NCC-WCH

Final version 1.0

Diabetes (type 1 and type 2) in children and young people:

diagnosis and management

NICE Guideline 18

Appendices

August 2015

Final version

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Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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Contents

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Appendix A: Recommendations from NICE clinical guideline 15 (2004) that have been amended

Recommendations are labelled **[2004, amended 2015]** if the evidence has not been reviewed but:

- changes have been made to the recommendation wording that change the meaning; or
- NICE has made editorial changes to the original wording to clarify the action to be taken; or
- the recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.

Recommendation numbers in the table refer to the numbering in the NICE guideline.

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
The diagnosis of type 1 diabetes in children and young people should be based on the criteria specified in the 1999 World Health Organization report on the diagnosis and classification of diabetes mellitus.[1] The symptoms and signs of type 1 diabetes include: hyperglycaemia (random blood glucose more than 11 mmol/litre), polyuria, polydipsia and weight loss. (1.1.1.1)	Be aware that the characteristics of type 1 diabetes in children and young people include: • hyperglycaemia (random plasma glucose more than 11 mmol/litre) • polyuria • polydipsia • weight loss • excessive tiredness. (1.1.1) Confirm type 1 diabetes in children and young people using the plasma glucose criteria specified in the World Health Organization's 2006 report on the diagnosis and classification of diabetes mellitus. (1.1.3)	The WHO updated their report on the diagnosis and classification of diabetes in 2006. The population has been added to this recommendation for clarification. In addition, this recommendation has been split into 2 recommendations to make it easier to understand. 'Symptoms and signs' has been replaced with 'characteristics' as the guideline development group felt this was a more accurate term for the list of conditions in this recommendation. Excessive tiredness was added at the request of stakeholders commenting on the draft for consultation of the 2015 update as this is a recognised symptom of diabetes. 'Plasma glucose' was added to the second recommendation, to make it clear that diagnosis should be confirmed using the WHO plasma glucose criteria and not their HbA1c criteria.
Children and young people with suspected type 1 diabetes should be offered immediate (same day) referral to a multidisciplinary paediatric diabetes care team that has the competencies needed to	Refer children and young people with suspected type 1 diabetes immediately (on the same day) to a multidisciplinary paediatric diabetes care team with the competencies needed to	The action was changed from 'offer' to 'refer', as the 2012 NICE guidelines manual used to develop this update has a specific definition of the word 'offer' that was not used when the original 2004 guideline was published.

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
confirm diagnosis and to provide immediate care. (1.1.1.2)	confirm diagnosis and to provide immediate care. (1.1.2)	
Consideration should be given to the possibility of other types of diabetes (such as early-onset type 2 diabetes, other insulin resistance syndromes, maturity-onset diabetes in the young and molecular/enzymatic abnormalities) in children and young people with suspected type 1 diabetes who: • have a strong family history of diabetes • are obese at presentation • are of black or Asian origin • have an insulin requirement of less than 0.5 units/kg body weight/day outside a partial remission phase • have no insulin requirement • rarely or never produce ketone bodies in the urine (ketonuria) during episodes of hyperglycaemia • show evidence of insulin resistance (for example, acanthosis nigricans) • have associated features, such as eye disease, deafness, or another systemic illness or syndrome. (1.1.1.3)	Think about the possibility of type 2 diabetes in children and young people with suspected diabetes who: • have a strong family history of type 2 diabetes • are obese at presentation • are of black or Asian family origin • have no insulin requirement, or have an insulin requirement of less than 0.5 units/kg body weight/day after the partial remission phase • show evidence of insulin resistance (for example, acanthosis nigricans). (1.1.5) Think about the possibility of types of diabetes other than types 1 or 2 (such as other insulin resistance syndromes, or monogenic or mitochondrial diabetes) in children and young people with suspected diabetes who have any of the following features: • diabetes in the first year of life • rarely or never develop ketone bodies in the blood (ketonaemia) during episodes of hyperglycaemia • associated features, such as optic atrophy, retinitis pigmentosa, deafness, or another systemic illness or syndrome. (1.1.6)	This recommendation has been split into two, as the guideline development group felt that type 2 diabetes should be considered separately from the rarer conditions now that it is covered in this guideline. In addition, not all of the factors listed applied to type 2 diabetes or to the rarer conditions. Because of this, the guideline development group felt that separating them into two lists makes it clearer which factors apply to which condition. In the second recommendation, maturity onset diabetes in the young and molecular/enzymatic abnormalities have been replaced by monogenic diabetes and mitochondrial diabetes to cover diabetes more generally; diabetes in the first year of life has been added to cover neonatal diabetes; the reference to ketone bodies in the urine has been changed to ketone bodies in the blood to mirror the recommendations elsewhere in the guideline; and 'eye' disease' has been replaced with 'optic atrophy and retinitis pigmentosa', as the guideline development group felt that 'eye disease' was not specific enough and could be mistaken for diabetic retinopathy.
Young people with type 1 diabetes should be encouraged to attend clinics on a regular basis (three or four times per year) because regular attendance is associated with good glycaemic control. (1.5.2.1)	Encourage young people with type 1 diabetes to attend clinic 4 times a year because regular contact is associated with optimal blood glucose control. (1.2.3)	The recommended number of contacts has been updated to reflect the Paediatric Diabetes Best Practice Tariff Criteria. In addition, 4 clinic attendances is standard in current clinical practice.
Children and young people with type 1 diabetes and their families should be informed	Explain to children and young people with type 1 diabetes and their family	An explanation has been added to the bullet on eye examination to make it clear this refers to

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
that, as for other children, regular dental examinations[2] and eye examinations (every 2 years) are recommended. (1.3.5.4)	members or carers (as appropriate) that like others they are advised to have • regular dental examinations (see the NICE guideline on dental recall) • an eye examination by an optician every 2 years. (1.2.4)	standard eye tests rather than retinopathy monitoring. In addition, 'recommended' has been changed to 'advised to have' as part of the editorial changes to make this sentence active.
Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) how to find information about benefits from government disability support. (1.5.1.4)	Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) how to find information about government disability benefits. (1.2.8)	The phrasing has been changed to refer to government disability benefits in general rather than implying that a specific benefit is applicable.
Children and young people with type 1 diabetes wishing to participate in restricted sports (such as scuba diving) should be offered comprehensive advice by their diabetes team. Additional information may be available from local and/or national patient support groups and organisations. (1.2.8.3)	Children and young people with type 1 diabetes wishing to participate in sports that may have particular risks for people with diabetes should be offered comprehensive advice by their diabetes team. Additional information may be available from local and/or national support groups and organisations, including sports organisations. (1.2.10)	The reference to restricted sports has been deleted because this is no longer meaningful. The phrasing has been changed to emphasise that the recommendation is about sports that may have particular risks for people with diabetes, and the specific reference to scuba diving has been deleted. The reference to support organisations has been amended to cover sports organisations as well as patient support organisations.
Encourage children and young people with type 1 diabetes not to start smoking. (1.2.9.5)	Encourage children and young people with type 1 diabetes not to start smoking. See also the NICE guidelines on preventing the uptake of smoking by children and young people and school-based interventions to prevent smoking. (1.2.13)	A reference to related NICE guidance on prevention of smoking in children and young people has been added.
Offer smoking cessation programmes to children and young people with type 1 diabetes who smoke. (1.2.9.6)	Offer smoking cessation programmes to children and young people with type 1 diabetes who smoke. See also the NICE guidelines on brief interventions and referral for smoking cessation, smoking cessation services, harm reduction approaches to smoking, and smoking cessation in secondary care. (1.2.14)	A reference to related NICE guidance on smoking cessation has been added.
Children and young people with type 1 diabetes and their families should be informed	Explain to children and young people with type 1 diabetes and their family	This recommendation has been updated to reflect guidance from

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
that the Department of Health[7] recommends immunisation against pneumococcal infection for children and young people with diabetes over the age of 2 months. (1.2.11.2)	members or carers (as appropriate) that the Department of Health's Green Book recommends immunisation against pneumococcal infection for children and young people with diabetes who need insulin or oral hypoglycaemic medicines. (1.2.17)	the Department of Health's Green Book.
Encourage children and young people with type 1 diabetes who are using multiple daily insulin regimens and their family members or carers (as appropriate) to adjust the insulin dose if appropriate after each pre-meal, bedtime and occasional night-time blood glucose measurement. (12.6.10)	Encourage children and young people with type 1 diabetes who are using multiple daily insulin injection regimens and their family members or carers (as appropriate) to adjust the insulin dose if appropriate after each blood glucose measurement. (1.2.20)	The reference to the timing of blood glucose measurements has been deleted because the recommendations about blood glucose measurements state the minimum number of times measurements should be made, but not the specific timing of the measurements.
Children and young people with newly diagnosed type 1 diabetes should be informed that they may experience a partial remission phase (or 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 7%. (1.1.3.1)	Explain to children and young people with newly diagnosed type 1 diabetes and their family members or carers (as appropriate) that they may experience a partial remission phase (a 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 48 mmol/mol (6.5%). (1.2.24)	This recommendation has been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person's treatment. In addition, the target HbA1c level has been updated to match the new recommendations on HbA1c target levels.
Children and young people with type 1 diabetes using insulin injection regimens should be offered needles that are of an appropriate length for their body fat (short needles are appropriate for children and young people with less body fat; longer needles are appropriate for children and young people with more body fat). (1.2.4.2)	Provide children and young people with type 1 with insulin injection needles that are of an appropriate length for their body fat. (1.2.26)	The information on what needle length is appropriate for a child has been deleted from this recommendation, as the guideline development group felt that this was well known and did not need defining in the recommendation.
Children and young people with type 1 diabetes should be offered: • annual foot care reviews • investigation of the state of injection sites at each clinic visit. (1.3.5.3)	Offer children and young people with type 1 diabetes a review of injection sites at each clinic visit. (1.2.28)	The text on foot care has been removed from this recommendation, as it is covered by the new NICE guideline on diabetic foot care.
Children and young people with type 1 diabetes and their families should be informed	Explain to children and young people with type 1 diabetes and their family	The text on total daily energy intake distribution and eating 5 portions of fruit and vegetables

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows: • carbohydrates – more than 50% • protein – 10–15% • fat – 30–35%. The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs. (1.2.7.2)	members or carers (as appropriate) that children and young people with type 1 diabetes have the same basic nutritional requirements as other children and young people. Children and young people's food should provide sufficient energy and nutrients for optimal growth and development. (1.2.36)	per day has been removed from this recommendation, as the 2015 recommendation 1.2.41 covers this. In addition, the specific energy intake levels were removed, as these are applicable to all children and not just those with type 1 diabetes.
Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. (1.3.5.5)	At each clinic visit for children and young people with type 1 diabetes measure height and weight and plot on an appropriate growth chart. Check for normal growth and/or significant changes in weight because these may reflect changes in blood glucose control. (1.2.45)	This recommendation has been heavily edited for clarity, and the second part of the recommendation has been rewritten to make it easier to follow. The reference to measuring BMI has been deleted because it is not necessary to measure this at every clinic visit.
Encourage all children and young people, including those with type 1 diabetes, to exercise on a regular basis because this reduces the risks of developing macrovascular disease in the long term. (1.2.8.1)	Encourage all children and young people, including those with type 1 diabetes, to exercise on a regular basis because this reduces the risks of developing cardiovascular disease in the long term. (1.2.47)	The term macrovascular has been changed to cardiovascular to clarify the meaning.
Children and young people with type 1 diabetes and their families should be informed about the effects of exercise on blood glucose levels and about strategies for preventing exercise-induced hypoglycaemia during and/or after physical activity. (1.2.8.4)	Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) about the effects of exercise on blood glucose levels and about strategies for avoiding hypo- or hyperglycaemia during or after physical activity. (1.2.49)	The term 'exercise-induced' has been removed from this recommendation, as the guideline development group felt that the cause of hypoglycaemia did not need stating here. In addition, hyperglycaemia caused by exercise has been added to this recommendation, as this is also a complication that children and young people with type 1

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		diabetes and their family members or carers (as appropriate) should be aware of. In addition, this recommendation has been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person's treatment.
Children and young people with type 1 diabetes should be offered testing of their HbA1c levels two to four times per year (more frequent testing may be appropriate if there is concern about poor glycaemic control). (1.2.6.2)	Offer children and young people with type 1 diabetes measurement of their HbA1c level 4 times a year (more frequent testing may be appropriate if there is concern about suboptimal blood glucose control). (1.2.71)	The recommended number of measurements has been updated to reflect the Paediatric Diabetes Best Practice Tariff Criteria. In addition, 4 clinic attendances is standard in current clinical practice.
Children and young people with type 1 diabetes, their parents and other carers should be informed that they should always have access to an immediate source of carbohydrate (glucose or sucrose) and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. (1.3.1.1)	Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that they should always have access to an immediate source of fast-acting glucose and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. (1.2.78)	The type of carbohydrate suitable for safe management of hypoglycaemia has been changed from 'glucose or sucrose' to 'fast-acting glucose', as the guideline development group felt this was what was recommended in current practice.
Parents and, where appropriate, school nurses and other carers should have access to glucagon for subcutaneous or intramuscular use in an emergency, especially when there is a high risk of severe hypoglycaemia. (1.3.1.6)	Family members or carers and, where appropriate, school nurses and other carers should be trained and equipped to give intramuscular glucagon for severe hypoglycaemia in an emergency. (1.2.79)	Subcutaneous glucagon has been removed from this recommendation, as the guideline development group did not think this was used in current practice.
		The recommendation has been reworded to make it clear that intramuscular glucagon would only be given for severe hypoglycaemia.
		In addition, 'have access' has been replaced with 'trained and equipped', as the guideline development group felt that this was an important point that was left out of the original recommendation.
Children and young people with mild to moderate hypoglycaemia should be treated as follows. • Take immediate action. • The first line of treatment should be the consumption of rapidly absorbed simple carbohydrate (for example,	Immediately treat mild to moderate hypoglycaemia in children and young people as follows. • Give fast-acting glucose (for example, 10 to 20 g) by mouth (liquid carbohydrate may be taken more easily than solid).	This recommendation has been reworded and reordered to make it easier to understand. In addition, the type of carbohydrate suitable for safe management of hypoglycaemia has been changed from 'glucose or sucrose' to 'fast-acting glucose', as the guideline

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
10–20 g carbohydrate given by mouth). • The simple carbohydrate should raise blood glucose levels within 5 to 15 minutes. • Carbohydrate given in liquid form may be taken more easily. • It may be appropriate to give small amounts of rapidly absorbed simple carbohydrate frequently because hypoglycaemia may cause vomiting. • As symptoms improve or normoglycaemia is restored additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels unless a snack or meal is imminent. • Additional complex long-acting carbohydrate is not required for children and young people using continuous subcutaneous insulin infusion. • Blood glucose levels should be rechecked within 15 minutes. (1.3.1.4)	• Be aware that fast-acting glucose may need to be given in frequent small amounts, because hypoglycaemia can cause vomiting. • Recheck blood glucose levels within 15 minutes (fast-acting glucose should raise blood glucose levels within 5–15 minutes) and repeat fast-acting glucose if hypoglycaemia persists. • As symptoms improve or normoglycaemia is restored, give oral complex long-acting carbohydrate to maintain blood glucose levels, unless the child or young person is: ○ about to have a snack or meal ○ receiving a continuous subcutaneous insulin infusion. (1.2.80)	development group felt this was what was recommended in current practice. The recommendation also clarifies that administration of fast-acting glucose should be repeated if hypoglycaemia persists.
Children and young people with severe hypoglycaemia should be treated as follows. • In a hospital setting, 10% intravenous glucose should be used when rapid intravenous access is possible (up to 500 mg/kg body weight – 10% glucose is 100 mg/ml). • Outside hospital, or where intravenous access is not practicable, intramuscular glucagon or concentrated oral glucose solution (e.g. Hypostop) may be used. • Children and young people over 8 years old (or body weight more than 25 kg) should be given 1 mg glucagon. • Children under 8 years old (or body weight less than 25 kg) should be given 500 micrograms of glucagon.	Treat severe hypoglycaemia in children and young people who are in hospital and in whom rapid intravenous access is possible by giving 10% intravenous glucose. Give a maximum dose of 500 mg/kg body weight (equivalent to a maximum of 5 ml/kg). (1.2.81) • Treat severe hypoglycaemia in children and young people who are not in hospital or who do not have rapid intravenous access available as follows. • Use intramuscular glucagon or concentrated oral glucose solution (for example Glucogel). Do not use oral glucose solution if the level of consciousness is reduced as this could be dangerous. • If using intramuscular glucagon:	This recommendation has been reworded, reordered, and split into 2 separate recommendations to make it easier to understand. The dose for children and young people who weigh 25 kg has been added to the recommendation. In addition, the action in the section on intramuscular glucagon and concentrated oral glucose solution has changed from ‘may be used’ to ‘Use’. This is because the guideline development group felt that these 2 were the only standard treatment options rather than 2 options out of several, as was suggested by the original wording. The reference to ‘Hypostop’ has been changed to ‘Glucogel’, as the guideline development group felt that this was the preparation commonly used in clinical practice.

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
• Blood glucose levels should respond within 10 minutes. • As symptoms improve or normoglycaemia is restored, in children and young people who are sufficiently awake, additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels.	○ give children and young people over 8 years old (or who weigh 25 kg or more) 1 mg glucagon. ○ give children under 8 years old (or who weigh 25 kg or more) 500 micrograms of glucagon.	A warning on using oral glucose solution in children with reduced levels of consciousness has been added, as the guideline development group felt that this is being missed in clinical practice. This was an important safety issue and was alluded to in the 2004 recommendation but it was not made clear that it applied at this stage. It is vitally important that caution is exercised when giving Glucogel at first presentation as this is the stage at which reduced conscious level is most likely to occur
• Some children and young people may continue to have reduced consciousness for several hours after a severe hypoglycaemic episode, and repeat blood glucose measurements will be required to determine whether further glucose is necessary. • Medical assistance should be sought for children and young people whose blood glucose levels fail to respond and those in whom symptoms persist for more than 10 minutes. (1.3.1.5)	• Seek medical assistance if blood glucose levels do not respond or symptoms persist for more than 10 minutes. • As symptoms improve or normoglycaemia is restored, and once the child or young person is sufficiently awake, give oral complex long-acting carbohydrate to maintain blood glucose levels. • Recheck the blood glucose repeatedly in children and young people who have persistently reduced consciousness after a severe hypoglycaemic episode, to determine whether further glucose is needed. (1.2.82)	
Young people with type 1 diabetes should be informed about the specific effects of alcohol consumption on glycaemic control, particularly the risk of (nocturnal) hypoglycaemia. (1.2.9.1)	Explain to young people with type 1 diabetes the effects of alcohol consumption on blood glucose control, and in particular that there is an increased risk of hypoglycaemia including hypoglycaemia while sleeping. (1.2.83)	The term ‘nocturnal hypoglycaemia’ has been changed to ‘hypoglycaemia while sleeping’, as the guideline development group did not think the original term was common in clinical practice.
Non-adherence to therapy should be considered in children and young people with type 1 diabetes who have poor glycaemic control, especially in adolescence. (1.4.6.1)	Think about the possibility of non-adherence to therapy in children and young people with type 1 diabetes who have suboptimal blood glucose control, especially in adolescence. (1.2.87)	The action was changed from ‘consider’ to ‘think about’, as the 2012 NICE guidelines manual used to develop this update has a specific definition of the word ‘consider’ that was not used when the original 2004 guideline was published.
Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than other children and young people. (1.4.1.1)	Diabetes teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural difficulties. (1.2.94)	This recommendation has been amended, as the original suggested that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than all other children

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		and young people, which is not the case.
Young people with 'brittle diabetes' (that is, those who present with frequent episodes of diabetic ketoacidosis over a relatively short time) should have their emotional and psychological well-being assessed. (1.4.6.3)	Assess the emotional and psychological wellbeing of young people with type 1 diabetes who present with frequent episodes of diabetic ketoacidosis (DKA). (1.2.96)	The term 'brittle diabetes' has been removed from this recommendation, as the guideline development group felt that this term was no longer commonly used in clinical practice.
Children and young people with type 1 diabetes and their families should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being. (1.4.7.5)	Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) timely and ongoing access to mental health professionals with an understanding of diabetes because they may experience psychological problems (such as anxiety, depression, behavioural and conduct disorders and family conflict) or psychosocial difficulties that can impact on the management of diabetes and wellbeing. (1.2.98)	The reference to mental health professionals has been amended to clarify that those involved in caring for children and young people with diabetes should be knowledgeable about diabetes. The importance of psychosocial difficulties has also been emphasised by adding this to the recommendation.
Diabetes care teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. (1.4.3.1)	Diabetes teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. See also the NICE guideline on eating disorders. (1.2.107)	A cross-reference to the NICE guideline on eating disorders has been added for information.
Diabetes care teams should be aware that children and young people with type 1 diabetes who have eating disorders may have associated problems of persistent hyperglycaemia, recurrent hypoglycaemia and/or symptoms associated with gastric paresis. (1.4.3.2)	Be aware that children and young people with type 1 diabetes who have eating disorders may have associated difficulties with • suboptimal blood glucose control (both hyperglycaemia and hypoglycaemia) • symptoms of gastroparesis. (1.2.108)	The terms 'persistent hyperglycaemia' and 'recurrent hypoglycaemia' have been replaced with the text on poor blood glucose control, covering both hyperglycaemia and hypoglycaemia. This is because the guideline development group felt that these two complications are both indicative of 'poor blood glucose control', so it would be simpler to use this phrase in the recommendation.
		In addition, the phrase 'symptoms associated with gastric paresis' has been changed, as the guideline development group felt that the use of 'associated' made this recommendation vague. 'gastric paresis' has been changed to 'gastroparesis', as

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		this is the term currently used in practice.
Children and young people with type 1 diabetes in whom eating disorders are identified by their diabetes care team should be offered joint management involving their diabetes care team and child mental health professionals. (1.4.3.3)	For children and young people with type 1 diabetes in whom eating disorders are identified, offer joint management involving their diabetes team and child mental health professionals. (1.2.109)	This recommendation has been amended as healthcare professionals outside of the diabetes team (such as GPs) can also identify eating disorders.
Children and young people with type 1 diabetes and their families should be informed that, as for other children, regular dental examinations[3] and eye examinations (every 2 years) are recommended. (1.3.5.4)	Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that like others they are advised to have: • regular dental examinations[4] • an eye examination by an optician every 2 years. (1.3.3)	An explanation has been added to the bullet on eye examination to make it clear this refers to standard eye tests rather than retinopathy monitoring. 'recommended' has been changed to 'advised to have' as part of the editorial changes to make this sentence active. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.
Children and young people with type 1 diabetes and their families should be offered information about the existence of and means of contacting local and/or national diabetes support groups and organisations, and the potential benefits of membership. This should be done in the time following diagnosis and periodically thereafter. (1.5.1.1)	Give children and young people with type 2 diabetes and their family members or carers (as appropriate) information about local and/or national diabetes support groups and organisations, and the potential benefits of membership. Give this information after diagnosis and regularly afterwards. (1.3.5)	NICE has made editorial changes to the original wording to clarify the action to be taken (no change to meaning): a verb has been added, or the verb used has been changed. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.
Children and young people with type 1 diabetes and their families should be advised how to obtain information about benefits in relation to government disability support. (1.5.1.4)	Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) how to find information about possible government disability benefits. (1.3.6)	The word 'possible' has been added, as the benefits available to children and young people with type 2 diabetes can be different to those available to children and young people with type 1 diabetes. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
Children and young people with type 1 diabetes and their families should be informed that the Department of Health[5] recommends annual immunisation against influenza for children and young people with diabetes over the age of 6 months. (1.2.11.1)	Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that the Department of Health's Green Book recommends annual immunisation against influenza for children and young people with diabetes. (1.3.12)	This recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population. In addition, 'over 6 months' has been taken out of this recommendation, as type 2 diabetes normally only occurs in young people or adults, and never in children under 6 months.
Children and young people with type 1 diabetes and their families should be informed that the Department of Health7 recommends immunisation against pneumococcal infection for children and young people with diabetes over the age of 2 months. (1.2.11.2)	Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that the Department of Health's Green Book recommends immunisation against pneumococcal infection for children and young people with diabetes who need insulin or oral hypoglycaemia medicines. (1.3.13)	This recommendation has been updated to reflect guidance from the Department of Health's Green Book. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population. In addition, 'over the age of 2 months' has been taken out of this recommendation, as type 2 diabetes normally only occurs in young people or adults, and never in children under 2 months.
Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. (1.3.5.5)	At each clinic visit for children and young people with type 2 diabetes: • measure height and weight and plot on an appropriate growth chart • calculate body mass index.	This recommendation has been heavily edited for clarity, and the second part of the recommendation has been rewritten to make it easier to follow. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.
	Check for normal growth and/or significant changes in weight because these may reflect changes in blood glucose control. (1.3.21)	
Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural	Diabetes teams should be aware that children and young people with type 2 diabetes have a greater risk	This recommendation has been amended, as the original suggested that children and young people with diabetes have a greater risk of emotional and behavioural problems than all

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
problems than other children and young people. (1.4.1.1)	of emotional and behavioural difficulties. (1.3.33)	other children and young people, which is not the case. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been amended to include type 2 diabetes as it is applicable to this population.
Children with type 1 diabetes who are younger than 2 years of age and children and young people who have social or emotional difficulties, or who live a long way from hospital should be offered inpatient initial management. (1.1.2.6)	Offer initial inpatient management to children with diabetes who are aged under 2 years. (1.5.5) Think about initial inpatient management for children and young people with diabetes if there are social or emotional factors that would make home-based management inappropriate, or if they live a long distance from the hospital. (1.5.6)	This recommendation has been split into 2 recommendations to make the differences in care for the 2 populations clearer. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been amended to include type 2 diabetes as it is applicable to this population.
Explain to young people with type 1 diabetes who are preparing for transition to adult services that some aspects of diabetes care will change at transition. The main changes relate to targets for short-term blood glucose control and screening for complications. (1.5.2.7)	Explain to young people with type 1 diabetes who are preparing for transition to adult services that some aspects of diabetes care will change at transition. (1.5.13)	The examples of changes at transition have been deleted because those specified in the 2004 recommendation no longer apply to the same extent and there is now much greater harmony generally between the recommendations for children and young people and those for adults
	1.2.3, 1.2.30, 1.2.71, 1.2.87, 1.2.104, 1.2.108, 1.3.40	The terms ‘good’ and ‘satisfactory’ have been changed to ‘optimal’ and the term ‘poor’ has been changed to ‘suboptimal’ throughout the recommendations to avoid them appearing judgemental.
	1.2.21, 1.2.23	The terms ‘preprandial’ and ‘postprandial’ have been changed to ‘pre-meal’, ‘before meals’, and ‘after meals’ when appropriate, as the guideline development group felt that these terms are simpler and more commonly used.
	1.2.21, 1.2.22, 1.2.23, 1.2.24, 1.2.26, 1.2.40, 1.2.50	These recommendations have been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person’s treatment.
	1.2.6, 1.2.22, 1.2.32, 1.2.93, 1.2.96, 1.2.109, 1.4.64, 1.5.7, 1.5.12	NICE has made editorial changes to the original wording to clarify the action to be taken (no change to meaning): a verb has been

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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		added, or the verb used has been changed.
	1.3.3, 1.3.5, 1.3.6, 1.3.7, 1.3.8, 1.3.9, 1.3.10, 1.3.11, 1.3.12, 1.3.13, 1.3.16, 1.3.21, 1.3.22, 1.3.29, 1.3.30, 1.3.31, 1.3.32, 1.3.33, 1.3.34, 1.3.35, 1.3.36, 1.3.37, 1.3.38, 1.3.40, 1.3.41, 1.5.1, 1.5.2, 1.5.3, 1.5.4, 1.5.5, 1.5.6, 1.5.8, 1.5.9, 1.5.10, 1.5.11, 1.5.12	These recommendations originally only applied to type 1 diabetes in children and young people, but have been included in the section of this guideline on type 2 diabetes as they are applicable to this population.
	1.2.52	The term 'blood' has been changed to 'plasma' as this recommendation is referring to a concentration value.

[1] World Health Organization (1999)

[2] Dental recall: Recall interval between routine dental examinations. NICE clinical guideline 19 (2004).

[3] Dental recall: Recall interval between routine dental examinations. NICE clinical guideline 19 (2004).

[4] Dental recall: Recall interval between routine dental examinations NICE clinical guideline 19 (2004).

[5] Salisbury, D. M. and Department of Health, Welsh Office, Scottish Office Department of Health, DHSS (Northern Ireland): 1996. Update for pneumococcal vaccination.

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Appendix B: 2015 update scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Diabetes in children and young people: diagnosis and management of type 1 and type 2 diabetes in children and young people

1.1 Short title

Diabetes in children and young people

2 The remit

This is an update of Type 1 diabetes (NICE clinical guideline 15). See section 4.3.1 for details of which sections will be updated for children and young people. We will also carry out an editorial review of all recommendations to ensure that they comply with NICE's duties under equalities legislation.

This update is being undertaken as part of the guideline review cycle.

The guideline is also being extended to cover type 2 diabetes in children and young people.

This is the scope for 1 of 4 NICE clinical guidelines being developed that address diabetes care. Included below is a summary of the content for each guideline and of the NICE steering committee.

Guideline 1 – Diabetes in children and young people (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update Type 1 diabetes in children, young people and adults (NICE clinical guideline 15). It will cover the diagnosis and management of type 1 and type 2 diabetes in children and young people (younger than 18 years). It will include: structured education programmes, behavioural interventions to improve adherence, glucose monitoring strategies, ketone

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monitoring, insulin regimens for type 1 diabetes and metformin monotherapy for type 2 diabetes.

Guideline 2 – Diabetes in pregnancy (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update Diabetes in pregnancy (NICE clinical guideline 63). It will cover women of reproductive age who have pre-existing diabetes or who develop diabetes during pregnancy and it will also cover their newborn babies. It will include: target glucose ranges in the preconception period and during pregnancy, glucose monitoring strategies during pregnancy, screening, diagnosis and treatment of gestational diabetes, and postnatal testing for type 2 diabetes.

Guideline 3 – Type 1 diabetes in adults (developed by the National Clinical Guideline Centre)

This guideline will update Type 1 diabetes in children, young people and adults (NICE clinical guideline 15). It will cover adults (18 years or older) with type 1 diabetes. It will include: tests to differentiate type 1 diabetes from type 2 diabetes, structured education programmes, clinical monitoring of glucose control, insulin regimens, ketone monitoring, dietary advice on carbohydrate counting and glycaemic index, and treatment and monitoring of specific complications.

Guideline 4 –Type 2 diabetes in adults (developed by the Internal Clinical Guidelines Programme, Centre for Clinical Practice, NICE)

This guideline will update Type 2 diabetes (NICE clinical guideline 66) and Type 2 diabetes: newer agents (NICE clinical guideline 87). It will cover adults (18 years or older) with type 2 diabetes. It will include: pharmacological management of blood glucose levels, target values for blood glucose control, self-monitoring of blood glucose levels for blood glucose control, antithrombotic therapy and drug therapy for erectile dysfunction.

NICE steering committee

NICE has set up a steering committee to oversee the production of these clinical guidelines. The group, which includes the Guideline Development Groups' chairs, together with staff from the 3 guidance-producing centres and NICE, will identify and act on any gaps or overlaps across the different guidance topics to ensure that the final guidelines are complementary and consistent. It is intended that the guidance-producing centres will share systematic reviews and cross-refer to recommendations in the other guidelines where appropriate. This update is being undertaken as part of the guideline review cycle.

3 Clinical need for the guideline

3.1 Epidemiology

3.1.1 Type 1 diabetes

a) Type 1 diabetes is an autoimmune disorder resulting in the destruction of insulin-producing cells in the pancreas. It is predominantly diagnosed in children and young people and inevitably needs insulin replacement treatment.

b) Around 26,500 children and young people in the UK are estimated to have type 1 diabetes needing insulin replacement therapy.

c) Most children and young people diagnosed with type 1 diabetes do not have a family member with the condition, although there may be related disorders such as thyroid or rheumatoid disease in the family. However, a family history of type 1 diabetes does increase a child's risk of developing type 1 diabetes. For children with an identical twin with type 1 diabetes, the risk of developing the disorder is 1 in 3, for children with a father with type 1 diabetes the risk is 1 in 16, and for children with a mother with type 1 diabetes the risk is 1 in 40. By comparison, the population risk is roughly 1 in 500, although this varies with geographical location.

d) Children and young people with type 1 diabetes have poorer glucose control and the higher rates of acute metabolic complications such as diabetic ketoacidosis in comparison with children and young people with type 2 diabetes. Nine per cent of children and young people with diabetes experienced at least 1 episode of diabetic ketoacidosis in 2009–2010.

e) Systems of surveillance for the early detection of complications in children and young people with type 1 diabetes are important, as is effective management of late complications when they occur.

f) Good blood glucose control is known to prevent or delay the long-term complications of both type 1 and type 2 diabetes.

3.1.2 Type 2 diabetes

g) In 2011, around 300 children and young people in the UK had a confirmed diagnosis of type 2 diabetes.

h) Type 2 diabetes is initially an insulin-resistant state, the primary treatment for which is weight loss and exercise. Pharmacological measures to increase insulin sensitivity or to increase insulin release can be added to lifestyle interventions, but insulin may be needed because of the continuing failure of insulin secretion. Like type 1 diabetes, type 2 diabetes has a significant impact on lifestyle in the short term, and is associated with major long-term complications and reduced life expectancy.

i) Obesity is the most common risk factor for type 2 diabetes. Type 2 diabetes is more common in people of South Asian, Chinese, black African and African–Caribbean origin. In Europeans, type 2 diabetes in children is associated with the most severe degrees of obesity.

j) People from the most deprived socioeconomic backgrounds are 2.5 times more likely than average to have type 2 diabetes at any given age.

3.2 *Current practice*

a) Fewer than 20% of children and young people with diabetes receive the basic care recommended by NICE guidelines.

b) Current standard care for children and young people with diabetes includes patient education, dietary advice, psychological support and management of complications.

c) Standard care for children and young people with type 1 diabetes also includes insulin therapy.

d) For children and young people with type 2 diabetes, first-line care often includes advice on the need for weight loss and the importance of adopting a healthy lifestyle. Metformin may also be used to improve glycaemic control by increasing insulin sensitivity. If good glycaemic control is not achieved then additional insulin or other agents may be needed.

e) The aim of patient education is to enable children and young people and their parents or carers to live a normal life and minimise the risk of complications. It includes advice on diet, improving glycaemic control and how complications are managed.

f) Management of hypoglycaemia depends on its severity. Hospital care may be needed if the child or young person is unresponsive or unconscious, but some children and young people can be cared for at home.

g) It is considered good practice that children and young people with diabetes receive an integrated package of care and that this is delivered by a multidisciplinary care team with expertise in paediatric diabetes, including its clinical, educational, dietetic, lifestyle and psychological management.

h) Children and young people with type 1 diabetes are monitored for growth and pubertal development, blood pressure, injection site

complications, thyroid disease and coeliac disease. Long-term glycaemic control is monitored using haemoglobin A_{1c} (HbA_{1c}). From the age of 12 years they are also monitored for retinopathy and nephropathy by the measurement of microalbuminuria. Rare associated conditions (juvenile cataracts, necrobiosis lipoidica, rheumatoid disease and Addison's disease, among others) may also be considered.

i) Children and young people with type 1 or type 2 diabetes receive annual foot care reviews from the age of 12 years. Minor problems (ingrown toenails or verrucas) are common and may be treated by a chiropodist. Serious foot problems are very rare in children and young people.

j) Psychological and social issues are also important to consider at each clinic visit, and treatment or advice is given where necessary.

k) There is a process of transition so that from the age of 13 years, young people are prepared for eventual transfer to adult care. This includes agreed protocols and joint clinics if possible. Young people are given time to familiarise themselves with this process and it is only completed when they are ready to move to adult services. The timing of transition depends on the young person's physical development, emotional maturity, stability of health, other life changes and local circumstances.

l) Since the publication of Type 1 diabetes (NICE clinical guideline 15), new evidence has been published (or is anticipated) to warrant reconsideration of the following areas of care for children and young people with type 1 diabetes:

- structured education programmes
- behavioural interventions to improve adherence
- insulin regimens (multiple daily injections versus mixed insulin injections)
- strategies for glucose and ketone monitoring

- dietetic advice
- recognition and management of diabetic ketoacidosis
- recognition of complications and comorbidities.

m) Consideration is also being given to the following areas of care for children and young people with type 2 diabetes based on clinical priorities and likely availability of evidence:

- structured education programmes
- behavioural interventions to improve adherence
- dietetic advice
- weight management
- metformin monotherapy
- targets for HbA_{1c}
- recognition and management of diabetic ketoacidosis
- recognition of complications and comorbidities.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Children and young people (younger than 18 years) with type 1 diabetes.

b) Children and young people (younger than 18 years) with type 2 diabetes (new 2012).

c) Where the evidence supports it, the following subgroups will be given special consideration:

- children and young people with an ethnicity associated with a high prevalence of diabetes
- disabilities (including learning disabilities)
- children and young people with comorbidities (medical or psychological conditions)
- children and young people with poor educational achievement.

4.1.2 Groups that will not be covered

a) Young women with diabetes who wish to conceive or who are pregnant.

b) Children and young people with other forms of diabetes mellitus (for example, monogenic diabetes and cystic fibrosis-related diabetes) (new 2012).

c) Adults (aged 18 years and older) with type 1 diabetes.

d) Adults (aged 18 years and older) with type 2 diabetes.

4.2 Healthcare setting

All settings in which NHS care is received or commissioned.

The guideline will address the support and advice that the NHS should offer to crèches, nurseries, schools and other institutions.

The guideline will also be relevant to the work, but will not cover the practice, of:

- social services and the voluntary sector

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- services supplied by secondary and tertiary specialties for late complications of diabetes (for example, renal, cardiology, urology and ophthalmology services) to which patients have been referred
- the education sector.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Areas from the original guideline that will be updated

a) The role of c-peptide and antibody testing in the diagnosis of type 1 and type 2 diabetes.

b) Structured education programmes for children and young people with type 1 diabetes.

c) Behavioural interventions to improve adherence in children and young people with type 1 diabetes.

d) Multiple daily injections versus mixed insulin injections in children and young people with type 1 diabetes.

e) HbA_{1c} targets for children and young people with type 1 diabetes.

f) Glucose monitoring strategies in children and young people with type 1 diabetes, including:

- blood glucose targets
- frequency of intermittent testing (finger-prick read by meter)
- continuous glucose monitoring with retrospective (intermittent) versus real-time (long-term) adjustment of treatment.

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g) Blood ketone monitoring compared with urine ketone monitoring in children and young people with type 1 diabetes.

h) Dietetic advice, including carbohydrate counting and glycaemic index, for children and young people with type 1 diabetes.

i) Recognition and management of diabetic ketoacidosis in children and young people with type 1 diabetes:

- recognition based on symptoms, signs and biochemical abnormalities
- immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration)
- clinical assessment and investigations at presentation to guide management
- fluid management, including:
  - assessment of dehydration
  - route of administration
  - rate and volume of administration
  - choice of fluid
  - other additives (for example, glucose, potassium and bicarbonate)
- insulin therapy, including:
  - timing
  - route of administration
  - dosage
- anticoagulant prophylaxis to prevent venous thrombosis
- clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status

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  - fluid balance
  - neurological observations
  - electrocardiographic (ECG) monitoring
- laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including:
  - blood glucose
  - blood or urine ketones
  - serum urea and electrolytes
  - acid/base status.

j) Recognition of complications and comorbidities in children and young people with type 1 diabetes (retinopathy and nephropathy).

Areas not in the original guideline that will be included in the update

k) Structured education programmes for children and young people with type 2 diabetes.

l) Behavioural interventions to improve adherence in children and young people with type 2 diabetes.

m) Dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes.

n) Weight management in children and young people with type 2 diabetes who are overweight or obese to improve glycaemic control.

o) Metformin monotherapy for children and young people with type 2 diabetes.

p) HbA_{1c} targets for children and young people with type 2 diabetes.

q) Recognition and management of diabetic ketoacidosis in children and young people with type 2 diabetes (the specific aspects to be

covered for this area will be the same as those in section 4.3.1, point h)).

r) Recognition of complications and comorbidities in children and young people with type 2 diabetes (hypertension, dyslipidaemia, retinopathy and nephropathy).

4.3.2 Clinical issues that will not be covered

Areas from the original guideline that will not be updated

The following areas addressed in Type 1 diabetes (NICE clinical guideline 15) will not be updated (the existing recommendations will remain as current guidance):

a) All aspects of diagnosis and initial management in children and young people other than those listed in section 4.3.1, including:

- location of initial management after diagnosis
- advice on the natural history of type 1 diabetes.

b) All aspects of ongoing management other than those listed in section 4.3.1, including:

- insulin preparations, including new short- and long-acting insulins
- methods of delivering insulin
- metformin in addition to insulin for type 1 diabetes
- exercise
- advice on alcohol, smoking and recreational drugs
- long-distance travel
- immunisation.

c) All aspects of complications and associated conditions other than those listed in section 4.3.1, including:

- hypoglycaemia
- care during surgery

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- monitoring for complications and comorbidities of type 1 diabetes other than those specified.

d) All aspects of psychological and social issues other than those listed in section 4.3.1, including:

- emotional and behavioural problems, anxiety, depression and eating disorders
- cognitive disorders
- behavioural and conduct disorders
- psychosocial support
- adolescence.

e) Continuity of care, including:

- communication between organisations
- transition from paediatric to adult care.

Areas not covered by the original guideline or the update

f) Management of hypoglycaemia unawareness in children and young people with type 1 diabetes.

g) Glycaemic monitoring strategies for children and young people with type 2 diabetes.

h) Treatment for children and young people with type 2 diabetes in whom glycaemic control is not maintained with metformin.

i) Bariatric surgery for children and young people with type 2 diabetes.

j) Monitoring for complications and comorbidities of type 2 diabetes other than those specified in section 4.3.1.

k) Management of complications and comorbidities of type 1 or type 2 diabetes.

l) Contraceptive, pre-pregnancy and conception advice for children and young people with type 1 or type 2 diabetes.

m) Foot care for children and young people with type 1 or type 2 diabetes.

4.4 Main outcomes

a) Glycaemic control.

b) Any adverse effects of interventions used to manage type 1 or type 2 diabetes.

c) Health-related quality of life (validated questionnaire), for example, diabetes-specific health-related quality of life.

d) Complications of diabetes.

e) Mortality.

f) Psychological outcomes.

g) Patient satisfaction.

4.5 Review questions

These are draft review questions and the final questions will be agreed by the Guideline Development Group during development.

Type 1 diabetes

- What is the effectiveness of c-peptide and antibody tests to distinguish type 1 and type 2 diabetes?
- What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?
- What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

- What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?
- What is the optimal HbA_{1c} target for children and young people with type 1 diabetes?
- What are the optimal blood glucose targets for children and young people with type 1 diabetes?
- How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?
- What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?
- What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?
- What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?
- What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?
- What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?
- What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?
- What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?
- At what rate should children and young people with diabetic ketoacidosis be rehydrated?
- What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

- When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?
- How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?
- What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?
- Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status
  - fluid balance
  - neurological observations
  - ECG monitoring?
- Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
  - blood glucose
  - blood or urine ketones
  - serum urea or electrolytes
  - acid/base status?
- What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?
- What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Type 2 diabetes

- What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

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- What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?
- What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?
- What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?
- Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA_{1c}?
- What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?
- What is the optimal HbA_{1c} target for children and young people with type 2 diabetes?
- What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?
- What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?
- What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?
- At what rate should children and young people with diabetic ketoacidosis be rehydrated?
- What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?
- When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?
- How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

- What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?
- Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status
  - fluid balance
  - neurological observations
  - ECG monitoring?
- Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
  - blood glucose
  - blood or urine ketones
  - serum urea or electrolytes
  - acid/base status?
- What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?
- What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?
- What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?
- What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and

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analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

Scope

This is the final scope.

Timing

The development of the guideline recommendations will begin in October 2012.

5 Related NICE guidance

5.1 Published guidance

Related NICE guidance

- Preventing type 2 diabetes: risk identification and interventions for individuals at high risk. NICE public health guidance 38 (2012).
- Anxiety. NICE clinical guideline 113 (2011).
- Preventing type 2 diabetes: population and community interventions. NICE public health guidance 35 (2011).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2010).
- Type 2 diabetes. NICE clinical guideline 87 (2009).
- Coeliac disease. NICE clinical guideline 86 (2009).
- Medicines adherence. NICE clinical guideline 76 (2009).
- Promoting physical activity for children and young people. NICE public health guidance 17 (2009).
- Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. NICE technology appraisal guidance 151 (2008).

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- Obesity. NICE clinical guideline 43 (2006).
- Four commonly used methods to increase physical activity. NICE public health guidance 2 (2006).
- Type 2 diabetes: footcare. NICE clinical guideline 10 (2004).
- Guidance on the use of patient-education models for diabetes. NICE technology appraisal guidance 60 (2003).
- Guidance on the use of long-acting insulin analogues for the treatment of diabetes – insulin glargine. NICE technology appraisal guidance 53 (2002).

5.2 *Guidance under development*

NICE is currently developing the following related guidance (details available from the NICE website):

- Obesity – working with local communities. NICE public health guidance. Publication expected November 2012.
- Overweight and obese children and young people – lifestyle weight management services. NICE public health guidance. Publication expected October 2013.
- Type 1 diabetes in adults (update). NICE clinical guideline. Publication expected July 2014.
- Type 2 diabetes in adults (update). NICE clinical guideline. Publication expected July 2014.
- Diabetes in pregnancy (update). NICE clinical guideline. Publication expected June 2014.
- Lipid modification (update). NICE clinical guideline. Publication date to be confirmed.
- Buccal insulin for the management of type 1 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'.

Information on the progress of the guideline will also be available from the NICE website.

Appendix C: Stakeholder organisations

C.1 Original (2004) stakeholder organisations

A. Menarini Diagnostics Ltd

Abbott Laboratories Limited (BASF/Knoll)

Afiya Trust

African and Caribbean Diabetes Association

Ambulance Service Association

Association of British Clinical Diabetologists

Association of British Health-Care Industries

Association of Clinical Biochemists

Association of the British Pharmaceuticals Industry

AstraZeneca UK Ltd

Atkins Nutritional Inc

Aventis Pasteur MSD

Aventis Pharma

Blood Pressure Association

Bournemouth Diabetes and Endocrine Centre

British Association of Prosthetists and Orthotists

British Association of Sport and Exercise Sciences

British Dietetic Association

British Geriatrics Society Special Interest Group in Diabetes

British Hypertension Society

British In Vitro Diagnostics Association

British Medical Association

British National Formulary

British Psychological Society

British Society for Paediatric Endocrinology and Diabetes

British Society of Periodontology

BUPA

Chartered Society of Physiotherapy

Cheshire West PCT and Ellesmere Port & Neston PCT Diabetes NSF LIT

Commission for Health Improvement

College of Optometrists

Coloplast Limited

Community District Nurses Association

ConvaTec

Department of Health

Depression Alliance

Diabetes UK

Eli Lilly and Company Ltd

Faculty of Dental Surgery

Faculty of Public Health

Fibroid Network Charity

General Medical Council

Health Development Agency

Heart UK

Institute of Sport and Recreation Management

Insulin Dependent Diabetes Trust

Johnson & Johnson Medical

Kidney Alliance

LifeScan

Limbless Association

Long Term Medical Conditions Alliance

Maternity Health Links

Medicines and Healthcare products Regulatory Agency

Medtronic Limited

Merck Sharp & Dohme

National Association of Theatre Nurses

Type 1 diabetes

National Council for Disabled People, Black, Minority and Ethnic Community

National Public Health Service

Newcastle PCT

NHS Information Authority

NHS Quality Improvement Scotland

Norfolk and Norwich University Hospital NHS Trust

Novo Nordisk Limited

Ortho Biotech

Patient Involvement Unit for NICE

Pfizer Limited

Prodigy

Provalis Diagnostics Ltd

Roche Diagnostics Limited

Royal College of Anaesthetists

Royal College of General Practitioners

Royal College of General Practitioners Wales

Royal College of Midwives

Royal College of Nursing

Royal College of Ophthalmologists

Royal College of Paediatrics and Child Health

Royal College of Pathologists

Royal College of Physicians of London

Royal College of Psychiatrists

Royal College of Surgeons of England

Royal National Institute of the Blind

Royal Pharmaceutical Society of Great Britain

Scottish Intercollegiate Guidelines Network

Sheffield Teaching Hospitals NHS Trust

Society of Chiropodists and Podiatrists

The Royal Society of Medicine

Tissue Viability Nurses Association

Tissue Viability Society

TOAST (The Obesity Awareness and Solutions Trust)

UK National Screening Committee

UK Pain Society

UK Thalassaemia Society

Welsh Assembly Government (formerly National Assembly for Wales)

Westmeria Healthcare Ltd

C.2 2015 update

5 Boroughs Partnership NHS Foundation Trust

Abbott Diabetes Care

Abbott Laboratories

Abertawe Bro Morgannwg University NHS Trust

Action for Sick Children

activeNewham

Advisory Committee for Community Dentistry

Africa Advocacy Foundation

African Health Policy Network

Alder Hey Children's NHS Foundation Trust

Alere

Allocate Software plc

Amateur Swimming Association

AMORE Studies Group

Anglian Community Enterprise

Association for Clinical Biochemistry and Laboratory Medicine

Association for Dance Movement Psychotherapy UK

Association for Family Therapy and Systemic Practice in the UK

Association for the Study of Obesity

Association of Ambulance Chief Executives

Association of Anaesthetists of Great Britain and Ireland

Association of Breastfeeding Mothers

Association of British Clinical Diabetologists

Association of British Healthcare Industries

Association of British Insurers

Association of Child Psychotherapists, The

Association of Children’s Diabetes Clinicians

Association of Clinical Pathologists

Association of Directors of Children's Services

Association of Renal Industries

Association of School and College Leaders

Astrazeneca UK Ltd

Update 2015

B. Braun Medical Ltd

Bailey Instruments Ltd

Bard Limited

Barnardo's

Barnsley Hospital NHS Foundation Trust

Baxter Healthcare

Bayer HealthCare

Bayer plc

BD U.K. Ltd

BEAT

Becton Dickinson

Belfast Health and Social Care Trust

Berkshire Local Pharmaceutical Committees

Birmingham Children's Hospital NHS Foundation Trust

Birmingham Women's Health Care NHS Trust

Black and Ethnic Minority Diabetes Association

Black Country Partnership Foundation Trust

Blackpool, Fylde and Wyre Hospitals NHS Foundation Trust

Boehringer Ingelheim

Bolton Hospitals NHS Trust

Boots

Bradford District Care Trust

Breakspear Medical Group Ltd

Brighton and Sussex University Hospital NHS Trust

Bristol Myers Squibb Pharmaceuticals Ltd

British Association for Adoption and Fostering

British Association for Community Child Health

British Association for Counselling and Psychotherapy

British Association of Behavioural and Cognitive Psychotherapies

British Association of Prosthetists & Orthotists

British Association of Psychodrama and Sociodrama

British Association of Social Workers

British Dental Association

British Dietetic Association

British Geriatrics Society

British Heart Foundation

British Hypertension Society

British Infection Association

British Liver Trust

British Medical Association

British Medical Journal

British National Formulary

British Nuclear Cardiology Society

British Obesity Surgery Society

British Paediatric Mental Health Group

British Paediatric Respiratory Society

British Pain Society

British Pharmacological Society

British Psychodrama Association

British Psychological Society

British Red Cross

British Renal Society

British Society for Human Genetics

British Society for Immunology

British Society for Paediatric Endocrinology and Diabetes

British Society of Interventional Radiology

BUPA Foundation

Cambridge University Hospitals NHS Foundation Trust

Camden Link

Camden Provider Services

Caplond Services

Capsulation PPS

Cardiff and Vale NHS Trust

Cardiff Research Consortium

Care Quality Commission

CareTech Community Services

Cegedimrx

Central & North West London NHS Foundation Trust

Central London Community Health Care NHS Trust

Centrepoint

Cheshire Diabetes Network

Children with Diabetes

Children, Young People and Families NHS Network

Children's Commissioner for Wales

Children's Law Centre

CIS' ters

Clarity Informatics Ltd

Clinical Council for Eye Health Commissioning

Coeliac UK

Collaboration for Leadership in Applied Health Research and Care

College of Mental Health Pharmacy

College of Optometrists

Company Chemists Association Ltd

Cook Medical Inc.

Countess of Chester Hospital NHS Foundation Trust

County Durham and Darlington Acute Hospitals NHS Trust

Coventry and Warwickshire Cardiac Network

Covidien Ltd.

Croydon Clinical Commissioning Group

Croydon Council

Croydon Health Services NHS Trust

Croydon University Hospital

Cumbria Partnership NHS Foundation Trust

CVAA

CWHHE Collaborative Clinical Commissioning Groups

Cystic Fibrosis Trust

Cytori Therapeutics Inc

Daiichi Sankyo UK

Deaf Diabetes UK

Department of Health

Department of Health, Social Services and Public Safety Northern Ireland

Derbyshire County Council

Dexcom

Diabetes Management and Education Group

Diabetes Power

Diabetes Reference Group Conwy and Denbighshire

Diabetes UK

Diabetics with Eating Disorders

Dialog Devices

Diet Plate Ltd, The

Diving Diseases Research Centre, The

Division of Education and Child Psychology

DJO UK Ltd

Ealing Hospital NHS Trust

EASD

East and North Hertfordshire NHS Trust

East Kent Hospitals University NHS Foundation Trust

East Lancashire Hospitals NHS Trust

East Midlands Ambulance Service NHS Trust

East of England Children and Young People's Diabetes Network

East Riding of Yorkshire Council

Economic and Social Research Council

Education for Health

Eisai Ltd

Elective Cesarean

Equalities National Council

ESyDoc

Ethical Medicines Industry Group

European Atherosclerosis Society

Expert Patients Programme CIC

Experts in Severe and Complex Obesity

Faculty of Dental Surgery

Faculty of General Dental Practice

Faculty of Pharmaceutical Medicine

Faculty of Public Health

Faculty of Sport and Exercise Medicine

Fair Play for Children

Families With Diabetes National Network

Federation of Ophthalmic and Dispensing Opticians

Ferring Pharmaceuticals

Food and Drink Federation

George Eliot Hospital NHS Trust

GlaxoSmithKline

Gloucestershire Hospitals NHS Foundation Trust

Gloucestershire Link

Glysure

GP Care

GP update / Red Whale

Great Western Hospitals NHS Foundation Trust

Greater Manchester West Mental Health NHS Foundation Trust

Greater Manchester, Lancashire and South Cumbria Strategic Clinical Network

Group B Strep Support

Guildford and Waverley Local Implementation Team

Guy's and St Thomas' NHS Foundation Trust

Haag Streit UK

Healing Honey International Ltd

Health and Care Professions Council

Health and Social Care Information Centre

Healthcare Improvement Scotland

Healthcare Infection Society

Healthcare Quality Improvement Partnership

Healthwatch East Sussex

HEART UK

Herts Valleys Clinical Commissioning Group

Hindu Council UK

Update 2015

Hockley Medical Practice

HQT Diagnostics

Humber NHS Foundation Trust

Independent Children's Homes Association

InDependent Diabetes Trust

Infant and Toddler Forum

INPUT Patient Advocacy

Institute Metabolic Science

Institute of Biomedical Science

Institute of Child Health

Insulin Pump Awareness Group Scotland

Johnson & Johnson Medical Ltd

Juvenile Diabetes Research Foundation

Keele University

Kidney Research UK

King Fahd Military Medical Complex

Kowa Research Europe Ltd

LINC Medical

Lactation Consultants of Great Britain

Lancashire Care NHS Foundation Trust

Lancashire Teaching Hospitals NHS Trust

Leeds Community Healthcare NHS Trust

Leeds North Clinical Commisioning Group

Leicester City Council

Leicestershire Partnership NHS Trust

LifeScan

Lilly UK

Limbless Association

Llandudno and District Diabetes UK

Local Government Association

London Ambulance Service NHS Trust

London Diabetes Strategic Clinical Network

London North West Healthcare NHS Trust

Luton and Dunstable Hospital NHS Trust

Maquet UK Ltd

Mastercall Healthcare

Medical Directorate Services

Medicines and Healthcare products Regulatory Agency

Medicines for Children Research Network

MedTech Europe

Medtronic

Menarini Diagnostics UK

Mental Health and Substance Use: Dual Diagnosis

Mental Health Group British Dietetic Association

Merck Sharp & Dohme UK Ltd

Mid Cheshire Hospitals NHS Trust

Ministry of Defence

Morecambe Bay Hospitals NHS Trust

Muslim Doctors and Dentists Association

National Association of Primary Care

National Children and Young People's Diabetes Network

National Clinical Guideline Centre

National Collaborating Centre for Cancer

National Collaborating Centre for Mental Health

National Collaborating Centre for Women's and Children's Health

National Deaf Children's Society

National Diabetes Audit

National Institute for Health Research Health Technology Assessment Programme

National Institute for Health Research

National Patient Safety Agency

National Pharmacy Association

NDR UK

Neonatal & Paediatric Pharmacists Group

Newcastle upon Tyne Hospitals NHS Foundation Trust

NHS Barnsley Clinical Commissioning Group

NHS Bolton Clinical Commissioning Group

NHS Brent Clinical Commissioning Group

NHS Choices

NHS Chorley and South Ribble Clinical Commissioning Group

NHS Confederation

NHS Connecting for Health

NHS County Durham and Darlington

NHS Cumbria Clinical Commissioning Group

NHS Eastbourne, Hailsham and Seaford Clinical Commissioning Group

NHS England

NHS Hardwick Clinical Commissioning Group

NHS Health at Work

NHS Improvement

NHS Luton Clinical Commissioning Group

NHS Medway

NHS Medway Clinical Commissioning Group

NHS North East Lincolnshire Clinical Commissioning Group

NHS North Somerset Clinical Commissioning Group

NHS Plus

NHS Sheffield

NHS South Cheshire Clinical Commissioning Group

NHS Trafford Clinical Commissioning Group

NHS Wakefield Clinical Commissioning Group

NHS Warwickshire North Clinical Commissioning Group

NHS West Cheshire Clinical Commissioning Group

NHS West Hampshire Clinical Commissioning Group

NHSCC

Norfolk Community Health and Care NHS Trust

North Cheshire Hospitals NHS Trust

North East London Foundation Trust

North Essex Mental Health Partnership Trust

North of England Commissioning Support

North Tees and Hartlepool NHS Foundation Trust

North West Commissioning Support Unit

North West London Perinatal Network

Northamptonshire County Council

Northern Health and Social Care Trust

Northumberland Hills Hospital, Ontario

Nottingham Children's Hospital

Nottingham City Hospital

Nottinghamshire Healthcare NHS Foundation Trust

Nova Biomedical UK

Novartis Pharmaceuticals

Novo Nordisk Ltd

Nursing and Midwifery Council

Nutricia Advanced Medical Nutrition

Nutrition and Diet Resources UK

Optical Confederation

Owen Mumford Ltd

Oxford Centre for Diabetes, Endocrinology and Metabolism

Oxford Health NHS Foundation Trust

Oxfordshire Clinical Commissioning Group

Oxleas NHS Foundation Trust

Parkwood Healthcare

Patient Assembly

Pennine Acute Trust

Perspectum Diagnostics Ltd

Peterborough City Hospital

Pharmametrics GmbH

Picker Institute Europe

PrescQIPP NHS Programme

Primary Care Cardiovascular Society

Primary Care Dermatology Society

Primary Care Diabetes Society

Primary Care Pharmacists Association

Primrose Bank Medical Centre

Public Health Agency

Public Health England

Public Health Wales NHS Trust

Rainbows Children's Hospice

Randox Laboratories Limited

Renal Nutrition Group, British Dietetic Association

Rethink Mental Illness

RioMed Ltd

Roche Diagnostics

Roche Products

Royal Belfast Hospital for Sick Children

Royal Berkshire NHS Foundation Trust

Royal Brompton Hospital & Harefield NHS Trust

Royal College of Anaesthetists

Royal College of Emergency Medicine

Royal College of General Practitioners

Royal College of General Practitioners in Wales

Royal College of Midwives

Royal College of Nursing

Royal College of Obstetricians and Gynaecologists

Royal College of Ophthalmologists

Royal College of Paediatrics and Child Health

Royal College of Pathologists

Royal College of Physicians

Royal College of Physicians and Surgeons of Glasgow

Royal College of Psychiatrists

Royal College of Radiologists

Royal College of Speech and Language Therapists

Royal College of Surgeons of England

Royal Cornwall Hospitals NHS Trust

Royal Free Hospital NHS Foundation Trust

Royal Manchester Children's Hospital

Royal National Institute of Blind People

Royal Pharmaceutical Society

Royal Society of Medicine

Royal United Hospitals Bath NHS Foundation Trust

Salford Royal NHS Foundation Trust

Sanctuary Care

Sandoz Ltd

Sanofi

School And Public Health Nurses Association

Scottish Intercollegiate Guidelines Network

Sebia

SEC & London Paediatric Diabetes Partnership

SeeAbility

Self Management UK

Sheffield Children's Hospital

Sheffield Children's NHS Trust

Sheffield Teaching Hospitals NHS Foundation Trust

Shrewsbury and Telford Hospital NHS Trust

Sirona Care & Health CIC

Slimming World

SNDRi

Social Care Institute for Excellence

Society for Cardiological Science and Technology

Society for Endocrinology

Society for Vascular Technology of Great Britain and Ireland

Society of Chiropodists & Podiatrists

Solvay

South Asian Health Foundation

South Belfast Partnership Board

South Devon Healthcare NHS Foundation Trust

South East Coast Ambulance Service

South East Coast Strategic Clinical Network

South Eastern Health and Social Care Trust

South Essex Partnership University Foundation Trust

South London & Maudsley NHS Trust

South West Paediatric Diabetes Network

South West Yorkshire Partnership NHS Foundation Trust

South Western Ambulance Service NHS Foundation Trust

Southend Hospitals NHS Foundation Trust

Southern Health & Social Care Trust

Southport and Ormskirk Hospital NHS Trust

Spectranetics Corporation

Spirit Healthcare

St Mary's Hospital

Staffordshire and Stoke on Trent Partnership NHS Trust

Staffordshire University

Stockport Clinical Commissioning Group

Stockport Clinical Commissioning Pathfinder

Successful Diabetes

Suffolk County Council

Sunderland Diabetes Network

Sustrans

Swansea NHS Trust

Takeda UK Ltd

TCV

Teva UK

Thames Reach

The African Eye Trust

The Brecon Group

The British In Vitro Diagnostics Association

The College & Fellowship of Podiatric Medicine

The Medicines Management Partnership

The National LGB&T Partnership

The Natural Ketosis Company

The Patients Association

The Portland Hospital for Women and Children

The Rotherham NHS Foundation Trust

Transport & Health Study Group

Tunstall Healthcare UK Ltd

UK Clinical Pharmacy Association

UK National Screening Committee

UK Ophthalmic Pharmacy Group

UK Society for Behavioural Medicine

UK Thalassaemia Society

uMotif Digital Health

Unite the Union

University College London

University College London Hospital NHS Foundation Trust

University Hospital Aintree

University Hospital Birmingham NHS Foundation Trust

University Hospitals Bristol NHS Foundation Trust

University Hospitals of Leicester NHS Trust

University of Huddersfield

University of Liverpool

University of Nottingham

Walsall Hospitals NHS Trust

Walsall Local Involvement Network

Wandsworth Borough Council

Warrington and Halton Hospitals NHS Foundation Trust

Waterfront Surgery

Weight Concern

Welsh Endocrine and Diabetes Society

Welsh Government

Welsh Scientific Advisory Committee

West Herts Hospitals NHS Trust

West London Mental Health NHS Trust

West Midlands Ambulance Service NHS Trust

West Suffolk Hospital NHS Trust

Western Health and Social Care Trust

Western Sussex Hospitals NHS Trust

Wigan Borough Clinical Commissioning Group

Wirral University Teaching Hospital NHS Foundation Trust

Wockhardt UK Ltd

Worcestershire Acute Hospitals Trust

Worcestershire Health and Care NHS Trust

Wrightington, Wigan and Leigh NHS Foundation Trust

Wye Valley NHS Trust

York Hospitals NHS Foundation Trust

York Teaching Hospotal NHS Foundation Trust

Yorkshire and Humber Strategic Clinical Network

Young Diabetlolgists Forum

Appendix D: Declarations of interest

D.1 2015 update

All guideline development group members' interests were recorded on declaration forms provided by NICE. The forms covered consultancies, fee-paid work, share holdings, fellowships and support from the healthcare industry. Guideline development group members' interests are listed in this section. Note that the guideline development group chair, members and expert advisers were appointed under NICE's April 2007 Code of Practice for Declaring and Dealing with Conflicts of Interest.

Table 1: Guideline development group members' declarations of interest

Guideline development group member	Interest
Jerry Wales (Chair)	Non-personal pecuniary Sheffield Children's Hospital Foundation Trust clinical research faculty received funding from Merck Sharp & Dohme (MSD) and Parexel via the Medicines for Children Research Network (MCRN) for Jerry Wales's participation in research into the pharmacokinetics of novel medications for type 2 diabetes (both projects yet to start), from Novo Nordisk for Jerry Wales's participation in a Paediatric Investigation Protocol for a new long-acting insulin for type 1 diabetes (historical declaration only, no ongoing interests), and from 9 companies manufacturing medications or equipment for diabetes (Abbott, Bayer, LifeScan (Johnson and Johnson), Lilly, Novo Nordisk, Owen Mumford, Roche, Sanofi, and Ypsomed) to support the Yorkshire Regional Paediatric Diabetes Network meeting 2011 (historical declaration only, no ongoing interests). Personal non-pecuniary Member of the British Society for Paediatric Endocrinology and Diabetes (BSPED), Diabetes UK, the European Society for Paediatric Endocrinology (ESPE) and the International Society for Pediatric and Adolescent Diabetes (ISPAD); published and lectured on bariatric surgery in young people; joint chief investigator on a project funded by Diabetes UK but receives no money directly and has no managerial responsibility for the budget.
Francesca Annan	Personal pecuniary Received funding from Eli Lilly for speaking at the Eli Lilly National Paediatric Diabetes Meeting in May 2014 on topics related to the management of diabetes that were not specific to the scope of the guideline (fat and protein counting and exercise); invited chair at International Diabetes Federation (IDF) World Congress, Dubai 2011 and received funding from Novo Nordisk, Roche and Sanofi towards travel and accommodation expenses; received funding to cover travel and accommodation expenses from the ISPAD to attend and speak as an expert panel member on the management of diabetes at the 40th ISPAD conference in Toronto, Canada in September 2014; invited speaker at the ISPAD annual meeting 2012 and received funding from Roche towards accommodation expenses; invited speaker (on the topic of exercise and diabetes

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Guideline development group member	Interest
	management) at the Juvenile Diabetes Research Foundation (JDRF) 'Type 1 diabetes discovery weekend' and received funding from JDRF towards travel expenses, the conference was supported by industry sponsorship; received educational grant (£250) from Novo Nordisk to cover the cost of ISPAD conference registration fee, the conference was supported by industry sponsorship; received funding from the JDRF to cover travel, accommodation and an honorarium to attend a JDRF PEAK programme expert panel meeting on exercise and diabetes; received funding from the organisers of an Italian paediatric diabetes meeting to cover travel, accommodation and an honorarium as an invited speaker on ISPAD nutrition guidelines (the meeting was sponsored by Eli Lilly). Non-personal pecuniary Co-applicant for the following Health Technology Assessment (HTA) funded trials: Child and Adolescent Structured Competencies Approach to Diabetes Education (CASCADE), randomised controllted trial (RCT) of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes (Subcutaneous Insulin, Pumps or Injections [SCIPI]); organised an educational meeting on the topic of 'exercise in diabetes'. Funds were received from Novo Nordisk to cover the costs of food and the venue. Francesca Annan did not receive these funds directly. Personal non-pecuniary Member of British Dietetic Association, Diabetes Management & Education Group (DMEG), Diabetes UK, ISPAD, Sports Dietitians UK; regular teaching commitments related to nutritional management of diabetes, and exercise and diabetes at University of York, University of Warwick, Coventry University, Birmingham Children's Hospital; contributed to ISPAD guidelines on nutritional management and exercise; wrote articles on exercise and diabetes management and nutritional management of diabetes for Complete Nutrition and Diabetes Care for Children & Young People; presentations at national and international meetings on exercise and diabetes management; reviewed patient information content of Diabetes UK publications and pharmaceutical company literature (Lilly and Roche); chair of Paediatric Sub Group of Diabetes Management and Education Group (a specialist group of The British Dietetic Association) from April 2013; member of the writing group for ISPAD consensus guidelines.
Jo Dalton	Personal pecuniary Post as paediatric diabetes specialist nurse during guideline development funded by a diabetes charity within the Royal London Hospital; received funding from current employer (a hospital trust) to attend the Diabetes UK annual Professional Conference and a study day on insulin pump therapy sponsored by Roche; received funding from the organisers of an international group called BEYOND TEENS to attend a meeting as a member of the group which is taking forward results of the TEEN project focusing

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Guideline development group member	Interest
	on wellbeing and quality of life for young people and young adults (the group is sponsored by Sanofi Aventis). Personal non-pecuniary Member of the guideline development group for the 2004 NICE guideline on type 1 diabetes in children and young people; member of the Royal College of Nursing (RCN), ISPAD, Primary Care Diabetes Society (PCDS), professional member of Diabetes UK, attended a study day funded by Medtronic on a topic that is not specific to the guideline scope (continuous subcutaneous insulin infusion therapy); registered for a symposium funded by Novo Nordisk in Leicester on paediatric diabetes in October 2014 but could not attend.
Jacqueline Double	Personal pecuniary Honorarium from NHS Diabetes as Chair of national Parent Reference Group; invited speaker at 2 Friends For Life conferences and received free travel and food, the conferences were supported by industry sponsorship; received funding to cover travel expenses to attend a meeting in Australia funded by a number of commercial sources; gave a presentation at an IDF meeting in Melbourne. Travel expenses were paid by the organisation. Personal family interest Husband received funding to cover travel expenses from Children with Diabetes (a US not-for-profit organisation) to attend a Family Conference in the USA. Personal non-pecuniary Spoke for NHS Technology Adoption Centre (NTAC) and NHS Diabetes; ran workshops on schools, advocacy and mother's emotional needs; member of Diabetes UK and JDRF; director of INPUT (a patient-run organisation that advocates for access to insulin pumps and diabetes technology in the UK) until December 2012; member of UK Children with Diabetes Advocacy Group.
Sarah Eaton	Non-personal pecuniary Member of conference planning team for conferences organised by Diabetes UK and the Universities of York and Huddersfield (the conferences are sponsored by a number of pharmaceutical companies but Sarah Eaton does not receive any funding personally and is not responsible for management of the funds); honorarium from the University of York for a discussion regarding the GP's role in transitional care. Personal non-pecuniary Attended GP education meetings funded by Ashfield In2 Focus, Bayer Healthcare, Boehringer Ingelheim, HRA Pharma, Napp Pharmaceuticals, Pfizer, Reckit Benckiser; professional member of Diabetes UK, volunteer for Diabetes UK children's care events; member of team (also involving Diabetes UK, University of Huddersfield and University of York) planning a conference on new developments in diabetes management in primary care.
Julie Edge (Chair of the diabetic ketoacidosis (DKA) subgroup)	Personal pecuniary Honoraria for writing on type 1 diabetes for the British National Formulary for Children; honoraria for writing on type 1 diabetes for Practical Diabetes; attended the ISPAD

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Guideline development group member	Interest
	annual meeting in Gothenburg as invited speaker and received expenses (travel, registration, 3 nights' hotel accommodation and one evening meal) from ISPAD; received funding from the IDF to cover the cost of travel and accommodation expenses incurred when attending their meeting in Melbourne; received funding from the Australia Paediatric Society to cover registration and travel expenses to speak on the topic of cerebral oedema in children and young people with DKA at their Diabetes Meeting, the event was funded by a number of commercial sources; received funding from Diabetes UK to cover travel expenses to attend their Diabetes UK conference; honorarium from the University of York as an invited speaker on a master's module on DKA. Non-personal pecuniary Julie Edge holds managerial responsibility for departmental funding from Oxford Medical Diagnostics for a research project on a device not directly linked to any of the topics in the scope, from Aventis, Novo Nordisk, and Roche for sponsorship of educational meetings, and from the British Heart Foundation, Diabetes UK, JDRF, National Institute for Health Research Comprehensive Clinical Research Network (NIHR CCRN) via the Comprehensive Local Research Networks (CLRNs) and Thames Valley Diabetes Research Network (TVRN) for the following research projects for which Julie Edge is the local principle investigator: Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT); Diabetes Genome Anatomy Project (DGAP); and studies about insulin for diabetes including an RCT of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes (SCIPI); holds managerial responsibility for departmental funding from Advanced Therapeutics, Animas/LifeScan (part of Johnson and Johnson), Glucomen, Lilly, Novo Nordisk and Roche for sponsorship of educational meetings in 2013; holds managerial responsibility for departmental funding from Advanced Therapeutics, Aventis, Novo Nordisk and Roche for sponsorship of educational meetings in 2014; received funding from Novo Nordisk to cover travel expenses to attend and speak at a symposium (also funded by Novo Nordisk) in Leicester on paediatric diabetes in October 2014; chief investigator on a study of a new glucose sensor funded by abbot diabetes Care and local principal investigator on the same study (the funding contributes to a research trust fund managed by Julie Edge). Personal non-pecuniary Involved over many years in research on the management of DKA; lectured and prepared guidelines on DKA; member of Association of Children's Diabetes Clinicians (ACDC), BSPED, Diabetes UK and ISPAD; member of the writing group for ISPAD consensus guidelines; attended a half-day training course organised by Medtronic about continuous intravenous insulin therapy pumps; author of a paper looking at the timing of insulin therapy which was included in the guideline systematic review for the same topic; joint author on a paper looking at the rate of fluid administration

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Guideline development group member	Interest
	which was included in the guideline systematic review for the same topic.
Nikhil Gokani	Personal pecuniary Payment received for systematic reviewing work not directly linked to any of the topics in the guideline scope; researcher in public health and law with consultancy in the same field but not related to diabetes; honorarium from the NIHR for peer review of research applications on topics not related directly to any areas covered by the guideline scope; honorarium from the NIHR for peer review of Health Technology Assessment (HTA) on psychological interventions in children and young people with long-term health conditions. Personal non-pecuniary Supporting member of Diabetes UK, member of its groups and committees and volunteer; PhD candidate in public health and law; member of the National Diabetes Audit Partnership Board; member of Royal College of Physicians (RCP) joint specialty committee on endocrinology and diabetes mellitus; member of the specialist advisory committee on endocrinology and diabetes mellitus at the Joint Royal Colleges of Physicians Training Board; member of the Delphi consensus panel on pressure ulcers in children and young people at the National Clinical Guideline Centre (NCGC) member of the NICE Appeal Panel; discussed possible funding of a children and young people's version of the guideline with Diabetes UK, the Association of British Clinical Diabetologists and Abbott (no discussions regarding content of the guideline, and contact established only after final changes to recommendations had been made following stakeholder consultation on the draft guideline).
William Lamb	Personal pecuniary Honoraria from Practical Diabetes for writing an article about adolescent diabetes and from Medtronic Ltd for lecturing on continuous glucose monitoring; honoraria from eMedicine.com (part of Medscape from WebMD) for writing and updating articles about diabetes and DKA; attended an educational meeting organised by Francesca Annan on the topic of exercise in diabetes, the meeting was sponsored by Novo Nordisk and travel expenses were paid by the conference organisers; received payment for medico-legal work (expert testimony and a report) in a case pertaining to paediatric diabetes care that was not specific to the scope of the guideline (neglect); received funding to cover travel expenses to speak at a conference on diabetes and exercise, the conference was sponsored by a number of insulin pump manufacturers; received funding from university employer to cover travel expenses to speak at a training course on the use of insulin pumps, the course was sponsored by a number of insulin pump manufacturers; received funding from Diabetes UK to cover travel, accommodation and conference fees to attend the Diabetes UK annual Professional conference as an invited speaker (did not speak about and topics related directly to any areas covered by the guideline scope).

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Guideline development group member	Interest
	Personal non-pecuniary Professional member of Diabetes UK; member of ACDC, BSPED and ISPAD; volunteer for Diabetes UK and JDRF; associate editor of Clinical Diabetes; attended meetings supported by various industry sponsors unknown to William Lamb as part of continuing professional development. Spoke at JDRF 'Type 1 diabetes discovery weekend', the event was supported by industry sponsorship but William Lamb received no funding.
Carol Metcalfe	Personal pecuniary Received funding from Novo Nordisk to attend the Diabetes UK annual Professional Conference in March 2014 and from Eli Lily to attend the Eli Lilly National Paediatric Diabetes Meeting in May 2014; received funding from Roche to cover accommodation costs while attending a study day (also funded by Roche) on a topic that is not specific to the guideline scope (continuous subcutaneous insulin infusion therapy); received funding from Novo Nordisk to cover accommodation expenses while attending a symposium (also funded by Novo Nordisk) in Leicester on paediatric diabetes in October 2014. Personal non-pecuniary interest Volunteer for Diabetes UK; senior nurse on family events and organiser of young person event for Diabetes UK; adviser to Diabetes UK on volunteer and safeguarding guidelines.
Claire Pesterfield	Non-personal pecuniary Addenbrookes Charitable Trust will receive honoraria from Abbott, Animas, Roche and Medtronic for Claire Pesterfield presenting clinical case studies regarding diabetes care and preparing 2 articles for publication (1 about an education event (sports day) for Diabetes Care of Children and Young People and the other about management of neonatal diabetes for Diabetes Management). Personal non-pecuniary Volunteer for Diabetes UK; IDF young leader programme mentor; wrote article about parental attitudes to a closed-loop blood glucose trial for Diabetes Technology and Therapeutics (2010); co-founder and director of Team Blood Glucose, a not-for-profit social enterprise that provides peer support and education resources to encourage people with or at risk of diabetes to participate in exercise.

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Table 2: NCC-WCH staff members' declarations of interest

Staff member	Interest
Sarah Bailey	No interests declared
Frauke Becker	No interests declared
Zosia Beckles	No interests declared
Anne Carty	No interests declared
Rupert Franklin	No interests declared
Yelan Guo	No interests declared
Paul Jacklin	No interests declared
Sadia Janjua	No interests declared

Staff member	Interest
Juliet Kenny	No interests declared
Hugh McGuire	No interests declared
Paul Mitchell	No interests declared
Moira Mugglestone	No interests declared
M Stephen Murphy	No interests declared
Su Park	No interests declared
Nitara Prasannan	No interests declared
Wendy Riches	No interests declared
Grammati Sarri	No interests declared
Lilian Stevens	No interests declared
Cristina Visintin	No interests declared
Amy Wang	No interests declared
Katie Webster	No interests declared

Table 3: Expert advisers' declarations of interest

Expert adviser	Interest
Katharine Barnard	Personal pecuniary interest Honorarium from Animas to attend advisory board meetings in January and July 2014 for the CHOICE study – the study looks at treatment satisfaction with insulin pump therapy; honorarium from Johnson and Johnson to provide expert advice on impact of diabetes-related devices (until October 2014); honorarium from Novo Nordisk to attend advisory board meetings for the DAWN2 study – the study looks at psychosocial attitudes of adults and family members with type 1 diabetes (until March 2014); honorarium from Roche Diagnostics to act as Global Advisory Board member (ongoing) providing advice on the topic of psychosocial impact of devices for adults with type 1 diabetes; honorarium from Sanofi to attend one-off meeting on behavioural aspects of diabetes (February 2014).
Andrew Durward	No interests declared

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Appendix E: Review protocols

E.1 Diagnosis

The systematic review for the following question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'. The style of the review protocol differs slightly from the style used elsewhere in this guideline.

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

Diagnosis	
Review question for update	What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes? Note that the evidence review was prepared by the guidance-producing centre for type 1 diabetes in adults who used the following as a working version of the review question for compatibility with the evidence review for the adult's guideline *In young people with diabetes, what is the best marker (C-peptides plus or minus antibodies) to distinguish between a diagnosis of type 1 diabetes, type 2 diabetes and other forms of diabetes?*
Objectives	The aim of this review is to determine whether the presence of C-peptides and/or antibodies in people with diabetes distinguishes between type 1 diabetes, type 2 diabetes, and other forms of diabetes, in order to make an accurate diagnosis. Also what titre or concentration of each of these markers is present and distinguishes the types. • What is the best test or combination of tests to give you the highest level of certainty in discriminating type 1 diabetes from type 2 diabetes? • When does uncertainty exist, and what should be done when uncertainty exists?
Population	Young people with all types of diabetes: • young people is defined as aged at least 11 years and younger than 18 years • diabetes types are: type 1 diabetes, type 2 diabetes, latent autoimmune diabetes of adulthood (LADA) and maturity onset diabetes of the young (MODY)
Subgroups	The following groups will be considered separately if data are available: • young people
Diagnostic tests	C-peptide: • plasma C-peptide (stimulated) • urinary C-peptide • urinary C-peptide:creatinine ratio Antibody tests: • anti-islet cell antibody (ICA) • anti-glutamic acid decarboxylase 65 antibody or anti-glutamic acid decarboxylase antibody (GADA) • insulinoma-associated (IA-2 / ICA512) autoantibody • other (zinc transporter 8 (ZnT8), islet-specific glucose-6-phosphatase catalytic subunit (IGRP), anti-ZnT8)
Outcomes	• Presence of marker (number or percentage of participants with marker) • Concentration of marker (ug/ml)

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Diagnosis	
	• Change in marker over time (number or percentage of participants with marker) • Change in concentration of marker over time (ug/ml)
Importance of outcomes	Critical outcomes • not relevant
Study design	All study types
Population size and directness	Studies will be excluded if any of the following apply. • The population is mixed, with no young people subgroup analyses. Mixed populations excluded are: ○ children and young people ○ children, young people and adults • The population is exclusively children (age <11 years) • They are validation studies • They are treatment studies • They are pre-diabetes populations (we are not going to look at studies that use markers as predictors of the future development of diabetes) • They are detecting markers in relatives of people with diabetes Sample size restrictions. We will exclude studies if any of the following apply. • Adults and young people with sample size of n<50 if we retrieve >20 studies that have been conducted in young people and adults separately • Young people with a sample size of n<50 if there are >20 young people studies retrieved
Setting	All settings (as per scope)
Search strategy	Search will be restricted to studies published since the original guideline for type 1 diabetes in adults (2003). If only a few studies are found, then we will extend the search to all years
Review strategy	Appraisal of methodological quality/evidence synthesis • The methodological quality of each study will be assessed using NICE checklists and a narrative synthesis of the evidence will be provided
Notes	If no/insufficient evidence is found we will (in order of preference): • consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • move to guideline development group consensus

Diagnosis – health economic evidence	
Objectives	To identify economic studies relevant to the review question set out above
Criteria	Populations, interventions and comparators as specified in the individual review protocol above. Must be a relevant economic study design (cost-utility analysis, cost-benefit analysis, cost effectiveness analysis, cost-consequence analysis, comparative cost analysis)
Search strategy	An economic study search was undertaken using population specific terms and an economic study filter
Review strategy	Each study is assessed using the NICE economic evaluation checklist - NICE guidelines manual (2009 edition) Inclusion/exclusion criteria • If a study is rated as both 'Directly applicable' and 'Minor limitations' (using the NICE economic evaluation checklist) then it should be included in the guideline. An

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Diagnosis – health economic evidence	
	evidence table should be completed and it should be included in the economic profile. • If a study is rated as either 'Not applicable' or 'Very serious limitations' then it should be excluded from the guideline. It should not be included in the economic profile and there is no need to include an evidence table. • If a study is rated as 'Partially applicable' and/or 'Potentially serious limitations' then there is discretion over whether it should be included. The health economist should make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline development group if required. The ultimate aim being to include studies that are helpful for decision making in the context of the guideline and current NHS setting. Where exclusions occur on this basis, this should be noted in the relevant section of the guideline with references. Also exclude: • unpublished reports unless submitted as part of a call for evidence • abstract-only studies • letters • editorials • reviews of economic evaluations • foreign language articles. **Where there is discretion** The health economist should be guided by the following hierarchies. *Setting:* • UK NHS • OECD countries with predominantly public health insurance systems (for example, France, Germany and Sweden) • OECD countries with predominantly private health insurance systems (for example, the USA and Switzerland) • Non-OECD settings (always 'Not applicable') *Economic study type:* • cost-utility analysis • other type of full economic evaluation (cost-benefit analysis, cost effectiveness analysis, cost-consequence analysis) • comparative cost analysis • non-comparative cost analyses including cost of illness studies (always 'Not applicable') *Year of analysis:* • the more recent the study, the more applicable it is *Quality and relevance of effectiveness data used in the economic analysis:* • the more closely the effectiveness data used in the economic analysis matches with the studies included for the review of clinical evidence the more useful the analysis will be to decision making for the guideline
Notes	Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered

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E.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Type 1 diabetes – education		
Existing recommendation(s) in 2004 guideline	Children and young people with newly diagnosed type 1 diabetes should be offered a structured programme of education covering the aims of insulin therapy, delivery of insulin, self-monitoring of blood glucose, the effects of diet, physical activity and intercurrent illness on glycaemic control, and the detection and management of hypoglycaemia. Children and young people with type 1 diabetes and their families should be offered timely and ongoing opportunities to access information about the development, management and effects of type 1 diabetes. The information provided should be accurate and consistent and it should support informed decision-making. Children and young people with type 1 diabetes and their families should be offered opportunities to discuss particular issues and to ask questions at each clinic visit. The method of delivering education and content will depend on the individual and should be appropriate for the child's or young person's age, maturity, culture, wishes and existing knowledge within the family. Particular care should be given to communication and the provision of information when children and young people with type 1 diabetes and/or their parents have special needs, such as those associated with physical and sensory disabilities, or difficulties in speaking or reading English. The 2004 guideline includes recommendations about education at diagnosis and as part of ongoing management for type 1 diabetes An external adviser has been appointed to advise the guideline development group on technical aspects of clinical research relating to behavioural interventions and the interface with education programmes	
Review question for update	What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?	
Objectives	To determine the effectiveness of structured education programmes in improving outcomes for children and young people with type 1 diabetes. Structured education programmes deliver information to the child or young person, or their family, with the intention of improving outcomes and using a process which includes (see ISPAD Clinical Practice Consensus Guidelines 2009, Chapter 5 [Diabetes education in children and adolescents]): • a structured, agreed, written curriculum • use of trained educators • quality assurance • audit	
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion The next step might be to include systematic reviews of RCTs and non-randomised comparative studies

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Type 1 diabetes – education		
		(but not individual non-randomised studies)
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)
Population	Children and young people with type 1 diabetes less than 18 years of age	This review question will focus solely on 'patient' education (that is, education of healthcare professionals will be excluded)
Intervention or index test	Structured education programmes specific to type 1 diabetes (education aimed at children and young people or their families) This review should cover: • all settings (diabetes clinics, schools, etc.), while recognising that recommendations will be limited to the clinical practice context • all forms of delivery of education (for example, one-to-one, brief, face-to-face and remote [telemedicine, including text messaging])	
Comparator or reference standard	Alternative models of structured education Usual care	Usual care in this context usually includes unstructured, informal education, provision of information leaflets or multimedia
Clinical outcomes	Physical outcomes • glycaemic control ○ HbA1c (minimum follow-up 6 months after completion of primary intervention) • severe hypoglycaemic episodes • diabetic ketoacidosis (DKA; number of episodes) • adherence to diabetes management (including self-management) • adherence to education intervention. Psychosocial outcomes • health-related quality of life • children and young people's and families' satisfaction with intervention (education intervention) • risk-taking behaviours (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction).	The guideline development group initially identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required. The minimum duration of follow-up was subsequently relaxed to cover follow-up from baseline (rather than completion of the primary intervention) to allow inclusion of clinically relevant evidence HbA1c MID is 0.5 percentage points (5.5 mmol/mol) Severe hypoglycaemic episodes defined according to either of the following criteria. International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from

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Type 1 diabetes – education		
		another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3) No long-term interventions needed to be prioritised as outcomes because HbA1c will determine these
Health economic outcomes	This question was prioritised for health economic analysis Relevant outcomes: • health-related quality of life and quality adjusted life years (QALYs) • adherence to education intervention.	It will only be necessary to consider the cost effectiveness of structured education programmes if there is some evidence of benefit. If education programmes have a mixture of harms and benefits then a QALY approach could facilitate the appropriate trade-off. There may also be a need to model longer-term QALY gains or losses from intermediate trial or study outcomes (for example, changes in weight)
Other criteria for inclusion/ exclusion of studies	None	Studies that evaluate education programmes for healthcare professionals will be excluded (see above) Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected). Note that there are age-specific structured education programmes (mainly for young people) Subgroup analysis according to the presence of associated conditions such as autism spectrum disorder or learning difficulties, and according to language and culture-specific interventions would be useful if the evidence allows this
Search strategies	See separate document	Search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	

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Type 1 diabetes – education		
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The notes above relating to subgroup analysis by associated conditions, language and cultural considerations reflect the importance of equalities issues in this question

E.3 Type 1 diabetes – psychological interventions

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Type 1 diabetes – psychological interventions		
Existing recommendation(s) in 2004 guideline	Behavioural and conduct disorders Children and young people with type 1 diabetes who have behavioural or conduct disorders, and their families, should be offered access to appropriate mental health professionals. Non-adherence to therapy should be considered in children and young people with type 1 diabetes who have poor glycaemic control, especially in adolescence. Non-adherence to therapy should be considered in children and young people with established type 1 diabetes who present with diabetic ketoacidosis, especially if the diabetic ketoacidosis is recurrent. Young people with 'brittle diabetes' (that is, those who present with frequent episodes of diabetic ketoacidosis over a relatively short time) should have their emotional and psychological well-being assessed. The issue of non-adherence to therapy should be raised with children and young people and their families in a sensitive manner. Psychosocial support Diabetes care teams should be aware that poor psychosocial support has a negative impact on a variety of outcomes of type 1 diabetes in children and young people, including glycaemic control and self-esteem. Children and young people with type 1 diabetes, especially young people using multiple daily injection regimens, should be offered structured psychological intervention	The 2004 guideline does not make specific recommendations about psychological interventions to improve outcomes in children and young people with type 1 diabetes, but it includes the recommendations listed which refer to related topics on behavioural and conduct disorders, non-adherence, psychosocial support and adolescence An external adviser has been appointed to advise the guideline development group on technical aspects of clinical research relating to psychological interventions and the interface with education programmes

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Type 1 diabetes – psychological interventions		
	strategies because these may improve psychological well-being and glycaemic control. Young people with type 1 diabetes should be offered specific support strategies, such as mentoring and self-monitoring of blood glucose levels supported by problem solving, to improve their self-esteem and glycaemic control. Families of children and young people with type 1 diabetes should be offered specific support strategies (such as behavioural family systems therapy) to reduce diabetes-related conflict between family members. Children and young people with type 1 diabetes and their families should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being. Diabetes care teams should have appropriate access to mental health professionals to support them in the assessment of psychological dysfunction and the delivery of psychosocial support. Adolescence Diabetes care teams should be aware that adolescence can be a period of worsening glycaemic control, which may in part be due to non-adherence to therapy.	
Review question for update	What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 1 diabetes?	
Objectives	To determine the effectiveness of psychological interventions in improving outcomes for children and young people with type 1 diabetes. The question is sufficiently broad to cover interventions aimed at families and healthcare professionals as well as those aimed at the child or young person. The guideline development group prioritised psychological interventions that should be addressed in this question as follows. • Family therapy (including behavioural family systems therapy [BFST]): this is always delivered to one family unit but it can include separate sessions with	

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Type 1 diabetes – psychological interventions		
	different members (individuals/groups) within the unit. • Cognitive behavioural therapy (CBT): this can be delivered one-to-one or in groups. The intervention focuses on recognising specific triggers for maladaptive behaviour and bringing about changes to behaviour. • Motivational interviewing: this can be delivered one-to-one or in groups. The intervention focuses on general exploration of ambivalence around maladaptive behaviours and what the person wants to do or should do. The intervention develops insight into maladaptive behaviour. • Counselling: this is delivered one-to-one but the content of interventions termed counselling may vary. • Mentoring: this can be delivered one-to-one or in groups. The mentor is typically older than the person receiving mentoring or is influential in the community. • Peer support: this can be delivered one-to-one or in groups. The intervention typically involves people of similar age to the person receiving peer support.	
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered for any of the prioritised interventions only if no RCT evidence is identified for inclusion for that intervention The next step might be to include systematic reviews of RCTs and non-randomised comparative studies (but not individual non-randomised studies)
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles) The aim is to retain general recommendations that have not become outdated and to add specific recommendations about psychological interventions if relevant
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years

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Type 1 diabetes – psychological interventions		
Intervention or index test	Psychological interventions specific to the management of type 1 diabetes in children and young people (this could involve interventions aimed at families and healthcare professionals as well as those aimed at the child or young person) • Family therapy (include only validated therapies such as BFST – expert adviser to advise in relation to search results); it is likely that RCTs will be available for this type of intervention. • CBT; it is likely that RCTs will be available for this type of intervention. • Motivational interviewing; it is possible that RCTs will be available for this intervention, although it is more likely to have been used in young people and adults rather than children. • Counselling; it is possible that RCTs will be available for this type of intervention. • Mentoring; there may be no RCTs evaluating this type of intervention. • Peer support; there may be no RCTs evaluating this type of intervention.	Use the terms specific to the prioritised psychological interventions when conducting the searches for this question http://www.ahrq.gov/clinic/tp/diabedtp.htm) The following search terms from the AHRQ 2008 systematic review were considered by the guideline development group and expert adviser as part of the prioritisation of psychological interventions for this question but they were not selected for the reasons given and they should not be used as search terms for this question: • adherence (an outcome not an intervention) • behavioural therapy (poorly defined so not a priority) • biofeedback (more relevant to the question relating to education programmes) • cognitive therapy (not a priority because it focuses on awareness of behaviour but not changing behaviour) • conjoint therapy (refers to any two therapies joined together) • educational therapy (will be addressed in the education question) • psychological interventions (not specific) • psychological therapy (not specific) • solution-focused therapy (not specific – refers to any therapy that focuses on solutions rather than problems; several of the prioritised interventions are solution-focused) • therapy (not specific). This review should cover: • all settings (diabetes clinics, schools, etc.), while recognising that recommendations will be limited to the clinical practice context • all forms of delivery of the prioritised psychological interventions (for example, one-to-one, brief, face-to-face and remote [telemedicine]).
Comparator or reference standard	An alternative psychological intervention listed above An alternative and well defined psychological intervention not listed above	Usual care in this context usually includes education, no therapy, provision of information leaflets or

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Type 1 diabetes – psychological interventions		
	(expert adviser to advise on what is well defined in relation to search results) Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management Usual care (this will be the most common comparator)	multimedia (DVDs, CDs, websites, apps)
Clinical outcomes	Physical outcomes • glycaemic control ○ HbA1c (minimum follow-up 6 months after completion of primary intervention) • adherence to diabetes management (the scope requires this; to include self-management) • adverse events (for example, severe hypoglycaemic episodes, diabetic ketoacidosis (DKA) or self-harm) Psychosocial outcomes • health-related quality of life • children and young people's and families' satisfaction with intervention • depression or anxiety • school performance or attendance (this will be very important for this question) • risk-taking behaviours (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction).	The guideline development group initially identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required. The minimum duration of follow-up was subsequently relaxed to cover follow-up from baseline (rather than completion of the primary intervention) to allow inclusion of clinically relevant evidence The guideline development group noted that change in body mass index (BMI) standard deviation score (SDS) would be more important than DKA for the corresponding question for type 2 diabetes HbA1c MID is 0.5 percentage points (5.5 mmol/mol) Severe hypoglycaemic episodes defined according to either of the following criteria. • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3).

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Type 1 diabetes – psychological interventions		
		No long-term interventions needed to be prioritised as outcomes because HbA1c will determine these
Health economic outcomes	This question was not prioritised for health economic analysis Outcomes: • health-related quality of life and quality adjusted life years (QALYs) • adherence to treatment It may be possible attach a QALY to various long-term complications – this could be a longer list than the seven outcomes considered for the GRADE profiles	This question was rated as a medium (but not high) priority for health economic analysis, but it could be considered if resources allow, especially as there are parallels with the question on structured education packages, which was selected as a high priority for health economic analysis guideline development group to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hyperglycaemia and mortality It would only be necessary to consider the cost effectiveness of psychological interventions if there were some evidence of clinical benefit. If psychological interventions have a mixture of harms and benefits then a QALY approach could facilitate the appropriate trade-off. There may also be a need to model longer-term QALY gains or losses from intermediate trial or study outcomes (for example, changes in weight)
Other criteria for inclusion/ exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected). Subgroup analysis by ages within these groups would also be useful if it is feasible Evidence tables should document who delivered the intervention(s), the frequency of contact with healthcare or other relevant professionals to deliver the intervention(s), and process evaluation information
Search strategies	See section F.19	NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)	

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Type 1 diabetes – psychological interventions		
	A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

E.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Type 1 diabetes – multiple daily injections		
Existing recommendation(s) in 2004 guideline	Pre-school and primary school children with type 1 diabetes should be offered the most appropriate individualised regimens to optimise their glycaemic control. Young people with type 1 diabetes should be offered multiple daily injection regimens to help optimise their glycaemic control. Young people who do not achieve satisfactory glycaemic control with multiple daily injection regimens should be offered additional support and, if appropriate, alternative insulin therapy (once-, twice- or three-times daily mixed insulin regimens or continuous subcutaneous insulin infusion using an insulin pump). Young people with type 1 diabetes who have difficulty adhering to multiple daily injection regimens should be offered twice-daily injection regimens.	The 2004 guideline contains the following definitions: • pre-school children – children aged 1 year or older, and younger than 5 years • primary school children – children aged 5 years or older, and younger than11 years • young people – people aged 11 years or older, and younger than 18 years.
Review question for update	What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?	
Objectives	To establish the effectiveness of different insulin regimens in children and young people with type 1 diabetes	
Language	English	
Study design	Systematic reviews and RCTs only Comparative observation studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	Although this is an update of part of a review question considered in the 2004 guideline, no date limit will be applied to searches to ensure that all relevant articles are identified and allow extraction

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Type 1 diabetes – multiple daily injections		
		of data in the form of GRADE profiles
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years Exclude studies involving children or young people with type 2 diabetes unless the results for children and young people with type 1 diabetes are reported separately
Intervention or index test	Multiple daily injections of insulin, with or without carbohydrate counting	The definition of multiple daily injections will be four or more injections per day using unmixed insulin (meaning insulins that are not mixed in the syringe) The 2004 guideline defines multiple daily injections as follows: the person has injections of short-acting insulin or rapid-acting insulin analogue before meals, together with one or more separate daily injections of intermediate-acting insulin or long-acting insulin analogue Evidence tables should record additional care received (carbohydrate counting, advice, monitoring, etc.) Any articles in which four or more injections were given but it was not clear from the title or abstract whether mixed or unmixed insulin was used should be ordered and discussed with the guideline development group The guideline development group noted that studies in which short-term intensive insulin treatment is used from diagnosis are not relevant for this question Report the following types of studies separately: • those in which all participants are studied from diagnosis • those in which all participants receive a change in treatment simultaneously

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Type 1 diabetes – multiple daily injections		
		• those in which selected children and young people receive a change in treatment (for example, because usual treatment has failed).
Comparator or reference standard	Fewer than four injections or occasions of injecting per day. Predominantly mixed insulin regimens – combinations of insulins with different durations of action given in a single injection – also includes regimens where such insulins are given in separate injections but at the same time. Two injections given at the same time will count as one mixed injection 25:75 and 30:70 mixes are currently available in the UK, but studies involving other mixes (for example, 40:60) or free-mixed insulin are also eligible for inclusion	The definition of a mixed insulin regimen will be one in which fewer than four injections per day using mixed insulin (meaning insulin with different durations of action mixed in the syringe) are administered The 2004 guideline defines fewer than four injections per day as follows: injections of short-acting insulin or rapid-acting insulin analogue mixed with intermediate-acting insulin. The insulin preparations may be mixed by the patient at the time of injection. For example, mixtures of 25 to 30% short-acting analogue with an intermediate insulin (such as Humalog mix[25]) Any articles in which fewer than four injections were given but it was not clear from the title or abstract whether mixed or unmixed insulin was used should be ordered and discussed with the guideline development group

Clinical outcomes	Physical outcomes
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months)
	  ○ severe hypoglycaemic episodes
	  ○ diabetic ketoacidosis (DKA; number of episodes)
	• adherence to diabetes management (including self-management)
	• changes in body mass index (BMI) standard deviation score (SDS).
	
	Psychosocial outcomes
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention.
		The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		Severe hypoglycaemic episodes defined according to either of the following criteria.
		• International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with

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Type 1 diabetes – multiple daily injections		
		or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3). BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions
Health economics outcomes	This question was prioritised for health economic analysis Outcomes: • health-related quality of life (measured using quality adjusted life years [QALYs]) • adherence to diabetes management (including self-management) It may be possible attach a QALY weight to various long-term complications – this could be a longer list than the seven outcomes considered for GRADE profiles	
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	Results will be pooled using meta-analysis if possible
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

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E.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Type 1 diabetes – HbA1c targets		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and that their care package should be designed to attempt to achieve this.	
Review question for update	What is the optimal HbA1c target for children and young people with type 1 diabetes?	
Objectives	To determine the optimal HbA1c target value in terms of minimising the risk of long-term complications without incurring an increased risk of hypoglycaemic episodes as an adverse effect	The threshold of 7.5% in the 2004 guideline recommendations comes from the Diabetes Control and Complications Trial (DCCT); the lower HbA1c the lower the risk of complications, and there is no lower limit at which the risk stops reducing; but at very low levels of HbA1c the risk of hypoglycaemia is unacceptable (for type 1 diabetes the risk of hypoglycaemia is great) This review question should, therefore, consider studies that focus on hypoglycaemia risk related to HbA1c
Language	English	
Study design	Systematic reviews and RCTs Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion No RCTs that report results specific to children and young people are expected. Only consider studies involving adults if no RCTs or observational studies report data for children and young, and then only by cross-referring to the type 1 diabetes in adults guideline in which HbA1c targets are being updated
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles). Note that newer studies will be more relevant to current diabetes management

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Type 1 diabetes – HbA1c targets		
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years Note, however, that inclusion/exclusion of studies will be based on time at diagnosis and application of HbA1c targets, whereas long-term follow-up into adulthood will be relevant for this question
Intervention	Specified target value for HbA1c or HbA1c values achieved (recorded)	Comparisons might, for example, relate to differences between clinics
Comparator or reference standard	Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded)	

Clinical outcomes	Physical outcomes
	• glycaemic control
	  ○ severe hypoglycaemic episodes (frequency)
	  ○ nocturnal hypoglycaemic episodes (frequency)
	  ○ any hypoglycaemic episode (however defined; frequency)
	• contact with the diabetes care team as a measure of healthcare utilisation.
	
	Psychosocial outcomes
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention (acceptability and comfort associated with testing, and anxiety or stress associated with trying to meet specific targets would be reflected here, but these were not expected to be reported frequently enough to warrant consideration as separate outcomes).
		• The guideline development group used the review protocol for the question related to blood glucose monitoring for type 1 diabetes as the starting point for the outcomes to be considered for this question
		
		• Outcomes related to hypoglycaemia were prioritised for inclusion because the risk of hypoglycaemia is important with type 1 diabetes; this contrasts with the corresponding protocol for HbA1c targets for type 2 diabetes where the risk of long-term complications is more important
		
		• The guideline development group identified a minimum follow-up period of 4 months after completion of the primary intervention for all prioritised outcomes). Include further follow-up if reported, for example, if a top-up intervention is required
		
		Severe hypoglycaemic episodes defined according to either of the following criteria:
		• International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment

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Type 1 diabetes – HbA1c targets		
		(glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3).
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

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E.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Type 1 diabetes – blood glucose targets		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be informed that the optimal targets for short-term glycaemic control are a pre-prandial blood glucose level of 4–8 mmol/litre and a post-prandial blood glucose level of less than 10 mmol/litre.	
Review question for update	What are the optimal blood glucose targets for children and young people with type 1 diabetes?	
Objectives	To determine the optimal blood glucose target range in terms of minimising the HbA1c level (as a surrogate for long-term complications) without incurring hypoglycaemia as an adverse effect. This question should include consideration of the timing of testing, for example, before or after meals	
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion

Type 1 diabetes – blood glucose targets		
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention	Specified target ranges for blood glucose or blood glucose values achieved (recorded)	
Comparator or reference standard	Comparisons to be made between outcomes according to target ranges for blood glucose and/or blood glucose values achieved (recorded)	

Clinical outcomes	Physical outcomes:
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months)
	  ○ severe hypoglycaemic episodes
	  ○ nocturnal hypoglycaemic episodes
	  ○ diabetic ketoacidosis (DKA; number of episodes)
	• contact with the diabetes care team as a measure of healthcare utilisation
	
	Psychosocial outcomes:
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention (acceptability and comfort associated with testing, and anxiety or stress associated with trying to meet specific targets would be reflected here, but these were not expected to be reported frequently enough to warrant consideration as separate outcomes).
		The guideline development group identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		Severe hypoglycaemic episodes defined according to either of the following criteria.
		• International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or
		• ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3).

Health economic outcomes	This question was not prioritised for health economic analysis	

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Type 1 diabetes – blood glucose targets	
Other criteria for inclusion/ exclusion of studies	None
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)

E.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

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Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing	
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care teams. Children and young people with type 1 diabetes who are trying to optimise their glycaemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day. Children and young people with type 1 diabetes should be encouraged to monitor their blood glucose levels before and after exercise so that they can: • identify when changes in insulin or food intake are necessary • learn the glycaemic response to different exercise conditions • be aware of exercise-induced hypoglycaemia • be aware that hypoglycaemia may occur several hours • after prolonged exercise. Young people with type 1 diabetes who drink alcohol should be informed that they should: • eat food containing carbohydrate before and after drinking • monitor their blood glucose levels regularly and aim to keep the levels within the recommended range by • eating food containing carbohydrate.

Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
	Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	
Review question for update	How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?	
Objectives	To identify the optimal frequency of capillary blood glucose testing (at any site) in children and young people with type 1 diabetes. The question is designed to identify which frequency (or range of frequencies) of testing is associated with optimal glycaemic control and thus a reduced risk of long-term complications	Notes from the guideline development group: • frequent blood glucose testing helps to mitigate against hypoglycaemia unawareness • blood glucose level- anxiety is related to excessive testing • excessive testing can be more expensive that continuous glucose monitoring, and so clinicians often use excessive testing as a rationale for requesting funding for continuous monitoring systems
Language	English	
Study design	Systematic reviews and RCTs and observational studies	
Status	Published articles (no limitation on year of publication)	The original guideline did not consider non-comparative, observational studies and so no date limit will be applied to searches
Population	Children and young people with type 1 diabetes	
Intervention or index test	• RCTs: 5 or more finger-prick tests per day • Observational studies: frequency varies with lower limit of 0 tests per day and no upper limit	It is not expected that there will be RCTs that fully answer this question and so no restriction in study design will be applied to the literature searches. This reflects the following considerations: • there are unlimited possibilities in terms of the frequency of testing • it might be difficult ethically to randomise any participants to just a few tests • including observational studies will allow consideration of no testing at all, which would never be recommended practice.
Comparator or reference standard	• RCTs: 4 or fewer finger-prick tests per day • Observational studies: different frequencies of testing	
Clinical outcomes	Physical outcomes: • glycaemic control ○ HbA1c (minimum follow-up 6 months) ○ severe hypoglycaemic episodes ○ nocturnal hypoglycaemic episodes ○ diabetic ketoacidosis (DKA; number of episodes)	The guideline development group selected 7 outcomes and agreed to use them across the three questions relating to blood glucose monitoring (with the exception of DKA which is used in this question but is replaced in the CGMS questions by mean blood glucose levels):

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Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
	• adherence to diabetes management (including self-management) Psychosocial outcomes: • health-related quality of life • children and young people's and families' satisfaction with intervention (impact of pain to be reflected here).	• frequency of finger-prick (capillary) testing, • sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and • finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring. Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes HbA1c MID is 0.5 percentage points (5.5 mmol/mol) Severe hypoglycaemic episodes defined according to either of the following criteria. • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)

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Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
Health economics outcomes	This question was prioritised for health economic analysis Outcomes: • Health-related quality of life (measured using quality adjusted life years [QALYs]). In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes	The guideline development group's view was that commissioners ration testing strips because they are expensive and so this becomes a barrier to implementation
Other criteria for inclusion/ exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (frequency of testing is likely to depend on age)
Search strategies	See Section F.7	A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	School regulations can be a barrier to uptake, which creates variations in practice The guideline development group noted that it can be helpful if spare pens, meters and strips are available in schools

Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems. Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction. Research recommendation: Research is needed to evaluate the clinical effectiveness of the routine use of invasive and noninvasive continuous glucose monitoring systems for optimising glycaemic control in children and young people with type 1 diabetes.	Update needs to be clear about which children and young people would benefit from using continuous glucose monitoring systems Devices without memories are no longer available and so this recommendation may be obsolete now

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Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
Review question for update	What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?	Continuous glucose monitoring can be used daily or just at night. Monitoring devices are often supplied by the diabetes care team for short-term use (4 to 5 days) for trouble-shooting multiple daily injection regimens, for example, to get an idea of when hypoglycaemia occurs (often at night). More recently, they have been made available to the child or young person for long-term use The child or young person may not see the results that are recorded – the results may be transmitted to the diabetes care team and analysed retrospectively This question covers all forms of finger-prick testing and continuous glucose monitoring
Objectives	To identify the circumstances in which children and young people with type 1 diabetes should be offered continuous subcutaneous glucose monitoring in addition to capillary blood testing (finger-prick testing)	
Language	English	
Study design	Systematic reviews and RCTs only	
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles), although it is unlikely that many of them will be relevant because technology has moved on. Short-term use and loan of monitoring devices is, however, still relevant
Population	Children and young people with type 1 diabetes	
Intervention or index test	Any form of continuous subcutaneous glucose monitoring, including • sustained use of continuous subcutaneous glucose monitoring (providing real-time, ongoing output) • continuous subcutaneous glucose monitoring performed intermittently and analysed retrospectively without the child or young person seeing the measurements	In all instances, finger-prick testing needs to be used alongside continuous subcutaneous glucose monitoring for the purposes of calibrating the continuous monitoring device All monitoring methods that involve a subcutaneous cannula are of interest in this question, but evidence relating to any version of glucowatch (which is now obsolete) should be excluded
Comparator or reference standard	Any form of capillary blood glucose testing, including: • finger-prick testing • testing at another anatomical site • any frequency of testing.	Self-monitoring of blood glucose (SMBG) is standard term in clinical practice and research articles

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Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
		The guideline development group agreed that all frequencies of SMBG will be included

Clinical outcomes	Physical outcomes:
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months – if not available then use 3-month follow-up)
	  ○ mean blood glucose levels
	  ○ severe hypoglycaemic episodes
	  ○ nocturnal hypoglycaemic episodes
	• adherence to diabetes management (including self-management).
	
	Psychosocial outcomes:
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention (impact of pain to be reflected here).
		The guideline development group selected 7 outcomes and agreed to use these across the three questions relating to blood glucose monitoring (with the exception of mean blood glucose levels which would be excluded from the frequency question and replaced with DKA):
		• frequency of finger-prick (capillary) testing,
		• sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and
		• finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring
		
		Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control
		
		The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		Severe hypoglycaemic episodes defined according to either of the following criteria:
		• International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or

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Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
		without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3).
Health economics outcomes	This question was prioritised for health economic analysis Health-related quality of life (measured using quality adjusted life years [QALYs]) In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes	
Other criteria for inclusion/ exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this Subgroup analysis for insulin pump therapy versus multiple daily injections would be of interest Subgroup analysis based on how continuous subcutaneous glucose monitoring is used (sustained versus intermittent) would be of interest
Search strategies	A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The possibility of providing spare pens, meters, strips and continuous subcutaneous glucose monitoring devices to keep in school was raised by the guideline development group

Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems.	Update needs to be clear about which children and young people would benefit from using continuous glucose monitoring systems

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Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
	Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction.	
Review question for update	What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?	Continuous glucose monitoring can be used daily or just at night. Monitoring devices are often supplied by the diabetes care team for short-term use (4 to 5 days) for trouble-shooting multiple daily injection regimens, for example, to get an idea of when hypoglycaemia occurs (often at night). More recently, they have been made available to the child or young person for long-term use The child or young person may not see the results that are recorded – the results may be transmitted to the diabetes care team and analysed retrospectively
Objectives	To identify the optimal use of continuous subcutaneous glucose monitoring (sustained use with real-time adjustment versus intermittent use with retrospective adjustment) in children and young people with type 1 diabetes. The question focuses on the comparative effectiveness in children and young people with type 1 diabetes of: • sustained continuous subcutaneous glucose monitoring (providing real-time, ongoing output and adjustment to insulin treatment where appropriate), and • continuous subcutaneous glucose monitoring performed intermittently with retrospective adjustment of insulin treatment. In all instances, finger-prick testing needs to be used alongside continuous subcutaneous glucose monitoring for the purposes of calibrating the continuous monitoring device.	Evidence relating to insulin pumps that perform a continuous glucose monitoring function can be considered in this review (alongside evidence relating to standalone continuous glucose monitoring devices).
Language	English	
Study design	Systematic reviews and RCTs only	A 2012 Cochrane review 'Continuous glucose monitoring systems for type 1 diabetes mellitus' contains seven RCTs published since 2004
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the

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Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
		update review (involving extraction of data in the form of GRADE profiles), although it is unlikely that many of them will be relevant because technology has moved on. Short-term use and loan of monitoring devices is, however, still relevant
Population	Children and young people with type 1 diabetes	
Intervention or index test	Sustained use of continuous subcutaneous glucose monitoring (providing real-time, ongoing output)	
Comparator or reference standard	Continuous subcutaneous glucose monitoring performed intermittently and analysed retrospectively without the child or young person seeing the measurements	All monitoring methods that involve a subcutaneous cannula are of interest in this question, but evidence relating to any version of glucowatch (which is now obsolete) should be excluded

Clinical outcomes	Physical outcomes:
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months)
	  ○ mean blood glucose levels
	  ○ severe hypoglycaemic episodes
	  ○ nocturnal hypoglycaemic episodes
	• adherence to diabetes management (including self-management).
	
	Psychosocial outcomes:
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention (impact of pain to be reflected here).
		The guideline development group selected 7 outcomes and agreed to use these across the three questions relating to blood glucose monitoring (with the exception of mean blood glucose levels which would be excluded from the frequency question and replaced with DKA):
		• frequency of finger-prick (capillary) testing,
		• sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and
		• finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring.
		
		Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control
		
		The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes

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Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
		HbA1c MID)is 0.5 percentage points (5.5 mmol/mol) Severe hypoglycaemic episodes defined according to either of the following criteria. • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3).
Health economics outcomes	This question was prioritised for health economic analysis Outcomes: • Health-related quality of life (measured using quality adjusted life years [QALYs]). In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes	
Other criteria for inclusion/ exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this Subgroup analysis for insulin pump therapy versus multiple daily injections would be of interest
Search strategies	See separate document	A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The possibility of providing spare devices to keep in school was raised by the guideline development group

Update 2015

E.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Type 1 diabetes – blood ketone monitoring		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness.	The 2004 guideline also includes a recommendation for further research to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis (DKA) in children and young people with type 1 diabetes
Review question for update	What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of DKA?	
Objectives	To compare the clinical and cost effectiveness of blood ketone monitoring and urine ketone monitoring in the prevention or early detection of DKA in children and young people with type 1 diabetes. The question relates to home monitoring of ketones (rather than monitoring in hospital during treatment for DKA). It should include consideration of the frequency of monitoring, and the potential use of ketone monitoring will be interpreted more broadly than in relation to intercurrent illness. Comparisons between monitoring during intercurrent illness and at other times, depending on the insulin regimen being used (and especially when using insulin pump therapy), will be considered if the evidence allows	
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Blood ketone monitoring	
Comparator or reference standard	Urine ketone monitoring	Historically urine ketone monitoring would have been usual practice
Clinical outcomes	Physical outcomes: • development of DKA (number of episodes)	The group did not prioritise adherence to diabetes

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Type 1 diabetes – blood ketone monitoring		
	• severity of DKA (measured by pH at admission) • hospital admission rates • mortality • contact with the diabetes care team (for example, to interpret ketone measurements and determine appropriate action) as a measure of healthcare utilization • adherence to diabetes management (including self-management). Psychosocial outcomes: • health-related quality of life • children and young people's and families' satisfaction with intervention.	management (including self-management) as an outcome for extraction initially because it was unlikely to be reported in clinical studies. The group did, however, note that discouraging the use of out-of-date testing strips might be discussed in the evidence to recommendations section of the guideline Due to the sparsity of evidence identified for inclusion, the NCC-WCH technical team extracted data on adherence to diabetes management (percentage of time the test was used during sick days)
Health economics outcomes	This question was prioritised for health economic analysis Outcomes: • health-related quality of life (measured using quality adjusted life years [QALYs]) • hospitalisation episodes.	Full recovery usually occurs with appropriate management, although a risk of long-term intellectual impairment may occur even in children and young people without cerebral oedema. DKA is the most common form of diabetic related death in children and young people with a 2 to 5% mortality from cases Most of the potential QALY gain from monitoring is, therefore, likely to arise from averted mortality, although there is additionally some long-term morbidity from neurological deficits in about 35% of children and young people who survive an episode of cerebral oedema In addition to the QALY gain, cost-effectiveness will be dependent on monitoring averting expensive episodes of hospitalisation
Other criteria for inclusion/ exclusion of studies	None	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	

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Type 1 diabetes – blood ketone monitoring	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)

E.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Type 1 diabetes – dietary advice – carbohydrate counting		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be informed that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows: • carbohydrates – more than 50% • protein – 10–15% • fat – 30–35%. The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs. Children and young people using multiple daily injection regimens should be offered education about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake.	The 2004 guideline does not make specific recommendations about carbohydrate counting, but it includes the recommendations listed which refer to carbohydrate intake as a percentage of the total diet and adjusting insulin doses to reflect carbohydrate intake
Review question for update	What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?	
Objectives	To determine whether dietetic advice using carbohydrate counting is effective in children and young people with type 1 diabetes. The term carbohydrate counting is taken here to mean the calculation of insulin:carbohydrate ratios, as used with multiple daily injection regimens or insulin pump therapy (that is, level 3 carbohydrate counting in the American Dietetic Association classification)	Note that dietary management using glycaemic index, which can be used with or without carbohydrate counting, is considered in a separate review question References for the American Dietetic Association classification are as follows:

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Type 1 diabetes – dietary advice – carbohydrate counting		
	The American Dietetic Association classifies approaches to carbohydrate counting using the following three levels (see Gillespie 1998 and Rabasa-Lhoret 1999) • Level 1 – consistent carbohydrate intake. At this level the patient is introduced to the fundamental concept that carbohydrate is the food component that raises blood glucose. A consistent intake of carbohydrate is encouraged based on predefined quantities of food • Level 2 – pattern management principles. At this level, patients continue to eat regular carbohydrate, use a consistent baseline insulin dose and monitor blood glucose levels frequently. They recognise patterns of blood glucose response to carbohydrate (and other food) intake, and changes that occur with insulin and exercise. They learn to adjust their insulin dose, or change carbohydrate intake or timing of exercise, to meet blood glucose targets • Level 3 – insulin:carbohydrate ratios. At this level, which is appropriate for people on multiple daily injection regimens or insulin pump therapy, calculation of insulin:carbohydrate ratios are individualised according to age, sex, pubertal status, duration of diabetes, time of day, and activity. Adjustment of pre-meal insulin according to the estimated carbohydrate content of the meal or snack is then undertaken using the specified insulin:carbohydrate ratios	• Gillespie SJ, Kulkarni KD, Daly AE. Using carbohydrate counting in diabetes clinical practice. J Am Diet Assoc 1998: 98: 897–905. • Rabasha-Lhoret R, Garon J, Langelier. Effects of meal carbohydrate content on insulin requirements in Type 1 diabetic patients treated with Ultralente-Regular) insulin regimen. Diabetes Care 1999: 22: 667–673.
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Dietetic advice involving carbohydrate counting (level 3 in the American Dietetic Association classification)	Include studies only if dietetic advice includes direct contact and training with healthcare professionals (for example, providing an information leaflet is not enough) Exclude studies in which advice about carbohydrate counting is

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Type 1 diabetes – dietary advice – carbohydrate counting		
		given, but insulin is not adjusted according to carbohydrate intake (level 3 carbohydrate counting implies participants will be using multiple daily injection regimens or insulin pump therapy) Evidence tables should document the insulin regimen in the intervention and comparison groups
Comparator or reference standard	Usual care	Usual care could include dietetic advice which does not incorporate specific advice about carbohydrate counting, including levels 1 and 2 in the American Dietetic Association classification

Clinical outcomes	Physical outcomes:
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months)
	  ○ aevere hypoglycaemic episodes
	  ○ postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve)
	• adherence to diabetes management (including self-management)
	• changes in body mass index (BMI) standard deviation score (SDS).
	
	Psychosocial outcomes:
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention.
		The guideline development group selected the same priority outcomes for the questions on carbohydrate counting and glycaemic index, and the outcomes selected were the same as those for the question on multiple daily injection regimens except that postprandial hyperglycaemia was substituted for diabetic ketoacidosis (DKA)
		
		The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		Severe hypoglycaemic episodes defined according to either of the following criteria:
		• International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or

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Type 1 diabetes – dietary advice – carbohydrate counting		
		• ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3).
Health economic outcomes	This question was prioritised for health economic analysis, but only in connection with the question on multiple daily injections Outcomes: • health-related quality of life and quality adjusted life years (QALYs) • adherence to diabetes management (including self-management) It may be possible attach a QALY to various long-term complications – long-term outcomes are not prioritised per se but might be affected through glycaemic control	Guideline development group to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hypoglycaemia and mortality
Other criteria for inclusion/ exclusion of studies		Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allow this (although the availability of such studies is not expected)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

Type 1 diabetes – dietary advice – glycaemic index		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be informed of the importance of healthy eating in reducing the risk of cardiovascular disease (including foods with a low glycaemic index, fruit and vegetables, and types and amounts of fats), and means of making appropriate nutritional changes in the period after diagnosis and according to need and interest at intervals thereafter. Children and young people using multiple daily injection regimens should be offered education about insulin and dietary management as part of their diabetes	The 2004 guideline does not make specific recommendations about glycaemic intake in children and young people, but it includes the recommendations listed which refer to the importance of foods with low glycaemic index as part of a healthy diet, and adjusting insulin doses to reflect carbohydrate intake The type 1 diabetes in adults guideline update includes a parallel question for which the initial systematic review was undertaken by the NCC-WCH team; material differences between the two reviews are indicated here

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Type 1 diabetes – dietary advice – glycaemic index		
	care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake.	
Review question for update	What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?	
Objectives	To determine whether dietetic advice using glycaemic index is effective in children and young people with type 1 diabetes in terms of maintaining glycaemic control. The guideline development group noted that knowledge about foods with a low glycaemic index and those with a high glycaemic index could be relevant for the update	
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Dietetic advice taking account of the glycaemic index of carbohydrates	
Comparator or reference standard	Dietetic advice that does not take account of glycaemic index Carbohydrate counting without taking account of glycaemic index	The only difference between the intervention and comparator arms should be the use of glycaemic index Evidence tables should document the insulin regimen and whether or not carbohydrate counting was used
Clinical outcomes	Physical outcomes: • glycaemic control ○ HbA1c (minimum follow-up 6 months) ○ severe hypoglycaemic episodes ○ postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve) • adherence to diabetes management (including self-management) • changes in body mass index (BMI) standard deviation score (SDS). Psychosocial outcomes: • health-related quality of life • children and young people's and families' satisfaction with intervention.	The guideline development group for diabetes in children and young people selected the same priority outcomes for the review questions on carbohydrate counting and glycaemic index, and the outcomes selected were the same as those for the question on multiple daily injection (MDI) regimens except that postprandial hyperglycaemia was substituted for diabetic ketoacidosis (DKA) The guideline development group for type 1 diabetes in adults selected the same priority outcomes as for children and young people, except that nocturnal hypoglycaemia was substituted for changes in BMI SDS. The latter was considered to be more important in children and young people with type 1 diabetes across the questions about dietetic advice and MDI regimens because any dietetic

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Type 1 diabetes – dietary advice – glycaemic index		
		intervention might affect weight gain, whereas daytime food intake is unlikely to result in nocturnal hypoglycaemia because food intake will be covered by administration of short-acting insulin that will generally have little effect during sleep The guideline development group for diabetes in children and young people considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes. The same approach was used in the question related to adults with type 1 diabetes HbA1c MID is 0.5 percentage points (5.5 mmol/mol) Severe hypoglycaemic episodes defined according to either of the following criteria: • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economic outcomes	This question was not prioritised for health economic analysis Outcomes: • health-related quality of life and quality adjusted life years (QALYs) • adherence to diabetes management (including self-management) It may be possible attach a QALY to various long-term complications – long-	Guideline development group to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hypoglycaemia and mortality

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Type 1 diabetes – dietary advice – glycaemic index		
	term outcomes are not prioritised per se but might be affected through glycaemic control	
Other criteria for inclusion/ exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

E.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

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Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline The 2004 guideline was specific to type 1 diabetes The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The

Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
	Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	full Guideline development group will ratify all conclusions and recommendations based on the DKA evidence
Review question for update	What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of DKA in children and young people?	
Objectives	To evaluate the predictive value of symptoms, signs and biochemical abnormalities as indicators of DKA in children and young people with type 1 or type 2 diabetes. These questions cover children and young people who have either type 1 or type 2 diabetes. The diagnosis of diabetes may have been made previously, or they may be presenting for the first time with DKA	
Language	English	
Study design	• Systematic reviews and RCTs only • Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion The Guideline development group noted that for these questions RCTs are unlikely to be identified, and so the systematic search for evidence should encompass observational studies from the outset The Guideline development group discussed the feasibility of identifying prospective observational studies for inclusion and concluded that it might be necessary to consider retrospective studies (for example, case-control studies, because of the rarity of DKA) despite their potential limitations
Status	Published articles (no limitation on year of publication)	Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people (in whom type 1 or type 2 diabetes may or may not have been recognised previously)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years

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Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
		The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Symptoms, signs and biochemical abnormalities that are suggestive of DKA and their predictive values individually or in combination Symptoms and signs: • polydypsia • polyuria (possibly manifesting as bedwetting, that is, secondary enuresis) • weight loss • dehydration • nausea or vomiting • abdominal pain • respiratory distress • altered level of consciousness. Biochemical abnormalities: • hyperglycaemia • acidosis • ketosis.	The clinical problem is that DKA is not always recognised (rather than it being overdiagnosed) The guideline development group agreed to consider the symptoms, signs and biochemical abnormalities listed in terms of their value as predictive features The order in which the symptoms and signs are currently listed reflects increasing severity of DKA; it might be useful to reflect this in the review guideline development group to consider tests (capillary blood glucose), recognition, prevention at diagnosis somewhere in the guideline (not directly this question)
Comparator or reference standard	Hospital-based diagnosis of DKA (based on pH or bicarbonate, blood glucose and blood or urine ketones)	
Clinical outcomes	Diagnostic test (predictive) accuracy (sensitivity, specificity and positive and negative likelihood ratios) applied to symptoms, signs and biochemical abnormalities individually or in groups	
Health economics outcomes	These questions were not prioritised for health economic analysis	This will remain true provided the recommendations arising from these questions are restricted to giving a list of symptoms, signs and biochemical abnormalities to look out for, rather than interventions that should follow based on them
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation

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Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
		Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See Section F.10	A single search for evidence will be undertaken across the two questions
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes Communication problems (young children and neurodisabilities) might also be of relevance for this question

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E.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**

- **serum urea or electrolytes**
- **acid/base status?**

Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full guideline development group will ratify all conclusions and recommendations based on the DKA evidence
Review question for update	What routine assessments and investigations should be used to inform management in children and young people who present with DKA? Which of the following should be performed as clinical monitoring during treatment of DKA in children and young people: • general observations (for example, heart and respiratory rate and blood pressure) • body weight • hydration status • fluid balance • neurological observations • electrocardiographic (ECG) monitoring?	The review questions for type 1 and type 2 diabetes are identical The guideline development group needs to address assessment of, and typical degree of, dehydration somewhere, and volume of fluids for rehydration, and this protocol is intended to be broad enough to accommodate this The guideline development group might want to consider

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Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
	Which of the following laboratory investigations should be performed to monitor children and young people during treatment for DKA: • blood glucose • blood or urine ketones • serum urea or electrolytes • acid/base status?	recommending the use of early warning scores
Objectives	To identify the appropriate clinical assessments and laboratory investigations that should be performed in order to guide treatment for children and young people with DKA, and to monitor the response during treatment. The guideline scope requires the guideline development group to consider all of the following: • immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration) • clinical assessment and investigations at presentation to guide management • fluid management, including: ○ assessment of dehydration ○ volume of administration • clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including: ○ general observations (for example, heart and respiratory rate and blood pressure) ○ body weight ○ hydration status ○ fluid balance ○ neurological observations ○ ECG monitoring • laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including: ○ blood glucose ○ blood or urine ketones ○ serum urea and electrolytes ○ acid/base status.	Other aspects of fluid management (route and rate of administration, choice of fluid, and additives) are addressed through separate questions and a different protocol
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	There are unlikely to be any RCTs for this question and so the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	No date limit will be applied to searches for these specific review questions to ensure that

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Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
		all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Any approach to clinical assessment and/or laboratory investigations for children and young people presenting with DKA or during treatment	Although the intervention and comparison are specified very broadly, the guideline scope requires the guideline development group to address all of the following, whether or not relevant evidence is identified through the systematic search Immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration) Clinical assessment and investigations at presentation to guide management Fluid management, including: • assessment of dehydration • volume of administration • (other aspects of fluid management will be addressed through separate questions and a different protocol). Clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including: • general observations (for example, heart and

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Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
		respiratory rate and blood pressure) • body weight • hydration status • fluid balance • neurological observations • ECG monitoring. Laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including: • blood glucose • blood or urine ketones • serum urea and electrolytes • acid/base status. The guideline development group noted that the following terminology might be helpful when selecting search terms Clinical assessment: • general observations (vital signs): ○ temperature ○ level of consciousness • clinical signs of dehydration: ○ altered skin colour ○ sunken eyes ○ cold extremities ○ prolonged capillary refill time ○ dry mucous membranes ○ reduced skin turgor ○ reduced urine output • signs of deep vein thrombosis (including leg pain or swelling). Laboratory investigations: • blood ketones to include near-patient testing • plasma osmolality (tonicity). The evidence identified for inclusion could provide guidance on the frequency and duration with which to perform laboratory investigations

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Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
Comparator or reference standard	Any other approach to clinical assessment and/or laboratory investigations for children and young people presenting with DKA or during treatment	There may be few comparative studies identified for inclusion, but where necessary the guideline development group will be able to use informal consensus based on knowledge and experience to formulate recommendations addressing all areas required by the scope There may be comparative studies relating to blood ketone testing

Clinical outcomes	Physical outcomes:
	• mortality
	• degree of dehydration confirmed by post-recovery weight
	• detection of hypovolaemia
	• detection of laboratory abnormalities:
	  ○ hypoglycaemia
	  ○ hypokalaemia
	  ○ hyponatraemia
	  ○ persistent acidosis
	  ○ persistent ketosis
	• detection of complications:
	  ○ cerebral oedema
	  ○ venous thrombosis
	  ○ aspiration
	• healthcare utilisation (for example, duration of admission, requirement for ventilation [as a proxy for severity of DKA or presence of cerebral oedema]).
		Include consideration of frequency of monitoring and intervals

Health economics outcomes	These questions were not selected as priorities for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See Section F.11	A single search for evidence will be undertaken across the six questions to cover all the aspects of interest in this protocol

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Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

E.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

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Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
	Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full guideline development group will ratify all conclusions and recommendations based on the DKA evidence
Review question for update	What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis? At what rate should children and young people with diabetic ketoacidosis be rehydrated? What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?	The review questions for type 1 and type 2 diabetes are identical All six questions will be covered by a single protocol. The available evidence will be presented in such a way as to emphasise the difference between the questions

Objectives	To determine the optimal fluid management regimen for children and young people with DKA. The review will address the following aspects of fluid management:
	• route of administration ('route' in the table of outcomes below)
	• rate of administration ('rate' in the table of outcomes below)
	• choice of fluid (including sodium chloride content; 'fluid/sodium' in the table of outcomes below)
	• other additives (for example,
	  ○ glucose ('glucose' in the table of outcomes below)
	  ○ potassium ('potassium' in the table of outcomes below)
	  ○ bicarbonate ('bicarbonate' in the table of outcomes below)
	  ○ phosphate ['phosphate' in the table of outcomes below]).
		The scope also requires consideration of assessment of dehydration and the volume of fluid administration; these will be covered by separate review questions linked to the questions about clinical assessment and investigations at presentation and during management of DKA
		
		The questions relating to route of administration should include consideration of the effectiveness of intraosseus administration

Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	There are unlikely to be RCTs that fully address all of these question and so the systematic search for evidence should encompass observational studies from the outset and the review itself will

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Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

		cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Any fluid management regimen for children and young people presenting with DKA	
Comparator or reference standard	Any other fluid management regimen for children and young people presenting with DKA	
Clinical outcomes	Physical outcomes	The guideline development group prioritised different outcomes for the different aspects of the review questions covered by this protocol ('route', 'rate', 'fluid/sodium', 'glucose', 'potassium', 'bicarbonate' and 'phosphate'); 'Y' in the cells of the table indicates that an

	Route	Rate	Fluid/sodium	Glucose	carbon e	
Mortality	Y	Y	Y	Y		
Time to resolution of dehydration	Y	Y	Y			
Rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be)		Y		Y		
Incidence of hypoglycaemia				Y		

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Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

	Resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations)	Y	Y	Y	Y	outcome was prioritised for the corresponding aspect of the questions covered by the protocol. Some outcomes (for example, mortality) are common to all aspects of the questions The guideline development group discussed whether serum urea concentration was an important outcome to consider for these questions and concluded that it was not because it is a marker of severity of DKA but it will not have an impact on management For some aspects, the guideline development group prioritised 8 outcomes initially and this remained acceptable because of the sparsity of the evidence identified for inclusion guideline development group to consider changing terminology from 'hypokalaemia' to 'serum potassium concentration', etc. in review questions related to DKA
	Resolution of blood ketosis	Y			Y	
	Serum chloride concentration (a raised concentration is linked to acidosis)		Y	Y		
	Incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema	Y	Y	Y	Y	
	Hypokalaemia (this is important because people with DKA die of this)					
	Serum sodium concentration	Y	Y	Y		
	Serum calcium concentration					
	Carbon dioxide (CO2) concentration			Y		
	Healthcare utilisation (for example, duration of admission, requirement for ventilation [as a proxy for severity of DKA or presence of cerebral oedema])	Y	Y	Y	Y	
Health economics outcomes	These questions were not prioritised for health economic analysis					
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total					Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
		Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See Section F.12	A single search for evidence will be undertaken across the questions relating to fluid management in children and young people presenting with DKA Possible search terms to include the following For fluid composition: • sodium chloride or sodium lactate concentration • pH • specific fluids such as Ringer's solution, Hartmann's solution, isolyte and plasmalyte. For route of administration: • intravenous • intraosseus • oral • not intramuscular.
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first

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Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
		presentation with diabetes

E.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full guideline development group will ratify all conclusions and recommendations based on the DKA evidence

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Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents		
Review question for update	What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?	
Objectives	To assess the effectiveness of intravenous osmotic agents in the treatment of cerebral oedema associated with DKA in children and young people	The main intervention of interest from the guideline development group is the urgent administration of mannitol whilst the child is still on a general paediatric ward Note the setting in which agents are administered and the duration of treatment in the evidence tables
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	
Population	Children and young people with DKA and cerebral oedema	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Any treatment based on administration of intravenous osmotic agents	For example, mannitol, hypertonic saline or a combination of the two May also be referred to as osmotic therapy or osmotherapy
Comparator or reference standard	Any other treatment based on administration of intravenous osmotic agents No treatment with osmotic agents	
Clinical outcomes	Physical outcomes: • mortality • persistent neurological deficit Healthcare utilisation (for example, duration of admission, requirement for ventilation [as a proxy for severity of DKA or presence of cerebral oedema])	
Health economics outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously

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Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents		
		recognised diabetes or first presentation Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

Update 2015

E.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
	Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	development of the remainder of the guideline. The full guideline development group will ratify all conclusions and recommendations based on the DKA evidence
Review question for update	When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To determine when intravenous insulin therapy should be started and stopped in children and young people with DKA. The two aspects of the review question will be addressed separately. Cerebral oedema is a potential adverse consequence of starting intravenous insulin therapy too early (during intravenous infusion of fluids without glucose), whereas the optimal time to stop intravenous insulin therapy is likely to be determined by the timescale for continuing intravenous glucose infusion once ketoacidosis has been resolved. In some children and young people with DKA or ketonaemia who are not very ill it may not be necessary to use intravenous insulin therapy at all, and the question also covers this scenario. The guideline development group may also wish to make recommendations for the insulin regimen to be used immediately after stopping intravenous insulin therapy (taking into account the fact that the child or young person may or may not have been recognised as having type 1 or type 2 diabetes before presenting with DKA). Overall the guideline development group noted that the part of the question that deals with when to start intravenous insulin therapy was of greater clinical importance (as it could be associated with a risk of mortality)	
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	For the part of the question about when to start intravenous insulin infusion: there may be no RCTs but some comparative observational studies

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Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
		For the part of the question about when to stop intravenous insulin infusion: it is very unlikely that there will be any RCTs and evidence from observational studies will be considered The guideline development group noted, therefore, that for these questions the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	For the part of the question about when to start intravenous insulin infusion: delayed insulin (delaying the start of intravenous insulin therapy until intravenous fluid therapy is established) For the part of the question about when to stop intravenous insulin infusion: outcomes should be compared according to the blood ketone concentration at which intravenous insulin is stopped	For the part of the question about when to start intravenous insulin infusion: the important consideration is the timing of intravenous insulin in relation to the timing of intravenous fluids For the part of the question about when to stop intravenous insulin infusion: there may be evidence in terms of retrospective comparison of outcomes before and after resolution of ketosis
Comparator or reference standard	For the part of the question about when to start intravenous insulin infusion: immediate insulin (starting intravenous insulin therapy before or at the same time as starting intravenous fluids)	

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Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
	For the part of the question about when to stop intravenous insulin infusion: outcomes should be compared according to the blood ketone concentration at which intravenous insulin is stopped	
Clinical outcomes	<u>For the part of the question about when to start intravenous insulin infusion</u> Physical outcomes: • mortality • rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be) • incidence of hypoglycaemia • resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations) • incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema • hypokalaemia (this is important because people with DKA die of this) • healthcare utilisation (for example, duration of admission, requirement for ventilation [as a proxy for severity of DKA or presence of cerebral oedema]) <u>For the part of the question about when to stop intravenous insulin infusion</u> Physical outcomes: • resolution of blood ketosis • healthcare utilisation (for example, duration of admission, requirement for ventilation [as a proxy for severity of DKA or presence of cerebral oedema]) Terminology: • diabetic coma might be relevant to cerebral oedema but is too general a term to use in the extraction/description of evidence • consider using 'serum potassium concentration' rather than 'hypokalaemia' etc.	
Health economics outcomes	These questions were not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See Section F.14	A single search for evidence will be undertaken across the questions relating to timing of intravenous insulin therapy and calculation of the insulin dosage
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)	

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Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
	A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The 2004 guideline was specific to type 1 diabetes The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full guideline development group will ratify all conclusions and recommendations based on the DKA evidence
Review question for update	How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To determine the optimal insulin dosage for children and young people with DKA. A smoother recovery from ketoacidosis and a lower risk of cerebral oedema might be achieved with a 'small' dosage of intravenous insulin (for example, a low-dose intravenous insulin infusion with no initial bolus [higher dose]). Current practice is typically to use a dosage of 0.1 units/kg/hour and the review for this question will	

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Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
	focus on comparison of outcomes for this conventional dosage with those for alternative dosages, such as 0.05 units/kg/hour or 0.025 units/kg/hour	
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Insulin dosage of 0.05 units/kg/hour or lower	There may be some small studies to answer this question. Most studies are likely to compare 0.05 units/kg/hour with 0.1 units/kg/hour; a few might compare 0.025 units/kg/hour with 0.05 units/kg/hour or 0.1 units/kg/hour
Comparator or reference standard	Insulin dosage of 0.1 units/kg/hour	0.1 units/kg/hour, 0.05 units/kg/hour, and 0.025 units/kg/hour are the dosages likely to be used; the intended starting dosage will be important and evidence tables and GRADE profiles should reflect this
Clinical outcomes	Physical outcomes: • mortality • rate of change of blood glucose concentration (this is likely to be reported in research	The guideline development group prioritised 8 outcomes initially (based on those selected for the question on when to start and stop

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Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
	studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be) • incidence of hypoglycaemia • resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations) • resolution of blood ketosis • incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema • hypokalaemia (this is important because people with DKA die of this) • healthcare utilisation (for example, duration of admission, requirement for ventilation [as a proxy for severity of DKA or presence of cerebral oedema])	intravenous insulin infusion in children and young people with DKA); this was found to be acceptable based on the sparsity of evidence identified for inclusion guideline development group to consider using the terminology 'serum potassium concentration' rather than 'hypokalaemia' etc.
Health economics outcomes	These questions were not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See Section F.14	A single search for evidence will be undertaken across the questions relating to timing of intravenous insulin therapy and calculation of the insulin dosage
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young

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Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
		people with DKA at the first presentation with diabetes

E.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis		
Existing recommendation(s) in 2004 guideline	Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline The 2004 guideline was specific to type 1 diabetes The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the guideline development group plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full guideline development group will ratify all conclusions and recommendations based on the DKA evidence
Review question for update	What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with DKA?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To determine whether anticoagulant prophylaxis is effective in preventing venous	Children and young people with DKA who have central venous lines

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Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis		
	thrombosis in children and young people with DKA. The guideline development group noted that deep vein thrombosis, visceral thrombosis, and cerebral thrombosis would all be relevant in this review question	inserted are at greater risk of developing central venous thrombosis. Current practice is typically to provide prophylactic anticoagulation to these children and young people. The review for this question will focus on comparison of outcomes for some form of prophylactic anticoagulation compared with no anticoagulation
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	As this is a new question which was not considered in the original 2004 guideline, no date limit will be applied to searches for these review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The guideline development group noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Any anticoagulation prophylaxis regimen	The following terminology may be useful in relation to specifying search terms relevant to anticoagulation regimens: • aspirin • dalterparin • dicoumarol • fragmin • heparin • low-dose heparin • synthetic warfarins (these newer products are not licensed for use in children and young people but any relevant evidence can still be considered as part of the review) • warfarin

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Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis		
Comparator or reference standard	No anticoagulation prophylaxis regimen	The review will not compare different anticoagulation regimens with one another
Clinical outcomes	Physical outcomes: • mortality • incidence of venous thrombosis (of any type, including deep vein thrombosis, visceral thrombosis and cerebral thrombosis) • incidence of pulmonary embolism • healthcare utilisation (for example, duration of admission, admission to intensive care) • adverse events, including bleeding and thrombocytopaenia Psychosocial outcomes: • children and young people's and families' satisfaction with intervention	
Health economics outcomes	These questions were not prioritised for health economic analysis	If any evidence is identified in relation to healthcare utilisation the decision not to prioritise this question for health economic analysis might be revisited
Other criteria for inclusion/ exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See Section F.15	A single search for evidence will be undertaken for both type 1 and type 2 diabetes
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The guideline development group's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

Update 2015

E.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Type 1 diabetes – retinopathy		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes should be offered screening for: • coeliac disease at diagnosis • thyroid disease at diagnosis and annually thereafter until transfer to adult services • retinopathy annually from the age of 12 years • microalbuminuria annually from the age of 12 years • blood pressure annually from the age of 12 years.	Only those aspects relating to retinopathy and nephropathy in the 2004 recommendation about screening for complications in children and young people with type 1 diabetes are being updated The reason for updating this recommendation is to reconsider the time at which to test (age/duration of diabetes), not how to test
Review question for update	What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?	
Objectives	To determine when retinopathy screening should start following diagnosis of type 1 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of the severity (grade) of retinopathy, including the clinical importance of any background retinopathy	Note that background retinopathy can revert to normal, giving rise to intermittent retinopathy The guideline development group's recommendations should take into account the practicalities of starting screening based on duration of diabetes rather than age (because screening for retinopathy requires referral to an ophthalmologist and ophthalmology services may not have access to information about duration of diabetes)
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is different to the review questions considered in the 2004 guideline and so no date limitations will be applied during the search for evidence
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years,

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Type 1 diabetes – retinopathy		
		these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes) Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis
Intervention or index test	Universal retinopathy screening using digital retinal photography	Digital retinal photography is the method currently recommended in the NHS Diabetic Eye Screening Programme Exclude studies which consider only fluorescein angiography or ophthalmoscopy
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	• prevalence of retinopathy at different timepoints after diagnosis (this might include data obtained via 'survival analysis' methods) • incidence of retinopathy over time • when available, severity (grade) of retinopathy will be reported based on the NHS Diabetic Eye Screening Programme (see, for example, http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm)	• Look at finding the earliest time at which retinopathy becomes sufficiently common/severe to warrant screening • The guideline development group may need to consider not just the existence of retinopathy but also the severity (grade) of retinopathy • Current practice is to refer children and young people with diabetes to an ophthalmologist only if they have sight-threatening diabetic retinopathy, and this is unlikely in people younger than 12 years; as noted above, background retinopathy can revert to normal • It might be worth identifying retinopathy that will not lead to referral to an ophthalmologist if this would support provision of education about risks associated with retinopathy • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	

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Type 1 diabetes – retinopathy		
Other criteria for inclusion/ exclusion of studies	Exclude studies that do not: • report prevalence of retinopathy at a particular timepoint after diagnosis have a systematic approach to screening, as opposed to selective patient screening based on individual concerns	
Search strategies	See Section F.16	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for retinopathy (type 1 diabetes and type 2 diabetes)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The practicalities of offering screening for retinopathy will vary according to the child or young person's age and whether or not they have learning difficulties (because digital retinal photography requires the person to sit still and stare at a fixed point)

E.17 Type 1 diabetes – nephropathy

Update 2015

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Type 1 diabetes – nephropathy		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes should be offered screening for: • coeliac disease at diagnosis • thyroid disease at diagnosis and annually thereafter until transfer to adult services • retinopathy annually from the age of 12 years • microalbuminuria annually from the age of 12 years • blood pressure annually from the age of 12 years.	Only those aspects relating to retinopathy and nephropathy in the 2004 recommendation about screening for complications in children and young people with type 1 diabetes are being updated The existing recommendation about screening for microalbuminuria relates to testing based on urine albumin:creatinine ratio. The reason for updating this recommendation is to reconsider the time at which to test (age/duration of diabetes) not how to test If the guideline development group intends to recommend screening for microalbuminuria (as a marker of nephropathy) from an age lower than 12 years then the possibility of revising the recommendation about when to start monitoring blood pressure should be raised with NICE

Type 1 diabetes – nephropathy		
		(because hypertension is also associated with nephropathy)
Review question for update	What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?	
Objectives	To determine when nephropathy screening should start following diagnosis of type 1 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of issues such as the clinical importance of intermittent microalbuminuria	
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is different to the review questions considered in the 2004 guideline and so no date limitations will be applied during the search for evidence
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes) Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis
Intervention or index test	Screening for microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio [ACR])	The guidelines relating to type 1 diabetes in adults and type 2 diabetes in adults include specific recommendations on: • repeated measurement of ACR over a 4-month period to establish a diagnosis of microalbuminuria

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Type 1 diabetes – nephropathy		
		• measuring serum creatinine at the same time, and • in type 2 diabetes, estimating the glomerular filtration rate (GFR) at the same time (using the method-abbreviated modification of diet in renal disease four-variable equation) Usual practice is to measure only microalbuminuria in children and young people with type 1 diabetes (serum creatinine concentration is measured only if the microalbuminuria measurement is abnormal because this provides evidence of renal damage from microalbuminuria or hypertension); an abnormal urine ACR is the first feature of nephropathy, whereas abnormal serum creatinine concentration is a later feature that is not relevant in children and young people with type 1 diabetes because they are unlikely to have nephropathy at diagnosis Urine ACR is the practice for screening of microalbuminuria in the UK. For studies which report on albumin excretion rate (AER) rather than ACR for the confirmation of microalbimuria, convert to ACR measurements using separate conversion equations for males and females (Schultz 1999) Using ACR >2.5 mg/mmol for males and ACR >3.5 mg/mmol for females (at least 2 of 3 consecutive collections over a period of 3 to 4 months) which are the standards for confirming microalbuminuria in UK adults, exclude studies where the ACR measurement falls below 2.5 mg/mmol or 3.5 mg/mmol for males and females, respectively
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	• Prevalence of microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio) • Incidence of microalbuminuria over time	Evidence tables should document cut-offs and definitions of microalbuminuria used in included studies NCC-WCH to discuss with guideline development group to determine which studies should be included if necessary

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Type 1 diabetes – nephropathy		
		Note that the 2004 guideline on type 1 diabetes in adults, and the 2008 guideline on type 2 diabetes in adults use repeated tests of ACR >2.5 mg/mmol for men, and >3.5 mg/mmol for women (in at least 2 of 3 consecutive collections over a period of 3 to 4 months) to confirm microalbuminuria It will be important to consider the severity of microalbuminuria and how should this be reported (for example, thresholds for 'severe microalbuminuria', etc.)
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies that do not: • report prevalence of microalbuminuria • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns.	
Search strategies	See Section F.17	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for nephropathy (type 1 diabetes and type 2 diabetes) The search terms microalbuminuria and diabetes should identify relevant studies
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

Update 2015

E.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Type 2 diabetes – education		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes An external adviser has been appointed to advise the guideline development group on technical aspects of clinical research

Type 2 diabetes – education		
		relating to behavioural interventions and the interface with education programmes
Review question for update	What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?	
Objectives	To determine the effectiveness of structured education programmes in improving outcomes for children and young people with type 2 diabetes	
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion The next step might be to include systematic reviews of RCTs and non-randomised comparative studies (but not individual non-randomised studies)
Status	Published papers (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years This review question will focus solely on 'patient' education (that is, education of healthcare professionals will be excluded)
Intervention	Structured education programmes specific to type 2 diabetes (education aimed at children and young people or their families)	This review should cover: all settings (diabetes clinics, schools, etc.), while recognising that recommendations will be limited to the clinical practice context all forms of delivery of education (for example, one-to-one, brief, face-to-face, and remote [telemedicine, including text messaging])
Comparator or reference standard	Alternative models of education Usual care	Usual care in this context usually includes unstructured, informal education, provision of information leaflets or multimedia
Clinical Outcomes	Physical outcomes: • glycaemic control ○ HbA1c (minimum follow-up 6 months after completion of primary intervention) • adherence to education intervention • changes in body mass index (BMI) standard deviation score (SDS) • achievement and maintenance of weight loss during the programme	The priority outcomes selected by the guideline development group are different to those for the review questions on psychological interventions because psychosocial outcomes are more relevant there The guideline development group identified a minimum follow-up

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Type 2 diabetes – education		
	• change in level of physical activity (for example, hours of exercise per week; minimum follow-up 6 months after completion of primary intervention). Psychosocial outcomes: • health-related quality of life. • Children and young people's and families' satisfaction with intervention (education intervention)	period of 6 months after completion of the primary intervention for HbA1c and change in level of physical activity, and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required HbA1c MID is 0.5 percentage points (5.5 mmol/mol) BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would case hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently Adherence to diabetes management, including self-management was not prioritised as an outcome for this question. The guideline development group agreed that this was a lower priority than adherence to the educational intervention itself because insulin is not always used in the treatment of type 2 diabetes No long-term complications needed to be prioritised as outcomes because HbA1c will determine these
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	Studies that evaluate education programmes for healthcare professionals will be excluded (see above) Subgroup analysis according to the presence of associated conditions such as autism

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Type 2 diabetes – education		
		spectrum disorder or learning difficulties, and according to language and culture-specific interventions would be useful if the evidence allows this Subgroup analysis by ethnicity may be of interest
Search strategies	See Section F.18	NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

Update 2015

E.19 Type 2 diabetes – psychological interventions

Review questions:

What is the effectiveness of psychological interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?

Type 2 diabetes – psychological interventions		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes An expert adviser has been appointed to advise the guideline development group on technical aspects of clinical research relating to psychological interventions and the interface with education programmes
Review question for update	What is the effectiveness of psychological interventions to promote engagement with	Both questions will be covered by a single protocol. The available evidence will be presented in such a

Type 2 diabetes – psychological interventions		
	clinical services in children and young people with type 2 diabetes? What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?	way as to emphasise the difference between the two questions
Objectives	To determine the effectiveness of psychological interventions in promoting engagement with clinical services in children and young people with type 2 diabetes and improving outcomes of care. The question is sufficiently broad to cover interventions aimed at families and healthcare professionals as well as those aimed at the child or young person. The guideline development group prioritised psychological interventions that should be addressed in this question as follows: • Family therapy (including behavioural family systems therapy [BFST]): this is always delivered to one family unit but it can include separate sessions with different members (individuals/groups) within the unit. • Cognitive behavioural therapy (CBT): this can be delivered one-to-one or in groups. The intervention focuses on recognising specific triggers for maladaptive behaviour and bringing about changes to behaviour. • Motivational interviewing: this can be delivered one-to-one or in groups. The intervention focuses on general exploration of ambivalence around maladaptive behaviours and what the person wants to do or should do. The intervention develops insight into maladaptive behaviour. • Counselling: this is delivered one-to-one but the content of interventions termed counselling may vary. • Mentoring: this can be delivered one-to-one or in groups. The mentor is typically older than the person receiving mentoring or is influential in the community. • Peer support (and peer-led interventions): these can be delivered one-to-one or in groups. The intervention typically involves people of similar age to the person receiving peer support.	
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion The next step might be to include systematic reviews of RCTs and non-randomised comparative studies (but not individual non-randomised studies)
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Psychological interventions specific to the management of type 2 diabetes in children and young people (this could involve interventions aimed at families and healthcare professionals as well as those aimed at the child or young person)	Use the terms specific to the prioritised psychological interventions when conducting the searches for this question This review should cover:

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Type 2 diabetes – psychological interventions		
	• family therapy (include only validated therapies such as BFST – expert adviser to advise in relation to search results) • CBT • motivational interviewing • counselling • mentoring • peer support (and peer-led interventions)	• all settings (diabetes clinics, schools, etc.), while recognising that recommendations will be limited to the clinical practice context • all forms of delivery of the prioritised behavioural interventions (for example, one-to-one, brief, face-to-face, and remote [telemedicine]).
Comparator or reference standard	An alternative psychological intervention listed above An alternative and well defined psychological intervention not listed above (expert adviser to advise on what is well defined in relation to search results) Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management Usual care (this will be the most common comparator)	Usual care in this context usually includes education, no therapy, provision of information leaflets or multimedia (DVDs, CDs, websites, apps)

Clinical outcomes	For the question about engagement with clinical services
	Physical outcomes:
	• adherence to diabetes management (the scope requires this; to include self-management).
	
	Psychosocial outcomes:
	• children and young people's and families' satisfaction with intervention
	• risk-taking behaviours (such as smoking)
	• engagement with clinical services (for example, attendance at clinic appointments).
	
	For the general question about improving outcomes
	Physical outcomes:
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months after completion of primary intervention)
	  ○ adverse events (for example, diabetes-related hospital admission or self-harm)
	• changes in body mass index (BMI) standard deviation score (SDS)
	• achievement and maintenance of weight loss during the programme (NCC-WCH to seek clarification from guideline development group about whether
		The guideline development group identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and change in level of physical activity, and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required
		
		The guideline development group agreed that change in body mass index (BMI) standard deviation score (SDS) would be more important than DKA than in the corresponding question for type 1 diabetes
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions
		
		No long-term complications needed to be prioritised as outcomes because HbA1c will determine these

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Type 2 diabetes – psychological interventions		
	weight-loss outcomes are relevant after searches have been completed) • change in level of physical activity (for example, hours of exercise per week; minimum follow-up 6 months after completion of primary intervention). Psychosocial outcomes: • health-related quality of life (this outcome might capture bullying about weight) • depression or anxiety.	
Health economic outcomes	This question was not prioritised for health economic analysis	The guideline development group might wish to evaluate the cost effectiveness of psychological interventions for type 2 diabetes – see notes on protocol for weight loss in type 2 diabetes
Other criteria for inclusion/ exclusion of studies	None	Evidence tables should document who delivered the intervention(s) and the frequency of contact with healthcare or other relevant professionals to deliver the intervention(s)
Search strategies	See Section F.19	A single search will be used to cover both questions NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

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E.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Type 2 diabetes – dietary advice		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?	
Objectives	To identify the dietetic advice to be given to children and young people with type 2 diabetes to optimise glycaemic control. The question includes evaluation of the effectiveness of different forms of dietetic advice in terms of achieving outcomes relating to glycaemic control	Dietetic advice for type 2 diabetes will usually focus on dietary advice to achieve weight loss; weight loss will improve glycaemic control The guideline development group agreed that the objectives of the question should remain open to allow consideration of evidence relating to any form of dietetic advice relevant to type 2 diabetes, although the intention was to look for evidence relating to improving glycaemic control
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Dietetic advice intended to optimise glycaemic control	Include studies only if dietetic advice includes direct contact and training with healthcare professionals (for example, providing an information leaflet is not enough) Evidence tables should document any pharmacological treatment (for example, metformin or insulin) in the intervention and comparison groups
Comparator or reference standard	Usual care	Usual care could include dietetic advice which does not incorporate specific advice about optimising glycaemic control, or dietary advice

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Type 2 diabetes – dietary advice		
		that does not involve direct contact and/or training with healthcare professionals (for example, providing an information leaflet only)

Clinical outcomes	Physical outcomes:
	• glycaemic control
	  ○ HbA1c (minimum follow-up 6 months)
	  ○ postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve)
	• adherence to dietary advice
	• adverse events (for example, changes in body mass index (BMI) standard deviation score (SDS) or changes in weight)
	
	Psychosocial outcomes:
	• health-related quality of life
	• children and young people's and families' satisfaction with intervention
		The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions
		
		Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would case hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently

Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Type 2 diabetes – weight loss		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by haemoglobin A1c (HbA1c)?	
Objectives	To evaluate the effectiveness of weight loss (by whatever means) in children and young people with type 2 diabetes who are overweight or obese in improving glycaemic control. The primary measure of glycaemic control to be considered in this question is HbA1c. The purpose of including this topic in the guideline update is to form the basis for advising weight loss to improve glycaemic control. The means for achieving weight loss will not be addressed in this guideline (except to document in the evidence tables the method of weight management used in the included studies) but through a cross-reference to the NICE clinical guideline on obesity. This guideline is currently being updated.	The NICE clinical guideline on obesity includes the following recommendations. Bariatric surgery is recommended as a treatment option for people with obesity if all of the following criteria are fulfilled: • they have a body mass index (BMI) of 40 kg/m2 or more, or between 35 kg/m2 and 40 kg/m2 and other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight [other bullets in this recommendation omitted for brevity] Bariatric surgery may be considered for young people only in exceptional circumstances, and if they have achieved or nearly achieved physiological maturity.
Language	English	
Study design	Systematic reviews and RCTs Observational studies	It is not expected that there will be RCTs that fully answer this question (in terms of the association between weight loss and glycaemic control) and so no restriction in study design will be applied to this question
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes who are overweight or obese	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	RCTs: Weight loss interventions specific to the management of type 2 diabetes in children and young people. Note that the	The specified interventions assume that RCTs are available but as noted above the review will include

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Type 2 diabetes – weight loss		
	guideline scope relates specifically to children and young people with diabetes, and so studies that focus on prevention of type 2 diabetes should be excluded Observational studies: Any study that reports weight change in children and young people with type 2 diabetes	consideration of observational studies from the outset so that any association between weight loss and glycaemic control can be evaluated Evidence tables should document any pharmacological treatment (for example, metformin or insulin) in the intervention and comparison groups
Comparator or reference standard	RCTs: An alternative weight loss intervention or usual care Observational studies: Weight change in relation to glycaemic control	Usual care could include informal, general advice or programmes relating to weight loss Weight change or a comparable measure such as change in body mass index (BMI) standard deviation score (SDS)
Clinical outcomes	Physical outcomes: • glycaemic control ○ HbA1c (minimum follow-up 6 months) • adherence to diabetes management, including self-management • changes in body mass index (BMI) standard deviation score (SDS) • remission of diabetes (normal HbA1c and no treatment for diabetes, for example at 1 year after starting the weight loss intervention) • time to treatment failure (when insulin is required to manage diabetes; the physiological basis for this is that initial management should postpone the need for insulin, but insulin will be needed eventually as insulin resistance changes and secretion of insulin by the pancreas stops) Psychosocial outcomes: • health-related quality of life • children and young people's and families' satisfaction with intervention	The guideline development group considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes HbA1c MID is 0.5 percentage points (5.5 mmol/mol) BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would case hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently
Health economic outcomes	This question was not prioritised for health economic analysis	This question was proposed as the top priority for health economic analysis among the questions relating to type 2 diabetes, but the NCC-WCH will refer to the guidelines on obesity (update) and type 2 diabetes in adults rather than undertaking any modelling for this guideline
Other criteria for inclusion/	None	

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Type 2 diabetes – weight loss		
exclusion of studies		
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Type 2 diabetes – metformin		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?	
Objectives	To determine the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes	
Language	English	
Study design	Systematic reviews and RCTs only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Metformin	
Comparator or reference standard	• Usual care • Placebo	Usual care in this instance includes lifestyle advice, education, etc.

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Type 2 diabetes – metformin		
Clinical outcomes	• Haemoglobin A1c (HbA1c) • Number needing rescue medication • Number of dropouts • Number with any adverse events, including diabetic ketoacidosis (DKA) • Changes in fasting plasma glucose (FPG) • Changes in body mass index (BMI) standard deviation score (SDS)Patient satisfaction with the intervention	
Health economic outcomes	This question was not prioritised for health economic analysis Most of the outcomes above, but should not necessarily be limited to seven and could be extended to include generic measures of health-related quality of life	
Other criteria for inclusion/ exclusion of studies	None	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

Update 2015

E.23 Type 2 diabetes – HbA1c targets

Review question: what is the optimal HbA1c target for children and young people with type 2 diabetes?

Type 2 diabetes – HbA1c targets		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal HbA1c target for children and young people with type 2 diabetes?	
Objectives	To determine the optimal HbA1c target value in terms of minimising the risk of long-term complications without incurring an increased risk of hypoglycaemic episodes as an adverse effect	
Language	English	
Study design	• Systematic reviews and RCTs • Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion

Type 2 diabetes – HbA1c targets		
		No RCTs that report results specific to children and young people are expected. A large RCT (involving adults) by Turner R, UKPDS Intervention Group, Lancet, 1998, and a meta-analysis by Hemmingsen B, BMJ, 2011 may be relevant. NCC-WCH to check whether these report any evidence specific to children and young people. Only consider studies involving adults if no RCTs or observational studies report data for children and young, and then only by cross-referring to the type 2 diabetes in adults guideline in which HbA1c targets are being updated
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years Note, however, that inclusion/exclusion of studies will be based on time at diagnosis and application of HbA1c targets, whereas long-term follow-up into adulthood will be relevant for this question
Intervention	Specified target value for HbA1c or HbA1c values achieved (recorded)	
Comparator or reference standard	Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded)	

Clinical outcomes	Physical outcomes:
	• development or worsening of long-term complications
	  ○ hypertension (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese)
	  ○ retinopathy
	  ○ nephropathy (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese)
	• glycaemic control
	  ○ Severe hypoglycaemic episodes (including nocturnal hypoglycaemia, although neither is very important in type 2 diabetes treated using metformin)
	• changes in body mass index (BMI) standard deviation score (SDS).
		Development or worsening of long-term complications are the most important outcomes for this question
		
		The guideline development group identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required
		
		HbA1c MID is 0.5 percentage points (5.5 mmol/mol)
		
		Severe hypoglycaemic episodes defined according to either of the following criteria:
		• International Society for Paediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child

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Type 2 diabetes – HbA1c targets		
	Psychosocial outcomes: • health-related quality of life • children and young people's and families' satisfaction with intervention (the impact of blood sampling would be reflected here).	or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose), or • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3) BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

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E.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Type 2 diabetes – hypertension		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?	
Objectives	To determine when monitoring for hypertension should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The	This review will need to consider how to identify hypertension, in terms of:

Type 2 diabetes – hypertension		
	review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter	• which parameters to measure (systolic and/or diastolic blood pressure) • which thresholds to use for parameters of interest (for example, ≥95th or ≥98th centile for sex, age and height), and • how many measurements to use (for example, measure once and if above the chosen threshold measure again at same clinic visit; if still elevated measure a third time at same visit; and accept the lowest value recorded). guideline development group to note that in children and young people in whom clinic blood pressure measurements suggest hypertension, confirmation will be necessary using ambulatory 24-hour monitoring or home blood pressure monitoring, for example, as described in the NICE guideline on hypertension in adults (CG127). The guideline comments on the choice and maintenance of devices used to measure blood pressure. The guideline development group may wish to consider cuff size to be used when measuring blood pressure in children and young people with type 2 diabetes
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years Studies will be included only if they provide data on prevalence for specific groups of children or young people

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Type 2 diabetes – hypertension		
		(stratified by age or duration of diabetes) Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis
Intervention or index test	Screening for hypertension	Inclusion of studies will not be restricted by the approach to defining hypertension, but the guideline development group can consider whether the thresholds used in included studies are appropriate for children and young people in the UK
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	Prevalence of hypertension at different timepoints after diagnosis Incidence of hypertension over time	• Look at finding the earliest time at which hypertension becomes sufficiently common/severe to warrant screening • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies that do not: • report prevalence of hypertension at a particular timepoint after diagnosis have a systematic approach to screening, as opposed to selective patient screening based on individual concerns	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	Type 2 diabetes is associated with obesity and so the guideline development group may wish to consider the appropriate cuff size to use when measuring blood pressure in children and young people with type 2 diabetes

Update 2015

E.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

Type 2 diabetes – dyslipidaemia		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?	The NICE guideline on lipid modification (adults; CG67) is being updated and a cross-reference may be relevant; the draft for consultation of the guideline on lipid modification (update) was published in February 2014
Objectives	To determine when monitoring for dyslipidaemia should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter	This review will need to consider how to identify dyslipidaemia, in terms of which serum lipids to measure, for example: • total cholesterol • high-density lipoprotein (HDL) cholesterol • low-density lipoprotein (LDL) cholesterol • triglycerides. The ratio of HDL:total cholesterol is also of interest
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years

Update 2015

Type 2 diabetes – dyslipidaemia		
		Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes) Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis
Intervention or index test	Measurement of any of the following serum lipids: • total cholesterol • HDL cholesterol • LDL cholesterol • triglycerides. The ratio of HDL:total cholesterol is also of interest	The terms in the bullet list to the left, plus lipoprotein (US synonym for cholesterol) should be used as search terms Evidence tables should document whether the evidence identified for inclusion relates to fasting or non-fasting measurements (both are of interest)
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	Prevalence of dyslipidaemia at different timepoints after diagnosis Incidence of dyslipidaemia over time	• Look at finding the earliest time at which dyslipidaemia becomes sufficiently common to warrant screening • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies that do not: • report prevalence of dyslipidaemia at a particular timepoint after diagnosis have a systematic approach to screening, as opposed to selective patient screening based on individual concerns	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

Update 2015

E.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Type 2 diabetes – retinopathy		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?	
Objectives	To determine when retinopathy screening should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of the severity (grade) of retinopathy, including the clinical importance of any background retinopathy	Note that background retinopathy can revert to normal, giving rise to intermittent retinopathy The guideline development group's recommendations should take into account the practicalities of starting screening based on duration of diabetes rather than age (because screening for retinopathy requires referral to an ophthalmologist and ophthalmology services may not have access to information about duration of diabetes)
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years Studies will be included only if they provide data on prevalence

Update 2015

Type 2 diabetes – retinopathy		
		for specific groups of children or young people (stratified by age or duration of diabetes) Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis
Intervention or index test	Universal retinopathy screening using digital retinal photography	Digital retinal photography is the method currently recommended in the NHS Diabetic Eye Screening Programme
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	Prevalence of retinopathy at different timepoints after diagnosis (this might include data obtained via 'survival analysis' methods) Incidence of retinopathy over time When available, severity (grade) of retinopathy will be reported based on the NHS Diabetic Eye Screening Programme (see, for example, http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm)	• Look at finding the earliest time at which retinopathy becomes sufficiently common/severe to warrant screening. • The guideline development group may need to consider not just the existence of retinopathy but also the severity (grade) of retinopathy. • Current practice is to refer children and young people with diabetes to an ophthalmologist only if they have sight-threatening diabetic retinopathy, and this is unlikely in people younger than 12 years; as noted above, background retinopathy can revert to normal. • It might be worth identifying retinopathy that will not lead to referral to an ophthalmologist if this would support provision of education about risks associated with retinopathy. • Subgroup analysis based on age may be relevant.
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies that do not: • report prevalence of retinopathy at a particular timepoint after diagnosis have a systematic approach to screening, as opposed to selective patient screening based on individual concerns	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	

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Type 2 diabetes – retinopathy		
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The practicalities of offering screening for retinopathy will vary according to the child or young person's age and whether or not they have learning difficulties (because digital retinal photography requires the person to sit still and stare at a fixed point); learning difficulties are more often associated with type 2 diabetes than with type 1 diabetes

E.27 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Type 2 diabetes – nephropathy		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?	
Objectives	To determine when nephropathy screening should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of issues such as the clinical importance of intermittent microalbuminuria	
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤

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Type 2 diabetes – nephropathy		
		18 years or if more than 50% of group participants are aged ≤ 18 years Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes) Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis
Intervention or index test	• Screening for microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio [ACR]) • Screening using serum creatinine concentration	The guidelines relating to type 1 diabetes in adults and type 2 diabetes in adults include specific recommendations on: • repeated measurement of ACR over a 4-month period to establish a diagnosis of microalbuminuria • measuring serum creatinine at the same time, and • in type 2 diabetes, estimating the glomerular filtration rate (GFR) at the same time (using the method-abbreviated modification of diet in renal disease four-variable equation). An abnormal urine ACR is the first feature of nephropathy, whereas abnormal serum creatinine concentration is a later feature; both may be relevant in children and young people with type 2 diabetes because they may have nephropathy at diagnosis (because the diabetes can go undetected for longer in the case of type 2 diabetes); children and young people with type 2 diabetes are also likely to have hypertension at diagnosis and/or to be obese, and both of these are independent risk factors for impaired renal function Urine ACR is the practice for screening of microalbuminuria in the UK. For studies which report on albumin excretion rate (AER) rather than ACR for the confirmation of microalbimuria,

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Type 2 diabetes – nephropathy		
		convert to ACR measurements using separate conversion equations for males and females (Schultz 1999) Using ACR >2.5mg/mmol for males and ACR >3.5 mg/mmol for females (at least 2 of 3 consecutive collections over a period of 3 to 4 months) which are the standards for confirming microalbuminuria in UK adults, exclude studies where the ACR measurement falls below 2.5 mg/mmol or 3.5 mg/mmol for males and females, respectively
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	Prevalence of microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio [ACR]) Incidence of microalbuminuria over time Prevalence of elevated serum creatinine (and/or reduced estimated GFR) using serum creatinine concentration	Evidence tables should document cut-offs and definitions of microalbuminuria used in included studies Note that the 2004 guideline on type 1 diabetes in adults, and the 2008 guideline on type 2 diabetes in adults use repeated tests of ACR >2.5mg/mmol for men, and >3.5mg/mmol for women (in at least 2 of 3 consecutive collections over a period of 3 to 4 months) to confirm microalbuminuria It will be important to consider the severity of microalbuminuria and how should this be reported (for example, thresholds for 'severe microalbuminuria', etc.)
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude studies that do not: • report either prevalence of microalbuminuria or prevalence of elevated serum creatinine at a particular time-point after diagnosis • have a systematic approach to screening as opposed to selective patient screening based on individual concerns.	
Search strategies	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for nephropathy (type 1 diabetes and type 2 diabetes) The search terms microalbuminuria and diabetes should identify relevant studies	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	

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Type 2 diabetes – nephropathy		
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

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Appendix F: Search strategies

F.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline on type 1 diabetes in adults.

Database(s): Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily Update

#	Searches
1	Diabetes mellitus, type 1/
2	Diabetic ketoacidosis/
3	((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
4	(diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
5	(LADA or MODY).ti,ab.
6	(diabet* adj2 (brittle or labile)).ti,ab.
7	(diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
8	(diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
9	(dm1 or iddm or t1d* or dka).ti,ab.
10	((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
11	diabetes mellitus.ti.
12	or/1-11
13	(pregnan* or gestation*).ti.
14	12 not 13
15	letter/
16	editorial/
17	news/
18	exp historical article/
19	Anecdotes as Topic/
20	comment/
21	case report/
22	(letter or comment*).ti.
23	or/15-22
24	23 not (randomized controlled trial/ or random*.ti,ab.)
25	animals/ not humans/
26	exp Animals, Laboratory/
27	exp Animal Experimentation/
28	exp Models, Animal/
29	exp Rodentia/
30	(rat or rats or mouse or mice).ti.
31	or/24-30
32	14 not 31
33	limit 32 to english language
34	C-peptide/
35	*Autoantibodies/
36	Glutamate decarboxylase/
37	Insulinoma/
38	Glucose-6-phosphatase/

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39	C peptide*.ti,ab.
40	((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
41	zinc transporter 8.ti,ab.
42	(islet adj5 (phosphatase or catalytic)).ti,ab.
43	(IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
44	or/34-43
45	33 and 44
46	(diagnos* or screen* or test*).ti,ab,hw.
47	exp "sensitivity and specificity"/
48	ROC Curve/
49	Area Under Curve/
50	Proportional Hazards Models/
51	(ROC or AUC or (area and curve)).ti,ab.
52	(sensitivity or specificity).ti,ab.
53	gold standard.ab.
54	(predictive value* or PPV or NPV).ti,ab.
55	likelihood ratio*.ti,ab.
56	or/46-55
57	45 and 56
58	randomized controlled trial.pt.
59	controlled clinical trial.pt.
60	randomi#ed.ab.
61	placebo.ab.
62	randomly.ab.
63	Clinical Trials as topic.sh.
64	trial*.ti.
65	or/58-64
66	Meta-Analysis/
67	Meta-Analysis as Topic/
68	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
69	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
70	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
71	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
72	(search* adj4 literature).ab.
73	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
74	cochrane.jw.
75	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
76	or/66-75
77	Epidemiologic studies/
78	exp case control studies/
79	exp cohort studies/
80	Cross-sectional studies/
81	case control.ti,ab.
82	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
83	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
84	(study and (participant* or patient* or subject* or group*)).ti,ab.
85	cohort*.ti,ab.
86	or/77-85

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87	57 and (65 or 76 or 86)
88	(2003$ or 2004$ or 2005$ or 2006$ or 2007$ or 2008$ or 2009$ or 2010$ or 2011$ or 2012$ or 2013$).ed,dc.
89	87 and 88

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	Diabetes mellitus, type 1/
2	Diabetic ketoacidosis/
3	((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
4	(diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
5	(LADA or MODY).ti,ab.
6	(diabet* adj2 (brittle or labile)).ti,ab.
7	(diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
8	(diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
9	(dm1 or iddm or t1d* or dka).ti,ab.
10	((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
11	diabetes mellitus.ti.
12	or/1-11
13	(pregnan* or gestation*).ti.
14	12 not 13
15	letter/
16	editorial/
17	news/
18	exp historical article/
19	Anecdotes as Topic/
20	comment/
21	case report/
22	(letter or comment*).ti.
23	or/15-22
24	23 not (randomized controlled trial/ or random*.ti,ab.)
25	animals/ not humans/
26	exp Animals, Laboratory/
27	exp Animal Experimentation/
28	exp Models, Animal/
29	exp Rodentia/
30	(rat or rats or mouse or mice).ti.
31	or/24-30
32	14 not 31
33	limit 32 to english language
34	C-peptide/
35	*Autoantibodies/
36	Glutamate decarboxylase/
37	Insulinoma/
38	Glucose-6-phosphatase/
39	C peptide*.ti,ab.
40	((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
41	zinc transporter 8.ti,ab.
42	(islet adj5 (phosphatase or catalytic)).ti,ab.
43	[or/34-43]
44	[or/46-55]

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45	[or/58-64]
46	[or/66-75]
47	[or/77-85]
48	Diabetes mellitus, type 1/
49	Diabetic ketoacidosis/
50	((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
51	(diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
52	(LADA or MODY).ti,ab.
53	(diabet* adj2 (brittle or labile)).ti,ab.
54	(diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
55	(diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
56	(dm1 or iddm or t1d* or dka).ti,ab.
57	((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
58	diabetes mellitus.ti.
59	or/48-58
60	(pregnan* or gestation*).ti.
61	59 not 60
62	letter/
63	editorial/
64	news/
65	exp historical article/
66	Anecdotes as Topic/
67	comment/
68	case report/
69	(letter or comment*).ti.
70	or/62-69
71	70 not (randomized controlled trial/ or random*.ti,ab.)
72	animals/ not humans/
73	exp Animals, Laboratory/
74	exp Animal Experimentation/
75	exp Models, Animal/
76	exp Rodentia/
77	(rat or rats or mouse or mice).ti.
78	or/71-77
79	61 not 78
80	limit 79 to english language
81	C-peptide/
82	*Autoantibodies/
83	Glutamate decarboxylase/
84	Insulinoma/
85	Glucose-6-phosphatase/
86	C peptide*.ti,ab.
87	((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
88	zinc transporter 8.ti,ab.
89	(islet adj5 (phosphatase or catalytic)).ti,ab.
90	(IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
91	or/81-90
92	80 and 91
93	(diagnos* or screen* or test*).ti,ab,hw.
94	exp "sensitivity and specificity"/
95	ROC Curve/
96	Area Under Curve/

Update 2015

97	Proportional Hazards Models/
98	(ROC or AUC or (area and curve)).ti,ab.
99	(sensitivity or specificity).ti,ab.
100	gold standard.ab.
101	(predictive value* or PPV or NPV).ti,ab.
102	likelihood ratio*.ti,ab.
103	or/93-102
104	92 and 103
105	randomized controlled trial.pt.
106	controlled clinical trial.pt.
107	randomi#ed.ab.
108	placebo.ab.
109	randomly.ab.
110	Clinical Trials as topic.sh.
111	trial*.ti.
112	or/105-111
113	Meta-Analysis/
114	Meta-Analysis as Topic/
115	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
116	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
117	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
118	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
119	(search* adj4 literature).ab.
120	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
121	cochrane.jw.
122	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
123	or/113-122
124	Epidemiologic studies/
125	exp case control studies/
126	exp cohort studies/
127	Cross-sectional studies/
128	case control.ti,ab.
129	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
130	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
131	(study and (participant* or patient* or subject* or group*)).ti,ab.
132	cohort*.ti,ab.
133	or/124-132
134	104 and (112 or 123 or 133)
135	(201402* or201403* or 201404* or 201405* or 201406* or 201407* or 201408*).ed,dc.
136	134 and 135

Database(s): Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment, Database of Abstracts of Reviews of Effects, NHS Economic Evaluation Database

No.	Search terms
#1	MeSH descriptor: [Diabetes Mellitus, Type 1] explode all trees
#2	MeSH descriptor: [Diabetic Ketoacidosis] this term only
#3	((diabet* or DM) near/4 ("type 1" or type1 or "type I" or "type one")):ti,ab
#4	(diabet* near/2 (autoimmun* or "auto immun*")):ti,ab

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#5	(diabet* near/2 (brittle or labile)):ti,ab
#6	(diabet* near/2 ("sudden onset" or "maturity onset" or juvenile or child*)):ti,ab
#7	(diabet* near/3 (keto* or acido* or gastropare*)):ti,ab
#8	(dm1 or iddm or t1d* or dka or LADA or MODY):ti,ab
#9	(diabet* near/2 (insulin next depend*)):ti,ab
#10	#9 and not "non insulin dependent"
#11	diabetes mellitus:ti
#12	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13	(pregnan* or gestation*):ti
#14	#12 not #13
#15	#14 from 2003 to 2012
#16	MeSH descriptor: [C-Peptide] this term only
#17	MeSH descriptor: [Autoantibodies] this term only
#18	MeSH descriptor: [Glutamate Decarboxylase] this term only
#19	MeSH descriptor: [Insulinoma] this term only
#20	MeSH descriptor: [Glucose-6-Phosphatase] this term only
#21	(C next (peptide or peptides)):ti,ab
#22	((“islet cell” or decarboxylase or glutamic or insulinoma) and (antibody or antibodies or “anti body” or “anti bodies” or autoantibody or autoantibodies)):ti,ab
#23	(“zinc transporter 8”):ti,ab
#24	(islet* and (phosphatase or catalytic)):ti,ab
#25	(IGRP* or ICA* or “IA-2” or IA2* or ZnT8* or GAD*):ti,ab
#26	#16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25
#27	#15 and #26
#28	MeSH descriptor: [Diagnosis] explode all trees
#29	(diagnos* or screen* or test*):ti,ab
#30	MeSH descriptor: [Sensitivity and Specificity] explode all trees
#31	MeSH descriptor: [Area Under Curve] this term only
#32	MeSH descriptor: [Proportional Hazards Models] this term only
#33	((ROC or AUC) or (area and curve)):ti,ab
#34	(sensitivity or specificity):ti,ab
#35	“gold standard”:ab
#36	(“predictive value” or PPV or NPV):ti,ab
#37	“likelihood ratio”:ti,ab
#38	#28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37
#39	#38 and #27

Update 2015

Database(s): Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment, Database of Abstracts of Reviews of Effects, NHS Economic Evaluation Database

No.	Search terms
#1	MeSH descriptor: [Diabetes Mellitus, Type 1] explode all trees
#2	MeSH descriptor: [Diabetic Ketoacidosis] this term only
#3	((diabet* or DM) near/4 ("type 1" or type1 or "type I" or "type one")):ti,ab
#4	(diabet* near/2 (autoimmun* or "auto immun*")):ti,ab
#5	(diabet* near/2 (brittle or labile)):ti,ab
#6	(diabet* near/2 ("sudden onset" or juvenile or child*)):ti,ab
#7	(diabet* near/3 (keto* or acido* or gastropare*)):ti,ab
#8	(dm1 or iddm or t1d* or dka or LADA):ti,ab
#9	(diabet* near/2 (insulin next depend*)):ti,ab
#10	#9 and not "non insulin dependent"
#11	diabetes mellitus:ti
#12	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #10 or #11)

#13	(pregnan* or gestation*):ti
#14	#12 not #13
#15	MeSH descriptor: [C-Peptide] this term only
#16	MeSH descriptor: [Autoantibodies] this term only
#17	MeSH descriptor: [Glutamate Decarboxylase] this term only
#18	MeSH descriptor: [Insulinoma] this term only
#19	MeSH descriptor: [Glucose-6-Phosphatase] this term only
#20	(C next (peptide or peptides)):ti,ab
#21	(("islet cell" or decarboxylase or glutamic or insulinoma) and (antibody or antibodies or "anti body" or "anti bodies" or autoantibody or autoantibodies)):ti,ab
#22	("zinc transporter 8"):ti,ab
#23	(islet* and (phosphatase or catalytic)):ti,ab
#24	(IGRP* or ICA* or "IA-2" or IA2* or ZnT8* or GAD*):ti,ab
#25	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
#26	#14 and #25
#27	MeSH descriptor: [Diagnosis] explode all trees
#28	(diagnos* or screen* or test*):ti,ab
#29	MeSH descriptor: [Sensitivity and Specificity] explode all trees
#30	MeSH descriptor: [Area Under Curve] this term only
#31	MeSH descriptor: [Proportional Hazards Models] this term only
#32	((ROC or AUC) or (area and curve)):ti,ab
#33	(sensitivity or specificity):ti,ab
#34	gold standard:ab
#35	("predictive value" or PPV or NPV):ti,ab
#36	likelihood ratio:ti,ab
#37	#27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36
#38	#26 and #37

Database(s): Embase

No.	Search terms
1	Insulin dependent diabetes mellitus/
2	Juvenile diabetes mellitus/
3	Diabetic ketoacidosis/
4	((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
5	(diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
6	(LADA or MODY).ti,ab.
7	(diabet* adj2 (brittle or labile)).ti,ab.
8	(diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
9	(diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
10	(dm1 or iddm or t1d* or dka).ti,ab.
11	((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
12	diabetes mellitus.ti.
13	or/1-12
14	(pregnan* or gestation*).ti.
15	13 not 14
16	letter.pt. or letter/
17	note.pt.
18	editorial.pt.
19	case report/ or case study/
20	(letter or comment*).ti.
21	or/16-20
22	21 not (randomized controlled trial/ or random*.ti,ab.)
23	animal/ not human/

Update 2015

24	nonhuman/
25	exp Animal Experiment/
26	exp Experimental Animal/
27	animal model/
28	exp Rodent/
29	(rat or rats or mouse or mice).ti.
30	or/22-29
31	15 not 30
32	(2003$ or 2004$ or 2005$ or 2006$ or 2007$ or 2008$ or 2009$ or 2010$ or 2011$ or 2012$ or 2013$).em.
33	31 and 32
34	C peptide/
35	Glutamate decarboxylase 65 antibody/
36	Insulinoma/
37	*Autoantibody/
38	Glucose 6 phosphatase/
39	((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
40	zinc transporter 8.ti,ab.
41	(islet adj5 (phosphatase or catalytic)).ti,ab.
42	(IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
43	or/34-42
44	33 and 43
45	(diagnos* or screen* or test*).ti,ab,hw.
46	exp "sensitivity and specificity"/
47	Receiver operating characteristic/
48	Area under the curve/
49	Proportional hazards model/
50	(ROC or AUC or (area and curve)).ti,ab.
51	(sensitivity or specificity).ti,ab.
52	gold standard.ab.
53	(predictive value* or PPV or NPV).ti,ab.
54	likelihood ratio*.ti,ab.
55	or/45-54
56	44 and 55
57	random*.ti,ab.
58	factorial*.ti,ab.
59	(crossover* or cross over*).ti,ab.
60	((doubl* or singl*) adj blind*).ti,ab.
61	(assign* or allocat* or volunteer* or placebo*).ti,ab.
62	crossover procedure/
63	single blind procedure/
64	randomized controlled trial/
65	double blind procedure/
66	or/57-65
67	Meta-Analysis/
68	Meta-Analysis as Topic/
69	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
70	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
71	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
72	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
73	(search* adj4 literature).ab.

Update 2015

74	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
75	cochrane.jw.
76	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
77	or/67-76
78	Clinical study/
79	exp case control study/
80	family study/
81	longitudinal study/
82	retrospective study/
83	prospective study/
84	cross-sectional study/
85	cohort analysis/
86	case control.ti,ab.
87	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
88	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
89	(study and (participant* or patient* or subject* or group*)).ti,ab.
90	cohort*.ti,ab.
91	or/78-90
92	56 and (66 or 77 or 91)
93	limit 92 to english language

Database(s): Embase

#	Searches
1	Insulin dependent diabetes mellitus/
2	Juvenile diabetes mellitus/
3	Diabetic ketoacidosis/
4	((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
5	(diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
6	(LADA or MODY).ti,ab.
7	(diabet* adj2 (brittle or labile)).ti,ab.
8	(diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
9	(diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
10	(dm1 or iddm or t1d* or dka).ti,ab.
11	((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
12	diabetes mellitus.ti.
13	or/1-12
14	(pregnan* or gestation*).ti.
15	13 not 14
16	letter.pt. or letter/
17	note.pt.
18	editorial.pt.
19	case report/ or case study/
20	(letter or comment*).ti.
21	or/16-20
22	21 not (randomized controlled trial/ or random*.ti,ab.)
23	animal/ not human/
24	nonhuman/
25	exp Animal Experiment/
26	exp Experimental Animal/
27	animal model/

Update 2015

28 exp Rodent/
29 (rat or rats or mouse or mice).ti.
30 or/22-29
31 15 not 30
32 ("201406" or "201407" or "201408" or "201409" or 20141* or 20142* or 20143*).em.
33 31 and 32
34 C peptide/
35 Glutamate decarboxylase 65 antibody/
36 Insulinoma/
37 *Autoantibody/
38 Glucose 6 phosphatase/
39 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
40 zinc transporter 8.ti,ab.
41 (islet adj5 (phosphatase or catalytic)).ti,ab.
42 [or/34-42]
43 [or/45-54]
44 [or/57-65]
45 [or/67-76]
46 [or/78-90]
47 [limit 92 to english language]
48 Insulin dependent diabetes mellitus/
49 Juvenile diabetes mellitus/
50 Diabetic ketoacidosis/
51 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
52 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
53 (LADA or MODY).ti,ab.
54 (diabet* adj2 (brittle or labile)).ti,ab.
55 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
56 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
57 (dm1 or iddm or t1d* or dka).ti,ab.
58 ((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
59 diabetes mellitus.ti.
60 or/48-59
61 (pregnan* or gestation*).ti.
62 60 not 61
63 letter.pt. or letter/
64 note.pt.
65 editorial.pt.
66 case report/ or case study/
67 (letter or comment*).ti.
68 or/63-67
69 68 not (randomized controlled trial/ or random*.ti,ab.)
70 animal/ not human/
71 nonhuman/
72 exp Animal Experiment/
73 exp Experimental Animal/
74 animal model/
75 exp Rodent/
76 (rat or rats or mouse or mice).ti.
77 or/69-76
78 62 not 77
79 ("201406" or "201407" or "201408" or "201409" or 20141* or 20142* or 20143*).em.

Update 2015

80	78 and 79
81	C peptide/
82	Glutamate decarboxylase 65 antibody/
83	Insulinoma/
84	*Autoantibody/
85	Glucose 6 phosphatase/
86	((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
87	zinc transporter 8.ti,ab.
88	(islet adj5 (phosphatase or catalytic)).ti,ab.
89	(IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
90	or/81-89
91	80 and 90
92	(diagnos* or screen* or test*).ti,ab,hw.
93	exp "sensitivity and specificity"/
94	Receiver operating characteristic/
95	Area under the curve/
96	Proportional hazards model/
97	(ROC or AUC or (area and curve)).ti,ab.
98	(sensitivity or specificity).ti,ab.
99	gold standard.ab.
100	(predictive value* or PPV or NPV).ti,ab.
101	likelihood ratio*.ti,ab.
102	or/92-101
103	91 and 102
104	random*.ti,ab.
105	factorial*.ti,ab.
106	(crossover* or cross over*).ti,ab.
107	((doubl* or singl*) adj blind*).ti,ab.
108	(assign* or allocat* or volunteer* or placebo*).ti,ab.
109	crossover procedure/
110	single blind procedure/
111	randomized controlled trial/
112	double blind procedure/
113	or/104-112
114	Meta-Analysis/
115	Meta-Analysis as Topic/
116	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
117	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
118	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
119	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
120	(search* adj4 literature).ab.
121	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
122	cochrane.jw.
123	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
124	or/114-123
125	Clinical study/
126	exp case control study/
127	family study/
128	longitudinal study/
129	retrospective study/

Update 2015

130	prospective study/
131	cross-sectional study/
132	cohort analysis/
133	case control.ti,ab.
134	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
135	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
136	(study and (participant* or patient* or subject* or group*)).ti,ab.
137	cohort*.ti,ab.
138	or/125-137
139	103 and (113 or 124 or 138)
140	limit 139 to english language

F.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7	or/1-6
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
9	clinical trial.pt.
10	exp CLINICAL TRIAL/
11	exp CLINICAL TRIALS AS TOPIC/
12	(clinic$ adj5 trial$).tw,sh.
13	PLACEBOS/
14	placebo$.tw,sh.
15	random$.tw,sh.
16	or/8-15
17	or/7,16
18	META ANALYSIS/
19	META ANALYSIS AS TOPIC/
20	meta analysis.pt.
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
22	(systematic$ adj5 (review$ or overview$)).tw,sh.
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.
24	or/18-23
25	review$.pt.
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
27	((hand or manual$) adj2 search$).tw.
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
29	(pooling or pooled or mantel haenszel).tw,sh.

Update 2015

30	(peto or dersimonian or der simonian or fixed effect).tw,sh.
31	or/26-30
32	and/25,31
33	or/24,32
34	letter.pt.
35	case report.tw.
36	comment.pt.
37	editorial.pt.
38	historical article.pt.
39	or/34-38
40	17 not 39
41	33 not 39
42	or/40-41
43	ADOLESCENT/ or MINORS/
44	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
45	exp CHILD/
46	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
47	exp INFANT/
48	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
49	exp PEDIATRICS/ or exp PUBERTY/
50	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
51	or/43-50
52	exp DIABETES MELLITUS, TYPE 1/
53	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
54	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
55	or/52-54
56	and/51,55
57	PATIENT EDUCATION AS TOPIC/
58	PROBLEM SOLVING/
59	ed.fs.
60	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
61	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
62	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
63	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
64	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
65	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
66	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
67	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
68	or/57-67
69	and/56,68
70	and/42,69

Update 2015

71	limit 70 to english language
72	LETTER/
73	EDITORIAL/
74	NEWS/
75	exp HISTORICAL ARTICLE/
76	ANECDOTES AS TOPIC/
77	COMMENT/
78	CASE REPORT/
79	(letter or comment* or abstracts).ti.
80	or/72-79
81	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
82	80 not 81
83	ANIMALS/ not HUMANS/
84	exp ANIMALS, LABORATORY/
85	exp ANIMAL EXPERIMENTATION/
86	exp MODELS, ANIMAL/
87	exp RODENTIA/
88	(rat or rats or mouse or mice).ti.
89	or/82-88
90	71 not 89

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	and/5,8
10	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
11	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
12	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
13	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
14	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
15	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
16	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
17	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
18	or/10-17

Update 2015

19	and/9,18
20	limit 19 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	and/9,13
15	PATIENT EDUCATION AS TOPIC/
16	PROBLEM SOLVING/
17	ed.fs.
18	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
19	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
20	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
21	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
22	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
23	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
24	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
25	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
26	or/15-25
27	and/14,26

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,ti,ab,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,ti,ab,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,ti,ab,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,ti,ab,jw,rw.
5	or/1-4

Update 2015

6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).kw,ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).kw,ti,ab.
8	or/6-7
9	and/5,8
10	"PATIENT EDUCATION AS TOPIC".kw.
11	"PROBLEM SOLVING".kw.
12	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).tw,tx.
13	(problem-solving or "problem solving" or problem-based or "problem based").tw,tx.
14	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw,tx.
15	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).tw,tx.
16	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw,tx.
17	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw,tx.
18	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw,tx.
19	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).tw,tx.
20	or/10-19
21	and/9,20

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	and/9,13
15	PATIENT EDUCATION AS TOPIC/
16	PROBLEM SOLVING/
17	ed.fs.
18	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).tw.
19	(problem-solving or "problem solving" or problem-based or "problem based").tw.
20	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw.

Update 2015

21	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).tw.
22	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw.
23	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw.
24	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw.
25	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).tw.
26	or/15-25
27	and/14,26
28	limit 27 to english language

Embase

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).ti,ab,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.ti,ab,sh.
9	random$.ti,ab,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	or/18,28
30	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31	13 not 30
32	29 not 30
33	or/31-32

Update 2015

34	exp ADOLESCENT/
35	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
36	exp CHILD/
37	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
38	exp INFANT/
39	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
40	exp PEDIATRICS/ or exp PUBERTY/
41	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
42	or/34-41
43	INSULIN DEPENDENT DIABETES MELLITUS/
44	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
45	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
46	or/43-45
47	JUVENILE DIABETES MELLITUS/
48	and/42,46
49	or/47-48
50	PATIENT EDUCATION/
51	DIABETES EDUCATION/
52	DIABETES EDUCATOR/
53	EDUCATION PROGRAM/
54	PROBLEM SOLVING/
55	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
56	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
57	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
58	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
59	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
60	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
61	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
62	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
63	or/50-62
64	and/49,63
65	and/33,64
66	conference abstract.pt.
67	letter.pt. or LETTER/
68	note.pt.
69	editorial.pt.
70	CASE REPORT/ or CASE STUDY/
71	(letter or comment* or abstracts).ti.
72	or/66-71
73	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
74	72 not 73

Update 2015

75	ANIMAL/ not HUMAN/
76	NONHUMAN/
77	exp ANIMAL EXPERIMENT/
78	exp EXPERIMENTAL ANIMAL/
79	ANIMAL MODEL/
80	exp RODENT/
81	(rat or rats or mouse or mice).ti.
82	or/74-81
83	65 not 82
84	limit 83 to english language

PsycINFO

#	Searches
1	LITERATURE REVIEW/
2	EXPERIMENTAL DESIGN/
3	RANDOM SAMPLING/
4	META-ANALYSIS/
5	exp TREATMENT/
6	(random$ or search$ or control$ or risk$).tw.
7	(meta-analys#s or metaanalys#s).ti.
8	(systematic$ adj (review$ or overview$)).ti.
9	((single or double or triple) adj (blind$ or mask$)).ti.
10	rct.tw.
11	or/1-10
12	adolescen$.ag.
13	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
14	(child$ or school$ or preschool$).ag.
15	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,id,jw.
16	(infan$ or neonat$).ag.
17	(infan$ or neonat$ or newborn$ or baby or babies or p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,id,jw.
18	or/12-17
19	DIABETES MELLITUS/
20	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab,id.
21	(IDDM or T1D or TID or DM1 or DMI).ti,ab,id.
22	or/19-21
23	and/18,22
24	CLIENT EDUCATION/
25	EDUCATIONAL PROGRAMS/ or EDUCATIONAL THERAPY/
26	PROBLEM SOLVING/
27	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab,id.
28	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab,id.
29	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.
30	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab,id.
31	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.

Update 2015

32	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab,id.
33	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.
34	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab,id.
35	or/24-34
36	and/23,35
37	and/11,36
38	limit 37 to english language

CINAHL with Full Text

#	Query	Limiters/Expanders
S31	S6 AND S29	Limiters - English Language; Exclude MEDLINE records Search modes - Boolean/Phrase
S30	S6 AND S29	Search modes - Boolean/Phrase
S29	S16 AND S28	Search modes - Boolean/Phrase
S28	S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27	Search modes - Boolean/Phrase
S27	TI ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N3 information) OR AB ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N3 information)	Search modes - Boolean/Phrase
S26	TI ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes))	Search modes - Boolean/Phrase
S25	TI ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information)	Search modes - Boolean/Phrase
S24	TI ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes))	Search modes - Boolean/Phrase
S23	TI ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information)	Search modes - Boolean/Phrase
S22	TI ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes))	Search modes - Boolean/Phrase
S21	TI (problem-solving or "problem solving" or problem-based or "problem based") OR AB (problem-solving or "problem solving" or problem-based or "problem based")	Search modes - Boolean/Phrase

Update 2015

S20	TI ((educat* or training) N6 (intervention* or program# or programme or programmes)) OR AB ((educat* or training) N6 (intervention* or program# or programme or programmes)) Search modes - Boolean/Phrase
S19	MW "ED" Search modes - Boolean/Phrase
S18	(MH "Problem Solving+") Search modes - Boolean/Phrase
S17	(MH "Patient Education") OR (MH "Diabetes Education") Search modes - Boolean/Phrase
S16	S12 AND S15 Search modes - Boolean/Phrase
S15	S13 OR S14 Search modes - Boolean/Phrase
S14	TI (diabet* N5 ("type one" or "type 1" or "type I" or “insulin depend*” or juvenile or child* or earl* or labile or brittle or “sudden onset” or “auto immun*” or autoimmun* or “auto-immun*)) OR AB (diabet* N5 ("type one" or "type 1" or "type I" or “insulin depend*” or juvenile or child* or earl* or labile or brittle or “sudden onset” or “auto immun*” or autoimmun* or “auto-immun*)) Search modes - Boolean/Phrase
S13	(MH "Diabetes Mellitus, Type 1+") Search modes - Boolean/Phrase
S12	S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase
S11	TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
S10	TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
S9	TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
S8	TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S7	(MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase
S6	S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
S5	PT systematic review Search modes - Boolean/Phrase
S4	PT review Search modes - Boolean/Phrase
S3	TX meta-analysis OR "meta analysis" Search modes - Boolean/Phrase
S2	TX random* Search modes - Boolean/Phrase
S1	(MH "Treatment Outcomes+") OR (MH "Experimental Studies+") Search modes - Boolean/Phrase

F.3 Type 1 diabetes – psychological interventions

Review question: What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/

Update 2015

6	RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7	or/1-6
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
9	clinical trial.pt.
10	exp CLINICAL TRIAL/
11	exp CLINICAL TRIALS AS TOPIC/
12	(clinic$ adj5 trial$).tw,sh.
13	PLACEBOS/
14	placebo$.tw,sh.
15	random$.tw,sh.
16	or/8-15
17	or/7,16
18	META ANALYSIS/
19	META ANALYSIS AS TOPIC/
20	meta analysis.pt.
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
22	(systematic$ adj5 (review$ or overview$)).tw,sh.
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.
24	or/18-23
25	review$.pt.
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
27	((hand or manual$) adj2 search$).tw.
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
29	(pooling or pooled or mantel haenszel).tw,sh.
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.
31	or/26-30
32	and/25,31
33	or/24,32
34	letter.pt.
35	case report.tw.
36	comment.pt.
37	editorial.pt.
38	historical article.pt.
39	or/34-38
40	17 not 39
41	33 not 39
42	or/40-41
43	ADOLESCENT/ or MINORS/
44	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
45	exp CHILD/
46	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
47	exp INFANT/
48	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
49	exp PEDIATRICS/ or exp PUBERTY/
50	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
51	or/43-50
52	exp DIABETES MELLITUS, TYPE 1/
53	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
54	(IDDM or T1D or TID or DM1 or DMI).ti,ab.

Update 2015

55	or/52-54
56	and/51,55
57	BEHAVIOR THERAPY/
58	COGNITIVE THERAPY/
59	PSYCHOTHERAPY/
60	PSYCHOTHERAPY, GROUP/
61	FAMILY THERAPY/
62	(psychotherap$ or BFST or CBT).ti,ab.
63	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
64	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
65	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
66	COUNSELING/
67	MOTIVATIONAL INTERVIEWING/
68	MENTORS/
69	SOCIAL SUPPORT/
70	SELF-HELP GROUPS/
71	(motivation$ or counsel?ing or mentor$).ti,ab.
72	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
73	or/57-72
74	and/42,56,73
75	limit 74 to english language
76	LETTER/
77	EDITORIAL/
78	NEWS/
79	exp HISTORICAL ARTICLE/
80	ANECDOTES AS TOPIC/
81	COMMENT/
82	CASE REPORT/
83	(letter or comment* or abstracts).ti.
84	or/76-83
85	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
86	84 not 85
87	ANIMALS/ not HUMANS/
88	exp ANIMALS, LABORATORY/
89	exp ANIMAL EXPERIMENTATION/
90	exp MODELS, ANIMAL/
91	exp RODENTIA/
92	(rat or rats or mouse or mice).ti.
93	or/86-92
94	75 not 93

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.

Update 2015

7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	and/5,8
10	(psychotherap$ or BFST or CBT).ti,ab.
11	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
12	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
13	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
14	(motivation$ or counsel?ing or mentor$).ti,ab.
15	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
16	or/10-15
17	and/9,16
18	limit 17 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	and/9,13
15	BEHAVIOR THERAPY/
16	COGNITIVE THERAPY/
17	PSYCHOTHERAPY/
18	PSYCHOTHERAPY, GROUP/
19	FAMILY THERAPY/
20	(psychotherap$ or BFST or CBT).ti,ab.
21	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
22	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
23	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
24	COUNSELING/
25	MOTIVATIONAL INTERVIEWING/
26	MENTORS/
27	SOCIAL SUPPORT/
28	SELF-HELP GROUPS/
29	(motivation$ or counsel?ing or mentor$).ti,ab.
30	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
31	or/15-30
32	and/14,31

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,ti,ab,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,ti,ab,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,ti,ab,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,ti,ab,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).kw,ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).kw,ti,ab.
8	or/6-7
9	and/5,8
10	BEHAVIOR THERAPY.kw.
11	COGNITIVE THERAPY.kw.
12	PSYCHOTHERAPY.kw.
13	PSYCHOTHERAPY, GROUP.kw.
14	FAMILY THERAPY.kw.
15	(psychotherap$ or BFST or CBT).tw,tx.
16	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).tw,tx.
17	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).tw,tx.
18	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).tw,tx.
19	COUNSELING.kw.
20	MOTIVATIONAL INTERVIEWING.kw.
21	MENTORS.kw.
22	SOCIAL SUPPORT.kw.
23	SELF-HELP GROUPS.kw.
24	(motivation$ or counsel?ing or mentor$).tw,tx.
25	((peer or social$ or self help or self-help) adj3 (group? or support?)).tw,tx.
26	or/10-25
27	and/9,26

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	and/9,13

Update 2015

15	BEHAVIOR THERAPY/
16	COGNITIVE THERAPY/
17	PSYCHOTHERAPY/
18	PSYCHOTHERAPY, GROUP/
19	FAMILY THERAPY/
20	(psychotherap$ or BFST or CBT).tw.
21	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).tw.
22	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).tw.
23	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).tw.
24	COUNSELING/
25	MOTIVATIONAL INTERVIEWING/
26	MENTORS/
27	SOCIAL SUPPORT/
28	SELF-HELP GROUPS/
29	(motivation$ or counsel?ing or mentor$).tw.
30	((peer or social$ or self help or self-help) adj3 (group? or support?)).tw.
31	or/15-30
32	and/14,31
33	limit 32 to english language

Embase 1974 to 2014 Week 13

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).ti,ab,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.ti,ab,sh.
9	random$.ti,ab,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27

Update 2015

29	or/18,28
30	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31	13 not 30
32	29 not 30
33	or/31-32
34	exp ADOLESCENT/
35	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
36	exp CHILD/
37	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
38	exp INFANT/
39	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
40	exp PEDIATRICS/ or exp PUBERTY/
41	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
42	or/34-41
43	INSULIN DEPENDENT DIABETES MELLITUS/
44	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
45	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
46	or/43-45
47	JUVENILE DIABETES MELLITUS/
48	and/42,46
49	or/47-48
50	BEHAVIOR THERAPY/
51	BEHAVIOR MODIFICATION/
52	COGNITIVE THERAPY/
53	PSYCHOTHERAPY/
54	FAMILY THERAPY/
55	GROUP THERAPY/
56	MOTIVATIONAL INTERVIEWING/
57	(psychotherap$ or BFST or CBT).ti,ab.
58	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
59	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
60	((family$ or families or parent$) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
61	COUNSELING/
62	FAMILY COUNSELING/
63	PARENT COUNSELING/
64	PATIENT COUNSELING/
65	PEER COUNSELING/
66	TEACHER/
67	SOCIAL SUPPORT/
68	SUPPORT GROUP/
69	SELF HELP/
70	(motivation$ or counsel?ing or mentor$).ti,ab.
71	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
72	or/50-71
73	and/33,49,72
74	limit 73 to english language
75	conference abstract.pt.
76	letter.pt. or LETTER/
77	note.pt.

Update 2015

78	editorial.pt.
79	CASE REPORT/ or CASE STUDY/
80	(letter or comment* or abstracts).ti.
81	or/75-80
82	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
83	81 not 82
84	ANIMAL/ not HUMAN/
85	NONHUMAN/
86	exp ANIMAL EXPERIMENT/
87	exp EXPERIMENTAL ANIMAL/
88	ANIMAL MODEL/
89	exp RODENT/
90	(rat or rats or mouse or mice).ti.
91	or/83-90
92	74 not 91

PsycINFO 1967 to March Week 4 2014

#	Searches
1	LITERATURE REVIEW/
2	EXPERIMENTAL DESIGN/
3	RANDOM SAMPLING/
4	META-ANALYSIS/
5	exp TREATMENT/
6	(random$ or search$ or control$ or risk$).tw.
7	(meta-analys#s or metaanalys#s).ti.
8	(systematic$ adj (review$ or overview$)).ti.
9	((single or double or triple) adj (blind$ or mask$)).ti.
10	rct.tw.
11	or/1-10
12	adolescen$.ag.
13	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
14	(child$ or school$ or preschool$).ag.
15	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,id,jw.
16	(infan$ or neonat$).ag.
17	(infan$ or neonat$ or newborn$ or baby or babies or p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,id,jw.
18	or/12-17
19	DIABETES MELLITUS/
20	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab,id.
21	(IDDM or T1D or TID or DM1 or DMI).ti,ab,id.
22	or/19-21
23	and/18,22
24	BEHAVIOR THERAPY/
25	COGNITIVE THERAPY/
26	COGNITIVE BEHAVIOR THERAPY/
27	PSYCHOTHERAPY/
28	ADOLESCENT PSYCHOTHERAPY/
29	CHILD PSYCHOTHERAPY/
30	GROUP PSYCHOTHERAPY/
31	FAMILY THERAPY/
32	FAMILY INTERVENTION/

Update 2015

33	MOTIVATIONAL INTERVIEWING/
34	(psychotherap$ or BFST or CBT).ti,ab.
35	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
36	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
37	((family$ or families or parent$) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
38	COUNSELING/
39	GROUP COUNSELING/
40	PEER COUNSELING/
41	MENTOR/
42	SOCIAL SUPPORT/
43	SUPPORT GROUPS/
44	SELF HELP TECHNIQUES/
45	(motivation$ or counsel?ing or mentor$).ti,ab.
46	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
47	or/24-46
48	and/23,47
49	and/11,48
50	limit 49 to english language

CINAHL with Full Text

#	Query	Limiters/Expanders
S33	S6 AND S31	Limiters - English Language; Exclude MEDLINE records Search modes - Boolean/Phrase
S32	S6 AND S31	Search modes - Boolean/Phrase
S31	S16 AND S30	Search modes - Boolean/Phrase
S30	S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29	Search modes - Boolean/Phrase
S29	TI ((peer or social* or “self help” or self-help) N3 (group# or support#)) OR AB ((peer or social* or “self help” or self-help) N3 (group# or support#))	Search modes - Boolean/Phrase
S28	TI (motivation* or counsel#ing or mentor*) OR AB (motivation* or counsel#ing or mentor*)	Search modes - Boolean/Phrase
S27	(MH "Support Groups")	Search modes - Boolean/Phrase
S26	(MH "Mentorship")	Search modes - Boolean/Phrase
S25	(MH "Counseling") OR (MH "Peer Counseling")	Search modes - Boolean/Phrase
S24	TI ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*)) OR AB ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*))	Search modes - Boolean/Phrase
S23	TI ((behavi* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) OR AB ((behavi* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*))	Search modes - Boolean/Phrase
S22	TI ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) OR AB ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*))	Search modes - Boolean/Phrase
S21	TI (psychotherap* or BFST or CBT) OR AB (psychotherap* or BFST or CBT)	Search modes - Boolean/Phrase
S20	(MH "Motivational Interviewing")	Search modes - Boolean/Phrase
S19	(MH "Psychotherapy, Group") OR (MH "Family Therapy")	Search modes - Boolean/Phrase
S18	(MH "Psychotherapy")	Search modes - Boolean/Phrase
S17	(MH "Behavior Therapy+") OR (MH "Cognitive Therapy")	Search modes - Boolean/Phrase
S16	S12 AND S15	Search modes - Boolean/Phrase
S15	S13 OR S14	Search modes - Boolean/Phrase

Update 2015

S14	TI (diabet* N5 ("type one" or "type 1" or "type I" or “insulin depend*” or juvenile or child* or earl* or labile or brittle or “sudden onset” or “auto immun*” or autoimmun* or “auto-immun*)) OR AB (diabet* N5 ("type one" or "type 1" or "type I" or “insulin depend*” or juvenile or child* or earl* or labile or brittle or “sudden onset” or “auto immun*” or autoimmun* or “auto-immun*)) Search modes - Boolean/Phrase
S13	(MH "Diabetes Mellitus, Type 1+") Search modes - Boolean/Phrase
S12	S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase
S11	TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
S10	TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
S9	TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
S8	TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S7	(MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase
S6	S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
S5	PT systematic review Search modes - Boolean/Phrase
S4	PT review Search modes - Boolean/Phrase
S3	TX meta-analysis OR "meta analysis" Search modes - Boolean/Phrase
S2	TX random* Search modes - Boolean/Phrase
S1	(MH "Treatment Outcomes+") OR (MH "Experimental Studies+") Search modes - Boolean/Phrase

Update 2015

F.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.

12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	and/9,13
15	exp INSULIN/ad, tu [Administration & Dosage, Therapeutic Use]
16	exp INSULINS/ad, tu [Administration & Dosage, Therapeutic Use]
17	(insulin$ or Hagedorn).kw.
18	or/15-17
19	exp DRUG ADMINISTRATION SCHEDULE/
20	DOSE-RESPONSE RELATIONSHIP, DRUG/
21	exp INJECTIONS, SUBCUTANEOUS/
22	((insulin$ or inject$) adj (regim$ or schedul$)).ti,ab.
23	((intensiv$ or conventional or flexib$ or basal$ or bolus$) adj3 (treatment? or therap$ or regime$ or manag$ or control$ or program$ or schedul$)).ti,ab.
24	((multiple or prandial$ or preprandial$ or postprandial$ or meal$ or premeal$ or postmeal$ or basal$ or bolus$) adj3 (inject$ or insulin$ or dose? or dosage?)).ti,ab.
25	((mix$ or premix$ or freemix$ or self titrat$ or biphasic$) adj5 insulin$).ti,ab.
26	(MDI or FMDI).ti,ab.
27	or/19-26
28	and/14,18,27
29	limit 28 to english language
30	LETTER/
31	EDITORIAL/
32	NEWS/
33	exp HISTORICAL ARTICLE/
34	ANECDOTES AS TOPIC/
35	COMMENT/
36	CASE REPORT/
37	(letter or comment* or abstracts).ti.
38	or/30-37
39	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
40	38 not 39
41	ANIMALS/ not HUMANS/
42	exp ANIMALS, LABORATORY/
43	exp ANIMAL EXPERIMENTATION/
44	exp MODELS, ANIMAL/
45	exp RODENTIA/
46	(rat or rats or mouse or mice).ti.
47	or/40-46
48	29 not 47

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	((insulin$ or inject$) adj (regim$ or schedul$)).ti,ab.

Update 2015

10	((intensiv$ or conventional or flexib$ or basal$ or bolus$) adj3 (treatment? or therap$ or regime$ or manag$ or control$ or program$ or schedul$)).ti,ab.
11	((multiple or prandial$ or preprandial$ or postprandial$ or meal$ or premeal$ or postmeal$ or basal$ or bolus$) adj3 (inject$ or insulin$ or dose? or dosage?)).ti,ab.
12	((mix$ or premix$ or freemix$ or self titrat$ or biphasic$) adj5 insulin$).ti,ab.
13	(MDI or FMDI).ti,ab.
14	or/9-13
15	and/5,8,14

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	and/9,13
15	exp INSULIN/ad, tu [Administration & Dosage, Therapeutic Use]
16	exp INSULINS/ad, tu [Administration & Dosage, Therapeutic Use]
17	(insulin$ or Hagedorn).kw.
18	or/15-17
19	exp DRUG ADMINISTRATION SCHEDULE/
20	DOSE-RESPONSE RELATIONSHIP, DRUG/
21	exp INJECTIONS, SUBCUTANEOUS/
22	((insulin$ or inject$) adj (regim$ or schedul$)).ti,ab.
23	((intensiv$ or conventional or flexib$ or basal$ or bolus$) adj3 (treatment? or therap$ or regime$ or manag$ or control$ or program$ or schedul$)).ti,ab.
24	((multiple or prandial$ or preprandial$ or postprandial$ or meal$ or premeal$ or postmeal$ or basal$ or bolus$) adj3 (inject$ or insulin$ or dose? or dosage?)).ti,ab.
25	((mix$ or premix$ or freemix$ or self titrat$ or biphasic$) adj5 insulin$).ti,ab.
26	(MDI or FMDI).ti,ab.
27	or/19-26
28	and/14,18,27

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,ti,ab,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,ti,ab,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,ti,ab,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,ti,ab,jw,rw.
5	or/1-4

Update 2015

6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).kw,ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).kw,ti,ab.
8	or/6-7
9	and/5,8
10	INSULIN.kw.
11	INSULINS.kw.
12	(insulin$ or Hagedorn).tw,tx.
13	or/10-12
14	DRUG ADMINISTRATION SCHEDULE.kw.
15	DOSE-RESPONSE RELATIONSHIP, DRUG.kw.
16	INJECTIONS, SUBCUTANEOUS.kw.
17	((insulin$ or inject$) adj (regim$ or schedul$)).tw,tx.
18	((intensiv$ or conventional or flexib$ or basal$ or bolus$) adj3 (treatment? or therap$ or regime$ or manag$ or control$ or program$ or schedul$)).tw,tx.
19	((multiple or prandial$ or preprandial$ or postprandial$ or meal$ or premeal$ or postmeal$ or basal$ or bolus$) adj3 (inject$ or insulin$ or dose? or dosage?)).tw,tx.
20	((mix$ or premix$ or freemix$ or self titrat$ or biphasic$) adj5 insulin$).tw,tx.
21	(MDI or FMDI).tw,tx.
22	or/14-21
23	and/9,13,22

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	and/9,13
15	exp INSULIN/ad, tu [Administration & Dosage, Therapeutic Use]
16	exp INSULINS/ad, tu [Administration & Dosage, Therapeutic Use]
17	(insulin$ or Hagedorn).tw.
18	or/15-17
19	exp DRUG ADMINISTRATION SCHEDULE/
20	DOSE-RESPONSE RELATIONSHIP, DRUG/
21	exp INJECTIONS, SUBCUTANEOUS/
22	((insulin$ or inject$) adj (regim$ or schedul$)).tw.
23	((intensiv$ or conventional or flexib$ or basal$ or bolus$) adj3 (treatment? or therap$ or regime$ or manag$ or control$ or program$ or schedul$)).tw.
24	((multiple or prandial$ or preprandial$ or postprandial$ or meal$ or premeal$ or postmeal$ or basal$ or bolus$) adj3 (inject$ or insulin$ or dose? or dosage?)).tw.
25	((mix$ or premix$ or freemix$ or self titrat$ or biphasic$) adj5 insulin$).tw.
26	(MDI or FMDI).tw.

Update 2015

27	or/19-26
28	and/14,18,27

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	JUVENILE DIABETES MELLITUS/
15	and/9,13
16	or/14-15
17	exp INSULIN DERIVATIVE/co, do, dt [Drug Combination, Drug Dose, Drug Therapy]
18	(insulin$ or Hagedorn).kw.
19	or/17-18
20	INSULIN TREATMENT/
21	NEUTRAL INSULIN INJECTION/
22	DRUG ADMINISTRATION/
23	DOSE CALCULATION/
24	DRUG DOSE REGIMEN/
25	DOSAGE SCHEDULE COMPARISON/
26	exp INJECTION/
27	SUBCUTANEOUS DRUG ADMINISTRATION/
28	((insulin$ or inject$) adj (regim$ or schedul$)).ti,ab.
29	((intensiv$ or conventional or flexib$ or basal$ or bolus$) adj3 (treatment? or therap$ or regime$ or manag$ or control$ or program$ or schedul$)).ti,ab.
30	((multiple or prandial$ or preprandial$ or postprandial$ or meal$ or premeal$ or postmeal$ or basal$ or bolus$) adj3 (inject$ or insulin$ or dose? or dosage?)).ti,ab.
31	((mix$ or premix$ or freemix$ or self titrat$ or biphasic$) adj5 insulin$).ti,ab.
32	(MDI or FMDI).ti,ab.
33	or/20-32
34	and/16,19,33
35	limit 34 to english language
36	conference abstract.pt.
37	letter.pt. or LETTER/
38	note.pt.
39	editorial.pt.
40	CASE REPORT/ or CASE STUDY/
41	(letter or comment* or abstracts).ti.
42	or/36-41
43	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
44	42 not 43

Update 2015

45	ANIMAL/ not HUMAN/
46	NONHUMAN/
47	exp ANIMAL EXPERIMENT/
48	exp EXPERIMENTAL ANIMAL/
49	ANIMAL MODEL/
50	exp RODENT/
51	(rat or rats or mouse or mice).ti.
52	or/44-51
53	35 not 52

F.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	or/1-5
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
8	clinical trial.pt.
9	exp CLINICAL TRIAL/
10	exp CLINICAL TRIALS AS TOPIC/
11	(clinic$ adj5 trial$).tw,sh.
12	PLACEBOS/
13	placebo$.tw,sh.
14	random$.tw,sh.
15	or/7-14
16	or/6-15
17	META ANALYSIS/
18	META ANALYSIS AS TOPIC/
19	meta analysis.pt.
20	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21	(systematic$ adj5 (review$ or overview$)).tw,sh.
22	(methodologic$ adj5 (review$ or overview$)).tw,sh.
23	or/17-22
24	review$.pt.
25	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
26	((hand or manual$) adj2 search$).tw.
27	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
28	(pooling or pooled or mantel haenszel).tw,sh.
29	(peto or dersimonian or der simonian or fixed effect).tw,sh.
30	or/25-29
31	and/24,30
32	exp CASE-CONTROL STUDIES/

Update 2015

33	(case$ adj2 control$).tw.
34	exp COHORT STUDIES/
35	cohort$.tw.
36	or/32-35
37	letter.pt.
38	or/16,23,31,36
39	comparative study.pt.
40	or/38-39
41	ADOLESCENT/ or MINORS/
42	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
43	exp CHILD/
44	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
45	exp INFANT/
46	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
47	exp PEDIATRICS/ or exp PUBERTY/
48	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
49	or/41-48
50	exp DIABETES MELLITUS, TYPE 1/
51	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
52	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
53	or/50-52
54	HEMOGLOBIN A, GLYCOSYLATED/
55	(h?emoglobin? adj3 glycosylat$).ti,ab.
56	(glycated adj3 h?emoglobin?).ti,ab.
57	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
58	"hemoglobin A1c protein, human".nm.
59	or/54-58
60	REFERENCE STANDARDS/ or REFERENCE VALUES/
61	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
62	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
63	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
64	or/60-63
65	and/49,53,59,64
66	and/40,65
67	LETTER/
68	EDITORIAL/
69	NEWS/
70	exp HISTORICAL ARTICLE/
71	ANECDOTES AS TOPIC/
72	COMMENT/
73	CASE REPORT/
74	(letter or comment* or abstracts).ti.
75	or/67-74
76	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
77	75 not 76
78	ANIMALS/ not HUMANS/
79	exp ANIMALS, LABORATORY/
80	exp ANIMAL EXPERIMENTATION/
81	exp MODELS, ANIMAL/

Update 2015

82	exp RODENTIA/
83	(rat or rats or mouse or mice).ti.
84	or/77-83
85	66 not 84
86	limit 85 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	(h?emoglobin? adj3 glycosylat$).ti,ab.
10	(glycated adj3 h?emoglobin?).ti,ab.
11	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
12	or/9-11
13	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
14	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
15	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
16	or/13-15
17	and/5,8,12,16

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	HEMOGLOBIN A, GLYCOSYLATED/
15	(h?emoglobin? adj3 glycosylat$).ti,ab.
16	(glycated adj3 h?emoglobin?).ti,ab.
17	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
18	or/14-17
19	REFERENCE STANDARDS/ or REFERENCE VALUES/

Update 2015

20	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
21	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
22	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
23	or/19-22
24	and/9,13,18,23
25	limit 24 to yr="2013 -Current"

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(ADOLESCENT or MINORS).kw.
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,jw,rw.
3	CHILD.kw.
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,jw,rw.
5	INFANT.kw.
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,jw,rw.
7	(PEDIATRICS or PUBERTY).kw.
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,jw,rw.
9	or/1-8
10	DIABETES MELLITUS, TYPE 1.kw.
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx.
12	(IDDM or T1D or TID or DM1 or DMI).tw,tx.
13	or/10-12
14	HEMOGLOBIN A, GLYCOSYLATED.kw.
15	(h?emoglobin? adj3 glycosylat$).tw,tx.
16	(glycated adj3 h?emoglobin?).tw,tx.
17	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).tw,tx.
18	or/14-17
19	(REFERENCE STANDARDS or REFERENCE VALUES).kw.
20	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).tw,tx.
21	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).tw,tx.
22	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).tw,tx.
23	or/19-22
24	and/9,13,18,23

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/

Update 2015

11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	HEMOGLOBIN A, GLYCOSYLATED/
15	(h?emoglobin? adj3 glycosylat$).tw.
16	(glycated adj3 h?emoglobin?).tw.
17	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).tw.
18	or/14-17
19	REFERENCE STANDARDS/ or REFERENCE VALUES/
20	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).tw.
21	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).tw.
22	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).tw.
23	or/19-22
24	and/9,13,18,23

Embase

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).tw,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.tw,sh.
9	random$.tw,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.
16	(systematic$ adj5 (review$ or overview$)).tw,sh.
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	exp CASE CONTROL STUDY/
30	RETROSPECTIVE STUDY/
31	(case$ adj2 control$).tw.
32	COHORT ANALYSIS/

Update 2015

33	LONGITUDINAL STUDY/
34	FOLLOW UP/
35	PROSPECTIVE STUDY/
36	cohort$.tw.
37	or/29-36
38	or/13,18,28,37
39	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40	38 not 39
41	COMPARATIVE STUDY/
42	(compar$ adj3 stud$).tw.
43	or/41-42
44	or/40,43
45	exp ADOLESCENT/
46	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
47	exp CHILD/
48	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
49	exp INFANT/
50	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
51	exp PEDIATRICS/ or exp PUBERTY/
52	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
53	or/45-52
54	INSULIN DEPENDENT DIABETES MELLITUS/
55	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
56	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
57	JUVENILE DIABETES MELLITUS/
58	or/54-57
59	HEMOGLOBIN A1c/
60	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
61	(h?emoglobin? adj3 glycosylat$).ti,ab.
62	(glycated adj3 h?emoglobin?).ti,ab.
63	or/59-62
64	STANDARD/
65	REFERENCE VALUE/
66	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
67	or/64-66
68	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
69	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
70	or/67-69
71	and/53,58,63,70
72	and/44,71
73	conference abstract.pt.
74	letter.pt. or LETTER/
75	note.pt.
76	editorial.pt.
77	CASE REPORT/ or CASE STUDY/
78	(letter or comment* or abstracts).ti.
79	or/73-78
80	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
81	79 not 80

Update 2015

82	ANIMAL/ not HUMAN/
83	NONHUMAN/
84	exp ANIMAL EXPERIMENT/
85	exp EXPERIMENTAL ANIMAL/
86	ANIMAL MODEL/
87	exp RODENT/
88	(rat or rats or mouse or mice).ti.
89	or/81-88
90	72 not 89
91	limit 90 to english language

F.6 Type 1 diabetes blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	BLOOD GLUCOSE/
15	BLOOD GLUCOSE SELF-MONITORING/
16	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
17	(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
18	(normoglyc?emi$ or euglyc?emi$).ti,ab.
19	(glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.
20	or/14-19
21	REFERENCE STANDARDS/ or REFERENCE VALUES/
22	GOALS/
23	((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).ti,ab.
24	target$.ti.
25	target$.ab. /freq=2
26	((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).ti,ab.
27	or/21-26
28	and/20,27
29	(("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.

Update 2015

30	(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
31	or/28-30
32	TIME FACTORS/
33	((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
34	or/32-33
35	and/20,34
36	or/31,35
37	and/9,13,36
38	limit 37 to english language
39	LETTER/
40	EDITORIAL/
41	NEWS/
42	exp HISTORICAL ARTICLE/
43	ANECDOTES AS TOPIC/
44	COMMENT/
45	CASE REPORT/
46	(letter or comment* or abstracts).ti.
47	or/39-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMALS/ not HUMANS/
51	exp ANIMALS, LABORATORY/
52	exp ANIMAL EXPERIMENTATION/
53	exp MODELS, ANIMAL/
54	exp RODENTIA/
55	(rat or rats or mouse or mice).ti.
56	or/49-55
57	38 not 56

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
10	(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
11	(normoglyc?emi$ or euglyc?emi$).ti,ab.
12	(glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.
13	or/9-12
14	((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).ti,ab.
15	target$.ti.
16	target$.ab. /freq=2
17	((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).ti,ab.

Update 2015

18	or/14-17
19	and/13,18
20	(("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
21	(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
22	or/19-21
23	((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
24	and/13,23
25	or/22,24
26	and/5,8,25

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	BLOOD GLUCOSE/
15	BLOOD GLUCOSE SELF-MONITORING/
16	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
17	(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
18	(normoglyc?emi$ or euglyc?emi$).ti,ab.
19	(glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.
20	or/14-19
21	REFERENCE STANDARDS/ or REFERENCE VALUES/
22	GOALS/
23	((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).ti,ab.
24	target$.ti.
25	target$.ab. /freq=2
26	((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).ti,ab.
27	or/21-26
28	and/20,27
29	(("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
30	(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
31	or/28-30
32	TIME FACTORS/

Update 2015

33	((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
34	or/32-33
35	and/20,34
36	or/31,35
37	and/9,13,36

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.
7	(IDDM or T1D or TID or DM1 or DMI).tw,tx.
8	or/6-7
9	((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
10	(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).tw,tx.
11	(normoglyc?emi$ or euglyc?emi$).tw,tx.
12	(glyc?emi$ adj3 (norm$ or near?norm$)).tw,tx.
13	or/9-12
14	(REFERENCE STANDARDS or REFERENCE VALUES).kw.
15	GOALS.kw.
16	((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).tw,tx.
17	target$.tw,tx,kw.
18	((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).tw,tx.
19	or/14-18
20	and/13,19
21	(("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).tw,tx.
22	(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).tw,tx.
23	or/20-22
24	TIME.kw.
25	((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).tw,tx.
26	or/24-25
27	and/13,26
28	or/23,27
29	and/5,8,28

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw.

Update 2015

5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	BLOOD GLUCOSE/
15	BLOOD GLUCOSE SELF-MONITORING/
16	((blood or plasma) adj3 (glucose or sugar?)).tw.
17	(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).tw.
18	(normoglyc?emi$ or euglyc?emi$).tw.
19	(glyc?emi$ adj3 (norm$ or near?norm$)).tw.
20	or/14-19
21	REFERENCE STANDARDS/ or REFERENCE VALUES/
22	GOALS/
23	((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).tw.
24	target$.tw.
25	((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).tw.
26	or/21-25
27	and/20,26
28	(("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).tw.
29	(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).tw.
30	or/27-29
31	TIME FACTORS/
32	((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).tw.
33	or/31-32
34	and/20,33
35	or/30,34
36	and/9,13,35

Update 2015

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp NEWBORN/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.

12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	JUVENILE DIABETES MELLITUS/
15	and/9,13
16	or/14-15
17	GLUCOSE BLOOD LEVEL/
18	BLOOD GLUCOSE MONITORING/
19	GLYCEMIC CONTROL/
20	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
21	(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
22	(normoglyc?emi$ or euglyc?emi$).ti,ab.
23	(glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.
24	or/17-23
25	STANDARD/
26	REFERENCE VALUE/ or NORMAL VALUE/
27	MOTIVATION/
28	((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).ti,ab.
29	target$.ti.
30	target$.ab. /freq=2
31	((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).ti,ab.
32	or/25-31
33	and/24,32
34	(("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
35	(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
36	or/33-35
37	TIME/
38	((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
39	or/37-38
40	and/24,39
41	or/36,40
42	and/16,41
43	limit 42 to english language
44	conference abstract.pt.
45	letter.pt. or LETTER/
46	note.pt.
47	editorial.pt.
48	CASE REPORT/ or CASE STUDY/
49	(letter or comment* or abstracts).ti.
50	or/44-49
51	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
52	50 not 51
53	ANIMAL/ not HUMAN/
54	NONHUMAN/
55	exp ANIMAL EXPERIMENT/
56	exp EXPERIMENTAL ANIMAL/
57	ANIMAL MODEL/
58	exp RODENT/
59	(rat or rats or mouse or mice).ti.

Update 2015

60	or/52-59
61	43 not 60

F.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	and/9,13
15	BLOOD GLUCOSE SELF-MONITORING/
16	((glucose or blood sugar$ or insulin$) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.
17	(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
18	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
19	or/15-18
20	and/14,19
21	limit 20 to english language
22	LETTER/
23	EDITORIAL/
24	NEWS/
25	exp HISTORICAL ARTICLE/
26	ANECDOTES AS TOPIC/
27	COMMENT/
28	CASE REPORT/
29	(letter or comment* or abstracts).ti.
30	or/22-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

Update 2015

32	30 not 31
33	ANIMALS/ not HUMANS/
34	exp ANIMALS, LABORATORY/
35	exp ANIMAL EXPERIMENTATION/
36	exp MODELS, ANIMAL/
37	exp RODENTIA/
38	(rat or rats or mouse or mice).ti.
39	or/32-38
40	21 not 39

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	and/5,8
10	((glucose or blood sugar$ or insulin$) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.
11	(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
12	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
13	or/10-12
14	and/9,13
15	limit 14 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	and/9,13
15	BLOOD GLUCOSE SELF-MONITORING/
16	((glucose or blood sugar$ or insulin$) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.
17	(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.

Update 2015

18	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
19	or/15-18
20	and/14,19

Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,ti,ab,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,ti,ab,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,ti,ab,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,ti,ab,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).kw,ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).kw,ti,ab.
8	or/6-7
9	and/5,8
10	((glucose or blood sugar$ or insulin) adj3 (meter$ or monitor$ or sensor$ or capillary)).tw,tx,kw.
11	(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).tw,tx.
12	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw,tx.
13	or/10-12
14	and/9,13

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	and/9,13
15	BLOOD GLUCOSE SELF-MONITORING/
16	((glucose or blood sugar$ or insulin) adj3 (meter$ or monitor$ or sensor$ or capillary)).tw.
17	(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).tw.
18	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw.
19	or/15-18
20	and/14,19

Update 2015

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	JUVENILE DIABETES MELLITUS/
15	and/9,13
16	or/14-15
17	BLOOD GLUCOSE MONITORING/
18	((glucose or blood sugar$ or insulin$) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.
19	(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
20	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
21	or/17-20
22	and/16,21
23	limit 22 to english language
24	conference abstract.pt.
25	letter.pt. or LETTER/
26	note.pt.
27	editorial.pt.
28	CASE REPORT/ or CASE STUDY/
29	(letter or comment* or abstracts).ti.
30	or/24-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32	30 not 31
33	ANIMAL/ not HUMAN/
34	NONHUMAN/
35	exp ANIMAL EXPERIMENT/
36	exp EXPERIMENTAL ANIMAL/
37	ANIMAL MODEL/
38	exp RODENT/
39	(rat or rats or mouse or mice).ti.
40	or/32-39
41	23 not 40

Update 2015

F.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	exp KETOSIS/
14	(ketosis or ketoacid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	(DK or DKA).ti,ab.
16	or/10-15
17	exp KETONES/
18	HYDROXYBUTYRATES/
19	(ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but$ or hydroxybut$ or betahydroxybut$ or 3hydroxybut$).ti,ab.
20	or/17-19
21	and/9,16,20
22	limit 21 to english language
23	LETTER/
24	EDITORIAL/
25	NEWS/
26	exp HISTORICAL ARTICLE/
27	ANECDOTES AS TOPIC/
28	COMMENT/
29	CASE REPORT/
30	(letter or comment* or abstracts).ti.
31	or/23-30
32	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
33	31 not 32
34	ANIMALS/ not HUMANS/
35	exp ANIMALS, LABORATORY/
36	exp ANIMAL EXPERIMENTATION/
37	exp MODELS, ANIMAL/
38	exp RODENTIA/
39	(rat or rats or mouse or mice).ti.
40	or/33-39
41	22 not 40

Update 2015

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	(ketosis or ketoacid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
9	(DK or DKA).ti,ab.
10	or/6-9
11	(ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but$ or hydroxybut$ or betahydroxybut$ or 3hydroxybut$).ti,ab.
12	and/5,10-11

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	exp KETOSIS/
14	(ketosis or ketoacid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	(DK or DKA).ti,ab.
16	or/10-15
17	exp KETONES/
18	HYDROXYBUTYRATES/
19	(ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but$ or hydroxybut$ or betahydroxybut$ or 3hydroxybut$).ti,ab.
20	or/17-19
21	and/9,16,20

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw.

Update 2015

4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.
7	(IDDM or T1D or TID or DM1 or DMI).tw,tx.
8	(ketosis or ketoacid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw,tx,kw.
9	(DK or DKA).tw,tx.
10	or/6-9
11	(ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but$ or hydroxybut$ or betahydroxybut$ or 3hydroxybut$).tw,tx,kw.
12	and/5,10-11

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/
14	KETONURIA/
15	(ketosis or ketoacid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
16	(DK or DKA).ti,ab.
17	or/10-16
18	and/9,17
19	JUVENILE DIABETES MELLITUS/
20	or/18-19
21	exp KETONE/
22	3 HYDROXYBUTYRIC ACID/ or HYDROXYBUTYRIC ACID/
23	(ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but$ or hydroxybut$ or betahydroxybut$ or 3hydroxybut$).ti,ab.
24	or/21-23
25	and/20,24
26	limit 25 to english language
27	conference abstract.pt.
28	letter.pt. or LETTER/
29	note.pt.
30	editorial.pt.
31	CASE REPORT/ or CASE STUDY/
32	(letter or comment* or abstracts).ti.
33	or/27-32
34	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
35	33 not 34

Update 2015

36	ANIMAL/ not HUMAN/
37	NONHUMAN/
38	exp ANIMAL EXPERIMENT/
39	exp EXPERIMENTAL ANIMAL/
40	ANIMAL MODEL/
41	exp RODENT/
42	(rat or rats or mouse or mice).ti.
43	or/35-42
44	26 not 43

F.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	GLYCEMIC INDEX/
15	DIETARY CARBOHYDRATES/
16	(glyc?emic adj3 (index or indice? or load)).ti,ab.
17	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).ti,ab.
18	(CHOx or GI).ti,ab.
19	or/14-18
20	and/9,13,19
21	limit 20 to english language
22	LETTER/
23	EDITORIAL/
24	NEWS/
25	exp HISTORICAL ARTICLE/
26	ANECDOTES AS TOPIC/
27	COMMENT/
28	CASE REPORT/

Update 2015

29	(letter or comment* or abstracts).ti.
30	or/22-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32	30 not 31
33	ANIMALS/ not HUMANS/
34	exp ANIMALS, LABORATORY/
35	exp ANIMAL EXPERIMENTATION/
36	exp MODELS, ANIMAL/
37	exp RODENTIA/
38	(rat or rats or mouse or mice).ti.
39	or/32-38
40	21 not 39

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	or/6-7
9	(glyc?emic adj3 (index or indice? or load)).ti,ab.
10	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).ti,ab.
11	(CHOx or GI).ti,ab.
12	or/9-11
13	and/5,8,12
14	limit 13 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	GLYCEMIC INDEX/
15	DIETARY CARBOHYDRATES/
16	(glyc?emic adj3 (index or indice? or load)).ti,ab.
17	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).ti,ab.

Update 2015

18	(CHOx or GI).ti,ab.
19	or/14-18
20	and/9,13,19

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,tw,tx,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).kw,tw,tx.
7	(IDDM or T1D or TID or DM1 or DMI).kw,tw,tx.
8	or/6-7
9	(glyc?emic adj3 (index or indice? or load)).tw,tx,kw.
10	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).tw,tx,kw.
11	(CHOx or GI).tw,tx.
12	or/9-11
13	and/5,8,12

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	GLYCEMIC INDEX/
15	DIETARY CARBOHYDRATES/
16	(glyc?emic adj3 (index or indice? or load)).tw.
17	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).tw.
18	(CHOx or GI).tw.
19	or/14-18
20	and/9,13,19

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/

Update 2015

4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	JUVENILE DIABETES MELLITUS/
15	and/9,13
16	or/14-15
17	GLYCEMIC INDEX/
18	CARBOHYDRATE DIET/
19	exp CARBOHYDRATE INTAKE/
20	(glyc?emic adj3 (index or indice? or load)).ti,ab.
21	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).ti,ab.
22	(CHOx or GI).ti,ab.
23	or/17-22
24	and/16,23
25	limit 24 to english language
26	conference abstract.pt.
27	letter.pt. or LETTER/
28	note.pt.
29	editorial.pt.
30	CASE REPORT/ or CASE STUDY/
31	(letter or comment* or abstracts).ti.
32	or/26-31
33	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
34	32 not 33
35	ANIMAL/ not HUMAN/
36	NONHUMAN/
37	exp ANIMAL EXPERIMENT/
38	exp EXPERIMENTAL ANIMAL/
39	ANIMAL MODEL/
40	exp RODENT/
41	(rat or rats or mouse or mice).ti.
42	or/34-41
43	25 not 42

PsycINFO

#	Searches
1	adolescen$.ag.
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
3	(child$ or school$ or preschool$).ag.
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,id,jw.
5	(infan$ or neonat$).ag.
6	(infan$ or neonat$ or newborn$ or baby or babies or p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,id,jw.

Update 2015

7	or/1-6
8	DIABETES MELLITUS/
9	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab,id.
10	(IDDM or T1D or TID or DM1 or DMI).ti,ab,id.
11	or/8-10
12	DIETS/
13	exp CARBOHYDRATES/
14	(glyc?emic adj3 (index or indice? or load)).ti,ab,id.
15	((carbohydrate? or CHO) adj3 (count$ or quant$ or exchang$ or diet$ or intake)).ti,ab,id.
16	(CHOx or GI).ti,ab,id.
17	or/12-16
18	and/7,11,17
19	limit 18 to english language
20	(book or dissertation abstract or encyclopedia).pt.
21	19 not 20

CINAHL with Full Text

#	Query	Limiters/Expanders
S21	S6 AND S9 AND S20	Limiters - English Language; Exclude MEDLINE records
Search modes - Boolean/Phrase		
S20	S16 OR S19	Search modes - Boolean/Phrase
S19	S17 AND S18	Search modes - Boolean/Phrase
S18	TI (count* or quant* or exchang* or diet* or intake) or AB (count* or quant* or exchang* or diet* or intake)	Search modes - Boolean/Phrase
S17	TI (carbohydrate* or CHO) or AB (carbohydrate* or CHO)	Search modes - Boolean/Phrase
S16	S10 OR S11 OR S12 OR S13 OR S14 OR S15	Search modes - Boolean/Phrase
S15	TI (glycaemic load*) or AB (glycaemic load*)	Search modes - Boolean/Phrase
S14	TI (glycemic load*) or AB (glycemic load*)	Search modes - Boolean/Phrase
S13	AB (glycemic index) or AB (glycaemic index)	Search modes - Boolean/Phrase
S12	TI (glycemic index) or TI (glycaemic index)	Search modes - Boolean/Phrase
S11	(MH "Dietary Carbohydrates+")	Search modes - Boolean/Phrase
S10	(MH "Glycemic Load") OR (MH "Glycemic Index")	Search modes - Boolean/Phrase
S9	S7 OR S8	Search modes - Boolean/Phrase
S8	TI (diabet* N5 ("type one" or "type 1" or "type I" or “insulin depend*” or juvenile or child* or earl* or labile or brittle or “sudden onset” or “auto immun*” or autoimmun* or “auto-immun*)) OR AB (diabet* N5 ("type one" or "type 1" or "type I" or “insulin depend*” or juvenile or child* or earl* or labile or brittle or “sudden onset” or “auto immun*” or autoimmun* or “auto-immun*))	Search modes - Boolean/Phrase
S7	(MH "Diabetes Mellitus, Type 1+")	Search modes - Boolean/Phrase
S6	S1 OR S2 OR S3 OR S4 OR S5	Search modes - Boolean/Phrase
S5	TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*)	Search modes - Boolean/Phrase
S4	TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies)	Search modes - Boolean/Phrase
S3	TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#)	Search modes - Boolean/Phrase

Update 2015

S2	TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S1	(MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase

F.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	POLYDIPSIA/
22	DRINKING BEHAVIOR/
23	THIRST/
24	(polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).ti,ab.
25	or/21-24
26	POLYURIA/
27	(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).ti,ab.
28	or/26-27
29	WEIGHT LOSS/
30	(weight adj3 (loss or lost or reduc$)).ti,ab.
31	or/29-30
32	DEHYDRATION/
33	(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).ti,ab.

Update 2015

34	or/32-33
35	NAUSEA/ or VOMITING/
36	(nausea or emesis or vomit$).ti,ab.
37	or/35-36
38	ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39	((abdom#n$ adj3 pain$) or acute abdomen).ti,ab.
40	or/38-39
41	DYSPNEA/
42	TACHYPNEA/
43	HYPERVENTILATION/
44	(respirat$ adj (distress or rate)).ti,ab.
45	(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).ti,ab.
46	(gasping or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).ti,ab.
47	or/41-46
48	CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49	(conscious$ or confus$ or deliri$ or mental state$).ti,ab.
50	or/48-49
51	"SIGNS AND SYMPTOMS"/
52	(sign? or symptom? or indicat$ or presentation).ti,ab.
53	((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?)).ti,ab.
54	or/51-53
55	or/25,28,31,34,37,40,47,50,54
56	exp HYPERGLYCEMIA/
57	hyperglyc?emi$.ti,ab.
58	((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?)).ti,ab.
59	BLOOD GLUCOSE/an
60	(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
61	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
62	or/56-61
63	exp KETOSIS/
64	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).ti,ab.
65	KETONES/
66	3-HYDROXYBUTYRIC ACID/
67	HYDROXYBUTYRATES/
68	or/65-67
69	URINALYSIS/
70	BLOOD CHEMICAL ANALYSIS/
71	or/69-70
72	and/68,71
73	KETONES/an, bl, ur [Analysis, Blood, Urine]
74	3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]
75	HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]
76	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
77	((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
78	or/63-64,72-77
79	ACIDOSIS/
80	(acidosis or (blood? adj3 acid$) or acid?emi$).ti,ab.

Update 2015

81	HYDROGEN-ION CONCENTRATION/
82	ACID-BASE EQUILIBRIUM/
83	ACID-BASE IMBALANCE/
84	BICARBONATES/
85	ELECTROLYTES/
86	or/81-85
87	BLOOD GAS ANALYSIS/
88	BLOOD CHEMICAL ANALYSIS/
89	or/87-88
90	and/86,89
91	HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]
92	ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]
93	ACID-BASE IMBALANCE/bl, ur [Blood, Urine]
94	BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
95	ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
96	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).ti,ab.
97	(blood gas or ABG or blood test$).ti,ab.
98	or/79-80,90-97
99	(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).ti,ab.
100	or/62,78,98-99
101	or/55,100
102	exp "SENSITIVITY AND SPECIFICITY"/
103	exp BLOOD CHEMICAL ANALYSIS/
104	URINALYSIS/
105	(detect$ or diagnos$ or predict$ or sensitiv$ or accuracy or test$).mp.
106	or/102-105
107	and/20,101,106
108	limit 107 to english language
109	LETTER/
110	EDITORIAL/
111	NEWS/
112	exp HISTORICAL ARTICLE/
113	ANECDOTES AS TOPIC/
114	COMMENT/
115	CASE REPORT/
116	(letter or comment* or abstracts).ti.
117	or/109-116
118	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
119	117 not 118
120	ANIMALS/ not HUMANS/
121	exp ANIMALS, LABORATORY/
122	exp ANIMAL EXPERIMENTATION/
123	exp MODELS, ANIMAL/
124	exp RODENTIA/
125	(rat or rats or mouse or mice).ti.
126	or/119-125
127	108 not 126

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.

Update 2015

2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
5	or/1-4
6	(diabetic ketoacidosis or DK or DKA).ti,ab.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
8	diabet$.mp.
9	and/7-8
10	5 and (6 or 9)
11	(polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).ti,ab.
12	(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).ti,ab.
13	(weight adj3 (loss or lost or reduc$)).ti,ab.
14	(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).ti,ab.
15	(nausea or emesis or vomit$).ti,ab.
16	((abdom#n$ adj3 pain$) or acute abdomen).ti,ab.
17	(respirat$ adj (distress or rate)).ti,ab.
18	(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).ti,ab.
19	(gasping or kussmaul or dyspnea or tchypnea or breathless$ or hyperventilat$).ti,ab.
20	(conscious$ or confus$ or deliri$ or mental state$).ti,ab.
21	(sign? or symptom? or indicat$ or presentation).ti,ab.
22	((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?)).ti,ab.
23	or/11-22
24	hyperglyc?emi$.ti,ab.
25	((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?)).ti,ab.
26	(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
27	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
28	or/24-27
29	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).ti,ab.
30	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
31	((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
32	or/29-31
33	(acidosis or (blood? adj3 acid$) or acid?emi$).ti,ab.
34	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).ti,ab.
35	(blood gas or ABG or blood test$).ti,ab.
36	or/33-35
37	(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).ti,ab.
38	or/23,28,32,36-37
39	(detect$ or diagnos$ or predict$ or sensitiv$ or accuracy or test$).mp.
40	and/10,38-39

Update 2015

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	POLYDIPSIA/
22	DRINKING BEHAVIOR/
23	THIRST/
24	(polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).ti,ab.
25	or/21-24
26	POLYURIA/
27	(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).ti,ab.
28	or/26-27
29	WEIGHT LOSS/
30	(weight adj3 (loss or lost or reduc$)).ti,ab.
31	or/29-30
32	DEHYDRATION/
33	(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).ti,ab.
34	or/32-33
35	NAUSEA/ or VOMITING/
36	(nausea or emesis or vomit$).ti,ab.
37	or/35-36
38	ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39	((abdom#n$ adj3 pain$) or acute abdomen).ti,ab.
40	or/38-39
41	DYSPNEA/
42	TACHYPNEA/
43	HYPERVENTILATION/
44	(respirat$ adj (distress or rate)).ti,ab.
45	(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).ti,ab.

Update 2015

46	(gasping or kussmaul or dyspnea or tchypnea or breathless$ or hyperventilat$).ti,ab.
47	or/41-46
48	CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49	(conscious$ or confus$ or deliri$ or mental state$).ti,ab.
50	or/48-49
51	"SIGNS AND SYMPTOMS"/
52	(sign? or symptom? or indicat$ or presentation).ti,ab.
53	((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?)).ti,ab.
54	or/51-53
55	or/25,28,31,34,37,40,47,50,54
56	exp HYPERGLYCEMIA/
57	hyperglyc?emi$.ti,ab.
58	((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?)).ti,ab.
59	BLOOD GLUCOSE/an
60	(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
61	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
62	or/56-61
63	exp KETOSIS/
64	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).ti,ab.
65	KETONES/
66	3-HYDROXYBUTYRIC ACID/
67	HYDROXYBUTYRATES/
68	or/65-67
69	URINALYSIS/
70	BLOOD CHEMICAL ANALYSIS/
71	or/69-70
72	and/68,71
73	KETONES/an, bl, ur [Analysis, Blood, Urine]
74	3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]
75	HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]
76	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
77	((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
78	or/63-64,72-77
79	ACIDOSIS/
80	(acidosis or (blood? adj3 acid$) or acid?emi$).ti,ab.
81	HYDROGEN-ION CONCENTRATION/
82	ACID-BASE EQUILIBRIUM/
83	ACID-BASE IMBALANCE/
84	BICARBONATES/
85	ELECTROLYTES/
86	or/81-85
87	BLOOD GAS ANALYSIS/
88	BLOOD CHEMICAL ANALYSIS/
89	or/87-88
90	and/86,89
91	HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]
92	ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]

Update 2015

93	ACID-BASE IMBALANCE/bl, ur [Blood, Urine]
94	BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
95	ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
96	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).ti,ab.
97	(blood gas or ABG or blood test$).ti,ab.
98	or/79-80,90-97
99	(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).ti,ab.
100	or/62,78,98-99
101	55 or 100
102	20 and 101
103	exp "SENSITIVITY AND SPECIFICITY"/
104	exp BLOOD CHEMICAL ANALYSIS/
105	URINALYSIS/
106	(detect$ or diagnos$ or predict$ or sensitiv$ or accuracy or test$).mp.
107	or/103-106
108	102 and 107

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).kw,tw,tx,jw,rw.
5	or/1-4
6	(diabetic ketoacidosis or DK or DKA).kw,tw,tx.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).kw,tw,tx.
8	diabet$.kw,tw,tx.
9	and/7-8
10	5 and (6 or 9)
11	POLYDIPSIA.kw.
12	DRINKING BEHAVIOR.kw.
13	THIRST.kw.
14	(polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).tw,tx.
15	or/11-14
16	POLYURIA.kw.
17	(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).tw,tx.
18	or/16-17
19	WEIGHT LOSS.kw.
20	(weight adj3 (loss or lost or reduc$)).tw,tx.
21	or/19-20
22	DEHYDRATION.kw.
23	(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).tw,tx.
24	or/22-23
25	(NAUSEA or VOMITING).kw.
26	(nausea or emesis or vomit$).tw,tx.
27	or/25-26

Update 2015

28	(ABDOMINAL PAIN or ABDOMEN, ACUTE).kw.
29	((abdom#n$ adj3 pain$) or acute abdomen).tw,tx.
30	or/28-29
31	DYSPNEA.kw.
32	TACHYPNEA.kw.
33	HYPERVENTILATION.kw.
34	(respirat$ adj (distress or rate)).tw,tx.
35	(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).tw,tx.
36	(gasping or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).tw,tx.
37	or/31-36
38	(CONSCIOUSNESS DISORDERS or CONFUSION or DELIRIUM).kw.
39	(conscious$ or confus$ or deliri$ or mental state$).tw,tx.
40	or/38-39
41	"SIGNS AND SYMPTOMS".kw.
42	(sign? or symptom? or indicat$ or presentation).tw,tx.
43	((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?)).tw,tx.
44	or/41-43
45	or/15,18,21,24,27,30,37,40,44
46	(HYPERGLYCEMIA or GLUCOSE INTOLERANCE).kw.
47	hyperglyc?emi$.tw,tx.
48	((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?)).tw,tx.
49	(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).tw,tx.
50	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw,tx.
51	or/46-50
52	(KETOSIS or DIABETIC KETOACIDOSIS).kw.
53	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).tw,tx.
54	KETONES.kw.
55	3-HYDROXYBUTYRIC ACID.kw.
56	HYDROXYBUTYRATES.kw.
57	or/54-56
58	URINALYSIS.kw.
59	BLOOD CHEMICAL ANALYSIS.kw.
60	or/58-59
61	and/57,60
62	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.
63	((urine or urinary) adj3 (dipstick or dip test)).tw,tx.
64	or/52-53,61-63
65	ACIDOSIS.kw.
66	(acidosis or (blood? adj3 acid$) or acid?emi$).tw,tx.
67	HYDROGEN-ION CONCENTRATION.kw.
68	ACID-BASE EQUILIBRIUM.kw.
69	ACID-BASE IMBALANCE.kw.
70	BICARBONATES.kw.
71	ELECTROLYTES.kw.
72	or/67-71
73	BLOOD GAS ANALYSIS.kw.
74	BLOOD CHEMICAL ANALYSIS.kw.

Update 2015

75	or/73-74
76	and/72,75
77	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).tw,tx.
78	(blood gas or ABG or blood test$).tw,tx.
79	or/65-66,76-78
80	(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).tw,tx.
81	or/51,64,79-80
82	or/45,81
83	"SENSITIVITY AND SPECIFICITY".kw.
84	"PREDICTIVE VALUE OF TESTS".kw.
85	BLOOD CHEMICAL ANALYSIS.kw.
86	BLOOD GAS ANALYSIS.kw.
87	URINALYSIS.kw.
88	(detect$ or diagnos$ or predict$ or sensitiv$ or accuracy or test$).mp.
89	or/83-88
90	and/10,82,89

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).tw,jx,rw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).tw.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	POLYDIPSIA/
22	DRINKING BEHAVIOR/
23	THIRST/
24	(polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).tw.
25	or/21-24
26	POLYURIA/
27	(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).tw.
28	or/26-27
29	WEIGHT LOSS/

Update 2015

30	(weight adj3 (loss or lost or reduc$)).tw.
31	or/29-30
32	DEHYDRATION/
33	(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).tw.
34	or/32-33
35	NAUSEA/ or VOMITING/
36	(nausea or emesis or vomit$).tw.
37	or/35-36
38	ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39	((abdom#n$ adj3 pain$) or acute abdomen).tw.
40	or/38-39
41	DYSPNEA/
42	TACHYPNEA/
43	HYPERVENTILATION/
44	(respirat$ adj (distress or rate)).tw.
45	(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).tw.
46	(gasping or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).tw.
47	or/41-46
48	CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49	(conscious$ or confus$ or deliri$ or mental state$).tw.
50	or/48-49
51	"SIGNS AND SYMPTOMS"/
52	(sign? or symptom? or indicat$ or presentation).tw.
53	((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?)).tw.
54	or/51-53
55	or/25,28,31,34,37,40,47,50,54
56	exp HYPERGLYCEMIA/
57	hyperglyc?emi$.tw.
58	((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?)).tw.
59	BLOOD GLUCOSE/an
60	(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).tw.
61	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw.
62	or/56-61
63	exp KETOSIS/
64	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).tw.
65	KETONES/
66	3-HYDROXYBUTYRIC ACID/
67	HYDROXYBUTYRATES/
68	or/65-67
69	URINALYSIS/
70	BLOOD CHEMICAL ANALYSIS/
71	or/69-70
72	and/68,71
73	KETONES/an, bl, ur [Analysis, Blood, Urine]
74	3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]
75	HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]
76	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.

Update 2015

77	((urine or urinary) adj3 (dipstick or dip test)).tw.
78	or/63-64,72-77
79	ACIDOSIS/
80	(acidosis or (blood? adj3 acid$) or acid?emi$).tw.
81	HYDROGEN-ION CONCENTRATION/
82	ACID-BASE EQUILIBRIUM/
83	ACID-BASE IMBALANCE/
84	BICARBONATES/
85	ELECTROLYTES/
86	or/81-85
87	BLOOD GAS ANALYSIS/
88	BLOOD CHEMICAL ANALYSIS/
89	or/87-88
90	and/86,89
91	HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]
92	ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]
93	ACID-BASE IMBALANCE/bl, ur [Blood, Urine]
94	BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
95	ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
96	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).tw.
97	(blood gas or ABG or blood test$).tw.
98	or/79-80,90-97
99	(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).tw.
100	or/62,78,98-99
101	55 or 100
102	20 and 101
103	exp "SENSITIVITY AND SPECIFICITY"/
104	exp BLOOD CHEMICAL ANALYSIS/
105	URINALYSIS/
106	(detect$ or diagnos$ or predict$ or sensitiv$ or accuracy or test$).mp.
107	or/103-106
108	102 and 107

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	KETOACIDOSIS/
11	KETONURIA/
12	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS/
15	diabet$.mp.

Update 2015

16	or/14-15
17	and/13,16
18	DIABETIC KETOACIDOSIS/
19	(DK or DKA).ti,ab.
20	or/18-19
21	9 and (17 or 20)
22	POLYDIPSIA/
23	THIRST/
24	(polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).ti,ab.
25	or/22-24
26	POLYURIA/
27	(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).ti,ab.
28	or/26-27
29	WEIGHT REDUCTION/
30	(weight adj3 (loss or lost or reduc$)).ti,ab.
31	or/29-30
32	DEHYDRATION/
33	(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).ti,ab.
34	or/32-33
35	NAUSEA/ or VOMITING/
36	(nausea or emesis or vomit$).ti,ab.
37	or/35-36
38	exp ABDOMINAL PAIN/ or ACUTE ABDOMEN/
39	((abdom#n$ adj3 pain$) or acute abdomen).ti,ab.
40	or/38-39
41	DYSPNEA/ or TACHYPNEA/ or HYPERVENTILATION/
42	(respirat$ adj (distress or rate)).ti,ab.
43	(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).ti,ab.
44	(gasping or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).ti,ab.
45	or/41-44
46	CONSCIOUSNESS LEVEL/
47	CONFUSION/ or DELIRIUM/
48	(conscious$ or confus$ or deliri$ or mental state$).ti,ab.
49	or/46-48
50	PHYSICAL DISEASE BY BODY FUNCTION/
51	(sign? or symptom? or indicat$ or presentation).ti,ab.
52	((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?)).ti,ab.
53	or/50-52
54	or/25,28,31,34,37,40,45,49,53
55	HYPERGLYCEMIA/
56	hyperglyc?emi$.ti,ab.
57	((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?)).ti,ab.
58	GLUCOSE BLOOD LEVEL/
59	BLOOD GLUCOSE MONITORING/
60	BLOOD GLUCOSE METER/
61	(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
62	(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
63	or/55-62
64	KETOACIDOSIS/

Update 2015

65	KETONEMIA/
66	KETONURIA/
67	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).ti,ab.
68	KETONE/
69	KETONE BODY/
70	3-HYDROXYBUTYRIC ACID/
71	HYDROXYBUTYRIC ACID/
72	or/68-71
73	URINALYSIS/ or BLOOD ANALYSIS/ or BLOOD CHEMISTRY/
74	and/72-73
75	KETONE/an [Drug Analysis]
76	KETONE BODY/an [Drug Analysis]
77	3-HYDROXYBUTYRIC ACID/an [Drug Analysis]
78	HYDROXYBUTYRIC ACID/an [Drug Analysis]
79	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
80	((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
81	or/64-67,74-80
82	ACIDOSIS/
83	(acidosis or (blood? adj3 acid$) or acid?emi$).ti,ab.
84	ACID BASE BALANCE/
85	BLOOD pH/
86	BICARBONATE/
87	ELECTROLYTE/
88	or/84-87
89	BLOOD ANALYSIS/ or BLOOD CHEMISTRY/ or BLOOD GAS ANALYSIS/
90	and/88-89
91	BICARBONATE BLOOD LEVEL/
92	exp ELECTROLYTE BLOOD LEVEL/
93	ACID BASE BALANCE/an [Drug Analysis]
94	BICARBONATE/an [Drug Analysis]
95	ELECTROLYTE/an [Drug Analysis]
96	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).ti,ab.
97	(blood gas or ABG or blood test$).ti,ab.
98	or/82-83,90-97
99	(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).ti,ab.
100	or/63,81,98-99
101	or/54,100
102	"SENSITIVITY AND SPECIFICITY"/
103	DIAGNOSTIC ACCURACY/
104	DIAGNOSTIC TEST/
105	DIAGNOSTIC VALUE/
106	PREDICTIVE VALUE/
107	(detect$ or diagnos$ or predict$ or sensitiv$ or specificity).tw.
108	or/102-107
109	and/21,101,108
110	limit 109 to english language
111	conference abstract.pt.
112	letter.pt. or LETTER/

Update 2015

113	note.pt.
114	editorial.pt.
115	CASE REPORT/ or CASE STUDY/
116	(letter or comment* or abstracts).ti.
117	or/111-116
118	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
119	117 not 118
120	ANIMAL/ not HUMAN/
121	NONHUMAN/
122	exp ANIMAL EXPERIMENT/
123	exp EXPERIMENTAL ANIMAL/
124	ANIMAL MODEL/
125	exp RODENT/
126	(rat or rats or mouse or mice).ti.
127	or/119-126
128	110 not 127

F.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**
- **acid/base status?**

Update 2015

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/

6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	exp VITAL SIGNS/
22	SYMPTOM ASSESSMENT/
23	exp AIRWAY MANAGEMENT/
24	exp INTUBATION/
25	exp NEUROLOGIC EXAMINATION/
26	BLOOD PRESSURE DETERMINATION/
27	exp CONFUSION/
28	CONSCIOUSNESS DISORDERS/
29	GLASGOW COMA SCALE/
30	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ti.
31	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ab. /freq=2
32	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ti.
33	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ab. /freq=2
34	or/21-33
35	and/20,34
36	exp BODY WEIGHT CHANGES/
37	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.
38	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab. /freq=2
39	or/36-38
40	and/20,39
41	DEHYDRATION/
42	(dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.
43	WATER-ELECTROLYTE BALANCE/
44	WATER-ELECTROLYTE IMBALANCE/
45	exp FLUID THERAPY/
46	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ti.
47	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
48	(volume adj3 expan$).ti,ab.
49	OLIGURIA/
50	((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.
51	REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)

Update 2015

52	capillary refill$.ti,ab.
53	SKIN/
54	(skin turgor or skin colo?r or pinch test).ti,ab.
55	EYE/
56	sunken eye?.ti,ab.
57	exp LOWER EXTREMITY/
58	exp UPPER EXTREMITY/
59	(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
60	MOUTH MUCOSA/
61	(mucosa or mucous membrane?).ti,ab.
62	or/41-61
63	and/20,62
64	ELECTROCARDIOGRAPHY/
65	(electrocardio$ or ECG).ti,ab.
66	or/64-65
67	and/20,66
68	or/35,40,63,67
69	CLINICAL LABORATORY TECHNIQUES/
70	BLOOD GAS ANALYSIS/
71	URINALYSIS/
72	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
73	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
74	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
75	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
76	or/69-75
77	and/20,76
78	BLOOD GLUCOSE/an [Analysis]
79	GLUCOSE TOLERANCE TEST/
80	(OGTT or FPG or fasting plasma glucose).ti,ab.
81	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ti.
82	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ab. /freq=2
83	or/78-82
84	and/20,83
85	KETONES/an, bl, ur [Analysis, Blood, Urine]
86	exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
87	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
88	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
89	or/85-88
90	POINT-OF-CARE SYSTEMS/
91	(near patient or bedside or bed side or point of care).ti,ab.
92	or/89-91
93	and/20,92
94	PLASMA/ and OSMOLAR CONCENTRATION/

Update 2015

95	((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.
96	HYDROGEN-ION CONCENTRATION/
97	ACID-BASE EQUILIBRIUM/
98	ACID-BASE IMBALANCE/
99	BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
100	ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
101	SODIUM/an, bl, ur [Analysis, Blood, Urine]
102	POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
103	exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
104	UREA/an, bl, ur [Analysis, Blood, Urine]
105	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).ti,ab.
106	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).ti,ab.
107	(blood gas or ABG).ti,ab.
108	or/94-107
109	and/20,108
110	or/77,84,93,109
111	or/68,110
112	*HYPOVOLEMIA/
113	*HYPOGLYCEMIA/
114	*HYPOKALEMIA/
115	*HYPONATREMIA/
116	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ti.
117	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2
118	*ACIDOSIS/
119	(acidosis or (blood? adj3 acid$) or acid?emi$).ti.
120	(acidosis or (blood? adj3 acid$) or acid?emi$).ab. /freq=2
121	*BRAIN EDEMA/
122	((cerebral or brain) adj3 (oedema? or edema?)).ti.
123	((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
124	*VENOUS THROMBOSIS/
125	(DVT or deep vein thrombo$).ti.
126	(DVT or deep vein thrombo$).ab. /freq=2
127	exp *RESPIRATORY ASPIRATION/
128	exp *PNEUMONIA, ASPIRATION/
129	aspiration.ti. or aspiration.ab. /freq=2
130	or/112-129
131	exp "SENSITIVITY AND SPECIFICITY"/
132	((pre test or pretest or post test or posttest) adj probability).ti,ab.
133	(predictive value$ or PPV or NPV).ti,ab.
134	likelihood ratio$.ti,ab.
135	LIKELIHOOD FUNCTIONS/
136	(ROC curve$ or AUC).ti,ab.
137	(detect$ or diagnos$ or predict$ or accuracy or test$).ti,ab.
138	di.xs.
139	or/131-138
140	and/20,130,139
141	or/111,140
142	LETTER/
143	EDITORIAL/
144	NEWS/

Update 2015

145	exp HISTORICAL ARTICLE/
146	ANECDOTES AS TOPIC/
147	COMMENT/
148	CASE REPORT/
149	(letter or comment* or abstracts).ti.
150	or/142-149
151	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
152	150 not 151
153	ANIMALS/ not HUMANS/
154	exp ANIMALS, LABORATORY/
155	exp ANIMAL EXPERIMENTATION/
156	exp MODELS, ANIMAL/
157	exp RODENTIA/
158	(rat or rats or mouse or mice).ti.
159	or/152-158
160	141 not 159
161	limit 160 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
5	or/1-4
6	(diabetic ketoacidosis or DK or DKA).ti,ab.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
8	diabet$.mp.
9	and/7-8
10	5 and (6 or 9)
11	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ti.
12	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ab. /freq=2
13	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ti.
14	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ab. /freq=2
15	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.
16	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab. /freq=2
17	(dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.
18	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ti.

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19	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
20	(volume adj3 expan$).ti,ab.
21	((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.
22	capillary refill$.ti,ab.
23	(skin turgor or skin colo?r or pinch test).ti,ab.
24	sunken eye?.ti,ab.
25	(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
26	(mucosa or mucous membrane?).ti,ab.
27	(electrocardio$ or ECG).ti,ab.
28	or/11-27
29	and/10,28
30	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
31	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
32	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
33	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
34	(OGTT or FPG or fasting plasma glucose).ti,ab.
35	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ti.
36	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ab. /freq=2
37	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
38	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
39	(near patient or bedside or bed side or point of care).ti,ab.
40	((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.
41	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).ti,ab.
42	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).ti,ab.
43	(blood gas or ABG).ti,ab.
44	or/30-43
45	and/10,44
46	or/29,45
47	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ti.
48	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2
49	(acidosis or (blood? adj3 acid$) or acid?emi$).ti.
50	(acidosis or (blood? adj3 acid$) or acid?emi$).ab. /freq=2
51	((cerebral or brain) adj3 (oedema? or edema?)).ti.
52	((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
53	(DVT or deep vein thrombo$).ti.
54	(DVT or deep vein thrombo$).ab. /freq=2

Update 2015

55	aspiration.ti. or aspiration.ab. /freq=2
56	or/47-55
57	((pre test or pretest or post test or posttest) adj probability).ti,ab.
58	(predictive value$ or PPV or NPV).ti,ab.
59	likelihood ratio$.ti,ab.
60	(ROC curve$ or AUC).ti,ab.
61	(detect$ or diagnos$ or predict$ or accuracy or test$).ti,ab.
62	or/57-61
63	and/10,56,62
64	or/46,63

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	exp VITAL SIGNS/
22	SYMPTOM ASSESSMENT/
23	exp AIRWAY MANAGEMENT/
24	exp INTUBATION/
25	exp NEUROLOGIC EXAMINATION/
26	BLOOD PRESSURE DETERMINATION/
27	exp CONFUSION/
28	CONSCIOUSNESS DISORDERS/
29	GLASGOW COMA SCALE/
30	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ti.
31	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ab. /freq=2
32	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$

Update 2015

	or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ti.
33	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ab. /freq=2
34	or/21-33
35	and/20,34
36	exp BODY WEIGHT CHANGES/
37	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.
38	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab. /freq=2
39	or/36-38
40	and/20,39
41	DEHYDRATION/
42	(dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.
43	WATER-ELECTROLYTE BALANCE/
44	WATER-ELECTROLYTE IMBALANCE/
45	exp FLUID THERAPY/
46	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ti.
47	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
48	(volume adj3 expan$).ti,ab.
49	OLIGURIA/
50	((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.
51	REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)
52	capillary refill$.ti,ab.
53	SKIN/
54	(skin turgor or skin colo?r or pinch test).ti,ab.
55	EYE/
56	sunken eye?.ti,ab.
57	exp LOWER EXTREMITY/
58	exp UPPER EXTREMITY/
59	(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
60	MOUTH MUCOSA/
61	(mucosa or mucous membrane?).ti,ab.
62	or/41-61
63	and/20,62
64	ELECTROCARDIOGRAPHY/
65	(electrocardio$ or ECG).ti,ab.
66	or/64-65
67	and/20,66
68	or/35,40,63,67
69	CLINICAL LABORATORY TECHNIQUES/
70	BLOOD GAS ANALYSIS/
71	URINALYSIS/
72	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
73	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2

Update 2015

74	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
75	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
76	or/69-75
77	and/20,76
78	BLOOD GLUCOSE/an [Analysis]
79	GLUCOSE TOLERANCE TEST/
80	(OGTT or FPG or fasting plasma glucose).ti,ab.
81	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ti.
82	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ab. /freq=2
83	or/78-82
84	and/20,83
85	KETONES/an, bl, ur [Analysis, Blood, Urine]
86	exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
87	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
88	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
89	or/85-88
90	POINT-OF-CARE SYSTEMS/
91	(near patient or bedside or bed side or point of care).ti,ab.
92	or/89-91
93	and/20,92
94	PLASMA/ and OSMOLAR CONCENTRATION/
95	((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.
96	HYDROGEN-ION CONCENTRATION/
97	ACID-BASE EQUILIBRIUM/
98	ACID-BASE IMBALANCE/
99	BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
100	ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
101	SODIUM/an, bl, ur [Analysis, Blood, Urine]
102	POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
103	exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
104	UREA/an, bl, ur [Analysis, Blood, Urine]
105	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).ti,ab.
106	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).ti,ab.
107	(blood gas or ABG).ti,ab.
108	or/94-107
109	and/20,108
110	or/77,84,93,109
111	or/68,110
112	*HYPOVOLEMIA/

Update 2015

113	*HYPOGLYCEMIA/
114	*HYPOKALEMIA/
115	*HYPONATREMIA/
116	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ti.
117	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2
118	*ACIDOSIS/
119	(acidosis or (blood? adj3 acid$) or acid?emi$).ti.
120	(acidosis or (blood? adj3 acid$) or acid?emi$).ab. /freq=2
121	*BRAIN EDEMA/
122	((cerebral or brain) adj3 (oedema? or edema?)).ti.
123	((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
124	*VENOUS THROMBOSIS/
125	(DVT or deep vein thrombo$).ti.
126	(DVT or deep vein thrombo$).ab. /freq=2
127	exp *RESPIRATORY ASPIRATION/
128	exp *PNEUMONIA, ASPIRATION/
129	aspiration.ti. or aspiration.ab. /freq=2
130	or/112-129
131	exp "SENSITIVITY AND SPECIFICITY"/
132	((pre test or pretest or post test or posttest) adj probability).ti,ab.
133	(predictive value$ or PPV or NPV).ti,ab.
134	likelihood ratio$.ti,ab.
135	LIKELIHOOD FUNCTIONS/
136	(ROC curve$ or AUC).ti,ab.
137	(detect$ or diagnos$ or predict$ or accuracy or test$).ti,ab.
138	di.xs.
139	or/131-138
140	and/20,130,139
141	or/111,140

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).tw,kw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,kw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,kw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).tw,kw,tx,jw,rw.
5	or/1-4
6	(diabetic ketoacidosis or DK or DKA).tw,kw,tx.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw,kw,tx.
8	diabet$.tw,kw,tx.
9	and/7-8
10	5 and (6 or 9)
11	SYMPTOM ASSESSMENT.kw.
12	INTUBATION.kw.
13	(NEUROLOGIC EXAMINATION or REFLEX).kw.
14	BLOOD PRESSURE DETERMINATION.kw.
15	CONSCIOUSNESS DISORDERS.kw.
16	GLASGOW COMA SCALE.kw.

17	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).tw,tx.
18	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).tw,kw,tx.
19	or/11-18
20	and/10,19
21	(BODY WEIGHT CHANGES or WEIGHT GAIN or WEIGHT LOSS).kw.
22	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).tw,tx.
23	or/21-22
24	and/10,23
25	(dehydrat$ or hydration status or rehydrate$ or re hydrat$).tw,kw,tx.
26	WATER-ELECTROLYTE BALANCE.kw.
27	WATER-ELECTROLYTE IMBALANCE.kw.
28	(FLUID THERAPY or HYPODERMOCLYSIS).kw.
29	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).tw,tx.
30	(volume adj3 expan$).tw,tx.
31	OLIGURIA.kw.
32	((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).tw,tx.
33	(REGIONAL BLOOD FLOW and (FINGERS or CAPILLARIES)).kw.
34	capillary refill$.tw,tx.
35	SKIN.kw.
36	(skin turgor or skin colo?r or pinch test).tw,tx.
37	EYE.kw.
38	sunken eye?.tw,tx.
39	(LOWER EXTREMITY or FOOT or TOES).kw.
40	(UPPER EXTREMITY or HAND or FINGERS).kw.
41	(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).tw,tx.
42	MOUTH MUCOSA.kw.
43	(mucosa or mucous membrane?).tw,tx.
44	or/25-43
45	and/10,44
46	ELECTROCARDIOGRAPHY.kw.
47	(electrocardio$ or ECG).tw,tx.
48	or/46-47
49	and/10,48
50	or/20,24,45,49
51	CLINICAL LABORATORY TECHNIQUES.kw.
52	BLOOD GAS ANALYSIS.kw.
53	URINALYSIS.kw.
54	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).tw,tx.
55	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).tw,tx.
56	or/51-55
57	and/10,56
58	BLOOD GLUCOSE.kw.
59	GLUCOSE TOLERANCE TEST.kw.
60	(OGTT or FPG or fasting plasma glucose).tw,tx.

Update 2015

61	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).tw,tx.
62	or/58-61
63	and/10,62
64	KETONES.kw.
65	(KETONE BODIES or 3-HYDROXYBUTYRIC ACID or HYDROXYBUTYRATES or ACETOACETATES or ACETONE).kw.
66	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.
67	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.
68	or/64-67
69	POINT-OF-CARE SYSTEMS.kw.
70	(near patient or bedside or bed side or point of care).tw,tx.
71	or/68-70
72	and/10,71
73	(PLASMA and OSMOLAR CONCENTRATION).kw.
74	((plasma or serum or blood) adj3 (osmola$ or tonicity)).tw,tx.
75	HYDROGEN-ION CONCENTRATION.kw.
76	ACID-BASE EQUILIBRIUM.kw.
77	ACID-BASE IMBALANCE.kw.
78	BICARBONATES.kw.
79	ELECTROLYTES.kw.
80	SODIUM.kw.
81	POTASSIUM.kw.
82	(CHLORIDES or SODIUM CHLORIDE or POTASSIUM CHLORIDE).kw.
83	UREA.kw.
84	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).tw,tx.
85	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).tw,tx.
86	(blood gas or ABG).tw,tx.
87	or/73-86
88	and/10,87
89	or/57,63,72,88
90	or/50,89
91	HYPOVOLEMIA.kw.
92	HYPOGLYCEMIA.kw.
93	HYPOKALEMIA.kw.
94	HYPONATREMIA.kw.
95	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).tw,tx.
96	ACIDOSIS.kw.
97	(acidosis or (blood? adj3 acid$) or acid?emi$).tw,tx.
98	BRAIN EDEMA.kw.
99	((cerebral or brain) adj3 (oedema? or edema?)).tw,tx.
100	VENOUS THROMBOSIS.kw.
101	(DVT or deep vein thrombo$).tw,tx.
102	aspiration.tw,kw,tx.

Update 2015

103	or/91-102
104	("SENSITIVITY AND SPECIFICITY" or "PREDICTIVE VALUE OF TESTS").kw.
105	((pre test or pretest or post test or posttest) adj probability).tw,tx.
106	(predictive value$ or PPV or NPV).tw,tx.
107	likelihood ratio$.tw,tx.
108	LIKELIHOOD FUNCTIONS.kw.
109	(ROC curve$ or AUC).tw,tx.
110	(detect$ or diagnos$ or predict$ or accuracy or test$).tw,tx.
111	or/104-110
112	and/10,103,111
113	or/90,112

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).tw,jx,rw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).tw.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	exp VITAL SIGNS/
22	SYMPTOM ASSESSMENT/
23	exp AIRWAY MANAGEMENT/
24	exp INTUBATION/
25	exp NEUROLOGIC EXAMINATION/
26	BLOOD PRESSURE DETERMINATION/
27	exp CONFUSION/
28	CONSCIOUSNESS DISORDERS/
29	GLASGOW COMA SCALE/
30	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).tw.
31	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).tw.
32	or/21-31

Update 2015

33	and/20,32
34	exp BODY WEIGHT CHANGES/
35	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).tw.
36	or/34-35
37	and/20,36
38	DEHYDRATION/
39	(dehydrat$ or hydration status or rehydrate$ or re hydrat$).tw.
40	WATER-ELECTROLYTE BALANCE/
41	WATER-ELECTROLYTE IMBALANCE/
42	exp FLUID THERAPY/
43	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).tw.
44	(volume adj3 expan$).tw.
45	OLIGURIA/
46	((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).tw.
47	REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)
48	capillary refill$.tw.
49	SKIN/
50	(skin turgor or skin colo?r or pinch test).tw.
51	EYE/
52	sunken eye?.tw.
53	exp LOWER EXTREMITY/
54	exp UPPER EXTREMITY/
55	(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).tw.
56	MOUTH MUCOSA/
57	(mucosa or mucous membrane?).tw.
58	or/38-57
59	and/20,58
60	ELECTROCARDIOGRAPHY/
61	(electrocardio$ or ECG).tw.
62	or/60-61
63	and/20,62
64	or/33,37,59,63
65	CLINICAL LABORATORY TECHNIQUES/
66	BLOOD GAS ANALYSIS/
67	URINALYSIS/
68	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).tw.
69	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).tw.
70	or/65-69
71	and/20,70
72	BLOOD GLUCOSE/an [Analysis]
73	GLUCOSE TOLERANCE TEST/
74	(OGTT or FPG or fasting plasma glucose).tw.
75	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).tw.
76	or/72-75
77	and/20,76
78	KETONES/an, bl, ur [Analysis, Blood, Urine]
79	exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]

Update 2015

80	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.
81	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.
82	or/78-81
83	POINT-OF-CARE SYSTEMS/
84	(near patient or bedside or bed side or point of care).tw.
85	or/82-84
86	and/20,85
87	PLASMA/ and OSMOLAR CONCENTRATION/
88	((plasma or serum or blood) adj3 (osmola$ or tonicity)).tw.
89	HYDROGEN-ION CONCENTRATION/
90	ACID-BASE EQUILIBRIUM/
91	ACID-BASE IMBALANCE/
92	BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
93	ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
94	SODIUM/an, bl, ur [Analysis, Blood, Urine]
95	POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
96	exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
97	UREA/an, bl, ur [Analysis, Blood, Urine]
98	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).tw.
99	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).tw.
100	(blood gas or ABG).tw.
101	or/87-100
102	and/20,101
103	or/71,77,86,102
104	or/64,103
105	*HYPOVOLEMIA/
106	*HYPOGLYCEMIA/
107	*HYPOKALEMIA/
108	*HYPONATREMIA/
109	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).tw.
110	*ACIDOSIS/
111	(acidosis or (blood? adj3 acid$) or acid?emi$).tw.
112	*BRAIN EDEMA/
113	((cerebral or brain) adj3 (oedema? or edema?)).tw.
114	*VENOUS THROMBOSIS/
115	(DVT or deep vein thrombo$).tw.
116	exp *RESPIRATORY ASPIRATION/
117	exp *PNEUMONIA, ASPIRATION/
118	aspiration.tw.
119	or/105-118
120	exp "SENSITIVITY AND SPECIFICITY"/
121	((pre test or pretest or post test or posttest) adj probability).tw.
122	(predictive value$ or PPV or NPV).tw.
123	likelihood ratio$.tw.

Update 2015

124	LIKELIHOOD FUNCTIONS/
125	(ROC curve$ or AUC).tw.
126	(detect$ or diagnos$ or predict$ or accuracy or test$).tw.
127	di.xs.
128	or/120-127
129	and/20,119,128
130	or/104,129

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	NON INSULIN DEPENDENT DIABETES MELLITUS/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	JUVENILE DIABETES MELLITUS/
20	or/13,18-19
21	KETOACIDOSIS/
22	KETONURIA/
23	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
24	or/21-23
25	and/20,24
26	DIABETIC KETOACIDOSIS/
27	(DK or DKA).ti,ab.
28	or/26-27
29	9 and (25 or 28)
30	VITAL SIGN/
31	CLINICAL OBSERVATION/
32	CLINICAL ASSESSMENT/
33	PATIENT ASSESSMENT/
34	SYMPTOM ASSESSMENT/
35	BODY TEMPERATURE MEASUREMENT/
36	BLOOD PRESSURE MEASUREMENT/
37	BLOOD PRESSURE MONITORING/
38	HEART RATE/
39	PULSE RATE/

Update 2015

40	BREATHING RATE/
41	RESPIRATION CONTROL/
42	exp RESPIRATORY TRACT INTUBATION/
43	STOMACH INTUBATION/
44	CONSCIOUSNESS LEVEL/
45	CONSCIOUSNESS DISORDER/
46	exp CONFUSION/
47	exp DELIRIUM/
48	NEUROLOGIC EXAMINATION/
49	GLASGOW COMA SCALE/
50	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ti.
51	((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ab. /freq=2
52	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ti.
53	(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ab. /freq=2
54	or/30-53
55	and/29,54
56	WEIGHT CHANGE/
57	WEIGHT FLUCTUATION/
58	WEIGHT GAIN/
59	WEIGHT REDUCTION/
60	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.
61	(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab. /freq=2
62	or/56-61
63	and/29,62
64	DEHYDRATION/
65	(dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.
66	FLUID BALANCE/
67	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ti.
68	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
69	(volume adj3 expan$).ti,ab.
70	OLIGURIA/
71	URINE OUTPUT/
72	((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.
73	CAPILLARY FLOW/
74	capillary refill$.ti,ab.
75	SKIN TURGOR/
76	(skin turgor or skin colo?r or pinch test).ti,ab.
77	EYE/
78	sunken eye?.ti,ab.
79	COLD LIMB/
80	(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.

Update 2015

81	MUCOSAL DRYNESS/
82	(mucosa or mucous membrane?).ti,ab.
83	or/64-82
84	and/29,83
85	ELECTROCARDIOGRAPHY/
86	(electrocardio$ or ECG).ti,ab.
87	or/85-86
88	and/29,87
89	or/55,63,84,88
90	exp *LABORATORY DIAGNOSIS/
91	exp *BLOOD GAS ANALYSIS/
92	*URINALYSIS/
93	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
94	(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
95	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
96	((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
97	or/90-96
98	and/29,97
99	BLOOD GLUCOSE MONITORING/
100	GLUCOSE BLOOD LEVEL/
101	exp GLUCOSE TOLERANCE TEST/
102	(OGTT or FPG or fasting plasma glucose).ti,ab.
103	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ti.
104	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ab. /freq=2
105	or/99-104
106	and/29,105
107	KETONE/an [Drug Analysis]
108	KETONE BODY/an [Drug Analysis]
109	3-HYDROXYBUTYRIC ACID/an [Drug Analysis]
110	HYDROXYBUTYRIC ACID/an [Drug Analysis]
111	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
112	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
113	"POINT OF CARE TESTING"/
114	(near patient or bedside or bed side or point of care).ti,ab.
115	or/107-114
116	and/29,115
117	exp OSMOLALITY/
118	((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.
119	BLOOD pH/
120	ACID BASE BALANCE/

Update 2015

121	BICARBONATE BLOOD LEVEL/
122	exp ELECTROLYTE BLOOD LEVEL/
123	exp URINE LEVEL/
124	UREA BLOOD LEVEL/
125	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).ti,ab.
126	((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).ti,ab.
127	(blood gas or ABG).ti,ab.
128	or/117-127
129	and/29,128
130	or/98,106,116,129
131	or/89,130
132	exp *HYPOVOLEMIA/
133	*HYPOGLYCAEMIA/
134	*HYPOKALEMIA/
135	*HYPONATREMIA/
136	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ti.
137	(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2
138	*ACIDOSIS/
139	(acidosis or (blood? adj3 acid$) or acid?emi$).ti.
140	(acidosis or (blood? adj3 acid$) or acid?emi$).ab. /freq=2
141	*BRAIN EDEMA/
142	((cerebral or brain) adj3 (oedema? or edema?)).ti.
143	((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
144	*DEEP VEIN THROMBOSIS/
145	(DVT or deep vein thrombo$).ti.
146	(DVT or deep vein thrombo$).ab. /freq=2
147	*PULMONARY ASPIRATION/
148	*ASPIRATION PNEUMONIA/
149	aspiration.ti. or aspiration.ab. /freq=2
150	or/132-149
151	"SENSITIVITY AND SPECIFICITY"/
152	PREDICTIVE VALUE/
153	DIAGNOSTIC VALUE/
154	DIAGNOSTIC ACCURACY/
155	((pre test or pretest or post test or posttest) adj probability).ti,ab.
156	(predictive value$ or PPV or NPV).ti,ab.
157	likelihood ratio$.ti,ab.
158	di.fs.
159	or/151-158
160	and/29,150,159
161	or/131,160
162	conference abstract.pt.
163	letter.pt. or LETTER/
164	note.pt.
165	editorial.pt.
166	CASE REPORT/ or CASE STUDY/
167	(letter or comment* or abstracts).ti.
168	or/162-167
169	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
170	168 not 169

Update 2015

171	ANIMAL/ not HUMAN/
172	NONHUMAN/
173	exp ANIMAL EXPERIMENT/
174	exp EXPERIMENTAL ANIMAL/
175	ANIMAL MODEL/
176	exp RODENT/
177	(rat or rats or mouse or mice).ti.
178	or/170-177
179	161 not 178
180	limit 179 to english language

F.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Update 2015

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	exp FLUID THERAPY/
22	REHYDRATION SOLUTIONS/
23	WATER-ELECTROLYTE BALANCE/

24	WATER-ELECTROLYTE IMBALANCE/
25	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).ti,ab.
26	or/21-25
27	and/20,26
28	DRUG ADMINISTRATION ROUTES/
29	ADMINISTRATION, ORAL/
30	ADMINISTRATION, INTRAVENOUS/
31	INFUSIONS, INTRAVENOUS/
32	INFUSIONS, INTRAOSSEOUS/
33	exp INFUSIONS, SUBCUTANEOUS/
34	INFUSION PUMP/
35	INTUBATION, GASTROINTESTINAL/
36	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).ti,ab.
37	(fluid bolus or two bag or ORT).ti,ab.
38	or/28-37
39	and/20,38
40	TIME FACTORS/
41	DRUG ADMINISTRATION SCHEDULE/
42	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).ti,ab.
43	or/40-42
44	and/20,43
45	SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
46	exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
47	GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
48	GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
49	SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
50	exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
51	POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
52	PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
53	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
54	or/45-53
55	and/20,54
56	or/27,39,44,55
57	LETTER/
58	EDITORIAL/
59	NEWS/
60	exp HISTORICAL ARTICLE/
61	ANECDOTES AS TOPIC/
62	COMMENT/
63	CASE REPORT/
64	(letter or comment* or abstracts).ti.
65	or/57-64

Update 2015

66	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
67	65 not 66
68	ANIMALS/ not HUMANS/
69	exp ANIMALS, LABORATORY/
70	exp ANIMAL EXPERIMENTATION/
71	exp MODELS, ANIMAL/
72	exp RODENTIA/
73	(rat or rats or mouse or mice).ti.
74	or/67-73
75	56 not 74
76	limit 75 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
5	or/1-4
6	(diabetic ketoacidosis or DK or DKA).ti,ab.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
8	diabet$.mp.
9	and/7-8
10	5 and (6 or 9)
11	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).ti,ab.
12	and/10-11
13	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).ti,ab.
14	(fluid bolus or two bag or ORT).ti,ab.
15	or/13-14
16	and/10,15
17	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).ti,ab.
18	and/10,17
19	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
20	and/10,19
21	or/12,16,18,20
22	limit 21 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/

Update 2015

2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	exp FLUID THERAPY/
22	REHYDRATION SOLUTIONS/
23	WATER-ELECTROLYTE BALANCE/
24	WATER-ELECTROLYTE IMBALANCE/
25	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).ti,ab.
26	or/21-25
27	and/20,26
28	DRUG ADMINISTRATION ROUTES/
29	ADMINISTRATION, ORAL/
30	ADMINISTRATION, INTRAVENOUS/
31	INFUSIONS, INTRAVENOUS/
32	INFUSIONS, INTRAOSSEOUS/
33	exp INFUSIONS, SUBCUTANEOUS/
34	INFUSION PUMP/
35	INTUBATION, GASTROINTESTINAL/
36	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).ti,ab.
37	(fluid bolus or two bag or ORT).ti,ab.
38	or/28-37
39	and/20,38
40	TIME FACTORS/
41	DRUG ADMINISTRATION SCHEDULE/
42	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).ti,ab.
43	or/40-42
44	and/20,43

Update 2015

45	SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
46	exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
47	GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
48	GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
49	SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
50	exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
51	POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
52	PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
53	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
54	or/45-53
55	and/20,54
56	or/27,39,44,55

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).kw,tw,tx,jw,rw.
5	or/1-4
6	(diabetic ketoacidosis or DK or DKA).kw,tw,tx.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).kw,tw,tx.
8	diabet$.kw,tw,tx.
9	and/7-8
10	5 and (6 or 9)
11	(FLUID THERAPY or HYPODERMOCLYSIS).kw.
12	REHYDRATION SOLUTIONS.kw.
13	WATER-ELECTROLYTE BALANCE.kw.
14	WATER-ELECTROLYTE IMBALANCE.kw.
15	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).tw,tx.
16	or/11-15
17	and/10,16
18	DRUG ADMINISTRATION ROUTES.kw.
19	ADMINISTRATION, ORAL.kw.
20	ADMINISTRATION, INTRAVENOUS.kw.
21	INFUSIONS, INTRAVENOUS.kw.
22	INFUSIONS, INTRAOSSEOUS.kw.
23	INFUSIONS, SUBCUTANEOUS.kw.
24	INFUSION PUMP.kw.
25	INTUBATION, GASTROINTESTINAL.kw.
26	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).tw,tx.

Update 2015

27	(fluid bolus or two bag or ORT).tw,tx.
28	or/18-27
29	and/10,28
30	TIME FACTORS.kw.
31	DRUG ADMINISTRATION SCHEDULE.kw.
32	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).tw,tx.
33	or/30-32
34	and/10,33
35	SODIUM.kw.
36	CHLORIDE?.kw.
37	GLUCOSE.kw.
38	GLUCOSE SOLUTION, HYPERTONIC.kw.
39	SALINE SOLUTION, HYPERTONIC.kw.
40	BICARBONATE?.kw.
41	POTASSIUM.kw.
42	PHOSPHATES.kw.
43	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).tw,tx.
44	or/35-43
45	and/10,44
46	or/17,29,34,45

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).tw,jx,rw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).tw.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	exp FLUID THERAPY/

Update 2015

22	REHYDRATION SOLUTIONS/
23	WATER-ELECTROLYTE BALANCE/
24	WATER-ELECTROLYTE IMBALANCE/
25	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).tw.
26	or/21-25
27	and/20,26
28	DRUG ADMINISTRATION ROUTES/
29	ADMINISTRATION, ORAL/
30	ADMINISTRATION, INTRAVENOUS/
31	INFUSIONS, INTRAVENOUS/
32	INFUSIONS, INTRAOSSEOUS/
33	exp INFUSIONS, SUBCUTANEOUS/
34	INFUSION PUMP/
35	INTUBATION, GASTROINTESTINAL/
36	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).tw.
37	(fluid bolus or two bag or ORT).tw.
38	or/28-37
39	and/20,38
40	TIME FACTORS/
41	DRUG ADMINISTRATION SCHEDULE/
42	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).tw.
43	or/40-42
44	and/20,43
45	SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
46	exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
47	GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
48	GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
49	SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
50	exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
51	POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
52	PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
53	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).tw.
54	or/45-53
55	and/20,54
56	or/27,39,44,55

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/

Update 2015

4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	NON INSULIN DEPENDENT DIABETES MELLITUS/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	JUVENILE DIABETES MELLITUS/
20	or/13,18-19
21	KETOACIDOSIS/
22	KETONURIA/
23	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
24	or/21-23
25	and/20,24
26	DIABETIC KETOACIDOSIS/
27	(DK or DKA).ti,ab.
28	or/26-27
29	9 and (25 or 28)
30	FLUID THERAPY/
31	FLUID RESUSCITATION/
32	exp REHYDRATION/
33	exp ELECTROLYTE BALANCE/
34	exp ELECTROLYTE DISTURBANCE/
35	((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).ti,ab.
36	or/30-35
37	and/29,36
38	DRUG ADMINISTRATION ROUTE/
39	INTRAVENOUS ADMINISTRATION/
40	INTRAGASTRIC DRUG ADMINISTRATION/
41	INTRAOSSEOUS DRUG ADMINISTRATION/
42	INTRAPERITONEAL DRUG ADMINISTRATION/
43	SUBCUTANEOUS DRUG ADMINISTRATION/
44	STOMACH INTUBATION/
45	ORAL REHYDRATION THERAPY/
46	ORAL REHYDRATION SOLUTION/
47	INFUSION SYSTEM/
48	INFUSION PUMP/
49	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).ti,ab.

Update 2015

50	(fluid bolus or two bag or ORT).ti,ab.
51	or/38-50
52	and/29,51
53	INFUSION RATE/
54	DRUG DOSE REGIMEN/
55	DRUG ADMINISTRATION/
56	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).ti,ab.
57	or/53-56
58	and/29,57
59	INFUSION FLUID/ad, dt, ig, os, iv, po, pa, sc [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration]
60	SODIUM/ad, dt, ip, iv, po, pa, sc, th [Drug Administration, Drug Therapy, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
61	CHLORIDE/ad, dt, ip, iv, po, pa, sc, th [Drug Administration, Drug Therapy, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
62	SODIUM CHLORIDE/ad, dt, dl, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intradermal Drug Administration, Intragastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
63	GLUCOSE/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
64	GLUCOSE INFUSION/
65	BICARBONATE/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
66	POTASSIUM/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
67	PHOSPHATE/ad, dt, ig, ip, iv, po, pa, rc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Therapy]
68	exp ELECTROLYTE BLOOD LEVEL/
69	BICARBONATE BLOOD LEVEL/
70	GLUCOSE BLOOD LEVEL/
71	PHOSPHATE BLOOD LEVEL/
72	((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid? or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
73	or/59-72
74	and/29,73
75	or/37,52,58,74
76	conference abstract.pt.
77	letter.pt. or LETTER/
78	note.pt.

Update 2015

79	editorial.pt.
80	CASE REPORT/ or CASE STUDY/
81	(letter or comment* or abstracts).ti.
82	or/76-81
83	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
84	82 not 83
85	ANIMAL/ not HUMAN/
86	NONHUMAN/
87	exp ANIMAL EXPERIMENT/
88	exp EXPERIMENTAL ANIMAL/
89	ANIMAL MODEL/
90	exp RODENT/
91	(rat or rats or mouse or mice).ti.
92	or/84-91
93	75 not 92
94	limit 93 to english language

F.13 Type 1 and type 2 diabetes – diabetic ketoacidosis intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Update 2015

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	BRAIN EDEMA/
22	((brain or cerebral) adj3 (edema? or oedema? or swell$)).ti,ab.
23	INTRACRANIAL PRESSURE/
24	INTRACRANIAL HYPERTENSION/

25	((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens$)).ti,ab.
26	ICP.ti,ab.
27	or/21-26
28	DIURETICS, OSMOTIC/
29	osmotherap$.ti,ab.
30	(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).ti,ab.
31	SALINE SOLUTION, HYPERTONIC/
32	SODIUM CHLORIDE/
33	(hyperton$ adj3 (saline or solution?)).ti,ab.
34	(saline or sodium chloride or NaCl).ti,ab.
35	MANNITOL/
36	(mannitol or viaflo or viaflex).ti,ab.
37	or/28-36
38	and/20,27,37
39	limit 38 to english language
40	LETTER/
41	EDITORIAL/
42	NEWS/
43	exp HISTORICAL ARTICLE/
44	ANECDOTES AS TOPIC/
45	COMMENT/
46	CASE REPORT/
47	(letter or comment* or abstracts).ti.
48	or/40-47
49	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50	48 not 49
51	ANIMALS/ not HUMANS/
52	exp ANIMALS, LABORATORY/
53	exp ANIMAL EXPERIMENTATION/
54	exp MODELS, ANIMAL/
55	exp RODENTIA/
56	(rat or rats or mouse or mice).ti.
57	or/50-56
58	39 not 57

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(DK or DKA).ti,ab.
7	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
8	diabet$.mp.
9	and/7-8
10	5 and (6 or 9)
11	((brain or cerebral) adj3 (edema? or oedema? or swell$)).ti,ab.
12	((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens$)).ti,ab.

Update 2015

13	ICP.ti,ab.
14	or/11-13
15	osmotherap$.ti,ab.
16	(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).ti,ab.
17	(hyperton$ adj3 (saline or solution?)).ti,ab.
18	(saline or sodium chloride or NaCl).ti,ab.
19	(mannitol or viaflo or viaflex).ti,ab.
20	or/15-19
21	and/10,14,20
22	limit 21 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15	or/13-14
16	exp DIABETES MELLITUS/
17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	BRAIN EDEMA/
22	((brain or cerebral) adj3 (edema? or oedema? or swell$)).ti,ab.
23	INTRACRANIAL PRESSURE/
24	INTRACRANIAL HYPERTENSION/
25	((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens$)).ti,ab.
26	ICP.ti,ab.
27	or/21-26
28	DIURETICS, OSMOTIC/
29	osmotherap$.ti,ab.
30	(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).ti,ab.
31	SALINE SOLUTION, HYPERTONIC/
32	SODIUM CHLORIDE/
33	(hyperton$ adj3 (saline or solution?)).ti,ab.
34	(saline or sodium chloride or NaCl).ti,ab.
35	MANNITOL/
36	(mannitol or viaflo or viaflex).ti,ab.
37	or/28-36

Update 2015

38	and/20,27,37

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw.
5	or/1-4
6	DIABETIC KETOACIDOSIS.kw.
7	(DK or DKA).tw,tx.
8	or/6-7
9	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw,tx,kw.
10	diabet$.tw,tx,kw.
11	and/9-10
12	5 and (8 or 11)
13	((brain or cerebral) adj3 (edema? or oedema? or swell$)).tw,tx,kw.
14	((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens$)).tw,tx,kw.
15	ICP.tw,tx.
16	or/13-15
17	DIURETICS, OSMOTIC.kw.
18	osmotherap$.tw,tx.
19	(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).tw,tx.
20	(hyperton$ adj3 (saline or solution?)).tw,tx,kw.
21	(saline or sodium chloride or NaCl).tw,tx,kw.
22	(mannitol or viaflo or viaflex).tw,tx,kw.
23	or/17-22
24	and/12,16,23

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).tw.
12	or/10-11
13	exp KETOSIS/
14	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
15	or/13-14
16	exp DIABETES MELLITUS/

Update 2015

17	diabet$.mp.
18	or/16-17
19	and/15,18
20	9 and (12 or 19)
21	BRAIN EDEMA/
22	((brain or cerebral) adj3 (edema? or oedema? or swell$)).tw.
23	INTRACRANIAL PRESSURE/
24	INTRACRANIAL HYPERTENSION/
25	((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens$)).tw.
26	ICP.tw.
27	or/21-26
28	DIURETICS, OSMOTIC/
29	osmotherap$.tw.
30	(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).tw.
31	SALINE SOLUTION, HYPERTONIC/
32	SODIUM CHLORIDE/
33	(hyperton$ adj3 (saline or solution?)).tw.
34	(saline or sodium chloride or NaCl).tw.
35	MANNITOL/
36	(mannitol or viaflo or viaflex).tw.
37	or/28-36
38	and/20,27,37

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(DK or DKA).ti,ab.
12	or/10-11
13	KETOACIDOSIS/
14	KETONURIA/
15	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
16	or/13-15
17	exp DIABETES MELLITUS/
18	diabet$.mp.
19	or/17-18
20	and/16,19
21	9 and (12 or 20)
22	BRAIN EDEMA/
23	((brain or cerebral) adj3 (edema? or oedema? or swell$)).ti,ab.
24	INTRACRANIAL PRESSURE/
25	INTRACRANIAL HYPERTENSION/

Update 2015

26	((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens$)).ti,ab.
27	ICP.ti,ab.
28	or/22-27
29	exp OSMOTIC AGENT/
30	osmotherap$.ti,ab.
31	(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).ti,ab.
32	HYPERTONIC SOLUTION/
33	SODIUM CHLORIDE/
34	(hyperton$ adj3 (saline or solution?)).ti,ab.
35	(saline or sodium chloride or NaCl).ti,ab.
36	MANNITOL/
37	(mannitol or viaflo or viaflex).ti,ab.
38	or/29-37
39	and/21,28,38
40	limit 39 to english language
41	conference abstract.pt.
42	letter.pt. or LETTER/
43	note.pt.
44	editorial.pt.
45	CASE REPORT/ or CASE STUDY/
46	(letter or comment* or abstracts).ti.
47	or/41-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMAL/ not HUMAN/
51	NONHUMAN/
52	exp ANIMAL EXPERIMENT/
53	exp EXPERIMENTAL ANIMAL/
54	ANIMAL MODEL/
55	exp RODENT/
56	(rat or rats or mouse or mice).ti.
57	or/49-56
58	40 not 57

Update 2015

F.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/

6	RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7	or/1-6
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
9	clinical trial.pt.
10	exp CLINICAL TRIAL/
11	exp CLINICAL TRIALS AS TOPIC/
12	(clinic$ adj5 trial$).tw,sh.
13	PLACEBOS/
14	placebo$.tw,sh.
15	random$.tw,sh.
16	or/8-15
17	or/7,16
18	META ANALYSIS/
19	META ANALYSIS AS TOPIC/
20	meta analysis.pt.
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
22	(systematic$ adj5 (review$ or overview$)).tw,sh.
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.
24	or/18-23
25	review$.pt.
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
27	((hand or manual$) adj2 search$).tw.
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
29	(pooling or pooled or mantel haenszel).tw,sh.
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.
31	or/26-30
32	and/25,31
33	exp CASE-CONTROL STUDIES/
34	(case$ adj2 control$).tw.
35	exp COHORT STUDIES/
36	cohort$.tw.
37	or/33-36
38	or/17,24,32,37
39	letter.pt.
40	comment.pt.
41	editorial.pt.
42	historical article.pt.
43	or/39-42
44	38 not 43
45	ADOLESCENT/ or MINORS/
46	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
47	exp CHILD/
48	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
49	exp INFANT/
50	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
51	exp PEDIATRICS/ or exp PUBERTY/
52	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
53	or/45-52
54	exp KETOSIS/

Update 2015

55	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
56	(DK or DKA).ti,ab.
57	or/54-56
58	exp DIABETES MELLITUS/
59	diabet$.mp.
60	or/58-59
61	and/53,57,60
62	exp INSULINS/
63	INSULIN INFUSION SYSTEMS/
64	or/62-63
65	exp DRUG ADMINISTRATION SCHEDULE/
66	TIME FACTORS/
67	DOSE-RESPONSE RELATIONSHIP, DRUG/
68	DRUG DOSAGE CALCULATIONS/
69	or/65-68
70	and/64,69
71	exp INSULINS/ad [Administration & Dosage]
72	(insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or intermittent$ or time or timing)).ti,ab.
73	(insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading)).ti,ab.
74	or/70-73
75	and/61,74
76	and/44,75
77	LETTER/
78	EDITORIAL/
79	NEWS/
80	exp HISTORICAL ARTICLE/
81	ANECDOTES AS TOPIC/
82	COMMENT/
83	CASE REPORT/
84	(letter or comment* or abstracts).ti.
85	or/77-84
86	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
87	85 not 86
88	ANIMALS/ not HUMANS/
89	exp ANIMALS, LABORATORY/
90	exp ANIMAL EXPERIMENTATION/
91	exp MODELS, ANIMAL/
92	exp RODENTIA/
93	(rat or rats or mouse or mice).ti.
94	or/87-93
95	76 not 94
96	limit 95 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.

Update 2015

5	or/1-4
6	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
7	(DK or DKA).ti,ab.
8	or/6-7
9	diabet$.mp.
10	and/5,8-9
11	(insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or intermittent$ or time or timing)).ti,ab.
12	(insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading)).ti,ab.
13	or/11-12
14	and/10,13

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp KETOSIS/
11	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
12	(DK or DKA).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS/
15	diabet$.mp.
16	or/14-15
17	and/9,13,16
18	exp INSULINS/
19	INSULIN INFUSION SYSTEMS/
20	or/18-19
21	exp DRUG ADMINISTRATION SCHEDULE/
22	TIME FACTORS/
23	DOSE-RESPONSE RELATIONSHIP, DRUG/
24	DRUG DOSAGE CALCULATIONS/
25	or/21-24
26	and/20,25
27	exp INSULINS/ad [Administration & Dosage]
28	(insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or intermittent$ or time or timing)).ti,ab.
29	(insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading)).ti,ab.
30	or/26-29
31	and/17,30

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw,rw.
5	or/1-4
6	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw,tx,kw.
7	(DK or DKA).tw,tx.
8	or/6-7
9	diabet$.tw,tx,kw.
10	and/5,8-9
11	insulin$.tw,tx,kw.
12	TIME FACTORS.kw.
13	DOSE-RESPONSE.kw.
14	DRUG DOSAGE CALCULATIONS.kw.
15	or/12-14
16	and/11,15
17	(insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or intermittent$ or time or timing)).tw,tx.
18	(insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading)).tw,tx.
19	or/16-18
20	and/10,19

NHS Economic Evaluation Database

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	DIABETIC KETOACIDOSIS/
11	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
12	(DK or DKA).tw.
13	or/10-12
14	exp DIABETES MELLITUS/
15	diabet$.mp.
16	or/14-15
17	and/9,13,16
18	exp INSULIN/
19	INSULIN INFUSION SYSTEMS/
20	or/18-19
21	exp DRUG ADMINISTRATION SCHEDULE/

Update 2015

22	TIME FACTORS/
23	DOSE-RESPONSE RELATIONSHIP, DRUG/
24	DRUG DOSAGE CALCULATIONS/
25	or/21-24
26	and/20,25
27	(insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or intermittent$ or time or timing)).tw.
28	(insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading)).tw.
29	or/26-28
30	and/17,29

Embase

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).tw,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.tw,sh.
9	random$.tw,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.
16	(systematic$ adj5 (review$ or overview$)).tw,sh.
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	exp CASE CONTROL STUDY/
30	RETROSPECTIVE STUDY/
31	(case$ adj2 control$).tw.
32	COHORT ANALYSIS/
33	LONGITUDINAL STUDY/
34	FOLLOW UP/
35	PROSPECTIVE STUDY/
36	cohort$.tw.
37	or/29-36
38	or/13,18,28,37

Update 2015

39	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40	38 not 39
41	exp ADOLESCENT/
42	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
43	exp CHILD/
44	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
45	exp INFANT/
46	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
47	exp PEDIATRICS/ or exp PUBERTY/
48	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
49	or/41-48
50	KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/
51	KETONURIA/
52	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
53	(DK or DKA).ti,ab.
54	or/50-53
55	exp DIABETES MELLITUS/
56	diabet$.mp.
57	or/55-56
58	and/49,54,57
59	exp INSULIN DERIVATIVE/
60	INSULIN TREATMENT/ or INSULIN INFUSION/
61	or/59-60
62	DRUG DOSE/ or DOSE CALCULATION/ or DOSAGE SCHEDULE COMPARISON/ or DRUG DOSE COMPARISON/ or DRUG DOSE ESCALATION/ or DRUG DOSE INCREASE/ or DRUG DOSE INTENSIFICATION/ or DRUG DOSE REDUCTION/ or DRUG DOSE REGIMEN/ or LOADING DRUG DOSE/ or LOW DRUG DOSE/ or MAINTENANCE DRUG DOSE/ or OPTIMAL DRUG DOSE/
63	EARLY INTERVENTION/
64	TREATMENT DURATION/
65	THERAPY DELAY/
66	or/62-65
67	and/61,66
68	exp INSULIN DERIVATIVE/do, iv [Drug Dose, Intravenous Drug Administration]
69	(insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading)).ti,ab.
70	(insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or time or timing)).ti,ab.
71	or/67-70
72	and/58,71
73	and/40,72
74	conference abstract.pt.
75	letter.pt. or LETTER/
76	note.pt.
77	editorial.pt.
78	CASE REPORT/ or CASE STUDY/
79	(letter or comment* or abstracts).ti.
80	or/74-79
81	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
82	80 not 81
83	ANIMAL/ not HUMAN/
84	NONHUMAN/

Update 2015

85	exp ANIMAL EXPERIMENT/
86	exp EXPERIMENTAL ANIMAL/
87	ANIMAL MODEL/
88	exp RODENT/
89	(rat or rats or mouse or mice).ti.
90	or/82-89
91	73 not 90
92	limit 91 to english language

F.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp KETOSIS/
11	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
12	(DK or DKA).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS/
15	diabet$.mp.
16	or/14-15
17	and/9,13,16
18	exp ANTICOAGULANTS/
19	exp FIBRINOLYTIC AGENTS/
20	exp THROMBOLYTIC THERAPY/
21	ASPIRIN/
22	DICUMAROL/
23	WARFARIN/
24	exp HEPARIN/
25	(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinoly$).ti,ab,nm.
26	or/18-25
27	exp "EMBOLISM AND THROMBOSIS"/
28	exp HEMORRHAGE/
29	(mo or ut or ae or co).fs.
30	PATIENT SATISFACTION/

Update 2015

31	(thromboprophyla$ or thrombus$ or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocyt$ or thrombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).ti,ab.
32	or/27-31
33	and/17,26,32
34	LETTER/
35	EDITORIAL/
36	NEWS/
37	exp HISTORICAL ARTICLE/
38	ANECDOTES AS TOPIC/
39	COMMENT/
40	CASE REPORT/
41	(letter or comment* or abstracts).ti.
42	or/34-41
43	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
44	42 not 43
45	ANIMALS/ not HUMANS/
46	exp ANIMALS, LABORATORY/
47	exp ANIMAL EXPERIMENTATION/
48	exp MODELS, ANIMAL/
49	exp RODENTIA/
50	(rat or rats or mouse or mice).ti.
51	or/44-50
52	33 not 51

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
7	(DK or DKA).ti,ab.
8	or/6-7
9	diabet$.mp.
10	and/5,8-9
11	(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinoly$).ti,ab.
12	(thromboprophyla$ or thrombus$ or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocyt$ or thrombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).ti,ab.
13	and/10-12

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/

Update 2015

6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp KETOSIS/
11	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
12	(DK or DKA).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS/
15	diabet$.mp.
16	or/14-15
17	and/9,13,16
18	exp ANTICOAGULANTS/
19	exp FIBRINOLYTIC AGENTS/
20	exp THROMBOLYTIC THERAPY/
21	ASPIRIN/
22	DICUMAROL/
23	WARFARIN/
24	exp HEPARIN/
25	(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinoly$).ti,ab.
26	or/18-25
27	exp "EMBOLISM AND THROMBOSIS"/
28	exp HEMORRHAGE/
29	(mo or ut or ae or co).fs.
30	PATIENT SATISFACTION/
31	(thromboprophyla$ or thrombus$ or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocyt$ or thrombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).ti,ab.
32	or/27-31
33	and/17,26,32

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,tw,tx,jw,rw.
5	or/1-4
6	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).kw,tw,tx.
7	(DK or DKA).kw,tw,tx.
8	or/6-7
9	diabet$.kw,tw,tx.
10	and/5,8-9
11	ANTICOAGULANT$.kw.
12	FIBRINOLYTIC$.kw.
13	(THROMBOL$ or HIRUDIN).kw.
14	ASPIRIN.kw.
15	DICUMAROL.kw.

16	WARFARIN.kw.
17	HEPARIN$.kw.
18	(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinoly$).tw,tx.
19	or/11-18
20	(EMBOLI$ or THROMBO$).kw.
21	HEMORRHAGE.kw.
22	SATISFACTION.kw.
23	(thromboprophyla$ or thrombus$ or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocyt$ or thrombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).tw,tx.
24	or/20-23
25	and/10,19,24

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp KETOSIS/
11	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
12	(DK or DKA).tw.
13	or/10-12
14	exp DIABETES MELLITUS/
15	diabet$.mp.
16	or/14-15
17	and/9,13,16
18	exp ANTICOAGULANTS/
19	exp FIBRINOLYTIC AGENTS/
20	exp THROMBOLYTIC THERAPY/
21	ASPIRIN/
22	DICUMAROL/
23	WARFARIN/
24	exp HEPARIN/
25	(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinoly$).tw.
26	or/18-25
27	exp "EMBOLISM AND THROMBOSIS"/
28	exp HEMORRHAGE/
29	(mo or ut or ae or co).fs.
30	PATIENT SATISFACTION/
31	(thromboprophyla$ or thrombus$ or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocyt$ or thrombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).tw.
32	or/27-31
33	and/17,26,32

Update 2015

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	NON INSULIN DEPENDENT DIABETES MELLITUS/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	JUVENILE DIABETES MELLITUS/
21	and/9,19
22	or/20-21
23	KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/
24	KETONURIA/
25	(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
26	(DK or DKA).ti,ab.
27	or/23-26
28	and/22,27
29	exp ANTICOAGULANT AGENT/
30	ANTICOAGULANT THERAPY/
31	FIBRINOLYTIC AGENT/
32	FIBRINOLYTIC THERAPY/
33	EMBOLISM PREVENTION/
34	THROMBOSIS PREVENTION/
35	ACETYLSALICYLIC ACID/
36	DICOUMAROL/
37	WARFARIN/
38	exp HEPARIN DERIVATIVE/
39	(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinoly$).ti,ab,rn.
40	or/29-39
41	exp THROMBOEMBOLISM/
42	exp THROMBOCYTOPENIA/
43	exp BLEEDING/
44	ADVERSE DRUG REACTION/
45	exp COMPLICATION/
46	MORTALITY/

Update 2015

47	HEALTH CARE UTILIZATION/
48	PATIENT SATISFACTION/
49	(thromboprophyla$ or thrombus$ or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocyt$ or thrombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).ti,ab.
50	or/41-49
51	and/28,40,50
52	conference abstract.pt.
53	letter.pt. or LETTER/
54	note.pt.
55	editorial.pt.
56	CASE REPORT/ or CASE STUDY/
57	(letter or comment* or abstracts).ti.
58	or/52-57
59	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
60	58 not 59
61	ANIMAL/ not HUMAN/
62	NONHUMAN/
63	exp ANIMAL EXPERIMENT/
64	exp EXPERIMENTAL ANIMAL/
65	ANIMAL MODEL/
66	exp RODENT/
67	(rat or rats or mouse or mice).ti.
68	or/60-67
69	51 not 68

Update 2015

F.16 Type 1 and type 2 diabetes – retinopathy

Review questions:

What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12

14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	DIABETIC RETINOPATHY/
21	(diabet$ adj3 retinopath$).ti,ab.
22	or/20-21
23	RETINAL DISEASES/
24	retinopath$.ti,ab.
25	or/23-24
26	DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
27	exp OPHTHALMOSCOPY/
28	FUNDUS OCULI/
29	RETINA/ or RETINAL VESSELS/
30	PHOTOGRAPHY/
31	and/29-30
32	((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
33	(op?thalmoscop$ or retinoscop$).ti,ab.
34	fundus oculi.ti,ab.
35	or/26-28,31-34
36	MASS SCREENING/
37	VISION SCREENING/
38	exp POPULATION SURVEILLANCE/
39	(undiagnos$ or estimate$).ti.
40	(screen$ or surveill$ or predict$ or detect$).ti.
41	or/36-40
42	SEVERITY OF ILLNESS INDEX/
43	INTERNATIONAL CLASSIFICATION OF DISEASES/
44	CLASSIFICATION/
45	(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).ti,ab.
46	or/42-45
47	exp EYE HEMORRHAGE/
48	h?emorrhag$.ti,ab.
49	exp ANEURYSM/
50	(microaneurysm? or micro aneurysm?).ti,ab.
51	"EXUDATES AND TRANSUDATES"/
52	exp EYE/
53	and/51-52
54	SUBRETINAL FLUID/
55	exudate?.ti,ab.
56	PAPILLEDEMA/
57	EDEMA/
58	exp EYE/
59	and/57-58
60	(papill?edem$ or papillitis or choked dis??).ti,ab.
61	((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
62	RETINAL NEOVASCULARIZATION/
63	NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64	exp EYE/ or RETINAL VESSELS/
65	and/63-64

Update 2015

66	exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67	neovascular$.ti,ab.
68	(new adj2 vessel adj2 form$).ti,ab.
69	((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.
70	(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
71	*MACULAR DEGENERATION/
72	MACULAR EDEMA/
73	(macular adj (degenerat$ or dysfunction$)).ti,ab.
74	(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
75	exp OCULAR HYPERTENSION/
76	(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.
77	OPTIC NEUROPATHY, ISCHEMIC/
78	(optic adj3 (isch?emi$ or neuropath$)).ti,ab.
79	cotton wool spot?.ti,ab.
80	RETINAL DETACHMENT/
81	((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis)).ti,ab.
82	VISION DISORDERS/
83	SCOTOMA/
84	VISION, LOW/
85	(scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
86	((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.
87	or/47-50,53-56,59-62,65-86
88	PREVALENCE/
89	INCIDENCE/
90	CROSS-SECTIONAL STUDIES/
91	exp MODELS, STATISTICAL/
92	LIFE TABLES/
93	exp RISK/
94	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
95	or/88-94
96	AGE FACTORS/
97	AGE DISTRIBUTION/
98	AGE OF ONSET/
99	TIME TO TREATMENT/
100	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
101	(disease adj3 (duration or onset)).ti,ab.
102	or/96-101
103	DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
104	22 and (35 or 41 or 46 or 95 or 102)
105	19 and 25 and (35 or 41 or 46 or 95 or 102)
106	19 and 87 and (95 or 102)
107	or/103-106
108	and/9,107
109	limit 108 to english language
110	LETTER/
111	EDITORIAL/
112	NEWS/
113	exp HISTORICAL ARTICLE/
114	ANECDOTES AS TOPIC/

Update 2015

115	COMMENT/
116	(letter or comment* or abstracts).ti.
117	or/110-116
118	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
119	117 not 118
120	ANIMALS/ not HUMANS/
121	exp ANIMALS, LABORATORY/
122	exp ANIMAL EXPERIMENTATION/
123	exp MODELS, ANIMAL/
124	exp RODENTIA/
125	(rat or rats or mouse or mice).ti.
126	or/119-125
127	109 not 126

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
9	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
10	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
11	or/6-10
12	(diabet$ adj3 retinopath$).ti,ab.
13	retinopath$.ti,ab.
14	((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
15	(op?thalmoscop$ or retinoscop$).ti,ab.
16	fundus oculi.ti,ab.
17	or/14-16
18	(undiagnos$ or estimate$).ti.
19	(screen$ or surveill$ or predict$ or detect$).ti.
20	or/18-19
21	(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).ti,ab.
22	h?emorrhag$.ti,ab.
23	(microaneurysm? or micro aneurysm?).ti,ab.
24	exudate?.ti,ab.
25	(papill?edem$ or papillitis or choked dis??).ti,ab.
26	((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
27	neovascular$.ti,ab.
28	(new adj2 vessel adj2 form$).ti,ab.
29	((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.
30	(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
31	(macular adj (degenerat$ or dysfunction$)).ti,ab.
32	(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
33	(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.

Update 2015

34	(optic adj3 (isch?emi$ or neuropath$)).ti,ab.
35	cotton wool spot?.ti,ab.
36	((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis)).ti,ab.
37	(scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
38	((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.
39	or/22-38
40	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
41	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
42	(disease adj3 (duration or onset)).ti,ab.
43	or/41-42
44	12 and (17 or 20 or 21 or 40 or 43)
45	11 and 13 and (17 or 20 or 21 or 40 or 43)
46	11 and 39 and (40 or 43)
47	or/44-46
48	and/5,47

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	DIABETIC RETINOPATHY/
21	(diabet$ adj3 retinopath$).ti,ab.
22	or/20-21
23	RETINAL DISEASES/
24	retinopath$.ti,ab.
25	or/23-24
26	DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
27	exp OPHTHALMOSCOPY/
28	FUNDUS OCULI/
29	RETINA/ or RETINAL VESSELS/
30	PHOTOGRAPHY/

Update 2015

31	and/29-30
32	((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
33	(op?thalmoscop$ or retinoscop$).ti,ab.
34	fundus oculi.ti,ab.
35	or/26-28,31-34
36	MASS SCREENING/
37	VISION SCREENING/
38	exp POPULATION SURVEILLANCE/
39	(undiagnos$ or estimate$).ti.
40	(screen$ or surveill$ or predict$ or detect$).ti.
41	or/36-40
42	SEVERITY OF ILLNESS INDEX/
43	INTERNATIONAL CLASSIFICATION OF DISEASES/
44	CLASSIFICATION/
45	(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).ti,ab.
46	or/42-45
47	exp EYE HEMORRHAGE/
48	h?emorrhag$.ti,ab.
49	exp ANEURYSM/
50	(microaneurysm? or micro aneurysm?).ti,ab.
51	"EXUDATES AND TRANSUDATES"/
52	exp EYE/
53	and/51-52
54	SUBRETINAL FLUID/
55	exudate?.ti,ab.
56	PAPILLEDEMA/
57	EDEMA/
58	exp EYE/
59	and/57-58
60	(papill?edem$ or papillitis or choked dis??).ti,ab.
61	((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
62	RETINAL NEOVASCULARIZATION/
63	NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64	exp EYE/ or RETINAL VESSELS/
65	and/63-64
66	exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67	neovascular$.ti,ab.
68	(new adj2 vessel adj2 form$).ti,ab.
69	((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.
70	(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
71	*MACULAR DEGENERATION/
72	MACULAR EDEMA/
73	(macular adj (degenerat$ or dysfunction$)).ti,ab.
74	(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
75	exp OCULAR HYPERTENSION/
76	(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.
77	OPTIC NEUROPATHY, ISCHEMIC/
78	(optic adj3 (isch?emi$ or neuropath$)).ti,ab.
79	cotton wool spot?.ti,ab.
80	RETINAL DETACHMENT/
81	((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis)).ti,ab.

Update 2015

82	VISION DISORDERS/
83	SCOTOMA/
84	VISION, LOW/
85	(scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
86	((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.
87	or/47-50,53-56,59-62,65-86
88	PREVALENCE/
89	INCIDENCE/
90	CROSS-SECTIONAL STUDIES/
91	exp MODELS, STATISTICAL/
92	LIFE TABLES/
93	exp RISK/
94	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
95	or/88-94
96	AGE FACTORS/
97	AGE DISTRIBUTION/
98	AGE OF ONSET/
99	TIME TO TREATMENT/
100	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
101	(disease adj3 (duration or onset)).ti,ab.
102	or/96-101
103	DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
104	22 and (35 or 41 or 46 or 95 or 102)
105	19 and 25 and (35 or 41 or 46 or 95 or 102)
106	19 and 87 and (95 or 102)
107	or/103-106
108	and/9,107

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.
7	(IDDM or T1D or TID or DM1 or DMI).tw,tx.
8	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
9	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
10	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
11	or/6-10
12	(diabet$ adj3 retinopath$).tw,tx,kw.
13	RETINAL DISEASES.kw.
14	retinopath$.tw,tx,kw.
15	or/13-14
16	DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL.kw.

17	((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).tw,tx,kw.
18	(op?thalmoscop$ or retinoscop$).tw,tx,kw.
19	fundus oculi.tw,tx,kw.
20	or/16-19
21	SCREENING.kw.
22	SURVEILLANCE.kw.
23	(undiagnos$ or estimate$).ti.
24	(screen$ or surveill$ or predict$ or detect$).ti.
25	or/21-24
26	SEVERITY OF ILLNESS INDEX.kw.
27	DISEASE SEVERITY.kw.
28	DISEASE COURSE.kw.
29	STAGING.kw.
30	INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
31	RATING SCALE.kw.
32	CLASSIFICATION.kw.
33	(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).tw,tx.
34	or/26-33
35	h?emorrhag$.tw,tx,kw.
36	ANEURYSM.kw.
37	(microaneurysm? or micro aneurysm?).tw,tx,kw.
38	SUBRETINAL FLUID.kw.
39	exudate?.tw,tx,kw.
40	(papill?edem$ or papillitis or choked dis??).tw,tx,kw.
41	((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).tw,tx,kw.
42	neovascular$.tw,tx,kw.
43	(new adj2 vessel adj2 form$).tw,tx.
44	((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).tw,tx,kw.
45	(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).tw,tx.
46	(macular adj (degenerat$ or dysfunction$)).tw,tx,kw.
47	(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).tw,tx,kw.
48	(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).tw,tx,kw.
49	(optic adj3 (isch?emi$ or neuropath$)).tw,tx,kw.
50	cotton wool spot?.tw,tx.
51	((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis)).tw,tx,kw.
52	(VISION DISORDERS or VISUAL DISORDER).kw.
53	(scotoma? or blind spot? or floater? or musca volitante?).tw,tx,kw.
54	((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).tw,tx,kw.
55	or/35-54
56	PREVALENCE.kw.
57	INCIDENCE.kw.
58	CROSS-SECTIONAL STUDIES.kw.
59	MODELS, STATISTICAL.kw.
60	LIFE TABLE$.kw.
61	RISK.kw.
62	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
63	or/56-62
64	AGE.kw.
65	TIME TO TREATMENT.kw.
66	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw,tx,kw.

Update 2015

67	(disease adj3 (duration or onset)).tw,tx,kw.
68	or/64-67
69	12 and (20 or 25 or 34 or 63 or 68)
70	11 and 15 and (20 or 25 or 34 or 63 or 68)
71	11 and 55 and (63 or 68)
72	or/69-71
73	and/5,72

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jw,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jw,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jw,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
17	(NIDDM or T2D or TIID or DM2 or DMII).tw.
18	or/14-17
19	or/13,18
20	DIABETIC RETINOPATHY/
21	(diabet$ adj3 retinopath$).tw.
22	or/20-21
23	RETINAL DISEASES/
24	retinopath$.tw.
25	or/23-24
26	DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
27	exp OPHTHALMOSCOPY/
28	FUNDUS OCULI/
29	RETINA/ or RETINAL VESSELS/
30	PHOTOGRAPHY/
31	and/29-30
32	((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).tw.
33	(op?thalmoscop$ or retinoscop$).tw.
34	fundus oculi.tw.
35	or/26-28,31-34
36	MASS SCREENING/
37	VISION SCREENING/
38	exp POPULATION SURVEILLANCE/
39	(undiagnos$ or estimate$).ti.
40	(screen$ or surveill$ or predict$ or detect$).ti.

Update 2015

41	or/36-40
42	SEVERITY OF ILLNESS INDEX/
43	INTERNATIONAL CLASSIFICATION OF DISEASES/
44	CLASSIFICATION/
45	(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).tw.
46	or/42-45
47	exp EYE HEMORRHAGE/
48	h?emorrhag$.tw.
49	exp ANEURYSM/
50	(microaneurysm? or micro aneurysm?).tw.
51	"EXUDATES AND TRANSUDATES"/
52	exp EYE/
53	and/51-52
54	SUBRETINAL FLUID/
55	exudate?.tw.
56	PAPILLEDEMA/
57	EDEMA/
58	exp EYE/
59	and/57-58
60	(papill?edem$ or papillitis or choked dis??).tw.
61	((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).tw.
62	RETINAL NEOVASCULARIZATION/
63	NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64	exp EYE/ or RETINAL VESSELS/
65	and/63-64
66	exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67	neovascular$.tw.
68	(new adj2 vessel adj2 form$).tw.
69	((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).tw.
70	(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).tw.
71	MACULAR DEGENERATION/
72	MACULAR EDEMA/
73	(macular adj (degenerat$ or dysfunction$)).tw.
74	(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).tw.
75	exp OCULAR HYPERTENSION/
76	(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).tw.
77	OPTIC NEUROPATHY, ISCHEMIC/
78	(optic adj3 (isch?emi$ or neuropath$)).tw.
79	cotton wool spot?.tw.
80	RETINAL DETACHMENT/
81	((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis)).tw.
82	VISION DISORDERS/
83	SCOTOMA/
84	VISION, LOW/
85	(scotoma? or blind spot? or floater? or musca volitante?).tw.
86	((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).tw.
87	or/47-50,53-56,59-62,65-86
88	PREVALENCE/
89	INCIDENCE/
90	CROSS-SECTIONAL STUDIES/

Update 2015

91	exp MODELS, STATISTICAL/
92	LIFE TABLES/
93	exp RISK/
94	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
95	or/88-94
96	AGE FACTORS/
97	AGE DISTRIBUTION/
98	AGE OF ONSET/
99	TIME TO TREATMENT/
100	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw.
101	(disease adj3 (duration or onset)).tw.
102	or/96-101
103	DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
104	22 and (35 or 41 or 46 or 95 or 102)
105	19 and 25 and (35 or 41 or 46 or 95 or 102)
106	19 and 87 and (95 or 102)
107	or/103-106
108	and/9,107

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	NON INSULIN DEPENDENT DIABETES MELLITUS/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	JUVENILE DIABETES MELLITUS/
21	DIABETIC RETINOPATHY/
22	(diabet$ adj3 retinopath$).ti,ab.
23	or/21-22
24	RETINOPATHY/
25	PROLIFERATIVE RETINOPATHY/
26	retinopath$.ti,ab.
27	or/24-26
28	EYE PHOTOGRAPHY/

Update 2015

29	exp RETINA EXAMINATION/
30	OPHTHALMOSCOPY/
31	RETINA/ or exp RETINA BLOOD VESSEL/
32	PHOTOGRAPHY/
33	and/31-32
34	exp OPHTHALMIC CAMERA/
35	((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
36	(op?thalmoscop$ or retinoscop$).ti,ab.
37	fundus oculi.ti,ab.
38	or/28-30,33-37
39	SCREENING/
40	MASS SCREENING/
41	SCREENING TEST/
42	RESCREENING/
43	exp DISEASE SURVEILLANCE/
44	(undiagnos$ or estimate$).ti.
45	(screen$ or surveill$ or predict$ or detect$).ti.
46	or/39-45
47	SEVERITY OF ILLNESS INDEX/
48	DISEASE SEVERITY/
49	STAGING/
50	exp INTERNATIONAL CLASSIFICATION OF DISEASES/
51	RATING SCALE/
52	CLASSIFICATION/
53	DISEASE CLASSIFICATION/
54	(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).ti,ab.
55	or/47-54
56	exp INTRAOCULAR HEMORRHAGE/
57	h?emorrhag$.ti,ab.
58	MICROANEURYSM/
59	(microaneurysm? or micro aneurysm?).ti,ab.
60	RETINA EXUDATE/
61	SUBRETINAL FLUID/
62	exudate?.ti,ab.
63	PAPILLEDEMA/
64	RETINAL EDEMA/
65	(papill?edem$ or papillitis or choked dis??).ti,ab.
66	((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
67	RETINA NEOVASCULARIZATION/
68	"NEOVASCULARIZATION (PATHOLOGY)"/
69	RETINA/ or exp RETINA BLOOD VESSEL/
70	and/68-69
71	neovascular$.ti,ab.
72	(new adj2 vessel adj2 form$).ti,ab.
73	((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.
74	(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
75	RETINA DEGENERATION/
76	RETINA MACULA DEGENERATION/
77	RETINA MACULOPATHY/
78	exp MACULAR EDEMA/
79	(macular adj (degenerat$ or dysfunction$)).ti,ab.
80	(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.

Update 2015

81	exp GLAUCOMA/
82	(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.
83	exp ISCHEMIC OPTIC NEUROPATHY/
84	(optic adj3 (isch?emi$ or neuropath$)).ti,ab.
85	cotton wool spot?.ti,ab.
86	RETINA DETACHMENT/
87	RETINA TEAR/
88	((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis)).ti,ab.
89	VISUAL DISORDER/
90	VISUAL IMPAIRMENT/
91	SCOTOMA/
92	VITREOUS FLOATERS/
93	(scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
94	((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.
95	or/56-67,70-94
96	PREVALENCE/
97	INCIDENCE/
98	STATISTICAL MODEL/
99	LIFE TABLE/
100	exp RISK/
101	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
102	or/96-101
103	AGE/
104	AGE DISTRIBUTION/
105	ONSET AGE/
106	DISEASE DURATION/
107	TIME TO TREATMENT/
108	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
109	(disease adj3 (duration or onset)).ti,ab.
110	or/103-109
111	DIABETIC RETINOPATHY/di, ep, pc [Diagnosis, Epidemiology, Prevention]
112	23 and (38 or 46 or 55 or 102 or 110)
113	19 and 27 and (38 or 46 or 55 or 102 or 110)
114	19 and 95 and (102 or 110)
115	or/111-114
116	and/9,115
117	20 and 23 and (38 or 46 or 55 or 102 or 110)
118	20 and 27 and (38 or 46 or 55 or 102 or 110)
119	20 and 95 and (102 or 110)
120	or/116-119
121	limit 120 to english language
122	conference abstract.pt.
123	letter.pt. or LETTER/
124	note.pt.
125	editorial.pt.
126	(letter or comment* or abstracts).ti.
127	or/122-126
128	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
129	127 not 128
130	ANIMAL/ not HUMAN/
131	NONHUMAN/

Update 2015

132	exp ANIMAL EXPERIMENT/
133	exp EXPERIMENTAL ANIMAL/
134	ANIMAL MODEL/
135	exp RODENT/
136	(rat or rats or mouse or mice).ti.
137	or/129-136
138	121 not 137

F.17 Type 1 and type 2 diabetes – nephropathy

Review questions:

What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	DIABETIC NEPHROPATHIES/
21	nephropath$.ti,ab.
22	glomerulosclerosis.ti,ab.
23	(Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
24	ALBUMINURIA/
25	PROTEINURIA/
26	SERUM ALBUMIN/
27	CREATININE/bl, ur [Blood, Urine]
28	(albuminuri$ or microalbuminuri$ or proteinuri$).ti,ab.
29	((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).ti,ab.

Update 2015

30	exp RENAL INSUFFICIENCY, CHRONIC/
31	((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).ti,ab.
32	or/20-31
33	SEVERITY OF ILLNESS INDEX/
34	DISEASE PROGRESSION/
35	INTERNATIONAL CLASSIFICATION OF DISEASES/
36	CLASSIFICATION/
37	or/33-36
38	or/20-28
39	and/37-38
40	((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).ti,ab.
41	or/39-40
42	MASS SCREENING/
43	exp POPULATION SURVEILLANCE/
44	(undiagnos$ or estimate$).ti.
45	(screen$ or surveill$ or predict$ or detect$).ti.
46	or/42-45
47	PREVALENCE/
48	INCIDENCE/
49	CROSS-SECTIONAL STUDIES/
50	exp MODELS, STATISTICAL/
51	LIFE TABLES/
52	exp RISK/
53	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
54	or/47-53
55	AGE FACTORS/
56	AGE DISTRIBUTION/
57	AGE OF ONSET/
58	TIME TO TREATMENT/
59	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
60	(disease adj3 (duration or onset)).ti,ab.
61	or/55-60
62	ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
63	32 and (46 or 54 or 61)
64	or/41,62-63
65	and/19,64
66	DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
67	or/65-66
68	and/9,67
69	limit 68 to english language
70	LETTER/
71	EDITORIAL/
72	NEWS/
73	exp HISTORICAL ARTICLE/
74	ANECDOTES AS TOPIC/
75	COMMENT/
76	(letter or comment* or abstracts).ti.
77	or/70-76
78	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
79	77 not 78
80	ANIMALS/ not HUMANS/

Update 2015

81	exp ANIMALS, LABORATORY/
82	exp ANIMAL EXPERIMENTATION/
83	exp MODELS, ANIMAL/
84	exp RODENTIA/
85	(rat or rats or mouse or mice).ti.
86	or/79-85
87	69 not 86

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
8	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
9	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
10	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
11	or/6-10
12	nephropath$.ti,ab.
13	glomerulosclerosis.ti,ab.
14	(Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
15	(albuminuri$ or microalbuminuri$ or proteinuri$).ti,ab.
16	((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).ti,ab.
17	((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).ti,ab.
18	or/12-17
19	((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).ti,ab.
20	(undiagnos$ or estimate$).ti.
21	(screen$ or surveill$ or predict$ or detect$).ti.
22	or/20-21
23	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
24	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
25	(disease adj3 (duration or onset)).ti,ab.
26	or/24-25
27	18 and (22 or 23 or 26)
28	or/19,27
29	and/5,11,28

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/

Update 2015

6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	DIABETIC NEPHROPATHIES/
21	nephropath$.ti,ab.
22	glomerulosclerosis.ti,ab.
23	(Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
24	ALBUMINURIA/
25	PROTEINURIA/
26	SERUM ALBUMIN/
27	CREATININE/bl, ur [Blood, Urine]
28	(albuminuri$ or microalbuminuri$ or proteinuri$).ti,ab.
29	((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).ti,ab.
30	exp RENAL INSUFFICIENCY, CHRONIC/
31	((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).ti,ab.
32	or/20-31
33	SEVERITY OF ILLNESS INDEX/
34	DISEASE PROGRESSION/
35	INTERNATIONAL CLASSIFICATION OF DISEASES/
36	CLASSIFICATION/
37	or/33-36
38	or/20-28
39	and/37-38
40	((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).ti,ab.
41	or/39-40
42	MASS SCREENING/
43	exp POPULATION SURVEILLANCE/
44	(undiagnos$ or estimate$).ti.
45	(screen$ or surveill$ or predict$ or detect$).ti.
46	or/42-45
47	PREVALENCE/
48	INCIDENCE/
49	CROSS-SECTIONAL STUDIES/
50	exp MODELS, STATISTICAL/
51	LIFE TABLES/
52	exp RISK/
53	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
54	or/47-53

Update 2015

55	AGE FACTORS/
56	AGE DISTRIBUTION/
57	AGE OF ONSET/
58	TIME TO TREATMENT/
59	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
60	(disease adj3 (duration or onset)).ti,ab.
61	or/55-60
62	ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
63	32 and (46 or 54 or 61)
64	or/41,62-63
65	and/19,64
66	DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
67	or/65-66
68	and/9,67

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.
7	(IDDM or T1D or TID or DM1 or DMI).tw,tx.
8	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
9	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
10	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
11	or/6-10
12	nephropath$.tw,tx,kw.
13	glomerulosclerosis.tw,tx.
14	(Kimmelstie?l Wilson adj (syndrome? or disease?)).tw,tx.
15	(albuminuri$ or microalbuminuri$ or proteinuri$).tw,tx,kw.
16	((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).tw,tx,kw.
17	((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).tw,tx,kw.
18	or/12-17
19	SEVERITY OF ILLNESS INDEX.kw.
20	(DISEASE PROGRESSION or DISEASE COURSE).kw.
21	INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
22	RATING SCALE.kw.
23	CLASSIFICATION.kw.
24	or/19-23
25	or/12-15
26	and/24-25
27	((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).tw,tx.
28	or/26-27
29	(SCREENING or RESCREENING).kw.

Update 2015

30	SURVEILLANCE.kw.
31	(undiagnos$ or estimate$).ti.
32	(screen$ or surveill$ or predict$ or detect$).ti.
33	or/29-32
34	PREVALENCE.kw.
35	INCIDENCE.kw.
36	(MODELS, STATISTICAL or STATISTICAL MODEL).kw.
37	LIFE TABLE?.kw.
38	RISK.kw.
39	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
40	or/34-39
41	AGE.kw.
42	TIME TO TREATMENT.kw.
43	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw,tx,kw.
44	(disease adj3 (duration or onset)).tw,tx,kw.
45	or/41-44
46	18 and (33 or 40 or 45)
47	or/28,46
48	and/5,11,47

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jw,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jw,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jw,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
17	(NIDDM or T2D or TIID or DM2 or DMII).tw.
18	or/14-17
19	or/13,18
20	DIABETIC NEPHROPATHIES/
21	nephropath$.tw.
22	glomerulosclerosis.tw.
23	(Kimmelstie?l Wilson adj (syndrome? or disease?)).tw.
24	ALBUMINURIA/
25	PROTEINURIA/
26	SERUM ALBUMIN/
27	CREATININE/bl, ur [Blood, Urine]
28	(albuminuri$ or microalbuminuri$ or proteinuri$).tw.

Update 2015

29	((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).tw.
30	exp RENAL INSUFFICIENCY, CHRONIC/
31	((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).tw.
32	or/20-31
33	SEVERITY OF ILLNESS INDEX/
34	DISEASE PROGRESSION/
35	INTERNATIONAL CLASSIFICATION OF DISEASES/
36	CLASSIFICATION/
37	or/33-36
38	or/20-28
39	and/37-38
40	((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).tw.
41	or/39-40
42	MASS SCREENING/
43	exp POPULATION SURVEILLANCE/
44	(undiagnos$ or estimate$).ti.
45	(screen$ or surveill$ or predict$ or detect$).ti.
46	or/42-45
47	PREVALENCE/
48	INCIDENCE/
49	CROSS-SECTIONAL STUDIES/
50	exp MODELS, STATISTICAL/
51	LIFE TABLES/
52	exp RISK/
53	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
54	or/47-53
55	AGE FACTORS/
56	AGE DISTRIBUTION/
57	AGE OF ONSET/
58	TIME TO TREATMENT/
59	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw.
60	(disease adj3 (duration or onset)).tw.
61	or/55-60
62	ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
63	32 and (46 or 54 or 61)
64	or/41,62-63
65	and/19,64
66	DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
67	or/65-66
68	and/9,67

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/

Update 2015

8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
13	or/10-12
14	NON INSULIN DEPENDENT DIABETES MELLITUS/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18	or/14-17
19	or/13,18
20	and/9,19
21	JUVENILE DIABETES MELLITUS/
22	or/20-21
23	DIABETIC NEPHROPATHY/
24	nephropath$.ti,ab.
25	glomerulosclerosis.ti,ab.
26	(Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
27	exp ALBUMINURIA/
28	PROTEINURIA/
29	PROTEIN URINE LEVEL/
30	SERUM ALBUMIN/
31	ALBUMIN BLOOD LEVEL/
32	CREATININE URINE LEVEL/
33	CREATININE BLOOD LEVEL/
34	(albuminuri$ or microalbuminuri$ or proteinuri$).ti,ab.
35	((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).ti,ab.
36	KIDNEY DISEASE/
37	KIDNEY FAILURE/
38	CHRONIC KIDNEY FAILURE/
39	((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).ti,ab.
40	or/23-39
41	SEVERITY OF ILLNESS INDEX/
42	DISEASE SEVERITY/
43	DISEASE COURSE/
44	STAGING/
45	exp INTERNATIONAL CLASSIFICATION OF DISEASES/
46	RATING SCALE/
47	CLASSIFICATION/
48	DISEASE CLASSIFICATION/
49	or/41-48
50	or/23-34
51	and/49-50
52	((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).ti,ab.
53	or/51-52
54	SCREENING/
55	MASS SCREENING/
56	SCREENING TEST/

Update 2015

57	RESCREENING/
58	exp DISEASE SURVEILLANCE/
59	(undiagnos$ or estimate$).ti.
60	(screen$ or surveill$ or predict$ or detect$).ti.
61	or/54-60
62	PREVALENCE/
63	INCIDENCE/
64	STATISTICAL MODEL/
65	LIFE TABLE/
66	exp RISK/
67	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
68	or/62-67
69	AGE/
70	AGE DISTRIBUTION/
71	ONSET AGE/
72	DISEASE DURATION/
73	TIME TO TREATMENT/
74	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
75	(disease adj3 (duration or onset)).ti,ab.
76	or/69-75
77	MICROALBUMINURIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
78	40 and (61 or 68 or 76)
79	or/53,77-78
80	and/22,79
81	DIABETIC NEPHROPATHY/di, ep, pc [Diagnosis, Epidemiology, Prevention]
82	and/9,81
83	or/80,82
84	limit 83 to english language
85	conference abstract.pt.
86	letter.pt. or LETTER/
87	note.pt.
88	editorial.pt.
89	(letter or comment* or abstracts).ti.
90	or/85-89
91	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
92	90 not 91
93	ANIMAL/ not HUMAN/
94	NONHUMAN/
95	exp ANIMAL EXPERIMENT/
96	exp EXPERIMENTAL ANIMAL/
97	ANIMAL MODEL/
98	exp RODENT/
99	(rat or rats or mouse or mice).ti.
100	or/92-99
101	84 not 100

Update 2015

F.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Database(s): Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7	or/1-6
8	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
9	clinical trial.pt.
10	exp CLINICAL TRIAL/
11	exp CLINICAL TRIALS AS TOPIC/
12	(clinic$ adj5 trial$).tw,sh.
13	PLACEBOS/
14	placebo$.tw,sh.
15	random$.tw,sh.
16	or/8-15
17	or/7,16
18	META ANALYSIS/
19	META ANALYSIS AS TOPIC/
20	meta analysis.pt.
21	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
22	(systematic$ adj5 (review$ or overview$)).tw,sh.
23	(methodologic$ adj5 (review$ or overview$)).tw,sh.
24	or/18-23
25	review$.pt.
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
27	((hand or manual$) adj2 search$).tw.
28	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
29	(pooling or pooled or mantel haenszel).tw,sh.
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.
31	or/26-30
32	and/25,31
33	or/24,32
34	letter.pt.
35	case report.tw.
36	comment.pt.
37	editorial.pt.
38	historical article.pt.
39	or/34-38
40	17 not 39
41	33 not 39
42	or/40-41

Update 2015

43	ADOLESCENT/ or MINORS/
44	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
45	exp CHILD/
46	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
47	exp INFANT/
48	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
49	exp PEDIATRICS/ or exp PUBERTY/
50	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
51	or/43-50
52	exp DIABETES MELLITUS, TYPE 2/
53	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
54	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
55	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
56	or/52-55
57	PATIENT EDUCATION AS TOPIC/
58	PROBLEM SOLVING/
59	ed.fs.
60	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
61	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
62	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
63	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
64	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
65	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
66	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
67	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
68	or/57-67
69	and/51,56,68
70	limit 69 to english language
71	LETTER/
72	EDITORIAL/
73	NEWS/
74	exp HISTORICAL ARTICLE/
75	ANECDOTES AS TOPIC/
76	COMMENT/
77	CASE REPORT/
78	(letter or comment* or abstracts).ti.
79	or/71-78
80	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
81	79 not 80
82	ANIMALS/ not HUMANS/
83	exp ANIMALS, LABORATORY/

Update 2015

84	exp ANIMAL EXPERIMENTATION/
85	exp MODELS, ANIMAL/
86	exp RODENTIA/
87	(rat or rats or mouse or mice).ti.
88	or/81-87
89	70 not 88
90	and/42,89

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
11	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
12	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
13	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
14	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
15	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
16	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
17	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
18	or/10-17
19	and/5,9,18
20	limit 19 to english language

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.

Update 2015

9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	PATIENT EDUCATION AS TOPIC/
16	PROBLEM SOLVING/
17	ed.fs.
18	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
19	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
20	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
21	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
22	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
23	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
24	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
25	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
26	or/15-25
27	and/9,14,26

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,tw,tx,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).kw,tw,tx.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).kw,tw,tx.
8	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9	or/6-8
10	PATIENT EDUCATION AS TOPIC.kw.
11	PROBLEM SOLVING.kw.
12	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).tw,tx.
13	(problem-solving or "problem solving" or problem-based or "problem based").tw,tx.
14	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw,tx.

15	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).tw,tx.
16	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw,tx.
17	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw,tx.
18	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw,tx.
19	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).tw,tx.
20	or/10-19
21	and/5,9,20

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	PATIENT EDUCATION AS TOPIC/
16	PROBLEM SOLVING/
17	ed.fs.
18	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).tw.
19	(problem-solving or "problem solving" or problem-based or "problem based").tw.
20	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw.
21	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).tw.
22	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw.
23	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw.
24	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).tw.

Update 2015

25	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).tw.
26	or/15-25
27	and/9,14,26

Embase

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).ti,ab,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.ti,ab,sh.
9	random$.ti,ab,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	or/18,28
30	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31	13 not 30
32	29 not 30
33	or/31-32
34	exp ADOLESCENT/
35	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
36	exp CHILD/
37	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
38	exp INFANT/
39	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
40	exp PEDIATRICS/ or exp PUBERTY/
41	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
42	or/34-41
43	NON INSULIN DEPENDENT DIABETES MELLITUS/

Update 2015

44	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
45	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
46	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
47	or/43-46
48	JUVENILE DIABETES MELLITUS/
49	and/42,47
50	or/48-49
51	PATIENT EDUCATION/
52	DIABETES EDUCATION/
53	DIABETES EDUCATOR/
54	EDUCATION PROGRAM/
55	PROBLEM SOLVING/
56	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
57	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
58	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
59	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab.
60	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
61	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
62	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
63	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
64	or/51-63
65	and/50,64
66	limit 65 to english language
67	conference abstract.pt.
68	letter.pt. or LETTER/
69	note.pt.
70	editorial.pt.
71	CASE REPORT/ or CASE STUDY/
72	(letter or comment* or abstracts).ti.
73	or/67-72
74	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
75	73 not 74
76	ANIMAL/ not HUMAN/
77	NONHUMAN/
78	exp ANIMAL EXPERIMENT/
79	exp EXPERIMENTAL ANIMAL/
80	ANIMAL MODEL/
81	exp RODENT/
82	(rat or rats or mouse or mice).ti.
83	or/75-82
84	66 not 83
85	and/33,84

Update 2015

PsycINFO

#	Searches
1	LITERATURE REVIEW/
2	EXPERIMENTAL DESIGN/
3	RANDOM SAMPLING/
4	META-ANALYSIS/
5	exp TREATMENT/
6	(random$ or search$ or control$ or risk$).tw.
7	(meta-analys#s or metaanalys#s).ti.
8	(systematic$ adj (review$ or overview$)).ti.
9	((single or double or triple) adj (blind$ or mask$)).ti.
10	rct.tw.
11	or/1-10
12	adolescen$.ag.
13	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
14	(child$ or school$ or preschool$).ag.
15	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,id,jw.
16	(infan$ or neonat$).ag.
17	(infan$ or neonat$ or newborn$ or baby or babies or p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,id,jw.
18	or/12-17
19	DIABETES MELLITUS/
20	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab,id.
21	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab,id.
22	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab,id.
23	BLOOD SUGAR/
24	or/19-23
25	EDUCATIONAL THERAPY/
26	CLIENT EDUCATION/
27	EDUCATIONAL PROGRAMS/
28	PROBLEM SOLVING/
29	((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab,id.
30	(problem-solving or "problem solving" or problem-based or "problem based").ti,ab,id.
31	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.
32	((patient? or parent? or parental or child$ or adolescen$ or young or youth? or family$ or families) adj3 information).ti,ab,id.
33	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.
34	((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab,id.
35	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.
36	((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab,id.
37	or/25-36
38	and/18,24,37

Update 2015

39 and/11,38
40 limit 39 to english language

CINAHL with Full Text

#	Query	Limiters/Expanders
S36	S6 AND S34	Limiters - English Language; Exclude MEDLINE records Search modes - Boolean/Phrase
S35	S6 AND S34	Search modes - Boolean/Phrase
S34	S21 AND S33	Search modes - Boolean/Phrase
S33	S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32	Search modes - Boolean/Phrase
S32	TI ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N3 information) OR AB ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N3 information)	Search modes - Boolean/Phrase
S31	TI ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes))	Search modes - Boolean/Phrase
S30	TI ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information)	Search modes - Boolean/Phrase
S29	TI ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes))	Search modes - Boolean/Phrase
S28	TI ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information)	Search modes - Boolean/Phrase
S27	TI ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes))	Search modes - Boolean/Phrase
S26	TI (problem-solving or "problem solving" or problem-based or "problem based") OR AB (problem-solving or "problem solving" or problem-based or "problem based")	Search modes - Boolean/Phrase
S25	TI ((educat* or training) N6 (intervention* or program# or programme or programmes)) OR AB ((educat* or training) N6 (intervention* or program# or programme or programmes))	Search modes - Boolean/Phrase
S24	MW "ED"	Search modes - Boolean/Phrase
S23	(MH "Problem Solving+")	Search modes - Boolean/Phrase
S22	(MH "Patient Education") OR (MH "Diabetes Education")	Search modes - Boolean/Phrase
S21	S12 AND S20	Search modes - Boolean/Phrase
S20	S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19	Search modes - Boolean/Phrase
S19	AB (NIDDM or T2D or TIID or DM2 or DMII)	Search modes - Boolean/Phrase
S18	TI (NIDDM or T2D or TIID or DM2 or DMII)	Search modes - Boolean/Phrase

Update 2015

S17	AB (diabet* adj5 non insulin or non-insulin) Search modes - Boolean/Phrase
S16	TI (diabet* adj5 non insulin or non-insulin) Search modes - Boolean/Phrase
S15	AB (diabet* N5 "type two" or "type 2" or "type II" or T2 or slow or late or stable or ketosis resistant or keto resist* or keto-resist* or non keto* or non-keto*) Search modes - Boolean/Phrase
S14	TI (diabet* N5 "type two" or "type 2" or "type II" or T2 or slow or late or stable or ketosis resistant or keto resist* or keto-resist* or non keto* or non-keto*) Search modes - Boolean/Phrase
S13	(MH "Diabetes Mellitus, Type 2") Search modes - Boolean/Phrase
S12	S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase
S11	TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
S10	TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
S9	TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
S8	TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S7	(MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase
S6	S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
S5	PT systematic review Search modes - Boolean/Phrase
S4	PT review Search modes - Boolean/Phrase
S3	TX meta-analysis OR "meta analysis" Search modes - Boolean/Phrase
S2	TX random* Search modes - Boolean/Phrase
S1	(MH "Treatment Outcomes+") OR (MH "Experimental Studies+") Search modes - Boolean/Phrase

Update 2015

F.19 Type 2 diabetes – psychological interventions

Review questions:

What is the effectiveness of psychological interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/

6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	and/9,14
16	BEHAVIOR THERAPY/
17	COGNITIVE THERAPY/
18	PSYCHOTHERAPY/
19	PSYCHOTHERAPY, GROUP/
20	FAMILY THERAPY/
21	(psychotherap$ or BFST or CBT).ti,ab.
22	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
23	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
24	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
25	COUNSELING/
26	MOTIVATIONAL INTERVIEWING/
27	MENTORS/
28	SOCIAL SUPPORT/
29	SELF-HELP GROUPS/
30	(motivation$ or counsel?ing or mentor$).ti,ab.
31	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
32	or/16-31
33	and/15,32
34	limit 33 to english language
35	LETTER/
36	EDITORIAL/
37	NEWS/
38	exp HISTORICAL ARTICLE/
39	ANECDOTES AS TOPIC/
40	COMMENT/
41	CASE REPORT/
42	(letter or comment* or abstracts).ti.
43	or/35-42
44	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
45	43 not 44
46	ANIMALS/ not HUMANS/
47	exp ANIMALS, LABORATORY/
48	exp ANIMAL EXPERIMENTATION/
49	exp MODELS, ANIMAL/
50	exp RODENTIA/
51	(rat or rats or mouse or mice).ti.
52	or/45-51
53	34 not 52

Update 2015

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	and/5,9
11	(psychotherap$ or BFST or CBT).ti,ab.
12	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
13	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
14	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
15	(motivation$ or counsel?ing or mentor$).ti,ab.
16	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
17	or/11-16
18	and/10,17
19	limit 18 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	and/9,14
16	BEHAVIOR THERAPY/
17	COGNITIVE THERAPY/
18	PSYCHOTHERAPY/
19	PSYCHOTHERAPY, GROUP/
20	FAMILY THERAPY/
21	(psychotherap$ or BFST or CBT).ti,ab.
22	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.

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23	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
24	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
25	COUNSELING/
26	MOTIVATIONAL INTERVIEWING/
27	MENTORS/
28	SOCIAL SUPPORT/
29	SELF-HELP GROUPS/
30	(motivation$ or counsel?ing or mentor$).ti,ab.
31	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
32	or/16-31
33	and/15,32

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,ti,ab,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,ti,ab,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,ti,ab,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,ti,ab,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab,kw.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab,kw.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	GROUP THERAPY.kw.
11	(psychotherap$ or BFST or CBT).tw,tx,kw.
12	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).tw,tx,kw.
13	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).tw,tx,kw.
14	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).tw,tx,kw.
15	TEACHER.kw.
16	SUPPORT GROUP.kw.
17	SELF HELP.kw.
18	(motivation$ or counsel?ing or mentor$).tw,tx,kw.
19	((peer or social$ or self help or self-help) adj3 (group? or support?)).tw,tx,kw.
20	or/10-19
21	and/5,9,20

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/

Update 2015

8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	BEHAVIOR THERAPY/
16	COGNITIVE THERAPY/
17	PSYCHOTHERAPY/
18	PSYCHOTHERAPY, GROUP/
19	FAMILY THERAPY/
20	(psychotherap$ or BFST or CBT).tw.
21	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).tw.
22	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).tw.
23	((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).tw.
24	COUNSELING/
25	MOTIVATIONAL INTERVIEWING/
26	MENTORS/
27	SOCIAL SUPPORT/
28	SELF-HELP GROUPS/
29	(motivation$ or counsel?ing or mentor$).tw.
30	((peer or social$ or self help or self-help) adj3 (group? or support?)).tw.
31	or/15-30
32	and/9,14,31

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	NON INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	JUVENILE DIABETES MELLITUS/
16	and/9,14
17	or/15-16
18	BEHAVIOR THERAPY/
19	BEHAVIOR MODIFICATION/
20	COGNITIVE THERAPY/

Update 2015

21	PSYCHOTHERAPY/
22	FAMILY THERAPY/
23	GROUP THERAPY/
24	MOTIVATIONAL INTERVIEWING/
25	(psychotherap$ or BFST or CBT).ti,ab.
26	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
27	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
28	((family$ or families or parent$) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
29	COUNSELING/
30	FAMILY COUNSELING/
31	PARENT COUNSELING/
32	PATIENT COUNSELING/
33	PEER COUNSELING/
34	TEACHER/
35	SOCIAL SUPPORT/
36	SUPPORT GROUP/
37	SELF HELP/
38	(motivation$ or counsel?ing or mentor$).ti,ab.
39	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
40	or/18-39
41	and/17,40
42	limit 41 to english language
43	conference abstract.pt.
44	letter.pt. or LETTER/
45	note.pt.
46	editorial.pt.
47	CASE REPORT/ or CASE STUDY/
48	(letter or comment* or abstracts).ti.
49	or/43-48
50	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
51	49 not 50
52	ANIMAL/ not HUMAN/
53	NONHUMAN/
54	exp ANIMAL EXPERIMENT/
55	exp EXPERIMENTAL ANIMAL/
56	ANIMAL MODEL/
57	exp RODENT/
58	(rat or rats or mouse or mice).ti.
59	or/51-58
60	42 not 59

PsycINFO

#	Searches
1	adolescen$.ag.
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
3	(child$ or school$ or preschool$).ag.
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,id,jw.
5	(infan$ or neonat$).ag.
6	(infan$ or neonat$ or newborn$ or baby or babies or p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,id,jw.

Update 2015

7	or/1-6
8	DIABETES MELLITUS/
9	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab,id.
10	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab,id.
11	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab,id.
12	or/8-11
13	BEHAVIOR THERAPY/
14	COGNITIVE THERAPY/
15	COGNITIVE BEHAVIOR THERAPY/
16	PSYCHOTHERAPY/
17	ADOLESCENT PSYCHOTHERAPY/
18	CHILD PSYCHOTHERAPY/
19	GROUP PSYCHOTHERAPY/
20	FAMILY THERAPY/
21	FAMILY INTERVENTION/
22	MOTIVATIONAL INTERVIEWING/
23	(psychotherap$ or BFST or CBT).ti,ab.
24	((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.
25	((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.
26	((family$ or families or parent$) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.
27	COUNSELING/
28	GROUP COUNSELING/
29	PEER COUNSELING/
30	MENTOR/
31	SOCIAL SUPPORT/
32	SUPPORT GROUPS/
33	SELF HELP TECHNIQUES/
34	(motivation$ or counsel?ing or mentor$).ti,ab.
35	((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.
36	or/13-35
37	and/7,12,36
38	limit 37 to english language
39	limit 38 to yr="2013 -Current"

Update 2015

CINAHL with Full Text

#	Query	Limiters/Expanders
S24	S6 AND S9 AND S23	Limiters - English Language; Exclude MEDLINE records Search modes - Boolean/Phrase
S23	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22	Search modes - Boolean/Phrase
S22	TI ((peer or social* or “self help” or self-help) N3 (group# or support#)) OR AB ((peer or social* or “self help” or self-help) N3 (group# or support#))	Search modes - Boolean/Phrase
S21	TI (motivation* or counsel#ing or mentor*) OR AB (motivation* or counsel#ing or mentor*)	Search modes - Boolean/Phrase
S20	(MH "Support Groups")	Search modes - Boolean/Phrase
S19	(MH "Mentorship")	Search modes - Boolean/Phrase
S18	(MH "Counseling") OR (MH "Peer Counseling")	Search modes - Boolean/Phrase
S17	TI ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*)) OR AB ((family* or families or parent#) N5 (intervention* or	

	treatment* or therap* or team# or teamwork* or team-work*)) Search modes - Boolean/Phrase
S16	TI ((behavio#r* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) OR AB ((behavio#r* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) Search modes - Boolean/Phrase
S15	TI ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) OR AB ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) Search modes - Boolean/Phrase
S14	TI (psychotherap* or BFST or CBT) OR AB (psychotherap* or BFST or CBT) Search modes - Boolean/Phrase
S13	(MH "Motivational Interviewing") Search modes - Boolean/Phrase
S12	(MH "Psychotherapy, Group") OR (MH "Family Therapy") Search modes - Boolean/Phrase
S11	(MH "Psychotherapy") Search modes - Boolean/Phrase
S10	(MH "Behavior Therapy+") OR (MH "Cognitive Therapy") Search modes - Boolean/Phrase
S9	S7 OR S8 Search modes - Boolean/Phrase
S8	TI (diabet* N5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)) OR AB (diabet* N5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)) Search modes - Boolean/Phrase
S7	(MH "Diabetes Mellitus, Type 2") Search modes - Boolean/Phrase
S6	S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
S5	TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
S4	TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
S3	TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
S2	TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S1	(MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase

Update 2015

F.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/

6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	exp DIET THERAPY/
16	NUTRITION THERAPY/
17	dh.fs.
18	or/15-17
19	exp FOOD HABITS/
20	exp DIET/
21	DIETETICS/
22	(diet$ or nutrition$ or food or feed$).ti,ab.
23	or/19-22
24	HEMOGLOBIN A, GLYCOSYLATED/
25	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
26	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
27	"hemoglobin A1c protein, human".nm.
28	BLOOD GLUCOSE/
29	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
31	exp HYPERGLYCEMIA/
32	hyperglyc?emi$.ti,ab.
33	REMISSION INDUCTION/
34	remission?.ti,ab.
35	((revers$ or regress$) adj5 diabet$).ti,ab.
36	or/24-35
37	and/23,36
38	or/18,37
39	and/9,14,38
40	limit 39 to english language
41	LETTER/
42	EDITORIAL/
43	NEWS/
44	exp HISTORICAL ARTICLE/
45	ANECDOTES AS TOPIC/
46	COMMENT/
47	CASE REPORT/
48	(letter or comment* or abstracts).ti.
49	or/41-48
50	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
51	49 not 50
52	ANIMALS/ not HUMANS/
53	exp ANIMALS, LABORATORY/
54	exp ANIMAL EXPERIMENTATION/
55	exp MODELS, ANIMAL/
56	exp RODENTIA/
57	(rat or rats or mouse or mice).ti.

Update 2015

58	or/51-57
59	40 not 58

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	(diet$ or nutrition$ or food or feed$).ti,ab.
11	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
12	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
13	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
14	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
15	hyperglyc?emi$.ti,ab.
16	remission?.ti,ab.
17	((revers$ or regress$) adj5 diabet$).ti,ab.
18	or/11-17
19	and/5,9-10,18
20	limit 19 to english language

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	exp DIET THERAPY/
16	NUTRITION THERAPY/
17	dh.fs.
18	or/15-17
19	exp FOOD HABITS/
20	exp DIET/
21	DIETETICS/

Update 2015

22	(diet$ or nutrition$ or food or feed$).ti,ab.
23	or/19-22
24	HEMOGLOBIN A, GLYCOSYLATED/
25	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
26	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
27	["hemoglobin A1c protein, human".nm.]
28	BLOOD GLUCOSE/
29	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
31	exp HYPERGLYCEMIA/
32	hyperglyc?emi$.ti,ab.
33	REMISSION INDUCTION/
34	remission?.ti,ab.
35	((revers$ or regress$) adj5 diabet$).ti,ab.
36	or/24-35
37	and/23,36
38	or/18,37
39	and/9,14,38

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,tw,tx,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,tw,tx,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
8	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9	or/6-8
10	DIET THERAPY.kw.
11	NUTRITION THERAPY.kw.
12	or/10-11
13	(diet$ or nutrition$ or food or feed$).tw,tx,kw.
14	(h?emoglobin? adj3 (glyc$ or A1?)).tw,tx,kw.
15	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).tw,tx,kw.
16	((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
17	(glyc?emi$ adj3 (control$ or parameter$ or status$)).tw,tx,kw.
18	hyperglyc?emi$.tw,tx,kw.
19	remission?.tw,tx,kw.
20	((revers$ or regress$) adj5 diabet$).tw,tx.
21	or/14-20
22	and/13,21
23	or/12,22
24	and/5,9,23

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/

Update 2015

2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	exp DIET THERAPY/
16	NUTRITION THERAPY/
17	dh.fs.
18	or/15-17
19	exp FOOD HABITS/
20	exp DIET/
21	DIETETICS/
22	(diet$ or nutrition$ or food or feed$).tw.
23	or/19-22
24	HEMOGLOBIN A, GLYCOSYLATED/
25	(h?emoglobin? adj3 (glyc$ or A1?)).tw.
26	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).tw.
27	BLOOD GLUCOSE/
28	((blood or plasma) adj3 (glucose or sugar?)).tw.
29	(glyc?emi$ adj3 (control$ or parameter$ or status$)).tw.
30	exp HYPERGLYCEMIA/
31	hyperglyc?emi$.tw.
32	REMISSION INDUCTION/
33	remission?.tw.
34	((revers$ or regress$) adj5 diabet$).tw.
35	or/24-34
36	and/23,35
37	or/18,36
38	and/9,14,37

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	NON INSULIN DEPENDENT DIABETES MELLITUS/

Update 2015

11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	JUVENILE DIABETES MELLITUS/
16	and/9,14
17	or/15-16
18	exp DIET THERAPY/
19	exp FEEDING BEHAVIOR/
20	exp DIET/ or DIETARY COMPLIANCE/
21	DIETETICS/
22	(diet$ or nutrition$ or food or feed$).ti,ab.
23	or/19-22
24	HEMOGLOBIN A1C/
25	GLYCOSYLATED HEMOGLOBIN/
26	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
27	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
28	GLUCOSE BLOOD LEVEL/
29	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30	GLYCEMIC CONTROL/
31	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
32	HYPERGLYCEMIA/
33	hyperglyc?emi$.ti,ab.
34	REMISSION/ or DISEASE CLEARANCE/
35	remission?.ti,ab.
36	((revers$ or regress$) adj5 diabet$).ti,ab.
37	or/24-36
38	and/23,37
39	or/18,38
40	and/17,39
41	limit 40 to english language
42	conference abstract.pt.
43	letter.pt. or LETTER/
44	note.pt.
45	editorial.pt.
46	CASE REPORT/ or CASE STUDY/
47	(letter or comment* or abstracts).ti.
48	or/42-47
49	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50	48 not 49
51	ANIMAL/ not HUMAN/
52	NONHUMAN/
53	exp ANIMAL EXPERIMENT/
54	exp EXPERIMENTAL ANIMAL/
55	ANIMAL MODEL/
56	exp RODENT/
57	(rat or rats or mouse or mice).ti.
58	or/50-57
59	41 not 58

PsycINFO

#	Searches

Update 2015

1	adolescen$.ag.
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
3	(child$ or school$ or preschool$).ag.
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,id,jw.
5	(infan$ or neonat$).ag.
6	(infan$ or neonat$ or newborn$ or baby or babies or p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,id,jw.
7	or/1-6
8	DIABETES MELLITUS/
9	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab,id.
10	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab,id.
11	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab,id.
12	or/8-11
13	DIETS/ or DIETARY RESTRAINT/ or EATING BEHAVIOUR/ or WEIGHT CONTROL/
14	(diet$ or nutrition$ or food or feed$).ti,ab,id.
15	or/13-14
16	BLOOD SUGAR/
17	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab,id.
18	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab,id.
19	((blood or plasma) adj3 (glucose or sugar?)).ti,ab,id.
20	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab,id.
21	HYPERGLYCEMIA/
22	hyperglyc?emi$.ti,ab,id.
23	exp "REMISSION (DISORDERS)"/
24	remission?.ti,ab,id.
25	((revers$ or regress$) adj5 diabet$).ti,ab.
26	or/16-25
27	and/7,12,15,26
28	limit 27 to english language
29	(book or dissertation abstract or encyclopedia).pt.
30	28 not 29

Update 2015

F.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/

11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	exp OVERWEIGHT/
16	exp OBESITY/
17	(obes$ or overweight or over weight).ti,ab.
18	or/15-17
19	exp BODY WEIGHT CHANGES/
20	((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).ti,ab.
21	SERVING SIZE/
22	PORTION SIZE/
23	((serving? or portion?) adj3 (size? or sizing)).ti,ab.
24	or/19-23
25	HEMOGLOBIN A, GLYCOSYLATED/
26	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
27	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
28	"hemoglobin A1c protein, human".nm.
29	BLOOD GLUCOSE/
30	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
31	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
32	exp HYPERGLYCEMIA/
33	hyperglyc?emi$.ti,ab.
34	exp HYPOGLYCEMIA/
35	hypoglyc?emi$.ti,ab.
36	REMISSION INDUCTION/
37	remission?.ti,ab.
38	((revers$ or regress$) adj5 diabet$).ti,ab.
39	or/25-38
40	and/9,14,18,24,39
41	limit 40 to english language
42	LETTER/
43	EDITORIAL/
44	NEWS/
45	exp HISTORICAL ARTICLE/
46	ANECDOTES AS TOPIC/
47	COMMENT/
48	(letter or comment* or abstracts).ti.
49	or/42-48
50	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
51	49 not 50
52	ANIMALS/ not HUMANS/
53	exp ANIMALS, LABORATORY/
54	exp ANIMAL EXPERIMENTATION/
55	exp MODELS, ANIMAL/
56	exp RODENTIA/
57	(rat or rats or mouse or mice).ti.
58	or/51-57
59	41 not 58

Update 2015

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	(obes$ or overweight or over weight).ti,ab.
11	((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).ti,ab.
12	((serving? or portion?) adj3 (size? or sizing)).ti,ab.
13	or/11-12
14	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
15	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
16	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
17	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
18	hyperglyc?emi$.ti,ab.
19	hypoglyc?emi$.ti,ab.
20	remission?.ti,ab.
21	((revers$ or regress$) adj5 diabet$).ti,ab.
22	or/14-21
23	and/5,9-10,13,22

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	exp OVERWEIGHT/
16	exp OBESITY/
17	(obes$ or overweight or over weight).ti,ab.
18	or/15-17
19	exp BODY WEIGHT CHANGES/

Update 2015

20	((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).ti,ab.
21	SERVING SIZE/
22	PORTION SIZE/
23	((serving? or portion?) adj3 (size? or sizing)).ti,ab.
24	or/19-23
25	HEMOGLOBIN A, GLYCOSYLATED/
26	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
27	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
28	BLOOD GLUCOSE/
29	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
31	exp HYPERGLYCEMIA/
32	hyperglyc?emi$.ti,ab.
33	exp HYPOGLYCEMIA/
34	hypoglyc?emi$.ti,ab.
35	REMISSION INDUCTION/
36	remission?.ti,ab.
37	((revers$ or regress$) adj5 diabet$).ti,ab.
38	or/25-37
39	and/9,14,18,24,38

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
8	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9	or/6-8
10	(obes$ or overweight or over weight).tw,tx,kw.
11	((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).tw,tx,kw.
12	(portion? or serv?).tw,tx,kw.
13	or/11-12
14	(h?emoglobin? adj3 (glyc$ or A1?)).tw,tx,kw.
15	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).tw,tx.
16	((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
17	(glyc?emi$ adj3 (control$ or parameter$ or status$)).tw,tx,kw.
18	hyperglyc?emi$.tw,tx,kw.
19	hypoglyc?emi$.tw,tx,kw.
20	remission?.tw,tx,kw.
21	((revers$ or regress$) adj5 diabet$).tw,tx.
22	or/14-21
23	and/5,9-10,13,22

Update 2015

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	exp OVERWEIGHT/
16	exp OBESITY/
17	(obes$ or overweight or over weight).tw.
18	or/15-17
19	exp BODY WEIGHT CHANGES/
20	(portion? or serv?).tw.
21	((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).tw.
22	or/19-20
23	HEMOGLOBIN A, GLYCOSYLATED/
24	(h?emoglobin? adj3 (glyc$ or A1?)).tw.
25	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).tw.
26	BLOOD GLUCOSE/
27	((blood or plasma) adj3 (glucose or sugar?)).tw.
28	(glyc?emi$ adj3 (control$ or parameter$ or status$)).tw.
29	exp HYPERGLYCEMIA/
30	hyperglyc?emi$.tw.
31	exp HYPOGLYCEMIA/
32	hypoglyc?emi$.tw.
33	REMISSION INDUCTION/
34	remission?.tw.
35	((revers$ or regress$) adj5 diabet$).tw.
36	or/23-35
37	and/9,14,18,22,36

Embase 1974 to 2014 April 03

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.

Update 2015

7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	NON INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	JUVENILE DIABETES MELLITUS/
16	and/9,14
17	or/15-16
18	exp OBESITY/
19	(obes$ or overweight or over weight).ti,ab.
20	or/18-19
21	WEIGHT CHANGE/ or WEIGHT CONTROL/ or WEIGHT GAIN/ or WEIGHT REDUCTION/
22	((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).ti,ab.
23	((serving? or portion?) adj3 (size? or sizing)).ti,ab.
24	or/21-23
25	HEMOGLOBIN A1C/
26	GLYCOSYLATED HEMOGLOBIN/
27	(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
28	(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA Ic or Hb A1c or Hb AIc).ti,ab.
29	GLUCOSE BLOOD LEVEL/
30	((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
31	GLYCEMIC CONTROL/
32	(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
33	HYPERGLYCEMIA/
34	hyperglyc?emi$.ti,ab.
35	HYPOGLYCEMIA/
36	hypoglyc?emi$.ti,ab.
37	REMISSION/
38	remission?.ti,ab.
39	((revers$ or regress$) adj5 diabet$).ti,ab.
40	or/25-39
41	and/17,20,24,40
42	limit 41 to english language
43	conference abstract.pt.
44	letter.pt. or LETTER/
45	note.pt.
46	editorial.pt.
47	(letter or comment* or abstracts).ti.
48	or/43-47
49	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50	48 not 49
51	ANIMAL/ not HUMAN/
52	NONHUMAN/
53	exp ANIMAL EXPERIMENT/
54	exp EXPERIMENTAL ANIMAL/
55	ANIMAL MODEL/
56	exp RODENT/

Update 2015

57	(rat or rats or mouse or mice).ti.
58	or/50-57
59	42 not 58

F.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	or/1-5
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
8	clinical trial.pt.
9	exp CLINICAL TRIAL/
10	exp CLINICAL TRIALS AS TOPIC/
11	(clinic$ adj5 trial$).tw,sh.
12	PLACEBOS/
13	placebo$.tw,sh.
14	random$.tw,sh.
15	or/7-14
16	or/6,15
17	META ANALYSIS/
18	META ANALYSIS AS TOPIC/
19	meta analysis.pt.
20	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21	(systematic$ adj5 (review$ or overview$)).tw,sh.
22	(methodologic$ adj5 (review$ or overview$)).tw,sh.
23	or/17-22
24	review$.pt.
25	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
26	((hand or manual$) adj2 search$).tw.
27	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
28	(pooling or pooled or mantel haenszel).tw,sh.
29	(peto or dersimonian or der simonian or fixed effect).tw,sh.
30	or/25-29
31	and/24,30
32	or/16,23,31
33	letter.pt.
34	case report.tw.
35	comment.pt.
36	editorial.pt.
37	historical article.pt.
38	or/33-37

Update 2015

39	32 not 38
40	ADOLESCENT/ or MINORS/
41	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
42	exp CHILD/
43	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
44	exp INFANT/
45	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
46	exp PEDIATRICS/ or exp PUBERTY/
47	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
48	or/40-47
49	exp DIABETES MELLITUS, TYPE 2/
50	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
51	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
52	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
53	or/49-52
54	METFORMIN/
55	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
56	or/54-55
57	and/48,53,56
58	and/39,57
59	limit 58 to english language
60	LETTER/
61	EDITORIAL/
62	NEWS/
63	exp HISTORICAL ARTICLE/
64	ANECDOTES AS TOPIC/
65	COMMENT/
66	CASE REPORT/
67	(letter or comment* or abstracts).ti.
68	or/60-67
69	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
70	68 not 69
71	ANIMALS/ not HUMANS/
72	exp ANIMALS, LABORATORY/
73	exp ANIMAL EXPERIMENTATION/
74	exp MODELS, ANIMAL/
75	exp RODENTIA/
76	(rat or rats or mouse or mice).ti.
77	or/70-76
78	59 not 77

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.

Update 2015

7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
11	and/5,9-10

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,kw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,kw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,kw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,kw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab,kw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab,kw.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	METFORMIN/
16	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab,kw.
17	or/15-16
18	and/9,14,17

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab,kw.
8	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9	or/6-8
10	(metformin or glucophage or glucient or metsol or bolamyn or metabet).tw,tx,kw.
11	and/5,9-10

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw.
3	exp CHILD/

Update 2015

4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	METFORMIN/
16	(metformin or glucophage or glucient or metsol or bolamyn or metabet).tw.
17	or/15-16
18	and/9,14,17

Embase

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).ti,ab,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.ti,ab,sh.
9	random$.ti,ab,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	or/18,28
30	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31	13 not 30
32	29 not 30

Update 2015

33	or/31-32
34	exp ADOLESCENT/
35	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
36	exp INFANT/
37	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
38	exp NEWBORN/
39	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
40	exp PEDIATRICS/ or exp PUBERTY/
41	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
42	or/34-41
43	NON INSULIN DEPENDENT DIABETES MELLITUS/
44	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
45	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
46	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
47	or/43-46
48	JUVENILE DIABETES MELLITUS/
49	and/42,47
50	or/48-49
51	METFORMIN/
52	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
53	or/51-52
54	and/50,53
55	limit 54 to english language
56	conference abstract.pt.
57	letter.pt. or LETTER/
58	note.pt.
59	editorial.pt.
60	CASE REPORT/ or CASE STUDY/
61	(letter or comment* or abstracts).ti.
62	or/56-61
63	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
64	62 not 63
65	ANIMAL/ not HUMAN/
66	NONHUMAN/
67	exp ANIMAL EXPERIMENT/
68	exp EXPERIMENTAL ANIMAL/
69	ANIMAL MODEL/
70	exp RODENT/
71	(rat or rats or mouse or mice).ti.
72	or/64-71
73	55 not 72
74	and/33,73

F.23 Type 2 diabetes – HbA1c targets

Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches

Update 2015

1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	or/1-5
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
8	clinical trial.pt.
9	exp CLINICAL TRIAL/
10	exp CLINICAL TRIALS AS TOPIC/
11	(clinic$ adj5 trial$).tw,sh.
12	PLACEBOS/
13	placebo$.tw,sh.
14	random$.tw,sh.
15	or/7-14
16	or/6,15
17	META ANALYSIS/
18	META ANALYSIS AS TOPIC/
19	meta analysis.pt.
20	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21	(systematic$ adj5 (review$ or overview$)).tw,sh.
22	(methodologic$ adj5 (review$ or overview$)).tw,sh.
23	or/17-22
24	review$.pt.
25	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
26	((hand or manual$) adj2 search$).tw.
27	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
28	(pooling or pooled or mantel haenszel).tw,sh.
29	(peto or dersimonian or der simonian or fixed effect).tw,sh.
30	or/25-29
31	and/24,30
32	exp CASE-CONTROL STUDIES/
33	(case$ adj2 control$).tw.
34	exp COHORT STUDIES/
35	cohort$.tw.
36	or/32-35
37	comparative study.pt.
38	(compar$ adj3 stud$).tw.
39	or/37-38
40	or/16,23,31,36,39
41	ADOLESCENT/ or MINORS/
42	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
43	exp CHILD/
44	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
45	exp INFANT/
46	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
47	exp PEDIATRICS/ or exp PUBERTY/
48	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
49	or/41-48
50	exp DIABETES MELLITUS, TYPE 2/

Update 2015

51	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
52	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
53	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
54	or/50-53
55	and/49,54
56	HEMOGLOBIN A, GLYCOSYLATED/
57	(h?emoglobin? adj3 glycosylat$).ti,ab.
58	(glycated adj3 h?emoglobin?).ti,ab.
59	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
60	"hemoglobin A1c protein, human".nm.
61	or/56-60
62	and/55,61
63	REFERENCE STANDARDS/ or REFERENCE VALUES/
64	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
65	or/63-64
66	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
67	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
68	or/65-67
69	and/62,68
70	and/55,69
71	LETTER/
72	EDITORIAL/
73	NEWS/
74	exp HISTORICAL ARTICLE/
75	ANECDOTES AS TOPIC/
76	COMMENT/
77	CASE REPORT/
78	(letter or comment* or abstracts).ti.
79	or/71-78
80	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
81	79 not 80
82	ANIMALS/ not HUMANS/
83	exp ANIMALS, LABORATORY/
84	exp ANIMAL EXPERIMENTATION/
85	exp MODELS, ANIMAL/
86	exp RODENTIA/
87	(rat or rats or mouse or mice).ti.
88	or/81-87
89	70 not 88
90	limit 89 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
5	or/1-4

Update 2015

6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$ or mellitus)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	(h?emoglobin? adj3 glycosylat$).ti,ab.
11	(glycated adj3 h?emoglobin?).ti,ab.
12	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
13	or/10-12
14	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
15	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
16	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
17	or/14-16
18	and/5,9,13,17

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	and/9,14
16	HEMOGLOBIN A, GLYCOSYLATED/
17	(h?emoglobin? adj3 glycosylat$).ti,ab.
18	(glycated adj3 h?emoglobin?).ti,ab.
19	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
20	or/16-19
21	REFERENCE STANDARDS/ or REFERENCE VALUES/
22	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
23	or/21-22
24	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
25	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
26	or/23-25
27	and/20,26
28	and/15,27

Update 2015

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(ADOLESCENT or MINORS).kw.
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx.
3	CHILD.kw.
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx.
5	INFANT.kw.
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx.
7	(PEDIATRICS or PUBERTY).kw.
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx.
9	or/1-8
10	DIABETES MELLITUS, TYPE 2.kw.
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
14	or/10-13
15	and/9,14
16	HEMOGLOBIN A, GLYCOSYLATED.kw.
17	(h?emoglobin? adj3 glycosylat$).tw,tx.
18	(glycated adj3 h?emoglobin?).tw,tx.
19	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).tw,tx.
20	or/16-19
21	(REFERENCE STANDARDS or REFERENCE VALUES).kw.
22	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).tw,tx.
23	or/21-22
24	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).tw,tx.
25	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).tw,tx.
26	or/23-25
27	and/20,26
28	and/15,27

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.

Update 2015

14	or/10-13
15	and/9,14
16	HEMOGLOBIN A, GLYCOSYLATED/
17	(h?emoglobin? adj3 glycosylat$).tw.
18	(glycated adj3 h?emoglobin?).tw.
19	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).tw.
20	or/16-19
21	REFERENCE STANDARDS/ or REFERENCE VALUES/
22	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).tw.
23	or/21-22
24	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).tw.
25	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).tw.
26	or/23-25
27	and/20,26
28	and/15,27

Embase

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).tw,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.tw,sh.
9	random$.tw,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.
16	(systematic$ adj5 (review$ or overview$)).tw,sh.
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	exp CASE CONTROL STUDY/
30	RETROSPECTIVE STUDY/
31	(case$ adj2 control$).tw.
32	COHORT ANALYSIS/

Update 2015

33	LONGITUDINAL STUDY/
34	FOLLOW UP/
35	PROSPECTIVE STUDY/
36	cohort$.tw.
37	or/29-36
38	or/13,18,28,37
39	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40	38 not 39
41	COMPARATIVE STUDY/
42	(compar$ adj3 stud$).tw.
43	or/41-42
44	or/40,43
45	exp ADOLESCENT/
46	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
47	exp CHILD/
48	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
49	exp INFANT/
50	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
51	exp PEDIATRICS/ or exp PUBERTY/
52	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
53	or/45-52
54	NON INSULIN DEPENDENT DIABETES MELLITUS/
55	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
56	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
57	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
58	or/54-57
59	JUVENILE DIABETES MELLITUS/
60	and/53,58
61	or/59-60
62	HEMOGLOBIN A1c/
63	(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
64	(h?emoglobin? adj3 glycosylat$).ti,ab.
65	(glycated adj3 h?emoglobin?).ti,ab.
66	or/62-65
67	and/61,66
68	STANDARD/
69	REFERENCE VALUE/
70	((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
71	or/68-70
72	((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
73	((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold?)).ti,ab.
74	or/71-73
75	and/67,74
76	and/44,75
77	conference abstract.pt.
78	letter.pt. or LETTER/
79	note.pt.
80	editorial.pt.
81	CASE REPORT/ or CASE STUDY/

Update 2015

82	(letter or comment* or abstracts).ti.
83	or/77-82
84	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
85	83 not 84
86	ANIMAL/ not HUMAN/
87	NONHUMAN/
88	exp ANIMAL EXPERIMENT/
89	exp EXPERIMENTAL ANIMAL/
90	ANIMAL MODEL/
91	exp RODENT/
92	(rat or rats or mouse or mice).ti.
93	or/85-92
94	76 not 93
95	limit 94 to english language

F.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	HYPERTENSION/
16	PREHYPERTENSION/
17	(hypertens$ or prehypertens$).ti,ab.
18	((high or elevat$ or increas$) adj3 blood pressur$).ti,ab.
19	or/15-18
20	BLOOD PRESSURE/
21	exp BLOOD PRESSURE DETERMINATION/
22	((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
23	or/20-22
24	SEVERITY OF ILLNESS INDEX/
25	DISEASE PROGRESSION/
26	INTERNATIONAL CLASSIFICATION OF DISEASES/
27	CLASSIFICATION/

Update 2015

28	((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
29	or/24-28
30	MASS SCREENING/
31	exp POPULATION SURVEILLANCE/
32	(undiagnos$ or estimate$).ti.
33	(screen$ or surveill$ or predict$ or detect$).ti.
34	or/30-33
35	PREVALENCE/
36	INCIDENCE/
37	exp COHORT STUDIES/
38	CROSS-SECTIONAL STUDIES/
39	exp MODELS, STATISTICAL/
40	LIFE TABLES/
41	exp RISK/
42	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
43	or/35-42
44	AGE FACTORS/
45	AGE DISTRIBUTION/
46	AGE OF ONSET/
47	TIME TO TREATMENT/
48	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
49	(disease adj3 (duration or onset)).ti,ab.
50	or/44-49
51	19 and (23 or 29 or 34 or 43 or 50)
52	*HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
53	*PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
54	or/51-53
55	and/9,14,54
56	*DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
57	and/9,56
58	*DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
59	*DIABETES COMPLICATIONS/ep [Epidemiology]
60	or/58-59
61	9 and (35 or 36) and 60
62	(diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
63	9 and 14 and (43 or 50) and 62
64	or/55,57,61,63
65	limit 64 to english language
66	LETTER/
67	EDITORIAL/
68	NEWS/
69	exp HISTORICAL ARTICLE/
70	ANECDOTES AS TOPIC/
71	COMMENT/
72	(letter or comment* or abstracts).ti.
73	or/66-72
74	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
75	73 not 74

Update 2015

76	ANIMALS/ not HUMANS/
77	exp ANIMALS, LABORATORY/
78	exp ANIMAL EXPERIMENTATION/
79	exp MODELS, ANIMAL/
80	exp RODENTIA/
81	(rat or rats or mouse or mice).ti.
82	or/75-81
83	65 not 82
84	limit 83 to yr="2013 -Current"

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	(hypertens$ or prehypertens$).ti,ab.
11	((high or elevat$ or increas$) adj3 blood pressur$).ti,ab.
12	or/10-11
13	((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
14	((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
15	(undiagnos$ or estimate$).ti.
16	(screen$ or surveill$ or predict$ or detect$).ti.
17	or/15-16
18	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
19	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
20	(disease adj3 (duration or onset)).ti,ab.
21	or/19-20
22	12 and (13 or 14 or 17 or 18 or 21)
23	and/5,9,22
24	(diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
25	5 and 9 and (18 or 21) and 24
26	or/23,25

Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/

Update 2015

8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	HYPERTENSION/
16	PREHYPERTENSION/
17	(hypertens$ or prehypertens$).ti,ab.
18	((high or elevat$ or increas$) adj3 blood pressur$).ti,ab.
19	or/15-18
20	BLOOD PRESSURE/
21	exp BLOOD PRESSURE DETERMINATION/
22	((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
23	or/20-22
24	SEVERITY OF ILLNESS INDEX/
25	DISEASE PROGRESSION/
26	INTERNATIONAL CLASSIFICATION OF DISEASES/
27	CLASSIFICATION/
28	((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
29	or/24-28
30	MASS SCREENING/
31	exp POPULATION SURVEILLANCE/
32	(undiagnos$ or estimate$).ti.
33	(screen$ or surveill$ or predict$ or detect$).ti.
34	or/30-33
35	PREVALENCE/
36	INCIDENCE/
37	exp COHORT STUDIES/
38	CROSS-SECTIONAL STUDIES/
39	exp MODELS, STATISTICAL/
40	LIFE TABLES/
41	exp RISK/
42	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
43	or/35-42
44	AGE FACTORS/
45	AGE DISTRIBUTION/
46	AGE OF ONSET/
47	TIME TO TREATMENT/
48	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
49	(disease adj3 (duration or onset)).ti,ab.
50	or/44-49
51	19 and (23 or 29 or 34 or 43 or 50)
52	*HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
53	*PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
54	or/51-53
55	and/9,14,54

Update 2015

56	*DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
57	and/9,56
58	*DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
59	*DIABETES COMPLICATIONS/ep [Epidemiology]
60	or/58-59
61	9 and (35 or 36) and 60
62	(diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
63	9 and 14 and (43 or 50) and 62
64	or/55,57,61,63

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
8	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9	or/6-8
10	(hypertens$ or prehypertens$).tw,tx,kw.
11	((high or elevat$ or increas$) adj3 blood pressur$).tw,tx.
12	or/10-11
13	((blood or systol$ or diastol$ or arterial) adj3 pressur$).tw,tx,kw.
14	SEVERITY OF ILLNESS INDEX.kw.
15	(DISEASE PROGRESSION or DISEASE SEVERITY or DISEASE COURSE).kw.
16	STAGING.kw.
17	INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
18	RATING SCALE.kw.
19	CLASSIFICATION.kw.
20	((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).tw,tx.
21	or/14-20
22	RESCREENING.kw.
23	(undiagnos$ or estimate$).ti.
24	(screen$ or surveill$ or predict$ or detect$).ti,kw.
25	or/22-24
26	CROSS-SECTIONAL STUD$.kw.
27	LONGITUDINAL STUD$.kw.
28	COHORT.kw.
29	LIFE TABLE?.kw.
30	(prevalen$ or incidence? or model$ or risk$ or rate?).ti,kw.
31	or/26-30
32	AGE.kw.
33	TIME TO TREATMENT.kw.
34	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw,tx,kw.

Update 2015

35	(disease adj3 (duration or onset)).tw,tx,kw.
36	or/32-35
37	12 and (13 or 21 or 25 or 31 or 36)
38	and/5,9,37
39	(diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
40	5 and 9 and (31 or 36) and 39
41	or/38,40

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	HYPERTENSION/
16	PREHYPERTENSION/
17	(hypertens$ or prehypertens$).tw.
18	((high or elevat$ or increas$) adj3 blood pressur$).tw.
19	or/15-18
20	BLOOD PRESSURE/
21	exp BLOOD PRESSURE DETERMINATION/
22	((blood or systol$ or diastol$ or arterial) adj3 pressur$).tw.
23	or/20-22
24	SEVERITY OF ILLNESS INDEX/
25	DISEASE PROGRESSION/
26	INTERNATIONAL CLASSIFICATION OF DISEASES/
27	CLASSIFICATION/
28	((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).tw.
29	or/24-28
30	MASS SCREENING/
31	exp POPULATION SURVEILLANCE/
32	(undiagnos$ or estimate$).ti.
33	(screen$ or surveill$ or predict$ or detect$).ti.
34	or/30-33
35	PREVALENCE/
36	INCIDENCE/
37	exp COHORT STUDIES/
38	CROSS-SECTIONAL STUDIES/
39	exp MODELS, STATISTICAL/

Update 2015

40	LIFE TABLES/
41	exp RISK/
42	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
43	or/35-42
44	AGE FACTORS/
45	AGE DISTRIBUTION/
46	AGE OF ONSET/
47	TIME TO TREATMENT/
48	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw.
49	(disease adj3 (duration or onset)).tw.
50	or/44-49
51	19 and (23 or 29 or 34 or 43 or 50)
52	HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
53	PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
54	or/51-53
55	and/9,14,54
56	DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
57	and/9,56
58	DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
59	DIABETES COMPLICATIONS/ep [Epidemiology]
60	or/58-59
61	9 and (35 or 36) and 60
62	(diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
63	9 and 14 and (43 or 50) and 62
64	or/55,57,61,63

Update 2015

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	NON INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	and/9,14
16	JUVENILE DIABETES MELLITUS/
17	or/15-16
18	HYPERTENSION/
19	DIABETIC HYPERTENSION/
20	PREHYPERTENSION/

21	(hypertens$ or prehypertens$).ti,ab.
22	((high or elevat$ or increas$) adj3 blood pressur$).ti,ab.
23	or/18-22
24	exp BLOOD PRESSURE/
25	exp BLOOD PRESSURE MEASUREMENT/
26	((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
27	or/24-26
28	SEVERITY OF ILLNESS INDEX/
29	DISEASE SEVERITY/
30	DISEASE COURSE/
31	STAGING/
32	exp INTERNATIONAL CLASSIFICATION OF DISEASES/
33	RATING SCALE/
34	CLASSIFICATION/
35	DISEASE CLASSIFICATION/
36	((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
37	or/28-36
38	SCREENING/
39	MASS SCREENING/
40	SCREENING TEST/
41	RESCREENING/
42	exp DISEASE SURVEILLANCE/
43	(undiagnos$ or estimate$).ti.
44	(screen$ or surveill$ or predict$ or detect$).ti.
45	or/38-44
46	PREVALENCE/
47	INCIDENCE/
48	CROSS-SECTIONAL STUDY/
49	LONGITUDINAL STUDY/
50	COHORT ANALYSIS/
51	STATISTICAL MODEL/
52	LIFE TABLE/
53	exp RISK/
54	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
55	or/46-54
56	AGE/
57	AGE DISTRIBUTION/
58	ONSET AGE/
59	DISEASE DURATION/
60	TIME TO TREATMENT/
61	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
62	(disease adj3 (duration or onset)).ti,ab.
63	or/56-62
64	23 and (27 or 37 or 45 or 55 or 63)
65	*HYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
66	*PREHYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
67	or/64-66
68	and/17,67
69	DIABETIC HYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
70	and/9,69
71	*NON INSULIN DEPENDENT DIABETES MELLITUS/co, ep [Complication, Epidemiology]
72	9 and (46 or 47) and 71

Update 2015

73	(diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
74	17 and (55 or 63) and 73
75	or/68,70,72,74
76	limit 75 to english language
77	conference abstract.pt.
78	letter.pt. or LETTER/
79	note.pt.
80	editorial.pt.
81	(letter or comment* or abstracts).ti.
82	or/77-81
83	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
84	82 not 83
85	ANIMAL/ not HUMAN/
86	NONHUMAN/
87	exp ANIMAL EXPERIMENT/
88	exp EXPERIMENTAL ANIMAL/
89	ANIMAL MODEL/
90	exp RODENT/
91	(rat or rats or mouse or mice).ti.
92	or/84-91
93	76 not 92

F.25 Type 2 diabetes – dyslipidaemia

Update 2015

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	exp DYSLIPIDEMIAS/
16	(d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).ti,ab.
17	or/15-16
18	LIPIDS/bl [Blood]
19	CHOLESTEROL/an, bl [Analysis, Blood]
20	CHOLESTEROL, HDL/an, bl [Analysis, Blood]

21	CHOLESTEROL, LDL/an, bl [Analysis, Blood]
22	LIPOPROTEINS/an, bl [Analysis, Blood]
23	LIPOPROTEINS, HDL/an, bl [Analysis, Blood]
24	LIPOPROTEINS, LDL/an, bl [Analysis, Blood]
25	exp TRIGLYCERIDES/an, bl [Analysis, Blood]
26	(cholester$ or epicholester$ or lipoprotein? or lipid?).ti,ab.
27	(alphalip$ or alpha lipoprotein$ or HDL cholester$).ti,ab.
28	(betalip$ or beta lipoprotein$ or LDL cholester$).ti,ab.
29	(triglyceride? or triacy?glycerol?).ti,ab.
30	((HDL or LDL) adj3 cholester$ adj3 ratio?).ti,ab.
31	or/18-30
32	PREVALENCE/
33	INCIDENCE/
34	exp COHORT STUDIES/
35	CROSS-SECTIONAL STUDIES/
36	exp MODELS, STATISTICAL/
37	LIFE TABLES/
38	exp RISK/
39	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
40	or/32-39
41	MASS SCREENING/
42	exp POPULATION SURVEILLANCE/
43	(undiagnos$ or estimate$).ti.
44	(screen$ or surveill$ or predict$ or detect$).ti.
45	or/41-44
46	SEVERITY OF ILLNESS INDEX/
47	DISEASE PROGRESSION/
48	INTERNATIONAL CLASSIFICATION OF DISEASES/
49	CLASSIFICATION/
50	(d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
51	or/46-50
52	AGE FACTORS/
53	AGE DISTRIBUTION/
54	AGE OF ONSET/
55	TIME TO TREATMENT/
56	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
57	(disease adj3 (duration or onset)).ti,ab.
58	or/52-57
59	17 and (31 or 40 or 45 or 51 or 58)
60	exp *DYSLIPIDEMIAS/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
61	or/59-60
62	and/9,14,61
63	DIABETES COMPLICATIONS/
64	and/9,14,31,63
65	(DIABETES MELLITUS, TYPE 2/ and COMORBIDITY/) or DIABETES MELLITUS, TYPE 2/co [Complications]
66	and/9,31,65
67	or/62,64,66
68	limit 67 to english language
69	LETTER/
70	EDITORIAL/

Update 2015

71	NEWS/
72	exp HISTORICAL ARTICLE/
73	ANECDOTES AS TOPIC/
74	COMMENT/
75	(letter or comment* or abstracts).ti.
76	or/69-75
77	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
78	76 not 77
79	ANIMALS/ not HUMANS/
80	exp ANIMALS, LABORATORY/
81	exp ANIMAL EXPERIMENTATION/
82	exp MODELS, ANIMAL/
83	exp RODENTIA/
84	(rat or rats or mouse or mice).ti.
85	or/78-84
86	68 not 85

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
3	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
8	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9	or/6-8
10	(d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).ti,ab.
11	(cholester$ or epicholester$ or lipoprotein? or lipid?).ti,ab.
12	(alphalip$ or alpha lipoprotein$ or HDL cholester$).ti,ab.
13	(betalip$ or beta lipoprotein$ or LDL cholester$).ti,ab.
14	(triglyceride? or triacy?glycerol?).ti,ab.
15	((HDL or LDL) adj3 cholester$ adj3 ratio?).ti,ab.
16	or/11-15
17	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
18	(undiagnos$ or estimate$).ti.
19	(screen$ or surveill$ or predict$ or detect$).ti.
20	or/18-19
21	(d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
22	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
23	(disease adj3 (duration or onset)).ti,ab.
24	or/22-23
25	10 and (16 or 17 or 20 or 21 or 24)
26	and/5,9,25

EBM Reviews - Cochrane Central Register of Controlled Trials

#	Searches
1	ADOLESCENT/ or MINORS/

Update 2015

2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	exp DYSLIPIDEMIAS/
16	(d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).ti,ab.
17	or/15-16
18	LIPIDS/bl [Blood]
19	CHOLESTEROL/an, bl [Analysis, Blood]
20	CHOLESTEROL, HDL/an, bl [Analysis, Blood]
21	CHOLESTEROL, LDL/an, bl [Analysis, Blood]
22	LIPOPROTEINS/an, bl [Analysis, Blood]
23	LIPOPROTEINS, HDL/an, bl [Analysis, Blood]
24	LIPOPROTEINS, LDL/an, bl [Analysis, Blood]
25	exp TRIGLYCERIDES/an, bl [Analysis, Blood]
26	(cholester$ or epicholester$ or lipoprotein? or lipid?).ti,ab.
27	(alphalip$ or alpha lipoprotein$ or HDL cholester$).ti,ab.
28	(betalip$ or beta lipoprotein$ or LDL cholester$).ti,ab.
29	(triglyceride? or triacy?glycerol?).ti,ab.
30	((HDL or LDL) adj3 cholester$ adj3 ratio?).ti,ab.
31	or/18-30
32	PREVALENCE/
33	INCIDENCE/
34	exp COHORT STUDIES/
35	CROSS-SECTIONAL STUDIES/
36	exp MODELS, STATISTICAL/
37	LIFE TABLES/
38	exp RISK/
39	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
40	or/32-39
41	MASS SCREENING/
42	exp POPULATION SURVEILLANCE/
43	(undiagnos$ or estimate$).ti.
44	(screen$ or surveill$ or predict$ or detect$).ti.
45	or/41-44
46	SEVERITY OF ILLNESS INDEX/
47	DISEASE PROGRESSION/
48	INTERNATIONAL CLASSIFICATION OF DISEASES/
49	CLASSIFICATION/
50	(d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.

Update 2015

51	or/46-50
52	AGE FACTORS/
53	AGE DISTRIBUTION/
54	AGE OF ONSET/
55	TIME TO TREATMENT/
56	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
57	(disease adj3 (duration or onset)).ti,ab.
58	or/52-57
59	17 and (31 or 40 or 45 or 51 or 58)
60	exp *DYSLIPIDEMIAS/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
61	or/59-60
62	and/9,14,61
63	DIABETES COMPLICATIONS/
64	and/9,14,31,63
65	(DIABETES MELLITUS, TYPE 2/ and COMORBIDITY/) or DIABETES MELLITUS, TYPE 2/co [Complications]
66	and/9,31,65
67	or/62,64,66

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

#	Searches
1	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw,rw.
2	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw,rw.
3	(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw,rw.
4	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw,rw.
5	or/1-4
6	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
7	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
8	(NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9	or/6-8
10	(d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).tw,tx,kw.
11	(cholester$ or epicholester$ or lipoprotein? or lipid?).tw,tx,kw.
12	(alphalip$ or alpha lipoprotein$ or HDL cholester$).tw,tx,kw.
13	(betalip$ or beta lipoprotein$ or LDL cholester$).tw,tx,kw.
14	(triglyceride? or triacy?glycerol?).tw,tx,kw.
15	((HDL or LDL) adj3 cholester$ adj3 ratio?).tw,tx.
16	or/11-15
17	LIFE TABLE$.kw.
18	(prevalen$ or incidence? or model$ or risk$ or rate?).ti,kw.
19	or/17-18
20	RESCREENING.kw.
21	(undiagnos$ or estimate$).ti.
22	(screen$ or surveill$ or predict$ or detect$).ti,kw.
23	or/20-22
24	SEVERITY OF ILLNESS INDEX.kw.
25	(DISEASE PROGRESSION or DISEASE COURSE or DISEASE SEVERITY).kw.
26	STAGING.kw.

Update 2015

27	INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
28	RATING SCALE.kw.
29	CLASSIFICATION.kw.
30	(d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).tw,tx.
31	or/24-30
32	AGE.kw.
33	TIME TO TREATMENT.kw.
34	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw,tx,kw.
35	(disease adj3 (duration or onset)).tw,tx,kw.
36	or/32-35
37	10 and (16 or 19 or 23 or 31 or 36)
38	DIABETES COMPLICATIONS.kw.
39	and/16,38
40	or/37,39
41	and/5,9,40
42	(COMORBIDITY and (DIABETES MELLITUS, TYPE 2 or NON INSULIN DEPENDENT DIABETES MELLITUS)).kw.
43	and/5,16,42
44	or/41,43

Health Technology Assessment

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 2/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13	(NIDDM or T2D or TIID or DM2 or DMII).tw.
14	or/10-13
15	exp DYSLIPIDEMIAS/
16	(d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).tw.
17	or/15-16
18	LIPIDS/
19	CHOLESTEROL/
20	CHOLESTEROL, HDL/
21	CHOLESTEROL, LDL/
22	LIPOPROTEINS/
23	LIPOPROTEINS, HDL/
24	LIPOPROTEINS, LDL/
25	exp TRIGLYCERIDES/
26	(cholester$ or epicholester$ or lipoprotein? or lipid?).tw.
27	(alphalip$ or alpha lipoprotein$ or HDL cholester$).tw.

Update 2015

28	(betalip$ or beta lipoprotein$ or LDL cholester$).tw.
29	(triglyceride? or triacy?glycerol?).tw.
30	((HDL or LDL) adj3 cholester$ adj3 ratio?).tw.
31	or/18-30
32	PREVALENCE/
33	INCIDENCE/
34	exp COHORT STUDIES/
35	CROSS-SECTIONAL STUDIES/
36	exp MODELS, STATISTICAL/
37	LIFE TABLES/
38	exp RISK/
39	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
40	or/32-39
41	MASS SCREENING/
42	exp POPULATION SURVEILLANCE/
43	(undiagnos$ or estimate$).ti.
44	(screen$ or surveill$ or predict$ or detect$).ti.
45	or/41-44
46	SEVERITY OF ILLNESS INDEX/
47	DISEASE PROGRESSION/
48	INTERNATIONAL CLASSIFICATION OF DISEASES/
49	CLASSIFICATION/
50	(d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).tw.
51	or/46-50
52	AGE FACTORS/
53	AGE DISTRIBUTION/
54	AGE OF ONSET/
55	TIME TO TREATMENT/
56	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw.
57	(disease adj3 (duration or onset)).tw.
58	or/52-57
59	17 and (31 or 40 or 45 or 51 or 58)
60	DIABETES COMPLICATIONS/
61	and/31,60
62	or/59,61
63	and/9,14,62
64	DIABETES MELLITUS, TYPE 2/ and COMORBIDITY/
65	and/9,31,64
66	or/63,65

Embase

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8

Update 2015

10	NON INSULIN DEPENDENT DIABETES MELLITUS/
11	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14	or/10-13
15	JUVENILE DIABETES MELLITUS/
16	and/9,14
17	or/15-16
18	exp "DISORDERS OF CHOLESTEROL METABOLISM"/
19	"DISORDERS OF LIPID METABOLISM"/
20	exp "DISORDERS OF LIPOPROTEIN METABOLISM"/
21	DYSLIPIDEMIA/
22	exp HYPERLIPIDEMIA/
23	HYPOLIPEMIA/
24	(d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).ti,ab.
25	or/18-24
26	exp LIPID BLOOD LEVEL/ or LIPID/ec [Endogenous Compound]
27	CHOLESTEROL/an, ec [Drug Analysis, Endogenous Compound]
28	HIGH DENSITY LIPOPROTEIN CHOLESTEROL/an, ec [Drug Analysis, Endogenous Compound]
29	LOW DENSITY LIPOPROTEIN CHOLESTEROL/an, ec [Drug Analysis, Endogenous Compound]
30	LIPOPROTEIN/an, ec [Drug Analysis, Endogenous Compound]
31	HIGH DENSITY LIPOPROTEIN/an, ec [Drug Analysis, Endogenous Compound]
32	LOW DENSITY LIPOPROTEIN/an, ec [Drug Analysis, Endogenous Compound]
33	TRIACYLGLYCEROL/an, ec [Drug Analysis, Endogenous Compound]
34	(cholester$ or epicholester$ or lipoprotein? or lipid?).ti,ab.
35	(alphalip$ or alpha lipoprotein$ or HDL cholester$).ti,ab.
36	(betalip$ or beta lipoprotein$ or LDL cholester$).ti,ab.
37	(triglyceride? or triacy?glycerol?).ti,ab.
38	((HDL or LDL) adj3 cholester$ adj3 ratio?).ti,ab.
39	or/26-38
40	PREVALENCE/
41	INCIDENCE/
42	STATISTICAL MODEL/
43	LIFE TABLE/
44	exp RISK/
45	(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
46	or/40-45
47	SCREENING/
48	MASS SCREENING/
49	SCREENING TEST/
50	RESCREENING/
51	exp DISEASE SURVEILLANCE/
52	(undiagnos$ or estimate$).ti.
53	(screen$ or surveill$ or predict$ or detect$).ti.
54	or/47-53
55	SEVERITY OF ILLNESS INDEX/
56	DISEASE SEVERITY/
57	DISEASE COURSE/
58	STAGING/

Update 2015

59	exp INTERNATIONAL CLASSIFICATION OF DISEASES/
60	RATING SCALE/
61	CLASSIFICATION/
62	DISEASE CLASSIFICATION/
63	(d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
64	or/55-63
65	AGE/
66	AGE DISTRIBUTION/
67	ONSET AGE/
68	DISEASE DURATION/
69	TIME TO TREATMENT/
70	(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
71	(disease adj3 (duration or onset)).ti,ab.
72	or/65-71
73	25 and (39 or 46 or 54 or 64 or 72)
74	exp *"DISORDERS OF CHOLESTEROL METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
75	*"DISORDERS OF LIPID METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
76	exp *"DISORDERS OF LIPOPROTEIN METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
77	*DYSLIPIDEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
78	exp *HYPERLIPIDEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
79	*HYPOLIPEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
80	or/73-79
81	and/17,80
82	(NON INSULIN DEPENDENT DIABETES MELLITUS/ and COMORBIDITY/) or NON INSULIN DEPENDENT DIABETES MELLITUS/co [Complication]
83	and/9,39,82
84	or/81,83
85	limit 84 to english language
86	conference abstract.pt.
87	letter.pt. or LETTER/
88	note.pt.
89	editorial.pt.
90	(letter or comment* or abstracts).ti.
91	or/86-90
92	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
93	91 not 92
94	ANIMAL/ not HUMAN/
95	NONHUMAN/
96	exp ANIMAL EXPERIMENT/
97	exp EXPERIMENTAL ANIMAL/
98	ANIMAL MODEL/
99	exp RODENT/
100	(rat or rats or mouse or mice).ti.
101	or/93-100
102	85 not 101

Update 2015

F.26 Health economics

Ovid MEDLINE(R)

#	Searches

1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	ADOLESCENT/ or MINORS/
23	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
24	exp CHILD/
25	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
26	exp INFANT/
27	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
28	exp PEDIATRICS/ or exp PUBERTY/
29	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
30	or/22-29
31	exp DIABETES MELLITUS, TYPE 1/
32	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
33	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
34	or/31-33
35	exp DIABETES MELLITUS, TYPE 2/
36	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
37	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
38	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
39	or/35-38
40	or/34,39
41	and/30,40
42	limit 41 to english language
43	LETTER/
44	EDITORIAL/
45	NEWS/
46	exp HISTORICAL ARTICLE/
47	ANECDOTES AS TOPIC/
48	COMMENT/
49	CASE REPORT/
50	(letter or comment* or abstracts).ti.

Update 2015

51	or/43-50
52	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
53	51 not 52
54	ANIMALS/ not HUMANS/
55	exp ANIMALS, LABORATORY/
56	exp ANIMAL EXPERIMENTATION/
57	exp MODELS, ANIMAL/
58	exp RODENTIA/
59	(rat or rats or mouse or mice).ti.
60	or/53-59
61	42 not 60
62	and/21,61

Cochrane Central Register of Controlled Trials

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	ADOLESCENT/ or MINORS/
23	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
24	exp CHILD/
25	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab.
26	exp INFANT/
27	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
28	exp PEDIATRICS/ or exp PUBERTY/
29	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
30	or/22-29
31	exp DIABETES MELLITUS, TYPE 1/
32	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
33	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
34	or/31-33
35	exp DIABETES MELLITUS, TYPE 2/

Update 2015

36	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
37	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
38	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
39	or/35-38
40	or/34,39
41	and/30,40

Health Technology Assessment, EBM Reviews - NHS Economic Evaluation Database

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).tw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw.
9	or/1-8
10	exp DIABETES MELLITUS, TYPE 1/
11	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
12	(IDDM or T1D or TID or DM1 or DMI).tw.
13	or/10-12
14	exp DIABETES MELLITUS, TYPE 2/
15	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
16	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
17	(NIDDM or T2D or TIID or DM2 or DMII).tw.
18	or/14-17
19	or/13,18
20	and/9,19

Embase

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16

Update 2015

18	exp ADOLESCENT/
19	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
20	exp CHILD/
21	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
22	exp NEWBORN/
23	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
24	exp PEDIATRICS/ or exp PUBERTY/
25	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,ec.
26	or/18-25
27	INSULIN DEPENDENT DIABETES MELLITUS/
28	(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
29	(IDDM or T1D or TID or DM1 or DMI).ti,ab.
30	or/27-29
31	NON INSULIN DEPENDENT DIABETES MELLITUS/
32	(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
33	(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
34	(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
35	or/31-34
36	or/30,35
37	JUVENILE DIABETES MELLITUS/
38	and/26,36
39	or/37-38
40	limit 39 to english language
41	conference abstract.pt.
42	letter.pt. or LETTER/
43	note.pt.
44	editorial.pt.
45	CASE REPORT/ or CASE STUDY/
46	(letter or comment* or abstracts).ti.
47	or/41-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMAL/ not HUMAN/
51	NONHUMAN/
52	exp ANIMAL EXPERIMENT/
53	exp EXPERIMENTAL ANIMAL/
54	ANIMAL MODEL/
55	exp RODENT/
56	(rat or rats or mouse or mice).ti.
57	or/49-56
58	40 not 57
59	and/17,58

Update 2015

Appendix G: Summary of identified studies

G.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline on type 1 diabetes in adults.

Number of papers identified, 2536

Number of papers weeded out, 2216

Number of papers excluded, 298

Number of papers included, 22

G.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Number of papers identified, 1280

Number of papers weeded out, 1204

Number of papers excluded, 68

Number of papers included, 8

Update 2015

G.3 Type 1 diabetes – psychological interventions

Review question: What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 1 diabetes?

Number of papers identified, 771

Number of papers weeded out, 656

Number of papers excluded, 100

Number of papers included, 15

G.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 3775

Number of papers weeded out, 3588

Number of papers excluded, 174

Number of papers included, 13

G.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Number of papers identified, 293

Number of papers weeded out, 291

Number of papers excluded, 2

Number of papers included, 0

G.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Number of papers identified, 1303

Number of papers weeded out, 1292

Number of papers excluded, 11

Number of papers included, 0

G.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

Number of papers identified, 2064

Number of papers weeded out, 2011

Number of papers excluded, 40

Number of papers included, 13

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Number of papers identified, 868

Number of papers weeded out, 821

Number of papers excluded, 43

Number of papers included, 4

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Number of papers identified, 1304

Number of papers weeded out, 1266

Number of papers excluded, 37

Number of papers included, 1

Update 2015

G.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Number of papers identified, 435

Number of papers weeded out, 419

Number of papers excluded, 15

Number of papers included, 1

G.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 729

Number of papers weeded out, 704

Number of papers excluded, 23

Number of papers included, 2

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 712

Number of papers weeded out, 699

Number of papers excluded, 11

Number of papers included, 2

Update 2015

G.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Number of papers identified, 1289

Number of papers weeded out, 1274

Number of papers excluded, 11

Number of papers included, 4

G.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Number of papers identified, 1576

Number of papers weeded out, 1576

Number of papers excluded, 0

Number of papers included, 0

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Number of papers identified, 1576

Number of papers weeded out, 1561

Number of papers excluded, 15

Number of papers included, 0

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**
- **acid/base status?**

Number of papers identified, 1576

Number of papers weeded out, 1572

Number of papers excluded, 1

Number of papers included, 3

Update 2015

G.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

Number of papers identified, 1108

Number of papers weeded out, 1108

Number of papers excluded, 0

Number of papers included, 0

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

Number of papers identified, 1108

Number of papers weeded out, 1098

Number of papers excluded, 4

Number of papers included, 6

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Number of papers identified, 1108

Number of papers weeded out, 1090

Number of papers excluded, 11

Number of papers included, 7

G.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Number of papers identified, 88

Number of papers weeded out, 80

Number of papers excluded, 7

Number of papers included, 1

G.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Update 2015

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

Number of papers identified, 389

Number of papers weeded out, 388

Number of papers excluded, 0

Number of papers included, 1

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Number of papers identified, 389

Number of papers weeded out, 386

Number of papers excluded, 0

Number of papers included, 3

G.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

Number of papers identified, 24

Number of papers weeded out, 24

Number of papers excluded, 0

Number of papers included, 0

G.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Number of papers identified, 5684

Number of papers weeded out, 5382

Number of papers excluded, 69

Number of papers included, 18

G.17 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Number of papers identified, 2924

Number of papers weeded out, 2819

Number of papers excluded, 91

Number of papers included, 14

Update 2015

G.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Number of papers identified, 1435

Number of papers weeded out, 1402

Number of papers excluded, 33

Number of papers included, 0

G.19 Type 2 diabetes – psychological interventions

Review questions:

What is the effectiveness of psychological interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

Number of papers identified, 1637

Number of papers weeded out, 1624

Number of papers excluded, 13

Number of papers included, 0

What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?

Number of papers identified, 1637

Number of papers weeded out, 1617

Number of papers excluded, 20

Number of papers included, 0

G.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Number of papers identified, 2605

Number of papers weeded out, 2588

Number of papers excluded, 16

Number of papers included, 1

G.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Number of papers identified, 697

Number of papers weeded out, 624

Number of papers excluded, 27

Number of papers included, 1

Update 2015

G.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Number of papers identified, 604

Number of papers weeded out, 581

Number of papers excluded, 22

Number of papers included, 1

G.23 Type 2 diabetes – HbA1c targets

Review question: what is the optimal HbA1c target for children and young people with type 2 diabetes?

Number of papers identified, 716

Number of papers weeded out, 706

Number of papers excluded, 10

Number of papers included, 0

G.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Number of papers identified, 3205

Number of papers weeded out, 3190

Number of papers excluded, 7

Number of papers included, 8

G.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

Number of papers identified, 1613

Number of papers weeded out, 1595

Number of papers excluded, 11

Number of papers included, 7

G.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Number of papers identified, 2594

Number of papers weeded out, 2575

Number of papers excluded, 17

Number of papers included, 2

G.27 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Number of papers identified, 2923

Number of papers weeded out, 2913

Number of papers excluded, 7

Number of papers included, 3

G.28 Health economics

Number of papers identified, 2754

Number of papers weeded out, 2731

Number of papers excluded, 19

Number of papers included, 2

Update 2015

Appendix H: Excluded studies

H.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline on type 1 diabetes in adults.

Study	Reason for exclusion
J. M. Wenzlau, O. Moua, S. A. Sarkar, L. Yu, M. Rewers, G. S. Eisenbarth, H. W. Davidson, and J. C. Hutton. SlC30A8 is a major target of humoral autoimmunity in type 1 diabetes and a predictive marker in prediabetes. Ann N Y Acad Sci 1150:256-259, 2008.	Age of population not reported
A. Zmyslowska, A. Szadkowska, B. Mianowska, I. Pietrzak, and W. Mlynarski. Association between adiponectin level and residual insulin secretion in type 1 diabetes in children. Prz.Pediatr. 41 (2):69-73, 2011.	Not in English
J. Dretzke, C. Cummins, J. Sandercock, A. Fry-Smith, T. Barrett, and A. Burls. Autoantibody testing in children with newly diagnosed type 1 diabetes mellitus. Health Technol.Assess. 8 (22):1-196, 2004.	HTA 2004 in T1D children. Wrong markers being assessed: auto-antibodies for celiac and thyroid disease
M. Galgani, R. Nugnes, M. Santopaolo, A. Franzese, S. Formisano, and G. Matarese. Meta-immunological profile of children with type 1 diabetes: Toward the possibility to predict progression of autoimmune diabetes. Am.J.Pathol. 181 (3 SUPPL. 1):S11, 2012.	Conference abstract
H. Takeda, E. Kawasaki, I. Shimizu, E. Konoue, M. Fujiyama, S. Murao, K. Tanaka, K. Mori, Y. Tarumi, I. Seto, Y. Fujii, et al. Clinical, autoimmune, and genetic characteristics of adult-onset diabetic patients with GAD autoantibodies in Japan (Ehime Study). Diabetes Care 25 (6):995-1001, 2002.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc.) but insulin-deficient and non-insulin deficient
A Balasubramanyam, G Garza, L Rodriguez, CS. Hampe, L Gaur, A Lernmark, and MR. Maldonado. Accuracy and predictive value of classification schemes for ketosis-prone diabetes. Diabetes Care 29 (12):2575-2579, 2006.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc.) but KPD (ketone-prone diabetes) subtypes. Wrong study design: sensitivity and specificity of classification schemes to determine KPD subtypes
JM. Barker, SH. Goehrig, K Barriga, M Hoffman, R Slover, GS. Eisenbarth, JM. Norris, G Klingensmith, M Rewers, and study DAISY. Clinical characteristics of children diagnosed with type 1 diabetes through intensive screening and follow-up. Diabetes Care 27 (6):1399-1404, 2004.	Wrong intervention and outcomes: does not look at any of our specified markers
D. Dabelea, C. Pihoker, J. W. Talton, Jr D'Agostino, W. Fujimoto, G. J. Klingensmith, J. M. Lawrence, B. Linder, S. M. Marcovina, E. J. Mayer-Davis, G. Imperatore, and L. M. Dolan. Etiological approach to characterization of diabetes type: The SEARCH for diabetes in youth study. Diabetes Care 34 (7):1628-1633, 2011.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc.)
E. Lindholm, E. Agardh, T. Tuomi, L. Groop, and C. D. Agardh. Classifying diabetes according to the new WHO clinical stages. Eur.J.Epidemiol. 17 (11):983-989, 2001.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc.) but insulin-requiring for control (IRC) and non-insulin requiring (NIR)
J. S. Sorensen, F. Vaziri-Sani, F. Pociot, K. Kristensen, C. Brorsson, L. Lyngsoe, B. Dolmer, and N. H. Birkebaek. ZnT8 autoantibody specificities at, and 3-5 years after clinical onset, associates with the age at diagnosis and the SLC30A8 gene polymorphism in Danish children with type 1 diabetes. Pediatr Diabetes 11:24, 2010.	Conference abstract
M. J. Redondo, L. M. Rodriguez, M. Escalante, A. Balasubramanyam, and M. Haymond. Forms of pediatric diabetes mellitus defined by antiislet autoimmunity and beta-cell function at diagnosis. Pediatr Diabetes 12:98, 2011.	Conference abstract
K. Seifert, K. Tornow, U. Walschus, H. Kenk, and M. Schlosser. Examination of GAD65 in human serum as a possible marker of ongoing beta cell destruction in autoimmune diabetes. Diabetologia 54:S74, 2011.	Conference abstract
Z. Huang, Y. Chen, F. Li, and Y. Li. Clinical heterogeneity of type 1 diabetes mellitus at onset. Diabetologia 53:S396, 2010.	Conference abstract
A Soderbergh, A Grethe Myhre, O Ekwall, G Gebre-Medhin, H Hedstrand, E Landgren, A Miettinen, P Eskelin, M Halonen et al. Prevalence and clinical associations of 10 defined autoantibodies in autoimmune polyendocrine syndrome type I. J.Clin.Endocrinol.Metab. 89 (2):557-562, 2004.	Wrong population: T1D with APECED (autoimmune polyendocrinpathy-candidiasis-ectodermal dystrophy)

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Study	Reason for exclusion
S Oak, L K. Gilliam, M Landin-Olsson, C Torn, I Kockum, CR. Pennington, M J. Rowley, MR. Christie, JP Banga, and CS. Hampe. The lack of anti-idiotypic antibodies, not the presence of the corresponding autoantibodies to glutamate decarboxylase, defines type 1 diabetes. Proc.Natl.Acad.Sci.U.S.A. 105 (14):5471-5476, 2008.	Wrong outcomes: not the presence of markers in T1D, as recruited patients who were already GAD65+
L. C. G. de Graaff, J. W. A. Smit, and J. K. Radder. Prevalence and clinical significance of organ-specific autoantibodies in type 1 diabetes mellitus. Neth.J.Med. 65 (7):235-247, 2007.	Wrong intervention and outcomes: does not look at any of our specified markers
EH. Hathout, N Hartwick, OR. Fagoaga, AR Colacino, J Sharkey, M Racine, S Nelsen-Cannarella, and JW. Mace. Clinical, autoimmune, and HLA characteristics of children diagnosed with type 1 diabetes before 5 years of age. Pediatrics 111 (4 Pt 1):860-863, 2003.	Wrong population: children <12 years old (both early and later childhood onset)
L Thumer, K Adler, E Bonifacio, F Hofmann, M Keller, C Milz, A Munte, and A Gabriele Ziegler. German new onset diabetes in the young incident cohort study: DiMelli study design and first-year results. Rev.diabet.stud. 7 (3):202-208, 2010.	Wrong population: children and young people
A. J. Al Abbasi and F. A. Al Jenaidi. Frequency of auto-antibodies in newly diagnosed Bahraini type I diabetes mellitus children and their healthy siblings. J.Bahrain Med.Soc. 15 (1):9-12, 2003.	Wrong population: children 1-13 years old
M. Desai and A. Clark. Autoimmune diabetes in adults: lessons from the UKPDS. Diabet.Med. 25 Suppl 2:30-34, 2008.	Literature review
A. W. van Deutekom, R. J. Heine, and S. Simsek. The islet autoantibody titres: their clinical relevance in latent autoimmune diabetes in adults (LADA) and the classification of diabetes mellitus. Diabet.Med. 25 (2):117-125, 2008.	Literature review
R. Jensen, L. Gilliam, C. Torn, M. Landin-Olsson, J. Palmer, K. Akesson, I. Kockum, B. Lernmark, A. F. Karlsson, K. F. Lynch, N. Breslow, A. Lernmark, G. Sundkvist, and Diabetes Incidence Study in Sweden group. Islet cell autoantibody levels after the diagnosis of young adult diabetic patients. Diabet.Med. 24 (11):1221-1228, 2007.	Wrong population: shows changes in markers over time but does not categorise the diabetes population into different types of diabetes
S. Allen, J. Huber, and D. Devendra. Prevalence of organ-specific autoantibodies in childhood- and adult-onset type 1 diabetes. Ann.N.Y.Acad.Sci. 1150:260-262, 2008.	Wrong markers being assessed
T. Kobayashi, S. Tanaka, N. Harii, K. Aida, H. Shimura, M. Ohmori, M. Kanesige, A. Shimada, and T. Maruyama. Immunopathological and genetic features in slowly progressive insulin-dependent diabetes mellitus and latent autoimmune diabetes in adults. Ann.N.Y.Acad.Sci. 1079:60-66, 2006.	Literature review
JC. Low, EI. Felner, AB. Muir, M Brown, M Dorcelet, L Peng, and G E. Umpierrez. Do obese children with diabetic ketoacidosis have type 1 or type 2 diabetes? Prim Care Diabetes 6 (1):61-65, 2012.	Wrong outcomes: pools together results for Islet cell Abs and GAD Abs so can't separate the two
BW Lee, SY Kim, JY Kim, KY Cho, YJ Chung, YK Min, JH Chung, MK Lee, MS Lee, and KW Kim. Heterogeneity of early-onset and ketosis-resistant diabetes in Korean subjects--is it possible to determine cut-off age of early-onset type 2 diabetes? Diabetes Res.Clin.Pract. 70 (1):38-45, 2005.	Wrong population: unclear – just says 'early onset diabetes'
JL. Mahon, JM. Sosenko, L Rafkin-Mervis, H Krause-Steinrauf, JM. Lachin, C Thompson, PJ. Bingley, E Bonifacio, JP. Palmer, GS. Eisenbarth, J Wolfsdorf, JS. Skyler, TrialNet Natural History Committee, and Diabetes TrialNet Study Group. The TrialNet Natural History Study of the Development of Type 1 Diabetes: objectives, design, and initial results. Pediatr Diabetes 10 (2):97-104, 2009.	Wrong outcomes: does not give Ab results for the T1D patients; this is just the screening and baseline risk assessment paper. Wrong study population and design – presence of Abs in relatives and see if predicts development of diabetes
X Li, Z Zhou, G Huang, H Su, X Yan, and L Yang. Metabolic syndrome in adult-onset latent autoimmune diabetes. Metab.syndr.relat.disord. 3 (2):174-180, 2005.	Wrong outcomes: prevalence of metabolic syndrome (patients already divided into GAD+ and GAD-
FJ. Quintana, G Getz, G Hed, E Domany, and IR. Cohen. Cluster analysis of human autoantibody reactivities in health and in type 1 diabetes mellitus: a bio-informatic approach to immune complexity. J.Autoimmun. 21 (1):65-75, 2003.	Wrong interventions and outcomes: different assays / quantification of various markers in antigen clusters
M Nagata, R Kotani, H Moriyama, K Yokono, BO. Roep, and M Peakman. Detection of autoreactive T cells in type 1 diabetes using coded autoantigens and an immunoglobulin-free cytokine ELISPOT assay: report from the fourth immunology of diabetes society T cell workshop. Ann.N.Y.Acad.Sci. 1037:10-15, 2004.	Wrong interventions and outcomes: testing different assays and antibody types for GAD65
S. Brophy, H. Davies, G. Dunseath, J. W. Stephens, J. Platts, H. Lane, C. Beaverstock, L. Wakeman, I. Russell, M. Williams, and D. R. Williams. Experience of the introduction of routine antibody testing in primary care and of running a trial for latent autoimmune diabetes in adults (LADA). Diabetes Res.Clin.Pract. 93 (1):e49-e52, 2011.	Age of population not given for the main group recruited
E. Ortqvist, B. Brooks-Worrell, K. Lynch, J. Radtke, L. M. Bekris, I. Kockum, C. D. Agardh, C. M. Cilio, A. L. Lethagen, B. Persson, A. Lernmark, J. Reichow, S. Oak, J. P. Palmer, and C. S. Hampe. Changes in GAD65Ab-specific antiidiotypic antibody levels correlate with changes in C-peptide levels and progression to islet cell autoimmunity. J.Clin.Endocrinol.Metab. 95 (11):E310-E318, 2010.	Adult patients were treated with anti-GADA and so this study is about treatment effect

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Study	Reason for exclusion
F Mauvais-Jarvis, E Sobngwi, R Porcher, JP Riveline, JP Kevorkian, C Vaisse, G Charpentier, PJ Guillausseau, P Vexiau, and JF Gautier. Ketosis-prone type 2 diabetes in patients of sub-Saharan African origin: clinical pathophysiology and natural history of beta-cell dysfunction and insulin resistance. Diabetes 53 (3):645-653, 2004.	Adult patients but results divided into ketosis-prone and non-ketosis prone patients
A. Rogowicz-Frontczak, D. Zozulinska-Ziolkiewicz, P. Niedzwiecki, M. Litwinowicz, and B. Wierusz-Wysocka. Does glucagon stimulation test help to predict autoimmunity in newly diagnosed non obese adults with diabetes? Exp.Clin.Endocrinol.Diabetes 120 (7):428-434, 2012.	Type of diabetes population unspecified
B. Littorin, L. Nystrom, B. Gullberg, L. Rastam, J. Ostman, H. J. Arnqvist, E. Bjork, G. Blohme, J. Bolinder, J. W. Eriksson, B. Schersten, and G. Sundkvist. Increasing body mass index at diagnosis of diabetes in young adult people during 1983-1999 in the Diabetes Incidence Study in Sweden (DISS). J.Intern.Med. 254 (3):251-256, 2003.	Does not give the % of marker in each type of diabetes
S Porksen, LB Laborie, L Nielsen, MLM Andersen, T Sandal, H de Wet, E Schwarcz, J Aman, P Swift, M Kocova, EJ. Schonle, C de Beaufort, P Hougaard, F Ashcroft, A Molven, Ml Knip, HB. Mortensen, L Hansen, PR. Njolstad, and Hyidore Study Group on Childhood Diabetes. Disease progression and search for monogenic diabetes among children with new onset type 1 diabetes negative for ICA, GAD- and IA-2 Antibodies. BMC Endocrine Disorders 10:16, 2010.	Does not give results for each of the markers separately
S. Bilgic, E. Aktas, F. Salman, G. Ersahin, G. Erten, M. T. Yilmaz, and G. Deniz. Intracytoplasmic cytokine levels and neutrophil functions in early clinical stage of type 1 diabetes. Diabetes Res.Clin.Pract. 79 (1):31-36, 2008.	Wrong markers
M. Khalangot, V. Kravchenko, M. Tronko, and V. Gur'ianov. Correlation between the prevalence of type 1 diabetes with the daily insulin dose and the autoimmune process against glutamic acid decarboxylase in adults. EUR.J.INTERN.MED. 20 (6):611-615, 2009.	Wrong markers
MWMD. Lutgens, M Meijer, B Peeters, ML Poulsen, MJ. Rutten, ML. Bots, GJMG. van der Heijden, and SS. Soedamah-Muthu. Easily obtainable clinical features increase the diagnostic accuracy for latent autoimmune diabetes in adults: an evidence-based report. Prim Care Diabetes 2 (4):207-211, 2008.	Clinical screening tool for LADA but does nut use our pre-specified markers
O. Rubio-Cabezas, E. L. Edghill, J. Argente, and A. T. Hattersley. Testing for monogenic diabetes among children and adolescents with antibody-negative clinically defined Type 1 diabetes. Diabet.Med. 26 (10):1070-1074, 2009.	Results are split into different genotypes of T1D, but not show the markers in each genotype
K. Zorena, J. Mysliwska, M. Mysliwiec, and A. Balcerska. Analysis of levels of angiogenin in children and adolescents with type 1 diabetes mellitus in relation to the duration of the disease. Int.Rev.Allergol.Clin.Immunol. 14 (3-4):98-100, 2008.	Wrong markers
A Makinen, T Harkonen, J Ilonen, M Knip, and Diabetes Register Finnish Pediatric. Characterization of the humoral immune response to islet antigen 2 in children with newly diagnosed type 1 diabetes. European journal of endocrinology 159 (1):19-26, 2008.	Results of patients categorised into responders and nn-responders to single of combination of markers. And specifically recruited patients of IA-2A negative T1D
BM. Brooks-Worrell, JL. Reichow, A Goel, H Ismail, and JP. Palmer. Identification of autoantibody-negative autoimmune type 2 diabetic patients. Diabetes Care 34 (1):168-173, 2011.	Results of patients categorised into T-cell + and – and combination of all 5 markers, rather than each marker separately
KATULANDA 2008 P. Katulanda, B. Shine, G. W. Katulanda, A. Silva, E. L. Asfir, R. Sheriff, N. Somasundaram, A. E. Long, P. J. Bingley, M. I. McCarthy, A. Clark, and D. R. Matthews. Diabetes mellitus among young adults in Sri Lanka--role of GAD antibodies in classification and treatment: the Sri Lanka Young Diabetes study. Diabetologia 51 (8):1368-1374, 2008.	Wrong population: mixtuire of T1D, T2D and LADA with no subgroup analyses for each of these. And further divided into GAD- and GAD+
S Fourlanos, C Perry, MS. Stein, J Stankovich, LC. Harrison, and PG. Colman. A clinical screening tool identifies autoimmune diabetes in adults. Diabetes Care 29 (5):970-975, 2006.	Risk scores which do not include our pre-specified markers
J. Bolinder, P. Fernlund, H. Borg, H. J. Arnqvist, E. Bjork, G. Blohme, J. W. Eriksson, L. Nystrom, J. Ostman, and G. Sundkvist. Hyperproinsulinemia segregates young adult patients with newly diagnosed autoimmune (type 1) and non-autoimmune (type 2) diabetes. Scand.J.Clin.Lab.Invest. 65 (7):585-594, 2005.	Wrong markers
C. Steele, W. A. Hagopian, S. Gitelman, U. Masharani, M. Cavaghan, K. I. Rother, D. Donaldson, D. M. Harlan, J. Bluestone, and K. C. Herold. Insulin secretion in type 1 diabetes. Diabetes 53 (2):426-433, 2004.	Wrong population: all ages with no subgroup analysis
M. Andrade Lima Gabbay, M. N. Sato, A. J. S. Duarte, and S. A. Dib. Serum titres of anti-glutamic acid decarboxylase-65 and anti-IA-2 autoantibodies are associated with different immunoregulatory milieu in newly diagnosed type 1 diabetes patients. Clin.Exp.Immunol. 168 (1):60-67, 2012.	Wrong population: all ages with no subgroup analysis
CJ. Greenbaum, CA. Beam, D Boulware, SE. Gitelman, PA. Gottlieb, KC. Herold, JM. Lachin, P McGee et al., and Diabetes TrialNet Study Group. Fall in C-peptide during first 2 years from diagnosis: evidence of at least two distinct phases from composite Type 1 Diabetes TrialNet data. Diabetes 61 (8):2066-2073, 2012.	Wrong population: all ages with no subgroup analysis

Study	Reason for exclusion
JM. Sosenko, JP. Palmer, L Rafkin-Mervis, JP. Krischer, D Cuthbertson, D Matheson, and JS. Skyler. Glucose and C-peptide changes in the perionset period of type 1 diabetes in the Diabetes Prevention Trial-Type 1. Diabetes Care 31 (11):2188-2192, 2008.	Wrong population: all ages with no subgroup analysis
A. G. Unnikrishnan, E. Bhatia, V. Bhatia, S. K. Bhadada, R. K. Sahay, A. Kannan, V. Kumaravel, D. Sarma, B. Ganapathy, N. Thomas, M. John, R. V. Jayakumar, H. Kumar, V. Nair, and C. B. Sanjeevi. Type 1 diabetes versus type 2 diabetes with onset in persons younger than 20 years of age: Results from an Indian multicenter study. Ann.N.Y.Acad.Sci. 1150:239-244, 2008.	Wrong population: all ages with no subgroup analysis
E Aguilera, R Casamitjana, G Ercilla, J Oriola, R Gomis, and I Conget. Adult-onset atypical (type 1) diabetes: additional insights and differences with type 1A diabetes in a European Mediterranean population. Diabetes Care 27 (5):1108-1114, 2004.	Adult population but M<50 (n=8)
O. Raha, B. N. Sarkar, L. V. K. S. Bhaskar, P. Veerraju, S. Chowdhury, S. Mukhopadhyay, T. K. Biswas, and V. R. Rao. Insulin (INS) promoter vntr polymorphisms: Interactions and association with type 1 diabetes mellitus in bengali speaking patients of Eastern India. Diabetol.Croat. 40 (4):99-106, 2011.	Wrong population: all ages with no subgroup analysis
V. Serban, A. Enache, A. Vlad, Alexandra Sima, Mihaela Rosu, Adriana Rosca, and Carmina Draghici. GADA and islet cell antibodies in Romanian children and adolescents with diabetes mellitus. Rom.J.Intern.Med. 42 (2):325-332, 2004.	Wrong population: all ages with no subgroup analysis
S Tanaka, T Endo, K Aida, H Shimura, N Yokomori, M Kaneshige, F Furuya, S Amemiya, M Mochizuki, K Nakanishi, and T Kobayashi. Distinct diagnostic criteria of fulminant type 1 diabetes based on serum C-peptide response and HbA1c levels at onset. Diabetes Care 27 (8):1936-1941, 2004.	Wrong population: all ages with no subgroup analysis
L Yang, S Luo, G Huang, J Peng, X Li, X Yan, J Lin, JM. Wenzlau, HW. Davidson, JC. Hutton, and Z Zhou. The diagnostic value of zinc transporter 8 autoantibody (ZnT8A) for type 1 diabetes in Chinese. Diabetes.Metab.Res.Rev. 26 (7):579-584, 2010.	Wrong population: all ages with no subgroup analysis
E. S. Siraj, D. G. Rogers, M. K. Gupta, and S. S. K. Reddy. A Simple Screening Method for Individuals at Risk of Developing Type 1 Diabetes: Measurement of Islet Cell Autoantibodies (GADA, IA-2A, and IAA) on Dried Capillary Blood Spots Collected on Filter Paper. Horm.Metab.Res. 44 (11):855-860, 2012.	Wrong population: all ages with no subgroup analysis
T Maruyama, S Oak, A Shimada, and CS. Hampe. GAD65 autoantibody responses in Japanese latent autoimmune diabetes in adult patients. Diabetes Care 31 (8):1602-1607, 2008.	Wrong population: all ages with no subgroup analysis
S. Dagdelen, G. Hascelik, and M. Bayraktar. Simultaneous triple organ specific autoantibody profiling in adult patients with type 1 diabetes mellitus and their first-degree relatives. Int.J.Clin.Pract. 63 (3):449-456, 2009.	Wrong population: all ages with no subgroup analysis
D Hickey, G Joshy, P Dunn, D Simmons, and R Lawrenson. Glycaemic control and antibody status among patients with newly diagnosed Type 1 diabetes. N.Z.Med.J. 120 (1262):U2732, 2007.	Mixed population of adults and young people in T1D, N,50 for this subgroup. T2D population mix of all ages with no subgroup analysis.
N. C. Schloot, P. Hanifi-Moghaddam, N. Aabenhus-Andersen, B. Z. Alizadeh, M. T. Saha, M. Knip, D. Devendra, T. Wilkin, E. Bonifacio, B. O. Roep, H. Kolb, and T. Mandrup-Poulsen. Association of immune mediators at diagnosis of Type 1 diabetes with later clinical remission. Diabet.Med. 24 (5):512-520, 2007.	Wrong population: all ages with no subgroup analysis
R. C. Silva, C. Sallorenzo, C. E. Kater, S. A. Dib, and A. Falorni. Autoantibodies against glutamic acid decarboxylase and 21-hydroxylase in Brazilian patients with type 1 diabetes or autoimmune thyroid diseases. Diabetes Nutr Metab 16 (3):160-168, 2003.	Wrong population: all ages with no subgroup analysis
W. Y. Ng, Y. S. Lee, A. L. Todd, K. F. Lui, K. Y. Loke, and A. C. Thai. Tyrosine phosphatase-like protein (IA-2) and glutamic acid decarboxylase (GAD65) autoantibodies: a study of Chinese patients with diabetes mellitus. Autoimmunity 35 (2):119-124, 2002.	Wrong population: all ages with no subgroup analysis
E Kawasaki, K Nakamura, G Kuriya, T Satoh, M Kobayashi, H Kuwahara, N Abiru, H Yamasaki, N Matsuura, J Miura, Y Uchigata, and K Eguchi. Differences in the humoral autoreactivity to zinc transporter 8 between childhood- and adult-onset type 1 diabetes in Japanese patients. Clin.Immunol. 138 (2):146-153, 2011.	Wrong population: all ages with no subgroup analysis
E Kawasaki, K Nakamura, G Kuriya, T Satoh, M Kobayashi, H Kuwahara, N Abiru, H Yamasaki, N Matsuura, J Miura, Y Uchigata, and K Eguchi. Zinc transporter 8 autoantibodies in fulminant, acute-onset, and slow-onset patients with type 1 diabetes. Diabetes.Metab.Res.Rev. 27 (8):895-898, 2011.	Wrong population: all ages with no subgroup analysis
T Maruyama, T Nakagawa, A Kasuga, and M Murata. Heterogeneity among patients with latent autoimmune diabetes in adults. Diabetes.Metab.Res.Rev. 27 (8):971-974, 2011.	Wrong population: all ages with no subgroup analysis
J. F. Louet, S. B. Smith, J. F. Gautier, M. Molokhia, M. L. Virally, J. P. Kevorkian, P. J. Guillausseau, P. Vexiau, G. Charpentier, M. S. German, C. Vaisse, M. Urbanek, and F. Mauvais-Jarvis. Gender and neurogenin3 influence the pathogenesis of ketosis-prone diabetes. Diabetes Obes Metab 10 (10):912-920, 2008.	Wrong population: all ages with no subgroup analysis

Study	Reason for exclusion
R Buzzetti, S Di Pietro, A Giaccari, A Petrone, M Locatelli, C Suraci, M Capizzi, M L Arpi, E Bazzigaluppi, F Dotta, E Bosi, and Non Insulin Requiring Autoimmune Diabetes Study Group. High titer of autoantibodies to GAD identifies a specific phenotype of adult-onset autoimmune diabetes. Diabetes Care 30 (4):932-938, 2007.	Wrong population: age groups not specified
V Tica, MW Hanif, A Andersson, G. Valsamakis, A. H. Barnett, S Kumar, and C. B. Sanjeevi. Frequency of latent autoimmune diabetes in adults in Asian patients diagnosed as type 2 diabetes in Birmingham, United Kingdom. Ann.N.Y.Acad.Sci. 1005:356-358, 2003.	Mixed/unclear age groups
J. Skupien, S. Gorczynska-Kosiorz, T. Klupa, K. Cyganek, K. Wanic, M. Borowiec, J. Sieradzki, and M. T. Malecki. Molecular background and clinical characteristics of HNF1A MODY in a Polish population. Diabetes Metab. 34 (5):524-528, 2008.	Mixed/unclear age groups
MC Moreira, GM Lara, R Linden, LR Feksa, R G Tavares, SE de Matos Almeida, and DB Berlese. Frequency of the anti-glutamic acid decarboxylase immunological marker in patients with diabetes duration longer than three years in southern Brazil. Sao Paulo Med J 129 (3):130-133, 2011.	Age range of population not specified
M. Prazny, J. Skrha, Z. Limanova, Z. Vanickova, J. Hilgertova, J. Prazna, M. Jaresova, and I. Striz. Screening for associated autoimmunity in type 1 diabetes mellitus with respect to diabetes control. Physiol.Res. 54 (1):41-48, 2005.	Age range of population not specified
Ju Xu, QH Dan, V Chan, NMS. Wat, S Tam, SC Tiu, KF Lee, SC Siu, MW Tsang, L M Fung, KW Chan, and KSL. Lam. Genetic and clinical characteristics of maturity-onset diabetes of the young in Chinese patients. Eur.J.Hum.Genet. 13 (4):422-427, 2005.	Age range of population not specified
AJ. Delli, Fariba Vaziri-Sani, Bengt Lindblad, Helena Elding-Larsson, Annelie Carlsson, Gun Forsander, Sten A. Ivarsson, et al. and Better Diabetes Diagnosis study group. Zinc transporter 8 autoantibodies and their association with SLC30A8 and HLA-DQ genes differ between immigrant and Swedish patients with newly diagnosed type 1 diabetes in the Better Diabetes Diagnosis study. Diabetes 61 (10):2556-2564, 2012.	Excluded even for children/young people guideline because doesn't give the actual % of people (or the titre) who are Ab+ for the young people or children's subgroup
N. A. Ali, E. Swelam, E. A. Al Banna, and A. Showkry. Role of beta-cell autoantibodies as a predictor marker in diabetic patients and their relationship to glycemic control. Egyptian journal of immunology / Egyptian Association of Immunologists 19 (1):39-49, 2012.	Adults and children mixed population – but adult subgroup analysis. Adult subgroup n<50. Children=mix of children and young people, also n<50
MH Black, Jean M. Lawrence, Catherine Pihoker, Lawrence M. Dolan, Andrea Anderson, Beatriz Rodriguez, Santica M. Marcovina, Elizabeth J. Mayer-Davis, Giuseppina Imperatore, Dana Dabelea, and SEARCH for Diabetes in Youth Study Group. HLA-associated phenotypes in youth with autoimmune diabetes. Pediatr.Diabetes 14 (2):121-128, 2013.	Mixed population of all ages, with no age subgroup analyses
M. Borowiec, W. Fendler, P. Dusatkova, K. Antosik, S. Pruhova, O. Cinek, M. Mysliwiec, P. Jarosz-Chobot, M. T. Malecki, and W. Mlynarski. HbA1c-based diabetes diagnosis among patients with glucokinase mutation (GCK-MODY) is affected by a genetic variant of glucose-6-phosphatase (G6PC2). Diabet.Med. 29 (11):1465-1469, 2012.	Does no give % of patients with the markers pre-specified in our protocol
C Chao, Gan Huang, Xia Li, Lin Yang, Jian Lin, Ping Jin, Shuo Ming Luo, Yi Yu Zhang, Ling Ling Pan, and Zhi Guang Zhou. Change of glutamic acid decarboxylase antibody and protein tyrosine phosphatase antibody in Chinese patients with acute-onset type 1 diabetes mellitus. Chin.Med.J.(Engl). 126 (21):4006-4012, 2013.	Wrong population: mixed population of all ages, with no age subgroup analysis
C. O. Ekpebegh and B. Longo-Mbenza. Clinical, immunologic and insulin secretory characteristics of young black South African patients with diabetes: Hospital based single centre study. Diabetes Res.Clin.Pract. 99 (3):380-384, 2013.	Wrong population: mixed population of all ages, with no age subgroup analysis
T. Eto, S. Inoue, and T. Kadowaki. Effects of once-daily teneligliptin on 24-h blood glucose control and safety in Japanese patients with type 2 diabetes mellitus: A 4-week, randomized, double-blind, placebo-controlled trial. Diabestes Obes.Metab. 14 (11):1040-1046, 2012.	Intervention study
R Fernandez, Ranjita Misra, Ramaswami Nalini, Christiane S. Hampe, Kerem Ozer, and Ashok Balasubramanyam. Characteristics of patients with ketosis-prone diabetes (KPD) presenting with acute pancreatitis: implications for the natural history and etiology of a KPD subgroup. Endocr Pract 19 (2):243-251, 2013.	Unclear if T1D or T2D – just says ketosis-prone diabetics
BN. Frederiksen, Miranda Kroehl, Tasha E. Fingerlin, Randall Wong, Andrea K. Steck, Marian Rewers, and Jill M. Norris. Association between vitamin D metabolism gene polymorphisms and risk of islet autoimmunity and progression to type 1 diabetes: the diabetes autoimmunity study in the young (DAISY). J.Clin.Endocrinol.Metab. 98 (11):E1845-E1851, 2013.	Does not answer question: markers as predictors of future development of T1D
I Hojsak, Noam Zevit, Orith Waisbourd-Zinman, Yoram Rosenbach, Yael Mozer-Glassberg, Shlomit Shalitin, Moshe Phillip, and Raanan Shamir. Concomitant autoantibodies in newly diagnosed diabetic children with transient celiac serology or proven celiac disease. J.Pediatr.Endocrinol.Metab. 26 (11-12):1099-1104, 2013.	Wrong population: mixed population of children and young plus, with no age subgroup analysis

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Study	Reason for exclusion
H. U. Irgens, J. Molnes, B. B. Johansson, M. Ringdal, T. Skrivarhaug, D. E. Undlien, O. Sovik, G. Joner, A. Molven, and P. R. Njolstad. Prevalence of monogenic diabetes in the population-based Norwegian Childhood Diabetes Registry. Diabetologia 56 (7):1512-1519, 2013.	Mixed population of children and young people; can get data for young people but this is incomplete (some is missing or not available)
K Johnson, Randall Wong, Katherine J. Barriga, Georgeanna Klingensmith, Anette G. Ziegler, Marian J. Rewers, and Andrea K. Steck. rs11203203 is associated with type 1 diabetes risk in population pre-screened for high-risk HLA-DR,DQ genotypes. Pediatr.Diabetes 13 (8):611-615, 2012.	Wrong population: children only
B. S. Karagun, F. Temiz, G. Ozer, B. Yuksel, A. K. Topaloglu, N. O. Mungan, M. Mazman, and G. M. Karagun. Chromium levels in healthy and newly diagnosed type 1 diabetic children. Pediatr Int 54 (6):780-785, 2012.	Wrong population: children only
S Krause, Ruth Chmiel, Ezio Bonifacio, Marlon Scholz, Michael Powell, Jadwiga Furmaniak, Bernard Rees Smith, Anette G. Ziegler, and Peter Achenbach. IA-2 autoantibody affinity in children at risk for type 1 diabetes. Clin.Immunol. 145 (3):224-229, 2012.	Wrong population: children only. Risk of future development of T1D
TH Lee, Ah Reum Kwon, Ye Jin Kim, Hyun Wook Chae, Ho Seong Kim, and Duk Hee Kim. The clinical measures associated with C-peptide decline in patients with type 1 diabetes over 15 years. J Korean Med Sci 28 (9):1340-1344, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
J. Lempainen, T. Harkonen, Ap Laine, M. Knip, J. Ilonen, and Diabetes Register Finnish Pediatric. Associations of polymorphisms in non-HLA loci with autoantibodies at the diagnosis of type 1 diabetes: INS and IKZF4 associate with insulin autoantibodies. Pediatr.Diabetes 14 (7):490-496, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
J Ludvigsson, Annelie Carlsson, Ahmed Deli, Gun Forsander, Sten A. Ivarsson, Ingrid Kockum, Bengt Lindblad, Claude Marcus, Ake Lernmark, and Ulf Samuelsson. Decline of C-peptide during the first year after diagnosis of Type 1 diabetes in children and adolescents. Diabetes Res.Clin.Pract. 100 (2):203-209, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
D Miao, K. Michelle Guyer, Fran Dong, Ling Jiang, Andrea K. Steck, Marian Rewers, George S. Eisenbarth, and Liping Yu. GAD65 autoantibodies detected by electrochemiluminescence assay identify high risk for type 1 diabetes. Diabetes 62 (12):4174-4178, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
S Miersch, Xiaofang Bian, Garrick Wallstrom, Sahar Sibani, Tanya Logvinenko, Clive H. Wasserfall, Desmond Schatz, Mark Atkinson, Ji Qiu, and Joshua LaBaer. Serological autoantibody profiling of type 1 diabetes by protein arrays. J Proteomics 94:486-496, 2013.	Doesn't give % of pple with Abs or the titre
M. Moritani, I. Yokota, K. Tsubouchi, R. Takaya, K. Takemoto, K. Minamitani, T. Urakami, T. Kawamura, N. Kikuchi, M. Itakura, T. Ogata, S. Sugihara, and S. Amemiya. Identification of INS and KCNJ11 gene mutations in type 1B diabetes in Japanese children with onset of diabetes before 5 year of age. Pediatr.Diabetes 14 (2):112-120, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis. Doesn't give results for our pre-specified markers
S. A. Mughal, R. Park, N. Nowak, A. L. Gloyn, F. Karpe, H. Matile, M. T. Malecki, M. I. McCarthy, M. Stoffel, and K. R. Owen. Apolipoprotein M can discriminate HNF1A-MODY from Type 1 diabetes. Diabet.Med. 30 (2):246-250, 2013.	Doesn't look at the markers pre-specified in our protocol
L. Petruzelkova, R. Ananieva-Jordanova, J. Vcelakova, Z. Vesely, K. Stechova, J. Lebl, P. Dusatkova, Z. Sumnik, R. Coles, M. Powell, J. Furmaniak, Smith B. Rees, and S. Kolouskova. The dynamic changes of zinc transporter 8 autoantibodies in Czech children from the onset of Type 1 diabetes mellitus. Diabet.Med. 31 (2):165-171, 2014.	Wrong population: mix of children and young people, with no age subgroup analysis
MN Pham, Hubert Kolb, Thomas Mandrup-Poulsen, Tadej Battelino, Johnny Ludvigsson, Paolo Pozzilli, Michael Roden, Nanette C. Schloot, and C. P. European. Serum adipokines as biomarkers of beta-cell function in patients with type 1 diabetes: positive association with leptin and resistin and negative association with adiponectin. Diabetes.Metab.Res.Rev. 29 (2):166-170, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
C Pihoker, Lisa K. Gilliam, Sian Ellard, Dana Dabelea, Cralen Davis,et al and SEARCH for Diabetes in Youth Study Group. Prevalence, characteristics and clinical diagnosis of maturity onset diabetes of the young due to mutations in HNF1A, HNF4A, and glucokinase: results from the SEARCH for Diabetes in Youth. J.Clin.Endocrinol.Metab. 98 (10):4055-4062, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
MJ. Redondo, Luisa M. Rodriguez, Mirna Escalante, E. O'Brian Smith, Ashok Balasubramanyam, and Morey W. Haymond. Beta cell function and BMI in ethnically diverse children with newly diagnosed autoimmune type 1 diabetes. Pediatr.Diabetes 13 (7):564-571, 2012.	Wrong population: mix of children and young people, with no age subgroup analysis
M. J. Redondo, L. M. Rodriguez, M. Escalante, E. O. Smith, A. Balasubramanyam, and M. W. Haymond. Types of pediatric diabetes mellitus defined by anti-islet autoimmunity and random C-peptide at diagnosis. Pediatr.Diabetes 14 (5):333-340, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
JL. Sherr, Tara Ghazi, Anna Wurtz, Linda Rink, and Kevan C. Herold. Characterization of residual beta cell function in long-standing type 1 diabetes. Diabetes.Metab.Res.Rev. 30 (2):154-162, 2014.	Wrong population: mix of all ages, with no age subgroup analysis
E Pettersen Sorgjerd, Frank Skorpen, Kirsti Kvaloy, Kristian Midthjell, and Valdemar Grill. Prevalence of ZnT8 antibody in relation to phenotype and SLC30A8 polymorphism in adult autoimmune diabetes: results from the HUNT study, Norway. Autoimmunity 46 (1):74-79, 2013.	Wrong population: mix of all ages, with no age subgroup analysis

Update 2015

Study	Reason for exclusion
JM. Sosenko, Jay S. Skyler, Jerry P. Palmer, Jeffrey P. Krischer, et al Diabetes TrialNet Study Group, and Prevention Trial-Type Diabetes. The prediction of type 1 diabetes by multiple autoantibody levels and their incorporation into an autoantibody risk score in relatives of type 1 diabetic patients. Diabetes Care 36 (9):2615-2620, 2013.	Does not answer the question: uses markers as predictors of future development of T1D
P Xu, Craig A. Beam, David Cuthbertson, Jay M. Sosenko, Jay S. Skyler, Jeffrey P. Krischer, and Study Group. Prognostic accuracy of immunologic and metabolic markers for type 1 diabetes in a high-risk population: receiver operating characteristic analysis. Diabetes Care 35 (10):1975-1980, 2012.	Does not answer the question: uses markers as predictors of future development of T1D
L Yu, Fran Dong, Dongmei Miao, Alexandra R. Fouts, Janet M. Wenzlau, and Andrea K. Steck. Proinsulin/Insulin autoantibodies measured with electrochemiluminescent assay are the earliest indicator of prediabetic islet autoimmunity. Diabetes Care 36 (8):2266-2270, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
SY Chai, Xiao Yu Pan, Ke Xiu Song, Yue Ye Huang, Fei Li, Xiao Yun Cheng, and Shen Qu. Differential patterns of insulin secretion and sensitivity in patients with type 2 diabetes mellitus and nonalcoholic fatty liver disease versus patients with type 2 diabetes mellitus alone. Lipids health dis. 13:7, 2014.	Adults but n<50
H. Demirbilek, Ozbek M. Nuri, and Baran R. Taner. Incidence of type 1 diabetes mellitus in Turkish children from the Southeastern region of the country: A regional report. JCRPE J.Clin.Res.Pediatr.Endocrinol. 5 (2):98-103, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
W Donelan, Hai Wang, Shi Wu Li, David Pittman, Yi Li, Shuhong Han, Yu Sun, Christopher Carter, Mark Atkinson, Westley Reeves, William E. Winter, and Li Jun Yang. Novel detection of pancreatic and duodenal homeobox 1 autoantibodies (PAA) in human sera using luciferase immunoprecipitation systems (LIPS) assay. Int J Clin Exp Pathol 6 (6):1202-1210, 2013.	Validation study of new methods for Ab detection
E. Ekholm, N. Shaat, and J. J. Holst. Characterization of beta cell and incretin function in patients with MODY1 (HNF4A MODY) and MODY3 (HNF1A MODY) in a Swedish patient collection. Acta Diabetol. 49 (5):349-354, 2012.	Adults but n<50
C Ekpebegh, Benjamin Longo-Mbenza, and Ernesto Blanco-Blanco. Islet immunity and beta cell reserve of indigenous Black South Africans with ketoacidosis at initial diagnosis of diabetes. Ethn Dis 23 (2):196-201, 2013.	Unclear population: just says DKA. Most were later recognised as T2D (in the discussion section), but no analysis done by type of diabetes
G Huang, Xuxu Mo, Muwen Li, Yufei Xiang, Xia Li, Shuoming Luo, and Zhiguang Zhou. Autoantibodies to CCL3 are of low sensitivity and specificity for the diagnosis of type 1 diabetes. Acta Diabetol. 49 (5):395-399, 2012.	Wrong population: mix of all ages, with no age subgroup analysis
N. M. Kamal Alanani and A. A. Alsulaimani. Epidemiological pattern of newly diagnosed children with type 1 diabetes mellitus, Taif, Saudi Arabia. Sci.World J. 2013, 2013.	Wrong population: children
I Kikkas, Roberto Mallone, Nadia Tubiana-Rufi, Didier Chevenne, Jean Claude Carel, Christophe Creminon, Herve Volland, Christian Boitard, and Nathalie Morel. A simple and fast non-radioactive bridging immunoassay for insulin autoantibodies. PloS one 8 (7):e69021, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
H Kolb, Kathrin Luckemeyer, Tim Heise, Christian Herder, Nanette C. Schloot, Wolfgang Koenig, Lutz Heinemann, Stephan Martin, and DIATOR Study Group. The systemic immune network in recent onset type 1 diabetes: central role of interleukin-1 receptor antagonist (DIATOR Trial). PloS one 8 (8):e72440, 2013.	Does not give levels or percentage of patients with markers; just correlations with other markers
S Masala, Maria Antonietta Zedda, Davide Cossu, Carlo Ripoli, Mario Palermo, and Leonardo A. Sechi. Zinc transporter 8 and MAP3865c homologous epitopes are recognized at T1D onset in Sardinian children. PloS one 8 (5):e63371, 2013.	Wrong population: children
RH. Muni, Radha P. Kohly, Eudocia Q. Lee, JoAnn E. Manson, Richard D. Semba, and Debra A. Schaumberg. Prospective study of inflammatory biomarkers and risk of diabetic retinopathy in the diabetes control and complications trial. JAMA Ophthalmol 131 (4):514-521, 2013.	Wrong markers: not those pre-specified in our protocol
A Parkkola, Taina Harkonen, Samppa J. Ryhanen, Jorma Ilonen, Mikael Knip, and Diabetes Register Finnish Pediatric. Extended family history of type 1 diabetes and phenotype and genotype of newly diagnosed children. Diabetes Care 36 (2):348-354, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
A Ryden and Maria Faresjo. Altered immune profile from pre-diabetes to manifestation of type 1 diabetes. Diabetes Res.Clin.Pract. 100 (1):74-84, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
H Skarstrand, L. B. Dahlin, A. Lernmark, and F. Vaziri-Sani. Neuropeptide Y autoantibodies in patients with long-term type 1 and type 2 diabetes and neuropathy. J.Diabetes Complications 27 (6):609-617, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
P Varadarajan, Thangavelu Sangaralingam, Senthil Senniappan, Suresh Jahnavi, Venkatesan Radha, and Viswanathan Mohan. Clinical profile and outcome of infantile onset diabetes mellitus in southern India. Indian Pediatr 50 (8):759-763, 2013.	Wrong population: children
J Vcelakova, Radek Blatny, Zbynek Halbhuber, Michal Kolar, Ales Neuwirth, et al. The effect of diabetes-associated autoantigens on cell processes in human PBMCs and their relevance to autoimmune diabetes development. J Diabetes Res 2013:589451, 2013.	Wrong population: mix of all ages, with no age subgroup analysis

Update 2015

Study	Reason for exclusion
K Warncke, M Krasmann, R Puff, D Dunstheimer, AG Ziegler, and A Beyerlein. Does diabetes appear in distinct phenotypes in young people? Results of the diabetes mellitus incidence Cohort Registry (DiMelli). PloS one 8 (9):e74339, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
AJ. K. Williams, SL. Thrower, IM. Sequeiros, A Ward, AS. Bickerton, JM. Triay, MP. Callaway, and CM. Dayan. Pancreatic volume is reduced in adult patients with recently diagnosed type 1 diabetes. J.Clin.Endocrinol.Metab. 97 (11):E2109-E2113, 2012.	Adults, but n<50
A M Zahran, KI Elsayh, and K A Metwalley. Regulatory T cells in children with recently diagnosed type 1 diabetes. Indian J Endocrinol Metab 16 (6):952-957, 2012.	Wrong population: children
AG. Ziegler, M Rewers, O Simell, T Simell, J Lempainen, A Steck, C Winkler, J Ilonen, R Veijola, M Knip, E Bonifacio, and GS. Eisenbarth. Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in children. JAMA 309 (23):2473-2479, 2013.	Does not answer the question: uses markers as predictors of future development of T1D
Hartemann A, Bensimon G, Payan CA, Jacqueminet S, Bourron O, Nicolas N et al. Low-dose interleukin 2 in patients with type 1 diabetes: A phase 1/2 randomised, double-blind, placebo-controlled trial. Lancet Diabetes and Endocrinology. 2013; 1(4):295-305	Treatment study. Article currently unavailable
DT. Papadimitriou, C Marakaki, A Fretzayas, P Nicolaidou, and A Papadimitriou. Negativation of type 1 diabetes-associated autoantibodies to glutamic acid decarboxylase and insulin in children treated with oral calcitriol. J Diabetes 5 (3):344-348, 2013.	Article currently unavailable
R. J. Aitken, I. V. Wilson, A. E. Long, A. J. K. Williams, T. J. McDonald, K. M. Gillespie, F. S. Wong, A. T. Hattersley, and P. J. Bingley. Residual beta cell function in long-standing childhood onset Type 1 diabetes. Diabet Med 31:19-20, 2014.	Conference abstract
A. Al-Farwi. The prevalence, autoimmune and genetic markers of latent autoimmune diabetes of adults in the coastal area/Syria. Diabetes Technol.Ther. 16:A135, 2014.	Conference abstract
C Andersson, M Kolmodin, S A Ivarsson, A Carlsson, G Forsander, B Lindblad, J Ludvigsson, I Kockum, C Marcus et al and Better Diabetes Diagnosis Study Group. Islet cell antibodies (ICA) identify autoimmunity in children with new onset diabetes mellitus negative for other islet cell antibodies. Pediatr Diabetes 15 (5):336-344, 2014	Unable to acquire article. Also in children
S. Axelsson, M. Hjorth, J. Ludvigsson, and R. Casas. Decreased GAD(65)-specific Th1/Tc1 phenotype in children with Type 1 diabetes treated with GAD-alum. Diabet Med 29 (10):1272-1278, 2012.	Does not give the results for our pre-specifed markers of interest
A. Bossowski, J. Furmaniak, J. Michalak, T. Diana, B. Glowin'ska-Olszewska, and G. Kahaly. Assessment of the occurance of the autoantibodies in children with diabetes type 1. Pediatr Diabetes 14:125, 2013.	Conference abstract
R. Braham, A. A. Zaid, R. Ahmed, M. Zitouni, S. Sobki, and F. A. Sabaan. Double diabetes in Saudi Arabia: A new entity or an underestimated condition? Diabetes 63:A402, 2014.	Conference abstract
V. Bravis, A. Kaur, H. Walkey, I. Godsland, C. Dayan, M. Peakman, P. Bingley, and D. G. Johnston. An incident and high-risk type 1 diabetes cohort-after diagnosis diabetes research support system-2 (address-2): Key initial findings. Diabetes 63:A645, 2014.	Conference abstract
B. A. Buckingham, P. Cheng, R. W. Beck, C. Kollman, K. Ruedy, S. A. Weinzimer, R. Slover, A. A. Bremer, W. V. Tamborlane, and J. Fuqua. Relationship of glycemic control and c-peptide levels 2 years following diagnosis of T1D. Diabetes 63:A392, 2014.	Conference abstract
L. E. Calliari, B. L. Barbosa, D. C. F. Lago, R. M. Noronha, and A. F. Reis. Maturity-onset diabetes of the young (MODY) type 2 in infancy and adolescence: Description of three families. Pediatr Diabetes 14:133, 2013.	Conference abstract
H. A. Castleden, A. E. Long, I. V. Wilson, R. J. Aitken, A. J. Williams, P. J. Bingley, and K. M. Gillespie. The characteristics of slow progression to Type 1 diabetes. Diabet Med 31:19, 2014.	Conference abstract
BM. Cerqueiro, L. Grahnquist, E. Ortqvist, A. Carlsson, and S. Ivarsson. Transglutaminas antibodies in Swedish children with type 1 diabetes in relation to HLA types and islet autoantibodies. Pediatr Diabetes 14:128-129, 2013.	Conference abstract
C. M. Chambers, A. R. Fouts, R. M. Sippl, K. Colclough, Z. X. Wang, Batish S. Dev, M. Jaremko, S. Ellard, A. T. Hattersley, G. J. Klingensmith, and A. K. Steck. Characteristics of maturity onset diabetes of the young in a large diabetes center. Diabetes 63:A363, 2014.	Conference abstract
K. K. Danielson, R. S. Monson, and T. J. Lecaire. Lower residual c-peptide at type 1 diabetes diagnosis and poor 10-year glycemic control independently predict higher pro-inflam matory tumor necrosis factor-alpha at 13-18 years diabetes duration. Diabetes 63:A409, 2014.	Conference abstract
L. A. Dimeglio, P. Cheng, R. W. Beck, C. Kollman, K. Ruedy, B. A. Buckingham, S. A. Weinzimer, R. Slover, A. A. Bremer, and T. Aye. Early predictors of stimulated C-peptide in persons with type 1 diabetes (T1D). Diabetes 63:A392, 2014.	Conference abstract

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Study	Reason for exclusion
LH. Elding, K. Vehik, P. Gesualdo, B. Akolkar, W. Hagopian, J. Krischer, A. Lernmark, M. Rewers, O. Simell, J.-X. She, A. Ziegler, and M. J. Haller. Children followed in the TEDDY study are diagnosed with type 1 diabetes at an early stage of disease. Pediatr Diabetes 15 (2):118-126, 2014.	Does not answer question: presence of Abs BEFORE diagnosis
H Fan, QingRong Pan, Pengrui Zhang, Jia Liu, Yuan Xu, and Xinchun Yang. Influence of islet function on typing and prognosis of new-onset diabetes after intensive insulin therapy. Med Sci Monit 19:787-793, 2013.	Already found this study in first set of reruns. Has been included in review
LA. Fernandez, Moreira Garcia, V, Gonzalez B. Laborda, Corona L. Marcos, N. Beridze, and Rodriguez E. Fernandez. Stability of C-peptide in blood specimens after delayed processing. Biochim.Clin. 37:S331, 2013.	Conference abstract
E. Graber, M. Regelmann, E. Wallach, L. Waldman, M. Goldis, M. Klein, D. Chia, and R. Rapaport. C-peptide is detected in 40% of youth with long-standing type 1 diabetes: A pilot study. Diabetes 63:A320, 2014.	Conference abstract
M. Habu, R. Kuwabara, M. Okuno, J. Suzuki, T. Urakami, and S. Takahashi. Prevalences of antibodies to IA-2 and GAD at the time of diagnosis in children with type1 diabetes. Pediatr Diabetes 14:123, 2013.	Conference abstract
C. C. Johnson, K. A. Mclaughlin, D. Morgan, R. G. Feltbower, and M. R. Christie. Fine mapping of epitopes for antibodies to the juxtamembrane domain of IA-2 in type 1 diabetes. Diabetes 63:A430, 2014.	Conference abstract
C. B. Juhl, U. Bradley, J. J. Holst, R. D. Leslie, K. B. Yderstraede, and S. Hunter. Similar weight-adjusted insulin secretion and insulin sensitivity in short-duration late autoimmune diabetes of adulthood (LADA) and Type 2 diabetes: Action LADA 8. Diabet Med 31 (8):941-945, 2014.	n<50
ES Jung, Dong Kyun Han, Eun Mi Yang, Min Sun Kim, Dae Yeol Lee, and Chan Jong Kim. Thyroid autoimmunity in children and adolescents with newly diagnosed type 1 diabetes mellitus. Ann.pediatr.endocrinol.metab. 19 (2):76-79, 2014.	Wrong population: children
N Mohamed Kamal Alanani and AA Alsulaimani. Epidemiological pattern of newly diagnosed children with type 1 diabetes mellitus, Taif, Saudi Arabia. ScientificWorldJournal 2013:421569, 2013.	Already found this study in first set of reruns. Has been excluded from review as children population
S. Kanthimathi, S. Jahnavi, K. Balamurugan, H. Ranjani, J. Sonya, S. Goswami, S. Chowdhury, V. Mohan, and V. Radha. Glucokinase gene mutations (MODY 2) in Asian Indians. Diabetes Technol.Ther. 16 (3):180-185, 2014.	Wrong population: not diabetic
E. Kawasaki, T. Maruyama, A. Imagawa, T. Awata, H. Ikegami, Y. Uchigata, H. Osawa, Y. Kawabata, T. Kobayashi, A. Shimada, I. Shimizu, K. Takahashi, M. Nagata, H. Makino, and T. Hanafusa. Diagnostic criteria for acute-onset type 1 diabetes mellitus (2012): Report of the committee of Japan diabetes society on the research of fulminant and acute-onset type 1 diabetes mellitus. J.diabetes investig. 5 (1):115-118, 2014.	Wrong population: fulminant and acute T1D
E Kawasaki, Megumi Tanaka, Masaki Miwa, Norio Abiru, and Atsushi Kawakami. Novel enzyme-linked immunosorbent assay for bivalent ZnT8 autoantibodies. Acta Diabetol 51 (3):429-434, 2014.	Wrong population: all ages mixed
B. Khodaghalian, A. U. Nayak, G. I. Varughese, and P. Raffeeq. Association of anti-GAD antibodies at diagnosis with glycaemia at 6 months in children with type 1 diabetes. Diabetes 63:A627, 2014.	Conference abstract
I Kikkas, Roberto Mallone, Etienne Larger, Herve Volland, and Nathalie Morel. A Rapid Lateral Flow Immunoassay for the Detection of Tyrosine Phosphatase-Like Protein IA-2 Autoantibodies in Human Serum. PloS one 9 (7):e103088, 2014.	Wrong sample size. n<50
YH Kong, Min Sun Kim, and Dae Yeol Lee. Comparison of the prevalence of islet autoantibodies according to age and disease duration in patients with type 1 diabetes mellitus. Ann.pediatr.endocrinol.metab. 18 (2):65-70, 2013.	Wrong sample size: adult subgroup is n<50; adult and young people mixed subgroup isalso n<50
B Kyung Koo, Sehyun Chae, Kristine M. Kim, Min Jueng Kang, Eunhee G. Kim, Soo Heon Kwak, Hye Seung Jung, et al. Identification of novel autoantibodies in type 1 diabetic patients using a high-density protein microarray. Diabetes 63 (9):3022-3032, 2014.	Unable to obtain article
M. K. Koskinen, R. Hermann, J. Matomaki, J. Mykkanen, M. Vaha-Makila, T. Simell, S. Simell, M. Makinen, V. Simell, M. Saarinen, J. Ilonen, M. Knip, and O. Simell. Insulin resistance, beta cell function and the effect of non-HLA genetic variants in Finnish DIPP study children with HLA-conferred risk for type 1 diabetes. Diabetologia 56:S229, 2013.	Conference abstract
JE Lee, Ji Woo Lee, Tatsuyoshi Fujii, Noriyoshi Fujii, and Jong Weon Choi. The ratio of estimated average glucose to fasting plasma glucose level is superior to glycated albumin, hemoglobin A1c, fructosamine, and GA/A1c ratio for assessing beta-cell function in childhood diabetes. Biomed Res Int 2014:370790, 2014.	Wrong population: children and young people
J. Lempainen, A.-P. Laine, A. Hammais, R. Veijola, O. Simell, M. Knip, and J. Ilonen. PTPN2 rs45450798 polymorphism is associated with accelerated progression of beta cell autoimmunity to clinical type 1 diabetes. Diabetologia 56:S18, 2013.	Conference abstract
A. Lernmark. The environmental determinants of diabetes in the young (TEDDY) and prospects of prevention. Pediatr Diabetes 14:1-2, 2013.	Conference abstract

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Study	Reason for exclusion
J. Lilleker, V. Biswas, and R. Mohanraj. Relevance of gad antibodies in adults with epilepsy: Experience in a tertiary clinic. J.Neurol.Neurosurg.Psychiatry 84 (11), 2013.	Conference abstract
J. Ludvigsson, D. Krisky, R. Casas, T. Battelino, L. Castano, J. Greening, O. Kordonouri, T. Otonkoski, P. Pozzilli, J. J. Robert, H. J. Veeze, and J. Palmer. GAD65 antigen therapy in recently diagnosed type 1 diabetes mellitus. Diabetes Technol.Ther. 15 (SUPPL.1):S92-S93, 2013.	Conference abstract
E. Maddaloni, N. Lessan, A. A. Tikriti, P. Pozzilli, and M. T. Barakat. Prevalence and features of adult-onset autoimmune diabetes in the United Arab Emirates (UAE). Diabetes 63:A399, 2014.	Conference abstract
S. Majidi, A. R. Fouts, T. Armstrong, R. M. Sippl, K. Colclough, Z. Wang, D. S. Batish, M. Jaremko, S. Ellard, A. T. Hattersley, G. J. Klingensmith, and A. K. Steck. Hla typing and C-peptide measurement to target mody genetic testing in antibody-negative diabetes. Diabetes 63:A354, 2014.	Conference abstract
S Masala, Davide Cossu, Simona Piccinini, Novella Rapini, Arianna Massimi, Ottavia Porzio, Silvia Pietrosanti, Roberta Lidano, Maria Luisa Manca Bitti, and Leonardo Antonio Sechi. Recognition of zinc transporter 8 and MAP3865c homologous epitopes by new-onset type 1 diabetes children from continental Italy. Acta Diabetol 51 (4):577-585, 2014.	Wrong population: children and young people
R. Matter, A. Adly, M. M. Abd El Aziz, and D. Toima. Serum CXC chemokine ligand 10 (CXCL10) in type 1 diabetic children, adolescents, and subjects at high risk of type 1 diabetes. Pediatr Diabetes 14:44, 2013.	Conference abstract
A. Maurizi, R. Strollo, P. Pozzilli, and N. Napoli. Osteocalcin and residual beta-cell function in type 1 diabetes. J.Bone Miner.Res. 26, 2011.	Conference abstract
M L Max Andersen, Lotte B. Nielsen, Jannet Svensson, Sven Porksen, Philip Hougaard, Craig Beam, Carla Greenbaum, Dorothy Becker, Jacob S. Petersen, Lars Hansen, and Henrik B. Mortensen. Disease progression among 446 children with newly diagnosed type 1 diabetes located in Scandinavia, Europe, and North America during the last 27yr. Pediatr Diabetes 15 (5):345-354, 2014.	Wrong population: children and young people
A. Messaaoui, S. Tenoutasse, C. Melot, and H. Dorchy. Inverse relationship between increased glomerular filtration rate and C-peptide level at diagnosis of type 1 diabetes in children and adolescents. Pediatr Diabetes 14:21-22, 2013.	Conference abstract
D. Mul, T. C. Sas, J. J. Schermer-Rotte, and H. J. Veeze. Completeness of immunological testing at diagnosis of diabetes mellitus in the Paediatric Diabetes Registry in the Netherlands (PDR.NL). Pediatr Diabetes 14:123-124, 2013.	Conference abstract
K. Nugent, C. M. McDonnell, and N. P. Murphy. Autoantibodies in type 1 diabetes: Are we different? Ir.J.Med.Sci. 181:S105, 2012.	Conference abstract
R. A. Oram, T. J. McDonald, B. M. Shields, E. R. Pearson, and A. T. Hattersley. A large, population-based study demonstrates that most people with long duration Type 1 diabetes are insulin microsecretors and produce their own endogenous insulin. Diabet Med 31:10, 2014.	Conference abstract
C. J. Padoa, P. Rheeder, and N. J. Crowther. Phenotypic and genotypic characterisation of type 1 diabetes mellitus in black South African patients. J.Endocrinol.Metab.Diabetes S.Afr. 18 (1):37, 2013.	Conference abstract
M L Pedersen, Peter Bjerregaard, and Marit Eika Jorgensen. GAD65 antibodies among Greenland Inuit and its relation to glucose intolerance. Acta Diabetol 51 (4):641-646, 2014.	Wrong population: not generalizable / applicable to UK population
R. Piekarski, J. Tabarkiewicz, A. Bojarska-Junak, and L. Szewczyk. Dynamic changes of the TH17 cell population in children with new-onset type 1 diabetes. Diabetes 63:A625-A626, 2014.	Conference abstract
R. Piekarski, B. Wilczyn'ska, A. Bojarska-Junak, and J. Tabarkiewicz. Th17 cells in children with new onset type 1 diabetes-preliminary report. Pediatr Diabetes 14:123, 2013.	Conference abstract
W. E. Powell, C. N. Janicki, A. Howell, A. Bishop, C. M. Dayan, and F. S. Wong. Developing an assay to detect B-cell responses to autoantigens GAD and IA-2 in Type 1 diabetes. Diabet Med 31:47, 2014.	Conference abstract
F Prodam, Francesco Cadario, Simonetta Bellone, Letizia Trovato, Stefania Moia, Erica Pozzi, Silvia Savastio, and Gianni Bona. Obestatin levels are associated with C-peptide and antiinsulin antibodies at the onset, whereas unacylated and acylated ghrelin levels are not predictive of long-term metabolic control in children with type 1 diabetes. J Clin Endocrinol Metab 99 (4):E599-E607, 2014.	Unable to obtain article
M. J. Redondo, N. Bansal, L. M. Rodriguez, J. A. Kushner, C. S. Hampe, and A. Balasubramanyam. Dpd epitope-specific GAD65 autoantibody is associated with older age of onset and obesity in pediatric type 1 diabetes. Diabetes 63:A8, 2014.	Conference abstract
M. Rewers, K. Waugh, K. Barriga, J. Norris, and J. Snell-Bergeon. Lower physical activity in children with persistent islet autoantibodies than in matched controls. Diabetologia 56:S132-S133, 2013.	Conference abstract
V. Serban, F. Fiera, and B. Timar. Basal C-peptide behavior and its clinical significance in Romanian children with type 1 diabetes. Pediatr Diabetes 14:80, 2013.	Conference abstract

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Study	Reason for exclusion
B. M. Shields, M. Hudson, M. Shepherd, R. Oram, T. J. McDonald, S. Ellard, E. R. Pearson, and A. T. Hattersley. Comparison of screening using clinical criteria and biomarkers to identify maturity-onset diabetes of the young (MODY) in a community based setting. Diabet Med 31:20, 2014.	Conference abstract
H. Siljander, A. Peet, V. Tillmann, T. Harkonen, O. Niemela, J. Ilonen, Hertzen L. Von, T. Haahtela, Mutius E. Von, and M. Knip. Relation between beta cell autoimmunity and levels of allergen-specific IgEs in young Finnish and Estonian children. Diabetologia 56:S18, 2013.	Conference abstract
H. Skarstrand, F. Vaziri-Sani, C. Andersson, H. Elding-Larsson, S. Ivarsson, and A. Lernmark. NPY minor autoantibodies in newly diagnosed type 1 diabetes patients. Diabetologia 56:S19, 2013.	Conference abstract
J. V. Stidsen, R. W. Thomsen, J. S. Nielsen, J. Rungby, S. P. Ulrichsen, K. Berensci, S. Friborg, I. Brandslund, A. A. Nielsen, J. S. Christiansen, H. Sorensen, A. A. Vaag, T. B. Olesen, M. H. Olsen, J. E. Henriksen, and H. Beck-Nielsen. Pathophysiological phenotypes of clinically diagnosed type 2 diabetes. Diabetes 63:A354-A355, 2014.	Conference abstract
M. S. Sunni, M. Farah, J. Smith, A. Dhunkal, M. D. Bellin, B. M. Nathan, P. A. Gottlieb, L. Yu, S. Babu, T. Armstrong, and A. Moran. HLA alleles and diabetes autoantibodies in a group of Somali children with type 1 diabetes in the Twin Cities, Minnesota: A pilot study. Pediatr Diabetes 14:129, 2013.	Conference abstract
J Takezawa, Kouichi Yamada, Akemi Morita, Naomi Aiba, and Shaw Watanabe. Preproghrelin gene polymorphisms in obese Japanese: Association with diabetes mellitus in men and with metabolic syndrome parameters in women. Obes Res Clin Pract 3 (4):179-191, 2009.	Wrong population: mixed diabetes subgroup
J. Urbanova, B. Rypackova, Z. Prochazkova, P. Kucera, M. Cerna, M. Andel, and P. Heneberg. Positivity for islet cell autoantibodies in patients with monogenic diabetes is associated with later diabetes onset and higher HbA1c level. Diabet Med 31 (4):466-471, 2014.	Wrong population: mixed agaes, and n<50
I. Wallace, S. Chan, M. Naidu, B. Secret, G. Braatvedt, and M. Khanolkar. A 6 year retrospective observational study: Autoantibodies to glutamic acid decarboxylase (GAD) and insulinoma antigen 2 (IA-2) in patients newly diagnosed with adult diabetes presenting with diabetic ketoacidosis. Diabet Med 31:181, 2014.	Conference abstract
K Warncke, Miriam Krasmann, Ramona Puff, Desiree Dunstheimer, Anette Gabriele Ziegler, and Andreas Beyerlein. Does diabetes appear in distinct phenotypes in young people? Results of the diabetes mellitus incidence Cohort Registry (DiMelli). PloS one 8 (9):e74339, 2013.	Already found article in first reruns. Was excluded from review as wrong population – mixed ages
R. A. Watkins, C. Evans-Molina, J. Terrell, K. Day, L. Guindon, R. G. Mirmira, J. S. Blum, and L. A. Di Meglio. Persistence of beta cell stress in the initial period following diagnosis of T1D in children. Pediatr Diabetes 14:68, 2013.	Conference abstract
K. Wilhelm, K. Tornow, V. Lampasona, U. Walschus, I. Rjasanowski, W. Kerner, and M. Schlosser. Prognostic and diagnostic relevance of ZnT8 antibodies in autoimmune diabetes. Diabetologia 56:S133, 2013.	Conference abstract
P. Xu, X. Qian, D. A. Schatz, D. Cuthbertson, and J. P. Krischer. Distribution of C-peptide and its determinants in North American children at risk for type 1 diabetes. Diabetes care 37 (7):1959-1965, 2014.	Wrong population: not diabetes, only those at risk for diabetes
AS. Yilmaz, Z. Aycan, S. Cetinkaya, V. N. Bas, A. Onder, H. N. Peltek Kendirci, and S. Ceylaner. Screening for mutations in children with a clinical diagnosis of maturity onset diabetes of youth (MODY). Pediatr Diabetes 14:132, 2013.	Conference abstract
S. Zago, M. Fabris, M. Liguori, M. Trevisan, M. Zanatta, A. Comici, G. Zanette, E. Tonutti, and F. Curcio. Improving the diagnostic approach to type I diabetes: The introduction of anti-zinc transporter protein autoantibodies (ZnT8A). FASEB J. 28 (1 SUPPL. 1), 2014.	Conference abstract
A. Zubkiewicz-Kucharska, A. Noczyn'ska, and L. Usnarska-Zubkiewicz. Prognostic significance of T lymphocytes in type 1 diabetes in children. Pediatr Diabetes 14:124, 2013.	Conference abstract
G. J. Tobon, A. Arango, V. Abad, J. Garcia, H. Cuervo, A. Velasquez, I. D. Angel, P. Vega, A. Abad, and J. M. Anaya. Clinical and immunological characteristics of type 1 diabetes mellitus in a northwestern Colombian population. Diabetes Res.Clin.Pract. 72 (2):170-175, 2006.	Mixed population: all ages with no adult or young people subgroup analysis
M. Koga, J. Murai, H. Saito, S. Kasayama, T. Kobayashi, A. Imagawa, and T. Hanafusa. Correlation of glycated albumin but not hemoglobin A1c with endogenous insulin secretion in fulminant type 1 diabetes mellitus. J.Diabetes Invest. 1 (6):279-282, 2010.	Mixed population: all ages with no adult ort young people subgroup analysis. Also wrong type of diabetes: fulminant T1D
M. K. Tulloch-Reid, M. S. Boyne, M. F. Smikle, E. G. Choo-Kang, R. H. Parkes, R. A. Wright-Pascoe, E. N. Barton, R. J. Wilks, and D. E. Williams. Clinical and laboratory features of youth onset type 2 diabetes in Jamaica. West Indian Med.J. 59 (2):131-138, 2010.	Mixed population: all ages with no adult or young people subgroup analysis
A Siafarikas, RJ. Johnston, MK. Bulsara, P O'Leary, TW. Jones, and EA. Davis. Early loss of the glucagon response to hypoglycemia in adolescents with type 1 diabetes. Diabetes Care 35 (8):1757-1762, 2012.	Mixed population: all ages with no adult or young people subgroup analysis

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Study	Reason for exclusion
C. Y. Pan, W. Y. So, B. A. K. Khalid, V. Mohan, A. C. Thai, P. Zimmet, C. S. Cockram, L. N. Jorgensen, J. P. Yeo, and ASDIAB Study Group. Metabolic, immunological and clinical characteristics in newly diagnosed Asian diabetes patients aged 12-40 years. Diabet.Med. 21 (9):1007-1013, 2004.	Mixed population: all ages with no adult or young people subgroup analysis
A. L. Todd, W. Y. Ng, K. F. Lui, and A. C. Thai. Low prevalence of autoimmune diabetes markers in a mixed ethnic population of Singaporean diabetics. Intern.Med.J. 34 (1-2):24-30, 2004.	Mixed population: all ages with no adult or young people subgroup analysis
M Rodacki, L Zajdenverg, RP Tortora, FA Reis, MS. Albernaz, MRB Goncalves, A Milech, and JEP de Oliveira. Characteristics of childhood and adult-onset type 1 diabetes in a multi-ethnic population. Diabetes Res.Clin.Pract. 69 (1):22-28, 2005.	Mixed population: all ages with no adult or young people subgroup analysis
A Szypowska and A Skorka. The risk factors of ketoacidosis in children with newly diagnosed type 1 diabetes mellitus. Pediatr Diabetes 12 (4 Pt 1):302-306, 2011.	Wrong population: children and young people
S. Hameed, S. Ellard, H. J. Woodhead, K. A. Neville, J. L. Walker, M. E. Craig, T. Armstrong, L. Yu, G. S. Eisenbarth, A. T. Hattersley, and C. F. Verge. Persistently autoantibody negative (PAN) type 1 diabetes mellitus in children. Pediatr Diabetes 12 (3 PART 1):142-149, 2011.	Wrong population: children and young people
RB. Lipton, ML. Drum, KK. Danielson, S Aw Greeley, GI. Bell, and WA. Hagopian. Onset features and subsequent clinical evolution of childhood diabetes over several years. Pediatr Diabetes 12 (4 Pt 1):326-334, 2011.	Wrong population: children and young people
Y Xin, M Yang, X Juan Chen, YJ Tong, and LH Zhang. Clinical features at the onset of childhood type 1 diabetes mellitus in Shenyang, China. J.Paediatr.Child Health 46 (4):171-175, 2010.	Wrong population: children and young people
HB. Mortensen, P Hougaard, P Swift, L Hansen, RW. Holl, H Hoey, H Bjoerndalen, C de Beaufort, F Chiarelli, T Danne, EJ. Schoenle, J Aman, and Hvidoere Study Group on Childhood Diabetes. New definition for the partial remission period in children and adolescents with type 1 diabetes. Diabetes Care 32 (8):1384-1390, 2009.	Wrong population: children and young people
T. Reinehr, E. Schober, S. Wiegand, A. Thon, R. Holl, and DPV-Wiss Study Group. Beta-cell autoantibodies in children with type 2 diabetes mellitus: subgroup or misclassification? Arch.Dis.Child. 91 (6):473-477, 2006.	Wrong population: children and young people
A. Amutha, M. Datta, R. Unnikrishnan, R. M. Anjana, and V. Mohan. Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India. Diabetes Technol Ther 14 (6):497-504, 2012.	Wrong population: children and young people
LE. Levitt Katz, SN Magge, ML. Hernandez, KM. Murphy, HM. McKnight, and T Lipman. Glycemic control in youth with type 2 diabetes declines as early as two years after diagnosis. J.Pediatr. 158 (1):106-111, 2011.	Wrong population: children and young people
J Matsui, N Tamasawa, J Tanabe, N Kasai, H Murakami, K Matsuki, and T Suda. Clinical characteristics of Japanese youth-onset type 2 diabetes with ketonuria. Diabetes Res.Clin.Pract. 70 (3):235-238, 2005.	Wrong population: children and young people
C Brorsson, F Vaziri-Sani, R Bergholdt, S Eising, A Nilsson, J Svensson, A Lernmark, F Pociot, and Danish Study Group of Childhood Diabetes. Correlations between islet autoantibody specificity and the SLC30A8 genotype with HLA-DQB1 and metabolic control in new onset type 1 diabetes. Autoimmunity 44 (2):107-114, 2011.	Wrong population: children and young people
H Manan, Al M Angham, and A Sitelbanat. Genetic and diabetic auto-antibody markers in Saudi children with type 1 diabetes. Hum.Immunol. 71 (12):1238-1242, 2010.	Wrong population: children and young people
A. M. N. E. Abd El Baky, S. M. Abd El Dayem, H. A. Atwa, and H. Rasmy. Assessment of interleukin 18 in children with type 1 diabetes and their relatives: Its relation to autoantibodies. J.Med.Sci.(Pakistan) 6 (4):603-608, 2006.	Wrong population: children and young people
M. S. Ronkainen, K. Savola, and M. Knip. Antibodies to GAD65 epitopes at diagnosis and over the first 10 years of clinical type 1 diabetes mellitus. Scand.J.Immunol. 59 (3):334-340, 2004.	Wrong population: children and young people
C. Andersson, K. Larsson, F. Vaziri-Sani, K. Lynch, A. Carlsson, E. Cedervall, B. Jonsson, J. Neiderud, M. Mansson, A. Nilsson, A. Lernmark, H. Elding Larsson, and S. A. Ivarsson. The three ZNT8 autoantibody variants together improve the diagnostic sensitivity of childhood and adolescent type 1 diabetes. Autoimmunity 44 (5):394-405, 2011.	Wrong population: children and young people
B. M. Brooks-Worrell, C. J. Greenbaum, J. P. Palmer, and C. Pihoker. Autoimmunity to Islet Proteins in Children Diagnosed with New-Onset Diabetes. J.Clin.Endocrinol.Metab. 89 (5):2222-2227, 2004.	Wrong population: children and young people
G Karaguzel, S Simsek, O Deger, and A Okten. Screening of diabetes, thyroid, and celiac diseases-related autoantibodies in a sample of Turkish children with type 1 diabetes and their siblings. Diabetes Res.Clin.Pract. 80 (2):238-243, 2008.	Wrong population: children and young people
A. Kaas, C. Pfleger, A. V. Kharagjitsingh, N. C. Schloot, L. Hansen, K. Buschard, B. P. C. Koeleman, B. O. Roep, H. B. Mortensen, B. Z. Alizadeh, and Hvidoere Study Group on Childhood Diabetes. Association between age, IL-10, IFNgamma, stimulated C-peptide and disease progression in children with newly diagnosed Type 1 diabetes. Diabet.Med. 29 (6):734-741, 2012.	Wrong population: children and young people

Update 2015

Study	Reason for exclusion
F. Lombardo, M. Valenzise, M. Wasniewska, M. F. Messina, C. Ruggeri, T. Arrigo, and F. De Luca. Two-year prospective evaluation of the factors affecting honeymoon frequency and duration in children with insulin dependent diabetes mellitus: the key-role of age at diagnosis. Diabetes Nutr Metab 15 (4):246-251, 2002.	Wrong population: children and young people
S. Salardi, S. Zucchini, A. Cicognani, E. Corbelli, R. Santoni, L. Ragni, D. Elleri, and E. Cacciari. The severity of clinical presentation of type 1 diabetes in children does not significantly influence the pattern of residual beta-cell function and long-term metabolic control. Pediatr Diabetes 4 (1):4-9, 2003.	Wrong population: children and young people
LE. Levitt Katz, A. F. J, J. Ganesh, M. Abraham, K. Murphy, and T. H. Lipman. Fasting c-peptide and insulin-like growth factor-binding protein-1 levels help to distinguish childhood type 1 and type 2 diabetes at diagnosis. Pediatr Diabetes 8 (2):53-59, 2007.	Wrong population: children and young people
Fu Sung Lo, Min Hai Yang, Luan Yin Chang, Yung Chun Ou, and Yang Hau Van. Clinical features of type 1 diabetic children at initial diagnosis. Acta Paediatr.Taiwan. 45 (4):218-223, 2004.	Wrong population: children and young people
J. Ludvigsson, A. Carlsson, G. Forsander, S. Ivarsson, I. Kockum, A. Lernmark, B. Lindblad, C. Marcus, and U. Samuelsson. C-peptide in the classification of diabetes in children and adolescents. Pediatr Diabetes 13 (1):45-50, 2012.	Wrong population: children and young people
A Kaas, MLM Andersen, S Fredheim, P Hougaard, K Buschard, JS Petersen, C de Beaufort, KJ. Robertson, L Hansen, HB. Mortensen, LB. Nielsen, and Hvidoere Study Group on Childhood Diabetes. Proinsulin, GLP-1, and glucagon are associated with partial remission in children and adolescents with newly diagnosed type 1 diabetes. Pediatr Diabetes 13 (1):51-58, 2012.	Wrong population: children and young people
A. Zmyslowska, W. Mlynarski, A. Szadkowska, and J. Bodalski. Prediction of the clinical remission using the C-peptide level in type 1 diabetes in children. Endokrynol.Diabetol.Choroby Przemiany Materii Wieku Rozwojowego 13 (2):71-74, 2007.	Wrong population: children and young people
HB. Mortensen, PGF. Swift, RW. Holl, P. Hougaard, L Hansen, H Bjoerndalen, CE. de Beaufort, M Knip, and Hvidoere Study Group on Childhood Diabetes. Multinational study in children and adolescents with newly diagnosed type 1 diabetes: association of age, ketoacidosis, HLA status, and autoantibodies on residual beta-cell function and glycemic control 12 months after diagnosis. Pediatr Diabetes 11 (4):218-226, 2010.	Wrong population: children and young people
C Pfleger, HB. Mortensen, L Hansen, C Herder, BO. Roep, H Hoey, HJ Aanstoot, M Kocova, NC. Schloot, and Hvidore Study Group on Childhood Diabetes. Association of IL-1ra and adiponectin with C-peptide and remission in patients with type 1 diabetes. Diabetes 57 (4):929-937, 2008.	Wrong population: children and young people
K. C. Copeland, P. Zeitler, M. Geffner, C. Guandalini, J. Higgins, K. Hirst, F. R. Kaufman, B. Linder, S. Marcovina, P. McGuigan, L. Pyle, W. Tamborlane, and S. Willi. Characteristics of adolescents and youth with recent-onset type 2 diabetes: The TODAY cohort at baseline. J.Clin.Endocrinol.Metab. 96 (1):159-167, 2011.	Wrong population: children and young people
GJ. Klingensmith, L Pyle, S Arslanian, KC. Copeland, L Cuttler, F Kaufman, L Laffel, S Marcovina, SE. Tollefsen, RS. Weinstock, B Linder, and TODAY Study Group. The presence of GAD and IA-2 antibodies in youth with a type 2 diabetes phenotype: results from the TODAY study. Diabetes Care 33 (9):1970-1975, 2010.	Wrong population: children and young people
H Holmberg, O Vaarala, V Sadauskaite-Kuehne, J Ilonen, Z Padaiga, and J Ludvigsson. Higher prevalence of autoantibodies to insulin and GAD65 in Swedish compared to Lithuanian children with type 1 diabetes. Diabetes Res.Clin.Pract. 72 (3):308-314, 2006.	Wrong population: children and young people
M. Rodacki, L. Zajdenverg, M. S. Albernaz, M. R. Bencke-Goncalves, A. Milech, and J. E. P. Oliveira. Relationship between the prevalence of anti-glutamic acid decarboxylase autoantibodies and duration of type 1 diabetes mellitus in Brazilian patients. Braz.J.Med.Biol.Res. 37 (11):1645-1650, 2004.	Wrong sample size: adults and young people n<50
E. Astorri, C. Guglielmi, M. Bombardieri, C. Alessandri, R. Buzzetti, D. Maggi, G. Valesini, C. Pitzalis, and P. Pozzilli. Circulating Reg1alpha proteins and autoantibodies to Reg1alpha proteins as biomarkers of beta-cell regeneration and damage in type 1 diabetes. Horm.Metab.Res. 42 (13):955-960, 2010.	Wrong sample size: adults and young people n<50
C Zheng, Z Zhou, L Yang, J Lin, G Huang, X Li, W Zhou, X Wang, and Z Liu. Fulminant type 1 diabetes mellitus exhibits distinct clinical and autoimmunity features from classical type 1 diabetes mellitus in Chinese. Diabetes.Metab.Res.Rev. 27 (1):70-78, 2011.	Wrong sample size: adults and young people n<50
T Mimura, H Funatsu, Y Uchigata, S Kitano, E Shimizu, S Amano, S Yamagami, H Noma, M Araie, and S Hori. Glutamic acid decarboxylase autoantibody prevalence and association with HLA genotype in patients with younger-onset type 1 diabetes and proliferative diabetic retinopathy. Ophthalmology 112 (11):1904-1909, 2005.	Wrong sample size: adults and young people n<50
AG. Unnikrishnan, V Kumaravel, V Nair, A Rao, RV. Jayakumar, H Kumar, and CB. Sanjeevi. TSH receptor antibodies in subjects with type 1 diabetes mellitus. Ann.n.Y.Acad.Sci. 1079:220-225, 2006.	Wrong sample size: adults and young people n<50
L Yang, Z Guang Zhou, G Huang, L Li Ouyang, X Li, and X Yan. Six-year follow-up of pancreatic beta cell function in adults with latent autoimmune diabetes. World J Gastroenterol 11 (19):2900-2905, 2005.	Wrong sample size: adults n<50

Update 2015

Study	Reason for exclusion
T. Tankova, L. Dakovska, G. Kirilov, and D. Koev. Intravenous glucose tolerance test and anti-GAD65 antibodies in the diagnosis of the type of diabetes mellitus. Pract.Diabetes Int. 20 (1):13-17, 2003.	Wrong sample size: adults n<50
Z. Milicevic, J. Knezevic, A. Sabioncello, G. Roglic, and B. Rocic. Beta-cell secretory function and CD25 + lymphocyte subsets in the early stage of type 1 diabetes mellitus. Exp.Clin.Endocrinol.Diabetes 112 (4):181-186, 2004.	Wrong sample size: adults n<50
NG 2002 W. Y. Ng, K. F. Lui, J. S. Cheah, and A. C. Thai. IgG1 subclass dominates autoimmune response to tyrosine phosphatase-like molecule IA-2 in Chinese type 1 diabetes patients. Horm.Metab.Res. 34 (10):596-600, 2002.	Wrong sample size: adults n<50
JM Gomez, R Vila, P Catalina, J Soler, L Badimon, and M Sahun. The markers of inflammation and endothelial dysfunction in correlation with glycated haemoglobin are present in type 2 diabetes mellitus patients but not in their relatives. Glycoconj.J. 25 (6):573-579, 2008.	Wrong sample size: adults n<50
C.-Y. Huang and S.-M. Lai. Low prevalence of latent autoimmune diabetes in adult type 2 diabetic patients with age of onset at 30-39 years in Taiwan. J.Intern.Med.Taiwan 15 (1):12-18, 2004.	Wrong sample size: adults n<50
M. Kurowska, J. S. Tarach, J. Malicka, H. Jankowska, and A. Dabrowska. Islet GAD autoantibodies in patients with newly diagnosed type 2 diabetes. Ann.Univ.Mariae Curie-Sklodowska Sect.DDD Pharm. 23 (3):101-106, 2010.	Wrong sample size: adults n<50
K. Agarwal, D. E. Jones, A. K. Daly, O. F. James, B. Vaidya, S. Pearce, and M. F. Bassendine. CTLA-4 gene polymorphism confers susceptibility to primary biliary cirrhosis. J Hepatol 32 (4):538-541, 2000.	Wrong population: adults only
Ch Amrouche, H. Jamoussi Kamoun, N. Trabelsi, and S. Blouza Chabchoub. Latent autoimmune diabetes in Tunisian adults (LADA): identification of autoimmune markers. Tunis Med 86 (4):316-318, 2008.	Wrong population: adults only
M. K. Andersen, M. Sterner, T. Forsen, A. Karajamaki, O. Rolandsson, C. Forsblom, P.-H. Groop, K. Lahti, P. M. Nilsson, L. Groop, and T. Tuomi. Type 2 diabetes susceptibility gene variants predispose to adult-onset autoimmune diabetes. Diabetologia 57 (9):1859-1868, 2014.	Wrong population: adults only
Ender Arikan, Tevfik Sabuncu, Esref M. Ozer, and Husrev Hatemi. The clinical characteristics of latent autoimmune diabetes in adults and its relation with chronic complications in metabolically poor controlled Turkish patients with Type 2 diabetes mellitus. J.Diabetes Complications 19 (5):254-258, 2005.	Wrong population: adults only
D Arslan, Alparslan Merdin, Deniz Tural, Mustafa Temizel, Olgun Akin, Seyda Gunduz, Ali Murat Tatli, Fatma Avci, and Mukremin Uysal. The effect of autoimmunity on the development time of microvascular complications in patients with type 1 diabetes mellitus. Med Sci Monit 20:1176-1179, 2014.	Wrong population: adults only
A. Barker, A. Lauria, N. Schloot, N. Hosszufalusi, J. Ludvigsson, C. Mathieu, D. Mauricio, M. Nordwall, B. Van Der Schueren, T. Mandrup-Poulsen, W. A. Scherbaum, I. Weets, F. K. Gorus, N. Wareham, R. D. Leslie, and P. Pozzilli. Age-dependent decline of beta-cell function in type 1 diabetes after diagnosis: a multi-centre longitudinal study. Diabetes Obesity and Metabolism 16 (3):262-267, 2014.	Wrong population: adults only
DS. H. Bell and Fernando Ovalle. The role of C-peptide levels in screening for latent autoimmune diabetes in adults. Am.J.Ther. 11 (4):308-311, 2004.	Wrong population: adults only
J. Bodalska-Lipinska, A. Szadkowska, and L. Markuszewski. Principles of diagnosis of latent autoimmune diabetes in adults (LADA). Diabetol.Dosw.Klin. 6 (2):69-74, 2006.	Wrong population: adults only
G. F. Bottazzo, E. Bosi, C. A. Cull, E. Bonifacio, M. Locatelli, P. Zimmet, I. R. Mackay, and R. R. Holman. IA-2 antibody prevalence and risk assessment of early insulin requirement in subjects presenting with type 2 diabetes (UKPDS 71). Diabetologia 48 (4):703-708, 2005.	Wrong population: adults only
H. A. J. Castleden, B. Shields, P. J. Bingley, A. J. K. Williams, M. Sampson, M. Walker, J. M. Gibson, M. I. McCarthy, G. A. Hitman, J. C. Levy, A. T. Hattersley, B. Vaidya, and E. R. Pearson. GAD antibodies in probands and their relatives in a cohort clinically selected for Type 2 diabetes. Diabet.Med. 23 (8):834-838, 2006.	Wrong population: adults only
M. Cerna, P. Novota, K. Kolostova, P. Cejkova, E. Zdarsky, D. Novakova, P. Kucera, J. Novak, and M. Andel. HLA in Czech adult patients with autoimmune diabetes mellitus: comparison with Czech children with type 1 diabetes and patients with type 2 diabetes. Eur.J.Immunogenet. 30 (6):401-407, 2003.	Wrong population: adults only
M. N. Chowta, P. M. Adhikari, N. K. Chowta, A. K. Shenoy, and S. D'Souza. Serum C peptide level and renal function in diabetes mellitus. Indian J.Nephrol. 20 (1):25-28, 2010.	Wrong population: adults only
H. Davies, S. Brophy, A. Fielding, P. Bingley, M. Chandler, I. Hilldrup, C. Brooks, and R. Williams. Latent autoimmune diabetes in adults (LADA) in South Wales: incidence and characterization. Diabet.Med. 25 (11):1354-1357, 2008.	Wrong population: adults only
T. M. E. Davis, Z. Mehta, I. R. Mackay, C. A. Cull, D. G. Bruce, S. Fida, M. J. Rowley, and R. R. Holman. Autoantibodies to the islet cell antigen SOX-13 are associated with duration but not type of diabetes. Diabet.Med. 20 (3):198-204, 2003.	Wrong population: adults only

Update 2015

Study	Reason for exclusion
M. Desai, C. A. Cull, V. A. Horton, M. R. Christie, E. Bonifacio, V. Lampasona, P. J. Bingley, J. C. Levy, I. R. Mackay, P. Zimmet, R. R. Holman, and A. Clark. GAD autoantibodies and epitope reactivities persist after diagnosis in latent autoimmune diabetes in adults but do not predict disease progression: UKPDS 77. Diabetologia 50 (10):2052-2060, 2007.	Wrong population: adults only
K Hamaguchi, Akinori Kimura, Yoichiro Kusuda, Tsutomu Yamashita, Michio Yasunami, Megumi Takahasi, Nobuyuki Abe, and Hironobu Yoshimatsu. Clinical and genetic characteristics of GAD-antibody positive patients initially diagnosed as having type 2 diabetes. Diabetes Res.Clin.Pract. 66 (2):163-171, 2004.	Wrong population: adults only
C S. Hampe, Murray E. Maitland, Lisa K. Gilliam, Thanh H. T. Phan, Ian R. Sweet, Jared R. Radtke, Vasile Bota, Bruce R. Ransom, and Irl B. Hirsch. High titers of autoantibodies to glutamate decarboxylase in type 1 diabetes patients: epitope analysis and inhibition of enzyme activity. Endocr Pract 19 (4):663-668, 2013.	Wrong population: adults only
MI. Hawa, Hubert Kolb, Nanette Schloot, Huriya Beyan, Stavroula A. Paschou, Raffaella Buzzetti, Didac Mauricio, Alberto de Leiva, Knud Yderstraede, Henning Beck-Neilsen, Jaakko Tuomilehto, Cinzia Sarti, Charles Thivolet, David Hadden, Steven Hunter, Guntram Schernthaner, Werner A. Scherbaum, Rhys Williams, Sinead Brophy, Paolo Pozzilli, Richard David Leslie, and Action LADA consortium. Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7. Diabetes Care 36 (4):908-913, 2013.	Wrong population: adults only
M. Hillman, C. Torn, M. Landin-Olsson, and DISS study group. The glutamic acid decarboxylase 65 immunoglobulin G subclass profile differs between adult-onset type 1 diabetes and latent autoimmune diabetes in adults (LADA) up to 3 years after clinical onset. Clin.Exp.Immunol. 157 (2):255-260, 2009.	Wrong population: adults only
S. V. Hope, A. G. Jones, E. Goodchild, M. Shepherd, R. E. J. Besser, B. Shields, T. McDonald, B. A. Knight, and A. Hattersley. Urinary C-peptide creatinine ratio detects absolute insulin deficiency in Type 2 diabetes. Diabet.Med. 30 (11):1342-1348, 2013.	Wrong population: adults only
N Hosszufalusi, Agnes Vatay, Katalin Rajczy, Zoltan Prohaszka, Eva Pozsonyi, Laura Horvath, Andrea Grosz, Laszlo Gero, Laszlo Madacsy, Laszlo Romics, Istvan Karadi, George Fust, and Pal Panczel. Similar genetic features and different islet cell autoantibody pattern of latent autoimmune diabetes in adults (LADA) compared with adult-onset type 1 diabetes with rapid progression. Diabetes Care 26 (2):452-457, 2003.	Wrong population: adults only
G Huang, Yufei Xiang, Lingling Pan, Xia Li, Shuoming Luo, and Zhiguang Zhou. Zinc transporter 8 autoantibody (ZnT8A) could help differentiate latent autoimmune diabetes in adults (LADA) from phenotypic type 2 diabetes mellitus. Diabetes.Metab.Res.Rev. 29 (5):363-368, 2013.	Wrong population: adults only
Y Hwangbo, Jin Taek Kim, Eun Ky Kim, Ah Reum Khang, Tae Jung Oh, Hak Chul Jang, Kyong Soo Park, Seong Yeon Kim, Hong Kyu Lee, and Young Min Cho. Prevalence and clinical characteristics of recently diagnosed type 2 diabetes patients with positive anti-glutamic Acid decarboxylase antibody. Diabetes & Metabolism 36 (2):136-143, 2012.	Wrong population: adults only
C. S. Kim, M. K. Song, J. S. Park, M. H. Cho, H. J. Kim, J. S. Nam, E. S. Kang, C. W. Ahn, B. S. Cha, E. G. Lee, S. K. Lim, K. R. Kim, H. C. Lee, and K. B. Huh. The clinical and immunogenetic characteristics of adult-onset type 1 diabetes mellitus in Korea. Acta Diabetol. 44 (2):45-54, 2007.	Wrong population: adults only
S. A. Lee, W. J. Lee, E. H. Kim, J. H. Yu, C. H. Jung, E. H. Koh, M. S. Kim, J. Y. Park, and K. U. Lee. Progression to insulin deficiency in Korean patients with Type 2 diabetes mellitus positive for anti-GAD antibody. Diabet.Med. 28 (3):319-324, 2011.	Wrong population: adults only
E Lindholm, Bengt Hallengren, and Carl David Agardh. Gender differences in GAD antibody-positive diabetes mellitus in relation to age at onset, C-peptide and other endocrine autoimmune diseases. Diabetes.Metab.Res.Rev. 20 (2):158-164, 2004.	Wrong population: adults only
YP. Mahadeb, Damien Gruson, Martin Buysschaert, and Michel P. Hermans. What are the characteristics of phenotypic type 2 diabetic patients with low-titer GAD65 antibodies? Acta Diabetol. 51 (1):103-111, 2014.	Wrong population: adults only
M. Maioli, G. M. Pes, G. Delitala, L. Puddu, A. Falorni, F. Tolu, R. Lampis, V. Orru, G. Secchi, A. M. Cicalo, R. Floris, G. F. Madau, R. M. Pilosu, M. Whalen, and F. Cucca. Number of autoantibodies and HLA genotype, more than high titers of glutamic acid decarboxylase autoantibodies, predict insulin dependence in latent autoimmune diabetes of adults. EUR.J.ENDOCRINOL. 163 (4):541-549, 2010.	Wrong population: adults only
J de Faria Maraschin, Leticia Schwerz Weinert, Nadia Murussi, Vanessa Witter, Ticiana da Costa Rodrigues, Egna Regina Rossato, and Sandra Pinho Silveiro. Influence of age at diagnosis and duration of diabetes on the positivity of glutamic acid decarboxylase antibody in South-Brazilian type 1 diabetes mellitus. Ann.Clin.Biochem. 50 (Pt 3):262-266, 2013.	Wrong population: adults only

Update 2015

Study	Reason for exclusion
T. J. McDonald, K. Colclough, R. Brown, B. Shields, M. Shepherd, P. Bingley, A. Williams, A. T. Hattersley, and Sian Ellard. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. Diabet.Med. 28 (9):1028-1033, 2011.	Wrong population: adults only
L. Monge, G. Bruno, S. Pinach, G. Grassi, G. Maghenzani, F. Dani, and G. Pagano. A clinically orientated approach increases the efficiency of screening for latent autoimmune diabetes in adults (LADA) in a large clinic-based cohort of patients with diabetes onset over 50 years. Diabet.Med. 21 (5):456-459, 2004.	Wrong population: adults only
S Murao, Shiori Kondo, Jun Ohashi, Yasuhisa Fujii, Ikki Shimizu, Masao Fujiyama, Keizo Ohno, Yasuharu Takada, Kazuaki Nakai, Yukio Yamane, Haruhiko Osawa, and Hideichi Makino. Anti-thyroid peroxidase antibody, IA-2 antibody, and fasting C-peptide levels predict beta cell failure in patients with latent autoimmune diabetes in adults (LADA)--a 5-year follow-up of the Ehime study. Diabetes Res.Clin.Pract. 80 (1):114-121, 2008.	Wrong population: adults only
A Paschke, Agata Grzelka, Agnieszka Zawada, and Dorota Zozulinska-Ziolkiewicz. Clinical characteristics and autoantibody pattern in newly diagnosed adult-onset autoimmune diabetes. Pol.Arch.Med.Wewn. 123 (7-8):401-408, 2013.	Wrong population: adults only
MA. Radtke, Kristian Midthjell, Tom I. L. Nilsen, and Valdemar Grill. Heterogeneity of patients with latent autoimmune diabetes in adults: linkage to autoimmunity is apparent only in those with perceived need for insulin treatment: results from the Nord-Trondelag Health (HUNT) study. Diabetes Care 32 (2):245-250, 2009.	Wrong population: adults only
A Rogowicz-Frontczak, Dorota Zozulilska-Ziolkiewicz, Monika Litwinowicz, Pawel Niedzwiecki, Krystyna Wyka, and Bogna Wierusz-Wysocka. Are zinc transporter type 8 antibodies a marker of autoimmune thyroiditis in non-obese adults with new-onset diabetes? EUR.J.ENDOCRINOL. 170 (4):651-658, 2014.	Wrong population: adults only
Mi Oh Roh, Chan Hee Jung, Bo Yeon Kim, Ji Oh Mok, and Chul Hee Kim. The prevalence and characteristics of latent autoimmune diabetes in adults (LADA) and its relation with chronic complications in a clinical department of a university hospital in Korea. Acta Diabetol. 50 (2):129-134, 2013.	Wrong population: adults only
K. Shishikura, K. Tanimoto, S. Sakai, Y. Tanimoto, J. Terasaki, and T. Hanafusa. Association between skeletal muscle mass and insulin secretion in patients with type 2 diabetes mellitus. Endocr.J. 61 (3):281-287, 2014.	Wrong population: adults only
E. P. Sorgjerd, F. Skorpen, K. Kvaloy, K. Midthjell, and V. Grill. Time dynamics of autoantibodies are coupled to phenotypes and add to the heterogeneity of autoimmune diabetes in adults: the HUNT study, Norway. Diabetologia 55 (5):1310-1318, 2012.	Wrong population: adults only
A. Szypowska, A. Ramotowska, K. Dzygalo, and D. Golicki. Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials. EUR.J.ENDOCRINOL. 166:567-574, 2012.	Wrong population: adults only
G Thanabalasingham, Aparna Pal, Mary P. Selwood, Christina Dudley, Karen Fisher, Polly J. Bingley, Sian Ellard, Andrew J. Farmer, Mark I. McCarthy, and Katharine R. Owen. Systematic assessment of etiology in adults with a clinical diagnosis of young-onset type 2 diabetes is a successful strategy for identifying maturity-onset diabetes of the young. Diabetes Care 35 (6):1206-1212, 2012.	Wrong population: adults only
A Trabucchi, Natalia I. Faccinetti, Luciano L. Guerra, Felix M. Puchulu, Gustavo D. Frechtel, Edgardo Poskus, and Silvina N. Valdez. Detection and characterization of ZnT8 autoantibodies could help to screen latent autoimmune diabetes in adult-onset patients with type 2 phenotype. Autoimmunity 45 (2):137-142, 2012.	Wrong population: adults only
F Vaziri-Sani, Shilpa Oak, Jared Radtke, Ke Lernmark, Kristian Lynch, Carl D. Agardh, Corrado M. Cilio, Asa L. Lethagen, Eva Ortqvist, Mona Landin-Olsson, Carina Torn, and Christiane S. Hampe. ZnT8 autoantibody titers in type 1 diabetes patients decline rapidly after clinical onset. Autoimmunity 43 (8):598-606, 2010.	Wrong population: adults only
I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G. Pipeleers, and F. K. Gorus. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. Diabetes Care 34 (8):1760-1765, 2011.	Wrong population: adults only
A. Vlad, V. Serban, Alexandra Sima, R. Timar, and Mihaela Rosu. The value of basal C peptide and its relationship with pancreatic autoantibodies in young adults with type 2 diabetes mellitus. Rom.J.Intern.Med. 42 (2):333-341, 2004.	Wrong population: adults only
H. Wilmot-Roussel, D. J. Levy, C. Carette, S. Caillat-Zucman, C. Boitard, J. Timsit, and D. Dubois-Laforgue. Factors associated with the presence of glutamic acid decarboxylase and islet antigen-2 autoantibodies in patients with long-standing type 1 diabetes. Diabetes & Metabolism 39 (3):244-249, 2013.	Wrong population: adults only
L. Yang, Z. G. Zhou, S. Z. Tan, G. Huang, P. Jin, X. Yan, X. Li, H. Peng, and W. Hagopian. Carboxypeptidase-H autoantibodies differentiate a more latent subset of autoimmune diabetes from phenotypic type 2 diabetes among Chinese adults. Ann.N.Y.Acad.Sci. 1150:263-266, 2008.	Wrong population: adults only

Update 2015

Study	Reason for exclusion
S Zampetti, Marco Capizzi, Marialuisa Spoletini, Giuseppe Campagna, Gaetano Leto, Laura Cipolloni, Claudio Tiberti, Emanuele Bosi, Alberto Falorni, Raffaella Buzzetti, and NIRAD Study Group. GADA titer-related risk for organ-specific autoimmunity in LADA subjects subdivided according to gender (NIRAD study 6). J.Clin.Endocrinol.Metab. 97 (10):3759-3765, 2012.	Wrong population: adults only
S Zhang, Qi Sun, Kai Feng, Yong Fu, Ou Wang, Fan Ping, and Yuxiu Li. Clinical, biochemical, and immunological characteristics of newly diagnosed nonobese diabetic patients aged 18-45 years in China. J.Diabetes Complications 26 (1):40-43, 2012.	Wrong population: adults only

H.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Study	Reason for exclusion
Ambrosino,J.M., Fennie,K., Whittemore,R., Jaser,S., Dowd,M.F., Grey,M., Short-term effects of coping skills training in school-age children with type 1 diabetes, Pediatric Diabetes, 9, 74-82, 2008	PICO not met: intervention not considered to be a form of structured education
Anderson,B.J., Wolf,F.M., Burkhart,M.T., Cornell,R.G., Bacon,G.E, Effects of peer-group intervention on metabolic control of adolescents with IDDM. Randomized outpatient study, Diabetes Care, 12, 179-183, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)
Armour,T.A., Norris,S.L., Jack,L.,Jr., Zhang,X., Fisher,L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], Diabetic Medicine, 22, 1295-1305, 2005	Systematic review: individual RCTs have been considered for inclusion
Barnes,L.P., The illiterate client: strategies in patient teaching, MCN: The American Journal of Maternal Child Nursing, 17, 127-127, 1992	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)
Bin-Abbas,B., Jabbari,M., Al-Fares,A., El-Dali,A., Al-Orifi,F., Effect of mobile phone short text messages on glycaemic control in children with type 1 diabetes, Journal of Telemedicine and Telecare, 20, 153-156, 2014	The study was not randomised, and included only 1 group using the intervention
Bloomfield,S., Calder,J.E., Chisholm,V., Kelnar,C.J., Steel,J.M., Farquhar,J.W., Elton,R., A project in diabetes education for children, Diabetic Medicine, 7, 137-142, 1990	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (study population unclear)
Brown,S.J., Lieberman,D.A., Germeny,B.A., Fan,Y.C., Wilson,D.M., Pasta,D.J., Educational video game for juvenile diabetes: results of a controlled trial, Medical Informatics, 22, 77-89, 1997	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)
Chaney,D., Coates,V., Shevlin,M., Carson,D., McDougall,A., Long,A., Bunting,B., Evaluation of the Carbohydrate, Insulin Collaborative Education (CHOICE) programme for young people with Type 1 diabetes, Diabetic Medicine, 28, 25-, 2011	Conference abstract
Chaney,David, Coates,Vivien, Shevlin,Mark, Running a complex educational intervention for adolescents with type 1 diabetes -- lessons learnt, Journal of Diabetes Nursing, 14, 370-, 2010	Discussion of issues from a RCT
Christie,D., Strange,V., Allen,E., Oliver,S., Wong,I.C., Smith,F., Cairns,J., Thompson,R., Hindmarsh,P., O'Neill,S., Bull,C., Viner,R., Elbourne,D., Maximising engagement, motivation and long term change in a Structured Intensive Education Programme in Diabetes for children, young people and their families: Child and Adolescent Structured Competencies Approach to Diabetes Education (CASCADE), BMC Pediatrics, 9, 57-, 2009	Protocol for a RCT (CASCADE)
Couch,R., Jetha,M., Dryden,D.M., Hooten,N., Liang,Y., Durec,T., Sumamo,E., Spooner,C., Milne,A., O'Gorman,K., Klassen,T.P., Diabetes education for children with type 1 diabetes mellitus and their families. [122 refs], Evidence Report/Technology Assessment, 1-144, 2008	Systematic review: individual RCT have been considered for inclusion
DeShazo,J., Harris,L., Pratt,W., Effective intervention or child's play? A review of video games for diabetes education, Diabetes Technology and Therapeutics, 12, 815-822, 2010	Systematic review: individual RCT have been considered for inclusion
Diabetes Education Program in Bulgaria (DEPB) Project Group., Diabetes education program in Bulgaria, Patient Education and Counseling, 43, 111-114, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no separate paediatric data reported)
Elamin,A., Eltayeb,B., Hasan,M., Hofvander,Y., Tuvemo,T., Effect of dietary education on metabolic control in children and adolescents with Type I diabetes mellitus, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 6, 223-229, 1993	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up too short)

Update 2015

Study	Reason for exclusion
Ellis,D.A., Yopp,J., Templin,T., Naar-King,S., Frey,M.A., Cunningham,P.B., Idalski,A., Niec,L.N., Family mediators and moderators of treatment outcomes among youths with poorly controlled type 1 diabetes: results from a randomized controlled trial, Journal of Pediatric Psychology, 32, 194-205, 2007	Did not consider a structured form of education
Gage,H., Hampson,S., Skinner,T.C., Hart,J., Storey,L., Foxcroft,D., Kimber,A., Cradock,S., McEvilly,E.A., Educational and psychosocial programmes for adolescents with diabetes: approaches, outcomes and cost-effectiveness. [122 refs], Patient Education and Counseling, 53, 333-346, 2004	Systematic review: individual RCT have been considered for inclusion
Grey,M., Jaser,S.S., Whittemore,R., Jeon,S., Lindemann,E., Coping skills training for parents of children with type 1 diabetes: 12-month outcomes, Nursing Research, 60, 173-181, 2011	Conference abstract
Grey,M., Whittemore,R., Jaser,S., Ambrosino,J., Lindemann,E., Liberti,L., Northrup,V., Dziura,J., Effects of coping skills training in school-age children with type 1 diabetes, Research in Nursing and Health, 32, 405-418, 2009	PICO not met: intervention not considered to be a form of structured education
Grey,M., Whittemore,R., Jeon,S., Jaser,S., Murphy,K., Faulkner,M., Delamater,A., Internet programs for youth with type 1 diabetes (T1D) improve outcomes, Diabetes, 61, A90-, 2012	PICO not met: intervention not considered to be a form of structured education
Hackett,A.F., Court,S., Mathews,J.N., McCowen,C., Do education groups help diabetics and their parents?, Archives of Disease in ChildhoodArch.Dis.Child., 64, 997-1003, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (study design unclear; not clearly an RCT)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review (Structured abstract), Health Technology Assessment Database, -, 2013	Abstract for a systematic review published in 2001
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Cradock,S., McEvilly,E.A., Behavioral interventions for adolescents with type 1 diabetes: how effective are they?. [68 refs], Diabetes Care, 23, 1416-1422, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (individual RCTs are included in the guideline review)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. [148 refs], Health Technology Assessment (Winchester, England), 5, 1-79, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (individual RCTs are included in the guideline review)
Hanberger,L., Ludvigsson,J., Nordfeldt,S., Use of a web 2.0 portal to improve education and communication in young patients with families: randomized controlled trial, Journal of medical Internet research, 15, e175-, 2013	Web 2.0 portal was not a 'structured' education programme (there was no structured curriculum); the use of the portal was designed to be self-initiated by participants and their parents whenever needed, although there was access to communication with healthcare professionals
Hill-Briggs,F., Gemmell,L., Problem solving in diabetes self-management and control: A systematic review of the literature, Diabetes Educator, 33, 1032-1050, 2007	Systematic review: individual RCT have been considered for inclusion
Hoff,A.L., Mullins,L.L., Gillaspy,S.R., Page,M.C., Van,PeltJ, Chaney,J.M., An intervention to decrease uncertainly and distress among parents of children newly diagnosed with diabetes: A pilot study, Families, Systems and Health, 23, 329-342, 2005	PICO not met: population was specifically the parents of children with diabetes
Holmes,C.S., Chen,R., Mackey,E., Grey,M., Streisand,R., Randomized clinical trial of clinic-integrated, low-intensity treatment to prevent deterioration of disease care in adolescents with type 1 diabetes, Diabetes Care, 37, 1535-1543, 2014	Wrong intervention (behavioural intervention)
Hood,K.K., Rohan,J.M., Peterson,C.M., Drotar,D., Interventions with adherence-promoting components in pediatric type 1 diabetes: meta-analysis of their impact on glycemic control, Diabetes Care, 33, 1658-1664, 2010	Systematic review: individual RCT have been considered for inclusion
Howells,L., Wilson,A.C., Skinner,T.C., Newton,R., Morris,A.D., Greene,S.A., A randomized control trial of the effect of negotiated telephone support on glycaemic control in young people with Type 1 diabetes, Diabetic Medicine, 19, 643-648, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)
Husted,G.R., Thorsteinsson,B., Esbensen,B.A., Hommel,E., Zoffmann,V., Improving glycaemic control and life skills in adolescents with type 1 diabetes: a randomised, controlled intervention study using the Guided Self-Determination-Young method in triads of adolescents, parents and healthcare providers integrated into routine paediatric outpatient clinics, BMC Pediatrics, 11, 55-, 2011	PICO not met: intervention not considered to be a form of structured education
Izquierdo,R., Morin,P.C., Bratt,K., Moreau,Z., Meyer,S., Ploutz-Snyder,R., Wade,M., Weinstock,R.S., School-centered telemedicine for children with type 1 diabetes mellitus, Journal of Pediatrics, 155, 374-379, 2009	PICO not met: intervention intended for improvement in education for school staff
Jonsson,L., Hallstrom,I., Lundqvist,A., A multi-disciplinary education process related to the discharging of children from hospital when the child has been diagnosed with type 1 diabetes--a qualitative study, BMC Pediatrics, 10, 36-, 2010	Not a RCT

Update 2015

Study	Reason for exclusion
Laffel,L.M.B., Vangsness,L., Connell,A., Goebel-Fabbri,A., Butler,D., Anderson,B.J., Impact of ambulatory, family-focused teamwork intervention on glycemic control in youth with type 1 diabetes, Journal of Pediatrics, 142, 409-416, 2003	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (intervention not considered to be a form of structured education)
Mannucci,E., Pala,L., Rotella,C.M., Long-term interactive group education for type 1 diabetic patients, Acta Diabetologica, 42, 1-6, 2005	Not a RCT
Massouh,S.R., Steele,T.M., Alseth,E.R., Diekmann,J.M., The effect of social learning intervention on metabolic control of insulin-dependent diabetes mellitus in adolescents, Diabetes Educator, 15, 518-521, 1989	Included in 2004 guideline review - did not meet inclusion criteria for 2015 update review (closer to a behavioural intervention than a structured education programme)
McBroom,L.A., Enriquez,M., Review of family-centered interventions to enhance the health outcomes of children with type 1 diabetes. [36 refs], Diabetes Educator, 35, 428-438, 2009	Systematic review: individual RCT have been considered for inclusion
McNabb,W.L., Quinn,M.T., Murphy,D.M., Thorp,F.K., Cook,S., Increasing children's responsibility for diabetes self-care: the In Control study, Diabetes Educator, 20, 121-124, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up period insufficient)
Mcpherson,A.C., Price,K., Does an interactive website provide additional support to young people participating in an educational intervention for type 1 diabetes?, Pediatric Diabetes, 13, 139-, 2012	Conference abstract
Moattari,Marzieh, Hashemi,Maryam, Dabbaghmanesh,Mohammad, The impact of electronic education on metabolic control indicators in patients with diabetes who need insulin: a randomised clinical control trial, Journal of Clinical Nursing, 22, 32-38, 2013	PICO not met: adult participants only
Muller,Nicolle, Kloos,Christof, Samann,Alexander, Wolf,Gunter, Muller,Ulrich Alfons, Evaluation of a treatment and teaching refresher programme for the optimization of intensified insulin therapy in type 1 diabetes, Patient Education and Counseling, 93, 108-113, 2013	Participants aged between 16 and 70 years
Mulvaney,S.A., Rothman,R.L., Osborn,C.Y., Lybarger,C., Dietrich,M.S., Wallston,K.A., Self-management problem solving for adolescents with type 1 diabetes: intervention processes associated with an Internet program, Patient Education and Counseling, 85, 140-142, 2011	Outcomes not compared between the comparative groups
Mulvaney,S.A., Rothman,R.L., Wallston,K.A., Lybarger,C., Dietrich,M.S., An internet-based program to improve self-management in adolescents with type 1 diabetes, Diabetes Care, 33, 602-604, 2010	PICO not met: intervention not considered to be a form of structured education
Murphy,H.R., Rayman,G., Skinner,T.C., Psycho-educational interventions for children and young people with Type 1 diabetes. [52 refs], Diabetic Medicine, 23, 935-943, 2006	Systematic review: individual RCT have been considered for inclusion
Nansel,T.R., Iannotti,R.J., Simons-Morton,B.G., Cox,C., Plotnick,L.P., Clark,L.M., Zeitzoff,L., Diabetes personal trainer outcomes: short-term and 1-year outcomes of a diabetes personal trainer intervention among youth with type 1 diabetes, Diabetes Care, 30, 2471-2477, 2007	PICO not met: intervention not considered to be a form of structured education
Nansel,T.R., Iannotti,R.J., Simons-Morton,B.G., Plotnick,L.P., Clark,L.M., Zeitzoff,L., Long-term maintenance of treatment outcomes: diabetes personal trainer intervention for youth with type 1 diabetes, Diabetes Care, 32, 807-809, 2009	A follow-up study of a RCT
Nicholas,D.B., Fellner,K.D., Frank,M., Small,M., Hetherington,R., Slater,R., Daneman,D., Evaluation of an online education and support intervention for adolescents with diabetes, Social Work in Health Care, 51, 815-827, 2012	Process evaluation
Nordfeldt,S., Johansson,C., Carlsson,E., Hammersjo,J.A., Persistent effects of a pedagogical device targeted at prevention of severe hypoglycaemia: a randomized, controlled study, Acta Paediatrica, 94, 1395-1401, 2005	A follow-up study of a RCT
Nordfeldt,S., Johansson,C., Carlsson,E., Hammersjo,J.A., Prevention of severe hypoglycaemia in type I diabetes: a randomised controlled population study, Archives of Disease in Childhood, 88, 240-245, 2003	Included in 2004 guideline review - does not meet criteria for 2015 update review (not a structured education programme)
Olmsted,M.P., Daneman,D., Rydall,A.C., Lawson,M.L., Rodin,G., The effects of psychoeducation on disturbed eating attitudes and behavior in young women with type 1 diabetes mellitus, International Journal of Eating Disorders, 32, 230-239, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population limited to young women with eating disturbance)
Pichert,J.W., Smeltzer,C., Snyder,G.M., Gregory,R.P., Smeltzer,R., Kinzer,C.K., Traditional versus anchored instruction for diabetes-related nutritional knowledge, skills, and behavior, Diabetes Educator, 20, 45-48, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 review (no outcomes of interest reported)
Pichert,J.W., Snyder,G.M., Kinzer,C.K., Boswell,E.J., Problem solving anchored instruction about sick days for adolescents with diabetes, Patient Education and Counseling, 23, 115-124, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 review (no outcomes of interest reported)
Price,K.J., Wales,J., Eiser,C., Knowles,J., Heller,S., Freeman,J., Brennan,A., McPherson,A., Wellington,J., Does an intensive self-management structured education course improve outcomes for children and young people with type 1 diabetes? The Kids In Control OF Food (KICk-OFF) cluster-randomised controlled trial protocol, BMJ Open, 3, -, 2013	A protocol for a RCT (KICk-OFF)
Sansom-Daly,U.M., Peate,M., Wakefield,C.E., Bryant,R.A., Cohn,R.J., A systematic review of psychological interventions for adolescents and young adults living with chronic illness, Health Psychology, 31, 380-393, 2012	Systematic review: individual RCT have been considered for inclusion

Update 2015

Study	Reason for exclusion
Satin,W., La Greca,A.M, Zigo,M.A, Skyler,J.S, Diabetes in adolescence: effects of multifamily group intervention and parent simulation of diabetes, Journal of Pediatric PsychologyJ.Pediatr.Psychol., 14, 259-275, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not considered to be a structured education programme)
Savage,E., Farrell,D., McManus,V., Grey,M., The science of intervention development for type 1 diabetes in childhood: systematic review, Journal of Advanced Nursing, 66, 2604-2619, 2010	Systematic review: individual RCT have been considered for inclusion
Sherifali,D., A case manager plus psychoeducation reduced adverse outcomes in youth with type 1 diabetes, Evidence Based Nursing, 7, 42-42, 2004	Abstract
Spiegel,G., Bortsov,A., Bishop,F.K., Owen,D., Klingensmith,G.J., Mayer-Davis,E.J., Maahs,D.M., Randomized Nutrition Education Intervention to Improve Carbohydrate Counting in Adolescents with Type 1 Diabetes Study: Is More Intensive Education Needed?, Journal of the Academy of Nutrition and Dietetics, , 1736-1746, 2012	PICO not met: outcomes of interest not reported
Srinivasan,B., Davies,M., Lawrence,I., Diabetes: glycaemic control in type 1, Clinical Evidence, 2008, 2008., -, 2008	Systematic review: individual RCT have been considered for inclusion
Suh,S., Jean,C., Koo,M., Lee,S.Y., Cho,M.J., Sim,K.H., Jin,S.M., Bae,J.C., Kim,J.H., A randomized controlled trial of an internet-based mentoring program for type 1 diabetes patients with inadequate glycemic control, Diabetes and Metabolism Journal, 38, 134-142, 2014	Adult population
Sullivan-Bolyai,Susan, Bova,Carol, Leung,Katherine, Trudeau,Allison, Lee,Mary, Gruppuso,Philip, Social Support to Empower Parents (STEP): An intervention for parents of young children newly diagnosed with type 1 diabetes, The Diabetes Educator, 36, 88-97, 2010	Population was mothers of children with type 1 diabetes
Sundelin,J., Forsander,G., Mattsson,S.E, Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, Acta PaediatricaActa Paediatr., 85, 49-55, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a form of structured education)
Urban,A.D., Berry,D., Grey,M., Optimizing outcomes in adolescents with type 1 diabetes and their families, Journal of Clinical Outcomes Management, 11, 299-306, 2004	Systematic review: individual RCT have been considered for inclusion
Viklund,G., Ortqvist,E., Wikblad,K., Assessment of an empowerment education programme. A randomized study in teenagers with diabetes, Diabetic medicine : a journal of the British Diabetic Association, 24, 550-556, 2007	PICO not met: intervention not considered to be a form of structured education
Wang,Y.C., Stewart,S.M., Mackenzie,M., Nakonezny,P.A., Edwards,D., White,P.C., A randomized controlled trial comparing motivational interviewing in education to structured diabetes education in teens with type 1 diabetes, Diabetes Care, 33, 1741-1743, 2010	This is a process evaluation study, not a clinical trial
Whittemore,R., Jaser,S.S., Jeon,S., Liberti,L., Delamater,A., Murphy,K., Faulkner,M.S., Grey,M., An internet coping skills training program for youth with type 1 diabetes: six-month outcomes, Nursing Research, 61, 395-404, 2012	PICO not met: intervention not considered to be a form of structured education
Wysocki,T., Harris,M.A, Greco,P., Harvey,L.M., McDonnell,K, Elder Danda,C.L, Bubb,J, White,N.H., Social validity of support group and behavior therapy interventions for families of adolescents with insulin-dependent diabetes mellitus, Journal of Pediatric PsychologyJ.Pediatr.Psychol., 22, 635-649, 1997	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no outcomes of interest reported and the original study was also excluded)
Wysocki,T., Harris,M.A., Buckloh,L.M., Mertlich,D., Lochrie,A.S., Taylor,A., Sadler,M., White,N.H., Randomized, controlled trial of Behavioral Family Systems Therapy for Diabetes: maintenance and generalization of effects on parent-adolescent communication, Behavior Therapy, 39, 33-46, 2008	Maintenance study for a RCT
Wysocki,T., Harris,M.A., Greco,P., Bubb,J., Danda,C.E., Harvey,L.M., McDonell,K., Taylor,A., White,N.H., Randomized, controlled trial of behavior therapy for families of adolescents with insulin-dependent diabetes mellitus, Journal of Pediatric Psychology, 25, 23-33, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (the original study Wysocki 1997 was excluded; this article has also been excluded as only results from the 3-month follow-up are reported)

Update 2015

H.3 Type 1 diabetes – psychological interventions

Review question: What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 1 diabetes?

Study	Reason for exclusion
Ambrosino,J.M., Fennie,K., Whittemore,R., Jaser,S., Dowd,M.F., Grey,M., Short-term effects of coping skills training in school-age children with type 1 diabetes, Pediatric Diabetes, 9, 74-82, 2008	PICO not met - follow-up length insufficient
Anderson,B.J., Wolf,F.M., Burkhart,M.T., Cornell,R.G., Bacon,G.E, Effects of peer-group intervention on metabolic control of adolescents with IDDM. Randomized outpatient study, Diabetes Care, 12, 179-183, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an intervention specified in the review protocol)

Study	Reason for exclusion
Berger,G., Muehlehner,M., Brunmayr,F., Waldhoer,T., Wondratsch,C., Lonsky,J., Koenig,M., Horak,E., Wagner,G., Hoertenhuber,T., Fritsch,M., Schober,E., Rami-Merhar,B., Motivational interviewing to improve metabolic control in adolescents with type 1 diabetes: It's worth talking to boys?, Pediatric Diabetes, 13, 27-, 2012	Conference abstract
Boardway,R.H., Delamater,A.M., Tomakowsky,J., Gutai,J.P., Stress management training for adolescents with diabetes, Journal of Pediatric Psychology, 18, 29-45, 1993	Included in 2004 guideline review does not meet inclusion criteria for 2015 update review (follow-up does not meet required duration)
Cakan,N., Ellis,D.A., Templin,T., Frey,M., Naar-King,S., The effects of weight status on treatment outcomes in a randomized clinical trial of multisystemic therapy for adolescents with type 1 diabetes and chronically poor metabolic control, Pediatric Diabetes, 8, 206-213, 2007	Secondary publication
Channon,S., Smith,V.J., Gregory,J.W., A pilot study of motivational interviewing in adolescents with diabetes, Archives of Disease in Childhood, 88, 680-683, 2003	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)
Chernoff,R.G., Ireys,H.T., DeVet,K.A., Kim,Y.J., A randomized, controlled trial of a community-based support program for families of children with chronic illness: pediatric outcomes, Archives of Pediatrics and Adolescent Medicine, 156, 533-539, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population does not match the inclusion criteria of the 2015 update review)
Chisholm,V., Gonzalez,A., Atkinson,L., Interpersonal engagement mediates the relation between maternal affect and externalising behaviour in young children with type 1 diabetes, PLoS ONE [Electronic Resource], 9, e97672-, 2014	Interventions are not of interest
Cho,E., Shin,S.H., Eun,S.H., Kim,J.Y., Nam,H.K., Lee,K.H., Rhie,Y.J., Psychological characteristics of Korean children and adolescents with type 1 diabetes mellitus, Annals of Pediatric Endocrinology and Metabolism, 18, 122-127, 2013	Wrong study design (case-control, not RCT)
Christie,D., Thompson,R., Sawtell,M., Allen,E., Cairns,J., Smith,F., Jamieson,E., Hargreaves,K., Ingold,A., Brooks,L., Wiggins,M., Oliver,S., Jones,R., Elbourne,D., Santos,A., Wong,I.C., O'Neill,S., Strange,V., Hindmarsh,P., Annan,F., Viner,R., Structured, intensive education maximising engagement, motivation and long-term change for children and young people with diabetes: a cluster randomised controlled trial with integral process and economic evaluation - the CASCADE study, Health Technology Assessment (Winchester, England), 18, 1-202, 2014	Wrong intervention (education)
Daley,B.J., Sponsorship for adolescents with diabetes, Health and Social Work, 17, 173-182, 1992	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population unclear, stated as teenagers with diabetes)
Delamater,A.M., Bubb,J., Davis,S.G, Smith,J.A, Schmidt,L., White,N.H, Santiago,J.V., Randomized prospective study of self-management training with newly diagnosed diabetic children. [erratum appears in Diabetes Care 1990 Jul;13(7):819], Diabetes Care, 13, 492-498, 1990	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (intervention is an education programme rather than a behavioural intervention)
Ellis,D., Naar-King,S., Templin,T., Frey,M., Cunningham,P., Sheidow,A., Cakan,N., Idalski,A., Multisystemic therapy for adolescents with poorly controlled type 1 diabetes: reduced diabetic ketoacidosis admissions and related costs over 24 months, Diabetes Care, 31, 1746-1747, 2008	Secondary publication
Ellis,D.A., Frey,M.A., Naar-King,S., Templin,T., Cunningham,P.B., Cakan,N., The effects of multisystemic therapy on diabetes stress among adolescents with chronically poorly controlled type 1 diabetes: findings from a randomized, controlled trial, Pediatrics, 116, e826-e832, 2005	Secondary publication
Ellis,D.A., Naar-King,S., Chen,X., Moltz,K., Cunningham,P.B., Idalski-Carcone,A., Multisystemic therapy compared to telephone support for youth with poorly controlled diabetes: findings from a randomized controlled trial, Annals of Behavioral Medicine, 44, 207-215, 2012	Secondary publication
Ellis,D.A., Naar-King,S., Frey,M., Templin,T., Rowland,M., Cakan,N., Multisystemic treatment of poorly controlled type 1 diabetes: effects on medical resource utilization, Journal of Pediatric Psychology, 30, 656-666, 2005	Secondary publication
Ellis,D.A., Naar-King,S., Templin,T., Frey,M.A., Cunningham,P.B., Improving health outcomes among youth with poorly controlled type I diabetes: the role of treatment fidelity in a randomized clinical trial of multisystemic therapy, Journal of Family Psychology, 21, 363-371, 2007	Secondary publication
Ellis,D.A., Templin,T., Naar-King,S., Frey,M.A., Cunningham,P.B., Podolski,C.L., Cakan,N., Multisystemic therapy for adolescents with poorly controlled type I diabetes: Stability of treatment effects in a randomized controlled trial, Journal of Consulting and Clinical Psychology, 75, 168-174, 2007	Secondary publication
Ellis,D.A., Yopp,J., Templin,T., Naar-King,S., Frey,M.A., Cunningham,P.B., Idalski,A., Niec,L.N., Family mediators and moderators of treatment outcomes among youths with poorly controlled type 1 diabetes: results from a randomized controlled trial, Journal of Pediatric Psychology, 32, 194-205, 2007	Secondary publication

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Study	Reason for exclusion
Franklin,V.L., Waller,A., Pagliari,C., Greene,S.A., A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes, Diabetic Medicine, 23, 1332-1338, 2006	PICO not met - support delivered by clinical staff not peers
Freeman,K.A., Duke,D.C., Harris,M.A., Behavioral health care for adolescents with poorly controlled diabetes via Skype: does working alliance remain intact?, Journal of Diabetes Science and Technology, 7, 727-735, 2013	Outcomes examined (working alliance inventory (WAI) subscale scores and the association between them and HbA1c) not of interest
Garcia-Perez,L., Perestelo-Perez,L., Serrano-Aguilar,P., Del,Mar Trujillo-Martin, Effectiveness of a psychoeducative intervention in a summer camp for children with type 1 diabetes mellitus, Diabetes Educator, 36, 310-317, 2010	PICO not met - intervention not relevant to this question
Gayes,L.A., Steele,R.G., A meta-analysis of motivational interviewing interventions for pediatric health behavior change, Journal of Consulting and Clinical Psychology, 82, 521-535, 2014	Meta-analysis - individual studies considered for guideline review
Greco,P., Pendley,J.S., McDonell,K., Reeves,G., A peer group intervention for adolescents with type 1 diabetes and their best friends, Journal of Pediatric Psychology, 26, 485-490, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a comparative study and therefore does not meet the study design inclusion criteria)
Gregory,J., Robling,M., Bennert,K., Channon,S., Cohen,D., Crowne,E., Hambly,H., Hawthorne,K., Hood,K., Longo,M., Lowes,L., McNamara,R., Pickles,T., Playle,R., Rollnick,S., Thomas-Jones,E., Development and evaluation by a cluster randomised trial of a psychosocial intervention in children and teenagers experiencing diabetes: the DEPICTED study, Health Technology Assessment (Winchester, England), 15, 1-202, 2011	Secondary publication
Gregory,J.W., Channon,S., Motivational interviewing to improve blood-glucose control in childhood diabetes, Paediatrics and Child Health, 19, 331-334, 2009	Commentary
Grey,M., Jaser,S.S., Whittemore,R., Jeon,S., Lindemann,E., Coping skills training for parents of children with type 1 diabetes: 12-month outcomes, Nursing Research, 60, 173-181, 2011	Pooled analysis of two separate RCT
Grey,M., Whittemore,R., Jaser,S., Ambrosino,J., Lindemann,E., Liberti,L., Northrup,V., Dziura,J., Effects of coping skills training in school-age children with type 1 diabetes, Research in Nursing and Health, 32, 405-418, 2009	PICO not met - outcome results not presented in a usable manner
Grey,M., Whittemore,R., Jeon,S., Murphy,K., Faulkner,M.S., Delamater,A., TeenCope Study Group., Internet psycho-education programs improve outcomes in youth with type 1 diabetes, Diabetes Care, 36, 2475-2482, 2013	Education rather than behavioural intervention programme
Grey,M., Whittemore,R., Liberti,L., Delamater,A., Murphy,K., Faulkner,M.S., A comparison of two internet programs for adolescents with type 1 diabetes: design and methods, Contemporary Clinical Trials, 33, 769-776, 2012	Protocol for a RCT
Grey,M., Boland,E.A., Davidson,M., Li,J., Tamborlane,W.V., Coping skills training for youth with diabetes mellitus has long-lasting effects on metabolic control and quality of life, Journal of Pediatrics, 137, 107-113, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population included participants up to the age of 20 years with no subgroups of younger participants reported)
Grey,M., Boland,E.A., Davidson,M., Yu,C., Sullivan-Bolyai,S., Tamborlane,W.V., Short-term effects of coping skills training as adjunct to intensive therapy in adolescents, Diabetes Care, 21, 902-908, 1998	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population includes participants up to the age of 20 years but does not report subgroups for younger participants, and length of follow-up does not meet the inclusion criteria)
Grey,M., Boland,E.A., Davidson,M., Yu,C., Tamborlane,W.V., Coping skills training for youths with diabetes on intensive therapy, Applied Nursing Research, 12, 3-12, 1999	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (participants aged <20 years and no subgroup analysis for ages relevant to guideline)
Gross,A.M., Heimann,L., Shapiro,R., Schulz,R.M., Children with diabetes. Social skills training and hemoglobin A1c levels, Behavior ModificationBehav.Modif., 7, 151-164, 1983	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (data are not extractable and therefore the study is excluded from the 2015 update)
Gross,AM, Magalnick,LJ, Richardson,P, Self management training with families of insulin dependent diabetic children: a controlled long term investigation, Child and Family Behavior Therapy, 7, 35-50, 1985	Included in 2004 guideline review â€“ does not meet inclusion criteria for 2015 update review (follow-up is not required duration)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Cradock,S., McEvilly,E.A., Behavioral interventions for adolescents with type 1 diabetes: how effective are they?. [68 refs], Diabetes Care, 23, 1416-1422, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (includes participants aged up to 21 years and does not report any subgroup analyses for younger participants)

Study	Reason for exclusion
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. [148 refs], Health Technology Assessment (Winchester, England), 5, 1-79, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (the broad inclusion criteria for this health technology assessment (HTA) report did not match the 2015 review update criteria, but the report was checked for relevance of individual studies)
Harris,MA, Greco,P, Wysocki,T, White,NH, Family therapy with adolescents with diabetes: a litmus test for clinically meaningful change, Families, Systems and Health, 24, 441-446, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no outcomes of interest)
Harris,MA, Mertlich,D, Piloting home-based behavioral family systems therapy for adolescents with poorly controlled diabetes, Children's Health Care, 32, 65-79, 2003	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)
Hernandez,C.A., Family focused teamwork prevented deterioration in diabetes control in children and adolescents, Evidence Based Nursing, 7, 10-10, 2004	Commentary
Hoff,A.L., Mullins,L.L., Gillaspy,S.R., Page,M.C., Van,PeltJ, Chaney,J.M., An intervention to decrease uncertainly and distress among parents of children newly diagnosed with diabetes: A pilot study, Families, Systems and Health, 23, 329-342, 2005	PICO not met - intervention not relevant to this question
Holmes,C.S., Chen,R., Mackey,E., Grey,M., Streisand,R., Randomized clinical trial of clinic-integrated, low-intensity treatment to prevent deterioration of disease care in adolescents with type 1 diabetes, Diabetes Care, 37, 1535-1543, 2014	Data in study cannot be extracted
Hood,K.K., Nansel,T.R., Commonalities in effective behavioral interventions for children and adolescents with type 1 diabetes: A review of reviews, Diabetes Spectrum, 20, 251-253, 2007	Review of reviews
Howe,C.J., Jawad,A.F., Tuttle,A.K., Moser,J.T., Preis,C., Buzby,M., Murphy,K.M., Education and telephone case management for children with type 1 diabetes: A randomized controlled trial, Journal of Pediatric Nursing, 20, 83-95, 2005	PICO not met - intervention not relevant to this question
Husted,G.R., Thorsteinsson,B., Esbensen,B.A., Hommel,E., Zoffmann,V., Improving glycaemic control and life skills in adolescents with type 1 diabetes: a randomised, controlled intervention study using the Guided Self-Determination-Young method in triads of adolescents, parents and health care providers integrated into routine paediatric outpatient clinics, BMC Pediatrics, 11, 55-, 2011	Protocol for a RCT
Insabella,G., Grey,M., Knafl,G., Tamborlane,W., The transition to young adulthood in youth with type 1 diabetes on intensive treatment, Pediatric Diabetes, 8, 228-234, 2007	PICO not met - age range of participants in original study was 12 to 20 years
Ireys,H.T., Chernoff,R., DeVet,K.A., Kim,Y., Maternal outcomes of a randomized controlled trial of a community-based support program for families of children with chronic illnesses, Archives of Pediatrics and Adolescent Medicine, 155, 771-777, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population not exclusively type 1 diabetes)
Jaser,S.S., Whittemore,R., Ambrosino,J.M., Lindemann,E., Grey,M., Mediators of depressive symptoms in children with type 1 diabetes and their mothers, Journal of Pediatric Psychology, 33, 509-519, 2008	Secondary publication
Kaplan,R.M., Chadwick,M.W., Schimmel,L.E., Social learning intervention to promote metabolic control in type I diabetes mellitus: pilot experiment results, Diabetes Care, 8, 152-155, 1985	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up did not meet the inclusion criteria)
Kawamura,T., Kawamura,K., Hirose,M., Hashimoto,T., Higashide,T., Kashihara,Y., Aono,S., Okajima,M., Oguru,M., Harai,H., Training of motivational interviewing to parents improved the glycemic control of the childhood and adolescent type 1 diabetes: A prospective randomized control trial, Pediatric Diabetes, 13, 26-, 2012	Conference abstract
Kharrazi,H., Improving healthy behaviors in type 1 diabetic patients by interactive frameworks, AMIA .., Annual Symposium Proceedings/AMIA Symposium. 2009, 322-326, 2009	PICO not met - no clinical outcomes reported
Kumar,V.S., Wentzell,K.J., Mikkelsen,T., Pentland,A., Laffel,L.M., The DAILY (Daily Automated Intensive Log for Youth) trial: a wireless, portable system to improve adherence and glycemic control in youth with diabetes, Diabetes Technology and Therapeutics, 6, 445-453, 2004	PICO not met - study included children and young people with either type 1 diabetes or type 2 diabetes
LÃ¸ding,R.N., Wold,J.E., Skavhaug,A., Graue,M., Evaluation of peer-group support and problem-solving training in the treatment of adolescents with type 1 diabetes, European Diabetes Nursing, 4, 28-33, 2007	Study is non-randomised
Lapp,J., White,N.H., Social networking and peer support (SNAPS) in adolescents with type 1 diabetes mellitus (T1D): A pilot study, Diabetes, 61, A195-, 2012	Conference abstract
Lehmkuhl,H.D., Storch,E.A., Cammarata,C., Meyer,K., Rahman,O., Silverstein,J., Malasanos,T., Geffken,G., Telehealth behavior therapy for the management of type 1 diabetes in adolescents, Journal of Diabetes Science and Technology, 4, 199-208, 2010	PICO not met: follow-up length insufficient

Update 2015

Study	Reason for exclusion
Marrero,DG, Myers,G, Golden,MP, West,D, Adjustment to misfortune: the use of a social support group for adolescent diabetes, Pediatric and Adolescent Endocrinology, 10, 213-218, 1982	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up did not meet the inclusion criteria for the 2015 update review)
Matam,P., Kumaraiah,V., Munichoodappa,C., Kumar,K.M., Aravind,S., Behavioural intervention in the management of compliance in young type-I diabetics, Journal of the Association of Physicians of India, 48, 967-971, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (participants aged <22 years with no subgroup analysis for ages relevant to the guideline)
McNamara,R., Robling,M., Hood,K., Bennert,K., Channon,S., Cohen,D., Crowne,E., Hambly,H., Hawthorne,K., Longo,M., Lowes,L., Playle,R., Rollnick,S., Gregory,J.W., Development and Evaluation of a Psychosocial Intervention for Children and Teenagers Experiencing Diabetes (DEPICTED): a protocol for a cluster randomised controlled trial of the effectiveness of a communication skills training programme for healthcare professionals working with young people with type 1 diabetes, BMC Health Services Research, 10, 36-, 2010	Secondary publication
Mendez,F.J., Belendez,M., Effects of a behavioral intervention on treatment adherence and stress management in adolescents with IDDM, Diabetes Care, 20, 1370-1375, 1997	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a comparative study)
Mulvaney,S.A., Rothman,R.L., Osborn,C.Y., Lybarger,C., Dietrich,M.S., Wallston,K.A., Self-management problem solving for adolescents with type 1 diabetes: intervention processes associated with an Internet program, Patient Education and Counseling, 85, 140-142, 2011	Secondary publication
Mulvaney,S.A., Rothman,R.L., Wallston,K.A., Lybarger,C., Dietrich,M.S., An internet-based program to improve self-management in adolescents with type 1 diabetes, Diabetes Care, 33, 602-604, 2010	PICO not met: insufficient follow-up period (12 weeks)
Murphy,H.R., Wadham,C., Hassler-Hurst,J., Rayman,G., Skinner,T.C., Families and Adolescents Communication and Teamwork Study (FACTS) Group., Randomized trial of a diabetes self-management education and family teamwork intervention in adolescents with Type 1 diabetes, Diabetic Medicine, 29, e249-e254, 2012	PICO not met - intervention not relevant to this question
Murphy,H.R., Wadham,C., Rayman,G., Skinner,T.C., Approaches to integrating paediatric diabetes care and structured education: experiences from the Families, Adolescents, and Children's Teamwork Study (FACTS), Diabetic Medicine, 24, 1261-1268, 2007	PICO not met - intervention not relevant to this question
Naar-King,S., Ellis,D.A., Idalski,A., Frey,M.A., Cunningham,P., Multisystemic therapy decreases parental overestimation of adolescent responsibility for Type 1 diabetes management in urban youth, Families, Systems and Health, 25, 178-189, 2007	Secondary publication
Nansel,T.R., Iannotti,R.J., Liu,A., Clinic-integrated behavioral intervention for families of youth with type 1 diabetes: randomized clinical trial, Pediatrics, 129, e866-e873, 2012	PICO not met - outcomes not reported in sufficient detail
Nansel,T.R., Iannotti,R.J., Simons-Morton,B.G., Plotnick,L.P., Clark,L.M., Zeitzoff,L., Long-term maintenance of treatment outcomes: diabetes personal trainer intervention for youth with type 1 diabetes, Diabetes Care, 32, 807-809, 2009	Secondary publication
Nardi,L., Zucchini,S., Petracci,E., Cavrini,G., Maltoni,G., Scipione,M., D'Alberton,F., A randomized controlled study on the effect of a group therapy for parents of youths with type 1 diabetes on quality of life, Pediatric Diabetes, 13, 156-, 2012	Conference abstract
Newton,K.T., Ashley,A., Pilot study of a web-based intervention for adolescents with type 1 diabetes, Journal of Telemedicine and Telecare, 19, 443-449, 2013	7-week intervention outcomes were assessed through an exit survey
Nunn,E., King,B., Smart,C., Anderson,D., A randomized controlled trial of telephone calls to young patients with poorly controlled type 1 diabetes, Pediatric Diabetes, 7, 254-279, 2006	PICO not met - intervention was support from a healthcare professional not peer support
Patel,A., Maissi,E., Chang,H.C., Rodrigues,I., Smith,M., Thomas,S., Chalder,T., Schmidt,U., Treasure,J., Ismail,K., Motivational enhancement therapy with and without cognitive behaviour therapy for Type 1 diabetes: economic evaluation from a randomized controlled trial, Diabetic medicine : a journal of the British Diabetic Association, 28, 470-479, 2011	PICO not met - study included adults
Paterson,B.L., Multisystemic therapy improved adherence to blood glucose testing in adolescents with type 1 diabetes, Evidence Based Nursing, 9, 14-14, 2006	Commentary
Pendley,J.S., Kasmen,L.J., Miller,D.L., Donze,J., Swenson,C., Reeves,G., Peer and family support in children and adolescents with type 1 diabetes, Journal of Pediatric Psychology, 27, 429-438, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (non-comparative study and therefore does not meet the study design inclusion criteria)
Powell,P.W., Hilliard,M.E., Anderson,B.J., Motivational interviewing to promote adherence behaviors in pediatric type 1 diabetes, Current Diabetes Reports, 14, 531-, 2014	This is a literature review

Study	Reason for exclusion
Ridge,K., Bartlett,J., Cheah,Y., Thomas,S., Lawrence-Smith,G., Winkley,K., Ismail,K., Do the effects of psychological treatments on improving glycemic control in type 1 diabetes persist over time? A long-term follow-up of a randomized controlled trial, Psychosomatic Medicine, 74, 319-323, 2012	Secondary publication
Ryden,O., Nevander,L., Johnsson,P., Hansson,K., Kronvall,P., Sjoblad,S., Westbom,L., Family therapy in poorly controlled juvenile IDDM: Effects on diabetic control, self-evaluation and behavioural symptoms, Acta Paediatrica, International Journal of Paediatrics, 83, 285-291, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up period not sufficient)
Sassmann,H., de,Hair M., Danne,T., Lange,K., Reducing stress and supporting positive relations in families of young children with type 1 diabetes: a randomized controlled study for evaluating the effects of the DELFIN parenting program, BMC Pediatrics, 12, 152-, 2012	Although families with children aged 2 to 10 years were selected for the study, the main target population of the intervention was parents; for outcomes related to children, only mean Hb1Ac at 3-month follow-up was reported
Satin,W., La Greca,A.M, Zigo,M.A, Skyler,J.S, Diabetes in adolescence: effects of multifamily group intervention and parent simulation of diabetes, Journal of Pediatric PsychologyJ.Pediatr.Psychol., 14, 259-275, 1989	Included in 2004 guideline review â€“ does not meet inclusion criteria for 2015 update review (follow-up does not meet required length)
Scaramuzza,A., Castellani,G., Lorini,R., Insulin abuse in an adolescent with insulin-dependent diabetes mellitus, European Journal of Pediatrics, 155, 526-, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (this is a letter)
Schachinger,H., Hegar,K., Hermannus,N., Straumann,M., Keller,U., Fehm-Wolfsdorf,G., Berger,W., Cox,D., Randomized controlled clinical trial of Blood Glucose Awareness Training (BGAT III) in Switzerland and Germany, Journal of Behavioral Medicine, 28, 587-594, 2005	Study involving adults
Schafer,L.C., Glasgow,R.E., McCaul,K.D., Increasing the adherence of diabetic adolescents, Journal of Behavioral Medicine, 5, 353-362, 1982	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (case series, not an RCT)
Serlachius,A., Frydenberg,E., Northam,E., Cameron,F., A randomised trial of a psychosocial program to improve glycaemic control and psychosocial wellbeing in adolescents with type 1 diabetes, Pediatric Diabetes, 12, 20-, 2011	Conference abstract
Skocic,Milena, Rudan,Vlasta, Brajkovic,Lovorka, Marcinko,Darko, Relationship among psychopathological dimensions, coping mechanisms, and glycemic control in a Croatian sample of adolescents with diabetes mellitus type 1, European Child & Adolescent Psychiatry, 19, 525-533, 2010	Wrong study design (cohort study not an RCT)
Suh,S., Jean,C., Koo,M., Lee,S.Y., Cho,M.J., Sim,K.H., Jin,S.M., Bae,J.C., Kim,J.H., A randomized controlled trial of an internet-based mentoring program for type 1 diabetes patients with inadequate glycemic control, Diabetes and Metabolism Journal, 38, 134-142, 2014	Adult population
Sullivan-Bolyai,S., Bova,C., Lee,M., Johnson,K., Development and pilot testing of a parent education intervention for type 1 diabetes: parent education through simulation-diabetes, Diabetes Educator, 38, 50-57, 2012	PICO not met - outcomes of interest not reported
Sullivan-Bolyai,S., Bova,C., Leung,K., Trudeau,A., Lee,M., Gruppuso,P., Social Support to Empower Parents (STEP): an intervention for parents of young children newly diagnosed with type 1 diabetes, Diabetes Educator, 36, 88-97, 2010	PICO not met - outcomes of interest not reported
Sullivan-Bolyai,S., Grey,M., Deatrick,J., Gruppuso,P., Giraitis,P., Tamborlane,W., Helping other mothers effectively work at raising young children with type 1 diabetes, Diabetes Educator, 30, 476-484, 2004	PICO not met - outcomes of interest not reported
Sullivan-Bolyai,Susan, Bova,Carol, Leung,Katherine, Trudeau,Allison, Lee,Mary, Gruppuso,Philip, Social Support to Empower Parents (STEP): An intervention for parents of young children newly diagnosed with type 1 diabetes, The Diabetes Educator, 36, 88-97, 2010	Intervention not of interest
Sundelin,J., Forsander,G., Mattsson,S.E, Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, Acta PaediatricaActa Paediatr., 85, 49-55, 1996	Included in 2004 guideline review does not meet inclusion criteria for 2015 update review (not intervention of interest)
Svoren,B.M., Butler,D., Levine,B.S., Anderson,B.J., Laffel,L.M., Reducing acute adverse outcomes in youths with type 1 diabetes: a randomized, controlled trial, Pediatrics, 112, 914-922, 2003	PICO not met - support given by a healthcare professional, not peers
Urban,A.D., Berry,D., Grey,M., Optimizing outcomes in adolescents with type 1 diabetes and their families, Journal of Clinical Outcomes Management, 11, 299-306, 2004	Clinical review, background reading
Viklund,G., Ortqvist,E., Wikblad,K., Assessment of an empowerment education programme. A randomized study in teenagers with diabetes, Diabetic medicine : a journal of the British Diabetic Association, 24, 550-556, 2007	PICO not met - intervention not of interest for this review
Weinger,K., Beverly,E.A., Lee,Y., Sitnokov,L., Ganda,O.P., Caballero,A.E., The effect of a structured behavioral intervention on poorly controlled diabetes: a randomized controlled trial, Archives of Internal Medicine, 171, 1990-1999, 2011	PICO not met - study included adults
Whittemore,R., Grey,M., Lindemann,E., Ambrosino,J., Jaser,S., Development of an Internet coping skills training program for teenagers with type 1 diabetes, CIN: Computers, Informatics, Nursing, 28, 103-111, 2010	Process evaluation

Update 2015

Study	Reason for exclusion
Whittemore,R., Jaser,S.S., Jeon,S., Liberti,L., Delamater,A., Murphy,K., Faulkner.M.S., Grey,M., An internet coping skills training program for youth with type 1 diabetes: six-month outcomes, Nursing Research, 61, 395-404, 2012	PICO not met - outcome results not presented in a usable manner
Wolanski,R., Sigman,T, Polychronakos,C., Assessment of blood glucose self-monitoring skills in a camp for diabetic children: the effects of individualized feedback counselling, Patient Education and CounselingPatient Educ.Couns., 29, 5-11, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up period insufficient)
Wysocki,T., Iannotti,R., Weissberg-Benchell,J., Laffel,L., Hood,K., Anderson,B., Chen,R., Family Management of Childhood Diabetes Steering Committee., Diabetes problem solving by youths with type 1 diabetes and their caregivers: measurement, validation, and longitudinal associations with glycemic control, Journal of Pediatric Psychology, 33, 875-884, 2008	PICO not met: outcome data not reported in sufficient detail
Wysocki,T., Harris,M.A., Buckloh,L.M., Mertlich,D., Lochrie,A.S., Taylor,A., Sadler,M., White,N.H. Randomized, controlled trial of Behavioral Family Systems Therapy for Diabetes: maintenance and generalization of effects on parent-adolescent communication , Behavior Therapy, Vol. 39, Issue 1, 33-46, 2008	Does not report outcomes of interest
Yopp,Justin M., - The impact of family functioning on treatment adherence and metabolic control for adolescents with poorly controlled type 1 diabetes, - Dissertation Abstracts International: Section B: The Sciences and Engineering, 66, 1744-, -32676	Dissertation abstract
Zoffmann,V., Lauritzen,T., Guided self-determination improves life skills with type 1 diabetes and A1C in randomized controlled trial, Patient Education and Counseling, 64, 78-86, 2006	PICO not met - study included adults

H.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Update 2015

Study	Reason for exclusion
Influence of intensive diabetes treatment on quality-of-life outcomes in the diabetes control and complications trial, Diabetes Care, 19, 195-203, 1996	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group, Journal of Pediatrics, 125, 177-188, 1994	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Weight gain associated with intensive therapy in the diabetes control and complications trial. The DCCT Research Group, Diabetes Care, 11, 567-573, 1988	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Effects of intensive diabetes therapy on neuropsychological function in adults in the Diabetes Control and Complications Trial, Annals of Internal Medicine, 124, 379-388, 1996	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Acharya,S.H., Philip,S., Viswanath,A.K., Boroujerdi,M., Waugh,N.R., Pearson,D.W.M., Glycaemic control and body mass index in late-adolescents and young adults with Type 1 diabetes mellitus: A population-based study, Diabetic Medicine, 25, 360-364, 2008	PICO (Patient Intervention Comparator Outcome) criteria not met - age range is 15 to 25 years, data for insulin regimen comparisons not reported separately for guideline age range
Al-Khawari,M., Al-Ruwayeh,A., Al-Doub,K., Allgrove,J., Adolescents on basal-bolus insulin can fast during Ramadan, Pediatric Diabetes, 11, 96-100, 2010	PICO criteria not met - participants are fasting during Ramadan with follow-up <4 months
Allen,C., LeCaire,T., Palta,M., Daniels,K., Meredith,M., D'Alessio,D.J., Wisconsin Diabetes,Registry Project, Risk factors for frequent and severe hypoglycemia in type 1 diabetes, Diabetes Care, 24, 1878-1881, 2001	PICO criteria not met - comparison is between 3 or more injections per day or continuous subcutaneous insulin infusion (CSII) and less than 3 injections per day
Anderson,D.G., Multiple daily injections in young patients using the ezy-BICC bolus insulin calculation card, compared to mixed insulin and CSII, Pediatric Diabetes, 10, 304-309, 2009	PICO criteria not met - age range is 1 to 20 years and data for relevant comparisons not reported separately for guideline age range
Azar,S.T., Birbari,A., Nocturnal blood pressure elevation in patients with type 1 diabetes receiving intensive insulin therapy compared with that in patients receiving conventional insulin therapy, Journal of Clinical Endocrinology and Metabolism, 83, 3190-3193, 1998	PICO criteria not met - comparison is between 2 and 3 or more injections per day

Study	Reason for exclusion
Azar,S.T., Zalloua,P.A., Zantout,M.S., Shahine,C.H., Salti,I., Leptin levels in patients with type 1 diabetes receiving intensive insulin therapy compared with those in patients receiving conventional insulin therapy, Journal of Endocrinological Investigation, 25, 724-726, 2002	PICO criteria not met - age range includes 18 years, guideline age range not reported separately
Bangstad,H.J., Danne,T., Deeb,L., Jarosz-Chobot,P., Urakami,T., Hanas,R., Insulin treatment in children and adolescents with diabetes, Pediatric Diabetes, 10, 82-99, 2009	Study criteria not met - consensus guideline
Baroni,M., Vialettes,B., Pozzilli,P., The glucose evaluation trial for remission (GETREM): A european effort to evaluate insulin-dependent diabetes mellitus in the first year after diagnosis, Diabetes and Metabolism, 23, 264-265, 1997	Study criteria not met - description of trial protocol only
Bayrakdar,A., Noureddine,S., Farhood,L., Nasrallah,M.P., Comparison of quality of life in a group of Lebanese type 1 diabetics on insulin pump and those on multiple daily injections, Journal Medical Libanais - Lebanese Medical Journal, 62, 22-26, 2014	The study does not show how many injections were given in the MDI group, wrong study design (cross-sectional study)
Beck,J.K., Lewis,T.V., Logan,K.J., Harrison,D.L., Gardner,A.W., Copeland,K.C., Intensive versus conventional insulin management initiated at diagnosis in children with diabetes: should payer source influence the choice of therapy?, Pediatric Diabetes, 10, 368-373, 2009	PICO criteria not met - cannot separate CSII and multiple daily injection results
Blair,J.C., Peak,M., Gregory,J.W., What is the best way to deliver subcutaneous insulin to infants, children, and young people with type 1 diabetes mellitus?, BMJ (Online), 343, -, 2011	PICO criteria not met - continuous subcutaneous insulin infusion versus multiple daily injections
Blasetti,A., Di,Giulio C., Tocco,A.M., Verrotti,A., Tumini,S., Chiarelli,F., Altobelli,E., Variables associated with severe hypoglycemia in children and adolescents with type 1 diabetes: a population-based study, Pediatric Diabetes, 12, 4-10, 2011	PICO criteria not met - all participants were using multiple daily injections
Bloomgarden,Z.T., Diabetes issues in women and children, Diabetes Care, 26, 2457-2463, 2003	Study criteria not met - narrative review
Bolli,G.B., Rationale for using combinations of short-acting insulin analogue and NPH insulin at mealtime in the treatment of type 1 diabetes mellitus. [18 refs], Journal of Pediatric Endocrinology, 12 Suppl 3, 737-744, 1999	Study criteria not met - narrative review
Bougneres,P.F., Landais,P., Mairesse,A.M., Jais,J.P., Jos,J., Peyraud,J., Wieliczko,M.C., Chavoix,P., Garandeau,P., Asensi,D., Improvement of diabetic control and acceptability of a three-injection insulin regimen in diabetic adolescents. A multicenter controlled study, Diabetes Care, 16, 94-102, 1993	PICO criteria not met - comparison is between 2 and 3 injections per day
Brinchmann-Hansen,O., Dahl-Jorgensen,K., Hanssen,K.F., Sandvik,L., Effects of intensified insulin treatment on various lesions of diabetic retinopathy, American Journal of Ophthalmology, , 644-653, 1985	PICO criteria not met - age range 18 to 45 years
Bulsara,M.K., Holman,C.D., Davis,E.A., Jones,T.W., The impact of a decade of changing treatment on rates of severe hypoglycemia in a population-based cohort of children with type 1 diabetes, Diabetes Care, 27, 2293-2298, 2004	PICO criteria not met - comparison is between 2 and 3 injections per day
Callaghan,Brian C., Little,Ann A., Feldman,Eva L., Hughes,AC Richard, Enhanced glucose control for preventing and treating diabetic neuropathy, Cochrane Database of Systematic Reviews, -, 2012	PICO criteria not met - interventions are a mixture of advice, insulin, and pancreas transplant; data for young people included but not reported separately; references checked
Cemeroglu,A.P., Kleis,L., Wood,A., Parkes,C., Wood,M.A., Davis,A.T., Comparison of the effect of insulin glulisine to insulin aspart on breakfast postprandial blood glucose levels in children with type 1 diabetes mellitus on multiple daily injections, Endocrine Practice, 19, 614-619, 2013	Case study, cross-over, not clear about frequency of MDI
Cengiz,E., Swan,K.L., Tamborlane,W.V., Sherr,J.L., Martin,M., Weinzimer,S.A., The alteration of aspart insulin pharmacodynamics when mixed with detemir insulin, Diabetes Care, 35, 690-692, 2012	PICO criteria not met - follow-up <4 months
Cengiz,E., Tamborlane,W.V., Martin-Fredericksen,M., Dziura,J., Weinzimer,S.A., Early pharmacokinetic and pharmacodynamic effects of mixing lispro with glargine insulin: results of glucose clamp studies in youth with type 1 diabetes, Diabetes Care, 33, 1009-1012, 2010	PICO criteria not met - follow-up <4 months
Centre for Reviews and Dissemination., Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes: a systematic review and meta-analysis (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2012	PICO criteria not met - age range is 18-50 years
Chapman,T.M., Noble,S., Goa,K.L., Insulin aspart: a review of its use in the management of type 1 and 2 diabetes mellitus. [100 refs][Erratum appears in Drugs. 2003;63(5):512.], Drugs, 62, 1945-1981, 2002	PICO criteria not met - comparison is between two multiple daily injection regimens
Chapman,T.M., Perry,C.M., Spotlight on insulin detemir in type 1 and 2 diabetes mellitus, Biodrugs, 19, 67-69, 2005	Study criteria not met - summary article; references checked
Chase,H.P., Rose,B., Hoops,S., Archer,P.G., Cribari,J.M., Techniques for improving glucose control in type I diabetes, Pediatrician, 12, 229-235, 1983	PICO criteria not met - number of injections per day not reported for all participants

Update 2015

Study	Reason for exclusion
Chase,H.P., Dixon,B., Pearson,J., Fiallo-Scharer,R., Walravens,P., Klingensmith,G., Rewers,M., Garg,S.K., Reduced hypoglycemic episodes and improved glycemic control in children with type 1 diabetes using insulin glargine and neutral protamine Hagedorn insulin, Journal of Pediatrics, 143, 737-740, 2003	PICO criteria not met - participants had a mixture of treatments before switching to basal-bolus regimen but these were not reported separately
Chase,H.P., Garg,S.K., Hoops,S.L., Harris,S., Wilcox,W., Use of the pen delivery system for intensive insulin therapy in college-age students with type I diabetes, Journal of Adolescent Health, 12, 373-376, 1991	PICO critera not met - age range includes 18 years, but data for guideline age range not reported separately
Clarke,W.L., The Diabetes Control and Complications Trial: new challenges for the primary physician, Virginia Medical Quarterly, 121, 185-188, 1994	PICO criteria not met - multiple daily injections defined as 3 injections per day
Craig,M.E., Jones,T.W., Silink,M., Ping,Y.J., Diabetes care, glycemic control, and complications in children with type 1 diabetes from Asia and the Western Pacific Region, Journal of Diabetes and its Complications, 21, 280-287, 2007	Incomplete data for comparisons of interest
Craig,M.E., Handelsman,P., Donaghue,K.C., Chan,A., Blades,B., Laina,R., Bradford,D., Middlehurst,A., Ambler,G., Verge,C.F., Crock,P., Moore,P., Silink,M., ACT,HbA, Predictors of glycaemic control and hypoglycaemia in children and adolescents with type 1 diabetes from NSW and the ACT, Medical Journal of Australia, 177, 235-238, 2002	Incomplete data for comparisons of interest
Da,SilvaJoseL, Cardoso-Demartini,A.D.A., Liberatore,JuniorR, Paulino,M.F.V.M., De,Lemos MariniS, Guerra-Junior,G., Rodrigues,A.G., Clinical and laboratory profile of pediatric and adolescent patients with type 1 diabetes, Jornal de Pediatria, 85, 490-494, 2009	PICO criteria not met - participants received 1, 2 or 3 injections per day; age range is 3-26 years
DAFNE Study Group, Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial, BMJ, 746-748, 2002	PICO criteria not met - age range is 18 years or older
Dahl-Jorgensen,K., Near-normoglycemia and late diabetic complications. The Oslo Study, Acta Endocrinologica, , 1-38, 1987	PICO criteria not met - age range 18 to 45 years
Dahl-Jorgensen,K., Bjoro,T., Kierulf,P., Sandvik,L., Bangstad,H.J., Hanssen,K.F., Long-term glycemic control and kidney function in insulin-dependent diabetes mellitus, Kidney International, , 920-923, 1992	PICO criteria not met - age range 18 to 45 years
Dahl-Jorgensen,K., Brinchmann-Hansen,O., Hanssen,K.F., Sandvik,L., Aagenaes,O., Rapid tightening of blood glucose control leads to transient deterioration of retinopathy in insulin dependent diabetes mellitus: the Oslo study, British Medical Journal Clinical Research Ed., , 811-815, 1985	PICO criteria not met - age range 18 to 45 years
Dahl-Jorgensen,K., Hanssen,K.F., Kierulf,P., Bjoro,T., Sandvik,L., Aagenaes,O., Reduction of urinary albumin excretion after 4 years of continuous subcutaneous insulin infusion in insulin-dependent diabetes mellitus. The Oslo Study, Acta Endocrinologica, , 19-25, 1988	PICO criteria not met - age range 18 to 45 years
Dahl-Jorgensen,K., Torjesen,P., Hanssen,K.F., Sandvik,L., Aagenaes,O., Increase in insulin antibodies during continuous subcutaneous insulin infusion and multiple-injection therapy in contrast to conventional treatment, Diabetes, , 1-5, 1987	PICO criteria not met - age range 18 to 42 years
Daneman,D., Wolfson,D.H., Becker,D.J., Drash,A.L., Factors affecting glycosylated hemoglobin values in children with insulin-dependent diabetes, Journal of Pediatrics, 99, 847-853, 1981	PICO criteria not met - comparison is between 1 and 2 injections per day
Danne,T., Mortensen,H.B., Hougaard,P., Lynggaard,H., Aanstoot,H.J., Chiarelli,F., Daneman,D., Dorchy,H., Garandeau,P., Greene,S.A., Hoey,H., Holl,R.W., Kaprio,E.A., Kocova,M., Martul,P., Matsuura,N., Robertson,K.J., Schoenle,E.J., Sovik,O., Swift,P.G., Tsou,R.M., Vanelli,M., Aman,J., Hvidore Study Group on Childhood Diabetes., Persistent differences among centers over 3 years in glycemic control and hypoglycemia in a study of 3,805 children and adolescents with type 1 diabetes from the Hvidore Study Group, Diabetes Care, 24, 1342-1347, 2001	PICO criteria not met - no data reported on absolute number of injections (change in number only)
de,BeaufortC, Hypoglycemia during intensified insulin therapy of young children, Journal of Pediatric Endocrinology and Metabolism, 11, 153-158, 1998	PICO criteria not met - comparison is between 1 to 2 and 3 or more injections per day
Deiss,D., Kordonouri,O., Hartmann,R., Hopfenmuller,W., Lupke,K., Danne,T., Treatment with insulin glargine reduces asymptomatic hypoglycemia detected by continuous subcutaneous glucose monitoring in children and adolescents with type 1 diabetes, Pediatric Diabetes, 8, 157-162, 2007	PICO criteria not met - follow up <4 months
Deja,G., Jarosz-Chobot,P., Polanska,J., The rate of improvement in metabolic control in children with diabetes mellitus type 1 on insulin glargine depends on age, Experimental and Clinical Endocrinology and Diabetes, 115, 662-668, 2007	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen

Update 2015

Study	Reason for exclusion
Distiller,L.A., Robertson,L.I., Moore,R., Bonnici,F., A bolus/basal multiple injection regimen in type I diabetes. A multicentre trial using a new 'fountain-pen' device for short-acting human insulin as well as long-acting human insulin, South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde. 71, 749-752, 1987	PICO criteria not met - follow up <4 months
Downie,E., Craig,M.E., Hing,S., Cusumano,J., Chan,A.K., Donaghue,K.C., Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glycemic control, Diabetes Care, 34, 2368-2373, 2011	PICO criteria not met - multiple daily injections defined as 3 injections per day and results combined with those for CSII
Dunn,C.J., Plosker,G.L., Keating,G.M., McKeage,K., Scott,L.J., Insulin glargine: an updated review of its use in the management of diabetes mellitus. [111 refs], Drugs, 63, 1743-1778, 2003	PICO criteria not met - comparison is between two multiple daily injection regimens
Ebeling,P., Jansson,P.A., Smith,U., Lalli,C., Bolli,G.B., Koivisto,V.A., Strategies toward improved control during insulin lispro therapy in IDDM. Importance of basal insulin, Diabetes Care, 20, 1287-1289, 1997	PICO criteria not met - age range 18 to 60 years
Egger,M, Smith,GD, Stettler,C, Diem,P, Risk of adverse effects of intensified treatment in insulin-dependent diabetes mellitus: a meta-analysis, Diabetic Medicine, , 919-928, 1997	PICO criteria not met - all included trials are in adults (outside guideline age range)
Fairchild,J.M., Ambler,G.R., Genoud-Lawton,C.H., Westman,E.A., Chan,A., Howard,N.J., Crock,P.A., Nunn,E.A., Silink,M., Insulin lispro versus regular insulin in children with type 1 diabetes on twice daily insulin, Pediatric Diabetes, 1, 135-141, 2000	PICO criteria not met - both treatment arms received 2 injections per day of mixed insulins
Fasching,P., Derfler,K., Maca,T., Kurzemann,S., Howorka,K., Schneider,B., Zirm,M., Waldhausl,W., Feasibility and efficacy of intensive insulin therapy in type 1 diabetes mellitus in primary care, Diabetic Medicine, 11, 836-842, 1994	PICO criteria not met - age range is 8 to 57 years
Fiallo-Scharer,R., Horner,B., McFann,K., Walravens,P., Chase,H.P., Mixing rapid-acting insulin analogues with insulin glargine in children with type 1 diabetes mellitus, Journal of Pediatrics, 148, 481-484, 2006	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Franklin,V.L., Khan,F., Kennedy,G., Belch,J.J., Greene,S.A., Intensive insulin therapy improves endothelial function and microvascular reactivity in young people with type 1 diabetes, Diabetologia, 51, 353-360, 2008	PICO criteria not met - cannot separate CSII and multiple daily injection results
Franklin,V.L., Waller,A., Pagliari,C., Greene,S.A., A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes, Diabetic Medicine, 23, 1332-1338, 2006	PICO criteria not met - cannot separate CSII and multiple daily injection results
Garg,S.K., Carmain,J.A., Braddy,K.C., Anderson,J.H., Vignati,L., Jennings,M.K., Chase,H.P., Pre-meal insulin analogue insulin lispro versus Humulin R insulin treatment in young subjects with type 1 diabetes, Diabetic Medicine, 13, 47-52, 1996	PICO criteria not met - age range includes 18 years, with the guideline age range not reported separately
Garnock-Jones,K.P., Plosker,G.L., Insulin glulisine: A review of its use in the management of diabetes mellitus, Drugs, 69, 1035-1057, 2009	PICO criteria not met - comparison is between two multiple daily injection regimens
Gerstl,E.M., Rabl,W., Rosenbauer,J., Grobe,H., Hofer,S.E., Krause,U., Holl,R.W., Metabolic control as reflectet by HbA1c in children, adolescents and young adults with type-1 diabetes mellitus: Combined longitudinal analysis including 27,035 patients from 207 centers in Germany and Austria during the last decade, European Journal of Pediatrics, 167, 447-453, 2008	PICO criteria not met - no data reported on insulin regimens
Gibb,D.M., Foot,A.B., May,B., Parish,H., Strang,S., Grant,D.B., Dunger,D.B., Human isophane or lente insulin? A double blind crossover trial in insulin dependent diabetes mellitus, Archives of Disease in Childhood, 65, 1334-1337, 1990	PICO criteria not met - both treatment arms received <4 injections per day
Golden,M.P., Russell,B.P., Ingersoll,G.M., Gray,D.L., Hummer,K.M., Management of diabetes mellitus in children younger than 5 years of age, American Journal of Diseases of Children, 139, 448-452, 1985	PICO criteria not met - all participants on two injections per day
Golenko,A., Noczynska,A., An evaluation of physical development and metabolic control in children with type 1 diabetes mellitus receiving treatment with various insulin regimens. Part 1, Diabetologia Doswiadczalna i Kliniczna, 8, 115-123, 2008	PICO criteria not met - number of injections not reported

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Study	Reason for exclusion
Gomes,M.B., Negrato,C.A., Cobas,R., Tannus,L.R.M., Goncalves,P.R., Da,SilvaP, Carneiro,J.R.I., Matheus,A.S.M., Dib,S.A., Azevedo,M.J., Nery,M., Rodacki,M., Zajdenverg,L., Montenegro,JuniorR, Sepulveda,J., Calliari,L.E., Jezini,D., Braga,N., Luescher,J.L., Berardo,R.S., rruda-Marques,M.C., Noronha,R.M., Manna,T.D., Salvodelli,R., Penha,F.G., Foss,M.C., Foss-Freitas,M.C., Pires,A.C., Robles,F.C., Guedes,M.D.F.S., Dualib,P., Silva,S.C., Sampaio,E., Rea,R., Faria,A.C.R., Tschiedel,B., Lavigne,S., Canani,L.H., Zucatti,A.T., Coral,M.H.C., Pereira,D.A., Araujo,L.A., Tolentino,M., Pedrosa,H.C., Prado,F.A., Rassi,N., Araujo,L.B., Fonseca,R.M.C., Guedes,A.D., Matos,O.S., Palma,C.C., Azulay,R., Forti,A.C., Facanha,C., Montenegro,A.P., Melo,N.H., Rezende,K.F., Ramos,A., Felicio,J.S., Santos,F.M., Determinants of intensive insulin therapeutic regimens in patients with type 1 diabetes: Data from a nationwide multicenter survey in Brazil, Diabetology and Metabolic Syndrome, 6, -, 2014	Interventions were 1 to 2 mixed versus monotherapy
Granado,F., Olmedilla,B., Botella,F., Simal,A., Blanco,I., Retinol and alpha-tocopherol in serum of type 1 diabetic patients with intensive insulin therapy: a long term follow-up study, Nutrition, 19, 128-132, 2003	PICO criteria not met - age range is 14 to 35 years
Greene,S.A., Robertson,L., Royle,P., Robertson,A., Waugh,N., Rae,P., Patterson,C., A longitudinal observational study of insulin therapy and glycaemic control in Scottish children with Type 1 diabetes: DIABAUD 3, Diabetic Medicine, 23, 1216-1221, 2006	PICO criteria not met - data reported for 2 and 3 injections per day only
Grey,M., Boland,E.A., Tamborlane,W.V., Use of lispro insulin and quality of life in adolescents on intensive therapy, Diabetes Educator, 25, 934-941, 1999	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Hanberger,L., Ludvigsson,J., Nordfeldt,S., Health-related quality of life in intensively treated young patients with type 1 diabetes, Pediatric Diabetes, 10, 374-381, 2009	Incomplete data for comparisons of interest
Hanssen,K.F., Dahl-Jorgensen,K., Brinchmann-Hansen,O., The influence of strict control on diabetic complications, Acta Endocrinologica, , 57-60, 1985	PICO criteria not met - age range is 18 to 42 years
Haugstvedt,A., Wentzel-Larsen,T., Rokne,B., Graue,M., Psychosocial family factors and glycemic control among children aged 1-15 years with type 1 diabetes: A population-based survey, BMC Pediatrics, 11 , 2011. Article Number, -, 2011	PICO criteria not met - all participants received multiple daily injections or CSII
Hayes,R.L., Garnett,S.P., Clarke,S.L., Harkin,N.M., Chan,A.K., Ambler,G.R., A flexible diet using an insulin to carbohydrate ratio for adolescents with type 1 diabetes - a pilot study, Clinical Nutrition, 31, 705-709, 2012	PICO criteria not met - all participants were using multiple daily injections
Heath,V., Diabetes: Basal insulin glargine decreases adolescent glycemic variability, Nature Reviews Endocrinology, 5, 183-, 2009	Summary of trial reported elsewhere (White 2009, weeded out)
Hecker,W., Grabert,M., Holl,R.W., Quality of paediatric IDDM care in germany: A multicentre analysis, Journal of Pediatric Endocrinology and Metabolism, 12, 31-38, 1999	PICO criteria not met - no comparative data reported
Hershey,T, Bhargava,N, Sadler,M, White,NH, Craft,S, Conventional versus intensive diabetes therapy in children with type 1 diabetes: effects on memory and motor speed, Diabetes Care, 1318-1324, 1999	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Holl,R.W., Swift,P.G., Mortensen,H.B., Lynggaard,H., Hougaard,P., Aanstoot,H.J., Chiarelli,F., Daneman,D., Danne,T., Dorchy,H., Garandeau,P., Greene,S., Hoey,H.M., Kaprio,E.A., Kocova,M., Martul,P., Matsuura,N., Robertson,K.J., Schoenle,E.J., Sovik,O., Tsou,R.M., Vanelli,M., Aman,J., Insulin injection regimens and metabolic control in an international survey of adolescents with type 1 diabetes over 3 years: results from the Hvidore study group, European Journal of Pediatrics, 162, 22-29, 2003	PICO criteria not met - cannot separate CSII and multiple daily injection results
Holman,RR, Mayon-White,V, Orde-Peckar,C, Steemson,J, Smith,B, McPerson,K, Prevention of deterioration of renal and sensory-nerve function by more intensive management of insulin-dependent diabetic patients. A two-year randomised prospective study, Lancet, 204-208, 1983	PICO criteria not met - age range is 21 to 60 years
HOSTOMSKA,L., KOPECKY,A., Insulin mixtures in the treatment of diabetes in children, Review of Czechoslovak Medicine, 2, 261-264, 1956	PICO criteria not met - no comparisons of interest reported
Houtzagers,C.M., van,der,V, Multiple daily insulin injections: a multicentre study on acceptability and efficacy, Netherlands Journal of Medicine, 33, 16-25, 1988	PICO criteria not met - age range is 14 to 70 years, and follow-up <4 months
Houtzagers,CM, Berntzen,PA, van der Stap,H, van Maarschalkerweerd,WW, Lanting,P, Boen-Tan,I, Efficacy and acceptance of two intensified conventional insulin therapy regimens: a long-term cross-over comparison, Diabetic Medicine, 416-421, 1989	PICO criteria not met - age range is 18 to 63 years
Houtzagers,CM, Visser,SP, Berntzen,PA, van der Stap,H, van Maarschalkerweerd,WW, Heine,RJ, Multiple daily insulin injections improve self-confidence, Diabetic Medicine, 512-519, 1989	PICO criteria not met - age range is 18 to 65 years

Study	Reason for exclusion
Institut fuer Qualitaet und Wirtschaftlichkeit im,Gesundheitswesen., Rapid-acting insulin analogues in the treatment of diabetes mellitus type 1 (Structured abstract), Health Technology Assessment Database, -, 2012	Non-English language
Jabbari,M., Bin-Abbas,B., Al-Fares,A., Basal-bolus insulin regimen using insulin detemir in type 1 diabetic Saudi children, Current Pediatric Research, 14, 108-110, 2010	PICO criteria not met - follow-up <4 months, <10 participants
Jackson,A., Ternand,C., Brunzell,C., Kleinschmidt,T., Dew,D., Milla,C., Moran,A., Insulin glargine improves hemoglobin A1c in children and adolescents with poorly controlled type 1 diabetes, Pediatric Diabetes, 4, 64-69, 2003	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Jarosz-Chobot,P., Guthrie,D.W., Otto-Buczkowska,E., Koehler,B., Self-care of young diabetics in practice, Medical Science Monitor, 6, 129-132, 2000	PICO criteria not met - details of insulin regimens not reported
Kaplan,W., Rodriguez,L.M., Smith,O.E., Haymond,M.W., Heptulla,R.A., Effects of mixing glargine and short-acting insulin analogs on glucose control, Diabetes Care, 27, 2739-2740, 2004	PICO criteria not met - follow-up <4 months
Karaguzel,G., Satilmis,A., Akcurin,S., Bircan,I., Comparison of breakfast and bedtime administration of insulin glargine in children and adolescents with Type 1 diabetes, Diabetes Research and Clinical Practice, 74, 15-20, 2006	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Katz,M.L., Volkening,L.K., Anderson,B.J., Laffel,L.M., Contemporary rates of severe hypoglycaemia in youth with Type 1 diabetes: variability by insulin regimen, Diabetic Medicine, 29, 926-932, 2012	PICO criteria not met - number of injections not stated and regimens unclear
Khadilkar,V.V., Khadilkar,A.V., Concomitant use of insulin glargine and NPH in type I diabetes, Indian Pediatrics, 42, 796-800, 2005	PICO criteria not met - comparison is between two regimens of 2 injections per day
Kimura,S., Nose,O., Tajiri,H., Miki,K., Yabuuchi,H., Shichiri,M., Harada,T., Efficacy of a multiple insulin injection regimen in teenagers with insulin-dependent diabetes. Carbohydrate and lipid oxidation measured by continuous indirect calorimetry, Diabetes Research and Clinical Practice, 4, 77-79, 1987	Study criteria not met - <10 participants
Knerr,I., Hofer,S.E., Holterhus,P.M., Nake,A., Rosenbauer,J., Weitzel,D., Wolf,J., Holl,R.W., Prevailing therapeutic regimes and predictive factors for prandial insulin substitution in 26 687 children and adolescents with Type 1 diabetes in Germany and Austria, Diabetic Medicine, 24, 1478-1481, 2007	PICO criteria not met - age range includes >18 years, guideline age range not reported separately
Laron,Z., Childhood diabetes towards the 21st century, Journal of Pediatric Endocrinology and Metabolism, 11, 387-402, 1998	Study criteria not met - narrative review
Lawson,M.L., Gerstein,H.C., Tsui,E., Zinman,B., Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes. A systematic review and meta-analysis, Diabetes Care, 22 Suppl 2, B35-B39, 1999	PICO criteria not met - all included trials were in adults
Leelarathna,L., Guzder,R., Muralidhara,K., Evans,M.L., Diabetes: glycaemic control in type 1, Clinical Evidence, 2011, 2011., -, 2011	PICO criteria not met - multiple daily injections versus CSII
Limbert,C., Schwingshandl,J., Haas,J., Roth,R., Borkenstein,M., Severe hypoglycemia in children and adolescents with IDDM: frequency and associated factors, Journal of Diabetes and its Complications, 7, 216-220, 1993	PICO criteria not met - age range is 4 to 25 years
Linn,T., Ortac,K., Laube,H., Federlin,K., Intensive therapy in adult insulin-dependent diabetes mellitus is associated with improved insulin sensitivity and reserve: a randomized, controlled, prospective study over 5 years in newly diagnosed patients, Metabolism: Clinical and Experimental, 45, 1508-1513, 1996	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Maiorino,M.I., Bellastella,G., Petrizzo,M., Improta,M.R., Brancario,C., Castaldo,F., Olita,L., Giugliano,D., Treatment satisfaction and glycemic control in young Type 1 diabetic patients in transition from pediatric health care: CSII versus MDI, Endocrine, 46, 256-262, 2014	Age group 18 to 25 years
Martin,D., Licha-Muntz,G., Grasset,E., Greneche,M.O., Nouet,D., Francois,L., Legrand,C., Polak,M., ugendre-Ferrante,B., Tubiana-Rufi,N., Robert,J.J., Efficacy of Humalog injections before an afternoon meal and their acceptance by children and adolescents with type 1 diabetes, Diabetic Medicine, 19, 1026-1031, 2002	PICO criteria not met - boths arms had fewer than 4 injections per day
McCaughey,E.S., Betts,P.R., Rowe,D.J., Improved diabetic control in adolescents using the Penject syringe for multiple insulin injections, Diabetic Medicine, 3, 234-236, 1986	PICO criteria not met - length of follow-up <4 months
McKeage,K., Goa,K.L., Insulin glargine: a review of its therapeutic use as a long-acting agent for the management of type 1 and 2 diabetes mellitus. [70 refs], Drugs, 61, 1599-1624, 2001	PICO criteria not met - comparison is between two multiple daily injection regimens
Menon,P.S.N., Virmani,A., Rationale of insulin therapy in insulin-dependent diabetes mellitus in children, Indian Pediatrics, 27, 1201-1208, 1990	Study criteria not met - narrative review

Study	Reason for exclusion
Microalbuminuria Collaborative Study Goup, Intensive therapy and progression to clinical albuminuria in patients with insulindependent diabetes mellitus and microalbuminuria, BMJ, 973-977, 1995	PICO criteria not met - age range 17 to 59 years
Mohn,A., Strang,S., Wernicke-Panten,K., Lang,A.M., Edge,J.A., Dunger,D.B., Nocturnal glucose control and free insulin levels in children with type 1 diabetes by use of the long-acting insulin HOE 901 as part of a three-injection regimen, Diabetes Care, 23, 557-559, 2000	PICO criteria not met - both treatment arms include fewer than than 4 injections per day
Mortensen,H.B., Outcome of quality management in pediatric diabetes care, Hormone Research, 50, 57-61, 1998	Incomplete data for comparisons of interest
Mortensen,H.B., Hougaard,P., Comparison of metabolic control in a cross-sectional study of 2,873 children and adolescents with IDDM from 18 countries. The Hvidore Study Group on Childhood Diabetes.[Erratum appears in Diabetes Care 1997 Jul;20(7):1216], Diabetes Care, 20, 714-720, 1997	Incomplete data for comparisons of interest
Mortensen,H.B., Robertson,K.J., Aanstoot,H.J., Danne,T., Holl,R.W., Hougaard,P., Atchison,J.A., Chiarelli,F., Daneman,D., Dinesen,B., Dorchy,H., Garandeau,P., Greene,S., Hoey,H., Kaprio,E.A., Kocova,M., Martul,P., Matsuura,N., Schoenle,E.J., Sovik,O., Swift,P.G., Tsou,R.M., Vanelli,M., Aman,J., Insulin management and metabolic control of type 1 diabetes mellitus in childhood and adolescence in 18 countries. Hvidore Study Group on Childhood Diabetes, Diabetic Medicine, 15, 752-759, 1998	PICO criteria not met - no relevant comparisons reported
Mortensen,H.B., Villumsen,J., Volund,A., Petersen,K.E., Nerup,J., Relationship between insulin injection regimen and metabolic control in young Danish type 1 diabetic patients. The Danish Study Group of Diabetes in Childhood, Diabetic Medicine, 9, 834-839, 1992	PICO criteria not met - multiple daily injections defined as 3 injections per day
Muhlhauser,I., Bruckner,I., Berger,M., Cheta,D., Jorgens,V., Ionescu-Tirgoviste,C., Scholz,V., Mincu,I., Evaluation of an intensified insulin treatment and teaching programme as routine management of type 1 (insulin-dependent) diabetes. The Bucharest-Dusseldorf Study, Diabetologia, 30, 681-690, 1987	PICO criteria not met - comparison is between 2 and >2 injections per day
Nathan,D.M., McKitrick,C., Larkin,M., Schaffran,R., Singer,D.E., Glycemic control in diabetes mellitus: Have changes in therapy made a difference?, American Journal of Medicine, 100, 157-163, 1996	PICO criteria not met - age range includes over 18 years, data for relevant comparisons not reported separately for guideline age range
Neu,A., Beyer,P., Burger-Busing,J., Danne,T., Etspuler,J., Heidtmann,B., Holl,R.W., Karges,B., Kiess,W., Knerr,I., Kordonouri,O., Lange,K., Lepler,R., Marg,W., Nake,A., Petersen,M., Podeswik,A., Stachow,R., Von,SengbuschS, Wagner,V., Ziegler,R., Holterhus,P.M., Diagnosis, therapy and control of diabetes mellitus in children and adolescents, Experimental and Clinical Endocrinology and Diabetes, 122, 425-434, 2014	This is a review
Nguyen,T.M., Renukuntla,V.S., Heptulla,R.A., Mixing insulin aspart with detemir does not affect glucose excursion in children with type 1 diabetes, Diabetes Care, 33, 1750-1752, 2010	PICO criteria not met - follow-up <4 months
Nordfeldt,S., Ludvigsson,J., Severe hypoglycemia in children with IDDM. A prospective population study, 1992-1994, Diabetes Care, 20, 497-503, 1997	PICO criteria not met - no comparison of insulin regimens
Ollenschlager,G, Hummerich,W, Steffen,M, Reincke,M, Allolio,B, Winelmann,W, Management and efficacy of intensified insulin therapy - starting in outpatients, Klinische Wochenschrift, 60-65, 1989	PICO criteria not met - mean age of participants outside guideline age range
Olsen,B.S., Johannesen,J., Sjolie,A.K., Borch-Johnsen,K., Hougaard,P., Thorsteinsson,B., Pramming,S., Marinelli,K., Mortensen,H.B., Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus, Diabetic Medicine, 16, 79-85, 1999	Incomplete data for comparisons of interest
Olsen,B.S., Sjolie,A.K., Hougaard,P., Johannesen,J., Borch-Johnsen,K., Marinelli,K., Thorsteinsson,B., Pramming,S., Mortensen,H.B., A 6-year nationwide cohort study of glycaemic control in young people with Type 1 diabetes: Risk markers for the development of retinopathy, nephropathy and neuropathy, Journal of Diabetes and its Complications, 14, 295-300, 2000	PICO criteria not met - no information on insulin regimens reported
Pais,V., Burkot,I., Buccino,J., Daneman,D., Is there a relationship between type of insulin regimen and dietary intake in adolescents with type 1 diabetes?, Canadian Journal of Diabetes, 34, 334-339, 2010	PICO criteria not met - no relevant outcomes reported
Palta,M., Shen,G., Allen,C., Klein,R., D'Alessio,D., Longitudinal patterns of glycemic control and diabetes care from diagnosis in a population-based cohort with type 1 diabetes, American Journal of Epidemiology, 144, 954-961, 1996	PICO criteria not met - no relevant comparisons reported
Paus,P.N., Jervell,J., Berg,T.J., Frosta,T., Larsen,S., [NovoPen. An aid in multi-injection insulin therapy], Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke, 106, 1943-1946, 1986	Non-English language
Pieber,T.R., Treichel,H.C., Hompesch,B., Philotheou,A., Mordhorst,L., Gall,M.A., Robertson,L.I., Comparison of insulin detemir and insulin glargine in subjects with Type 1 diabetes using intensive insulin therapy, Diabetic Medicine, 24, 635-642, 2007	PICO criteria not met - age range is 18 years and older

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Study	Reason for exclusion
Rabbone,I., Scaramuzza,A.E., Ignaccolo,M.G., Tinti,D., Sicignano,S., Redaelli,F., De,Angelis L., Bosetti,A., Zuccotti,G.V., Cerutti,F., Carbohydrate counting with an automated bolus calculator helps to improve glycaemic control in children with type 1 diabetes using multiple daily injection therapy: an 18-month observational study, Diabetes Research and Clinical Practice, 103, 388-394, 2014	This study is an observational study
Reichard,P, Berglund,A, Britz,A, Levander,S, Rosenqvist,U, Hypoglycaemic episodes during intensified insulin treatment: increased frequency but no effect on cognitive function, Journal of Internal Medicine, 9-16, 1991	PICO criteria not met - mean age of participants is outside guideline age range
Reichard,P, Berglund,B, Britz,A, Cars,I, Nilsson,BY, Rosenqvist,U, Intensified conventional insulin treatment retards the microvascular complications of insulin-dependent diabetes mellitus (IDDM): the Stockholm Diabetes Intervention Study (SDIS) after 5 years, Journal of Internal Medicine, 101-108, 1991	PICO criteria not met - mean age of participants is outside guideline age range
Rewers,M., Pihoker,C., Donaghue,K., Hanas,R., Swift,P., Klingensmith,G.J., Assessment and monitoring of glycemic control in children and adolescents with diabetes, Pediatric Diabetes, 10, 71-81, 2009	Study criteria not met - consensus guideline
Reynolds,N.A., Wagstaff,A.J., Insulin aspart: a review of its use in the management of type 1 or 2 diabetes mellitus. [63 refs], Drugs, 64, 1957-1974, 2004	PICO criteria not met - comparison is between two multiple daily injection regimens
Rogers,D.G., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, Clinical Pediatrics, 33, 378-, 1994	Study criteria not met - commentary article
Rosenbauer,J., Dost,A., Karges,B., Hungele,A., Stahl,A., Bachle,C., Gerstl,E.M., Kastendieck,C., Hofer,S.E., Holl,R.W., DPV Initiative and the German BMBF Competence Network Diabetes Mellitus., Improved metabolic control in children and adolescents with type 1 diabetes: a trend analysis using prospective multicenter data from Germany and Austria, Diabetes Care, 35, 80-86, 2012	PICO criteria not met - age of participants is <20 years, data for comparisons of interest not reported separately for guideline age range
Rosengren,A., Adlerberth,A., Bresater,L.E., Ehnberg,S., Welin,L., Multiple insulin injection therapy using an insulin pen - who benefits? A clinical 3-year follow-up study of 100 type 1 and 51 type 2 diabetic patients, Diabetes Research and Clinical Practice, 20, 69-74, 1993	PICO critera not met - age range is 17 to 72 years
Rosilio,M., Cotton,J.B., Wieliczko,M.C., Gendrault,B., Carel,J.C., Couvaras,O., Ser,N., Gillet,P., Soskin,S., Garandeau,P., Stuckens,C., Luyer,B.L.E., Jos,J., Bony-Trifunovic,H., Bertrand,A.M., Letlrcq,F., Lafuma,A., Bougneres,P.F., Factors associated with glycemic control: A cross-sectional nationwide study in 2,579 french children with type 1 diabetes, Diabetes Care, , 1146-1153, 1998	PICO criteria not met - comparison is between 1 to 2 and >3 injections per day
Rosilio,M., Cotton,J.B., Wieliczko,M.C., Gendrault,B., Carel,J.C., Couvaras,O., Ser,N., Gillet,P., Soskin,S., Garandeau,P., Stuckens,C., Le,Luyer B., Jos,J., Bony-Trifunovic,H., Bertrand,A.M., Leturcq,F., Lafuma,A., French Pediatric Diabetes Group, Bougneres,P.F., Factors associated with glycemic control. A cross-sectional nationwide study in 2,579 French children with type 1 diabetes. The French Pediatric Diabetes Group, Diabetes Care, 21, 1146-1153, 1998	PICO criteria not met - data reported for 2 versus 3 injections per day only
Rudolf,M.C., Sherwin,R.S., Markowitz,R., Bates,S.E., Genel,M., Hochstadt,J., Tamborlane,W.V., Effect of intensive insulin treatment on linear growth in the young diabetic patient, Journal of Pediatrics, 101, 333-339, 1982	Study criteria not met - <10 participants
Salardi,S., Cacciari,E., Zucchini,S., Donati,S., Steri,L., Gualandi,S., Mazzanti,L., Calliva,R., Modifications of metabolic control in type 1 diabetic children and adolescents: experience over the last 20 years, Journal of Pediatric Endocrinology, 10, 569-578, 1997	PICO criteria not met - comparison is between 3 and fewer than 3 injections per day
Schiffrin,A., Treatment of insulin-dependent diabetes with multiple subcutaneous insulin injections. [64 refs], Medical Clinics of North America, 66, 1251-1267, 1982	Study criteria not met - narrative review
Schiffrin,A.D., Desrosiers,M., Aleyassine,H., Belmonte,M.M., Intensified insulin therapy in the type I diabetic adolescent: a controlled trial, Diabetes Care, 7, 107-113, 1984	PICO criteria not met - multiple daily injections versus CSII
Schober,E., Schoenle,E., Van,Dyk J., Wernicke-Panten,K., Pediatric Study Group of Insulin Glargine, Comparative trial between insulin glargine and NPH insulin in children and adolescents with type 1 diabetes, Diabetes Care, 24, 2005-2006, 2001	PICO criteria not met - comparison is between two multiple daily injection regimens
Schober,E., Schoenle,E., Van,Dyk J., Wernicke-Panten,K., Pediatric Study Group of Insulin Glargine., Comparative trial between insulin glargine and NPH insulin in children and adolescents with type 1 diabetes mellitus, Journal of Pediatric Endocrinology, 15, 369-376, 2002	PICO criteria not met - comparison is between two multiple daily injection regimens
Service,F.J., Daube,J.R., O'Brien,P.C., Zimmerman,B.R., Swanson,C.J., Brennan,M.D., Dyck,P.J., Effect of blood glucose control on peripheral nerve function in diabetic patients, Mayo Clinic Proceedings, 58, 283-289, 1983	PICO criteria not met - median age is 31 years

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Study	Reason for exclusion
Shah,S.C., Malone,J.I., Simpson,N.E., A randomized trial of intensive insulin therapy in newly diagnosed insulin-dependent diabetes mellitus, New England Journal of Medicine, 320, 550-554, 1989	PICO criteria not met - comparison is between 2 injections per day and continuous subcutaneous insulin infusion
Shalitin,S., Phillip,M., Which factors predict glycemic control in children diagnosed with type 1 diabetes before 6.5 years of age?, Acta Diabetologica, 49, 355-362, 2012	PICO criteria not met - comparison is between multiple daily injections and CSII
Shamoon,H., Duffy,H., Fleischer,N., Engel,S., Saenger,P., Strelzyn,M., Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H., Fleischman,J., Pompi,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E., Thomashunis,A., Gonzalez,J., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, New England Journal of Medicine, 329, 977-986, 1993	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Shukla,V.K., Otten,N., Insulin lispro: a critical evaluation (Structured abstract), Health Technology Assessment Database, -, 2012	Study criteria not met - abstract only
Simpson,D., McCormack,P.L., Keating,G.M., Lyseng-Williamson,K.A., Insulin lispro: A review of its use in the management of diabetes mellitus, Drugs, 67, 407-434, 2007	PICO criteria not met - comparison is between two multiple daily injection regimens
Siu,A., Poon,C.Y., Pharmacologic management in pediatric type 1 diabetes mellitus, U.S, 33, -, 2008	Study criteria not met - narrative review
Small,M, MacRury,S, Boal,A, Paterson,KR, MacCuish,AC, Comparison of conventional twice daily subcutaneous insulin administration and a multiple injection regimen (using the NovoPen) in insulin-dependent diabetes mellitus, Diabetes Research, 85-89, 1988	PICO criteria not met - mean age of participants outside guideline age range
Smith,C.P., Dunger,D.B., Mitten,S., Hewitt,J., Spowart,K., Grant,D.B., Savage,M.O., A comparison of morning and bed-time ultralente administration when using multiple injections in adolescence, Diabetic Medicine, 5, 352-355, 1988	PICO criteria not met - follow-up <4 months
Soliman,A.T., Omar,M., Rizk,M.M., El,Awwa A., AlGhobashy,F.M., Glycaemic control with modified intensive insulin injections (MII) using insulin pens and premixed insulin in children with type-1 diabetes: a randomized controlled trial, Journal of Tropical Pediatrics, 52, 276-281, 2006	PICO criteria not met - both treatment arms received fewer than 4 injections per day
Srinivasan,B., Davies,M., Lawrence,I., Diabetes: glycaemic control in type 1, Clinical Evidence, 2008, 2008., -, 2008	PICO criteria not met - multiple daily injections versus CSII
Sundelin,J., Forsander,G., Mattson,S.E., Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, Acta Paediatrica, 85, 49-55, 1996	PICO criteria not met - educational intervention
Svensson,J., Johannesen,J., Mortensen,H.B., Nordly,S., Improved metabolic outcome in a Danish diabetic paediatric population aged 0-18 years: Results from a nationwide continuous Registration, Pediatric Diabetes, 10, 461-467, 2009	PICO criteria not met - no direct comparisons of interventions of interest
Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C., Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes, Journal of Pediatrics, 150, 279-285, 2007	PICO criteria not met - multiple daily injections defined as 3 or more injections per day
Swift,P.G., Diabetes in the young: from Leicester to Siena (via Oslo, Bethesda and Hvidore), Acta Bio-Medica de l Ateneo Parmense, 76 Suppl 3, 7-13, 2005	Study criteria not met - narrative review
Swift,P.G., Kennedy,J.D., Gerlis,L.S., Change to U-100 insulin does not appear to affect insulin absorption, British Medical Journal Clinical Research Ed., 286, 1015-, 1983	PICO criteria not met - follow-up <4 months
Tan,S.H., Lee,B.W., The use of twice-daily insulin regimes in insulin-dependent diabetic children, Journal of the Singapore Paediatric Society, 25, 70-74, 1983	PICO criteria not met - comparison is between 1 and 2 injections per day
The Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus, JAMA, 2563-2569, 2002	PICO criteria not met - comparison is between 3 or more injections per day and 1 to 2 injections per day
Thompson,R.J., Agostini,K., Potts,L., Luscombe,J., Christie,D., Viner,R., White,B., Hindmarsh,P.C., Deprivation and ethnicity impact on diabetes control and use of treatment regimen, Diabetic Medicine, 30, 491-494, 2013	The study only reported that the highest HbA1c was the highest in the twice-daily group and the lowest in the insulin therapy group in text; no comparison between MDI and mixed insulin injection was made.
Thomsett,M., Shield,G., Batch,J., Cotterill,A., How well are we doing? Metabolic control in patients with diabetes, Journal of Paediatrics and Child Health, 35, 479-482, 1999	PICO criteria not met - comparison is between 1 to 2 and >2 injections per day
Tonella,P., Fluck,C.E., Mullis,P.E., Metabolic control of type 1 diabetic patients followed at the University Children's Hospital in Berne: have we reached the goal?, Swiss Medical Weekly, 140, w13057-, 2010	Incomplete data for comparisons of interest

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Study	Reason for exclusion
Tubiana-Rufi,N., Levy-Marchal,C., Mugnier,E., Czernichow,P., Long term feasibility of multiple daily injections with insulin pens in children and adolescents with diabetes, European Journal of Pediatrics, 149, 80-83, 1989	PICO criteria not met - age range is 5 to 19.5 years, guideline age range not reported separately
Tupola,S., Rajantie,J., Maenpaa,J., Severe hypoglycaemia in children and adolescents during multiple-dose insulin therapy, Diabetic Medicine, 15, 695-699, 1998	PICO criteria not met - age range is 2 to 21 years, guideline age range not reported separately
Urakami,T., Kuwabara,R., Habu,M., Okuno,M., Suzuki,J., Takahashi,S., Basal insulin requirement of youth with type 1 diabetes differs according to age, Journal of Diabetes Investigation, 5, 442-444, 2014	No information on outcomes of interest
Urakami,T., Suzuki,J., Yoshida,A., Saito,H., Ishige,M., Takahashi,S., Mugishima,H., Association between sex, age, insulin regimens and glycemic control in children and adolescents with type 1 diabetes, Clinical Pediatric Endocrinology, 19, 1-6, 2010	PICO criteria not met - insulin regimen data not reported separately for guideline age range
Viberti,G.C., Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria, British Medical Journal, 311, 973-977, 1995	PICO criteria not met - age range 17 to 59 years
Vicens-Calvet,E., Gussinye,M., Albisu,M.A., Potau,N., Ibanez,L., Insulin treatment in adolescence, Journal of Endocrinological Investigation, 12, 109-112, 1989	Study criteria not met <10 participants in multiple daily injections arm
Wagner,V.M., Muller-Godeffroy,E., von,Sengbusch S., Hager,S., Thyen,U., Age, metabolic control and type of insulin regime influences health-related quality of life in children and adolescents with type 1 diabetes mellitus, European Journal of Pediatrics, 164, 491-496, 2005	PICO criteria not met - multiple daily injections defined as >3 injections per day
Wagner,V.M., Grabert,M., Holl,R.W., Severe hypoglycaemia, metabolic control and diabetes management in children with type 1 diabetes in the decade after the Diabetes Control and Complications Trial -- a large-scale multicentre study, European Journal of Pediatrics, 164, 73-79, 2005	PICO criteria not met - cannot separate CSII data from multiple daily injections
Wang,PH, Lau,J, Chalmers,TC, Meta-analysis of effects of intensive blood-glucose control on late complications of type 1 diabetes, Lancet, 1306-1309, 1993	Study criteria not met - brief report of systematic review. References checked.
Wheeler,K.A., Ahmed,M.L., Edge,J.A., Dunger,D.B., Comparison of cartridge insulin Penmix 50:50/Isophane with soluble/Isophane in type I diabetic adolescents using a multiple injection regimen, Diabetes Research, 22, 59-65, 1993	PICO criteria not met - comparison is between two multiple daily injection regimens
White,N.H., Intensive diabetes therapy is effective in children, American Family Physician, 50, 407-, 1994	PICO criteria not met - comparison is between 1 to 2 and 2 to 4 injections per day
White,N.H., Waltman,S.R., Krupin,T., Santiago,J.V., Reversal of neuropathic and gastrointestinal complications related to diabetes mellitus in adolescents with improved metabolic control, Journal of Pediatrics, 99, 41-45, 1981	Study criteria not met <10 participants
Wierusz-Wysocka,B., Wysocki,H., Byks,H., Zozulinska,D., Wykretowicz,A., Kazmierczak,M., Metabolic control quality and free radical activity in diabetic patients, Diabetes Research and Clinical Practice, 27, 193-197, 1995	PICO criteria not met - age range 17 to 51 years and follow-up <4 months
Williams,R.M., Dunger,D.B., Insulin treatment in children and adolescents. [50 refs], Acta Paediatrica, 93, 440-446, 2004	Study criteria not met - narrative review
Wilson,D.P., Fesmire,J.D., Endres,R.K., Blackett,P.R., Increased levels of HDL-cholesterol and apolipoprotein A-I after intensified insulin therapy for diabetes, Southern Medical Journal, 78, 636-638, 1985	PICO criteria not met - age range is 9 to 21 years, guideline age range not reported separately
Wintergerst,K.A., Hinkle,K.M., Barnes,C.N., Omoruyi,A.O., Foster,M.B., The impact of health insurance coverage on pediatric diabetes management, Diabetes Research and Clinical Practice, 90, 40-44, 2010	PICO criteria not met - age range includes 18 years, guideline age range not reported separately
Wolfsdorf,J.I., How effective is biphasic insulin aspart in the treatment of adolescents with type 1 diabetes?, Nature Clinical Practice Endocrinology and Metabolism, 2, 486-487, 2006	Summary of trial reported elsewhere (Mortensen 2006, weeded out)
Wysocki,T., Diabetes self-management profile for flexible insulin regimens: Cross-sectional and longitudinal analysis of psychometric properties in a pediatric sample, Diabetes Care, 28, 2034-2035, 2005	PICO criteria not met - comparison is continuous glucose monitoring versus usual monitoring
Wysocki,T., Harris,M.A., Buckloh,L.M., Wilkinson,K., Sadler,M., Mauras,N., White,N.H., Self-care autonomy and outcomes of intensive therapy or usual care in youth with type 1 diabetes, Journal of Pediatric Psychology, 31, 1036-1045, 2006	PICO criteria not met - cannot separate CSII and multiple daily injection results
Ying,A.K., Lairson,D.R., Giardino,A.P., Bondy,M.L., Zaheer,I., Haymond,M.W., Heptulla,R.A., Predictors of direct costs of diabetes care in pediatric patients with type 1 diabetes, Pediatric Diabetes, 12, 177-182, 2011	PICO criteria not met - multiple daily injections defined as 3 or more injections per day

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H.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Study	Reason for exclusion
Jarosz-Chobot,P., Polanska,J., Mysliwiec,M., Szadkowska,A., Fendler,W., Kaminska,H., Chumiecki,M., Mianowska,B., Techmanska,I., Sztangierska,B., Mlynarski,W., PolPeDiab study group., Multicenter cross-sectional analysis of values of glycated haemoglobin (HbA1c) in Polish children and adolescents with long-term type 1 diabetes in Poland: PolPeDiab study group, Pediatric endocrinology, diabetes, and metabolism, 18, 125-129, 2012	No targets specified. No threshold for HbA1c in analysis. No relevant outcomes reported. Study assesses whether children and young people with different HbA1c values have stable HbA1c levels.
Swift,P.G., Skinner,T.C., de Beaufort,C.E., Cameron,F.J., Aman,J., Aanstoot,H.J., Castano,L., Chiarelli,F., Daneman,D., Danne,T., Dorchy,H., Hoey,H., Kaprio,E.A., Kaufman,F., Kocova,M., Mortensen,H.B., Njolstad,P.R., Phillip,M., Robertson,K.J., Schoenle,E.J., Urakami,T., Vanelli,M., Ackermann,R.W., Skovlund,S.E., Hvidoere Study Group on Childhood Diabetes., Target setting in intensive insulin management is associated with metabolic control: the Hvidoere childhood diabetes study group centre differences study 2005, Pediatric Diabetes, 11, 271-278, 2010	No relevant outcomes were reported. Study addresses whether specifying tighter targets means a lower HbA1c is achieved, rather than the effect of a tighter HbA1c target on adverse outcomes.

H.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

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Study	Reason for exclusion
Ashwell,S.G., Gebbie,J., Home,P.D., Optimal timing of injection of once-daily insulin glargine in people with Type 1 diabetes using insulin lispro at meal-times, Diabetic Medicine, 23, 46-52, 2006	PICO not met: adult participants only
Boot,M., Volkening,L.K., Butler,D.A., Laffel,L.M., The impact of blood glucose and HbA(1c) goals on glycaemic control in children and adolescents with Type 1 diabetes, Diabetic Medicine, 30, 333-337, 2013	PICO not met: outcomes of interest not given
Fullerton,B., Jeitler,K., Seitz,M., Horvath,K., Berghold,A., Siebenhofer,A., Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus, Cochrane Database of Systematic Reviews, 2, CD009122-, 2014	The review was about both children and adults. The study on children (Wysocki 2003) does not meet the protocol in terms of intervention (that is, the comparison groups (intensive and usual care)not only differed in terms of Hb1Ac targets during treatment, but also other interventions such as education and behavioural interventions).
Fullerton,Birgit, Berghold,Andrea, Jeitler,Klaus, Siebenhofer,Andrea, Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2011	Protocol for a systematic review
Imran,S.A., Rabasa-Lhoret,R., Ross,S., Targets for Glycemic Control, Canadian Journal of Diabetes, 37, S31-S34, 2013	Clinical practice management guideline
Marcason,W., Is There a Recommended Target Range for Blood Glucose for the Type 1 Diabetic Endurance Athlete?, Journal of the Academy of Nutrition and Dietetics, 112, 2092-, 2012	Neither a study nor a systematic review
Nguyen,T.M., Mason,K.J., Sanders,C.G., Yazdani,P., Heptulla,R.A., Targeting blood glucose management in school improves glycemic control in children with poorly controlled type 1 diabetes mellitus, Journal of Pediatrics, 153, 575-578, 2008	PICO not met - interventions used did not include blood gluucose targets
Rankin,D., Cooke,D.D., Heller,S., Elliott,J., Amiel,S., Lawton,J., UK National Institute for Health Research (NIHR) Dose Adjustment for Normal Eating (DAFNE) Study Group., Experiences of using blood glucose targets when following an intensive insulin regimen: a qualitative longitudinal investigation involving patients with Type 1 diabetes, Diabetic Medicine, 29, 1079-1084, 2012	PICO not met: adult participants only
Scaramuzza,A.E., Iafusco,D., Santoro,L., Bosetti,A., De,Palma A., Spiri,D., Mameli,C., Zuccotti,G.V., Timing of bolus in children with type 1 diabetes using continuous subcutaneous insulin infusion (TiBoDi Study), Diabetes Technology and Therapeutics, 12, 149-152, 2010	PICO not met: no long-term outcomes assessed
Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C., Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes, Journal of Pediatrics, 150, 279-285, 2007	PICO not met - intervention examined did not include blood glucose targets

Study	Reason for exclusion
Swift,P.G., Skinner,T.C., de Beaufort,C.E., Cameron,F.J., Aman,J., Aanstoot,H.J., Castano,L., Chiarelli,F., Daneman,D., Danne,T., Dorchy,H., Hoey,H., Kaprio,E.A., Kaufman,F., Kocova,M., Mortensen,H.B., Njolstad,P.R., Phillip,M., Robertson,K.J., Schoenle,E.J., Urakami,T., Vanelli,M., Ackermann,R.W., Skovlund,S.E., Hvidoere Study Group on Childhood Diabetes., Target setting in intensive insulin management is associated with metabolic control: the Hvidoere childhood diabetes study group centre differences study 2005, Pediatric Diabetes, 11, 271-278, 2010	PICO not met - study does not report relationship between blood glucose levels and HbA1c

H.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

Study	Reason for exclusion
Allen,C., LeCaire,T., Palta,M., Daniels,K., Meredith,M., D'Alessio,D.J., Wisconsin Diabetes,Registry Project, Risk factors for frequent and severe hypoglycemia in type 1 diabetes, Diabetes Care, 24, 1878-1881, 2001	PICO not met - study included children, young people and adults but did not report findings separately
Anderson,B., Ho,J., Brackett,J., Finkelstein,D., Laffel,L., Parental involvement in diabetes management tasks: relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus, Journal of Pediatrics, 130, 257-265, 1997	PICO not met - study reported goodness of fit statistics for multiple variables, one of which was frequency of self-monitoring of blood glucose, so no data specific to self-monitoring of blood glucose are available
Anderson,B.J., Vangsness,L., Connell,A., Butler,D., Goebel-Fabbri,A., Laffel,L.M., Family conflict, adherence, and glycaemic control in youth with short duration Type 1 diabetes, Diabetic Medicine, 19, 635-642, 2002	PICO not met - study reported goodness of fit statistics for multiple variables, one of which was frequency of self-monitoring of blood glucose, so no data specific to self-monitoring of blood glucose are available
Beck,R.W., Tamborlane,W.V., Bergenstal,R.M., Miller,K.M., DuBose,S.N., Hall,C.A., Clinic Network,D.Exchange, The T1D Exchange clinic registry, Journal of Clinical Endocrinology and Metabolism, 97, 4383-4389, 2012	Report is a descriptive analysis of the 'T1D Exchange' registry
Belmonte,M.M., Schiffrin,A., Dufresne,J., Suissa,S., Goldman,H., Polychronakos,C., Impact of SMBG on control of diabetes as measured by HbA1. 3-year survey of a juvenile IDDM clinic, Diabetes Care, 11, 484-488, 1988	PICO not met - study does not report numerical data on the outcomes of interest
Brewer,K.W., Chase,H.P., Owen,S., Garg,S.K., Slicing the pie. Correlating HbA--values with average blood glucose values in a pie chart form, Diabetes Care, 21, 209-212, 1998	PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control
Cortina,S., Repaske,D.R., Hood,K.K., Sociodemographic and psychosocial factors associated with continuous subcutaneous insulin infusion in adolescents with type 1 diabetes, Pediatric Diabetes, 11, 337-344, 2010	PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control
Derr,R., Garrett,E., Stacy,G.A., Saudek,C.D., Is HbA(1c) affected by glycemic instability?, Diabetes Care, 26, 2728-2733, 2003	PICO not met - study did not include children or young people
Driscoll,K.A., Johnson,S.B., Tang,Y., Yang,F., Deeb,L.C., Silverstein,J.H., Does blood glucose monitoring increase prior to clinic visits in children with type 1 diabetes?, Diabetes Care, 34, 2170-2173, 2011	PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control
Evans,J.M.M., Newton,R.W., Ruta,D.A., MacDonald,T.M., Stevenson,R.J., Morris,A.D., Frequency of blood glucose monitoring in relation to glycaemic control: Observational study with diabetes database, British Medical Journal, 318, 83-86, 1999	PICO not met - study included children, young people and adults but did not report findings separately
Faustino,E.V.S., Hirshberg,E.L., Bogue,C.W., Hypoglycemia in critically ill children, Journal of Diabetes Science and Technology, 6, 48-57, 2012	The study did not report number of finger pricks and information on glycaemic control
Formosa,N., Blood glucose monitoring in children and adolescents with Type 1 Diabetes Mellitus, Malta Medical Journal, 25, 31-35, 2013	Systematic review where only studies showing significant associations between self-monitoring of blood glucose and Hb1Ac were included; the majority of included studies have been identified separately in guideline review

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Study	Reason for exclusion
Gomes,M.B., Cobas,R.A., Matheus,A.S., Tannus,L.R., Negrato,C.A., Rodacki,M., Braga,N., Cordeiro,M.M., Luescher,J.L., Berardo,R.S., Nery,M., Marques,M.A., Calliari,L.E., Noronha,R.M., Manna,T.D., Zajdenverg,L., Salvodelli,R., Penha,F.G., Foss,M.C., Foss-Freitas,M.C., Pires,A.C., Robles,F.C., Guedes,M., Dib,S.A., Dualib,P., Silva,S.C., Sepulvida,J., Almeida,H.G., Sampaio,E., Rea,R., Faria,A.C.R., Tschiedel,B., Lavigne,S., Cardozo,G.A., Azevedo,M.J., Canani,L.H., Zucatti,A.T., Coral,M.H.C., Pereira,D.A., Araujo,L.A., Tolentino,M., Pedrosa,H.C., Prado,F.A., Rassi,N., Araujo,L.B., Fonseca,R.M.C., Guedes,A.D., Matos,O.S., Faria,M., Azulay,R., Forti,A.C., Facanha,C., Montenegro,A.P., Montenegro,R., Melo,N.H., Rezende,K.F., Ramos,A., Felicio,J.S., Santos,F.M., Jezini,D.L., Cordeire,M.M., Regional differences in clinical care among patients with type 1 diabetes in Brazil: Brazilian Type 1 Diabetes Study Group, Diabetology and Metabolic Syndrome, 4, -, 2012	Paper is in Portuguese
Gomes,M.B., Negrato,C.A., Cobas,R., Tannus,L.R.M., Goncalves,P.R., Da,SilvaP, Carneiro,J.R.I., Matheus,A.S.M., Dib,S.A., Azevedo,M.J., Nery,M., Rodacki,M., Zajdenverg,L., Montenegro,JuniorR, Sepulveda,J., Calliari,L.E., Jezini,D., Braga,N., Luescher,J.L., Berardo,R.S., rruda-Marques,M.C., Noronha,R.M., Manna,T.D., Salvodelli,R., Penha,F.G., Foss,M.C., Foss-Freitas,M.C., Pires,A.C., Robles,F.C., Guedes,M.D.F.S., Dualib,P., Silva,S.C., Sampaio,E., Rea,R., Faria,A.C.R., Tschiedel,B., Lavigne,S., Canani,L.H., Zucatti,A.T., Coral,M.H.C., Pereira,D.A., Araujo,L.A., Tolentino,M., Pedrosa,H.C., Prado,F.A., Rassi,N., Araujo,L.B., Fonseca,R.M.C., Guedes,A.D., Matos,O.S., Palma,C.C., Azulay,R., Forti,A.C., Facanha,C., Montenegro,A.P., Melo,N.H., Rezende,K.F., Ramos,A., Felicio,J.S., Santos,F.M., Determinants of intensive insulin therapeutic regimens in patients with type 1 diabetes: Data from a nationwide multicenter survey in Brazil, Diabetology and Metabolic Syndrome, 6, -, 2014	The study included an adult population
Gomes,M.B., Tannus,L.R., Cobas,R.A., Matheus,A.S., Dualib,P., Zucatti,A.T., Cani,C., Guedes,A.D., Santos,F.M., Sepulveda,J., Tolentino,M., Facanha,M.C., Faria,A.C., Lavigne,S., Montenegro,A.P., Rodacki,M., de Fatima,Guedes M., Szundy,R., Cordeiro,M.M., Santos,P.T., Negrato,C.A., Brazilian,Type, Determinants of self-monitoring of blood glucose in patients with Type 1 diabetes: a multi-centre study in Brazil, Diabetic Medicine, 30, 1255-1262, 2013	The study did not report frequency of finger-prick according to age group as included population was of mixed ages
Gordon,D., Semple,C.G., Paterson,K.R., Do different frequencies of self-monitoring of blood glucose influence control in type 1 diabetic patients?, Diabetic MedicineDiabet.Med., 8, 679-682, 1991	PICO not met - both groups received 4 or fewer tests per day
Grady,M., Campbell,D., MacLeod,K., Srinivasan,A., Evaluation of a blood glucose monitoring system with automatic high- and low-pattern recognition software in insulin-using patients: Pattern detection and patient-reported insights, Journal of Diabetes Science and Technology, 7, 970-978, 2013	The study did not report different age groups as the population was of mixed ages
Grossi,S.A., Lottenberg,S.A., Lottenberg,A.M., Della,Manna T., Kuperman,H., Home blood glucose monitoring in type 1 diabetes mellitus, Revista Latino-Americana de Enfermagem, 17, 194-200, 2009	PICO not met - both groups performed fewer than 5 finger-prick tests per day
Hansen, M.V., Pedersen-Bjergaard, U., Heller, S.R., Wallace, T.M., Rasmussen, A.K., Jorgensen., H.V., Pramming, S., Thorsteinsson, B., Frequency and motives of blood glucose self-monitoring in type 1 diabetes, Diabetes Research and Clinical Practice, 85, 183-188, 2009	PICO not met - study included adults only
Haupt,E., Herrmann,R., ecke-Timp,A., Vogel,H., Haupt,A., Walter,C., The KID study IV: effects of inpatient rehabilitation on the frequency of glucose self-monitoring, quality of further primary care, on time being unable to work and on everyday psychic strain of type I and type II diabetics--a one-year follow-up. Kissingen Diabetes Intervention Study, Experimental and Clinical Endocrinology and Diabetes, 105, 21-31, 1997	PICO not met - study included adults only
Helgeson,V.S., Snyder,P.R., Seltman,H., Escobar,O., Becker,D., Siminerio,L., Brief report: trajectories of glycemic control over early to middle adolescence, Journal of Pediatric Psychology, 35, 1161-1167, 2010	PICO not met - study examined factors associated with 'good' glycaemic control compared with 'poor' glycaemic control
Hershey,T., Bhargava,N., Sadler,M., White,N.H., Craft,S., Conventional versus intensive diabetes therapy in children with type 1 diabetes: effects on memory and motor speed, Diabetes Care, 22, 1318-1324, 1999	PICO not met - both randomised groups used 4 or fewer blood glucose tests per day
McGrady,M.E., Peugh,J.L., Hood,K.K., Illness representations predict adherence in adolescents and young adults with type 1 diabetes, Psychology and Health, 29, 985-998, 2014	No comparator group, and data were not reported according to age groups as study included mixed ages
Messer,L., Ruedy,K., Xing,D., Coffey,J., Englert,K., Caswell,K., Ives,B., Educating families on real time continuous glucose monitoring: the DirecNet navigator pilot study experience, Diabetes Educator, 35, 124-135, 2009	PICO not met - study examined education in use of a real-time continuous glucose monitoring device
Mortensen,H.B., Hougaard,P., Comparison of metabolic control in a cross-sectional study of 2,873 children and adolescents with IDDM from 18 countries. The Hvidore Study Group on Childhood Diabetes, Diabetes Care, 20, 714-720, 1997	PICO not met - study does not report relationship between self-monitoring of blood glucose and glycaemic control
Olinder,A.L., Kernell,A., Smide,B., Missed bolus doses: devastating for metabolic control in CSII-treated adolescents with type 1 diabetes, Pediatric Diabetes, 10, 142-148, 2009	PICO not met - study does not report numerical data on the outcomes of interest

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Study	Reason for exclusion
Radermecker,R.P., Fayolle,C., Brun,J.F., Bringer,J., Renard,E., Accuracy assessment of online glucose monitoring by a subcutaneous enzymatic glucose sensor during exercise in patients with type 1 diabetes treated by continuous subcutaneous insulin infusion, Diabetes and Metabolism, 39, 258-262, 2013	Adult population
Schiffrin,A., Belmonte,M., Multiple daily self-glucose monitoring: Its essential role in long-term glucose control in insulin-dependent diabetic patients treated with pump and multiple subcutaneous injections, Diabetes Care, 5, 479-484, 1982	PICO not met - non-randomised study comparing 2 tests per day with 4 or more tests per day
Schutt,M., Kern,W., Busch,P., Dapp,A., Grziwotz,R., Mayer,I., Rosenbauer,J., Wagner,C., Zimmerman,A., Kerner,W., Holl,R.W, Is the frequency of self-monitoring of blood glucose related to long-term metabolic control? Multicentre analysis including 24 500 patients from 191 centers in Germany and Austria, Experimental and Clinical Endocrinology and Diabetes, 114 (7), 384-388, 2006	PICO not met - population was mixed type 1 and type 2 diabetes, and groups were not stratified
Service,F.J., O'Brien,P.C., Influence of glycemic variables on hemoglobin A1c, Endocrine Practice, 13, 350-354, 2007	PICO not met - study does not report data on outcome of interest (correlation of self-monitoring of blood glucose and glycaemic control)
Shalitin,S., Gil,M., Nimri,R., de Vries,L., Gavan,M.Y., Philip,M., Predictors of glycaemic control in patients with type 1 diabetes commencing continuous subcutaneous insulin infusion therapy, Diabetic Medicine, 27 (3), 339-347, 2010	Population was not stratified by age
Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C., Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes, Journal of Pediatrics, 150, 279-285, 2007	PICO not met - study did not report the correlation between self-monitoring of blood glucose and glycaemic control
Timar,B., Serban,V., Lacatusu,A., Barna,L., Fiera,F., Vlad,A., The relationship between quality of self-monitoring and glycemic control in Romanian children with type 1 diabetes mellitus, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 19, 237-244, 2012	Duration of measurement of HbA1c not reported
Vanelli,M., Cerutti,F., Chiarelli,F., Lorini,R., Meschi,F., MCDC-Italy Group., Nationwide cross-sectional survey of 3560 children and adolescents with diabetes in Italy.[Erratum appears in J Endocrinol Invest. 2005 Oct;28(9):868], Journal of Endocrinological Investigation, 28, 692-699, 2005	PICO not met - study did not report numerical data on the outcomes of interest
Vervoort,T., Goubert,L., Vandenbossche,H., van,AkenS, Matthys,D., Crombez,G., Child's and parents' catastrophizing about pain is associated with procedural fear in children: A study in children with diabetes and their mothers, Psychological Reports, 109, 879-895, 2011	The study did not have a comparator group; the participants appeared to have 1 finger prick test only
Wing,R.R., Lamparski,D.M., Zaslow,S., Betschart,J., Siminerio,L., Becker,D., Frequency and accuracy of self-monitoring of blood glucose in children: relationship to glycemic control, Diabetes Care, 8, 214-218, 1985	PICO not met - study did not report the correlation between self-monitoring of blood glucose and glycaemic control
Wilkinson,J., McFann,K., Chase,H.P., Factors affecting improved glycaemic control in youth using insulin pumps, Diabetic Medicine, 27(10), 1174-1177, 2010	PICO not met - study did not report the outcome stratified by age
Wyllie,H.R., McLaren,E.H., Self monitoring of blood glucose 'a walking stick and not a cane', Practical Diabetes, 11, 116-118, 1994	PICO not met - study includes both young people and adults but results not presented separately for both age groups
Wysocki,T., Green,L., Huxtable,K., Blood glucose monitoring by diabetic adolescents: compliance and metabolic control, Health Psychology, 8, 267-284, 1989	PICO not met - study examined incentives for self-monitoring of blood glucose, not different frequencies of self-monitoring
Yi-Frazier,J.P., Hood,K., Case,D., Waitzfelder,B., Anderson,A., Bloch,C.A., Naughton,M., Seid,M., Imperatore,G., Loots,B., Bell,R., Lawrence,J.M., SEARCH for Diabetes in Youth Study Group., Caregiver reports of provider recommended frequency of blood glucose monitoring and actual testing frequency for youth with type 1 diabetes, Diabetes Research and Clinical Practice, 95, 68-75, 2012	PICO not met - study did not report the correlation between self-monitoring of blood glucose and glycaemic control

Update 2015

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Study	Reason for exclusion
Battelino,T., Conget,I., Olsen,B., Schutz-Fuhrmann,I., Hommel,E., Hoogma,R., Schierloh,U., Sulli,N., Bolinder,J., SWITCH Study Group., The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial, Diabetologia, 55, 3155-3162, 2012	The study examined the efficacy of adding continuous glucose monitoring (CGMS) to insulin pump therapy in comparison with not adding CGMS to the therapy; comparator did not meet the review protocol inclusion criteria

Study	Reason for exclusion
Bergenstal,R.M., Tamborlane,W.V., Ahmann,A., Buse,J.B., Dailey,G., Davis,S.N., Joyce,C., Peoples,T., Perkins,B.A., Welsh,J.B., Willi,S.M., Wood,M.A., Study Group., Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes.[Erratum appears in N Engl J Med. 2010 Sep 9;363(11):1092], New England Journal of Medicine, 363, 311-320, 2010	PICO not met: participants were randomly assigned to insulin pump therapy or insulin injection therapy and then given a form of continuous glucose monitoring (CGMS); unable to tell whether any differences between groups are due to the form of CGMS used or to theinsulin regimen (non-parallel comparison), nor was the comparison between finger-prick blood glucose testing and CGMS
Bode,B.W., Clinical utility of the continuous glucose monitoring system, Diabetes Technology and Therapeutics, 2 Suppl 1, S35-S41, 2000	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (case study only)
Chase,H.P., Beck,R., Tamborlane,W., Buckingham,B., Mauras,N., Tsalikian,E., Wysocki,T., Weinzimer,S., Kollman,C., Ruedy,K., Xing,D., A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes, Diabetes Care, 28, 1101-1106, 2005	GlucoWatch G2 Biographer has been withdrawn from the market
Chase,H.P., Beck,R.W., Xing,D., Tamborlane,W.V., Coffey,J., Fox,L.A., Ives,B., Keady,J., Kollman,C., Laffel,L., Ruedy,K.J., Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the juvenile diabetes research foundation continuous glucose monitoring randomized trial, Diabetes Technology and Therapeutics, 12, 507-515, 2010	No comparative data between CGMS users and capillary blood glucose monitoring users
Chase,H.P., Kim,L.M., Owen,S.L., MacKenzie,T.A., Klingensmith,G.J., Murtfeldt,R., Garg,S.K., Continuous subcutaneous glucose monitoring in children with type 1 diabetes, Pediatrics, 107, 222-226, 2001	Included in the Cochrane systematic review (Langendam 2012) - also included in the 2004 guideline review
Chase,H.P., Roberts,M.D., Wightman,C., Klingensmith,G., Garg,S.K., Van,Wyhe M., Desai,S., Harper,W., Lopatin,M., Bartkowiak,M., Tamada,J., Eastman,R.C., Use of the GlucoWatch biographer in children with type 1 diabetes, Pediatrics, 111, 790-794, 2003	The first generation GlucoWatch Biographer was withdrawn from the market in 2008
Chase,H.P., Roberts,M.D., Wightman,C., Klingensmith,G., Garg,S.K., Van,Wyhe M., Desai,S., Harper,W., Lopatin,M., Bartkowiak,M., Tamada,J., Eastman,R.C., Use of the GlucoWatch biographer in children with type 1 diabetes, Pediatrics, 111, 790-794, 2003	GlucoWatch G2 Biographer has been withdrawn from the market
Chetty,V.T., Almulla,A., Odueyungbo.A., Thabane,L., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review, Diabetes Research and Clinical Practice, 81, 79-87, 2008	Superseded by more recent systematic reviews
Cobry,E., Chase,H.P., Burdick,P., McFann,K., Yetzer,H., Scrimgeour,L., Use of CoZmonitor in youth with type 1 diabetes, Pediatric Diabetes, 9, 148-151, 2008	PICO not met - study related to integration of capillary blood glucose monitoring and insulin pump therapy
Deiss,D., Hartmann,R., Schmidt,J., Kordonouri,O., Results of a randomised controlled cross-over trial on the effect of continuous subcutaneous glucose monitoring (CGMS) on glycaemic control in children and adolescents with type 1 diabetes, Experimental and Clinical Endocrinology and Diabetes, 114, 63-67, 2006	Included in the Cochrane systematic review (Langendam 2012)
Deiss,Dorothee, Bolinder,Jan, Riveline,Jean Pierre, Battelino,Tadej, Bosi,Emanuele, Tubiana-Rufi,Nadia, Kerr,David, Phillip,Moshe, Improved Glycemic Control in Poorly Controlled Patients with Type 1 Diabetes Using Real-Time Continuous Glucose Monitoring, Diabetes Care, 29, 2730-2732, 2006	Included in the Cochrane systematic review (Langendam 2012)
Gandhi,G.Y., Kovalaske,M., Kudva,Y., Walsh,K., Elamin,M.B., Beers,M., Coyle,C., Goalen,M., Murad,M.S., Erwin,P.J., Corpus,J., Montori,V.M., Murad,M.H., Efficacy of continuous glucose monitoring in improving glycemic control and reducing hypoglycemia: a systematic review and meta-analysis of randomized trials, Journal of Diabetes Science and Technology, 5, 952-965, 2011	Individual studies checked for inclusion and all except for the GlucoWatch studies are included in the Cochrane systematic review (Langendam 2012)
Guelho,D., Paiva,I., Batista,C., Barros,L., Carrilho,F., A1c, glucose variability and hypoglycemia risk in patients with type 1 diabetes, Minerva Endocrinologica, 39, 127-133, 2014	The study was carried out among adults; retrospective in design, and made no comparison between finger-prick blood glucose testing and CGMS
Hirsch,I.B., Abelseth,J., Bode,B.W., Fischer,J.S., Kaufman,F.R., Mastrototaro,J., Parkin,C.G., Wolpert,H.A., Buckingham,B.A., Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study, Diabetes Technology and Therapeutics, 10, 377-383, 2008	Included in the Cochrane systematic review (Langendam 2012)
Hoeks,L.B., Greven,W.L., de Valk,H.W., Real-time continuous glucose monitoring system for treatment of diabetes: a systematic review, Diabetic Medicine, 28, 386-94, 2011	Superseded by more recent systematic reviews

Update 2015

Study	Reason for exclusion
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Hirsch,I.B., Laffel,L., Tamborlane,W.V., Bode,B.W., Buckingham,B., Chase,P., Clemons,R., Fiallo-Scharer,R., Fox,L.A., Gilliam,L.K., Huang,E.S., Kollman,C., Kowalski,A.J., Lawrence,J.M., Lee,J., Mauras,N., O'Grady,M., Ruedy,K.J., Tansey,M., Tsalikian,E., Weinzimer,S.A., Wilson,D.M., Wolpert,H., Wysocki,T., Xing,D., The effect of continuous glucose monitoring in well-controlled type 1 diabetes, Diabetes Care, 32, 1378-1383, 2009	Included in the Cochrane systematic review (Langendam 2012)
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Lawrence,J.M., Laffel,L., Wysocki,T., Xing,D., Huang,E.S., Ives,B., Kollman,C., Lee,J., Ruedy,K.J., Tamborlane,W.V., Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial.[Erratum appears in Diabetes Care. 2010 Dec;33(12):2725], Diabetes Care, 33, 2175-2177, 2010	Included in the Cochrane systematic review (Langendam 2012)
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane,W.V., Beck,R.W., Bode,B.W., Buckingham,B., Chase,H.P., Clemons,R., Fiallo-Scharer,R., Fox,L.A., Gilliam,L.K., Hirsch,I.B., Huang,E.S., Kollman,C., Kowalski,A.J., Laffel,L., Lawrence,J.M., Lee,J., Mauras,N., O'Grady,M., Ruedy,K.J., Tansey,M., Tsalikian,E., Weinzimer,S., Wilson,D.M., Wolpert,H., Wysocki,T., Xing,D., Continuous glucose monitoring and intensive treatment of type 1 diabetes, New England Journal of Medicine, 359, 1464-1476, 2008	Included in the Cochrane systematic review (Langendam 2012)
Kaufman,F.R., Gibson,L.C., Halvorson,M., Carpenter,S., Fisher,L.K., Pitukcheewanont,P., A pilot study of the continuous glucose monitoring system: clinical decisions and glycemic control after its use in pediatric type 1 diabetic subjects, Diabetes Care, 24, 2030-2034, 2001	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (not a randomised study)
Kordonouri,O., Hartmann,R., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Lange,K., Danne,T., Follow-up of patients with sensor-augmented pump therapy during the first year of diabetes-pediatric onset study, Pediatric Diabetes, 12, 29-, 2011	An abstract
Kordonouri,O., Hartmann,R., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Lange,K., Danne,T., Sensor augmented pump therapy from onset of type 1 diabetes: late follow-up results of the Pediatric Onset Study, Pediatric Diabetes, 13, 515-518, 2012	Secondary publication of an included study
Kordonouri,O., Hartmann,R., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Lange,K., Danne,T., Sensor augmented pump therapy from onset of type 1 diabetes: Late follow-up results of the Pediatric ONSET Study, Diabetologia, 54, S41-, 2011	An abstract
Kordonouri,O., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Hartmann,R., Lange,K., Knip,M., Danne,T., Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment, Diabetologia, 53, 2487-2495, 2010	Included in the Cochrane systematic review (Langendam 2012)
Lagarde,W.H., Barrows,F.P., Davenport,M.L., Kang,M., Guess,H.A., Calikoglu,A.S., Continuous subcutaneous glucose monitoring in children with type 1 diabetes mellitus: a single-blind, randomized, controlled trial, Pediatric Diabetes, 7, 159-164, 2006	Included in the Cochrane systematic review (Langendam 2012)
Lange,K., Coutant,R., Danne,T., Kapellen,T., Pankowska,E., Rami,B., Aschemeier,B., Blasig,S., Hartmann,R., Krug,N., Marquardt,E., Remus,K., Kordonouri,O., High quality of life in children and psychological wellbeing in mothers 12 month after diabetes onset: Results of the paediatric onset-trial of sensor-enhanced CSII, Pediatric Diabetes, 11, 101-, 2010	An abstract
Lawson,M.L., Bradley,B., McAssey,K., Clarson,C., Kirsch,S.E., Mahmud,F.H., Curtis,J.R., Richardson,C., Courtney,J., Cooper,T., Downie,C.J., Rajamannar,G., Barrowman,N., CGM TIME Trial Study Group, JDRF Canadian Clinical Trial Network CCTN, The JDRF CCTN CGM TIME Trial: Timing of Initiation of continuous glucose Monitoring in Established pediatric type 1 diabetes: study protocol, recruitment and baseline characteristics, BMC Pediatrics, 14, 183-, 2014	This is a protocol and only reports baseline characteristics of participants
Ludvigsson,J., Hanas,R., Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study, Pediatrics, 111, 933-938, 2003	Included in the Cochrane systematic review(Langendam 2012)
Ly,T.T., Hewitt,J., Davey,R.J., Lim,E.M., Davis,E.A., Jones,T.W., Improving epinephrine responses in hypoglycemia unawareness with real-time continuous glucose monitoring in adolescents with type 1 diabetes, Diabetes Care, 34, 50-52, 2011	Minimum length of follow-up not met and objective not pertinent to this review question
Markowitz,J.T., Pratt,K., Aggarwal,J., Volkening,L.K., Laffel,L.M., Psychosocial correlates of continuous glucose monitoring use in youth and adults with type 1 diabetes and parents of youth, Diabetes Technology and Therapeutics, 14, 523-526, 2012	The original study (Juvenile Diabetes Research Foundation (JDRF) trial) was included in the Cochrane systematic review (Langendam 2012)
McGahan,L., Continuous glucose monitoring in the management of diabetes mellitus, Issues in Emerging Health Technologies, 1-4, 2002	Included in 2004 guideline review - copy could not be obtained for consideration in 2015 update review

Update 2015

Study	Reason for exclusion
O'Connell,M.A., Donath,S., O'Neal,D.N., Colman,P.G., Ambler,G.R., Jones,T.W., Davis,E.A., Cameron,F.J., Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial, Diabetologia, 52, 1250-1257, 2009	Included in the Cochrane systematic review (Langendam 2012)
Pickup,J.C., Freeman,S.C., Sutton,A.J., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, BMJ, 343, d3805-, 2011	Not strictly a systematic review and superseded by more recent systematic reviews; PICO not met - meta-analysis of RCTs comparing CGMS against self-monitoring of blood glucose (SMBG); mean age of participants over 18 years in all included trials
Poolsup,N., Suksomboon,N., Kyaw,A.M., Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes, Diabetology and Metabolic Syndrome, 5, -, 2013	Systematic review and meta-analysis of RCTs with results of the comparison between real-time CGMS and self-monitoring of blood glucose (SMBG), all relevant studies have been included in the review except Battelino 2012 which does not meet the review protocol inclusion criteria
Raccah,D., Sulmont,V., Reznik,Y., Guerci,B., Renard,E., Hanaire,H., Jeandidier,N., Nicolino,M., Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study, Diabetes Care, 32, 2245-2250, 2009	Included in the Cochrane systematic review (Langendam 2012)
Rami,B., Lange,K., Coutant,R., Danne,T., Aschemeier,B., Blasig,S., Hartmann,R., Marquardt,E., Walte,K., Krug,N., Kapellen,T., Pankowska,E., Kordonouri,O., Paediatric ONSET-Study: Impaired QoL in children and depressed mood in mothers at onset of diabetes mellitus type 1 in children, Diabetologia, 52, S28-, 2009	Objective is not relevant to the review question
Schiaffini,R., Ciampalini,P., Fierabracci,A., Spera,S., Borrelli,P., Bottazzo,G.F., Crino,A., The continuous glucose monitoring system (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk, Diabetes/metabolism research and reviews, 18, 324-329, 2002	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (cohort study only)
Sequeira,P.A., Montoya,L., Ruelas,V., Xing,D., Chen,V., Beck,R., Peters,A.L., Continuous glucose monitoring pilot in low-income type 1 diabetes patients, Diabetes Technology and Therapeutics, 15, 855-858, 2013	Age of participants was 18 years and over
Szypowska,A., Ramotowska,A., Dzygalo,K., Golicki,D., Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials, European Journal of Endocrinology, 166, 567-574, 2012	All the studies included are covered by the Cochrane systematic review (Langendam 2012)
Tansey,M., Laffel,L., Cheng,J., Beck,R., Coffey,J., Huang,E., Kollman,C., Lawrence,J., Lee,J., Ruedy,K., Tamborlane,W., Wysocki,T., Xing,D., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., Satisfaction with continuous glucose monitoring in adults and youths with Type 1 diabetes, Diabetic Medicine, 28, 1118-1122, 2011	Outcome not compared between intervention and comparator groups
Wojciechowski,P., Rys,P., Lipowska,A., Gaweska,M., Malecki,M.T., Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes: systematic review and meta-analysis, Polskie Archiwum Medycyny Wewnetrznej, 121, 333-343, 2011	All the studies included are covered by the Cochrane systematic review (Langendam 2012)
Yates,K., Hasnat,Milton A., Dear,K., Ambler,G., Continuous glucose monitoring-guided insulin adjustment in children and adolescents on near-physiological insulin regimens: a randomized controlled trial, Diabetes Care, 29, 1512-1517, 2006	Included in the Cochrane systematic review (Langendam 2012)
Yeh,H.C., Brown,T.T., Maruthur,N., Ranasinghe,P., Berger,Z., Suh,Y.D., Wilson,L.M., Haberl,E.B., Brick,J., Bass,E.B., Golden,S.H., Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: a systematic review and meta-analysis, Annals of Internal Medicine, 157, 336-347, 2012	All relevant included studies are covered by the Cochrane systematic review (Langendam 2012)

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Study	Reason for exclusion
Battelino,T., Bode,B.W., Continuous glucose monitoring in 2010, International Journal of Clinical Practice, Supplement., 10-15, 2011	Not a systematic review
Battelino,T., Conget,I., Olsen,B., Schutz-Fuhrmann,I., Hommel,E., Hoogma,R., Schierloh,U., Sulli,N., Bolinder,J., SWITCH Study Group., The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial, Diabetologia, 55, 3155-3162, 2012	The study examined the efficacy of adding continuous glucose monitoring (CGMS) to insulin pump therapy in comparison with not adding CGMS to the therapy; comparator did not meet the review protocol inclusion criteria.
Bergenstal,R.M., Tamborlane,W.V., Ahmann,A., Buse,J.B., Dailey,G., Davis,S.N., Joyce,C., Peoples,T., Perkins,B.A., Welsh,J.B., Willi,S.M., Wood,M.A., Study Group., Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes.[Erratum appears in N Engl J Med. 2010 Sep 9;363(11):1092], New England Journal of Medicine, 363, 311-320, 2010	Participants were randomly assigned to insulin pump therapy or insulin injection therapy and then given a form of continuous glucose monitoring (CGMS); unable to tell whether any differences between groups were due to the form of CGMS used or to the insulin regimen, and the comparison was not between intermittent and continuous CGMS either
Bode,B.W., Clinical utility of the continuous glucose monitoring system, Diabetes Technology and Therapeutics, 2 Suppl 1, S35-S41, 2000	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (case study only)
Chase,H.P., Beck,R.W., Xing,D., Tamborlane,W.V., Coffey,J., Fox,L.A., Ives,B., Keady,J., Kollman,C., Laffel,L., Ruedy,K.J., Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the juvenile diabetes research foundation continuous glucose monitoring randomized trial, Diabetes Technology and Therapeutics, 12, 507-515, 2010	A sub-study: the original study was excluded
Chetty,V.T., Almulla,A., Odueyungbo,A., Thabane,L., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review. [34 refs], Diabetes Research and Clinical Practice, 81, 79-87, 2008	PICO not met: comparator was self-monitoring of blood glucose
Danne,T., Lange,K., Kordonouri,O., Real-time glucose sensors in children and adolescents with type-1 diabetes. [64 refs], Hormone Research, 70, 193-202, 2008	Not a systematic review
Deiss,D., Hartmann,R., Schmidt,J., Kordonouri,O., Results of a randomised controlled cross-over trial on the effect of continuous subcutaneous glucose monitoring (CGMS) on glycaemic control in children and adolescents with type 1 diabetes, Experimental and Clinical Endocrinology and Diabetes, 114, 63-67, 2006	PICO not met: outcome data not been presented as specified in the protocol
Edelman,S.V., Bailey,T.S., Continuous glucose monitoring health outcomes, Diabetes Technology and Therapeutics, 11 Suppl 1, S68-S74, 2009	Review article: individual studies checked for inclusion
Halvorson,M., Carpenter,S., Kaiserman,K., Kaufman,F.R., A pilot trial in pediatrics with the sensor-augmented pump: combining real-time continuous glucose monitoring with the insulin pump, Journal of Pediatrics, 150, 103-105, 2007	Not an RCT
Hoeks,L.B., Greven,W.L., de Valk,H.W., Real-time continuous glucose monitoring system for treatment of diabetes: a systematic review, Diabetic Medicine, 28, 386-94, 2011	Systematic review: individual studies checked for inclusion
Hovorka,R., Elleri,D., Thabit,H., Allen,J.M., Leelarathna,L., El-Khairi,R., Kumareswaran,K., Caldwell,K., Calhoun,P., Kollman,C., Murphy,H.R., Acerini,C.L., Wilinska,M.E., Nodale,M., Dunger,D.B., Overnight closed-loop insulin delivery in young people with type 1 diabetes: A free-living, randomized clinical trial, Diabetes Care, 37, 1204-1211, 2014	The intervention and comparator were not as specified in the protocol (real-time CGMS versus real-time CGMS closed loop)
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Buckingham,B., Miller,K., Wolpert,H., Xing,D., Block,J.M., Chase,H.P., Hirsch,I., Kollman,C., Laffel,L., Lawrence,J.M., Milaszewski,K., Ruedy,K.J., Tamborlane,W.V., Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes, Diabetes Care, 32, 1947-1953, 2009	A secondary analysis of an RCT
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Lawrence,J.M., Laffel,L., Wysocki,T., Xing,D., Huang,E.S., Ives,B., Kollman,C., Lee,J., Ruedy,K.J., Tamborlane,W.V., Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial.[Erratum appears in Diabetes Care. 2010 Dec;33(12):2725], Diabetes Care, 33, 2175-2177, 2010	PICO not met: the comparator is self-monitoring of blood glucose only
Klonoff,D.C., Continuous glucose monitoring study does not demonstrate benefit in children and adolescents, Journal of Pediatrics, 154, 463-464, 2009	Not an RCT

Update 2015

Study	Reason for exclusion
Laffel,L.M., Hsu,W.C., McGill,J.B., Meneghini,L., Volkening,L.K., Continued use of an integrated meter with electronic logbook maintains improvements in glycemic control beyond a randomized, controlled trial, Diabetes Technology and Therapeutics, 9, 254-264, 2007	Paediatric data not reported separately; participants with type 1 diabetes and those with type 2 diabetes cannot be distinguished
Lagarde,W.H., Barrows,F.P., Davenport,M.L., Kang,M., Guess,H.A., Calikoglu,A.S., Continuous subcutaneous glucose monitoring in children with type 1 diabetes mellitus: a single-blind, randomized, controlled trial, Pediatric Diabetes, 7, 159-164, 2006	PICO not met: comparator was self-monitoring of blood glucose(although CGMS data were collected, they were not reported)
Langendam,M., Luijf,Y.M., Hooft,L., Devries,J.H., Mudde,A.H., Scholten,R.J., Continuous glucose monitoring systems for type 1 diabetes mellitus, Cochrane Database of Systematic Reviews, 1, CD008101-, 2012	Systematic review: individual articles checked for inclusion
Ludvigsson,J., Hanas,R., Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study, Pediatrics, 111, 933-938, 2003	PICO not met: comparator was self-monitoring of blood glucose(although CGMS data were collected they were not reported)
Ly,T.T., Hewitt,J., Davey,R.J., Lim,E.M., Davis,E.A., Jones,T.W., Improving epinephrine responses in hypoglycemia unawareness with real-time continuous glucose monitoring in adolescents with type 1 diabetes, Diabetes Care, 34, 50-52, 2011	PICO not met: comparator is 'standard therapy'- assumed that this refers to self-monitoring of blood glucose
Lynch, P., Attvall, S., Persson, S., Barsoe, C., Gerdtham, U., Routine use of personal continuous glucose monitoring system with insulin pump in Sweden, Diabetologica, 55, 432, 2012	Conference abstract
Maahs,D.M., Calhoun,P., Buckingham,B.A., Chase,H.P., Hramiak,I., Lum,J., Cameron,F., Bequette,B.W., Aye,T., Paul,T., Slover,R., Wadwa,R.P., Wilson,D.M., Kollman,C., Beck,R.W., A randomized trial of a home system to reduce nocturnal hypoglycemia in type 1 diabetes, Diabetes Care, 37, 1885-1891, 2014	The trial included participants aged 15-45 years, but results were not stratified by age group
Mauras,N., Fox,L., Englert,K., Beck,R.W., Continuous glucose monitoring in type 1 diabetes, Endocrine, 43, 41-50, 2013	Not a systematic review
Mauras,N., Beck,R., Xing,D., Ruedy,K., Buckingham,B., Tansey,M., White,N.H., Weinzimer,S.A., Tamborlane,W., Kollman,C., Diabetes Research in Children Network (DirecNet) Study Group., A randomized clinical trial to assess the efficacy and safety of real-time continuous glucose monitoring in the management of type 1 diabetes in young children aged 4 to <10 years, Diabetes Care, 35, 204-210, 2012	PICO not met: the comparator was self-monitoring of blood glucose only
McGahan,L., Continuous glucose monitoring in the management of diabetes mellitus, Issues in Emerging Health Technologies, 1-4, 2002	Included in 2004 guideline review - copy could not be obtained for consideration in 2015 update review
O'Connell,M.A., Donath,S., O'Neal,D.N., Colman,P.G., Ambler,G.R., Jones,T.W., Davis,E.A., Cameron,F.J., Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial, Diabetologia, 52, 1250-1257, 2009	PICO not met: the comparator was self-monitoring of blood glucose
Pickup,J.C., Freeman,S.C., Sutton,A.J., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, BMJ, 343, d3805-, 2011	PICO not met: meta-analysis of RCTs comparing CGMS against self-monitoring of blood glucose (SMBG); mean age of participants over 18 years in all included trials
Poolsup,N., Suksomboon,N., Kyaw,A.M., Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes, Diabetology and Metabolic Syndrome, 5, -, 2013	PICO not met: systematic review and meta-analysis of RCTs comparing real-time CGMS against self-monitoring of blood glucose (SMBG), and retrospective CGMS against SMBG, respectively
Raccah,D., Sulmont,V., Reznik,Y., Guerci,B., Renard,E., Hanaire,H., Jeandidier,N., Nicolino,M., Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study, Diabetes Care, 32, 2245-2250, 2009	Paediatric data not reported separately
Riveline,J.P., Schaepelynck,P., Chaillous,L., Renard,E., Sola-Gazagnes,A., Penfornis,A., Tubiana-Rufi,N., Sulmont,V., Catargi,B., Lukas,C., Radermecker,R.P., Thivolet,C., Moreau,F., Benhamou,P.Y., Guerci,B., Leguerrier,A.M., Millot,L., Sachon,C., Charpentier,G., Hanaire,H., EVADIAC Sensor Study Group., Assessment of patient-led or physician-driven continuous glucose monitoring in patients with poorly controlled type 1 diabetes using basal-bolus insulin regimens: a 1-year multicenter study, Diabetes Care, 35, 965-971, 2012	PICO not met: the results were not stratified by age
Schiaffini,R., Ciampalini,P., Fierabracci,A., Spera,S., Borrelli,P., Bottazzo,G.F., Crino,A., The continuous glucose monitoring system (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk, Diabetes/metabolism research and reviews, 18, 324-329, 2002	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (cohort study only)
Soliman,A., DeSanctis,V., Yassin,M., Elalaily,R., Eldarsy,N.E., Continuous glucose monitoring system and new era of early diagnosis of diabetes in high risk groups, Indian Journal of Endocrinology and Metabolism, 18, 274-282, 2014	Discussion paper related to CGMS as a diagnostic tool

Study	Reason for exclusion
Tamborlane,W.V., Insulin pumps and continuous glucose monitoring in pediatric patients with type 1 diabetes mellitus, Endocrine Practice, 18, 13-16, 2012	Not a systematic review
Tansey,M., Laffel,L., Cheng,J., Beck,R., Coffey,J., Huang,E., Kollman,C., Lawrence,J., Lee,J., Ruedy,K., Tamborlane,W., Wysocki,T., Xing,D., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., Satisfaction with continuous glucose monitoring in adults and youths with Type 1 diabetes, Diabetic Medicine, 28, 1118-1122, 2011	A sub-study: the original study was excluded
Tsalikian,E., Fox,L., Weinzimer,S., Buckingham,B., White,N.H., Beck,R., Kollman,C., Xing,D., Ruedy,K., Diabetes Research in Children Network Study Group., Feasibility of prolonged continuous glucose monitoring in toddlers with type 1 diabetes, Pediatric Diabetes, 13, 301-307, 2012	Not an RCT
Weinzimer,S., Xing,D., Tansey,M., Fiallo-Scharer,R., Mauras,N., Wysocki,T., Beck,R., Tamborlane,W., Ruedy,K., Diabetes Research in Children Network (DirecNet) Study Group., FreeStyle navigator continuous glucose monitoring system use in children with type 1 diabetes using glargine-based multiple daily dose regimens: results of a pilot trial Diabetes Research in Children Network (DirecNet) Study Group, Diabetes Care, 31, 525-527, 2008	Not an RCT
Weinzimer,S.A., Continuous glucose monitoring in young children: Satisfaction without success?, Diabetes Technology and Therapeutics, 14, 753-755, 2012	Not a systematic review

H.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Study	Reason for exclusion
Bashford,J., Acerini,C.L., How to use near-patient capillary ketone meters, Archives of Disease in Childhood Education and Practice, 97, 217-221, 2012	Narrative review article. Only relevant study cited is already included in review (Laffel 2006)
Bektas,F., Eray,O., Sari,R., Akbas,H., Point of care blood ketone testing of diabetic patients in the emergency department, Endocrine Research, 30, 395-402, 2004	Monitoring in hospital
Bismuth,E., Laffel,L., Can we prevent diabetic ketoacidosis in children?, Pediatric Diabetes, 8, 24-33, 2007	Not a systematic review
Charles,R.A., Bee,Y.M., Eng,P.H., Goh,S.Y., Point-of-care blood ketone testing: screening for diabetic ketoacidosis at the emergency department, Singapore Medical Journal, 48, 986-989, 2007	Monitoring in hospital
Chiari,G., Direct measurement of 3-B-hydroxybutyrate in the management of diabetic ketoacidosis in children: A cost effective enhancement in the management of diabetic ketoacidosis in children, Diabetes Technology and Therapeutics, 13, 178-179, 2011	Conference abstract
Donohoe,P.B., Kessler,R., Beattie,T.F., Exploring the clinical utility of blood ketone levels in the emergency department assessment of paediatric patients, Emergency Medicine Journal, 23, 783-787, 2006	Monitoring in hospital
Klocker,A.A., Phelan,H., Twigg,S.M., Craig,M.E., Blood beta-hydroxybutyrate versus urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review, Diabetic Medicine, 30, 818-824, 2013	Systematic review. References checked - only relevant article is already included in this review (Laffel 2006). Three other studies included in systematic review do not pertain to this question (all consider inpatient monitoring of ketones).
Lawrence,S.E., Diagnosis and treatment of diabetic ketoacidosis in children and adolescents, Paediatrics and Child Health, 10, 21-24, 2005	Review and recommendations (not a systematic review)
Meas,T., Taboulet,P., Sobngwi,E., Gautier,J.F., Is capillary ketone determination useful in clinical practice? In which circumstances?. [22 refs], Diabetes and Metabolism, 31, 299-303, 2005	Not a systematic review
Naunheim,R., Jang,T.J., Banet,G., Richmond,A., McGill,J., Point-of-care test identifies diabetic ketoacidosis at triage, Academic Emergency Medicine, 13, 683-685, 2006	Monitoring in hospital
Prisco,F., Picardi,A., Iafusco,D., Lorini,R., Minicucci,L., Martinucci,M.E., Toni,S., Cerutti,F., Rabbone,I., Buzzetti,R., Crino,A., Pozzilli,P., Blood ketone bodies in patients with recent-onset type 1 diabetes (a multicenter study), Pediatric Diabetes, 7, 223-228, 2006	Monitoring in hospital
Rewers,M., Pihoker,C., Donaghue,K., Hanas,R., Swift,P., Klingensmith,G.J., Assessment and monitoring of glycemic control in children and adolescents with diabetes. [94 refs], Pediatric Diabetes, 10 Suppl 12, 71-81, 2009	ISPAD Clinical Practice Consensus Guidelines 2009 Compendium

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Taboulet,P., Deconinck,N., Thurel,A., Haas,L., Manamani,J., Porcher,R., Schmit,C., Fontaine,J.P., Gautier,J.F., Correlation between urine ketones (acetoacetate) and capillary blood ketones (3-beta-hydroxybutyrate) in hyperglycaemic patients, Diabetes and Metabolism, 33, 135-139, 2007	Monitoring in hospital
Turan,S., Omar,A., Bereket,A., Comparison of capillary blood ketone measurement by electrochemical method and urinary ketone in treatment of diabetic ketosis and ketoacidosis in children, Acta Diabetologica, 45, 83-85, 2008	Monitoring in hospital
Vanelli,M., Chiari,G., Capuano,C., Iovane,B., Bernardini,A., Giacalone,T., The direct measurement of 3-beta-hydroxy butyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 16, 312-316, 2003	Monitoring in hospital

H.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Study	Reason for exclusion
Aguilar,Maria J., Garcia,Pedro A., Gonzalez,Emilio, Perez,Maria C., Padilla,Carlos A., A nursing educational intervention helped by One Touch UltraSmart improves monitoring and glycated haemoglobin levels in type I diabetic children, Journal of Clinical Nursing, 21, 1024-1032, 2012	Non-randomised study
Bell,K.J., Barclay,A.W., Petocz,P., Colagiuri,S., Brand-Miller,J.C., Efficacy of carbohydrate counting in type 1 diabetes: a systematic review and meta-analysis, The Lancet Diabetes and Endocrinology, 2, 133-140, 2014	Systematic review - only relevant paper included is Gilbertson 2001
Bishop,F.K., Maahs,D.M., Spiegel,G., Owen,D., Klingensmith,G.J., Bortsov,A., Thomas,J., Mayer-Davis,E.J., The carbohydrate counting in adolescents with type 1 diabetes (CCAT) study, Diabetes Spectrum, 22, 56-62, 2009	Not an RCT. Only assesses ability of children and young people to count carbohydrates, not outcomes associated with carbohydrate counting
Blazik,M., Pankowska,E., The impact of the bolus and food calculator "Diabetics" on decreasing postprandial glucose variability in children with type 1 diabetes treated with insulin pump: The results of RCT, Diabetologia, 54, S401-, 2011	Conference abstract
Buccino,J., Murray,K., Farmer,S., Assor,E., Daneman,D., Systematic review of the dietary management of children with type 1 diabetes, Canadian Journal of Diabetes, 28, 219-225, 2004	Systematic review. No relevant papers identified
Cadario,F., Prodam,F., Pasqualicchio,S., Bellone,S., Bonsignori,I., Demarchi,I., Monzani,A., Bona,G., Lipid profile and nutritional intake in children and adolescents with Type 1 diabetes improve after a structured dietician training to a Mediterranean-style diet, Journal of Endocrinological Investigation, 35, 160-168, 2012	Non-randomised study
Forsander,G., Malmodin,B., Eklund,C., Persson,B., Relationship between dietary intake in children with diabetes mellitus type I, their management at diagnosis, social factors, anthropometry and glycaemic control, Scandinavian Journal of Nutrition/Naringsforskning, 47, 75-84, 2003	PICO (Population Intervention Comparator Outcomes) not met - study examines different diabetic care programmes
Gilbertson,H.R., Brand-Miller,J.C., Thorburn,A.W., Evans,S., Chondros,P., Werther,G.A., Erratum: The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycemic control in children with type 1 diabetes (Diabetes Care [2001] 24 [1137-1143]), Diabetes Care, 36, 1056-, 2013	Erratum for excluded study only
Gilbertson,H.R., Brand-Miller,J.C., Thorburn,A.W., Evans,S., Chondros,P., Werther,G.A., The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycemic control in children with type 1 diabetes, Diabetes Care, 24, 1137-1143, 2001	PICO not met - study did not examine carbohydrate counting
Goksen,D., Darcan,S., Buyukinan,M., Kose,T., Erermis,S., Coker,M., The effect of insulin glargine and nutritional model on metabolic control, quality of life and behavior in children and adolescents with type 1 diabetes mellitus, Acta Diabetologica, 45, 47-52, 2008	Non-randomised study
Goksen,D., Ozen,S., Atik,AltinokY, Demir,G., Darcan,S., Effects of carbohydrate counting method on metabolic control in children with type 1 diabetes, Pediatric Diabetes, 13, 142-, 2012	Conference abstract only, therefore insufficient data for inclusion
Hayes,R.L., Garnett,S.P., Clarke,S.L., Harkin,N.M., Chan,A.K., Ambler,G.R., A flexible diet using an insulin to carbohydrate ratio for adolescents with type 1 diabetes - a pilot study, Clinical Nutrition, 31, 705-709, 2012	Longitudinal study, not an RCT

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Study	Reason for exclusion
Kaufman,F.R., Halvorson,M., Carpenter,S., Use of a plastic insulin dosage guide to correct blood glucose levels out of the target range and for carbohydrate counting in subjects with type 1 diabetes, Diabetes Care, 22, 1252-1257, 1999	PICO not met - study examined two different methods of calculating insulin based on carbohydrate counting and both groups used carbohydrate counting
Kawamura,T., The importance of carbohydrate counting in the treatment of children with diabetes, Pediatric Diabetes, 8, 57-62, 2007	Narrative review of carbohydrate counting
Lowe,J., Linjawi,S., Mensch,M., James,K., Attia,J., Flexible eating and flexible insulin dosing in patients with diabetes: Results of an intensive self-management course, Diabetes Research and Clinical Practice, 80, 439-443, 2008	Non-randomised study
Maffeis,C., Morandi,A., Ventura,E., Sabbion,A., Contreas,G., Tomasselli,F., Tommasi,M., Fasan,I., Costantini,S., Pinelli,L., Diet, physical, and biochemical characteristics of children and adolescents with type 1 diabetes: Relationship between dietary fat and glucose control, Pediatric Diabetes, 13, 137-146, 2012	Non-randomised study
Marigliano,M., Morandi,A., Maschio,M., Sabbion,A., Contreas,G., Tomasselli,F., Tommasi,M., Maffeis,C., Nutritional education and carbohydrate counting in children with type 1 diabetes treated with continuous subcutaneous insulin infusion: the effects on dietary habits, body composition and glycometabolic control, Acta Diabetologica, 50, 959-964, 2013	Not an RCT - longitudinal study
Marquard,J., Stahl,A., Lerch,C., Wolters,M., Grotzke-Leweling,M., Mayatepek,E., Meissner,T., A prospective clinical pilot-trial comparing the effect of an optimized mixed diet versus a flexible low-glycemic index diet on nutrient intake and HbA1c levels in children with type 1 diabetes, Journal of Pediatric Endocrinology and Metabolism, 24, 441-447, 2011	PICO not met - study did not examine carbohydrate counting
Rabbone,I., Scaramuzza,A.E., Ignaccolo,M.G., Tinti,D., Sicignano,S., Redaelli,F., De,Angelis L., Bosetti,A., Zuccotti,G.V., Cerutti,F., Carbohydrate counting with an automated bolus calculator helps to improve glycaemic control in children with type 1 diabetes using multiple daily injection therapy: an 18-month observational study, Diabetes Research and Clinical Practice, 103, 388-394, 2014	Observational study
Riccardi,G., Giacco,R., Parillo,M., Turco,S., Rivellese,A.A., Ventura,M.R., Contadini,S., Marra,G., Monteduro,M., Santeusanio,F., Brunetti,P., Librenti,M.C., Pontiroli,A.E., Vedani,P., Pozza,G., Bergamini,L., Bianchi,C., Efficacy and safety of acarbose in the treatment of Type 1 diabetes mellitus: a placebo-controlled, double-blind, multicentre study, Diabetic Medicine, 16, 228-232, 1999	PICO not met - study only included adults (aged between 18 and 65 years)
Schmidt,S., Meldgaard,M., Serifovski,N., Storm,C., Christensen,T.M., Gade-Rasmussen,B., Norgaard,K., Use of an automated bolus calculator in MDI-treated type 1 diabetes: the BolusCal Study, a randomized controlled pilot study, Diabetes Care, 35, 984-990, 2012	All participants aged >18 years
Spiegel,G., Bortsov,A., Bishop,F.K., Owen,D., Klingensmith,G.J., Mayer-Davis,E.J., Maahs,D.M., Randomized Nutrition Education Intervention to Improve Carbohydrate Counting in Adolescents with Type 1 Diabetes Study: Is More Intensive Education Needed?, Journal of the Academy of Nutrition and Dietetics, , 1736-1746, 2012	PICO not met - study examines carbohydrate counting in children and young people with poor carbohydrate counting accuracy
Waller,H., Eiser,C., Knowles,J., Rogers,N., Wharmby,S., Heller,S., Hall,C., Greenhalgh,S., Tinklin,T., Metcalfe,C., Millard,E., Parkin,V., Denial,M., Price,K., Pilot study of a novel educational programme for 11-16 year olds with type 1 diabetes mellitus: the KICk-OFF course, Archives of Disease in Childhood, 93, 927-931, 2008	Non-randomised pilot study for an RCT of carbohydrate counting and insulin dosage adjustment

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Study	Reason for exclusion
Brand-Miller,J., Hayne,S., Petocz,P., Colagiuri,S., Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials, Diabetes Care, 26, 2261-2267, 2003	Meta-analysis of trials of low glycaemic index diets. Studies included predominantly adults. Two studies identified which relate to children: Gilbertson, Collier
Buccino,J., Murray,K., Farmer,S., Assor,E., Daneman,D., Systematic review of the dietary management of children with type 1 diabetes, Canadian Journal of Diabetes, 28, 219-225, 2004	Systematic review that identifies no new studies
Forsander,G., Malmodin,B., Eklund,C., Persson,B., Relationship between dietary intake in children with diabetes mellitus type I, their management at diagnosis, social factors, anthropometry and glycaemic control, Scandinavian Journal of Nutrition/Naringsforskning, 47, 75-84, 2003	PICO (Population Intervention Comparator Outcomes) not met - study examines different diabetic care programmes

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Gilbertson,H.R., Thorburn,A.W., Brand-Miller,J.C., Chondros,P., Werther,G.A., Effect of low-glycemic-index dietary advice on dietary quality and food choice in children with type 1 diabetes, American Journal of Clinical Nutrition, 77, 83-90, 2003	Secondary publication of an included study (Gilbertson 2001)
Marquard,J., Stahl,A., Lerch,C., Wolters,M., Grotzke-Leweling,M., Mayatepek,E., Meissner,T., A prospective clinical pilot-trial comparing the effect of an optimized mixed diet versus a flexible low-glycemic index diet on nutrient intake and HbA1c levels in children with type 1 diabetes, Journal of Pediatric Endocrinology and Metabolism, 24, 441-447, 2011	PICO not met - study does not measure outcomes at >4 months
Nansel,T.R., Gellar,L., McGill,A., Effect of varying glycemic index meals on blood glucose control assessed with continuous glucose monitoring in youth with type 1 diabetes on basal-bolus insulin regimens, Diabetes Care, 31, 695-697, 2008	PICO not met - study does not measure outcomes at >4 months
Nansel,T.R., Gellar,L., Zeitzoff,L., Acceptability of lower glycemic index foods in the diabetes camp setting, Journal of Nutrition Education and Behavior, 38, 143-150, 2006	PICO not met - study does not measure outcomes at >4 months
Riccardi,G., Giacco,R., Parillo,M., Turco,S., Rivellese,A.A., Ventura,M.R., Contadini,S., Marra,G., Monteduro,M., Santeusanio,F., Brunetti,P., Librenti,M.C., Pontiroli,A.E., Vedani,P., Pozza,G., Bergamini,L., Bianchi,C., Efficacy and safety of acarbose in the treatment of Type 1 diabetes mellitus: a placebo-controlled, double-blind, multicentre study, Diabetic Medicine, 16, 228-232, 1999	PICO not met - population aged between 18 and 65 years
Rovner,A.J., Nansel,T.R., Gellar,L., The effect of a low-glycemic diet versus a standard diet on blood glucose levels and macronutrient intake in children with type 1 diabetes, Journal of the American Dietetic Association, 109, 303-307, 2009	PICO not met - study does not measure outcomes at >4 months
Ryan,R.L., King,B.R., Anderson,D.G., Attia,J.R., Collins,C.E., Smart,C.E., Influence of and optimal insulin therapy for a low-glycemic index meal in children with type 1 diabetes receiving intensive insulin therapy, Diabetes Care, 31, 1485-1490, 2008	PICO not met - study did not examine effectiveness of dietetic advice
Spiegel,G., Bortsov,A., Bishop,F.K., Owen,D., Klingensmith,G.J., Mayer-Davis,E.J., Maahs,D.M., Randomized Nutrition Education Intervention to Improve Carbohydrate Counting in Adolescents with Type 1 Diabetes Study: Is More Intensive Education Needed?, Journal of the Academy of Nutrition and Dietetics, , 1736-1746, 2012	PICO not met - study examines two forms of carbohydrate counting not glycaemic index

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H.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Study	Reason for exclusion
Bashford,James, Acerini,Carlo L., How to use near-patient capillary ketone meters, Archives of disease in childhood - Education & practice edition, 97, 217-221, 2012	Review article.
Bektas,F., Eray,O., Sari,R., Akbas,H., Point of care blood ketone testing of diabetic patients in the emergency department, Endocrine Research, 30, 395-402, 2004	PICO not met - adult participants only.
Bilan,N., Behbahan,A.G., Khosroshahi,A.J., Validity of venous blood gas analysis for diagnosis of acid-base imbalance in children admitted to pediatric intensive care unit, World Journal of Pediatrics, 4, 114-117, 2008	PICO not met - assesses correlation of arterial and venous blood gas measurement, but no reference to diagnosing DKA
Charles,R.A., Bee,Y.M., Eng,P.H., Goh,S.Y., Point-of-care blood ketone testing: screening for diabetic ketoacidosis at the emergency department, Singapore Medical Journal, 48, 986-989, 2007	PICO not met - no age restriction, but median age 60 years.
Ham,M.R., Okada,P., White,P.C., Bedside ketone determination in diabetic children with hyperglycemia and ketosis in the acute care setting, Pediatric Diabetes, 5, 39-43, 2004	PICO not met - outcomes of interest not reported, and not able to be calculated from data provided. Article only describes positive and negative predictive values. Cannot define 2×2 table to calculate other measures of diagnostic test accuracy.

Harris,S., Ng,R., Syed,H., Hillson,R., Near patient blood ketone measurements and their utility in predicting diabetic ketoacidosis, Diabetic Medicine, 22, 221-224, 2005	PICO not met - no age inclusion criteria. Age range in study 16 to 93 years but results for those aged <18 years not presented separately.
Hendey,G.W., Schwab,T., Soliz,T., Urine ketone dip test as a screen for ketonemia in diabetic ketoacidosis and ketosis in the emergency department, Annals of Emergency Medicine, 29, 735-738, 1997	PICO not met - participant mean age was 38 years, although range was 14 to 80 years. Number of participants under 18 years not reported. Results for participants under 18 years not reported separately.
Nadler,O.A., Finkelstein,M.J., Reid,S.R., How well does serum bicarbonate concentration predict the venous pH in children being evaluated for diabetic ketoacidosis?, Pediatric Emergency Care, 27, 907-910, 2011	PICO not met - outcomes of interest not reported, and not able to be calculated from data provided.
Naunheim,R., Jang,T.J., Banet,G., Richmond,A., McGill,J., Point-of-care test identifies diabetic ketoacidosis at triage, Academic Emergency Medicine, 13, 683-685, 2006	PICO not met - adult participants only.
Qiao,Y., Gao,Z., Liu,Y., Cheng,Y., Yu,M., Zhao,L., Duan,Y., Breath ketone testing: A new biomarker for diagnosis and therapeutic monitoring of diabetic ketosis, BioMed Research International, 2014 , 2014. Article Number, -, 2014	PICO not met - age range in study 11 to 85 years but results for those aged <18 years not presented separately.
Schwab,T.M., Hendey,G.W., Soliz,T.C., Screening for ketonemia in patients with diabetes, Annals of Emergency Medicine, 34, 342-346, 1999	PICO not met - adult participants only.

H.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**
- **acid/base status?**

These 3 questions were addressed through a single search and there is one combined list of excluded studies.

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Study	Reason for exclusion
Fagan,M.J., Avner,J., Khine,H., Initial fluid resuscitation for patients with diabetic ketoacidosis: how dry are they?, Clinical Pediatrics, 47, 851-855, 2008	Not a comparative study
Felner,E.I., White,P.C., Improving management of diabetic ketoacidosis in children, Pediatrics, 108, 735-740, 2001	PICO not met - intervention (two different DKA management protocols) not of interest

Study	Reason for exclusion
Glaser,N.S., Ghetti,S., Casper,T.C., Dean,J.M., Kuppermann,N., Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID Study Group., Pediatric diabetic ketoacidosis, fluid therapy, and cerebral injury: the design of a factorial randomized controlled trial, Pediatric Diabetes, 14, 435-446, 2013	Not a comparative study
Harris,G.D., Fiordalisi,I., Physiologic management of diabetic ketoacidemia. A 5-year prospective pediatric experience in 231 episodes, Archives of Pediatrics and Adolescent Medicine, 148, 1046-1052, 1994	Not a comparative study
Harrower,A.D., Campbell,I.W., Ewing,D.J., Murray,A., Neilson,J.M., Clarke,B.F., The value of continuous ECG monitoring during treatment of diabetic ketoacidosis. A computer study, Acta Diabetologica Latina, 15, 88-94, 1978	PICO not met - population were mainly adults
Jahagirdar,R.R., Khadilkar,V.V., Khadilkar,A.V., Lalwani,S.K., Management of diabetic ketoacidosis in PICU, Indian Journal of Pediatrics, 74, 551-554, 2007	Not a comparative study
Klocker,A.A., Phelan,H., Twigg,S.M., Craig,M.E., Blood beta-hydroxybutyrate versus urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review, Diabetic Medicine, 30, 818-824, 2013	Systematic review of blood versus urine ketone testing
Koves,I.H., Neutze,J., Donath,S., Lee,W., Werther,G.A., Barnett,P., Cameron,F.J., The accuracy of clinical assessment of dehydration during diabetic ketoacidosis in childhood, Diabetes Care, 27, 2485-2487, 2004	Not a comparative study
Ma,O.J., Rush,M.D., Godfrey,M.M., Gaddis,G., Arterial blood gas results rarely influence emergency physician management of patients with suspected diabetic ketoacidosis, Academic Emergency Medicine, 10, 836-841, 2003	Not a comparative study
McBride,M.E., Berkenbosch,J.W., Tobias,J.D., Transcutaneous carbon dioxide monitoring during diabetic ketoacidosis in children and adolescents, Paediatric Anaesthesia, 14, 167-171, 2004	PICO not met - interventions (different methods of carbon dioxide monitoring) not of interest
Naunheim,R., Jang,T.J., Banet,G., Richmond,A., McGill,J., Point-of-care test identifies diabetic ketoacidosis at triage, Academic Emergency Medicine, 13, 683-685, 2006	Not a comparative study
Rewers,A., McFann,K., Chase,H.P., Bedside monitoring of blood beta-hydroxybutyrate levels in the management of diabetic ketoacidosis in children, Diabetes Technology and Therapeutics, 8, 671-676, 2006	Not a comparative study
Sottosanti,M., Morrison,G.C., Singh,R.N., Sharma,A.P., Fraser,D.D., Alawi,K., Seabrook,J.A., Kornecki,A., Dehydration in children with diabetic ketoacidosis: a prospective study, Archives of Disease in Childhood, 97, 96-100, 2012	Not a comparative study
Turan,S., Omar,A., Bereket,A., Comparison of capillary blood ketone measurement by electrochemical method and urinary ketone in treatment of diabetic ketosis and ketoacidosis in children, Acta Diabetologica, 45, 83-85, 2008	PICO not met - outcomes of interest not reported
Wootton-Gorges,S.L., Buonocore,M.H., Kuppermann,N., Marcin,J., Dicarlo,J., Neely,E.K., Barnes,P.D., Glaser,N., Detection of cerebral {beta}-hydroxy butyrate, acetoacetate, and lactate on proton MR spectroscopy in children with diabetic ketoacidosis, Ajnr: American Journal of Neuroradiology, 26, 1286-1291, 2005	Not a comparative study

Update 2015

H.12 Type 1 and type 2 diabetes – diabetic ketoacidosis- fluids

Review questions

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

No articles were ordered for detailed consideration for this review question and so there is no excluded studies list.

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

Study	Reason for exclusion
Carcillo,J.A., Intravenous fluid choices in critically ill children, Current Opinion in Critical Care, 20, 396-401, 2014	Discussion paper for reference checking. Relevant studies have been included in the guideline review.
Duck,S.C., Wyatt,D.T., Factors associated with brain herniation in the treatment of diabetic ketoacidosis, Journal of Pediatrics, 113, 10-14, 1988	Not a comparative study.
Hom,J., Sinert,R., Evidence-based emergency medicine/critically appraised topic. Is fluid therapy associated with cerebral edema in children with diabetic ketoacidosis?. [12 refs], Annals of Emergency Medicine, 52, 69-75, 2008	Systematic review which includes papers already identified in the guideline search results.
Mel,J.M., Werther,G.A., Incidence and outcome of diabetic cerebral oedema in childhood: are there predictors?, Journal of Paediatrics and Child Health, 31, 17-20, 1995	Assesses risk factors for, and survival after, cerebral oedema. No comparison of the different fluid protocols.

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Study	Reason for exclusion
Basnet,S., Venepalli,P.K., Andoh,J., Verhulst,S., Koirala,J., Effect of normal saline and half normal saline on serum electrolytes during recovery phase of diabetic ketoacidosis, Journal of Intensive Care Medicine, 29, 38-42, 2014	Normal saline was compared with half-normal saline; no additives of interest to the guideline development group were assessed.
Duck,S.C., Wyatt,D.T., Factors associated with brain herniation in the treatment of diabetic ketoacidosis, Journal of Pediatrics, 113, 10-14, 1988	Not a comparative study.
Hale,P.J., Crase,J., Nattrass,M., Metabolic effects of bicarbonate in the treatment of diabetic ketoacidosis, British Medical Journal Clinical Research Ed., 289, 1035-1038, 1984	PICO not met: adult population, mean ages of 47 years and 41 years for each treatment group.
Krumlik,J.J., Ehrlich,R.M., Insulin and sodium bicarbonate treatment of diabetic acidosis: a retrospective review, Journal of Pediatrics, 83, 269-271, 1973	No comparative analysis of different fluid compositions.
Reddy,C.M., Orti,E., Crump,E.P., Treatment of diabetic ketoacidosis in children: A retrospective review, Clinical Research, 25, 68A-, 1977	Duplicate of previously weeded-out study with different title - abstract only.
Rother,K.I., Schwenk,W.F., Effect of rehydration fluid with 75 mmol/L of sodium on serum sodium concentration and serum osmolality in young patients with diabetic ketoacidosis, Mayo Clinic Proceedings, 69, 1149-1153, 1994	Not a comparative study.
Soler,N.G., Bennett,M.A., Dixon,K., Fitzgerald,M.G., Malins,J.M., Potassium balance during treatment of diabetic ketoacidosis with special reference to the use of bicarbonate, Lancet, 2, 665-667, 1972	PICO not met: adult population, age range 13 to 84 years. No subgroup analyses for age group of relevance in this guideline.
Thuzar,M., Malabu,U.H., Tisdell,B., Sangla,K.S., Use of a standardised diabetic ketoacidosis management protocol improved clinical outcomes, Diabetes Research and Clinical Practice, 104, E8-E11, 2014	Patients ≥16 years were included (mean age 30 years)
Toledo,J.D., Modesto,V., Peinador,M., Alvarez,P., Lopez-Prats,J.L., Sanchis,R., Vento,M., Sodium concentration in rehydration fluids for children with ketoacidotic diabetes: effect on serum sodium concentration, Journal of Pediatrics, 154, 895-900, 2009	Not a comparative study. Regression analysis only.
White,P.C., Dickson,B.A., Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids.[Erratum appears in J Pediatr. 2013 Sep;163(3):927], Journal of Pediatrics, 163, 761-766, 2013	The dextrose assessed in this study, which is a type of additive, was not included in the protocol.
Wilson,H.K., Keuer,S.P., Lea,A.S., Boyd,A.E.,III, Eknoyan,G., Phosphate therapy in diabetic ketoacidosis, Archives of Internal Medicine, 142, 517-520, 1982	PICO not met: adult population, mean age 26.8 years, range 14 to 58 years.

Update 2015

H.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Study	Reason for exclusion
Treating diabetic ketoacidosis in children requires careful management of fluid, electrolytes and insulin, Drugs and Therapy Perspectives, 25, 14-17, 2009	Management article
Rosenbloom,A.L., Cerebral edema in diabetic ketoacidosis and other acute devastating complications: Recent observations, Pediatric Diabetes, 6, 41-49, 2005	A review of reports
Rosenbloom,A.L., Intracerebral crises during treatment of diabetic ketoacidosis, Diabetes Care, 13, 22-33, 1990	Review of unpublished case records and published reports
Sherry,N.A., Levitsky,L.L., Management of diabetic ketoacidosis in children and adolescents. [49 refs], Paediatric Drugs, 10, 209-215, 2008	Exclude since it is a management article (used for checking references)
Tasker,R.C., Burns,J., Hypertonic saline therapy for cerebral edema in diabetic ketoacidosis: no change yet, please, Pediatric Critical Care Medicine, 15, 284-285, 2014	For reference checking
White,P.C., Dickson,B.A., Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids, Journal of Pediatrics, 163, 761-766, 2013	Case series
Wolfsdorf,J., Craig,M.E., Daneman,D., Dunger,D., Edge,J., Lee,W., Rosenbloom,A., Sperling,M., Hanas,R., Diabetic ketoacidosis in children and adolescents with diabetes, Pediatric Diabetes, 10, 118-133, 2009	Clinical practice consensus guidelines compendium

H.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

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Review question: When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

All articles order for detailed consideration for this review question were included in the review and so there is no excluded studies list.

Review question: How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

All articles order for detailed consideration for this review question were included in the review and so there is no excluded studies list.

H.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

No articles were ordered for detailed consideration for this review question and so there is no excluded studies list.

H.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Study	Reason for exclusion
When to screen for retinopathy in children with diabetes, Consultant, 38, 1320-, 1998	Summary of American Academy of Pediatrics guidelines only; no data reported
Progression of retinopathy with intensive versus conventional treatment in the Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group, Ophthalmology, 102, 647-661, 1995	Mean age 26.4 years; data on children and young people reported separately in an included study
Aiello,L.P., Diabetic retinopathy and other ocular findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study, Diabetes Care, 37, 17-23, 2014	No stratification by age; full DCCT cohort, therefore, mean age >18 years
Al-Fifi,S.H., Intensive insulin treatment versus conventional regimen for adolescents with type 1 diabetes, benefits and risks, Saudi Medical Journal, 24, 485-487, 2003	Population included 12 to 18 year-olds; no stratification of prevalence of retinopathy within this age range
Amutha,A., Datta,M., Unnikrishnan,R., Anjana,R.M., Mohan,V., Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India, Diabetes Technology and Therapeutics, 14, 497-504, 2012	No data on prevalence of retinopathy according to age or duration of diabetes
Betts,P.R., Logatchov,M., Volkov,I., Murphy,H., Dombrowskaya,N., Borzikh,S., Ivanova,I., Twyman,S., Vartan,J., An assessment of paediatric diabetes care in three centres in Russia and in Southampton, UK. The Paediatric Teams in Moscow, Tula, Tambov, Southampton, Diabetic Medicine, 16, 772-778, 1999	No stratification according to age or duration of diabetes; method of identifying retinopathy not reported
Bognetti,E., Calori,G., Meschi,F., Macellaro,P., Bonfanti,R., Chiumello,G., Prevalence and correlations of early microvascular complications in young type I diabetic patients: role of puberty, Journal of Pediatric Endocrinology, 10, 587-592, 1997	No stratification of prevalence according to age or duration of diabetes
Bonney,M., Hing,S.J., Fung,A.T., Stephens,M.M., Fairchild,J.M., Donaghue,K.C., Howard,N.J., Silink,M., Development and progression of diabetic retinopathy: adolescents at risk, Diabetic Medicine, 12, 967-973, 1995	Incidence data already included in Cheung 2008, and prevalence according to age already included in Cho 2011
Burger,W., Hovener,G., Dusterhus,R., Hartmann,R., Weber,B., Prevalence and development of retinopathy in children and adolescents with type 1 (insulin-dependent) diabetes mellitus. A longitudinal study, Diabetologia, 29, 17-22, 1986	Fluoroscein angiography used to identify retinopathy
Cahill,M., Wallace,D., Travers,S., Lipinski,H., Aldington,S., Costigan,C., Mooney,D., Detection and prevalence of early diabetic retinopathy in juvenile diabetics with diabetes for 10 years or more, Eye, 14, 847-850, 2000	No stratification of retinopathy prevalence within age group (population age range 11.4 to 22.6 years)
Chiumello,G., Bognetti,E., Meschi,F., Carra,M., Balzano,E., Early diagnosis of subclinical complications in insulin dependent diabetic children and adolescents, Journal of Endocrinological Investigation, 12, 101-104, 1989	Prevalence of retinopathy not grouped according to age or duration of diabetes; method of identifying retinopathy not reported
Cobuz,M., Cobuz,C., Chronic complications of type 1 diabetes mellitus in children, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 19, 301-309, 2012	Ophthalmoscopy used to identify retinopathy; no stratification of prevalence according to age or duration of diabetes
Danne,T., Kordonouri,O., Casani,A., Tumini,S., Chiarelli,F., Recent advances on the pathogenesis and management of both diabetic retinopathy and nephropathy with particular reference to children and adolescents with Type 1 diabetes. [87 refs], Diabetes, Nutrition and Metabolism - Clinical and Experimental, 12, 136-144, 1999	Narrative review
Dart,A.B., Martens,P.J., Rigatto,C., Brownell,M.D., Dean,H.J., Sellers,E.A., Earlier onset of complications in youth with type 2 diabetes, Diabetes Care, 37, 436-443, 2014	No stratification by age
Demirel,F., Tepe,D., Kara,O., Esen,I., Microvascular complications in adolescents with type 1 diabetes mellitus, JCRPE Journal of Clinical Research in Pediatric Endocrinology, 5, 145-149, 2013	No stratification by age or duration of diabetes
Donaghue,K.C., Chiarelli,F., Trotta,D., Allgrove,J., hl-Jorgensen,K., Microvascular and macrovascular complications associated with diabetes in children and adolescents, Pediatric Diabetes, 10, 195-203, 2009	Clinical guideline, no primary data
Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005	Prevalence of retinopathy recorded according to age, but data only provided graphically therefore unable to determine exact numbers
Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003	No data on prevalance stratified by age or duration of diabetes

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Study	Reason for exclusion
Donaghue,K.C., Fung,A.T., Hing,S., Fairchild,J., King,J., Chan,A., Howard,N.J., Silink,M., The effect of prepubertal diabetes duration on diabetes. Microvascular complications in early and late adolescence, Diabetes Care, 20, 77-80, 1997	No stratification of prevalence according to age or duration of diabetes
Donaghue,K.C., Fairchild,J.M., Chan,A., Hing,S.J., King,J., Howard,N.J., Silink,M., Diabetes microvascular complications in prepubertal children, Journal of Pediatric Endocrinology, 10, 579-585, 1997	Background population identical to that used in Donaghue et 1999
Downie,E., Craig,M.E., Hing,S., Cusumano,J., Chan,A.K., Donaghue,K.C., Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glycemic control, Diabetes Care, 34, 2368-2373, 2011	No data on prevalence of retinopathy according to age or duration of diabetes
El,AsrarM, Adly,A.A., El,HadidyE, Abdelwahab,M.A., D-dimer levels in type 1 and type 2 diabetic children and adolescents; Relation to microvascular complications and dyslipidemia "own data and review", Pediatric endocrinology reviews : PER, 9, 657-668, 2012	Ophthalmoscopy used to identify retinopathy; no stratification of prevalence according to age or duration of diabetes
Eppens,M.C., Craig,M.E., Cusumano,J., Hing,S., Chan,A.K., Howard,N.J., Silink,M., Donaghue,K.C., Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes, Diabetes Care, 29, 1300-1306, 2006	No assessment of prevalence of retinopathy according to age or duration of diabetes
Fairchild,J.M., Hing,S.J., Donaghue,K.C., Bonney,M.A., Fung,A.T., Stephens,M.M., Mitchell,P., Howard,N.J., Silink,M., Prevalence and risk factors for retinopathy in adolescents with type 1 diabetes, Medical Journal of Australia, 160, 757-762, 1994	No assessment of prevalence according to age or duration of diabetes
Falck,A.A., Kaar,M.L., Laatikainen,L.T., Prevalence and risk factors of retinopathy in children with diabetes. A population-based study on Finnish children, Acta Ophthalmologica, 71, 801-809, 1993	Data already included in Falck 1996
Florkowski,C.M., Scott,R.S., Coope,P.A., Graham,P.J., Moir,C.L., Age at diagnosis, glycaemic control and the development of retinopathy in a population-based cohort of Type 1 diabetic subjects in Canterbury, New Zealand, Diabetes Research and Clinical Practice, 52, 125-131, 2001	Ophthalmoscopy used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Frank,R.N., Hoffman,W.H., Podgor,M.J., Joondeph,H.C., Lewis,R.A., Margherio,R.R., Nachazel,D.P.,Jr., Weiss,H., Christopherson,K.W., Cronin,M.A., Retinopathy in juvenile-onset diabetes of short duration, Ophthalmology, 87, 1-9, 1980	Data already included in Frank 1982
Gallego,P.H., Craig,M.E., Hing,S., Donaghue,K.C., Role of blood pressure in development of early retinopathy in adolescents with type 1 diabetes: Prospective cohort study, BMJ, 337, 497-500, 2008	No stratification of prevalence according to age or duration of diabetes
Hammes,H.P., Kerner,W., Hofer,S., Kordonouri,O., Raile,K., Holl,R.W., DPV-Wiss Study Group., Diabetic retinopathy in type 1 diabetes-a contemporary analysis of 8,784 patients, Diabetologia, 54, 1977-1984, 2011	Ophthalmoscopy used to identify retinopathy; no stratification according to age or prevalence of diabetes
Holl,R.W., Lang,G.E., Grabert,M., Heinze,E., Lang,G.K., Debatin,K.M., Diabetic retinopathy in pediatric patients with type-1 diabetes: effect of diabetes duration, prepubertal and pubertal onset of diabetes, and metabolic control, Journal of Pediatrics, 132, 790-794, 1998	No assessment of prevalence of retinopathy according to age or duration of diabetes; data presented only graphically
Huo,B., Steffen,A.T., Swan,K., Sikes,K., Weinzimer,S.A., Tamborlane,W.V., Clinical outcomes and cost-effectiveness of retinopathy screening in youth with type 1 diabetes, Diabetes Care, 30, 362-363, 2007	Opthalmoscopy used to identify retinopathy; no data on prevalence of retinopathy according to age or duration of diabetes
itez-Aguirre,P., Craig,M.E., Sasongko,M.B., Jenkins,A.J., Wong,T.Y., Wang,J.J., Cheung,N., Donaghue,K.C., Retinal vascular geometry predicts incident retinopathy in young people with type 1 diabetes: a prospective cohort study from adolescence, Diabetes Care, 34, 1622-1627, 2011	No stratification according to age or duration of diabetes
Izumi,K., Hoshi,M., Kuno,S., Okuno,G., Yamazaki,Y., Isshiki,G., Sasaki,A., Glycemic control, growth and complications in children with insulin-dependent diabetes mellitus--a study of children enrolled in a Summer camp program for diabetics in Kinki district, Japan, Diabetes Research and Clinical Practice, 28, 185-190, 1995	Method of assessment of retinopathy not reported; no assessment of prevalence according to age or duration of diabetes
Jackson,R.L., Ide,C.H., Guthrie,R.A., James,R.D., Retinopathy in adolescents and young adults with onset of insulin-dependent diabetes in childhood, Ophthalmology, 89, 7-13, 1982	No assessment of prevalence of reetinopathy according to age or duration of diabetes
Johnson,B., Elliott,J., Scott,A., Heller,S., Eiser,C., Medical and psychological outcomes for young adults with Type 1 diabetes: No improvement despite recent advances in diabetes care, Diabetic Medicine, 31, 227-231, 2014	Mean age 18.1 years; no stratification by age group
Kalter-Leibovici,O., Leibovici,L., Loya,N., Kremer,I., xer-Siegel,R., Karp,M., Laron,Z., The development and progression of diabetic retinopathy in type I diabetic patients: a cohort study, Diabetic Medicine, 14, 858-866, 1997	Retinal photography only obtained when fundoscopy suggested abnormalities; prevalence not stratified by age or duration of diabetes
Kanematsu,S., Maruyama,H., Ishiba,S., Uchigata,Y., Otani,T., K,asaharaT., Yao,K., Kameyama,K., Omori,Y., Fukuyama,Y., Hirata,Y., Onset and prevalence of retinopathy in insulin-dependent diabetic Japanese children, Current status of prevention and treatment of diabetic complications: proceedings of the Third International Symposium on treatment of Diabetes Mellitus, 501-505, 1990	All participants >20 years old at time of examination
Klein,B.E., Moss,S.E., Klein,R., Is menarche associated with diabetic retinopathy?, Diabetes Care, 13, 1034-1038, 1990	No stratification of prevalence of retinopathy according to age or duration of diabetes

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Study	Reason for exclusion
Klein,R., Klein,B.E., Moss,S.E., Davis,M.D., DeMets,D.L., Retinopathy in young-onset diabetic patients, Diabetes Care, 8, 311-315, 1985	Data were obtained from same background population as Klein 1984, therefore already included in guideline review via that article
Kong,A., Donath,S., Harper,C.A., Werther,G.A., Cameron,F.J., Rates of diabetes mellitus-related complications in a contemporary adolescent cohort, Journal of Pediatric Endocrinology, 18, 247-255, 2005	Slit lamp examination/ophthalmoscopy only used to identify retinopathy
Kostraba,J.N., Dorman,J.S., Orchard,T.J., Becker,D.J., Ohki,Y., Ellis,D., Doft,B.H., Lobes,L.A., LaPorte,R.E., Drash,A.L., Contribution of diabetes duration before puberty to development of microvascular complications in IDDM subjects, Diabetes Care, 12, 686-693, 1989	No assessment of prevalence of retinopathy according to age or duration of diabetes, only according to puberty
Kovacs,M., Mukerji,P., Drash,A., Iyengar,S., Biomedical and psychiatric risk factors for retinopathy among children with IDDM, Diabetes Care, 18, 1592-1599, 1995	No stratification of prevalence of retinopathy according to age or duration of diabetes
Kubin,M., Tossavainen,P., Hannula,V., Lahti,S., Hautala,N., Falck,A., Prevalence of retinopathy in Finnish children and adolescents with type 1 diabetes: a cross-sectional population-based retrospective study, Archives of Disease in Childhood, 96, 963-968, 2011	No assessment of prevalence according to age or duration of diabetes
Lecaire,T., Palta,M., Zhang,H., Allen,C., Klein,R., D'Alessio,D., Lower-than-expected prevalence and severity of retinopathy in an incident cohort followed during the first 4-14 years of type 1 diabetes: the Wisconsin Diabetes Registry Study, American Journal of Epidemiology, 164, 143-150, 2006	Data on prevalence of retinopathy according to age and duration of diabetes reported only in graphical form
Levy-Shraga,Y., Lerner-Geva,L., Boyko,V., Graph-Barel,C., Mazor-Aronovitch,K., Modan-Moses,D., Pinhas-Hamiel,O., Type 1 diabetes in pre-school children--long-term metabolic control, associated autoimmunity and complications, Diabetic Medicine, 29, 1291-1296, 2012	No assessment of prevalence according to age or duration of diabetes; method of identifying retinopathy not reported
Lievre,M., Marre,M., Robert,J.J., Charpentier,G., Iannascoli,F., Passa,P., Cross-sectional study of care, socio-economic status and complications in young French patients with type 1 diabetes mellitus, Diabetes and Metabolism, 31, 41-46, 2005	Method of identifying retinopathy not reported; no assessment of prevalence according to age or duration of diabetes
Lim,S.W., Cheung,N., Wang,J.J., Donaghue,K.C., Liew,G., Islam,F.M., Jenkins,A.J., Wong,T.Y., Retinal vascular fractal dimension and risk of early diabetic retinopathy: A prospective study of children and adolescents with type 1 diabetes, Diabetes Care, 32, 2081-2083, 2009	No stratification according to age or duration of diabetes
Lueder,G.T., Pradhan,S., White,N.H., Risk of retinopathy in children with type 1 diabetes mellitus before 2 years of age, American Journal of Ophthalmology, 140, 930-931, 2005	Retinopathy identified with ophthalmoscopy
Maguire,A., Chan,A., Cusumano,J., Hing,S., Craig,M., Silink,M., Howard,N., Donaghue,K., The case for biennial retinopathy screening in children and adolescents.[Erratum appears in Diabetes Care. 2007 Apr;30(4):1035], Diabetes Care, 28, 509-513, 2005	Duplication of data already included in Donaghue 1999
Malone,J.I., Grizzard,S., Espinoza,L.R., Achenbach,K.E., Van Cader,T.C., Risk factors for diabetic retinopathy in youth, Pediatrics, 73, 756-761, 1984	Fluoroscein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Mayer-Davis,E.J., Davis,C., Saadine,J., D'Agostino,R.B.,Jr., Dabelea,D., Dolan,L., Garg,S., Lawrence,J.M., Pihoker,C., Rodriguez,B.L., Klein,B.E., Klein,R., SEARCH for Diabetes in Youth Study Group., Diabetic retinopathy in the SEARCH for Diabetes in Youth Cohort: a pilot study, Diabetic Medicine, 29, 1148-1152, 2012	Age of participants not reported; prevalence of retinopathy not reported according to age or duration of diabetes
Minuto,N., Emmanuele,V., Vannati,M., Russo,C., Rebora,C., Panarello,S., Pistorio,A., Lorini,R., d'Annunzio,G., Retinopathy screening in patients with type 1 diabetes diagnosed in young age using a non-mydriatic digital stereoscopic retinal imaging, Journal of Endocrinological Investigation, 35, 389-394, 2012	No stratification of results according to age or duration of diabetes
Mohsin,F., Craig,M.E., Cusumano,J., Chan,A.K., Hing,S., Lee,J.W., Silink,M., Howard,N.J., Donaghue,K.C., Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002, Diabetes Care, 28, 1974-1980, 2005	No stratification of prevalence of retinopathy according to age or duration of diabetes
Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,C., Christova,P., Relationship between anti-elastin IgG subclasses and the development of microvascular complications - A three-year follow-up study in children with Type 1 (insulin-dependent) diabetes mellitus, Central-European Journal of Immunology, 26, 12-16, 2001	No assessment of prevalence according to age or duration of diabetes
Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,Ch, Christova,P., An association of anti-elastin IgA antibodies with development of retinopathy in diabetic children, General Pharmacology: The Vascular System, 35, 83-87, 2000	Method of assessing retinopathy not reported; no assessment of prevalence according to age or duration of diabetes
North,R.V., Farrell,U., Banford,D., Jones,C., Gregory,J.W., Butler,G., Owens,D.R., Visual function in young IDDM patients over 8 years of age. A 4-year longitudinal study, Diabetes Care, 20, 1724-1730, 1997	Includes londitudinal data only but 13.5% of participants had retinopathy at baseline, and new incidence not reported; cannot assume new incidence for 4 years' follow up due to the potential for regression of retinopathy

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Study	Reason for exclusion
Olsen,B.S., Johannesen,J., Sjolie,A.K., Borch-Johnsen,K., Hougarrdss,P., Thorsteinsson,B., Prammingss,S., Marinelli,K., Mortensen,H.B., Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus. Danish Study Group of Diabetes in Childhood, Diabetic Medicine, 16, 79-85, 1999	Data on prevalence of retinopathy according to duration of diabetes presented only graphically; no data on prevalence stratified according to age
Owen,D.R., Farrell,U., Jones,C., North,R., Screening for diabetic retinopathy in young insulin-dependent diabetics (Type I), Pediatric Reviews and Communications, 8, 50-55, 1994	Data on prevalence of retinopathy at different ages reported only graphically; no data on prevalence after different durations of diabetes
Palmberg,P., Smith,M., Waltman,S., Krupin,T., Singer,P., Burgess,D., Wendtlant,T., Achtenberg,J., Cryer,P., Santiago,J., White,N., Kilo,C., Daughaday,W., The natural history of retinopathy in insulin-dependent juvenile-onset diabetes, Ophthalmology, 88, 613-618, 1981	Age of participants not reported; no assessment of prevalence according to age or duration of diabetes
Papali'i-Curtin,A.T., Dalziel,D.M., Prevalence of diabetic retinopathy and maculopathy in Northland, New Zealand: 2011-2012, New Zealand Medical Journal, 126, 20-28, 2013	Mean age 62.7 years
Raman,V., Campbell,F., Holland,P., Chapman,T., Dabbs,T., Bodansky,H.J., O'Neill,D.P., Retinopathy screening in children and adolescents with diabetes, Annals of the New York Academy of Sciences, 958, 387-389, 2002	No assessment of prevalence according to age or duration of diabetes
Rogers,D.G., White,N.H., Shalwitz,R.A., Palmberg,P., Smith,M.E., Santiago,J.V., The effect of puberty on the development of early diabetic microvascular disease in insulin-dependent diabetes, Diabetes Research and Clinical Practice, 3, 39-44, 1987	No assessment of prevalence according to age; although all participants had 5 to 7 years' duration of diabetes, the study did not include participants in puberty, or early post-pubertal stage therefore not representative of entire population of children and young people with type 1 diabetes
Salardi,S., Rubbi,F., Puglioli,R., Brancaleoni,A., Bacchi-Reggiani,L., Ragni,L., Cacciari,E., Diabetic retinopathy in childhood: long-term follow-up by fluorescein angiography beginning in the first months of disease, Journal of Pediatric Endocrinology, 14, 507-515, 2001	Fluoroscein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Shamoon,H., Duffy,H., Fleischer,N., Engel,S., Saenger,P., Strelyzn,M., Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H., Fleischman,J., Pompi,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E., Thomasunis,A., Gonzalez,J., The effect of intensive diabetes treatment on the progression of diabetic retinopathy in insulin-dependent diabetes mellitus: The diabetes control and complications trial, Archives of Ophthalmology, 113, 36-51, 1995	Mean age 26.5 years
Shamoon,H., Duffy,H., Fleischer,N., Engel,S., Saenger,P., Strelzyn,M., Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H., Fleischman,J., Pompi,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E., Thomashunis,A., Gonzalez,J., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, New England Journal of Medicine, 329, 977-986, 1993	Mean age for entire group was 26 /- 8 years (conventional treatment group) and 27 /- 7 years (intensive treatment group); data for age range of interest not reported separately
Verougstraete,C., Toussaint,D., De,SchepperJ, Haentjens,M., Dorchy,H., First microangiographic abnormalities in childhood diabetes - Types of lesions, Graefe's Archive for Clinical and Experimental Ophthalmology, 229, 24-32, 1991	Fluoroscein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999	Retinopathy assessed by ophthalmoscopy; mean age of participants 26.9 years
White,N.H., Cleary,P.A., Dahms,W., Goldstein,D., Malone,J., Tamborlane,W.V., Diabetes Control and Complications Trial (DCCT), Beneficial effects of intensive therapy of diabetes during adolescence: outcomes after the conclusion of the Diabetes Control and Complications Trial (DCCT), Journal of Pediatrics, 139, 804-812, 2001	No stratification of prevalence according to age or duration of diabetes
Wiltshire,E.J., Mohsin,F., Chan,A., Donaghue,K.C., Methylenetetrahydrofolate reductase and methionine synthase reductase gene polymorphisms and protection from microvascular complications in adolescents with type 1 diabetes, Pediatric Diabetes, 9, 348-353, 2008	No stratification of prevalence according to age or duration of diabetes

Update 2015

H.17 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Study	Reason for exclusion
Al-Agha,A.E., Ocheltree,A., Hakeem,A., Occurrence of microalbuminuria among children and adolescents with insulin-dependent diabetes mellitus, Saudi Journal of Kidney Diseases and Transplantation, 24, 1180-1188, 2013	Study from Saudi Arabia
Allen,T.J., Cooper,M.E., Gilbert,R.E., Winikoff,J., Skinni,S.L., Jerums,G., Serum total renin is increased before microalbuminuria in diabetes, Kidney International, 50, 902-907, 1996	Study involving adults
Alleyn,C.R., Volkening,L.K., Wolfson,J., Rodriguez-Ventura,A., Wood,J.R., Laffel,L.M., Occurrence of microalbuminuria in young people with Type 1 diabetes: importance of age and diabetes duration, Diabetic Medicine, 27, 532-537, 2010	The threshold (ACR >20 microg/mg)for confirmation of microalbuminuria used in the study corresponds to an ACR of >2.26 mg/mmol, which is lower than the UK standard of 2.5 mg/mmol for males and 3.5 mg/mmol for females
Amin,R., Bahu,T.K., Widmer,B., Dalton,R.N., Dunger,D.B., Longitudinal relation between limited joint mobility, height, insulin-like growth factor 1 levels, and risk of developing microalbuminuria: The Oxford Regional Prospective Study, Archives of Disease in Childhood, 90, 1039-1044, 2005	Only the numbers of microalbuminuria participants under or above 11 years were reported; no information about the population size in each age group and, therefore, prevalence cannot be calculated
Amin,R., Turner,C., Van,Aken S., Bahu,T.K., Watts,A., Lindsell,D.R., Dalton,R.N., Dunger,D.B., The relationship between microalbuminuria and glomerular filtration rate in young type 1 diabetic subjects: The Oxford Regional Prospective Study, Kidney International, 68, 1740-1749, 2005	Children and young people under 16 years diagnosed with type 1 diabetes were included; at 5 years' duration, when microalbuminuria was measured, some of them were already over 18 years
Amin,R., Widmer,B., Dalton,R.N., Dunger,D.B., Unchanged incidence of microalbuminuria in children with type 1 diabetes since 1986: a UK based inception cohort, Archives of Disease in Childhood, 94, 258-262, 2009	No cumulative prevalence before the age of 18 years was reported; prevalence by diabetes duration was reported in Kaplan-Meier graph only
Amin,R., Widmer,B., Prevost,A.T., Schwarze,P., Cooper,J., Edge,J., Marcovecchio,L., Neil,A., Dalton,R.N., Dunger,D.B., Risk of microalbuminuria and progression to macroalbuminuria in a cohort with childhood onset type 1 diabetes: prospective observational study, BMJ, 336, 697-701, 2008	Prevalence by age for all types of microalbuminuria(including intermittent and persistent) were reported together
Bakman,M., Yuksel,B., Topaloglu,A.K., Mungan,N.O., Ozer,G., Risk factors for microalbuminuria in children and adolescents with insulin dependent diabetes mellitus, Annals of Medical Sciences, 10, 156-159, 2001	Just an overall prevalence for all participants was reported, no stratification according to age
Barkai,L., Vamosi,I., Lukacs,K., Enhanced progression of urinary albumin excretion in IDDM during puberty, Diabetes Care, 21, 1019-1023, 1998	Just an overall prevalence was reported, no stratification according to age
Basiratnia,M., Abadi,S.F., Amirhakimi,G.H., Karamizadeh,Z., Karamifar,H., Ambulatory blood pressure monitoring in children and adolescents with type-1 diabetes mellitus and its relation to diabetic control and microalbuminuria, Saudi Journal of Kidney Diseases and Transplantation, 23, 311-315, 2012	Just an overall prevalence was reported, no stratification according to age
Bertalan,R., Gregory,J.W., Detecting diabetes complications in children, Practical Diabetes, 28, 352-357a, 2011	Background reading
Bojestig,M., Arnqvist,H.J., Karlberg,B.E., Ludvigsson,J., Unchanged incidence of severe retinopathy in a population of Type 1 diabetic patients with marked reduction of nephropathy, Diabetic Medicine, 15, 863-869, 1998	Only a cumulative incidence of nephropathy after 20 years' follow-up was reported
Bojestig,M., Arnqvist,H.J., Karlberg,B.E., Ludvigsson,J., Glycemic control and prognosis in type I diabetic patients with microalbuminuria, Diabetes Care, 19, 313-317, 1996	Just an overall prevalence was reported, no stratification according to age
Bruno,G., Pagano,G., Low prevalence of microalbuminuria in young Italian insulin-dependent diabetic patients with short duration of disease: a population-based study. Piedmont Study Group for Diabetes Epidemiology, Diabetic Medicine, 13, 889-893, 1996	Microalbuminuria was tested on 1 overnight urine sample only
Campbell,F.M., Microalbuminuria and nephropathy in insulin dependent diabetes mellitus, Archives of Disease in Childhood, 73, 4-7, 1995	Background reading
Chiarelli,F., Verrotti,A., Morgese,G., Glomerular hyperfiltration increases the risk of developing microalbuminuria in diabetic children, Pediatric Nephrology, 9, 154-158, 1995	Only participants with hyperfiltration >140 ml/minute per 1.73 square metres were included in the study to assess the development of microalbuminuria
Cizmecioglu,F.M., Noyes,K., Bath,L., Kelnar,C., Audit of microalbumin excretion in children with type I diabetes, Journal of clinical research in pediatric endocrinology, 1, 136-143, 2009	Just an overall prevalence for the age group 10 to 16 years was reported, no further stratification
Cobas,R.A., Santos,B., Da,SilvaP, Neves,R., Gomes,M.B., Progression to microalbuminuria in patients with type 1 diabetes: A seven-year prospective study, Diabetology and metabolic syndrome, 3, -, 2011	Study subjects included those who were older than 18 years

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Study	Reason for exclusion
Cobuz,M., Cobuz,C., Chronic complications of type 1 diabetes mellitus in children, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 19, 301-309, 2012	Just an overall prevalence was reported, no stratification according to age
Constantino,M.I., Molyneaux,L., Limacher-Gisler,F., Al-Saeed,A., Luo,C., Wu,T., Twigg,S.M., Yue,D.K., Wong,J., Long-term complications and mortality in young-onset diabetes: type 2 diabetes is more hazardous and lethal than type 1 diabetes, Diabetes Care, 36, 3863-3869, 2013	Study involving adults
Couper,J.J., Staples,A.J., Cocciolone,R., Nairn,J., Badcock,N., Henning,P., Relationship of smoking and albuminuria in children with insulin-dependent diabetes, Diabetic Medicine, 11, 666-669, 1994	Just the number of microalbuminuria participants was reported, prevalence cannot be calculated
Dahlquist,G., Rudberg,S., The prevalence of microalbuminuria in diabetic children and adolescents and its relation to puberty, Acta Paediatrica Scandinavica, 76, 795-800, 1987	AER was tested on 1 urine sample only, not in line with the UK standard (at least 2 out of 3 consecutive urine collections over a period of 3 to 4 months)
Dahlquist,G., Stattin,E.L., Rudberg,S., Urinary albumin excretion rate and glomerular filtration rate in the prediction of diabetic nephropathy; a long-term follow-up study of childhood onset type-1 diabetic patients, Nephrology Dialysis Transplantation, 16, 1382-1386, 2001	Only an overall prevalence for all participants after 8 years' follow-up was reported
D'Antonio,J.A., Ellis,D., Doft,B.H., Becker,D.J., Drash,A.L., Kuller,L.H., Orchard,T.J., Diabetes complications and glycemic control. The Pittsburgh Prospective Insulin-Dependent Diabetes Cohort Study Status Report after 5 years of IDDM, Diabetes Care, 12, 694-70, 1989	Microalbuminuria was tested on a 24-hour urine collection only
Demirel,F., Tepe,D., Kara,O., Esen,I., Microvascular complications in adolescents with type 1 diabetes mellitus, JCRPE Journal of Clinical Research in Pediatric Endocrinology, 5, 145-149, 2013	Only an overall prevalence for the duration between 2 and 15 years was reported; no data stratified by age
Doggen,K., Debacker,N., Beckers,D., Casteels,K., Coeckelberghs,M., Dooms,L., Dorchy,H., Lebrethon,M., Logghe,K., Maes,M., Massa,G., Mouraux,T., Rooman,R., Thiry-Counson,G., Van,Aken S., Vanbesien,J., Van,Casteren,V, Care delivery and outcomes among Belgian children and adolescents with type 1 diabetes, European Journal of Pediatrics, 171, 1679-1685, 2012	Just an overall prevalence for all participants was reported, no stratification according to age
Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005	Just an overall prevalence for all participants was reported; for prevalence by age group, just the numbers of microalbuminuric children and young people in each group reported, prevalence cannot be calculated
Donaghue,K.C., Fairchild,J.M., Chan,A., Hing,S.J., King,J., Howard,N.J., Silink,M., Diabetes microvascular complications in prepubertal children, Journal of Pediatric Endocrinology, 10, 579-585, 1997	The threshold (AER >15 microg/minute)used for confirmation of microalbuminuria in the study corresponds to ACR >2.65 mg/mmol for males or 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5 mg/mmol for females)
Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003	Longitudinal study, data analysed were from the lastest assessment when selected participants were already older than 18 years
Dost,A., Klinkert,C., Kapellen,T., Lemmer,A., Naeke,A., Grabert,M., Kreuder,J., Holl,R.W., DPV,Science,I, Arterial hypertension determined by ambulatory blood pressure profiles: contribution to microalbuminuria risk in a multicenter investigation in 2,105 children and adolescents with type 1 diabetes, Diabetes Care, 31, 720-725, 2008	Just an overall prevalence was reported, no stratification according to age
Ebeling,P., Koivisto,V.A., Occurrence and interrelationships of complications in insulin-dependent diabetes in Finland, Acta Diabetologica, 34, 33-38, 1997	The youngest age group assessed ranged from 15 to 27 years
Elamin,A., Ii Omer,M.I., Ismail,B., Tuvemo,T., Microalbuminuria in young Sudanese patients with type 1 diabetes, Annals of Saudi Medicine, 13, 493-497, 1993	The study was undertaken in Sudan
Gorman,D., Sochett,E., Daneman,D., The natural history of microalbuminuria in adolescents with type 1 diabetes, Journal of Pediatrics, 134, 333-337, 1999	Just an overall prevalence was reported, no stratification according to age
Harvey,J.N., Allagoa,B., The long-term renal and retinal outcome of childhood-onset Type 1 diabetes, Diabetic Medicine, 21, 26-31, 2004	Mean AER values by age at onset of diabetes rather than microalbuminuria prevalence by age were reported
Holl,R.W., Grabert,M., Thon,A., Heinze,E., Urinary excretion of albumin in adolescents with type 1 diabetes: persistent versus intermittent microalbuminuria and relationship to duration of diabetes, sex, and metabolic control, Diabetes Care, 22, 1555-1560, 1999	Just numbers of microalbuminuria patients by age were reported, no prevalence or incidence can be calculated
Ishikawa,K., Nagayoshi,M., Higa,S., Murakami,K., Kono,Y., Jinnouchi,T., Mimura,G., Frequency of diabetic nephropathy in childhood diabetics in southern districts of Kyusyu, Journal of Diabetic Complications, 5, 134-Sep, 1991	Available in abstract form only

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Study	Reason for exclusion
Izumi,K., Hoshi,M., Kuno,S., Okuno,G., Yamazaki,Y., Isshiki,G., Sasaki,A., Glycemic control, growth and complications in children with insulin-dependent diabetes mellitus--a study of children enrolled in a Summer camp program for diabetics in Kinki district, Japan, Diabetes Research and Clinical Practice, 28, 185-190, 1995	Just an overall prevalence for all participants was reported, no stratification according to age
Janner,M., Knill,S.E., Diem,P., Zuppinger,K.A., Mullis,P.E., Persistent microalbuminuria in adolescents with type I (insulin-dependent) diabetes mellitus is associated to early rather than late puberty. Results of a prospective longitudinal study, European Journal of Pediatrics, 153, 403-408, 1994	Just an overall prevalence for all participants was reported, no stratification according to age
Joner,G., Brinchmann-Hansen,O., Torres,C.G., Hanssen,K.F., A nationwide cross-sectional study of retinopathy and microalbuminuria in young Norwegian type 1 (insulin-dependent) diabetic patients, Diabetologia, 35, 1049-1054, 1992	Cut-off point for microalbuminuria was set at AER >15 microg/minute, which corresponds to ACR ≥2.65 mg/mmol for males or ≥2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5 mg/mmol for females)
Jones,C.A., Francis,M.E., Eberhardt,M.S., Chavers,B., Coresh,J., Engelgau,M., Kusek,J.W., Byrd-Holt,D., Narayan,K.M., Herman,W.H., Jones,C.P., Salive,M., Agodoa,L.Y., Microalbuminuria in the US population: third National Health and Nutrition Examination Survey, American Journal of Kidney Diseases, 39, 445-459, 2002	Microalbuminuria prevalence was stratified by age band, but the youngest group's age range was 6 to 19 years
Jones,C.A., Leese,G.P., Kerr,S., Bestwick,K., Isherwood,D.I., Vora,J.P., Hughes,D.A., Smith,C., Development and progression of microalbuminuria in a clinic sample of patients with insulin dependent diabetes mellitus, Archives of Disease in Childhood, 78, 518-523, 1998	Prevalence by age for all types of microalbuminuria(including intermittent and persistent) was reported
Karavanaki,K., Baum,J.D., Coexistence of impaired indices of autonomic neuropathy and diabetic nephropathy in a cohort of children with type 1 diabetes mellitus, Journal of Pediatric Endocrinology, 16, 79-90, 2003	Just the number of persistent microalbuminuria participants was reported, no population size of age groups and no prevalence can be calculated
Kim,N.H., Pavkov,M.E., Knowler,W.C., Hanson,R.L., Weil,E.J., Curtis,J.M., Bennett,P.H., Nelson,R.G., Predictive value of albuminuria in American Indian youth with or without type 2 diabetes, Pediatrics, 125, e844-e851, 2010	Study involving adults >18 years
Laborde,K., Levy-Marchal,C., Kindermans,C., Dechaux,M., Czernichow,P., Sachs,C., Glomerular function and microalbuminuria in children with insulin-dependent diabetes, Pediatric Nephrology, 4, 39-43, 1990	Microalbuminuria was determined by 1 urine sample in the morning only
Lee,T.H., Han,S.H., The prevalence of complications in Korean diabetic subjects, Tohoku Journal of Experimental Medicine, 141 Suppl, 361-365, 1983	The youngest group started from 19 years of age, and just the number of microalbuminuria participants was reported
Lee,T.H., Ryu,H.J., Chung,P.W., Lim,W.S., Chung,M.Y., The prevalence of diabetic complications in Korea, Korean Journal of Internal Medicine, 2, 42-47, 1987	The youngest age group started from 19 years
Levy-Shraga,Y., Lerner-Geva,L., Boyko,V., Graph-Barel,C., Mazor-Aronovitch,K., Modan-Moses,D., Pinhas-Hamiel,O., Type 1 diabetes in pre-school children--long-term metabolic control, associated autoimmunity and complications, Diabetic Medicine, 29, 1291-1296, 2012	Complications were grouped together and cumulative incidence of all complications was reported in a graph
Lievre,M., Marre,M., Robert,J.J., Charpentier,G., Iannascoli,F., Passa,P., DIabetes,therapeutic Strategies and COmplications (DISCO) investigators., Cross-sectional study of care, socio-economic status and complications in young French patients with type 1 diabetes mellitus, Diabetes and Metabolism, 31, 41-46, 2005	Just an overall prevalence for all participants was reported, no stratification according to age
Likitmaskul,S., Wacharasindhu,S., Rawdaree,P., Ngarmukos,C., Deerochanawong,C., Suwanwalaikorn,S., Chetthakul,T., Bunnag,P., Kosachunhanun,N., Plengvidhaya,N., Leelawatana,R., Krittiyawong,S., Benjasuratwong,Y., Pratipanawatr,T., Thailand Diabetes Registry Project: Type of diabetes, glycemic control and prevalence of microvascular complications in children and adolescents with diabetes, Journal of the Medical Association of Thailand, 89, S10-S16, 2006	No microalbuminuria prevalence was reported
Maahs,D.M., Snively,B.M., Beyer,J., Imperatore,G., Bell,R., Mayer-Davis,E.J., Dolan,L.M., Pettitt,D.J., Hirsch,I., Rodriguez,B., Dabelea,D., Birth weight [corrected] and elevated albumin to creatinine ratio in youth with diabetes: the SEARCH for Diabetes in Youth study.[Erratum appears in Pediatr Nephrol. 2009 Jan;24(1):221], Pediatric Nephrology, 23, 2255-2260, 2008	Just an overall prevalence was reported, no stratification according to age
Majaliwa,E.S., Munubhi,E., Ramaiya,K., Mpembeni,R., Sanyiwa,A., Mohn,A., Chiarelli,F., Survey on acute and chronic complications in children and adolescents with type 1 diabetes at Muhimbili National Hospital in Dar es Salaam, Tanzania, Diabetes Care, 30, 2187-2192, 2007	Just the numbers of microalbuminuric participants by age group were reported, no prevalence can be calculated
Marcovecchio,M.L., Dalton,R.N., Chiarelli,F., Dunger,D.B., A1C variability as an independent risk factor for microalbuminuria in young people with type 1 diabetes, Diabetes Care, 34, 1011-1013, 2011	Just an overall prevalence was reported, no stratification according to age

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Study	Reason for exclusion
Marshall,S.M., Hackett,A., Court,S., Parkin,M., Alberti,K.G., Albumin excretion in children and adolescents with insulin-dependent diabetes, Diabetes Research, 3, 345-348, 1986	Only an overall prevalence was reported, no stratification according to age
Mathiesen,E.R., Saurbrey,N., Hommel,E., Parving,H.H., Prevalence of microalbuminuria in children with type 1 (insulin-dependent) diabetes mellitus, Diabetologia, 29, 640-643, 1986	Cut-off point for microalbuminuria was set at AER >14 microg/min, which corresponds to ACR ≥2.48 mg/mmol for males or ≥2.71 mg/mmol for females (lower than the UK standards)
Matyka,K., Microalbuminuria in childhood diabetes, Journal of the Royal College of Physicians of Edinburgh, 39, 233-235, 2009	Not a primary study; summary of previous relevant publications
McVean,J.J., Eickhoff,J.C., MacDonald,M.J., Prevalence of early microalbuminuria in children with type 1 diabetes mellitus, Journal of Pediatric Endocrinology, 21, 469-471, 2008	ACR was tested on at least 1 random urine collection, including single urine sample
Midyett,L.K., Grunt,J., Simon,S.D., Noninvasive radial artery tonometry augmentation index and urinary albumin/creatinine levels in early adolescents with type 1 diabetes mellitus, Journal of Pediatric Endocrinology and Metabolism, 22, 531-537, 2009	ACRs by age and diabetes duration were only reported graphically
Moayeri,H., Dalili,H., Prevalence of microalbuminuria in children and adolescents with diabetes mellitus type I, Acta Medica Iranica, 44, 105-110, 2006	Just the number of microalbuminuria participants was reported, no prevalence by age can be calculated
Mogensen,C.E., Christensen,C.K., Predicting diabetic nephropathy in insulin-dependent patients, New England Journal of Medicine, 311, 89-93, 1984	Just an overall prevalence was reported, no stratification according to age
Mohsin,F., Craig,M.E., Cusumano,J., Chan,A.K., Hing,S., Lee,J.W., Silink,M., Howard,N.J., Donaghue,K.C., Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002, Diabetes Care, 28, 1974-1980, 2005	Just an overall prevalence was reported, no stratification according to age
Moore,T.H., Shield,J.P., Prevalence of abnormal urinary albumin excretion in adolescents and children with insulin dependent diabetes: the MIDAC study. Microalbinuria in Diabetic Adolescents and Children (MIDAC) research group, Archives of Disease in Childhood, 83, 239-243, 2000	Microalbuuminuria prevalence was stratified by puberty status (which was not defined by age)rather than by age
Moore,T.H., Shield,J.P., Microalbuminuria in diabetic adolescents and children--feasibility phase of a national cross-sectional study. MIDAC Research Group, Journal of Diabetes and its Complications, 13, 122-128, 1999	Just an overall prevalence for all participants was reported, not stratified by age
Morgese,G., Chiarelli,F., La,Penna G., Verrotti,A., Early detection of nephropathy in juvenile diabetes, Journal of Endocrinological Investigation, 12, 139-140, 1989	Just an overall prevalence for all participants was reported, no stratification according to age
Mortensen,H.B., Epidemiology of microalbuminuria among children with and without diabetes. Danish Study Group of Diabetes in Childhood, Journal of Diabetes and its Complications, 8, 164-165, 1994	Only an overall prevalence was reported, no stratification according to age
Mortensen,H.B., Hougaard,P., Ibsen,K.K., Parving,H.H., Petersen,K., Nerup,J., Marner,B., Holsteen,V., Haase,H., Saurbrey,N., Klinge,I., Bille,T., Kreutzfeldt,J., Lund,H.I., Pedersen,I.L., MacIntyre,B., Rasmussen,S.W., Hobolth,N., Brems,M., Relationship between blood pressure and urinary albumin excretion rate in young Danish Type 1 diabetic patients: Comparison to non-diabetic children, Diabetic Medicine, 11, 155-161, 1994	Just the numbers of microalbuminuria participants for different age groups were reported, no prevalence can be calculated
Mortensen,H.B., Marinelli,K., Norgaard,K., Main,K., Kastrup,K.W., Ibsen,K.K., Villumsen,J., Parving,H.H., A nation-wide cross-sectional study of urinary albumin excretion rate, arterial blood pressure and blood glucose control in Danish children with type 1 diabetes mellitus, Diabetic Medicine, 7, 887-897, 1990	Prevalence stratified by age and duration was only reported only graphically
Mullis,P., Kochli,H.P., Zuppinger,K., Schwarz,H.P., Intermittent microalbuminuria in children with type 1 diabetes mellitus without clinical evidence of nephropathy, European Journal of Pediatrics, 147, 385-388, 1988	The threshold (AER >15 microg/min)used for confirmation of microalbuminuria in the study corresponds to ACR >2.65 mg/mmol for males or 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5mg/mmol for males and 3.5 mg/mmol for females)
Nazim,J., Dziatkowiak,H., Sztefko,K., Six-year observation of adolescents with type 1 diabetes and microalbuminuria, Diabetologia Polska, 7, 166-170, 2000	Age of participants ranged from 2.2 to 24 years
Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,C., Christova,P., Detection of serum collagen type IV in children with type 1 (insulin-dependent) diabetes mellitus--a longitudinal study, Pediatric Diabetes, 2, 184-190, 2001	Only an overall prevalence for a wide age range (5 to 13 years) was reported
Okpere,A.N., Anochie,I.C., Eke,F.U., Prevalence of microalbuminuria among secondary school children, African Health Sciences, 12, 140-147, 2012	Study carried out in Nigeria
Quattrin,T., Waz,W.R., Duffy,L.C., Sheldon,M.W., Campos,S.P., Albini,C.H., Feld,L.G., Microalbuminuria in an adolescent cohort with insulin-dependent diabetes mellitus, Clinical Pediatrics, 34, 12-17, 1995	Just an overall prevalence for all participants was reported, no stratification according to age
Raile,K., Galler,A., Hofer,S., Herbst,A., Dunstheimer,D., Busch,P., Holl,R.W., Diabetic nephropathy in 27,805 children, adolescents, and adults with type 1 diabetes: effect of diabetes duration, A1C, hypertension, dyslipidemia, diabetes onset, and sex, Diabetes Care, 30, 2523-2528, 2007	Just an overall prevalence was reported, no stratification according to age

Study	Reason for exclusion
Rowe,D.J.F., Hayward,M., Bagga,H., Betts,P., Effect of glycaemic control and duration of disease on overnight albumin excretion in diabetic children, British Medical Journal, 289, 957-959, 1984	Just the number of microalbuminuria participants >12 years was reported, no prevalence can be calculated
Roy,M.S., Affouf,M., Roy,A., Six-year incidence of proteinuria in type 1 diabetic African Americans, Diabetes Care, 30, 1807-1812, 2007	The study was carried out only among African Americans in the USA
Salardi,S., Cacciari,E., Pascucci,M.G., Giambiasi,E., Tacconi,M., Tazzari,R., Cicognani,A., Boriani,F., Puglioli,R., Mantovani,W., Microalbuminuria in diabetic children and adolescents. Relationship with puberty and growth hormone, Acta Paediatrica Scandinavica, 79, 437-443, 1990	Cut-off point for microalbuminuria used in the study was 25mg/24h, which corresponds to ACR ≥3.06 mg/mmol in males and ≥3.19 mg/mmol in females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5mg/mmol for females)
Salgado,P.P., Silva,I.N., Vieira,E.C., Simoes e Silva AC., Risk factors for early onset of diabetic nephropathy in pediatric type 1 diabetes, Journal of Pediatric Endocrinology, 23, 1311-1320, 2010	Just an overall prevalence was reported, no stratification according to age
Santilli,F., Spagnoli,A., Mohn,A., Tumini,S., Verrotti,A., Cipollone,F., Mezzetti,A., Chiarelli,F., Increased vascular endothelial growth factor serum concentrations may help to identify patients with onset of type 1 diabetes during childhood at risk for developing persistent microalbuminuria, Journal of Clinical Endocrinology and Metabolism, 86, 3871-3876, 2001	Just an overall prevalence was reported after 8 years' follow-up, no stratification by age and participants' attained age could have reached more than 18 years
Schultz,C.J., Konopelska-Bahu,T., Dalton,R.N., Carroll,T.A., Stratton,I., Gale,E.A., Neil,A., Dunger,D.B., Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a longitudinal study. Oxford Regional Prospective Study Group, Diabetes Care, 22, 495-502, 1999	Only the number of microalbuminuria participants aged <11 years was reported without the whole number of this age group, prevalence cannot be calculated
Schultz,C.J., Neil,H.A., Dalton,R.N., Konopelska,Bahu T., Dunger,D.B., Oxford Regional Prospective Study Group., Blood pressure does not rise before the onset of microalbuminuria in children followed from diagnosis of type 1 diabetes. Oxford Regional Prospective Study Group, Diabetes Care, 24, 555-560, 2001	Just an overall prevalence was reported, no stratification according to age
Scott,A.R., Toomath,R., Bouchier,D., Bruce,R., Crook,N., Carroll,D., Cutfield,R., Dixon,P., Doran,J., Dunn,P., Hotu,C., Khant,M., Lonsdale,M., Lunt,H., Wiltshire,E., Wu,D., First national audit of the outcomes of care in young people with diabetes in New Zealand: High prevalence of nephropathy in Maori and Pacific Islanders, New Zealand Medical Journal, 119, -, 2006	Just an overall prevalence for participants aged between 12 and 26 years was reported
Sellers,E.A.C., Blydt-Hansen,T.D., Dean,H.J., Gibson,I.W., Birk,P.E., Ogborn,M., Macroalbuminuria and renal pathology in first nation youth with type 2 diabetes, Diabetes Care, 32, 786-790, 2009	Just an overall prevalence was reported, no stratification according to age
Sen,A., Buyukgebiz,A., Albumin excretion rate, serum insulin-like growth factor-I and glomerular filtration rate in type I diabetes mellitus at puberty, Journal of Pediatric Endocrinology, 10, 209-215, 1997	Mean values of AER for age groups such as 10 to 12 years, and 13 to 14 years, were reported, but prevalence cannot be calculated
Shield,J.P.H., Hunt,L.P., Karachaliou,F., Karavanaki,K., Baum,J.D., Is microalbuminuria progressive?, Archives of Disease in Childhood, 73, 512-514, 1995	Just an overall prevalence was reported, no stratification according to age
Simsek,D.G., Aycan,Z., Ozen,S., Cetinkaya,S., Kara,C., Abali,S., Demir,K., Tunc,O., Ucakturk,A., Asar,G., Bas,F., Cetinkaya,E., Aydin,M., Karaguzel,G., Orbak,Z., Siklar,Z., Altincik,A., Okten,A., Ozkan,B., Ocal,G., Semiz,S., Arslanoglu,I., Evliyaoglu,O., Bundak,R., Darcan,S., Diabetes care, glycemic control, complications, and concomitant autoimmune diseases in children with type 1 diabetes in Turkey: a multicenter study, Journal of clinical research in pediatric endocrinology, 5, 20-26, 2013	Only an overall prevalence was reported, no stratification by age or diabetes duration
Stone,M.L., Craig,M.E., Chan,A.K., Lee,J.W., Verge,C.F., Donaghue,K.C., Natural history and risk factors for microalbuminuria in adolescents with type 1 diabetes: a longitudinal study, Diabetes Care, 29, 2072-2077, 2006	Just an overall prevalence was reported, no stratification according to age
Svensson,M., Eriksson,J.W., Dahlquist,G., Early glycemic control, age at onset, and development of microvascular complications in childhood-onset type 1 diabetes: a population-based study in northern Sweden, Diabetes Care, 27, 955-962, 2004	Just an overall prevalence was reported, no stratification according to age
Tan,S.H., Lee,B.W., Low,P.S., Lee,C.P., Assessment of complications in children with insulin-dependent diabetes mellitus, Annals of the Academy of Medicine, Singapore, 14, 266-271, 1985	Participants' age ranged from 1 to 20 years (small sample size of 19 participants only)
Tsai,C.W., Kuo,C.C., Wu,C.F., Chien,K.L., Wu,V.C., Chen,M.F., Sung,F.C., Su,T.C., Associations of renal vascular resistance with albuminuria in adolescents and young adults, Nephrology Dialysis Transplantation, 26, 3943-3949, 2011	The overall prevalence was reported when participants had attained 21 years of age
Tuomilehto,J., Borch-Johnsen,K., Molarius,A., Jormanainen,V., Lounamaa,R., Gronhagen-Riska,C., Reunanen,A., Sarti,C., The unchanging incidence of hospitalization for diabetic nephropathy in a population-based cohort of IDDM patients in Finland.[Erratum appears in Diabetes Care 1997 Nov;20(11):1802], Diabetes Care, 20, 1081-1086, 1997	Nephropathy was identified by ICD codes of diabetic nephropathy diagnosis on hospital discharge records rather than by AER or ACR

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Study	Reason for exclusion
Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999	Study on young adults older than 18 years
Yokoyama,H., Uchigata,Y., Otani,T., Maruyama,A., Yano-Aoki,K., Kanematsu,S., Kasahara,T., Matsuura,N., Omori,Y., Development of diabetic nephropathy in Japanese patients with insulin-dependent diabetes mellitus: Tokyo Women's Medical College epidemiologic study, Journal of Diabetes and its Complications, 8, 7-12, 1994	Participants included those who were older than 18 years

H.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Study	Reason for exclusion
Armour,T.A., Norris,S.L., Jack,L.,Jr., Zhang,X., Fisher,L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], Diabetic Medicine, 22, 1295-1305, 2005	PICO not met - no studies included children or young people with type 2 diabetes. Interventions were generally behavioural in nature.
Atak,N., Gurkan,T., Kose,K., The effect of education on knowledge, self management behaviours and self efficacy of patients with type 2 diabetes, Australian Journal of Advanced Nursing, 26, 66-74, 2008	PICO not met - adult participants only
Avdal,Elif, Kizilci,Sevgi, Demirel,Neslihan, The effects of Web-based diabetes education on diabetes care results: a randomized control study, CIN: Computers, Informatics, Nursing, 29, TC29-TC34, 2011	PICO not met - adult participants only.
Babamoto,K.S., Sey,K.A., Camilleri,A.J., Karlan,V.J., Catalasan,J., Morisky,D.E., Improving diabetes care and health measures among hispanics using community health workers: results from a randomized controlled trial, Health Education and Behavior, 36, 113-126, 2009	PICO not met - adult participants only.
Borgermans,Liesbeth, Goderis,Geert, Carine, Verbeke,Geert, Carbonez,An, Ivanova,Anna, Mathieu,Chantal, Heyrman,Jan, Patients' experiences with patient-centred care are associated with documented outcome of care indicators for diabetes: findings from the Leuven Diabetes Project, International Journal of Care Pathways, 15, 65-75, 2011	PICO not met - although age not explicitly stated as an inclusion criterion, mean age of participants was 68 years (±12 years).
Brown,S.J., Lieberman,D.A., Gemeny,B.A., Fan,Y.C., Wilson,D.M., Pasta,D.J., Educational video game for juvenile diabetes: Results of a controlled trial, Medical Informatics, 22, 77-89, 1997	PICO not met - participants with type 1 diabetes only
Campbell,E.M., Redman,S., Moffitt,P.S., Sanson-Fisher,R.W., The relative effectiveness of educational and behavioral instruction programs for patients with NIDDM: a randomized trial, Diabetes Educator, 22, 379-386, 1996	PICO not met. Although inclusion criteria only state <80 years, mean age of participants was 58.3 years
Charron-Prochownik,D., Sereika,S.M., Becker,D., White,N.H., Schmitt,P., Powell,A.B.,III, Diaz,A.M., Jones,J., Herman,W.H., Fischl,A.F., McEwen,L., DiNardo,M., Guo,F., Downs,J., Long-term effects of the booster-enhanced READY-Girls preconception counseling program on intentions and behaviors for family planning in teens with diabetes, Diabetes Care, 36, 3870-3874, 2013	No outcomes of interest. Only considers preconception counselling and outcomes relevant to this.
Colquhoun,E., Drury,Michael I., Cregan,Deirdre, Keenan,Patricia, Group work with diabetic adolescents, Irish Journal of Psychological Medicine, 5, 37-40, 1988	PICO not met - participants with type 1 diabetes, psychosocial intervention.
DaniÃ¨le,Pacaud, Helen,Kelley, Angela,M., Mike,Chiasson, Successful Delivery of Diabetes Self-Care Education and Follow-Up through eHealth Media, Canadian Journal of Diabetes, 36, 257-262, 2012	PICO not met - adult participants only
Delamater,Alan M., Smith,Jeffrey A., Bubb,Jeanne, Davis,Susan Green, Gamble,Thomas, White,Neil H., Santiago,Julio V., Family-based behavior therapy for diabetic adolescents, Johnson, James H [Ed]; Johnson, Suzanne Bennett [Ed], , 293-306, 1991	PICO not met - type of diabetes not described (but likely type 1) and behavioural intervention, not educational.
Flamm,M., Panisch,S., Winkler,H., Johansson,T., Weitgasser,R., Sonnichsen,A.C., Effectiveness of the Austrian disease management programme "Therapie Aktiv" for type 2 diabetes regarding the improvement of metabolic control, risk profile and guideline adherence: 2 years of follow up, Wiener Klinische Wochenschrift, 124, 639-646, 2012	PICO not met - adult participants only

Update 2015

Study	Reason for exclusion
Gage,H., Hampson,S., Skinner,T.C., Hart,J., Storey,L., Foxcroft,D., Kimber,A., Cradock,S., McEvilly,E.A., Educational and psychosocial programmes for adolescents with diabetes: Approaches, outcomes and cost-effectiveness, Patient Education and Counseling, 53, 333-346, 2004	PICO not met - participants with type 1 diabetes only.
Heinrich,E., Schaper,N.C., de Vries,N.K., Self-management interventions for type 2 diabetes: a systematic review, European Diabetes Nursing, 7, 71-76, 2010	PICO not met - only adult studies included
Jeffreys,H.L., Hemoglobin A1C value for evaluating a community diabetes education series, Internet Journal of Advanced Nursing Practice, 9, -6p, 2008	PICO not met - not an RCT, and adult participants only
Johnson,S.T., Newton,A.S., Chopra,M., Buckingham,J., Huang,T.T.K., Franks,P.W., Jetha,M.M., Ball,G.D.C., In search of quality evidence for lifestyle management and glycemic control in children and adolescents with type 2 diabetes: a systematic review (Structured abstract), BMC Pediatrics, 10, 2010	Systematic review. Only includes one article which considers dietary modification rather than an educational intervention.
Keeratiyutawong,P., Hanucharurnkul,S., Melkus,G.D.E., Panpakdee,O., Vorapongsathorn,T., Effectiveness of a self-management program for Thais with type 2 diabetes, Thai Journal of Nursing Research, 10, 85-97, 2006	PICO not met - adult participants only
LEE,Haejung, KIM,Myoung Soo, PARK,Kyung Yeon, PARK,Hyoung Sook, KIM,In Joo, Effects of a problem-solving counseling program to facilitate intensified walking on Koreans with type 2 diabetes, Japan Journal of Nursing Science, 8, 129-139, 2011	PICO not met - adult participants only (>50 years), and not randomised
McIlhenny,C.,V, Guzic,B., Knee,D., Demuth,B., Roberts,J., Using technology to deliver healthcare education to rural patients, Rural and Remote Health, 11, 1-11, 2011	PICO not met - adult participants only
Moriyama,M., Nakano,M., Kuroe,Y., Nin,K., Niitani,M., Nakaya,T., Efficacy of a self-management education program for people with type 2 diabetes: results of a 12 month trial, Japan Journal of Nursing Science, 6, 51-63, 2009	No age restriction to enter study, but control and intervention groups had a mean age of 65.2 years (±8.5 years) and 66.4 years (±9.2 years), respectively.
Nichols,P.J., Norris,S.L., A systematic literature review of the effectiveness of diabetes education of school personnel, The Diabetes Educator, 28, 405-414, 2002	Systematic review that considers education of school teachers only. No reference to type 2 diabetes.
Norris,S.L., Nichols,P.J., Caspersen,C.J., Glasgow,R.E., Engelgau,M.M., Jack,Jr, Snyder,S.R., Carande-Kulis,V.G., Isham,G., Garfield,S., Briss,P., McCulloch,D., Increasing diabetes self-management education in community settings: A systematic review, American Journal of Preventive Medicine, 22, 39-66, 2002	PICO not met - 11 studies included young people but all had type 1 diabetes. One study looked at education of school personnel (type of diabetes not specified).
Norris,S.L., Engelgau,M.M., Narayan,K.M.V., Effectiveness of self management training in type 2 diabetes: a systematic review of randomized controlled trials, Diabetes Care, 24, 561-587, 2001	Only includes subjects >18 years of age.
Norris,S.L., Nichols,P.J., Caspersen,P.J., Glasgow,R.E,., Engelgau,M.M., Jack,L., Snyder, S.R., Carande-Kulis,V.G., Isham,G., Garfield,S., Briss,P., McCulloch,D., Increasing diabetes self-management education in community settings: a systematic review, American Journal of Preventive Medicine, 22, 39-66, 2002	Systematic review, predominantly considers educational interventions for adults or children and young people with type 1 diabetes. References checked and no relevant papers identified for children and young people with type 2 diabetes.
Pieter,Agema, Diana,Sherifali, Determining the impact of an intervention to increase problem-solving skills in diabetes self-management: The Diabetes Problem-Solving Passport Pilot Study, Canadian Journal of Diabetes, 36, 199-203, 2012	PICO not met - adult participants only.
Rothman,R.L., Malone,R., Bryant,B., Shintani,A.K., Crigler,B., Dewalt,D.A., Dittus,R.S., Weinberger,M., Pignone,M.P., A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes, The American journal of medicine, 118, 276-284, 2005	PICO not met - adult participants only
Sturt,J., One-to-one structured education using the Diabetes Manual: evidence of effectiveness, Journal of Diabetes Nursing, 12, 368-70, 372, 374, 2008	PICO not met - adult participants only
Sutcliffe,Paul, Martin,Steven, Sturt,Jackie, Powell,John, Griffiths,Frances, Adams,Ann, Dale,Jeremy, Systematic review of communication technologies to promote access and engagement of young people with diabetes into healthcare, BMC Endocrine Disorders, 11, 1-, 2011	PICO not met - studies included use of IT to communicate advice on diabetes management, rather than educational tools. Only one educational Internet site included, and this study was not an RCT.
Tjam,E.Y., Sherifali,D., Steinacher,N., Hett,S., Physiological outcomes of an Internet disease management program versus in-person counselling: a randomized, controlled trial, Canadian Journal of Diabetes, 30, 397-405, 2006	PICO not met - adults with type 1 or type 2 diabetes only

Update 2015

Study	Reason for exclusion
TODAY Study Group, A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes, New England Journal of MedicineN Engl J Med, 366, 2247-2256, 2012	PICO not met - behavioural intervention, not education
TODAY Study Group, Zeitler,P., Epstein,L., Grey,M., Hirst,K., Kaufman,F., Tamborlane,W., Wilfley,D., Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes, Pediatric Diabetes, 8, 74-87, 2007	Protocol for study - no results included.
Tshiananga,J.K.T., Kocher,S., Weber,C., Eerny-Albrecht,K., Berndt,K., Neeser,K.,, The effect of nurse-led diabetes self-management education on glycosylated hemoglobin and cardiovascular risk factors: a meta-analysis, The Diabetes Educator, 38, 108-123, 2012	Mean age of participants 52.8 years.
Tshiananga,Jacques Kande Tshiang, Kocher,Serge, Weber,Christian, Erny-Albrecht,Katrina, Berndt,Karsten, Neeser,Kurt, The Effect of Nurse-led Diabetes Self-management Education on Glycosylated Hemoglobin and Cardiovascular Risk Factors: A Meta-analysis, The Diabetes Educator, 38, 108-123, 2012	PICO not met - includes articles with either adult participants or children and young people with type 1 diabetes

H.19 Type 2 diabetes – psychological interventions

Review questions

What is the effectiveness of psychological interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?

These 2 questions were addressed through a single search and there is one combined list of excluded studies.

Update 2015

Study	Reason for exclusion
Boost glycemic control in teen diabetics through 'family focused teamwork', Disease Management Advisor, 9, 120-122, 117, 2003	Editorial for a study which assessed interventions in type 1 diabetes
Armour,T.A., Norris,S.L., Jack,L.,Jr., Zhang,X., Fisher,L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], Diabetic Medicine, 22, 1295-1305, 2005	PICO not met: adults with type 2 diabetes and children, young people and adults with type 1 diabetes
Bradshaw,B., The role of the family in managing therapy in minority children with type 2 diabetes mellitus, Journal of Pediatric Endocrinology, 15 Suppl 1, 547-551, 2002	Intervention not behavioural. Focused on administering care such as diet supervision
Calhoun,D., Brod,R., Kirlin,K., Howard,B.V., Schuldberg,D., Fiore,C., Effectiveness of motivational interviewing for improving self-care among Northern Plains Indians with type 2 diabetes, Diabetes Spectrum, 23, 107-114, 2010	PICO not met: adult population only. Mean age 54 years
Campbell,E.M., Redman,S., Moffitt,P.S., Sanson-Fisher,R.W., The relative effectiveness of educational and behavioral instruction programs for patients with NIDDM: a randomized trial, Diabetes Educator, 22, 379-386, 1996	PICO not met: adult population
Delamater,A.M., Jacobson,A.M., Anderson,B., Cox,D., Fisher,L., Lustman,P., Rubin,R., Wysocki,T., Psychosocial Therapies Working Group., Psychosocial therapies in diabetes: report of the Psychosocial Therapies Working Group. [111 refs], Diabetes Care, 24, 1286-1292, 2001	Not a systematic review; general literature review only with no data
Ellis,D.A., Naar-King,S., Chen,X., Moltz,K., Cunningham,P.B., Idalski-Carcone,A., Multisystemic therapy compared to telephone support for youth with poorly controlled diabetes: findings from a randomized controlled trial, Annals of Behavioral Medicine, 44, 207-215, 2012	Type 1 versus type 2 entered together as a confounding variable in a linear model. No analysis of the effect of the intervention on type 2 children and young people only
Grey,M., Boland,E.A., Davidson,M., Yu,C., Sullivan-Bolyai,S., Tamborlane,W.V., Short-term effects of coping skills training as adjunct to intensive therapy in adolescents, Diabetes Care, 21, 902-908, 1998	PICO not met: participants had type 1 diabetes only
Harris,M.A., Freeman,K.A., Beers,M., Family therapy for adolescents with poorly controlled diabetes: initial test of clinical significance, Journal of Pediatric Psychology, 34, 1097-1107, 2009	PICO not met: only 2 of 16 participants had type 2 diabetes

Study	Reason for exclusion
Henry,J.L., Wilson,P.H., Bruce,D.G., Chisholm,D.J., Rawling,P.J., Cognitive-behavioural stress management for patients with non-insulin dependent diabetes mellitus, Psychology, Health and Medicine, 2, 109-118, 1997	PICO not met: adult population. Mean age 59.8 years
Keeratiyutawong,P., Hanucharurnkul,S., Melkus,G.D.E., Panpakdee,O., Vorapongsathorn,T., Effectiveness of a self-management program for Thais with type 2 diabetes, Thai Journal of Nursing Research, 10, 85-97, 2006	PICO not met: adult population. Age range of 21 to 60 years
Keogh,K.M., White,P., Smith,S.M., McGilloway,S., O'Dowd,T., Gibney,J., Changing illness perceptions in patients with poorly controlled type 2 diabetes, a randomised controlled trial of a family-based intervention: protocol and pilot study, BMC Family Practice, 8, 36-, 2007	PICO not met: participants >18 years of age
LEE,Haejung, KIM,Myoung Soo, PARK,Kyung Yeon, PARK,Hyoung Sook, KIM,In Joo, Effects of a problem-solving counseling program to facilitate intensified walking on Koreans with type 2 diabetes, Japan Journal of Nursing Science, 8, 129-139, 2011	PICO not met: adult population >50 years
Lou,V.W.Q., Zhang,Y., Evaluating the effectiveness of a participatory empowerment group for Chinese type 2 diabetes patients, Research on Social Work Practice, 16, 491-499, 2006	PICO not met: adult population. Mean ages of 57.3 years and 56.8 years in each group
Moriyama,M., Nakano,M., Kuroe,Y., Nin,K., Niitani,M., Nakaya,T., Efficacy of a self-management education program for people with type 2 diabetes: results of a 12 month trial, Japan Journal of Nursing Science, 6, 51-63, 2009	PICO not met: adult population. Mean ages of 66.4 years and 65.2 years in each group
Partiprajak,Suphamas, Hanucharurnkul,Somchit, Piaseu,Noppawan, Brooten,Dorothy, Nityasuddhi,Dechavudh, Outcomes of an advanced practice nurse-led type-2 diabetes support group, Pacific Rim International Journal of Nursing Research, 15, 288-304, 2011	PICO not met: adult population. Age range 44 to 80 years
Sabourin,Brigitte, Vallis,T., Currie,Shannon, Development and pilot-testing of a brief psychosocial group intervention protocol for type 2 diabetes self-management, Canadian Journal of Diabetes, 35, 287-294, 2011	PICO not met: adult population. Age range 59 to 78 years
Satin,Wendy, la Greca,Annette M., Zigo,Marjorie A., Skyler,Jay S., Diabetes in adolescence: Effects of multifamily group intervention and parent simulation of diabetes, Journal of Pediatric Psychology, 14, 259-275, 1989	PICO not met: type 1 diabetes only
Smith,S., Paul,G., Kelly,A., Whitford,D., O'Shea,E., O'Dowd,T., Peer support for patients with type 2 diabetes: cluster randomised controlled trial, BMJ: British Medical Journal (Overseas and Retired Doctors Edition), 342, 482-482, 2011	PICO not met: adult population. Mean age ranges between 62.7 years and 66.1 years for each group
Tjam,E.Y., Sherifali,D., Steinacher,N., Hett,S., Physiological outcomes of an Internet disease management program versus in-person counselling: a randomized, controlled trial, Canadian Journal of Diabetes, 30, 397-405, 2006	PICO not met: adult population; 77% of participants >40 years

Update 2015

H.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Study	Reason for exclusion
Albarracin,C.A., Fuqua,B.C., Evans,J.L., Goldfine,I.D., Chromium picolinate and biotin combination improves glucose metabolism in treated, uncontrolled overweight to obese patients with type 2 diabetes, Diabetes/Metabolism Research Reviews, 24, 41-51, 2008	PICO not met: excluded people aged <18 years
Bantle,J.P., Laine,D.C., Thomas,J.W., Metabolic effects of dietary fructose and sucrose in types I and II diabetic subjects, JAMA, 256, 3241-3246, 1986	PICO not met: adults only for type 2 diabetes (36 to 80 years)
Brunner,S., Holub,I., Theis,S., Gostner,A., Melcher,R., Wolf,P., mann-Gassner,U., Scheppach,W., Hauner,H., Metabolic effects of replacing sucrose by isomaltulose in subjects with type 2 diabetes: a randomized double-blind trial, Diabetes Care, 35, 1249-1251, 2012	PICO not met: adult population only
Gellar,L., Nansel,T.R., High and low glycemic index mixed meals and blood glucose in youth with type 2 diabetes or impaired glucose tolerance.[Erratum appears in J Pediatr. 2009 Jun;154(6):937], Journal of Pediatrics, 154, 455-458, 2009	24 hour study only - meal not diet
Johnson,S.T., Newton,A.S., Chopra,M., Buckingham,J., Huang,T.T., Franks,P.W., Jetha,M.M., Ball,G.D., In search of quality evidence for lifestyle management and glycemic control in children and adolescents with type 2 diabetes: A systematic review, BMC Pediatrics, 10, 97-, 2010	Systematic review of non-RCT data; not included in evidence as the one study reviewed was identified in the non-RCT search
Kinmonth,A.L., Angus,R.M., Jenkins,P.A., Whole foods and increased dietary fibre improve blood glucose control in diabetic children, Archives of Disease in Childhood, 57, 187-194, 1982	Diabetes type not stated, appears to be type 1 based on background section

Study	Reason for exclusion
Kwak,J.H., Lee,J.H., Ahn,C.W., Park,S.H., Shim,S.T., Song,Y.D., Han,E.N., Lee,K.H., Chae,J.S., Black soy peptide supplementation improves glucose control in subjects with prediabetes and newly diagnosed type 2 diabetes mellitus, Journal of Medicinal Food, 13, 1307-1312, 2010	PICO not met: excluded people aged <18 years
MacLean,C.H., Mojica,W.A., Morton,S.C., Pencharz,J., Hasenfeld,Garland R., Tu,W., Newberry,S.J., Jungvig,L.K., Grossman,J., Khanna,P., Rhodes,S., Shekelle,P., Effects of omega-3 fatty acids on lipids and glycemic control in type II diabetes and the metabolic syndrome and on inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and osteoporosis, Evidence Report: Technology Assessment (Summary), 1-4, 2004	Short-term effects and insufficient follow-up of included studies
McCargar,L.J., Innis,S.M., Bowron,E., Leichter,J., Dawson,K., Toth,E., Wall,K., Effect of enteral nutritional products differing in carbohydrate and fat on indices of carbohydrate and lipid metabolism in patients with NIDDM, Molecular and Cellular Biochemistry, 188, 81-89, 1998	PICO not met: excluded people aged <18 years
Nansel,T.R., Gellar,L., Zeitzoff,L., Acceptability of lower glycemic index foods in the diabetes camp setting, Journal of Nutrition Education and Behavior, 38, 143-150, 2006	Type 1 and type 2 diabetes analysed together
Ooi,Peng Cheow, Loke,Cheong Seng, Sweet potato for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2012	PICO not met: adult population only, mean age >55 years
Ooi,Peng Cheow, Yassin,Zaitun, Hamid,TengkuAizan, Momordica charantia for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2012	PICO not met: people aged <18 years excluded
Sonksen,P.H., Lowy,C., Perkins,J.R., Lim,H.S., Non-insulin-dependent diabetes: 10-year outcome in relation to initial response to diet and subsequent sulfonylurea therapy, Diabetes Care, Vol.7 Suppl 1, pp.59-66, 1984 May-Jun., -66, 1984	PICO not met: people aged <18 years excluded
Thomas,Diana, Elliott,Elizabeth J., Low glycaemic index, or low glycaemic load, diets for diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009	PICO not met: all but one paper involved adult populations and the other paper did not state which type of diabetes was studied
Vivian,E.M., Type 2 diabetes in children and adolescents--the next epidemic?, Current Medical Research and Opinion, 22, 297-306, 2006	Review not systematic
Voss,A.C., Maki,K.C., Garvey,W.T., Hustead,D.S., Alish,C., Fix,B., Mustad,V.A., Effect of two carbohydrate-modified tube-feeding formulas on metabolic responses in patients with type 2 diabetes, Nutrition, 24, 990-997, 2008	PICO not met: people aged <18 years excluded

H.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Study	Reason for exclusion
Bohdjalian,A., Prager,G., Rosak,C., Weiner,R., Jung,R., Schramm,M., Aviv,R., Schindler,K., Haddad,W., Rosenthal,N., Ludvik,B., Improvement in glycemic control in morbidly obese type 2 diabetic subjects by gastric stimulation, Obesity Surgery, 19, 1221-1227, 2009	PICO not met: adults only
Copeland,K.C., Higgins,J., El,GhormliL, Delahanty,L., Grey,M., Kriska,A.M., Lipman,T.H., Pyle,L., Shepherd,J., Hirst,K., Treatment effects on measures of body composition in the TODAY clinical trial, Diabetes Care, 36, 1742-1748, 2013	No specific weight loss intervention; no assessment of correlation between weight loss and glycaemic indices
Garanty-Bogacka,B., Syrenicz,M., Goral,J., Krupa,B., Syrenicz,J., Walczak,M., Syrenicz,A., Changes in inflammatory biomarkers after successful lifestyle intervention in obese children, Endokrynologia Polska, 62, 499-505, 2011	PICO not met: proportion of participants with type 2 diabetes not reported
Gidding,S.S., Lima,J., Pyle,L., Payan,M., Hirst,K., Katz,L.E.L., Bacha,F., McKay,S., Relationship of LV mass, LA diameter, and LV geometry to cardiovascular risk factors in the today cohort of adolescents with type 2 diabetes (T2D), Circulation, 126, -, 2012	PICO not met: outcomes not of interest
Grinstein,G., Muzumdar,R., Aponte,L., Vuguin,P., Saenger,P., Martino-Nardi,J., Presentation and 5-year follow-up of type 2 diabetes mellitus in African-American and Caribbean-Hispanic adolescents, Hormone Research, 60, 121-126, 2003	Outcomes for participants with type 1 diabetes and type 2 diabetes not presented separately
Himpens,J., Verbrugghe,A., Cadiere,G.B., Everaerts,W., Greve,J.W., Long-term results of laparoscopic Roux-en-Y Gastric bypass: evaluation after 9 years, Obesity Surgery, 22, 1586-1593, 2012	PICO not met: adults only

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Study	Reason for exclusion
Horowitz,M., Flint,A., Jones,K.L., Hindsberger,C., Rasmussen,M.F., Kapitza,C., Doran,S., Jax,T., Zdravkovic,M., Chapman,I.M., Effect of the once-daily human GLP-1 analogue liraglutide on appetite, energy intake, energy expenditure and gastric emptying in type 2 diabetes, Diabetes Research and Clinical Practice, 97, 258-266, 2012	PICO not met: adults only
Inge,T.H., Miyano,G., Bean,J., Helmrath,M., Courcoulas,A., Harmon,C.M., Chen,M.K., Wilson,K., Daniels,S.R., Garcia,V.F., Brandt,M.L., Dolan,L.M., Reversal of type 2 diabetes mellitus and improvements in cardiovascular risk factors after surgical weight loss in adolescents, Pediatrics, 123, 214-222, 2009	An observational study with no correlation analysis between weight loss and glycaemic control
Jesudason,D.R., Pedersen,E., Clifton,P.M., Weight-loss diets in people with type 2 diabetes and renal disease: A randomized controlled trial of the effect of different dietary protein amounts, American Journal of Clinical Nutrition, 98, 494-501, 2013	All participants aged over 18 years
Kim,S., Richards,W.O., Long-term follow-up of the metabolic profiles in obese patients with type 2 diabetes mellitus after Roux-en-Y gastric bypass, Annals of Surgery, 251, 1049-1055, 2010	PICO not met: adults only
Kopelman,P., Groot,Gde H., Rissanen,A., Rossner,S., Toubro,S., Palmer,R., Hallam,R., Bryson,A., Hickling,R.I., Weight loss, HbA1c reduction, and tolerability of cetilistat in a randomized, placebo-controlled phase 2 trial in obese diabetics: comparison with orlistat (Xenical), Obesity, 18, 108-115, 2010	PICO not met: adults only
Korner,A., Wiegand,S., Hungele,A., Tuschy,S., Otto,K.P., l'Allemand-Jander,D., Widhalm,K., Kiess,W., Holl,R.W., APV,initiative, German Competence,Net Obesity, Longitudinal multicenter analysis on the course of glucose metabolism in obese children, International Journal of Obesity, 37, 931-936, 2013	No data specifically on children and young people with type 2 diabetes; population of obese people, 1.1% of whom had type 2 diabetes
Lawrence,J.M., Liese,A.D., Liu,L., Dabelea,D., Anderson,A., Imperatore,G., Bell,R., Weight-loss practices and weight-related issues among youth with type 1 or type 2 diabetes, Diabetes Care, 31, 2251-2257, 2008	PICO not met: no outcomes of interest
Lee,W.J., Chong,K., Ser,K.H., Chen,J.C., Lee,Y.C., Chen,S.C., Su,Y.H., Tsai,M.H., C-peptide predicts the remission of type 2 diabetes after bariatric surgery, Obesity Surgery, 22, 293-298, 2012	PICO not met: adults only
Leslie,D.B., Dorman,R.B., Serrot,F.J., Swan,T.W., Kellogg,T.A., Torres-Villalobos,G., Buchwald,H., Slusarek,B.M., Sampson,B.K., Bantle,J.P., Ikramuddin,S., Efficacy of the Roux-en-Y gastric bypass compared to medically managed controls in meeting the American Diabetes Association composite end point goals for management of type 2 diabetes mellitus, Obesity Surgery, 22, 367-374, 2012	PICO not met: adults only
Manning,R.M., Jung,R.T., Leese,G.P., Newton,R.W., The comparison of four weight reduction strategies aimed at overweight diabetic patients, Diabetic Medicine, 12, 409-415, 1995	Paediatric data not reported separately
Marinari,G.M., Papadia,F.S., Briatore,L., Adami,G., Scopinaro,N., Type 2 diabetes and weight loss following biliopancreatic diversion for obesity, Obesity Surgery, 16, 1440-1444, 2006	PICO not met: adults only
Narasimhan,S., Weinstock,R.S., Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study, Mayo Clinic Proceedings, 89, 806-816, 2014	This is a review of the TODAY RCT already included in the review
Pearson,E.R., Treating type 2 diabetes in youth: a depressing picture, Journal of the Royal College of Physicians of Edinburgh, 42, 228-, 2012	Expert opinion
Ramos,A.C., Galvao Neto,M.P., de Souza,Y.M., Galvao,M., Murakami,A.H., Silva,A.C., Canseco,E.G., Santamaria,R., Zambrano,T.A., Laparoscopic duodenal-jejunal exclusion in the treatment of type 2 diabetes mellitus in patients with BMI<30 kg/m2 (LBMI), Obesity Surgery, 19, 307-312, 2009	PICO not met: adults only
Reis,C.E., varez-Leite,J.I., Bressan,J., Alfenas,R.C., Role of bariatric-metabolic surgery in the treatment of obese type 2 diabetes with body mass index <35 kg/m2: a literature review, Diabetes Technology and Therapeutics, 14, 365-372, 2012	PICO not met: adults only
Scheen,A.J., Finer,N., Hollander,P., Jensen,M.D., Van Gaal,L.F., RIO-Diabetes Study Group., Efficacy and tolerability of rimonabant in overweight or obese patients with type 2 diabetes: a randomised controlled study.[Erratum appears in Lancet. 2006 Nov 11;368(9548):1650], Lancet, 368, 1660-1672, 2006	PICO not met: adults only
Shi,Y.F., Pan,C.Y., Hill,J., Gao,Y., Orlistat in the treatment of overweight or obese Chinese patients with newly diagnosed Type 2 diabetes, Diabetic Medicine, 22, 1737-1743, 2005	PICO not met: adults only
TODAY Study Group., Safety and Tolerability of the Treatment of Youth-Onset Type 2 Diabetes: The TODAY experience, Diabetes Care, 36, 1765-1771, 2013	PICO not met: outcomes not of interest
Tong,P.C., Lee,Z.S., Sea,M.M., Chow,C.C., Ko,G.T., Chan,W.B., So,W.Y., Ma,R.C., Ozaki,R., Woo,J., Cockram,C.S., Chan,J.C., The effect of orlistat-induced weight loss, without concomitant hypocaloric diet, on cardiovascular risk factors and insulin sensitivity in young obese Chinese subjects with or without type 2 diabetes, Archives of Internal Medicine, 162, 2428-2435, 2002	PICO not met: adults only

Study	Reason for exclusion
Toolabi,K., Arefanian,S., Golzarand,M., Arefanian,H., Effects of laparoscopic Roux-en-Y gastric bypass (LRYGB) on weight loss and biomarker parameters in morbidly obese patients: A 12-month follow-up, Obesity Surgery, 21, 1834-1842, 2011	PICO not met: predominantly adults
Varaschim,M., Nassif,P.A., Moreira,L.B., do Nascimento,M.M., Vieira,G.M., Garcia,R.F., Sue,K.M., Cruz,M.A., Changes in clinical and laboratory parameters in obese patients with type 2 diabetes mellitus submitted to Roux-en-y gastrojejunal bypass without ring, Revista do Colegio Brasileiro de Cirurgioes, 39, 178-182, 2012	PICO not met: adults only

H.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Study	Reason for exclusion
Metformin. Useful for some children with type 2 diabetes, Prescrire International, 16, 50-52, 2007	Study criteria not met - overview of metformin in children and young people with type 2 diabetes
Al-Shareef,M.A., Sanneh,A.F., Aljoudi,A.S., Clinical effect of Metformin in children and adolescents with type 2 diabetes mellitus: a systematic review and meta-analysis, Journal of Family and Community Medicine, 19, 68-73, 2012	Systematic review of trials including metformin; 3 trials in the meta-analysis, 1 already included in the evidence summary (Jones 2002). Remaining 2 trials excluded as do not compare metformin to placebo
Bernardita,PradoA, Veronica,GaeteP, Francisca,CoronaH, Eldreth,PeraltaV, Paula,DonosoA, Ximena,RaimannT, Metabolic effect of metformin in obese adolescents at risk of diabetes mellitus type 2Efecto metabolico de la metformina en adolescentes obesas con riesgo de diabetes mellitus tipo 2, Revista Chilena de Pediatria, 83, 48-57, 2012	PICO (Patient Intervention Comparator Outcome) criteria not met - population did not have type 2 diabetes
Burgert,T.S., Duran,E.J., Goldberg-Gell,R., Dziura,J., Yeckel,C.W., Katz,S., Tamborlane,W.V., Caprio,S., Short-term metabolic and cardiovascular effects of metformin in markedly obese adolescents with normal glucose tolerance, Pediatric Diabetes, 9, 567-576, 2008	PICO criteria not met - population did not have type 2 diabetes
Centre for Reviews and Dissemination., Efficacy of metformin in the treatment of NIDDM: meta-analysis (;Structured abstract);, Database of Abstracts of Reviews of Effects, -, 2012	Abstract of a published review
Centre for Reviews and Dissemination., Efficacy of metformin in the treatment of NIDDM: meta-analysis (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2014	No information in abstract
Clarson,C.L., Mahmud,F.H., Baker,J.E., Clark,H.E., McKay,W.M., Schauteet,V.D., Hill,D.J., Metformin in combination with structured lifestyle intervention improved body mass index in obese adolescents, but did not improve insulin resistance, Endocrine, 36, 141-146, 2009	PICO criteria not met - population did not have type 2 diabetes
Freemark,M., Liver dysfunction in paediatric obesity: a randomized, controlled trial of metformin, Acta Paediatrica, 96, 1326-1332, 2007	PICO criteria not met - population did not have type 2 diabetes
Freemark,M., Bursey,D., A therapeutic trial of metformin in obese adolescents predisposed to type 2 diabetes mellitus, Pediatric Research, 47, 128A, 2000-, 2000	PICO criteria not met - population did not have type 2 diabetes
Freemark,M., Bursey,D., The effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type 2 diabetes, Pediatrics, 107, E55-, 2001	PICO criteria not met - population did not have type 2 diabetes
Gemmill,J.A.L., Brown,R.J., Nandagopal,R., Rodriguez,L.M., Rother,K.I., Clinical trials in youth with type 2 diabetes, Pediatric Diabetes, 12, 50-57, 2011	Systematic review of trials in children and young people with type 2 diabetes
Gottschalk,M., Danne,T., Vlajnic,A., Cara,J.F., Glimepiride versus metformin as monotherapy in pediatric patients with type 2 diabetes: a randomized, single-blind comparative study, Diabetes Care, 30, 790-794, 2007	PICO not met - comparator was not placebo
Hess,A.M., Sullivan,D.L., Metformin for prevention of type 2 diabetes, Annals of Pharmacotherapy, 38, 1283-1285, 2004	PICO criteria not met - population did not have type 2 diabetes
Johansen,K., Efficacy of metformin in the treatment of NIDDM. Meta-analysis, Diabetes Care, 22, 33-37, 1999	No data reported for children or young people with type 2 diabetes
Kane,M.P., bu-Baker,A., Busch,R.S., The utility of oral diabetes medications in type 2 diabetes of the young. [58 refs], Current Diabetes Reviews, 1, 83-92, 2005	Study criteria not met - overview of medications for type 2 diabetes
Kay,J.P., Alemzadeh,R., Langley,G., D'Angelo,L., Smith,P., Holshouser,S., Beneficial effects of metformin in normoglycemic morbidly obese adolescents, Metabolism: Clinical and Experimental, 50, 1457-1461, 2001	PICO criteria not met - population did not have type 2 diabetes

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Study	Reason for exclusion
List,J.F., Woo,V., Morales,E., Tang,W., Fiedorek,F.T., Sodium-glucose cotransport inhibition with dapagliflozin in type 2 diabetes, Diabetes Care, 32, 650-657, 2009	PICO criteria not met - population aged 18-79 years
Narasimhan,S., Weinstock,R.S., Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study, Mayo Clinic Proceedings, 89, 806-816, 2014	This is a review of the TODAY study
Saenz,Antonio, FernandezEsteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2013	Participants aged over 18 years
Saenz,Antonio, Fernandez-Esteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009	Systematic review of metformin versus placebo in adults with type 2 diabetes
Srinivasan,S., Ambler,G.R., Baur,L.A., Garnett,S.P., Tepsa,M., Yap,F., Ward,G.M., Cowell,C.T., Randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents: improvement in body composition and fasting insulin, Journal of Clinical Endocrinology and Metabolism, 91, 2074-2080, 2006	PICO criteria not met - population did not have type 2 diabetes
TODAY Study Group, Zeitler,P., Hirst,K., Pyle,L., Linder,B., Copeland,K., Arslanian,S., Cuttler,L., Nathan,D.M., Tollefsen,S., Wilfley,D., Kaufman,F., A clinical trial to maintain glycemic control in youth with type 2 diabetes, New England Journal of Medicine, 366, 2247-2256, 2012	PICO criteria not met - participants in all groups received metformin

H.23 Type 2 diabetes – HbA1c targets

Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?

Study	Reason for exclusion
Bailey,C.J., Bagdonas,A., Rubes,J., McMorn,S.O., Donaldson,J., Biswas,N., Stewart,M.W., Rosiglitazone/metformin fixed-dose combination compared with uptitrated metformin alone in type 2 diabetes mellitus: a 24-week, multicenter, randomized, double-blind, parallel-group study, Clinical Therapeutics, 27, 1548-1561, 2005	PICO not met: excluded patients aged <18 years
Chou,H.S., Palmer,J.P., Jones,A.R., Waterhouse,B., Ferreira-Cornwell,C., Krebs,J., Goldstein,B.J., Initial treatment with fixed-dose combination rosiglitazone/glimepiride in patients with previously untreated type 2 diabetes, Diabetes, Obesity and Metabolism, 10, 626-637, 2008	PICO not met: excluded patients aged <18 years
Derosa,G., Maffioli,P., D'Angelo,A., Salvadeo,S.A., Ferrari,I., Fogari,E., Mereu,R., Gravina,A., Palumbo,I., Randazzo,S., Cicero,A.F., Effects of insulin therapy with continuous subcutaneous insulin infusion (CSII) in diabetic patients: comparison with multi-daily insulin injections therapy (MDI), Endocrine Journal, 56, 571-578, 2009	PICO not met: excluded patients aged <18 years
Dorchy,H., Roggemans,M.P., Willems,D., Glycated hemoglobin and related factors in diabetic children and adolescents under 18 years of age: a Belgian experience, Diabetes Care, 20, 2-6, 1997	PICO not met: type 1 diabetes only.
hl-Jorgensen,K., Near-normoglycemia and late diabetic complications. The Oslo Study, Acta Endocrinologica, Supplementum. 284, 1-38, 1987	PICO not met: type 1 diabetes only.
Jones,K.L., Arslanian,S., Peterokova,V.A., Park,J.S., Tomlinson,M.J., Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial, Diabetes Care, 25, 89-94, 2002	Intervention not relevant - not treat to target
Rosenstock,J., Rood,J., Cobitz,A., Biswas,N., Chou,H., Garber,A., Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes, Diabetes, Obesity and Metabolism, 8, 650-660, 2006	PICO not met: excluded patients aged <18 years.
Saenz,Antonio, FernandezEsteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009	PICO not met: excluded patients aged <18 years.
Sellers,E.A., Dean,H.J., Short-term insulin therapy in adolescents with type 2 diabetes mellitus, Journal of Pediatric Endocrinology, 17, 1561-1564, 2004	No comparator.

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Study	Reason for exclusion
Tong,P.C., Ko,G.T., So,W.Y., Chiang,S.C., Yang,X., Kong,A.P., Ozaki,R., Ma,R.C., Cockram,C.S., Chow,C.C., Chan,J.C., Use of anti-diabetic drugs and glycaemic control in type 2 diabetes-tThe Hong Kong Diabetes Registry, Diabetes Research and Clinical Practice, 82, 346-352, 2008	Children and young people were included in the study but no separate analyses were reported.

H.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Study	Reason for exclusion
Al-Agha,A.E., Ocheltree,A., Shata,N., Prevalence of hyperinsulinism, type 2 diabetes mellitus and metabolic syndrome among Saudi overweight and obese pediatric patients, Minerva Pediatrica, 64, 623-631, 2012	Prevalence estimates (measurements of blood pressure and lipids) are not provided with respect to a specific time since diagnosis - only mean age at diagnosis is provided with a wide age range
Bacha,F., Gidding,S.S., Caprio,S., Weinstock,R., Lynch,J., Hirst,K., High prevalence and rapid increase of cardiovascular disease risk factors in youth with type 2 diabetes: The today study group, Circulation, 127, -, 2013	Abstract only
Miller,J., Silverstein,J., How prevalent are diabetes-related complications in patients with youth-onset type 2 diabetes mellitus?, Nature Clinical Practice Endocrinology and Metabolism, 3, 12-13, 2007	Commentary on a study weeded out as it compared type 2 diabetes with type 1 diabetes
Schober,E., Holl,R.W., Grabert,M., Thon,A., Rami,B., Kapellen,T., Seewi,O., Reinehr,T., Diabetes mellitus type 2 in childhood and adolescence in Germany and parts of Austria, European Journal of Pediatrics, 164, 705-707, 2005	Data not presented at specific timepoints since diagnosis (all cases are grouped together regardless of age or time since diagnosis)
Scott,C.R., Smith,J.M., Cradock,M.M., Pihoker,C., Characteristics of youth-onset noninsulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus at diagnosis, Pediatrics, 100, 84-91, 1997	Data not reported according to time since diagnosis or by age group. Mean age and range are reported - range is very wide (8 to 19 years)
Urakami,T., Suzuki,J., Yoshida,A., Saito,H., Wada,M., Takahashi,S., Mugishima,H., Frequencies of factors of metabolic syndrome at diagnosis in children with T2DM, Pediatrics International, 51, 435-437, 2009	The same population was used by another included study. Methods are not clear about measurements taken pre-1990 (the included study states that blood pressure and lipids were not measured pre-1990)
Zdravkovic,V., Daneman,D., Hamilton,J., Presentation and course of Type 2 diabetes in youth in a large multi-ethnic city, Diabetic Medicine, 21, 1144-1148, 2004	Wide age range (8.8 to 17.5 years) with data not reported according to time since diagnosis

H.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Study	Reason for exclusion
Al-Agha,A.E., Ocheltree,A., Shata,N., Prevalence of hyperinsulinism, type 2 diabetes mellitus and metabolic syndrome among Saudi overweight and obese pediatric patients, Minerva Pediatrica, 64, 623-631, 2012	Prevalence estimates (measurements of blood pressure and lipids) are not provided with respect to a specific time since diagnosis - only mean age at diagnosis is provided with a wide age range
Alavudeen,S.S., Dhanapal,C.K., Khan,N.A., Al,AkhaliK, Paulliah,S.D., Prevalence and control of cardiovascular risk factors among type 2 diabetes mellitus patients in southern region of Saudi Arabia, Journal of Young Pharmacists, 5, 144-147, 2013	Adult population only. Mean age 53.9 ±10.02 years
Albers,J.J., Marcovina,S.M., Imperatore,G., Snively,B.M., Stafford,J., Fujimoto,W.Y., Mayer-Davis,E.J., Petitti,D.B., Pihoker,C., Dolan,L., Dabelea,D.M., Prevalence and determinants of elevated apolipoprotein B and dense low-density lipoprotein in youths with type 1 and type 2 diabetes, Journal of Clinical Endocrinology and Metabolism, 93, 735-742, 2008	Data are not presented according to specific time points since diagnosis
Bacha,F., Gidding,S.S., Caprio,S., Weinstock,R., Lynch,J., Hirst,K., High prevalence and rapid increase of cardiovascular disease risk factors in youth with type 2 diabetes: The today study group, Circulation, 127, -, 2013	Abstract only

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Study	Reason for exclusion
Kershnar,A.K., Daniels,S.R., Imperatore,G., Palla,S.L., Petitti,D.B., Pettitt,D.J., Marcovina,S., Dolan,L.M., Hamman,R.F., Liese,A.D., Pihoker,C., Rodriguez,B.L., Lipid abnormalities are prevalent in youth with type 1 and type 2 diabetes: the SEARCH for Diabetes in Youth Study, Journal of Pediatrics, 149, 314-319, 2006	Data presented as >10 years of age only which captures the entire type 2 diabetes population. Results are not presented according to time since diagnosis or age groups
Levitsky,L., Burden of comorbidities in youth in the TODAY trial, Pediatric Diabetes, 13, 11-, 2012	Abstract only
Newfield,R.S., Dewan,A.K., Jain,S., Dyslipidemia in children with type 2 diabetes versus obesity, Pediatric Diabetes, 9, 115-121, 2008	Data are not presented at specific time points and are grouped together across different time points
Schober,E., Holl,R.W., Grabert,M., Thon,A., Rami,B., Kapellen,T., Seewi,O., Reinehr,T., Diabetes mellitus type 2 in childhood and adolescence in Germany and parts of Austria, European Journal of Pediatrics, 164, 705-707, 2005	Data not presented at specific timepoints since diagnosis (all cases are grouped together regardless of age or time since diagnosis)
Sellers,E.A.C., Yung,G., Dean,H.J., Dyslipidemia and other cardiovascular risk factors in a Canadian First Nation pediatric population with type 2 diabetes mellitus, Pediatric Diabetes, 8, 384-390, 2007	Data not analysed by specific time points since diagnosis. Only mean age at diagnosis and mean age when study performed are reported and data for all participants are reported together
Sulehria,S.B., Awan,A.K., Comparison of pattern of dyslipidemia in type 1 & type 2 diabetes mellitus, Pakistan Journal of Medical and Health Sciences, 7, 911-912, 2013	Age range 13 to 85 years. No subgroup analyses
White,N.H., Pyle,L., Tamborlane,W.V., Geffner,M.E., Guandalini,C., Clinical characteristics and co-morbidities in a large cohort of youth with type 2 diabetes mellitus (T2DM) screened for the treatment options for type 2 diabetes in adolescents and youth (TODAY) study, Diabetes, 58 , 2009. Date of Publication, -, 2009	Abstract only. One data table is provided but only mean values, not prevalences, are reported

H.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

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Study	Reason for exclusion
Amutha,A., Datta,M., Unnikrishnan,R., Anjana,R.M., Mohan,V., Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India, Diabetes Technology and Therapeutics, 14, 497-504, 2012	Mean age at screening for retinopathy 22.2 years (±9.7 years). Prevalence of retinopathy stratified by duration of diabetes (<5, 5 to 10, 10 to 15 and >15 years) but not by age
Boussageon,R., Bejan-Angoulvant,T., Saadatian-Elahi,M., Lafont,S., Bergeonneay,C., Kassai,B., Erpeldinger,S., Wright, J.M., Gueyfflier,F., Cornu,C., Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials, BMJ, 343, d4169, 2011	All participants aged >18 years
Danne,T., Kordonouri,O., Casani,A., Chiarelli,F., Diabetic retinopathy in childhood and adolescents, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 12, 136-144, 1999	Narrative review article
Dart,A.B., Martens,P.J., Rigatto,C., Brownell,M.D., Dean,H.J., Sellers,E.A., Earlier onset of complications in youth with type 2 diabetes, Diabetes Care, 37, 436-443, 2014	No stratification by age
Donaghue,K.C., Chiarelli,F., Trotta,D., Allgrove,J., hl-Jorgensen,K., Microvascular and macrovascular complications associated with diabetes in children and adolescents, Pediatric Diabetes, 10, 195-203, 2009	Narrative review article
Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005	Type 1 diabetes
Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003	Type 1 diabetes. Data on prevalence of retinopathy stratified by age or duration of diabetes not reported. Data reported as survival analysis only
El,AsrarM, Adly,A.A., El,HadidyE, Abdelwahab,M.A., D-dimer levels in type 1 and type 2 diabetic children and adolescents; Relation to microvascular complications and dyslipidemia "own data and review", Pediatric endocrinology reviews : PER, 9, 657-668, 2012	Ophthalmoscopy used for identification of retinopathy. No stratification of prevalence according to age or duration of diabetes

Study	Reason for exclusion
Eppens,M.C., Craig,M.E., Cusumano,J., Hing,S., Chan,A.K., Howard,N.J., Silink,M., Donaghue,K.C., Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes, Diabetes Care, 29, 1300-1306, 2006	Prevalence of retinopathy not stratified by age or duration of diabetes. Age range for participants with type 2 diabetes not reported
Farah,S.E., Wals,K.T., Friedman,I.B., Pisacano,M.A., Martino-Nardi,J., Prevalence of retinopathy and microalbuminuria in pediatric type 2 diabetes mellitus, Journal of Pediatric Endocrinology, 19, 937-942, 2006	Ophthalmoscopy only used to identify retinopathy
Forster,A.S., Forbes,A., Dodhia,H., Connor,C., Du,CheminA, Sivaprasad,S., Mann,S., Gulliford,M.C., Changes in detection of retinopathy in type 2 diabetes in the first 4 years of a population-based diabetic eye screening program: Retrospective cohort study, Diabetes Care, 36, 2663-2669, 2013	Outcome not stratified by age. Population mean age not described, but likely to include adults as well as children and young people
Jialal,I., Welsh,N.H., Joubert,S.M., Rajput,M.C., Vascular complications in non-insulin-dependent diabetes in the young, South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde. 62, 155-157, 1982	Age of participants not fully reported, but age of participants with retinopathy reported as 24 to 52 years, therefore likely to be inappropriate age group
Mayer-Davis,E.J., Davis,C., Saadine,J., D'Agostino,R.B.,Jr., Dabelea,D., Dolan,L., Garg,S., Lawrence,J.M., Pihoker,C., Rodriguez,B.L., Klein,B.E., Klein,R., SEARCH for Diabetes in Youth Study Group., Diabetic retinopathy in the SEARCH for Diabetes in Youth Cohort: a pilot study, Diabetic Medicine, 29, 1148-1152, 2012	Mean age of participants with type 2 diabetes reported as 21.1 years (SD 2.8 years). Prevalence not stratified by age or duration of diabetes
Papali'i-Curtin,A.T., Dalziel,D.M., Prevalence of diabetic retinopathy and maculopathy in Northland, New Zealand: 2011-2012, New Zealand Medical Journal, 126, 20-28, 2013	Mean age 62.7 years
Raman,V., Campbell,F., Holland,P., Chapman,T., Dabbs,T., Bodansky,H.J., O'Neill,D.P., Retinopathy screening in children and adolescents with diabetes, Annals of the New York Academy of Sciences, 958, 387-389, 2002	Type 1 diabetes. No stratification by age or duration of diabetes. Detection of retinopathy was either by fundus photography or by slit lamp examination
Verougstraete,C., Toussaint,D., De,SchepperJ, Haentjens,M., Dorchy,H., First microangiographic abnormalities in childhood diabetes - Types of lesions, Graefe's Archive for Clinical and Experimental Ophthalmology, 229, 24-32, 1991	Type 1 diabetes. Intervention not relevant - fluoroscein angiography used to detect retinopathy
Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999	No description of prevalence of retinopathy for children and young people aged under 18

Update 2015

H.27 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Study	Reason for exclusion
Copeland,K.C., Zeitler,P., Geffner,M., Guandalini,C., Higgins,J., Hirst,K., Kaufman,F.R., Linder,B., Marcovina,S., McGuigan,P., Pyle,L., Tamborlane,W., Willi,S., Characteristics of adolescents and youth with recent-onset type 2 diabetes: The TODAY cohort at baseline, Journal of Clinical Endocrinology and Metabolism, 96, 159-167, 2011	The reported microalbuminuria prevalence was tested on one urine sample only rather than on two out of three as reported. (This was clarified by the Today Cohort Study Group in correspondence with NCC-WCH)
Ettinger,L.M., Freeman,K., Martino-Nardi,J.R., Flynn,J.T., Microalbuminuria and abnormal ambulatory blood pressure in adolescents with type 2 diabetes mellitus, Journal of Pediatrics, 147, 67-73, 2005	Just an overall prevalence was reported, no stratification according to age.
Kim,N.H., Pavkov,M.E., Knowler,W.C., Hanson,R.L., Weil,E.J., Curtis,J.M., Bennett,P.H., Nelson,R.G., Predictive value of albuminuria in American Indian youth with or without type 2 diabetes, Pediatrics, 125, e844-e851, 2010	The incidence of microalbuminuria by age was only reported only in a graph.
Krakoff,J., Lindsay,R.S., Looker,H.C., Nelson,R.G., Hanson,R.L., Knowler,W.C., Incidence of retinopathy and nephropathy in youth-onset compared with adult-onset type 2 diabetes, Diabetes Care, 26, 76-81, 2003	The incidence rate by age (10 to 15 years) was only reported in a graph.
Maahs,D.M., Snively,B.M., Bell,R.A., Dolan,L., Hirsch,I., Imperatore,G., Linder,B., Marcovina,S.M., Mayer-Davis,E.J., Pettitt,D.J., Rodriguez,B.L., Dabelea,D., Higher prevalence of elevated albumin excretion in youth with type 2 than type 1 diabetes: the SEARCH for Diabetes in Youth study, Diabetes Care, 30, 2593-2598, 2007	Just an overall prevalence was reported, no stratification according to age.

Study	Reason for exclusion
Shield,J.P.H., Lynn,R., Wan,K.C., Haines,L., Barrett,T.G., Management and 1 year outcome for UK children with type 2 diabetes, Archives of Disease in Childhood, 94, 206-209, 2009	Just an overall prevalence was reported, no stratification according to age.
TODAY Study Group., Rapid rise in hypertension and nephropathy in youth with type 2 diabetes: the TODAY clinical trial.[Erratum appears in Diabetes Care. 2013 Aug;36(8):2448], Diabetes Care, 36, 1735-1741, 2013	Publication with error corrected on the TODAY clinical trial, relevant data to this review(which remain intact) have been extracted from the original publication.

H.28 Health economics

Study	Reason for exclusion
Anderson,D.G., Multiple daily injections in young patients using the ezy-BICC bolus insulin calculation card, compared to mixed insulin and CSII, Pediatric Diabetes, 10, 304-309, 2009	Right comparator, but no costs included
Blair,J., Gregory,J.W., Peak,M., Insulin delivery by multiple daily injections or continuous subcutaneous insulin infusion in childhood: Addressing the evidence gap, Practical Diabetes, 29, 47-48, 2012	Commentary; no cost effectiveness
Centre for Reviews and Dissemination, The cost-effectiveness of continuous glucose monitoring in type 1 diabetes (Provisional abstract), NHS Economic Evaluation Database (NHSEED), -, 2010	Cost utility analysis (CUA) conducted only in adult cohort
Centre for Reviews and Dissemination, Continuous subcutaneous insulin infusion versus multiple daily injections of insulin: economic comparison in adult and adolescent Type 1 diabetes mellitus in Australia (Structured abstract), NHS Economic Evaluation Database (NHSEED), -, 2007	CSII was not included in the 2015 update scope
Chiari,G., Direct measurement of 3-B-hydroxybutyrate in the management of diabetic ketoacidosis in children: A cost effective enhancement in the management of diabetic ketoacidosis in children, Diabetes Technology and Therapeutics, 13, 178-179, 2011	Same study/data as Vanelli 2003: no economic evaluation, only limited information on clinical cost (test, ICU)
Couch,R., Jetha,M., Dryden,D.M., Hooton,N., Liang,Y., Durec,T., Sumamo,E., Spooner,C., Milne,A., Gorman,K., Klassen,T.P., Diabetes education for children with type 1 diabetes mellitus and their families (Structured abstract), Health Technology Assessment Database, -, 2013	No cost effectiveness model; comparator not clear
Gage,H., Hampson,S., Skinner,T.C., Hart,J., Storey,L., Foxcroft,D., Kimber,A., Cradock,S., McEvilly,E.A., Educational and psychosocial programmes for adolescents with diabetes: approaches, outcomes and cost-effectiveness. [122 refs], Patient Education and Counseling, 53, 333-346, 2004	No cost effectiveness model for structured education versus usual care
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. [148 refs], Health Technology Assessment (Winchester, England), 5, 1-79, 2001	No information on structured education programmes reported
Health,Technology Assessment, Randomised controlled trial of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type I diabetes mellitus (Project record), Health Technology Assessment Database, -, 2013	CSII was not included in the 2015 update scope
Health,Technology Assessment, Maximising engagement, motivation and long term change in a structured intensive education programme in diabetes for children, young people and their families: child and adolescent structured competencies approach to diabetes education (Project record), Health Technology Assessment Database, -, 2013	Not reporting results
Huang,E.S., O'Grady,M., Basu,A., Winn,A., John,P., Lee,J., Meltzer,D., Kollman,C., Laffel,L., Tamborlane,W., Weinzimer,S., Wysocki,T., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., The cost-effectiveness of continuous glucose monitoring in type 1 diabetes.[Erratum appears in Diabetes Care. 2010 Sep;33(9):2129], Diabetes Care, 33, 1269-1274, 2010	CUA conducted only in adult cohort
Huang,E.S., O'Grady,M., Basu,A., Winn,A., John,P., Lee,J., Meltzer,D., Kollman,C., Laffel,L., Tamborlane,W., Weinzimer,S., Wysocki,T., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., The cost-effectiveness of continuous glucose monitoring in type 1 diabetes.[Erratum appears in Diabetes Care. 2010 Sep;33(9):2129], Diabetes Care, 33, 1269-1274, 2010	Adult population
Laffel,L.M., Wentzell,K., Loughlin,C., Tovar,A., Moltz,K., Brink,S., Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces hospital visits in young people with T1DM: a randomized clinical trial, Diabetic Medicine, 23, 278-284, 2006	Right comparator, but no costs or cost effectiveness model
Meltzer,D., Egleston,B., Stoffel,D., Dasbach,E., Effect of future costs on cost-effectiveness of medical interventions among young adults: the example of intensive therapy for type 1 diabetes mellitus, Medical Care, 38, 679-685, 2000	DCCT model included participants aged 13 to 39 years, thus costs and benefits associated with children and young people cannot be estimated from this trial

Update 2015

Study	Reason for exclusion
Nahata,L., Insulin therapy in pediatric patients with type I diabetes: continuous subcutaneous insulin infusion versus multiple daily injections. [12 refs], Clinical Pediatrics, 45, 503-508, 2006	Literature review, no cost data
Price,K.J., Wales,J., Eiser,C., Knowles,J., Heller,S., Freeman,J., Brennan,A., McPherson,A., Wellington,J., Does an intensive self-management structured education course improve outcomes for children and young people with type 1 diabetes? The Kids In Control OF Food (KICk-OFF) clusterrandomised controlled trial protocol, BMJ Open, 3, -, 2013	Not reporting results
Slover,I.I.R.H., Continuous glucose monitoring in children and adolescents, Current Diabetes Reports, 12, 510-516, 2012	Literature review, cost effectiveness information from Huang 2010
St,Charles M., Lynch,P., Graham,C., Minshall,M.E., A cost-effectiveness analysis of continuous subcutaneous insulin injection versus multiple daily injections in type 1 diabetes patients: a third-party US payer perspective, Value in Health, 12, 674-686, 2009	CSII was not included in the 2015 update scope
Vanelli,M., Chiari,G., Capuano,C., Iovane,B., Bernardini,A., Giacalone,T., The direct measurement of 3-beta-hydroxy butyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 16, 312-316, 2003	No economic evaluation, only limited information on clinical cost (test, ICU)

Appendix I: Evidence tables

The evidence tables from the 2004 guideline are presented in a separate document.

The evidence tables from the 2015 update are presented in a separate document, except for those related to the review question about diagnosis which are presented below.

Update 2015

I.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline on type 1 diabetes in adults.

I.1.1 Population: young people only (all sample sizes)

Table 4: Andersson 2013

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
C. Andersson, F. Vaziri-Sani, Aj Delli, B. Lindblad, A. Carlsson, G. Forsander, J. Ludvigsson, C. Marcus, U. Samuelsson, Sa Ivarsson, A. Lernmark, H. Elding Larsson, and BDD Study Group. Triple specificity of ZnT8 autoantibodies in relation to HLA and other islet autoantibodies in childhood and adolescent type 1 diabetes. Pediatr.Diabetes 14 (2):97-105, 2013. REF ID: Andersson 2013	Observational: cross-sectional Sweden	N=427 young people aged 16 to 17.9 years Total n=3165 T1D young people and children Inclusion criteria: T1D (ADA criteria) Swedish SWEDIAL KIDS register Exclusion criteria: None given	Young people subgroup (age 16 to 17.9 years) Diabetes type: T1D	T1D: IAA GADA IA-2A Cut-offs for positivity GADA: >50 U/mL IA-2A: >10 U/mL IAA: >1RU (based on internal + and - standard samples)	Baseline	T1D young people (>15 years: 15 to 17.9 years)	Funding: Swedish Research Council and other non-pharmaceutical funded sources. Risk of bias: NA

Update 2015

Table 5: Barker 2014

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
A. Barker, A. Lauria, N. Schloot, N. Hosszufalusi, J. Ludvigsson, C. Mathieu, D. Mauricio, M. Nordwall, B. Van Der Schueren, T. Mandrup-Poulsen, W. A. Scherbaum, I. Weets, F. K. Gorus, N. Wareham, R. D. Leslie, and P. Pozzilli. Age-dependent decline of beta-cell function in type 1 diabetes after diagnosis: a multi-centre longitudinal study. Diabestes Obes.Metab. 16 (3):262-267, 2014. REF ID: Barker 2014	Observational: prospective case-series 7 European registries	n=995 young people subgroup Total n=3929 T1D adults, young people, and children Inclusion criteria: T1D (ADA and WHO criteria) Exclusion criteria: None given	Young people subgroup (age at onset >10 and ≤18 years) Diabetes type: T1D	T1D: Fasting C-pep Stimulated C-pep (results not given in study due to very small number of stim C-pep mmts made) Cut-offs for positivity C-pep: detection limit 0.01 nM	Baseline, 1 and 5 years	T1D young people	Funding: Centro Internazionale Studi Diabete. Risk of bias: NA lots of missing data at follow-up

Table 6: Tung 2008

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
Y C Tung, JS Lee, WY Tsai, and PH Hsiao. Evaluation of beta-cell function in diabetic Taiwanese children using a 6-min glucagon test.	Observational: cross-sectional study Single centre, Taiwan	Total n=118 T1D (n=20 T2D young people and n=98 T1D children and young people) Inclusion criteria: Newly diagnosed diabetes <18 years of age Received neither oral hypoglycaemic agents nor insulin therapy before the study	Young people with diabetes type 2D T2D n=20		T2D: fC-PEPTIDE Cut-offs for positivity fC-PEPTIDE+: 0.1 nmol/L	NA	T2D young people (n=20)		Funding: Not reported Risk of bias: NA
			Age, years, median (range)	13.3 (11.1 to 15.7)			fC-PEPTIDE+, nmol/L (range)	1.0 (0.5 to 5.1)	
			M/F %	40/60					

Update 2015

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
Eur.J.Pediatr. 167 (7):801-805, 2008. REFID: Tung 2008		IAA, GADA and IA-2 were measured to confirm the Diagnosis Exclusion criteria: None reported						

Table 7: Shivaprasad 2014

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
C. Shivaprasad, Rajneesh Mittal, Mala Dharmalingam, and Prasanna K. Kumar. Zinc transporter-8 autoantibodies can replace IA-2 autoantibodies as a serological marker for juvenile onset type 1 diabetes in India. Indian J Endocrinol Metab 18 (3):345-349, 2014. REF ID: Shivaprasad 2014	Observational: cross-sectional India	n=88 young people Inclusion criteria: Diabetes (ADA criteria) T1D Diagnosis: ketosis at presentation, lean phenotype, requirement for insulin, and/or low C-peptide Duration from Diagnosis <48 months Exclusion criteria: None given	Young people Diabetes type: T1D (n=21 newly Diagnosis)		T1D: ZnT8 GAD65 IA-2 Cut-offs for positivity ZnT8: ≥15 U/ml GAD65: >20 U/ml IA-2: >75 U/ml	Baseline	T1D young people		Funding: UGC Sri Lanka. Risk of bias: NA consecutive recruitment
				T1D all n=88			GAD65	64.7%	
			Age, mean (SD)	11.0 (4.2) years			IA-2	19.3%	
			HbA1c, % man (SD)	8.6 (1.3)			ZnT8	31.8%	
			Duration of diabetes, mean (SD)	11.5 (14.4) months			GAD+/ZnT8+	15.9%	
							GAD+/IA-2+	9.1%	
							GAD+/IA-2+/ZnT8+	5.7%	
							IA-2+/ZnT8+	2.3%	

Table 8: Vermeulan 2011

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G.	Observational: case-control study Single centre, Taiwan	Total n=655 T1D (extra n=761 controls) Data here are for young people only: aged 10 to 39 (most were >11 years) Inclusion criteria: Newly diagnosed diabetes <18 years of age	Young people diabetes type: T1D controls (health)		T1D: GADA IA-2 ZnT8 Combinations Cut-offs for positivity fC-PEPTIDE+: 0.1 nmol/L	NA	T1D young people (n=20)		Funding: Not reported Risk of bias: NA
				T1D n=655			fC-PEPTIDE+, nmol/L (range)	1.0 (0.5 to 5.1)	

Update 2015

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
Pipeleers, and F. K. Gorus. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. Diabetes Care 34 (8):1760-1765, 2011. Vermeula 2011		Received neither oral hypoglycaemic agents nor insulin therapy before the study IAA, GADA and IA-2 were measured to confirm the Diagnosis Exclusion criteria: None reported	Age, years, median (range) M/F %	13.3 (11.1 to 15.7) 40/60				

Table 9: Zanone 2003

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
M. M. Zanone, E. Catalfamo, S. L. Pietropaolo, I. Rabbone, C. Sacchetti, F. Cerutti, M. Trucco, and P. Cavallo-Perin. Glutamic acid decarboxylase and ICA512/IA-2 autoantibodies as disease markers and relationship to residual beta-cell function and glycemic control in young type 1 diabetic patients. Metabolism. 52 (1):25-29, 2003. REF ID: Zanone 2003	Observational: cross-sectional study Single centre, Italy	Total n=154 T1D (n=91 young people and n=63 children) Inclusion criteria: IDDM Adolescents (young people) Exclusion criteria: None reported	Young people Diabetes type: T1D		T1D: C-PEPTIDE GADA65 ICA IA-2 Cut-offs for positivity fC-PEPTIDE+: not given ICA512/IA-2+: Index* of 0.032 GAD65+: Index* of 0.069 ICA+: >5 JDF units *INDEX=sample cpm – negative control cpm /positive control cpm - negative control cpm	NA	T1D young people (n=91)		Funding: Not reported Risk of bias: NA
				T1D n=91			fC-PEPTIDE+,	n=23/91 (25%)	
			Age, years, mean (range; SD)	14.7 (11 to 18; 1.6)			fC-PEPTIDE+, ng/mL (SD)	0.11 (0.09)	
			Duration of diabetes, years, mean (SD)	7 (3.5)			ICA+	31 (34%)	
			M/F %	52/48			GAD65+	40 (44%)	
							IA-2 (ICA 512)+	41 (45%)	
							GAD+/IA-2+	19 (21%)	
							GAD+ and/or IA-2+	62 (68%)	
							ICA+, GAD+ and IA-2+	8 (9%)	
							ICA- / GAD+ and/or IA-2+	36 (40%)	
							ICA+ / GAD- and/or IA-2-	6 (6%)	

Update 2015

I.1.2 Population: young people and adults (mixed population studies); n ≥50

Table 10: Besser 2011

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
R. Besser, J. Ludvigsson, A. Jones, T. McDonald, B. Shields, B. Knight, and A. Hattersley. Urine C-peptide creatinine ratio is a noninvasive alternative to the mixed-meal tolerance test in children and adults with type 1 diabetes. Diabetes Care 34 (3):607-609, 2011. REF ID: Besser 2011	Observational: cohort study Adults from diabetes clinic, UK; young people from paediatric clinic, Sweden	Total n=72 T1D (mixture of young people and adults) Inclusion criteria: T1D Young people (<19 years) and adults (≥18 years) Age of Diagnosis: <30 years on insulin since diagnosis Exclusion criteria: known renal impairment (eGFR<60ml/min/1.73m2) severe hypoglyc. within last 3 months documented hypoglycaemia unawareness with a blood glucose <3mmol/L, and HbA1c >10%.	Young people (n=21) and adults diabetes type: T1D (n=72) Young (n=21) / Adults (n=51) Age, years, median (IQR): 14 (10.9 to 16.4) / 18 (13 to 24) M/F, %: 33/67 / 51/49 Diabetes duration, years, median (IQR): 2.6 (0.6 to 5.0) / 21.4 (2.8 to 41.0) HbA1c, median (IQR), %: 7.2 (6.6 to 7.9) / 7.8 (6.9 to 9.0) To enrich for patients who had endogenous insulin secretion, 43% patients were either within 5 years of Diagnosis or known to still secrete C-peptide when previously tested.	Patients underwent a standard mixed-meal tolerance test (MMTT) T1D: C-PEPTIDE (serum, sCP) Urine C-peptide creatinine ratio (UCPCR) sCP: collected at 0 and 90 min. Additional samples at 30, 60, and 120min in pediatric patients (n=18), allowing area under the curve (AUC) to be calculated. Urine was collected as a fasting second morning void immediately before the start of the MMTT (0 min) and after 120 min. Significant endogenous insulin secretion was defined as 90-min sCP ≥0.2 nmol/L, in accordance with the DCCT Urine: collected in boric acid 120 min after evening meal following a premeal void. Adult patients took further home urine samples 120 min after a standard 60 g CHO breakfast and following the patients' own lunch. Urine samples brought to the research centre within 24h.	n/A – immediate testing (up to 120 mins)	T1D (n=75) Association between 90-min sCP (1) and both the MMTT 120-min UCPCR and after the home evening meal In the pediatric cohort, correlations were also determined between AUC sCP and 120-min UCPCR. UCPCR cutoffs equivalent to 90-min sCP ≥0.2 nmol/L were derived using linear regression equations. UCPCR (120 min) following a home evening meal was compared with that after a MMTT. Results: MMTT 120-min UCPCR was highly correlated to 90-min sCP (r=0.97; p< 0.0001). UCPCR ≥0.53 nmol/mmol had 94% sensitivity/100% specificity for significant endogenous insulin secretion (90-min sCP ≥0.2 nmol/L). The 120-min postprandial evening meal UCPCR was highly correlated to 90-min sCP (r=0.91; p<0.0001). UCPCR ≥0.37 nmol/mmol had 84% sensitivity/97% specificity for sCP ≥0.2 nmol/L. AUTHORS' CONCLUSIONS: UCPCR measured during an MMTT or after a home meal is highly correlated with MMTT sCP. UCPCR testing is a	Funding: Diabteets UK, Peninsula NIHR Clinical Research Facility, EC program Collaborative European Effort to Develop Diabetes Diagnostics; arndiabetesfonden (The Swedish Child Diabetes Foundation) and the Swedish Research Council. Risk of bias: NA

Update 2015

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
						sensitive and specific method for detecting insulin secretion. UCPCR may be a practical alternative to serumC-peptide testing, avoiding the need for inpatient investigation.	

Table 11: Borg 2003

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
H. Borg, H. J. Arnqvist, E. Bjork, J. Bolinder, J. W. Eriksson, L. Nystrom, J. O. Jeppsson, and G. Sundkvist. Evaluation of the new ADA and WHO criteria for classification of diabetes mellitus in young adult people (15-34 years) in the Diabetes Incidence Study in Sweden (DISS). Diabetologia 46 (2):173-181, 2003. REF ID: Borg 2003	Observational: Cohort Registry, Sweden	Total n=422 T1D & T2D n=285 T1D, n=81 T2D (mixture of young people and adults) Inclusion criteria: Patients aged 15 to 34 at diagnosis Exclusion criteria: None stated	Young people and adults Diabetes type: T1D (n=285) T2D (n=81) Unclassified (n=85) T1D & T2D Age, years, median (IQR): 25 (10) M/F %: 254 (60%)/168 (40%)	T1D & T2D: ICA GADA GADA+ index IA-2A IA-2A index Any antibody + 3 Ab 2 Ab ICA & GADA ICA & IA-2A 1 Ab ICA GADA IA-2A C-PEPTIDE Cut-offs for positivity C-PEPTIDE+: 0.10 nmol/L ICA512/IA-2+: Index* of IA-2A: Index* of 1.0 GADA+: Index* of 4.6 ICA+: >4 JDF units *INDEX=sample cpm – negative control	1 year	T1D (n=285) ICA: n (%)=143 (54) GADA: 206 (77) GADA+ index: 53 (78) IA-2A: 123 (46) IA-2A index: 91 (90) Any antibody +: 220 (83) 3 Ab: 89 (40) 2 Ab: 74 (34) ICA & GADA: 47 (21) ICA & IA-2A: 6 (3) GADA & IA-2A: 21 (10) 1 Ab: 57 (26) ICA: 1 (0.5) GADA: 49 (22) IA-2A: 7 (3) T2D (n=81) ICA: 12 (15) GADA: 16 (21) GADA+ index: 72 (85)	Funding: Juvenile diabetes foundation-Wallenberg Diabetes research program, Lundstrom foundation, Novo-Nordisk foundation, Research funds of Malmo universityhospital, faculty of medicine at Lund university, Albert Pahlson Foundation, Swedish Diabetes association Risk of bias: NA

Update 2015

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
				cpm /positive control cpm -negative control cpm		IA-2A	12 (15)	
						IA-2A index	94 (101)	
						Any antibody +	18 (23)	
						3 Ab	7 (39)	
						2 Ab	8 (44)	
						ICA & GADA	3 (17)	
						ICA & IA-2A	2 (11)	
						GADA & IA-2A	3 (17)	
						1 Ab	3 (17)	
						ICA	0	
						GADA	3 (17)	
						IA-2A	0	
						P-C-PEPTIDE: Carried out in patients that were tested for C peptide within 1 week after diagnosis At diagnosis: Undetectable (<0.10 nmol/L): Ab+: 30/123 (24.4%) Ab-: 1/36 (2.8) Low (<0.25 nmol/L) Ab+: 72/123 (58.5) Ab-:2/36 (5.6) Follow up: Undetectable (<0.10 nmol/L): Ab+: 13/123 (10.6) Ab-: 3/36 (8.3) Aong all Ab- patients, 13/93 had low fasting P-C Peptide (0.25 nmol/L) and 12/13 had T1D		

Update 2015

Table 12: Brunova 2002

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
J. Brunova, J. Bruna, M. Koning, M. Meyer, G. Joubert, and W. Mollentze. GAD65Ab and primary hypothyroidism in type 1 and 2 diabetic subjects. J.Endocrinol.M	Observational: cross-sectional study Single centre, South Africa	Total n=192 (n=55 T1D and n=137 T2D) Inclusion criteria: Clinical Diagnosis of T1D and T2D Exclusion criteria: None reported	Adults and young people Diabetes type: T2D T1D		T1D: GAD65 T2D: fC-PEPTIDE GAD65 Cut-offs for positivity fC-PEPTIDE+: not given GAD65+: not given	NA	T1D (n=55)		Funding: Not reported Risk of bias: NA
							GAD65+	17/55 (30.9%)	
			T1D n=55; T2D n=137				T2D (n=137)		
			Age, years, (range)	13 to 85 years			GAD65+	9/137 (6.6%)	
							fC-PEPTIDE in GAD- patients, pmol/L (SD)	637.6 (503)	
							fC-PEPTIDE in GAD- patients, pmol/L (SD)	1168.1 (732)	
			M/F %	50/50					

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
etab.Diabetes S.Afr. 7 (1):6-8, 2002. REFID: Brunova 2002							The presence of GAD65 in T2D was associated with lower levels of fC-PEPTIDE	

Table 13: Laadhar 2007

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
L. Laadhar, M. Zitouni, M. Kallel-Sellami, R. Bouguerra, H. Chaabouni, and S. Makni. Spectrum of autoantibodies in Tunisian adult type 1 diabetes mellitus. Ann.N.Y.Acad. Sci. 1107:356-362, 2007. REFID: Laadhar 2007	Observational: cross-sectional study Single centre, Tunisia	Total n=261 T1D Inclusion criteria: Clinical diagnosis of T1D Exclusion criteria: None reported	Adults and young people Diabetes type: T1D		T1D: fC-PEPTIDE Cut-offs for positivity ICA+: not given	NA	T1D (n=261)		Funding: Not reported Risk of bias: NA
							ICA+	88 (33.7%)	
							ICA+ in patients <1 year diabetes	47.7%	
			T1D n=261						
			Age, years, mean (SD; range)	29.1 (1.9; 16 to 60)					
			Age at Diagnosis, years, mean (SD)	20.3 (10.3)					
			M/F %	48/52					

Table 14: Lu 2014

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes (baseline)		Comments
H Lu, F Hu, Y Zeng, L Zou, S Luo, Y Sun, H Liu, and L Sun. Ketosis onset type 2 diabetes had better islet beta-cell function	Observational: cross-sectionals tudy	n=140 Inclusion criteria: Newly diagnosed T2D Without islet-associated autoantibodies Age 16 to 68 years	Adults and young people Diabetes type: T2D	T2D: Fasting C-PEPTIDE	NA	T2D adults and young people		Funding: Not reported Risk of bias: NA
						f-C-PEP, pmol/L (SD)	Ketosis group: 475.8 (406)	
							Nonketotic group: 348.2 (283)	

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and more serious insulin resistance. J Diabetes Res 2014:510643, 2014. REF ID: Lu 2014	China	Diagnosis: WHO criteria If had Plasma glucose >250 mg/ml and positive urine ketone body=diabetic ketosis Diagnosis. Exclusion criteria: Evidence of other disease Taking agents known to affect CHO metabolism Obvious precipitating causes for the development of ketosis		Ketosis onset T2D n=62	Nonketotic onset T2D n=78	Cut-offs for positivity AUC			
			Age, years mean	44.8	47.0				
			M/F %	66	72				
			BMI, mean	25.0	24.4			T1D patients versus LADA: T1D were younger, lower age of onset. NS difference in number of patients with high GAD titer.	
			HbA1c	11.0%	11.8%				
			Drop-outs / missing data: none						

Table 15: McDonald 2011

Reference	Study type	Number of patients	Patient characteristics			Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
T.McDonald, K. Colclough, R. Brown, B. Shields, M. Shepherd, P. Bingley, A. Williams, A. Hattersley, and Sian Ellard. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. Diabet.Med. 28 (9):1028-1033, 2011. REF ID: McDonald 2011	Observational: cross-sectional study UK study	Total n=616 n=98 T1D – adults and young people n=508 MODY – but adults only Inclusion criteria: Clinical history of diabetes HbA1c <6.0% MODY Diagnosis by genetic testing T1D Diagnosis in last 6 mths Exclusion criteria: None given	Adults and young people Diabetes type: T1D MODY			T1D: GAD IA-2 MODY: GAD IA-2 Cut-offs for positivity GAD+: 64 WHO units/ml (99th percentile) IA-2+: 15 WHO units/ml (99th percentile; lowest calibrator)	NA	T1D		Funding: None reported Risk of bias: NA
				T1D n=98	MODY n=508			GAD+	24/98 (24.5%)	
			Age, years, median (IQR)	15 (12-25)	36 (18-50)			IA-2+	19/98 (94.5%)	
								GAD+ and/or IA-2)+	80/98 (82%)	
								GAD+ and IA-2+	37/98 (37.8%)	
			Duration of diabetes, years, median (IQR)	<6 months	9 (4 to 25)			MODY		
								GAD+	5 (1%)	
								IA-2+	0 (0%)	
								GAD+ and/or IA-2+	5/508 (1%)	

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Table 16: Oram 2014

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
R. A. Oram, A. G. Jones, R. E. J. Besser, B. A. Knight, B. M. Shields, R. J. Brown, A. T. Hattersley, and T. J. McDonald. The majority of patients with long-duration type 1 diabetes are insulin microsecretors and have functioning beta cells. Diabetologia 57 (1):187-191, 2014. REF ID: Oram 2014	Observational: cross-sectional UK	n=74 adults and young people Inclusion criteria: T1D for >5 years Diagnosis at either <30 years age (n=68) or >30 years age with islet autoAbs present (n=6) All patients on insulin since Diagnosis. Exclusion criteria: None given	Adults and young people diabetes type: T1D		T1D: UCPCR (urinary c-peptide:creatinine ratio) Fasting C-pep Stim C-pep Cut-offs for positivity C-PEPTIDE: 3.3 pmol/L	Baseline	T1D adults and young people		Funding: Diabetes UK, and NIHR. Risk of bias: NA
				T1D all n=74			Fasting C-Peptide	73%	
			Age at Diagnosis, median (IQR)	16 (9 to 23) years			Non-fasting C-Peptide	66%	
			Male	51%			Fasting UCPCR	68%	
			Duration of diabetes, median (IQR)	30 (19 to 41 years)			Non-fasting UCPCR	68%	
			BMI, median (IQR)	25 (23 to 28) kg/m2			C-peptide titres are compared using different assays; results not been extracted for this review as do not know which is the best (in terms of Diagnosis accuracy) assay method to us		
			HbA1c, median (IQR)	7.9 (7.2 to 9.0) kg/m2					

Table 17: Ota 2005

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
T Ota, T Takamura, Y Nagai, Y Bando, and R Usuda. Significance of IA-2 antibody in Japanese type 1 diabetes: its association with GAD antibody. Diabetes Res.Clin.Pract.	Observational: cross-sectional study	Total n=101 T1D Inclusion criteria: T1D classified by American diabetes association Exclusion criteria: None reported	ADULTS AND YOUNG PEOPLE DIABETES TYPE: T1D		T1D: C-PEPTIDE GADA65 IA-2A Cut-offs for positivity ICA512/IA-2: 0.4 U/mL GAD65+: 1.3 U/mL	NA	T1D (n=101)		Funding: Not reported
			T1D n=101				GAD65+	n=60/101 (59%)	
			Age, years, mean (range; SD)	41.3 (14.0 to 89.0; 15.3)			IA-2+	37/101 (37)	
			Duration of diabetes, years, mean (SD)	10.4 (9.6)			IA-2+/ GAD65-	10 (10)	
							GAD65+/ IA-2+	27 (27)	
							GAD65+/IA-2-	33 (32)	
			M/F %	47/54			Acute onset T1D (n=64)		Risk of bias: NA
							IA-2 Ab+: GAD Ab conc (U/mL) Mean (SD)	n=19 67.7 (97.2)	
							IA-2 Ab-: GAD Ab conc (U/mL)	n=45 31.1 (132.1)	

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Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
67 (1):63-69, 2005. REF ID: Ota 2005							GAD+: IA-2 Ab conc (U/mL) GAD-: IA-2 Ab conc (U/mL)	n=28 1.8 (3.0) n=36 1.0 (2.4)	

Table 18: Rajalakshmi

Reference	Study type	Number of patients	Patient characteristics			Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
R Rajalakshmi, A Amutha, Harish Ranjani, Mohammed K. Ali, Ranjit Unnikrishnan, Ranjit Mohan Anjana, K. M. V. Narayan, and Viswanathan Mohan. Prevalence and risk factors for diabetic retinopathy in Asian Indians with young onset type 1 and type 2 diabetes. J.Diabetes Complications 28 (3):291-297, 2014. REF ID: Rajalshmi 2014	Observational:cross-ectional study India	n=300 T1D and T2D (n=150 of each) Inclusion criteria: Diagnosis between ages 10 and 25 years Duration of diabetes >2 years Diagnosis: FPG ≥126 mg/dl, and/or 2hr post-load glc level ≥200 mg/dl, or self-reported diabetes treated by a physician or on hypoglyc. Medications or insulin. T1D Diagnosis: accompanied by abrupt onet of symptoms like polyuria, polydipsia, or unexplained wt loss, DKA, asent insuil reserve, requirement of insulin from time of Diagnosis for control of hyperglycaemia. T2D Diagnosis: absence of ketosis, good B-cell functional reserve, absence of pancreatic calculi, and good response to oral hypoglyc. Agents for >2 years. Exclusion criteria: None reported.	Adults and young people Diabetes type: T1D, T2D Adults and young people: T1D (n=150) / T2D (n=150) Age: 28 / 33			T1D and T2D: Fast C-pepide Stimulated C-peptide Cut-offs for positivity Not reported	NA	T1D adults and young people Fasting C-peptide, pmol/ml: 0.29 Stimulated C-peptide, pmol/ml: 0.32 T2D adults and young people Fasting C-peptide, pmol/ml: 0.79 Stimulated C-peptide, pmol/ml: 1.60		Funding: Global diabetes research centre. Risk of bias: NA no missing data

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Table 19: Samuelsson 2013

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
U. Samuelsson, B. Lindblad, A. Carlsson, G. Forsander, S. Ivarsson, I. Kockum, A. Lernmark, C. Marcus, J. Ludvigsson, and Better Diabetes Diagnosis study group. Residual beta cell function at diagnosis of type 1 diabetes in children and adolescents varies with gender and season. Diabetes.Metab.Res .Rev. 29 (1):85-89, 2013. REF ID: Samuelsson 2013	Observational: cross-sectional Sweden:43 centres	n=979 young people aged 11 to 18 years Total n=3824 T1D young people and children 0 to 18 years Inclusion criteria: T1D (ADA criteria) Swedish Better Diabetes Diagnosis, BDD register Exclusion criteria: None given	Young people subgroup (age 11-18 years) Diabetes type: T1D		T1D: Non-fasting C-Peptide Cut-offs for positivity Non-fasting C-PEPTIDE: 0.03 nmol/L	Baseline	T1D young people (11-18 years)		Funding: Swedish Child Diabetes Foundation. Risk of bias: NA
				T1D all n=3165			Non-fasting C-Peptide, nmol/L (SD)	0.34 (0.28)	
			Age range	0 to 18 years; mean of separated boys and girls=9.8years					
			Male	n=1913					

Table 20: Scholin 2004a

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
Anna Scholin, Agneta Siegbahn, Lars Lind, Christian Berne, Goran Sundkvist, Elisabeth Bjork, F. Anders Karlsson, and Diabetes Incidence Study in Sweden group. CRP and IL-6 concentrations are associated with poor glycemic control despite preserved beta-cell function during the first year after	Observational study: Diabetic incidence in Sweden study.	Total n=100 T1D . n=3ter excluded as pregnant. Inclusion criteria: Not pregnant. Exclusion criteria: None reported	Adult (15 to 34 years) Diabetes type: TID Age of T1D patients (n=97) at diagnosis	T1D: C-peptide ICA+ GADA+ IA-2A+ Cut-offs for positivity C-peptide: reference interval for fasting plasma concentration was 0.25 to 0.75 nmol/L GADA index: >4.6 u/ml IA-2A index: >1.0 ICA: Not reported	12 months	Assays divided into islet antibody positive (ab+) and negative (ab-) Ab+ (n=78)		Funding: Supported by Grant from the Swedish Research Council, the Swedish Heart Lung Foundation, the Swedish Diabetes Association, the family Ernfors Fund, and the Juvenile Diabetes
						C peptide (nmol/l)	0.25 (0.04 to 1.4)	
						ICA+	58/78 (74%)	
						GADA+	69/78 (88%)	
						IA-2A+	55/78 (70%)	
						Ab- (n=19 : 19.7%)		
						C peptide (nmol/l)	0.34 (0.08 to 1.41)	
						Total population (I have added Ab+ and Ab-)		
						ICA+	58/97 (59.8%)	
						GADA+	69/97 (71.1%)	
						IA-2A+	55/97 (56.7%)	

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Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
diagnosis of type 1 diabetes. Diabetes.Metab.Res.Rev. 20 (3):205-210, 2004. REF ID: Scholin 2004A			All (n=97)				C-peptide – mean of Ab+ and Ab- (nmol/l)	0.25 + 0.34 /2= 0.295	Foundation International and Knut and Alice Wallenberg Foundation.
			Age (years)	28.1 (15.3 to 34.8)					

Table 21: Scholin 2004b

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
A. Scholin, C. Torn, L. Nystrom, C. Berne, H. Arnqvist, G. Blohme, J. Bolinder, J. W. Eriksson, I. Kockum, M. Landin-Olsson, J. Ostman, F. A. Karlsson, G. Sundkvist, and E. Bjork. Normal weight promotes remission and low number of islet antibodies prolong the duration of remission in Type 1 diabetes. Diabet.Med. 21 (5):447-455, 2004. REF ID: Scholin 2004B	Observational: prospective cohort	Total n=362 T1D Inclusion criteria: People with T1D Aged 15 to 34 years Clinically classified as T1D according to WHO criteria Exclusion criteria: None reported	Adults and young people Diabetes type: T1D		T1D: C-PEPTIDE GADA ICA IA-2 IAA Cut-offs for positivity C-PEPTIDE+: 0.25 nmol/L ICA512/IA-2+: Index* of 0.05 GAD65+: Index* of 0.07 ICA+: >5 JDF units IAA: 0.7% *INDEX=sample cpm – negative control cpm /positive control cpm - negative control cpm	NA	T1D - All cases (n=362)		Funding: Juvenile diabetes foundation-Wallenberg Diabetes research program, Swedish Diabetes association, swedish society of medicine, Agnes & Mac Rudbergs foundation Risk of bias: NA
			T1D n=362				P-C-PEPTIDE+ (nmol/L) Median (range)	0.27 (0.10, 2.13)	
			Age, years, mean (range; SD)	24.7 (5.6)			ICA+	213/346 (62%)	
			Duration of diabetes, years, mean (SD)				IA-2A+	162/345 (47%)	
							GADA+	229/346 (66%)	
							IAA+	58/248 (23%)	
							T1D Ab+ (n=307)		
							P-C-PEPTIDE+ (nmol/L) Median (range)	0.26 (0.10, 2.13)	
							ICA+	213/295 (72%)	
							IA-2A+	162/294 (55%)	
							GADA+	229/295 (78%)	
							IAA+	58/215 (27%)	
							T1D Ab- (n=53)		
							P-C-PEPTIDE+ (nmol/L) Median (range)	0.38 (0.10, 1.63)	
			M/F %	242/120					

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Table 22: Scholin 2004c

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
A. Scholin, L. Bjorklund, H. Borg, H. Arnqvist, E. Bjork, G. Blohme, J. Bolinder, JW. Eriksson, S. Gudbjornsdottir, L. Nystrom and Diabetes Inc. Islet antibodies and remaining beta-cell function 8 years after diagnosis of diabetes in young adults: a prospective follow-up of the nationwide Diabetes Incidence Study in Sweden. J.Intern.Med. 255 (3):384-391, 2004. REF ID: SCHOLIN 2004C	Observational:	Total n=312 (patients with blood samples at diagnosis and follow up) n=254 T1D, n=30 T2D Inclusion criteria: Aged 15 to 34 years Diagnosed* with diabetes between 1987 to 1988 Exclusion criteria: None reported *diagnosis based on clinical judgement as reported by diagnosing clinician to DISS registry	Adults and young people Diabetes type: T1D T2D		T1D: C-PEPTIDE GADA ICA IA-2 ICA & IA-2A ICA & GADA GADA & IA-2A Cut-offs for positivity P-C-PEPTIDE+: <0.1 nmol/L ICA512/IA-2+: Index* of >1 GAD65+: Index* of >4.6 *INDEX=sample cpm – negative control cpm /positive control cpm - negative control cpm	8 years	T1D Baseline (n=312) ICA+ n=199/312 (64%) GADA 235/311 (76) IA-2A+ 143/311 (46) T1D: follow up (n=312) ICA+ 73/309 (24%) GADA 200/309 (65%) IA-2A+ 106/310 (34%) C-peptide at baseline ≥0.1 nmol/L: T1D: 25/42 (60%) T2D: 8/42 (21%) <0.1 nmol/L: T1D: 204/227 (90%) T2D: 10/227 (4%) C peptide at follow up ≥0.1 nmol/L: T1D: 31/42 (76) T2D: 8/42 (20) <0.1 nmol/L: T1D: 208/227 (95) T2D: 7/227 (3)		Funding: Juvenile diabetes foundation and Wallenberg diabetes research program, Lundstrom foundation, Novo-nordisk foundation, Albert Palson foundation, Swedish diabetes association, childrens diabetes fund, Swedish medical research council Risk of bias: NA
			T1D						
			Age, years, mean (range; SD)	24.8 (9.5)					
			M/F %	182 (58%)/ 130 (42%)					
			T1D	254 (81)					
			T2D	30 (10)					
			Unclassifiable Secondary	27 (9) 1 (0)					

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Table 23: Scholin 2011

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
A. Scholin, L. Nystrom, H. Arnqvist, J. Bolinder, E. Bjork, C. Berne, F. A. Karlsson, and Diabetes Incidence Study Group. Proinsulin/C-peptide ratio, glucagon and remission in new-onset	Observational: cross-sectional study and prospective Swedish study	Total recruited: n=203 n=78 T1D (had complete data at all the time-points and were confirmed T1D) Inclusion criteria: T1D Age 15 to 34 years In the nationwide Diabetes Study in Sweden (DISS)	Adults and young people Diabetes type: T1D		T1D: fC-PEPTIDE Cut-offs for positivity fC-PEPTIDE+: not given	3 years follow-up post Diagnosis.	T1D (n=78) FC-peptide over time: mths after Diagnosis nmol/L MEDIAN (min-max) Baseline 0.24 (0.04 to 1.4) 3 0.26 (0.04 to 1.8) 6 0.31 (0.04 to 1.3) 9 0.27 (0 to 1.9) 12 0.27 (0 to 1.6) 15 0.19 (0 to 1.7) 18 0.17 (0 to 1.1) 24 0.16 (0 to 1.5) 30 0.12 (0.04 to 1.3) 36 0.19 (0.02 to 1.8)		Funding: Not reported Risk of bias: NA
			T1D n=78						
			Age, years, mean (SD; range)	26.2 (6.0)					
			M/F %	60/40					
			Islet Ab+, %	86%					

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
Type 1 diabetes mellitus in young adults. Diabet.Med. 28 (2):156-161, 2011. REFID: Scholin 2011		T1D defined as islet-cell Ab+ and/or need for insulin treatment at Diagnosis) Blood samples taken Exclusion criteria: Pregnant T2D							

Table 24: Tridgell 2011

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
DM. Tridgell, C Spiekerman, Richard S. Wang, and Carla J. Greenbaum. Interaction of onset and duration of diabetes on the percent of gad and ia-2 antibody-positive subjects in the type 1 diabetes genetics consortium database. Diabetes Care 34 (4):988-993, 2011. REF ID: Tridgell 2011	Observational: cross-sectional study	Total n=5020 T1D Inclusion criteria: Diagnosed with T1D before aged 35 years Treated with insulin within 6 months of diagnosis without subsequent discontinuation of insulin treatment Families with at least 2 non-monozygotic siblings with T1D and families where there was a single affected child from a population with a low prevalence of T1D Exclusion criteria: None reported	Adults and young people Diabetes type: T1D		T1D: GADA IA-2A GADA and/or IA-2A Cut-offs for positivity GAD65+: NR ICA+: NR	NA	T1D: onset aged 2 to 7 (n=1739) -univariate analyses		Funding: T1D Genetics consortium, National institute of diabetes and digestive and kidney diseases, juvenile diabetes research foundation Risk of bias: NA
							GADA+	35.7%	
							IA-2+	43.1%	
							T1D: onset aged 8-13 years (n=1767) -univariate analyses		
							GADA+	47.6%	
							IA-2+	53.1%	
							T1D: onset aged ≥14 years (n=1514) -univariate analyses		
							GADA+	58.9%	
							IA-2+	40.6%	
							T1D: duration 0 to 5 years- univariate analyses		
			T1D n=5,020				GADA+	58.6%	
			Age, years, median (range)	10 (2 to 52) Data for adults and young people has been separated			IA-2+	60.4%	
							T1D: duration 6 to 13 years- univariate analyses (referent group 0-5 years duration)		
			Duration of diabetes, years, median (range)	8 (0 to 66)			GADA+	44.8%	
							IA-2+	47.2%	
							T1D: duration ≥14 years- univariate analyses (referent group 0 to 5 years duration)		
			M/F %	50.7%/49.3%			GADA+	35.6%	
							IA-2+	28.3%	

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Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
							GADA+	70.5%	
							IA-2A+	53.4%	
							GADA+ and/orIA-2A+	82.2%	
							T1D: duration 6-13 years-multivariate analyses		
							GADA+	65.3%	
							IA-2A+	42.7%	
							GADA+ and/orIA-2A+	73.8%	
							T1D: duration ≥14 years-multivariate analyses		
							GADA+	42.5%	
							IA-2A+	26.2%	
							GADA+ and/orIA-2A+	53.4%	

Table 25: Vermeulen 2011

Reference	Study type	Number of patients	Patient characteristics		Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G. Pipeleers, and F. K. Gorus. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. Diabetes Care 34 (8):1760-1765, 2011.	Observational: Case-control study Registry, Belgium	Total n=665 T1D (n=170 aged 0 to 9 years; n=223 aged 10 to 19 years; n=149 aged 20 to 29 years; n=113 aged 30 to 39 years) Inclusion criteria: Diagnosis with diabetes before age 40 Physician Diagnosis of T1D on clinical grounds and treated with insulin with 7 days after Diagnosis Blood sampled within 7 days after treatment started CONTROLS: sex-matched non-diabetic controls aged 0-39	Young people and adults (data separated for some age-groups and markers) DIABETES TYPE: T1D		T1D IA-2A IA-2βA ZnT8 IAA GADA Combinations Cut-offs for positivity IAA: ≥0.6% tracer binding IA-2A: ≥0.44% tracer binding	1 year	T1D Adults aged 20 to 29 (n=149)		Funding: Juvenile diabetes Research F, EU and Belgian fund for Scientific Research Risk of bias: NA
			T1D				MARKER	n (%)	
			Age, years,	n=170: 0 to 9 years n=223: 10 to 19 years n=149: 20 to 29 years n=113 30 to 39 years Median: 15 (IQR9-26) years			IA-2βA	47 (32)	
							ZnT8	76 (51)	
							T1D ADULTS aged 30 to 39 (n=113)		
							MARKER	n (%)	
							IA-2βA	21 (19)	
							ZnT8	44 (39)	
							T1D Young people aged 10 to 19 (n=223)		
			M/F	383/272			MARKER	n (%)	
							IA-2βA	105 (47)	

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REF ID: Vermeulen 2011		years. None had relatives with T1D. Exclusion criteria: None stated		IA-2βA: ≥0.39% tracer binding GADA+: ≥2.6% tracer binding ZnT8+: Age 0-14 years=≥1.28 % tracer binding Age15-39 years=≥1.02 % tracer binding		ZnT8	152 (68)	
						≥1 Ab+ (GADA, IA-2A or IAA)	207 (93)	
						≥1 Ab+ (GADA, IA-2A or ZnT8)	209 (94)	
						≥2 Ab+ (GADA, IA-2A and/or IAA)	154 (69)	
						≥2 Ab+ (GADA, IA-2A and/or ZnT8)	162 (73)	
						T1D ADULTS aged 20 to 39 (n=262)		
						≥1 Ab+ (GADA, IA-2A or IAA)	207 (79)	
						≥1 Ab+ (GADA, IA-2A or ZnT8)	206 (79)	
						≥2 Ab+ (GADA, IA-2A and/or IAA)	129 (49)	
						≥2 Ab+ (GADA, IA-2A and/or ZnT8)	139 (53)	
						Young people and adults: >age 15:		
						≥1 Ab+ (IAA, GADA and IA-2A)	82%	
						≥2 Ab+ (IAA, GADA or IA-2A)	51%	
						≥2 Ab+ (IA-2βA plus one of IAA, GADA or IA-2A)	56%	
						≥2 Ab+ (ZnT8 plus one of IAA, GADA or IA-2A)	63%	
						≥2 Ab+ (ZnT8 and IA-2βA plus one of IAA, GADA or IA-2A)	65%	
						The prevalence of IA-2βA and ZnT8 decreased with age at Diagnosis (esp after age 20 years).		

Table 26: Wenzlau 2010

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
J. M. Wenzlau, M. Walter, T. J. Gardner, L. M. Frisch, L. Yu, G. S. Eisenbarth, A. G. Ziegler, H. W. Davidson, and J.	Observational: cross-sectional study	Total n=506 Inclusion criteria: New onset patients within 6	Adults and young people Diabetes type: T1D	T1D: C-PEPTIDE ZnT8 GADA IA-2	Group 1: 2.5 years Group 2: 7 years Group 3: 3 to 10.9 years	Group 1: New onset diabetes (n=21) baseline		Funding: Childhood diabetes foundation, Denver; university of Colorado health
						ZnT8A+	85.7%	
						GADA+	95.2%	
						IA-2A+	90.5%	
						C Peptide+	100%	

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C. Hutton. Kinetics of the post-onset decline in zinc transporter 8 autoantibodies in type 1 diabetic human subjects. J.Clin.Endocrinol.Metab. 95 (10):4712-4719, 2010. REF ID: Wenzlau 2010		weeks of diagnosis T1D new onset patients (4 years duration) Patients with longstanding diabetes (>20 years) Exclusion criteria: None reported		1 (n=21)	2 (n=61)	3 (n=424)	Cut-offs for positivity C-PEPTIDE+:.3 pmol/mL ZnT8: index* of 0.015-0.020 ICA512/IA-2+: Index* of 0.032 GAD65+: Index* of 0.069 *INDEX=sample cpm – negative control cpm /positive control cpm -negative control cpm		Group 1: New onset diabetes (n=21) 2.5 years follow up		sciences centre diabetes endocrinology research centre (NIH), juvenile diabetes research foundation autoimmunity prevention centre grant Risk of bias: NA
			Age, years, median (SD; range)	20.3 (6.2; 12.2 to 34.6)	9.8 (5.2; 1.6 to 36.7)	11.4 (7.6; 0.5 to 52.7)			ZnT8A+	76.2%	
									GADA+	85.7%	
			Duration of diabetes, years, mean (SD)			26.3 (7.6; 12.0 to 57.1)			IA-2A+	90.5%	
									C Peptide+	85.7%	
									Group 1: new onset diabetes at 12 years follow up (prevalence)		
									GAD+	11.5%	
									CWCR	3.3%	
									IA2+	4.9%	
									GAD/CWCR	4.9%	
									GAD/ IA2	6.6%	
									IA2 / CWCR	21.3%	
									GAD/CWCR/IA2	41%	
									Group 2: New onset T1D diabetes (n=61) Baseline		
									ZnT8A+	80.3%	
									GADA+	63.0%	
									IA-2A+	73.8%	
									C Peptide+	NR	
									Group 2: New onset T1D diabetes (n=61) 12 years follow up		
									ZnT8A+	42.6%	
									GADA+	32.4%	
									IA-2A+	47.5%	
									C Peptide+ (detected >0.02 pmol/mL)	27.6%	
									Group 2: patients with 4 years duration of T1D at 12 years follow up (prevalence)		
									GAD+	10.7%	
									CWCR	8.9%	
									IA2+	16.1%	
									GAD/CWCR	3.6%	

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									GAD/ IA2	10.7%	
									IA2 / CWCR	19.6%	
									GAD/CWCR/IA2	20%	
									Group 3: Patients with longstanding diabetes(>20 years) (n=282) 12 year follow up (prevalence)		
									GAD+	11.0%	
									CWCR	1.4%	
									IA2+	7.8%	
									GAD/CWCR	0.7%	
									GAD/ IA2	7.1%	
									IA2 / CWCR	2.1%	
									GAD/CWCR/IA2	2.5%	

Update 2015

Appendix J: Forest plots

J.1 Original (2004) forest plots

J.1.1 Type 1 diabetes – insulin preparations

Figure 1: HbA1c – all included studies providing HbA1c levels; HbA1c is significantly lower with rapid-acting analogues than regular insulin; eleven parallel group studies with a total of 4246 patients showed a significant decrease in HbA1c levels (WMD −0.14%, 95% CI −0.19 to − 0.08%); twelve crossover studies with a total of 2441 patients showed no difference in HbA1c (WMD 0.00, 95% CI −0.09 to 0.08)

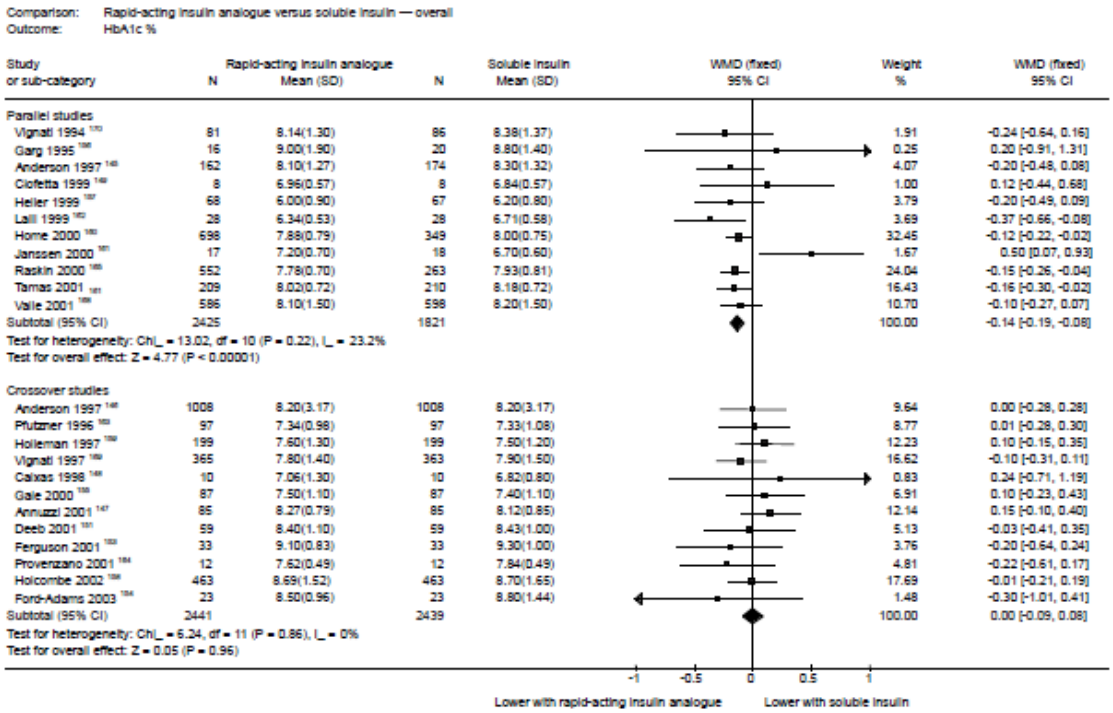


Figure 2: HbA1c – studies separated into children/young people and adults; three studies with a total of 545 children and young people investigated HbA1c levels; the studies did not show a significant difference between rapid-acting analogues and regular insulin (WMD −0.03%, 95% CI −0.21 to 0.14%); nine studies with a total of 1896 adult patients did not show a significant difference between rapid-acting analogues and regular insulin (WMD 0.01%, 95% CI −0.09 to 0.11%)

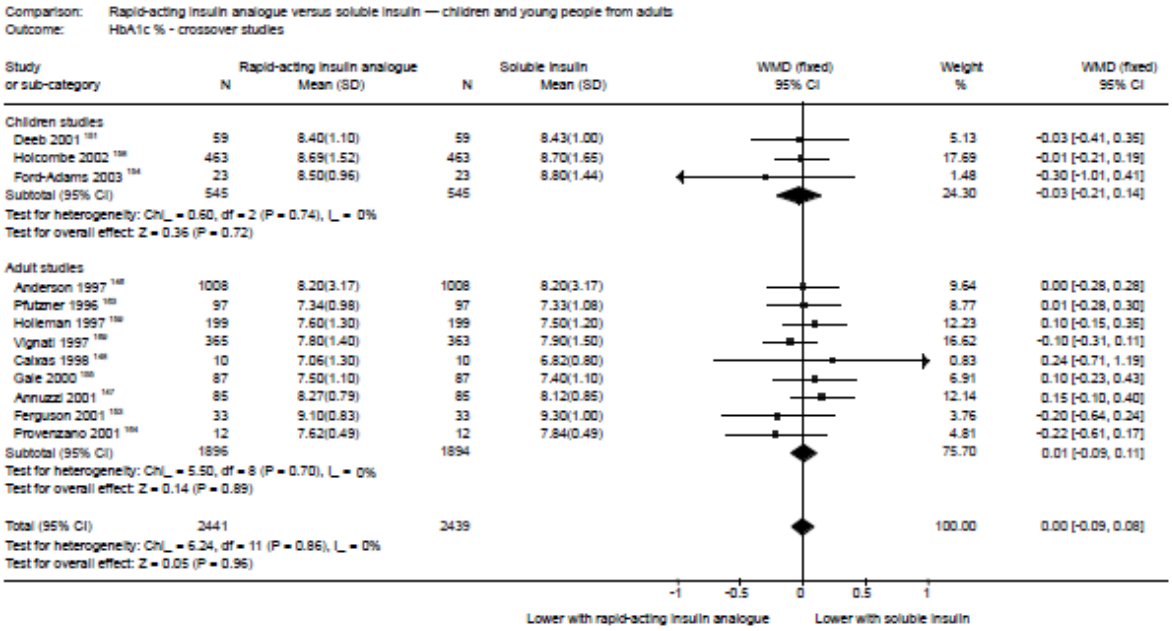


Figure 3: HbA1c – studies separated into type of analogue (insulin aspart and insulin lispro); HbA1c was significantly lower with both types of rapid-acting analogue when compared with regular insulin (insulin aspart with a total of 2281 patients: WMD −0.14% 95% CI −0.20 to − 0.07%; insulin lispro with a total of 1965 patients: WMD −0.13%, 95% CI −0.24 to −0.02%); there was no significant difference in HbA1c reduction between studies using insulin aspart or insulin lispro

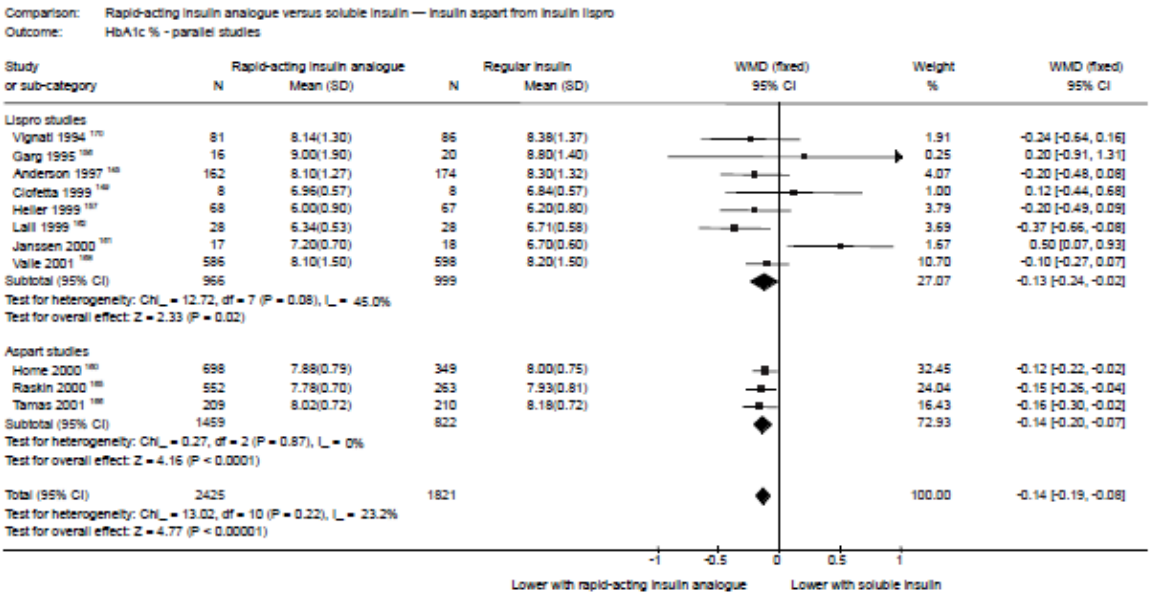


Figure 4: Hypoglycaemic episodes/30 days; there was no significant difference between rapid-acting analogues and regular insulin regarding hypoglycaemic episodes

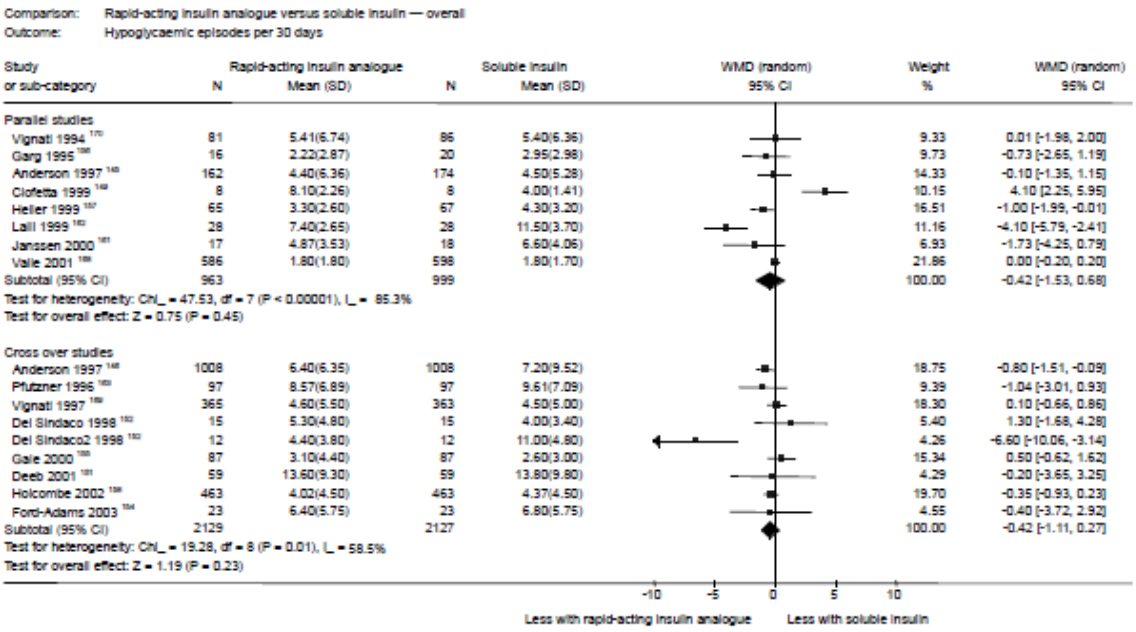


Figure 5: Hypoglycaemic episodes/30 days with adults' and children's/young people's studies separated; there was no significant difference between rapid-acting analogues and regular insulin regarding hypoglycaemic episodes in either adults or children/young people; furthermore, there was no apparent difference between children/young people and adults in terms of the number of hypoglycaemic episodes/30 days

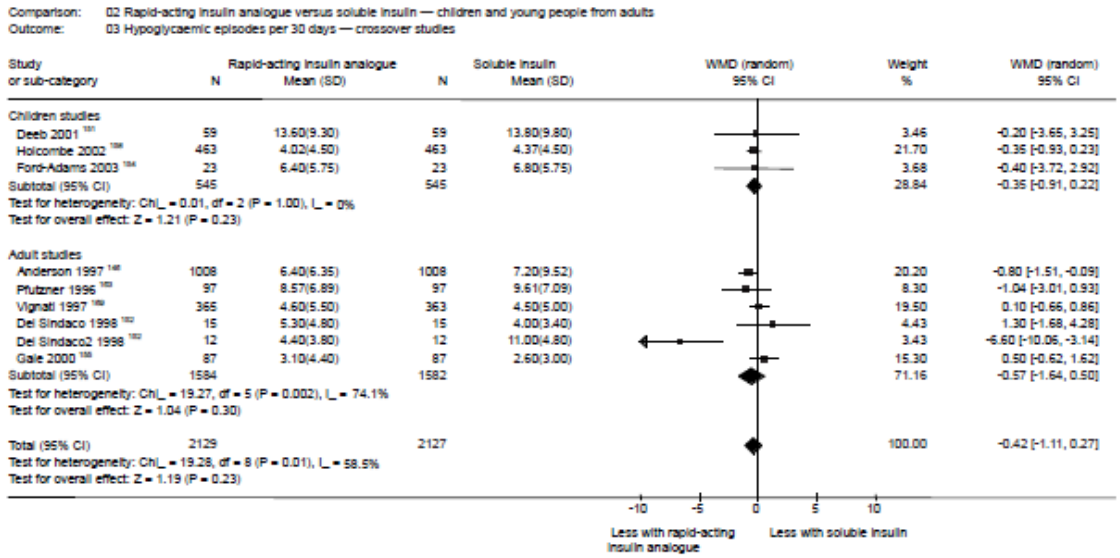


Figure 6: Patient preference – patients preferred rapid-acting analogues to regular insulin; the overall estimate contained significant heterogeneity, which could be due to statistical and/or clinical reasons; these data should, therefore, be interpreted with caution

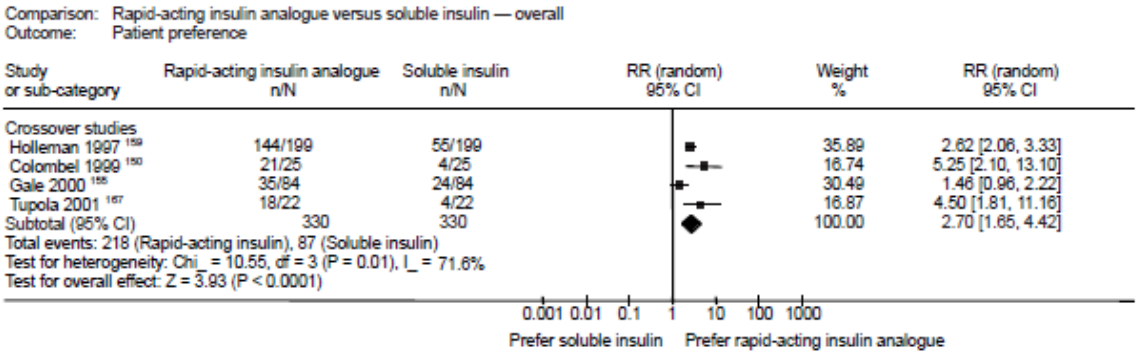
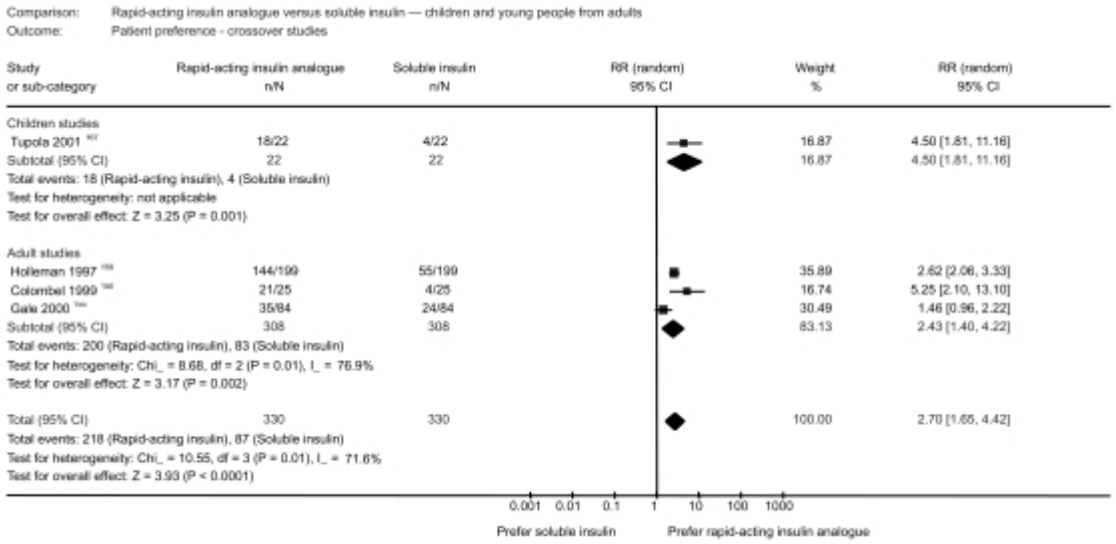
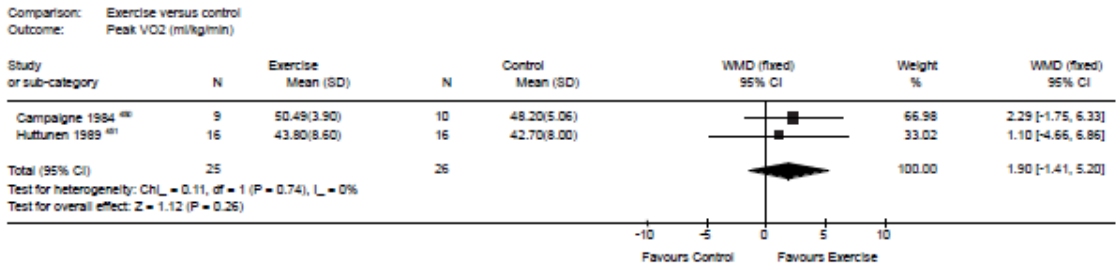


Figure 7: Patient preference – separated according to children's/young people's and adults' studies; both children/young people and adults preferred rapid-acting insulin analogue to regular insulin; the overall result was heterogeneous, and only one study contributed data for studies in children and young people; heterogeneity could be due to statistical and/or clinical reasons; these data should, therefore, be interpreted with caution



J.1.2 Type 1 diabetes – exercise

Figure 8: Ideal frequency of exercise – exercising one to three times/week compared with control (no exercise)



J.2 2015 update forest plots

J.2.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'.

No meta-analyses were conducted for this review question and so there are no forest plots.

Update 2015

J.2.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.3 Type 1 diabetes – psychological interventions

Review question: What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.7 Type 1 diabetes – blood glucose monitoring

Review questions:

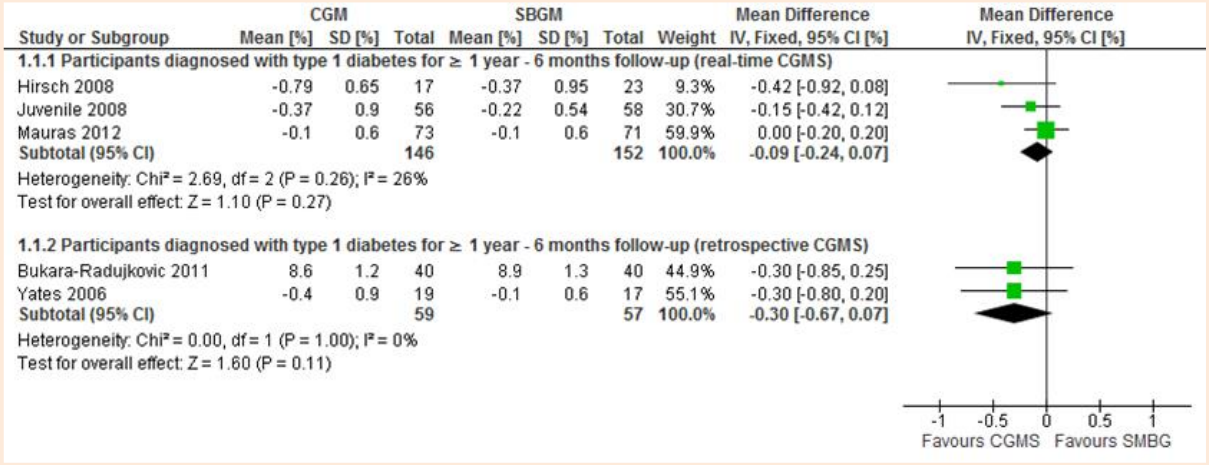
How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

Update 2015

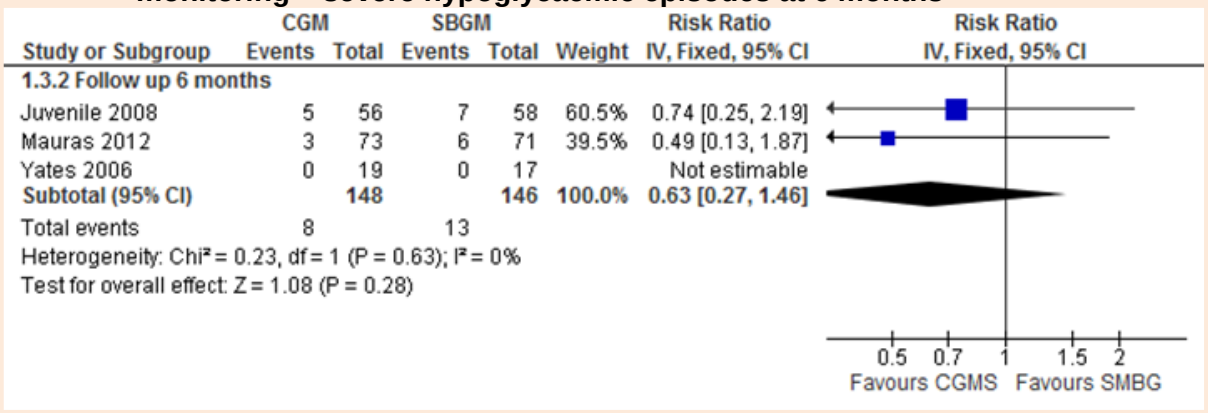
What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Figure 9: Continuous glucose monitoring versus capillary blood glucose monitoring – HbA1c at 6 months



Note: Hirsch 2008 Juvenile 2008 and Yates 2006 were reported in Langendam 2012 systematic review

Figure 10: Continuous glucose monitoring versus capillary blood glucose monitoring – severe hypoglycaemic episodes at 6 months



Note: Juvenile 2008 and Yates 2006 were reported in Langendam 2012 systematic review

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

Update 2015

J.2.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Figure 11: HbA1c at 12 months (2 studies)

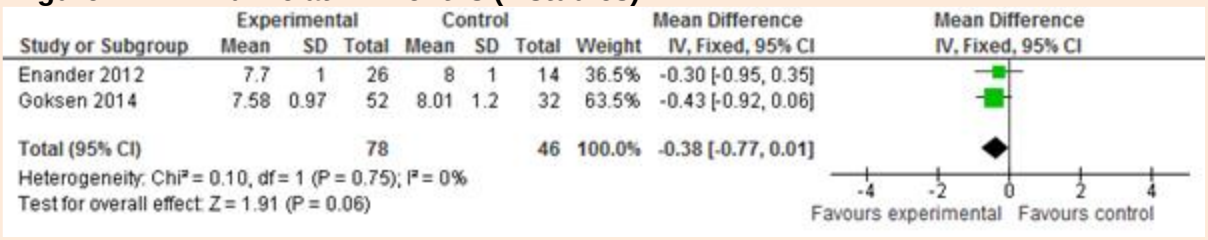
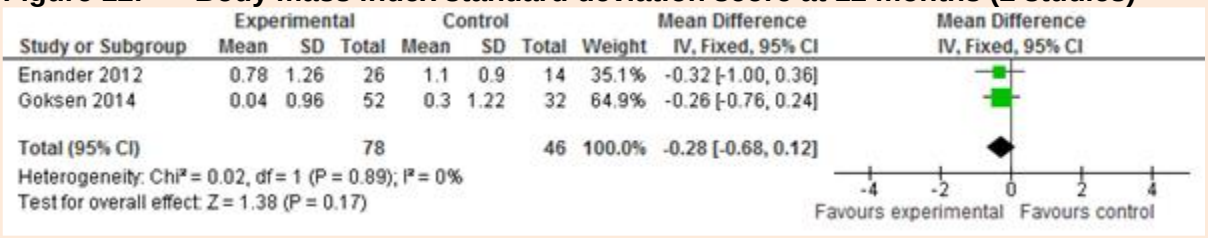


Figure 12: Body mass index standard deviation score at 12 months (2 studies)



What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

Update 2015

J.2.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**

- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

No meta-analyses were conducted for this review question and so there are no forest plots.

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**
- **acid/base status?**

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

No meta-analyses were conducted for this review question and so there are no forest plots.

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

Update 2015

J.2.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.15 Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.16.1 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.17 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

Update 2015

J.2.18 Type 2 diabetes – psychological interventions

Review questions:

What is the effectiveness of psychological interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.19 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.20 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.21 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.22 Type 2 diabetes – HbA1c targets

Review question: what is the optimal HbA1c target for children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.23 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

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J.2.24 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.25 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.26 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

Appendix K: GRADE tables

K.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'. There are no evidence profiles (GRADE tables) for this question because nearly all of the studies included in the evidence review were cross-sectional observational studies and thus were not able to be combined in a meta-analysis or GRADE evidence profile. All non-comparative observational studies included for this question were graded as low quality due to the inherent high risk of bias associated with these study designs. The specific methodological limitations of the included studies are summarised in the table below.

Table 27: Methodological limitations of non-comparative observational studies included for the review question about diagnosis

Study	Prospective or cross-sectional study design	Representative population sample	Outcomes measured adequately	Appropriate statistical analysis conducted (adjusted for confounders where applicable)	Quality
Zanone 2003	Yes	Yes	Yes	NA	Low
Tung 2008	Yes	Yes	Yes	NA	Low
Vermeulen 2011	Yes	Yes	Yes	NA	Low
Barker 2014	Yes	Yes	Yes	NA	Low
Andersson 2013	Yes	Yes	Yes	NA	Low
Samuelsson 2013	Yes	Yes	Yes	NA	Low
Shivaprasad 2014	Yes	Yes	Yes	NA	Low
Scholin 2004a	Yes	Yes	Yes	NA	Low
Borg 2003	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Besser 2011	Yes	Partially (mixed young people and adult population)	Yes	NA	Low

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Study	Prospective or cross-sectional study design	Representative population sample	Outcomes measured adequately	Appropriate statistical analysis conducted (adjusted for confounders where applicable)	Quality
Laadhar 2007	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Brunova 2002	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Ota 2005	Yes	Partially (mostly the population of interest based on the mean age of participants)	Yes	NA	Low
Scholin 2011	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Scholin 2004b	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Tridgell 2011	Yes	Partially (mostly the population of interest based on the mean age of participants)	Yes	NA	Low
Scholin 2004c	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Wenzlau 2010	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Mcdonald 2011	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
Oram 2014	Yes	Partially (mixed young people and adult population)	Yes	NA	Low

Update 2015

Study	Prospective or cross-sectional study design	Representative population sample	Outcomes measured adequately	Appropriate statistical analysis conducted (adjusted for confounders where applicable)	Quality
LU 2014	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
RAJALAKSHMI 2014	Yes	Partially (mixed young people and adult population)	Yes	NA	Low

NA not applicable

K.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Table 28: Evidence profile for effectiveness of structured education programmes in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mean HbA_{1c} at 6 months (education only versus standard care)											
1 (Howe 2005)	21	28	NA	MD 0.2 lower (1.21 lower to 0.81 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Mean HbA_{1c} at 6 months (education plus telephone case management versus standard care)											
1 (Howe 2005)	26	28	n/a	MD 0.4 lower (1.28 lower to 0.48 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[5]	None
Mean HbA_{1c} at 6 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	n/a	MD 0.02 higher (0.31 lower to 0.35 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 12 months (TeenCope versus Managing Diabetes)											

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Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Grey 2013)	167	153	NA	MD 0.18 lower (0.49 lower to 0.13 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 12 months (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.2 lower (0.55 lower to 0.15 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[5]	None
HbA_{1c} change over 12 months (family-centred group education versus waiting list)											
1 (Murphy 2007)	33	34	NA	MD 0.01 lower (0.17 lower to 0.15 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 12 months (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.1 lower (0.45 lower to 0.25 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 12 months (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0.1 higher (0.26 lower to 0.46 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 12 months (CASCADE versus control)											
1 (Christie 2014)	143	155	NA	MD 0.1 (0.28 lower to 0.50 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[6]	None
Mean HbA_{1c} at 12 months (supportive self-care versus conventional treatment)											
1 (Delamater 1990)	9	12	NA	MD 0.4 lower (not reported)[7]	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[7]	None
Mean HbA_{1c} at 24 months (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.2 lower (0.59 lower to 0.19 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[5]	None
Mean HbA_{1c} at 24 months (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0 (0.39 lower to 0.39 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Average mean HbA_{1c} at 24 months (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.1 lower (0.41 lower to 0.21 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Average mean HbA_{1c} at 24 months (care ambassador ultra versus standard care)											

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Katz 2014)	50	51	NA	MD 0 (0.36 lower to 0.36 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 24 months (CASCADE versus control)											
1 (Christie 2014)	135	149	NA	MD 0.03 (0.36 lower to 0.41 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Mean HbA_{1c} at 24 months (supportive self-care versus conventional treatment)											
1 (Delamater 1990)	9	12	NA	MD 0.9 lower (not reported)[7]	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[7]	None
Mean number of severe hypoglycaemic episodes (per participant) over 12 months (Family-centred group education versus Conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.05 lower (0.21 lower to 0.11 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Severe hypoglycaemic episodes (1 or more episodes versus no episodes, parent- or adult-reported) over 12 months (CASCADE versus control)											
1 (Christie. 2014)	143	155	OR 0.76[a] (0.32 lower to 2.59 higher)	NA	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Mean number of severe hypoglycaemic episodes (per participant) over 24 months (care ambassador plus psycho-education versus care ambassador only)											
1 (Svoren 2003)	97	94	NA	MD 0.17 higher (0.18 lower to 0.52 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[5]	None
Severe hypoglycaemic episodes (1 or more episodes versus no episodes, parent- or adult-reported) over 24 months (CASCADE versus control)											
1 (Christie 2014)	137	140	OR 0.92[a] (0.32 lower to 2.59 higher)	NA	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Mean number of episodes of diabetic ketoacidosis (per participant) over 12 months (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.01 higher (0.09 lower to 0.11 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Adherence to diabetes treatment (percentage of positive adherence) at 6 months (education versus standard care)											
1 (Howe 2005)	21	28	NA	MD 4.9 higher (10.39 lower to 20.19 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Children and young people's quality of life measured using DQOLY: impact, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.7 higher (3.28 lower to 4.68 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[6]	None
Children and young people's quality of life measured using DQOLY: worry, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 3 lower (5.51 lower to 0.49 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[4]	None
Children and young people's quality of life measured using DQOLY: parental involvement, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.3 lower (1.04 lower to 0.44 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[4]	
Children and young people's quality of life measured using PedsQL at 6 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 4.63 higher (2.18 lower to 7.08 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life measured using PedsQL at 12 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 3.62 higher (0.98 lower to 6.26 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life at 12 months measured using PedsQL, parent-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 2.7 higher (1.93 lower to 7.33 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life measured using PedsQL at 12 months, child- or young person-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.1 lower (3.07 lower to 2.87 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life measured using PedsQL at 12 months, parent-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 4.6 higher (0.06 lower to 9.26 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[5]	None

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Children and young people's quality of life measured using PedsQL at 12 months, child- or young person-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0.8 lower (3.78 lower to 2.18 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young person's quality of life measured using PedsQL: general module, at 12 months follow-up, young person-reported (CASCADE versus control)											
1 (Christie 2014)	148	159	NA	MD 1.09 lower (3.15 lower to 0.03 higher)	Low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[6]	None
Children and young people's quality of life measured using PedsQL: diabetes module, at 12 months, young person-reported (CASCADE versus control)											
1 (Christie 2014)	148	159	NA	MD 0.62 higher (2.35 lower to 3.04 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life measured using PedsQL at 24 months, parent-reported (care ambassador plus versus standard care)											
Children and young people's quality of life measured using PedsQL at 24 months, child- or young person-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 2.1 lower (5.46 lower to 1.26 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life measured using PedsQL at 24 months, parent-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0.2 higher (4.22 lower to 4.62 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young person's quality of life measured using PedsQL at 24 months, child- or young person-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 2.1 lower (5.44 lower to 1.24 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's quality of life measured using PedsQL: general module, at 24 months, young person-reported (CASCADE versus control)											
1 (Christie 2014)	144	151	NA	MD 0.33 lower (2.53 lower to 1.97 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young person's quality of life measured using PedsQL: diabetes module, at 24 months, young person-reported (CASCADE versus control)											
1 (Christie 2014)	144	151	NA	MD 0.02 lower (3.19 lower to 2.72 higher)	Very low	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
Children and young people's satisfaction with treatment or intervention, follow-up time not reported (TeenCope versus Managing Diabtes)											

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Grey 2013)	167	153	NA	MD 0.08 lower (0.22 lower to 0.06 higher)	Moderate	RCT	Serious[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None

CASCADE Child and Adult Structured Competencies Approach to Diabetes Education, MD mean difference, NA not applicable, OR odds ratio, RCT randomised controlled trial
a Adjusted for baseline and accounting for clustering within clinics
1 Some risk of bias due to identification of several limitations and absence of reported information
2 Single-study analysis
3 No serious indirectness
4 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')
5 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
6 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')
7 Unable to assess precision using data reported in the article, 12 months HbA1 self-management mean (SD) 8.1% ±1.5% versus conventional mean (SD) 9.3 ±1.7, p<0.01; 24 months HbA1 self-management mean (SD) 8.2±1.5 versus conventional mean (SD) 9.8 ±2.4, p <0.05

Update 2015

K.3 Type 1 diabetes – psychological interventions

Review question: What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 1 diabetes?

Table 29: Evidence profile for effectiveness of motivational interviewing versus support visits in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing	Support visits	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 12 months											
1 (Channon 2007)	35	25	NA	MD 0.5 lower (1.43 lower to 0.43 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious4	None
Depression (wellbeing questionnaire) at 12 months (lower scores indicate better outcomes)											
1 (Channon 2007)	35	25	NA	MD 1.77 lower (2.80 lower to 0.74 lower)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None
Health-related quality of life (Diabetes Quality of Life Measure for Youths, impact) at 12 months (lower scores indicate better outcomes)											

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing	Support visits	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Channon 2007)	35	25	NA	MD 10.56 lower (17.81 lower to 3.31 lower)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None

MD mean difference, NA not applicable,, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
5 No MID for wellbeing quality of life specified by guideline development group
6 No MID for diabetes quality of life for youths specified by guideline development group

Table 30: Evidence profile for effectiveness of motivational interviewing skills training versus awaiting treatment with the same intervention (placing patients on a waiting list)in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing delivered by trained HCPs	No motivational interviewing (waiting list)	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 15 months											
1 (Robling 2012)	342	318	NA	MD 0.2 higher (0.06 lower to 0.46 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[4]	None
Adherence to diabetes management (measured with Diabetes Mismanagement Questionnaire) at 15 months (lower scores indicate better outcomes)											
1 (Robling 2012)	186	163	NA	MD 4.6 lower (8.04 lower to 1.16 lower)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None
Health-related quality of life (measured with Diabetes Quality of Life Questionnaire, impact subscale) at 15 months (higher scores indicate better outcomes)											
1 (Robling 2012)	167	166	NA	MD 5.8 lower (9.85 lower to 1.75 lower)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None

MD mean difference, NA not applicable, RCT randomised controlled trial
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals entirely within one zone related to precision (see 'Methodology for 2015 update')
5 No MID for Diabetes Quality of Life Questionnaire specified by the guideline development group

Table 31: Evidence profile for effectiveness of motivational interviewing versus structured education in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing	Structured education	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 6 months											
1 (Wang 2010)	21	23	NA	MD 1.1 higher (0.27 higher to 1.93 higher)	Low	RCT	No serious risk of bias[1]	No serious inconsistency[2]	Serious[3]	Serious[4]	None
Depression (CES-D) at 6 months (lower scores indicate better outcomes)											
1 (Wang 2010)	21	23	NA	MD 0.07 higher (1.53 lower to 1.67 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	Serious[3]	No serious imprecision[5]	None
Health-related quality of life (EDIC-QoLY, lifestyle subscale) at 6 months (lower scores indicate better outcomes)											
1 (Wang 2010)	21	23	NA	MD 0.01 lower (1.61 lower to 1.59 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	Serious[3]	No serious imprecision[5]	None

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population and outcome as specified in the review protocol, but intervention was not delivered by psychologists and staff did not have an appropriate level of training
4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
5 No MID for EDIC-QoLY specified by guideline development group

Table 32: Evidence profile for effectiveness of cognitive behavioural therapy focused on quality of life versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Cognitive behavioural therapy focused on quality of life	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 12 months											
1 (de Wit 2008)	41	40	NA	MD 0.1 higher (0.53 lower to 0.73 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious[4]	None
Depression (CES-D) at 12 months (lower scores indicate better outcomes)											
1 (de Wit 2008)	41	40	NA	MD 1.04 higher (1.26 lower to 3.34 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Cognitive behavioural therapy focused on quality of life	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Health-related quality of life (CHQ-CF87, global health subscale) at 12 months (higher scores indicate better outcomes)											
1 (de Wit 2008)	41	40	NA	MD 10.08 higher (2.16 higher to 18 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None

CBT cognitive behavioural therapy, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference
1 Concerns about selection of participants and performance bias, but these are unlikely to affect outcome
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross three zones related to precision (see 'Methodology for 2015 update')
5 No MID for CHQ-CF87 specified by guideline development group

Table 33: Evidence profile for effectiveness of cognitive behavioural therapy not specifically focused on quality of life versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Cognitive behavioural therapy	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Adherence to diabetes management (measured with Diabetes Self- Management Profile, child domain) at 12 months											
1 (Nansel 2007)	40	41	NA	MD 0.01 lower (0.07 lower to 0.05 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[4]	None
Health-related quality of life (measured with Diabetes Quality of Life for Youth, impact subscale) at 15 months (higher scores indicate better outcomes)											
1 (Nansel 2007)	40	41	NA	MD 3.67 higher (3.1 higher to 4.24 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[4]	None

MD mean difference, NA not applicable, RCT randomised controlled trial
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 No MID for Diabetes Quality of Life for Youth specified by guideline development group

Update 2015

Table 34: Evidence profile for effectiveness of counselling versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Counselling	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 15 months											
1 (Graue 2005)	45	38	NA	MD 0.44 lower (1.04 lower to 0.16 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[4]	None
Adverse events (severe hypoglycaemic episodes at 15 months)											
1 (Graue 2005)	7/45 (15.6%)	5/38 (13.2%)	RR 1.18 (0.41 to 3.42)	24 more per 1000 (from 78 fewer to 318 more)	Low	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None
Health-related quality of life (measured with Diabetes Quality of Life Questionnaire, impact subscale) at 15 months (higher scores indicates better outcomes)											
1 (Graue 2005)	45	38	NA	MD 4.3 higher (0.16 higher to 8.44 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None

MD mean difference, NA not applicable, RCT randomised controlled trial
1 Concern about performance bias, but this is unlikely to affect outcome
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
5 No MID for Diabetes Quality of Life Questionnaire specified by the guideline development group
6 Confidence intervals cross three zones related to precision (see 'Methodology for 2015 update')

Table 35: Evidence profile for effectiveness of multi-systemic therapy (including behavioural family systems therapy) versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multi-systemic therapy	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 6 to 7 months' follow-up											
1 (Ellis 2004)	13	15	NR	MD 1.9 lower (4.24 lower to 0.44 higher)	Low	RCT	Serious risk of bias[12]	No serious inconsistency[6]	No serious indirectness[3]	Serious imprecision[10]	None
1 (Ellis 2005)	64	63	NR	MD 0.77 lower (1.35 to 0.19 lower)	Moderate	RCT	No serious risk of bias	No serious inconsistency[6]	No serious indirectness[3]	Serious imprecision[10]	None
HbA1c at 6 months' follow-up											

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multi-systemic therapy	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Wysocki 2001)	36	40	NR	MD 0.4 lower (not reported)	Very low	RCT	Very serious risk of bias[5]	No serious inconsistency[6]	No serious indirectness[3]	Very serious imprecision[7]	None
1 (Wysocki 2007)	36	32	NR	MD 0.7 lower (1.42 lower to 0.02 higher)	Low	RCT	Serious risk of bias[11]	No serious inconsistency[6]	No serious indirectness[3]	Serious imprecision[10]	None
HbA1c at 12 months' follow-up											
1 (Wysocki 2001)	36	40	NR	MD 0.2 lower (not reported)	Very low	RCT	Very serious risk of bias[5]	No serious inconsistency[6]	No serious indirectness[3]	Very serious imprecision[7]	None
1 (Wysocki 2007)	36	32	NR	MD 0.8 lower (1.57 to 0.03 lower)	Low	RCT	Serious risk of bias[11]	No serious inconsistency[6]	No serious indirectness[3]	Serious imprecision[10]	None
Adherence to diabetes treatment											
1 (Ellis 2004)	16	15	NR	MD 0.17 higher (0.53 lower to 0.87 higher)	Low	RCT	Serious risk of bias[12]	No serious inconsistency[6]	No serious indirectness[3]	Serious imprecision[10]	None
1 (Ellis 2005)	64	63	NR	MD 0.87 higher (0.46 to 1.28 higher)	Moderate	RCT	No serious risk of bias	No serious inconsistency[6]	No serious indirectness[3]	Serious imprecision[10]	None
Adherence to diabetes (measured with self-care inventory) at 6 months' follow-up (higher scores indicate better adherence)											
1 (Wysocki 2001)	36	40	NR	MD 4.4 higher (not reported)	Very low	RCT	Very serious risk of bias[5]	No serious inconsistency[6]	No serious indirectness[3]	Very serious imprecision[7]	None
1 (Wysocki 2007)	36	32	NR	MD 6.6 higher (1.77 to 11.43 higher)	Moderate	RCT	Serious risk of bias[11]	No inconsistency[6]	No serious indirectness[3]	No serious imprecision	None
Adherence to diabetes (measured with self-care inventory) at 12 months' follow-up (higher scores indicate better adherence)											
1 (Wysocki 2001)	34	38	NR	MD 8.7 higher (not reported)	Very low	RCT	Very serious risk of bias[5]	No serious inconsistency[5]	No serious indirectness[3]	Very serious imprecision[7]	None
1 (Wysocki 2007)	36	32	NR	MD 4 higher (1.08 lower to 9.08 higher)	Moderate	RCT	Serious risk of bias[11]	No serious inconsistency[6]	No serious indirectness[3]	No serious imprecision	None

MD mean difference, MID minimally important difference, NA not applicable, RCT randomised controlled trial
1 No apparent risk of bias in the included studies
2 No heterogeneity present (I-squared <33%)

Update 2015

3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
5 Concern about selection and performance bias, some participants received psychological support outside the study
6 Single-study analysis
7 Unable to assess precision using data reported in the article, 6 months HbA1 BFST mean (SD) 0.2% versus conventional treatment mean (SD) 0.6, not significant; 6 months self-care inventory BFST mean 1.8 versus conventional treatment mean -2.6, not significant; 12 months self-care inventory BFST mean 3.3 versus conventional treatment mean -5.4, not significant
8 Heterogeneity present (I-squared between 33% and 67%)
9 No MID for adherence specified by guideline development group
10 Confidence interval crosses one zone related to precision (MID -0.5 to +0.5; see 'Methodology for 2015 update')
11 Concern about attrition and detection bias
12 Concern about selection and performance bias (unclear reporting, lack of blinding)

Table 36: Evidence profile for effectiveness of family-based teamwork intervention versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Family-based teamwork intervention	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 12 months											
1 (Laffel 2003)	50	50	NA	MD 0.5 lower (1.02 lower to 0.02 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious imprecision[4]	None
1 (Anderson 1999)	28	27	NA	MD 0.2 higher (not reported)	Very low	RCT	Serious risk of bias[5]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[6]	None
Health-related quality of life (PedsQL) at 12 months (higher scores indicate better outcomes)											
1 (Laffel 2003)	50	50	NA	MD 0.4 higher (3.91 lower to 4.71 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[7]	None

MD mean difference, NA not applicable, RCT randomised controlled trial
1 Concern over performance bias possibly due to poor reporting, but this is unlikely to affects outcomes
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
5 Some risk of bias due to identification of several limitations and absence of reported information
6 Unable to assess precision using data reported in the article, 12 months HbA1 mean (SD) 8.9% ±1.05% versus standard care mean (SD) 8.7 ±0.63, not significant
7 No MID for PedsQL specified by guideline development group

Update 2015

Table 37: Evidence profile for effectiveness of family-based behavioural intervention not specifically based on teamwork versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Family-based behavioural intervention	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 6 months											
1 (Wysocki 2001a)	37	40	NR	MD 0.1 lower (not reported)	Very low	RCT	Very serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
1 (Wysocki 2007)[a]	36	32	NR	MD 0.3 lower (not reported)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[10]	None
HbA1c at 12 months											
1 (Nansel 2009)	58	58	NR	MD 0.2 higher (0.38 lower to 0.78 higher)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision 7	None
1 (Anderson 1999)b	30	27	NA	MD 0.0 (not reported)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[9]	No serious indirectness[3]	Very serious imprecision[4]	None
1 (Wysocki 2001a)	36	38	NR	MD 0.8 lower (not reported)	Very low	RCT	Very serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
1 (Wysocki 2007)[a]	36	32	NR	MD 0.1 lower (not reported)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[10]	None
Adherence to diabetes management (measured with Diabetes Self-Management Profile) at 12 months (higher scores indicate better outcomes)											
1 (Nansel 2009)	58	58	NR	MD 0.2 higher (3.45 lower to 3.85 higher)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[7]	None
1 (Wysocki 2007) [a]	28	29	NR	MD 6.6 higher (1.37 to 11.83 higher)	Moderate	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision	None
Adherence to diabetes (measured with Self-care inventory) at 6 months follow-up (higher scores indicate better adherence)											
1 (Wysocki 2001a)	37	40	NR	MD 2.3 higher (not reported)	Very low	RCT	Very serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
1 (Wysocki 2007) [a]	36	32	NR	MD 4 higher (1.4 lower to 9.4 higher)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[7]	None

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Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Family-based behavioural intervention	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Adherence to diabetes (measured with Self-care inventory) at 12 months follow-up (higher scores indicate better adherence)											
1 (Wysocki 2001a)	36	38	NR	MD 4.2 higher (not reported)	Very low	RCT	Very serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[4]	None
1 (Wysocki 2007)[a]	36	32	NR	MD 2 higher (3.26 lower to 7.26 higher)	Very low	RCT	Serious risk of bias[8]	No serious inconsistency[2]	No serious indirectness[3]	Very serious imprecision[7]	None

MD mean difference NA not applicable, NR not reported, RCT randomised controlled trial
a Education plus support versus conventional treatment (standard care)
b Attention control versus standard care
1 Concern about selection and performance bias, some participants received psychological support outside the study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Unable to assess precision using data reported in the article, 6 months HbA1 education support mean 0.5% versus conventional therapy mean 0.6%, not significant; 12 months HbA1 education support mean 0.3% versus conventional therapy mean 1.1%, not significant; 6 months SCI education support mean -0.3 versus conventional therapy mean -2.6, not significant; 12 months SCI education support mean -1.2 versus conventional therapy mean -5.4, not significant
5 Concern about performance bias, but this is unlikely to affect outcomes
6 Serious heterogeneity present (I-squared >67%)
7 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
8 Some risk of bias due to identification of several limitations and absence of reported information
9 No MID for Diabetes Self-Management Profile specified by guideline development group
10 Unable to assess precision using data reported in the article, 6 months post-intervention HbA1 education support mean 9.3% ±1.4% versus standard care mean 9.6% ±1.6; 12 months post-intervention HbA1 education support mean 9.5% ±1.5% versus standard care mean 9.6% ±1.7;

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K.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Table 38: Evidence profile for effectiveness of multiple daily injections in improving glycaemic control in children and young people newly diagnosed with type 1 diabetes when compared with mixed insulin injections

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c (%) change from baseline after 1 year											
1 (Abid 2011)	29 (changed from 9.1 at baseline to 7.9 at 1 year)	88 (changed from 11.4 at baseline to 9.1 at 1 year)	NA	MD 1.2 lower CI NC	Very low	Retrospective cohort study	Serious risk of bias[1]	NA	No serious indirectness[2]	Serious imprecision[c]	None
1 (Adhikari 2009)	212 (changed from 11.4 ±1.9 at baseline to 7.5 ±1.6 at 1 year)	247 (changed from 11.6 ±1.8 at baseline to 8.2 ±1.8 at 1 year)	NA	MD 0.7 lower (1.01 lower to 0.39 lower)	Very low	Retrospective cohort study	Serious risk of bias[4]	NA	No serious indirectness[5]	Serious imprecision[f]	None
HbA1c (%) change from baseline after 9 months											
1 (Adhikari 2009)	212 (changed from 11.4 ±1.9 at baseline to 7.2 ±1.7 at 9 months)	247 (changed from 11.6 ±1.8 at baseline to 7.9 ±1.4 at 9 months)	NA	MD 0.7 lower (0.98 lower to 0.42 lower)	Very low	Retrospective cohort study	Serious risk of bias[7]	NA	No serious indirectness[5]	Serious imprecision[f]	None
HbA1c (%) change from baseline after 6 months											
1 (Adhikari 2009)	212 (changed from 11.4 ±1.9 at baseline to 6.6 ±1.4 at 6 months)	247 (changed from 11.6 ±1.8 at baseline to 7.3 ±1.4 at 6 months)	NA	MD 0.7 lower (1.96 lower to 0.44 lower)	Very low	Retrospective cohort study	Serious risk of bias[8]	NA	No serious indirectness[5]	Serious imprecision[6]	None
BMI standard deviation score (SDS) change from baseline after 1 year											
1 (Abid 2011)	29 (changed from 0.28 at baseline to 0.56 at 1 year)	88 (changed from 0.41 at baseline to 0.9 at 1 year)	NA	MD 0.34 lower CI NC	Very low	Retrospective cohort study	Serious risk of bias[1]	NA	No serious indirectness[2]	Serious imprecision[3]	None

BMI body mass index, CI confidence interval, MD mean difference, NA not applicable, NC not calculable

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1 Multiple daily injections offered only to older children and young people
2 Comparison is between twice-daily injections and multiple daily injections
3 No estimates of precision reported
4 Participants allocated to treatment based on family or physician preference and high drop-out rate at 12 months reported in both thrice-daily injection cohort (44%) and multiple daily injections cohort (25%)
5 Comparison is between thrice-daily injections and multiple daily injections
6 Range of MD in HbA1c crosses two zones related to precision (see 'Methodology for 2015 update')
7 Participants allocated to treatment based on family or physician preference and high drop-out rate at 9 months in both thrice-daily injection cohort (36%) and multiple daily injections cohort (31%)
8 Participants allocated to treatment based on family or physician preference and high drop-out rate at 6 months in both thrice-daily injection cohort (26%) and multiple daily injections cohort (27%)

Table 39: Evidence profile for effectiveness of multiple daily injections in improving glycaemic control in children and young people with type 1 diabetes of at least 1 year's duration when compared with mixed insulin injections

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c (%) change from baseline after 2 years											
1 (Al-Fifi 2003)	24 (changed from 9.34 ±1.55 at baseline to 9.49 ±1.55 at 2 years)	57 (changed from 9.37 ±1.8 at baseline to 9.59 ±1.59 at 2 years)	NA	MD 0.1 lower (0.86 lower to 0.66 higher)	Very low	Retrospective cohort study	No serious risk of bias[1]	NA	Serious indirectness [2,3]	Serious imprecision[4]	None
HbA1c (%) change from baseline after 1 year											
1 (Al-Fifi 2003)	24 (changed from 9.34 ±1.55 at baseline to 9.2 ±1.7 at 1 year)	57 (changed from 9.37 ±1.8 at baseline to 9.46 ±1.61 at 1 year)	NA	MD 0.26 lower (1.05 lower to 0.53 higher)	Very low	Retrospective cohort study	No serious risk of bias[1]	NA	Serious indirectness [2,3]	Serious imprecision[d]	None
1 (Abid 2011)	36 (9.2 at 1 year)	36 (8.9 at treatment switch)	NA	MD 0.3 higher CI NC	Very low	Interrupted time series	Serious risk of bias[5]	NA	No serious indirectness [3]	Serious imprecision[f]	None
1 (Adhikari 2009)	118 (8.5 ±1.6 at 1 year)	198 (8.4 ±1.5 at treatment switch)	NA	MD 0.1 higher (0.25 lower to 0.45 higher)	Very low	Interrupted time series	Serious risk of bias[7]	NA	No serious indirectness [8]	No serious imprecision	None
1 (Alemzadeh 2003)	44 (8.1 ±1.0 at 1 year)	44 (9.2 ±1.1 at treatment switch)	NA	MD 1.1 lower (1.55 lower to 0.65 lower)	Very low	Interrupted time series	No serious risk of bias	NA	No serious indirectness [9]	No serious imprecision	None

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Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Karaguzel 2005)	25 (8.2 ±1.5 at 1 year)	25 (9.3 ±2.5 at treatment switch)	NA	MD 1.1 lower (2.27 lower to 0.07 higher)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness [3,10,11]	Serious imprecision[4]	None
HbA1c (%) change from baseline after 9 months											
1 (Adhikari 2009)	129 (8.5 ±1.6 at 9 months)	198 (8.4 ±1.5 at treatment switch)	NA	MD 0.1 higher (0.24 lower to 0.44 higher)	Very low	Interrupted time series	Serious risk of bias[12]	NA	no serious indirectness [8]	No serious imprecision	None
HbA1c (%) change from baseline after 6 months											
1 (Adhikari 2009)	142 (8.3 ±1.4 at 6 months)	198 (8.4 ±1.5 at treatment switch)	NA	MD 0.1 lower (0.42 lower to 0.22 higher)	Very low	Interrupted time series	Serious risk of bias[13]	NA	no serious indirectness [8]	No serious imprecision	None
1 (Bin-Abbas 2007)	10 (8.4 ±0.7 at endpoint)	10 (8.6 ±1.2 at treatment switch)	NA	MD 0.2 lower (1.12 lower to 0.72 higher)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness [c,n,o]	Serious imprecision[4]	None
1 (Bin-Abbas 2006	10 (8.6 ±0.5 at endpoint)	10 (10.6 ±1.2 at treatment switch)	NA	MD 2.0 lower (2.86 lower to 1.14 lower)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness [3,16,17]	No serious imprecision	None
1 (Karaguzel 2005)	25 (8.3 ±1.6 at 6 months)	25 (9.3 ±2.5 at treatment switch)	NA	MD 1.0 lower (2.19 lower to 0.19 higher)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness [3,10,11]	Serious imprecision[4]	None
HbA1c (%) during study period (cross-sectional observational data)											
1 (Alexander 2001)	30 (9.79 ±1.77)	1573 (9.04 ±1.53)	NA	MD 0.75 higher (0.20 higher to 1.30 higher)	Very low	Cross-sectional survey	No serious risk of bias	NA	Serious indirectnes[1] [8,19,20]	Serious imprecision[4]	None
1 (de Beaufort 2007)	926 (8.2 ±0.0)	524 (8.2 ±0.1)	NA	MD 0.0 (0.01 lower to 0.01 higher)	Low	Cross-sectional survey	No serious risk of bias[21]	NA	No serious indirectness [22]	No serious imprecision	None
1 (Dorchy 1997)	15 (6.6 ±1.1)	129 (6.6 ±1.2)	NA	MD 0.0 (0.64 lower to 0.64 higher)	Very low	Cross-sectional survey	No serious risk of bias	NA	Serious indirectness [3,23]	Serious imprecision[4]	None
1 (Vanelli 2005)	1911 (8.7 ±0.2)	1608 (8.3 ±0.1)	NA	MD 0.4 higher (0.39 higher to 0.41 higher)	Low	Cross-sectional survey	No serious risk of bias	NA	No serious indirectness [20]	No serious imprecision	None
Proportion achieving ADA age-specific HbA1c target24 (cross-sectional observational data)											

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Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Mohammad 2012)	31/42 (73.8%)	192/373 (51.5%)	RR 1.43 (1.17 to 1.76)	211 more per 1000 (from 88 more to 391 more)	Very low	Cross-sectional survey	No serious risk of bias	NA	No serious indirectness [25]	Serious imprecision [2, 6]	None
Number of severe hypoglycaemic episodes (ISPAD 2000 grades 2-3 or ISPAD 2009 'severe')											
1 (Al-Fifi 2003)	4/24 (16.7%)	16/57 (28.1%)	RR 0.59 (0.22 to 1.59)	115 fewer per 1000 (from 219 fewer to 166 more)	Very low	Retrospective cohort study	No serious risk of bias [1]	NA	Serious indirectness [3,27]	Very serious imprecision [28]	None
1 (Alemzadeh 2003)	7/44 (15.9%)	17/44 (38.6%)	RR 0.41 (0.19 to 0.89)	228 fewer per 1000 (from 43 fewer to 313 fewer)	Very low	Interrupted time series	No serious risk of bias	NA	no serious indirectness [9, 29]	Serious imprecision [26]	None
Number of episodes of DKA											
1 (Al-Fifi 2003)	6/24 (25%)	17/57 (29.8%)	RR 0.84 (0.38 to 1.86)	48 fewer per 1000 (from 185 fewer to 256 more)	Very low	Retrospective cohort study	No serious risk of bias [1]	NA	No serious indirectness [3,30]	Very serious imprecision [28]	None
1 (Alemzadeh 2003)	0/44 (0%)	2/44 (4.5%)	RR 0.2 (0.01 to 4.05) [32]	36 fewer per 1000 (from 45 fewer to 139 more)	Very low	Interrupted time series	No serious risk of bias	NA	No serious indirectness [9,31]	Very serious imprecision [ab]	None
1 (Bin Abbas 2007)	0/10 (0%)	0/10 (0%)	NC	NC	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness [3,33,34]	NA	None
1 (Bin Abbas 2006)	0/10 (0%)	0/10 (0%)	NC	NC	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness [3,34,35]	NA	None

ADA American Diabetes Association, CI confidence interval, DKA diabetic ketoacidosis, ISPAD International Society for Pedatric and Adolescent Diabetes, MD mean difference, NA not applicable, NC not calculable, RR relative risk
1 Participants matched for age, sex, body mass index (BMI), insulin dose and compliance
2 All participants enrolled into adolescent education programme at baseline
3 Comparison is between twice-daily injections and multiple daily injections
4 Range of MD in HbA1c crosses two zones related to precision (see 'Methodology for 2015 update')
5 Multiple daily injections offered only to older children and young people
6 No estimates of precision reported
7 Participants allocated to treatment according to family or physician preference and high drop-out rate at 12 months (40%)
8 Comparison is between thrice-daily injections and multiple daily injections
9 Comparison is between 2 to 3 injections per day and multiple daily injections
10 Length of time on twice-daily injections not reported
11 Participants had poor or moderate diabetes control before treatment switch
12 Participants allocated to treatment according to family or physician preference and high drop-out rate at 9 months (35%)

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13 Participants allocated to treatment according to family or physician preference and high drop-out rate at 6 months (28%)
14 HbA1c measured at different time points before and after treatment switch; mean during 3 months before switch and in last month after switch (6 to 10 months after switch)
15 Participants had poor diabetes control (HbA1c >8.5%) and recurrent daytime and nocturnal hypoglycaemia (>4 episodes per month) before treatment switch
16 HbA1c measured at different time points before and after treatment switch; mean during 6 months before switch, time point/span of measurement after switch not reported; follow-up 6 to 9 months
17 Participants had poor diabetes control (HbA1c >8.5%) and recurrent daytime and nocturnal hypoglycaemia (>8 episodes per month) before treatment switch
18 Study had only 2% participants using multiple daily injections
19 Duration of diabetes of participants was <6 months to >5 years
20 Participants had 1, 2 or 3 injections per day or multiple daily injections
21 Study had 11% loss to follow-up, duration of diabetes longer in those providing HbA1c data
22 Participants had 2 or 3 injections per day or a basal-bolus regimen (multiple daily injections)
23 Study had only 10% participants using multiple daily injections and included children and young people with duration of diabetes 5 months to 15 years
24 ADA age-specific targets: age <6 years, HbA1c 7.5 -8.5%; age 6 to 12 years, HbA1c ≤ 8%; age 13 to 18 years, HbA1c ≤7.5%
25 Participants had multiple daily injections, twice-daily injections, or a regimen of twice-daily intermediate-acting insulin plus 1 or more injections of regular-acting insulin (classified as <4 injections per day)
26 RR crosses two zones related to precision (see 'Methodology for 2015 update')
27 Severe hypoglycaemia defined in study methods as hypoglycaemia requiring assistance or leading to coma or convulsion but figures reported are for admissions for hypoglycaemia over 2 year study period
28 RR crosses three zones related to precision (see 'Methodology for 2015 update')
29 Severe hypoglycaemia defined as episodes of blood glucose <2.8 mmol/l with unconsciousness and with or without seizure
30 Outcome defined as number of admissions for DKA and length of follow-up 2 years
31 Length of follow-up 1 year
32 RR calculated by adding 0.5 to events in each arm
33 Frequency of DKA episodes measured at different times; 3 months before switch and 6 to 10 months after treatment switch
34 Length of follow-up 6 months
35 Frequency of DKA episodes may be measured at different times before and after treatment switch; follow-up 6 to 9 months after treatment switch and not reported before treatment switch

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K.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.7 Type 1 diabetes – blood glucose monitoring

Review question: How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

Table 40: Evidence profile for frequency of self-monitoring of blood glucose in children and young people with type 1 diabetes

Number of studies	Number of children and young people	Relative effect	Absolute effect	Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
Association between frequency of SMBG and HbA1c, reported as coefficients of associations										
5 (de Beaufort 2013; Haller 2004; Ingerski 2011; Levine 2001; Moreland 2004)	4794	NA	Increased frequency of SMBG was inversely correlated with HbA1c independent of other variables r=-0.17 (p <0.0001) to r=-0.45 (p <0.001)	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as the probability of frequency of SMBG being associated with excellent control of HbA1c in the previous 12 months compared with the poor control group, SMBG performed 3 to 4 times per day versus 0 to 2 times per day										
1 (Campbell 2014)	3272	Adjusted OR 1.7 (0.7 to 3.9)	NA	Very Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	Very serious imprecision[5]	None
Association between frequency of SMBG and HbA1c, reported as the probability of frequency of SMBG being associated with excellent control of HbA1c in the previous 12 months compared with the poor control group, SMBG performed 5 to 9 times per day versus 0 to 2 times per day										
1 (Campbell 2014)	3272	Adjusted OR 2.3 (1.0 to 5.1)	NA	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	Serious imprecision[6]	None
Association between frequency of SMBG and HbA1c, reported as the probability of frequency of SMBG being associated with excellent control of HbA1c in the previous 12 months compared with the poor control group, SMBG performed ≥10 times per day versus 0 to 2 times per day										
1 (Campbell 2014)	3272	Adjusted OR 7.0 (2.9 to 17.0)	NA	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 3 to 4 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.5%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 5 to 6 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.4%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 7 to 9 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.1%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None

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Number of studies	Number of children and young people	Relative effect	Absolute effect	Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed ≥ 10 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 7.8%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 3 to 4 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.7%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c leves among children aged 6 to 13 years, SMBG performed 5 to 6 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.4%	Low	Observational	No serious risk of bias1	Not calculated2	No serious indirectness3	No serious imprecision4	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 7 to 9 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.1%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed ≥ 10 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 7.8%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 0 to 3 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 10.3%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 3 to 4 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 9.0%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 5 to 6 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.5%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 7 to 9 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.2%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c levels among children aged 13 to 18 years, SMBG performed ≥ 10 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.0%	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None
Change in HbA1c for 1 additional test per day										
8 (Dorchy 1997; Haller 2004; Helgeson 2011; Levine 2001; McGrady 2009; Nordly 2005; Svensson 2009; Ziegler 2011)	31,083	NA	HbA1c decreased by between 0.056 percentage points and 0.4 percentage points for each additional test	Low	Observational	No serious risk of bias[1]	Not calculated[2]	No serious indirectness[3]	No serious imprecision[4]	None

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Number of studies	Number of children and young people	Relative effect	Absolute effect	Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
Association between frequency of SMBG and severe hypoglycaemic episodes										
1 (Ziegler 2011)	26,723	NA	2.38 (±0.54) additional events per 100 patient years for every 1 additional test	Low	Observational	No serious risk of bias[1]	No serious inconsistency	No serious indirectness[3]	No serious imprecision[4]	None

CI confidence interval, MID minimally important difference, NA not applicable, OR odds ratio, r correlation coefficient, SMBG self-monitoring of blood glucose
1 No apparent risk of bias in the included studies
2 No calculation of inconsistency performed
3 Population, intervention and outcome as specified in the review protocol
4 No MID specified by the guideline development group
5 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')
6 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
7 Single-study analysis

Review question: What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Table 41: Evidence profile for effectiveness of self-monitoring of blood glucose against continuous glucose monitoring systems in children and young people diagnosed with type 1 diabetes at least 1 year before enrolment to the study

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Change in HbA1c level – at 6 months (real-time CGMS)											
2 (Langendam 2012; Mauras 2012)	146	152	NA	MD 0.09 lower in CGMS group (0.24 lower to 0.07 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision4	None
Change in HbA1c level - at 6 months (retrospective CGMS)											
2 (Bukara-Radujković 2011; Langendam 2012)	59	57	NA	MD 0.3 lower (0.67 lower to 0.07 higher)	Low	RCT	Serious5	No serious inconsistency[6]	No serious indirectness[3]	Serious[7]	None

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Bukara-Radujković 2011)	40	40	NA	MD 0.7 lower (1.56 lower to 0.16 higher)	Very low	RCT	Serious8	No serious inconsistency[9]	No serious indirectness[3]	Very serious[10]	Yes[11]
Severe hypoglycaemic episodes – at 6 months											
2 (Langendam 2012; Mauras 2012)	8/148 (5.4%)	13/146 (8.9%)	RR 0.63 (0.27 to 1.46)	33 fewer per 1000 (from 65 fewer to 41 more)	Low	RCT	No serious risk of bias[1]	No serious inconsistency[6]	No serious indirectness[3]	Very serious[10]	None
Parental satisfaction with the intervention – change over 6 months (scale 1 to 3; higher score means greater satisfaction)											
1 (Mauras 2012)	69	68	NA	MD 0.3 higher (0.21 to 0.39 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[9]	No serious indirectness[3]	No serious imprecision[4]	None

CGMS continuous glucose monitoring system, CI confidence interval, MD mean difference, NA not applicable, QoL quality of life, RCT randomised controlled trial, RR relative risk, SMBG self-monitoring of blood glucose, SMD standardised mean difference
1 No apparent risk of bias in the included studies
2 Heterogeneity amongst the studies was low (I2=26%)
3 Population, intervention and outcome as specified in the review protocol
4 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')
5 In one of the included studies methods of randomisation and allocation concealment were unclear and the groups were not altogether comparable at baseline
6 No heterogeneity found between studies (I2=0%)
7 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
8 Methods of randomisation and allocation concealment were unclear and the groups were not altogether comparable at baseline
9 Single-study analysis
10 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')
11 There were statistically significant differences between the intervention and control groups at baseline in terms of age (p=0.016), diabetes duration (p=0.013), insulin dose (p=0.005) and mean blood glucose (p=0.031)

Update 2015

Table 42: Evidence profile for effectiveness of self-monitoring of blood glucose against continuous glucose monitoring systems in children and young people recently diagnosed with type 1 diabetes (less than 1 year before enrolment to the study)

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Change in HbA1c level - at 6 months (real-time CGMS)											
1 (Langendam 2012)	76	78	NA	MD 0.10 lower in CGMS group (0.46 lower to 0.66 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious[4]	None
Change in HbA1c level - at 12 months (real-time CGMS)											
1 (Langendam 2012)	76	78	NA	MD 0.10 higher (0.46 lower to 0.66 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious[4]	None
Severe hypoglycaemic episodes – at 12 months											
1 (Langendam 2012)	0/76 (0%)	4/78 (5.1%)	RR 0.11 (0.01 to 2.08)	46 fewer per 1000 (from 51 fewer to 55 more)	Low	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Very serious[5]	None
Quality of life of parents – at 6 months (scale 1 to 100; higher score means better quality of life)											
1 (Langendam 2012)	76	78	NA	MD 0.5 lower (7.64 lower to 6.64 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
Quality of life of parents – at 12 months (scale 1 to 100; higher score means better quality of life)											
1 (Langendam 2012)	76	78	NA	MD 1.9 higher (4.13 lower to 7.93 higher)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None

CGMS continuous glucose monitoring system, CI confidence interval, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMBG self-monitoring of blood glucose, SMD standardised mean difference
1 No apparent risk of bias in the included studies
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
5 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')
6 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')

Update 2015

Review question: What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Table 43: Evidence profile for effectiveness of continuous glucose monitoring performed in real-time compared with continuous glucose monitoring performed intermittently in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Real-time continuous glucose monitoring	Intermittent continuous glucose monitoring	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (%) - at 6 months											
1 (Battelino 2011)	27 (changed from 6.92 ±0.56 at baseline to 6.92 ±0.98 at 6 months)	26 (changed from 6.91 ±0.67 at baseline to 7.15 ±0.98 at 6 months)	NA	MD 0.23 lower in the real-time CGMS group (0.76 lower to 0.3 higher)	Low	RCT	No serious risk of bias[1]	No serious inconsistency [2]	Serious indirectness[3]	Serious imprecision[4]	None
Severe hypoglycaemic episodes – at 6 months											
1 (Battelino 2011)	0/27 (0%)	0/26 (0%)	NC5	NA	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency [2]	Serious indirectness[3]	NA	None

CGMS continuous glucose monitoring system, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial, RR relative risk,
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Intervention and comparison not as specified in the review protocol
4 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
5 Cannot be calculated as number of events in both intervention and control group is zero

Update 2015

K.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Table 44: Evidence profile for effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Blood ketone monitoring	Urine ketone monitoring	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Hospital admission rates: incidence of acute complications as a proxy for admission rates											
1 (Laffel 2005)	62	61	NA	MD 0.37 lower (0.74 lower to 0.00)	Low	RCT	Serious[1]	No serious inconsistency[2]	Serious indirectness[3]	No serious imprecision[4]	None
Adherence to ketone monitoring: percentage of time ketones checked on sick days											
1 (Laffel 2005)	62	61	NA	90.8% of time for blood ketone monitoring and 61.3% of time for urine ketone monitoring[a]	Low	RCT	Serious[1]	No serious inconsistency[2]	Serious indirectness[3]	Serious imprecision[6]	None

NA not applicable, MD mean difference, RCT randomised controlled trial
1 Several limitations identified which amounted to a serious risk of bias but these did not negate the study findings
2 Single-study analysis
3 People aged 18 years and over were included in the study but this did not negate the study findings
4 The guideline development group did not set a MID for this outcome
5 The study authors reported statistical significance of p <0.001

Update 2015

K.9 Type 1 diabetes – dietary advice

Review questions: What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Table 45: Evidence profile for effectiveness of dietary advice based on carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes

	Number of children and young people		Effect								
	Carbohydrate counting	Treatment as usual	Relative (95% confidence interval)	Absolute (95% confidence interval)	Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
HbA1c value (%) at 12 months											
2 (Enander 2012; Goksen 2014)	78	46	NA	WMD 0.38 lower (0.77 lower to 0.01 higher)	Moderate	RCT	Serious risk of bias[1]	No serious inconsistency	No serious indirectness[4]	Serious[4]	None
HbA1c value (%) at 24 months											
1 (Goksen 2014)	52	32	NA	MD 0.89 lower (1.61 to 0.17 lower)	Moderate	RCT	Serious risk of bias[1]	No serious inconsistency[3]	No serious indirectness[4]	Serious[4]	None
BMI-SDS at 12 months											
2 (Enander 2012; Goksen 2014)	78	46	NA	WMD 0.28 lower (0.68 lower to 012 higher)	Moderate	RCT	No serious risk of bias[2]	No serious inconsistency	No serious indirectness[4]	Serious[4]	None
BMI-SDS at 24 months											
1 (Goksen 2014)	52	32	NA	MD 0.14 lower (0.66 lower to 0.38 higher)	Moderate	RCT	Serious risk of bias[1]	No serious inconsistency[3]	No serious indirectness[4]	Serious[4]	None
Severe hypoglycaemic episodes (over the 12-month study)											
1 (Enander 2012)	0/30 (0%)	0/15 (0%)	NA[a]	MD 0.00 (NC)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[3]	No serious indirectness[4]	No serious imprecision[5]	None

BMI-SDS body mass index standard deviation score, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial, RR relative risk, WMD weighted mean difference
a Unknown as no events reported in either treatment group
1 Moderate risk of bias in the included studies
2 No apparent risk of bias in the included study
3 Single-study analysis
4 Population, intervention and outcome as specified in the review protocol
5 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

Update 2015

Review question: What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Table 46: Evidence profile for effectiveness of dietary advice based on glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes, glycaemic index diet versus standard diet

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Glycaemic index	Standard diet	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Postprandial hyperglycaemia											
1 (Collier 1988)	7	7	Blood glucose after standard meal reduced from baseline in low glycaemic index phase ($p < 0.05$) No significant change in blood glucose after standard meal when compared with baseline in normal diet phase.		Moderate	RCT	No Serious risk of bias[1]	No Serious inconsistency[2]	No Serious indirectness[3]	Serious[4]	None

RCT randomised controlled trial
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Data reported only graphically with an accompanying p value, therefore unable to calculate mean difference between the intervention and comparator groups – not currently reported in table

Table 47: Evidence profile for effectiveness of dietary advice based on glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes, glycaemic index diet versus carbohydrate exchange diet

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Glycaemic Index	Carbohydrate exchange	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (%) change from baseline to 12 months											
1 (Gilbert 2001)	51 (changed from 8.3 ±1.4 at baseline to 8.0 ±1.0 at 12 months)	38 (no change, was 8.6 ±1.4 at baseline and at 12 months)	NA	MD in change in values between groups 0.3 lower (0.89 lower to 0.29 higher)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	Serious[4]	None

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Glycaemic Index	Carbohydrate exchange	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mean number of hypoglycaemic episodes (preprandial blood glucose <3.5 mmol/l) per month											
1 (Gilbertson 2001)	51 (6.9 ±6.8 episodes at 12 months)	38 (5.8 ±5.5 episodes at 12 months)	NA	MD 1.1 more (1.46 more to 3.66 fewer)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No Serious indirectness[3]	No serious imprecision[5]	None
Mean number of hyperglycaemic episodes (preprandial blood glucose >15 mmol/l) per month											
1 (Gilbertson 2001)	51 (11.2 ±9.8 episodes at 12 months)	38 (16.8 ±11.8 episodes at 12 months)	NA	MD 5.6 fewer (10.22 to 0.98 fewer)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No Serious indirectness[3]	Serious[5]	None
Number adhering to treatment (up to 12 months)											
1 (Gilbertson 2001)	46/55 (83.6%)	32/49 (65.3%)	RR 1.28 (1.01 to 1.62)	183 more per 1000 (from 7 more to 405 more)	Moderate	RCT	No Serious risk of bias[1]	No Serious inconsistency[2]	No Serious indirectness[3]	Serious[5]	None

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Findings do not meet the guideline development group agreed MID of 0.5 percentage points for the change in HbA1c level
5 Confidence intervals cross two zones related to precision (see the 2015 methods section of the full guideline)

Update 2015

K.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Table 48: Evidence profile for diagnostic test accuracy of serum beta-hydroxybutyrate and end-tidal carbon dioxide as indicators of diabetic ketoacidosis

Number of studies	Number of children and young people	Measure of diagnostic test accuracy (95% CI)				Quality	Quality assessment					
		Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio		Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by serum bicarbonate ≤ 18 mEq/l)												
1 (Sheikh-Ali 2008)	129	0.92 (0.87 to 0.97)[a]	0.84 (0.70 to 0.91)[a]	5.86 (2.96 to 11.61)[a]	0.08 (0.04 to 0.18)[a]	Very low	Retrospective	Serious[1]	NA	No serious	Very serious[2]	None
Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by venous pH of <7.3)												
1 (Prisco 2006)	90	0.83 (NC)[b]	0.68 (NC)[b]	2.59 (NC)[b]	0.25 (NC)[b]	Moderate	Prospective	No serious	NA	No serious	Serious[3]	None
Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by blood glucose >13.9 mmol/l)												
1 (Prisco 2006)	110	0.57 (NC)[b]	0.83 (NC)[b]	3.35 (NC)[b]	0.52 (NC)[b]	Moderate	Prospective	No serious	NA	No serious	Serious[3]	None
End-tidal carbon dioxide (cut-point ≤ 29 mmHg) for detecting DKA												
1 (Fearon 2002)	44	0.83 (0.52 to 0.98)	1.0 (0.88 to 1.0)	NC	0.17 (0.05 to 0.59)[a]	Low	Prospective	No serious	NA	No serious	Very serious	Used 29 torr (≈ 29 mmHg)
1 (Gilhotra 2007)	63	0.93 (0.70 to 0.99)	0.91 (0.78 to 0.96)	10.03 (3.91 to 25.76)	0.07 (0.01 to 0.49)[a]	Low	Prospective	No serious	NA	No serious	Very serious	
End-tidal carbon dioxide (cut-point ≤30 mmHg) for detecting DKA												
1 (Gilhotra 2007)	58	1.0 (0.78 to 1.0)[c]	0.86 (0.72 to 0.95)[c]	7.17 (3.41 to 15.05)[a]	0 (NC)[a,d]	Low	Prospective	Low	NA	No serious	Very serious[2]	None
End-tidal carbon dioxide (cut-point <36 mmHg) for detecting DKA												
1 (Fearon 2002)	42	1.0 (0.74 to 1.0)[a]	0.67 (0.47 to 0.83)[a]	3.0 (1.81 to 4.98)[a]	0 (NC)[a,d]	High	Prospective	Low	NA	No serious	No serious	Used 36 torr (≈36 mmHg)

CI confidence interval, DKA diabetic ketoacidosis, NA not applicable, NC not calculable,
a Calculated by the NCC-WCH technical team from data reported in the article
b Point estimate reported only; unable to calculate 95% CI from data reported
c Point estimate reported only, CI calculated by NCC-WCH technical team from data reported in the article
d Sensitivity=1.0 therefore negative likelihood ratio=0, and CI not calculable

Update 2015

1 Highly selected population – only included participants where medical records stated 'diabetes with ketoacidosis'
2 Confidence interval for positive likelihood ratio ranges from not useful to definitely useful

Update 2015

K.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Update 2015

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**
- **acid/base status?**

Table 49: Evidence profile for comparison of blood ketone monitoring versus urine ketone monitoring during treatment of diabetic ketoacidosis

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Blood ketone monitoring	Urine ketone monitoring	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mortality											
1 (Vanelli 2003)	0/16 (0%)	0/17 (0%)	NC	NC	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision4	None
Time to resolution of ketosis (proxy measure for duration of treatment)											
1 (Vanelli 2003)	16	17	NA	MD 6.5 hours fewer (from 4 to 9.4 fewer)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision5	None
1 (Prisco 2006)	99	NA	NA	MD 2.3 hours fewer (from 9.42 hours fewer to 4.82 hours more)	Very low	Case series	No serious risk of bias[1]	No serious inconsistency[2]	Serious indirectness[6]	Serious imprecision[7]	None
1 (Noyes 2007)	28 episodes of DKA	NA	NA	Median difference 11 hours fewer (range 1 hour fewer to 36 hours fewer)	Low	Case series	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	Yes[8]

DKA diabetic ketoacidosis, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial
1 No apparent risk of bias
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 No events reported
5 No MID specified by the guideline development group
6 Population includes a majority of participants without DKA
7 Confidence interval crosses the line of no effect
8 The 25 participants experienced a total of 40 episodes of DKA during the study period; 28 of the episodes which were followed up until negative ketonuria was obtained and included in this analysis

Update 2015

K.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

There are no evidence profiles for this review question because no studies were identified for inclusion.

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

Table 50: Evidence profile for an increased rate of fluid administration in children and young people with diabetic ketoacidosis – case-control studies

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Cases (cerebral oedema)	Controls (no cerebral oedema)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Effect of a per 5 ml/kg/hour increase in fluids											
1 (Glaser 2001)	61	183	RR 1.1 (0.4 to 3.0)[a,b]	NA	Low	Retrospective case control	No serious bias[1]	NA[2]	No serious indirectness	Very serious[3]	None
Effect of a per 1ml/kg/hour increase in fluids											
1 (Lawrence 2005)	21	42	NA	MD 3.96 (0.80 to 7.12)[c]	Low	Prospective surveillance with retrospective case control	Serious[4]	NA[2]	No serious indirectness[5]	Serious[6]	Yes[7]
Effect of per tertile increases in fluids within the first 4 hours of treatment											
1 (Edge 2006)	43	169	OR 3.30 (0.71 to 15.27)[de,g]	NA	Low	Matched case control	No serious bias[8]	NA[2]	Serious[9]	Very serious[10]	None
1 (Edge 2006)	43	169	OR 6.55 (1.38 to 30.97)d[,f,g]	NA	Moderate	Matched case control	No serious bias[8]	NA[2]	Serious[9]	No serious imprecision[11]	None
Effect of the rate of fluid administration in the first 4 hours of treatment											
1 (Mahoney 1999)	9	186	NA	MD 36.4 (8.9 to 63.9)[h]	Very low	Retrospective chart review	Very serious[12,13,14]	NA[2]	No serious indirectness	No serious imprecision[15]	None

CI confidence interval, DKA diabetic ketoacidosis, MD mean difference, MID minimally important difference, NA not applicable, OR odds ratio, RR risk ratio
a Study used both matched and unmatched controls; results presented are for matched controls as unmatched analyses did not include treatment-related variables

Update 2015

b Reported as RR by study authors based on the rare disease assumption; effect estimate actually derived from conditional multivariate logistic regression; controls were matched to cases by age, onset of diabetes, venous pH at presentation and serum glucose at presentation
c Calculated by the NCC-WCH technical team using a standard deviation based on the t-distribution due to a small sample size
d Adjusted for matching variables: age, sex and whether diabetes was newly diagnosed as well as baseline acidosis
e OR represents the increase in risk of cerebral oedema for tertile 2 (512 ml to 879 ml) versus tertile 1 (referent category; 76 ml to 511 ml) of fluids administered
f OR represents the increase in risk of cerebral oedema for tertile 3 (892 ml to 4090 ml) versus tertile 1 (referent category: 76 ml to 511 ml) of fluids administered
g Evidence for an overall trend for the effect of increasing fluid administration was also tested, adjusted for age, sex, new or known diabetes and baseline acidosis; the p-value for this test was <0.02 indicating that increasing volumes of fluid increased the risk of cerebral oedema
h Calculated by the NCC-WCH technical team based on the normal distribution
1 Imputation of 12% of continuous variables due to missing data; method of imputation was not described
2 Single-study analysis
3 Confidence interval for the RR crosses all three zones related to precision (see 'Methodology for 2015 update')
4 To increase the numbers of cases identified a retrospective medical records search was undertaken and data combined with that from prospective surveillance
5 Diagnosis of cerebral oedema allowed inclusion of participants with normal neuroimaging based on the premise that clinical diagnosis is often sufficient
6 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.31 calculated by the NCC-WCH technical team using sample means and standard deviations
7 Diabetes type was not reported
8 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets
9 Indirectness due to the use of tertiles of fluid administration
10 Confidence interval for the OR cross all three zones related to precision (see 'Methodology for 2015 update')
11 Confidence interval for the OR is entirely within one zone related to precision (see 'Methodology for 2015 update')
12 More than one episode of DKA per participant was included in analyses for participants without cerebral oedema or brain herniation
13 Selection bias is likely as groups were not comparable for baseline characteristics
14 Groups did not receive the same care
15 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update') based on an MID of 3.85 calculated by the NCC-WCH technical team using sample means and standard deviations

Update 2015

Table 51: Evidence profile for a slower rate of fluid administration compared with a faster rate of fluid administration in children and young people with diabetic ketoacidosis – randomised study

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (slower rate)	Comparator (faster rate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Risk of mild cerebral oedema (brain swelling)[a]											
1 (Glaser 2013)	10/18	8/18	NA	Two-tailed p-value 0.63[b]	Very low[c]	RCT pilot study	No serious bias	NA[1]	Serious[2]	Very serious[3,4,5]	None

ADC apparent brain diffusion coefficient, CI confidence interval, MID minimally important difference, NA not applicable, RCT randomised controlled trial
a One group received a bolus of 0.9% saline of 20 ml/kg with two-thirds of fluid deficit replaced over the first 24 hours and the remaining third replaced over the next 24 hours (a fluid deficit of 10% was assumed); the other treatment group received a bolus of 0.9% saline of 10 ml/kg with fluid deficit replaced evenly over 48 hours (a fluid deficit of 7% was assumed)
b Calculated by the NCC-WCH technical team using the Wilcoxon rank sum test for non-parametric data using an online calculator at cs.fairfield.edu/~sawin/stats/templates/wilcoxon.xls; individual patient data were obtained from study authors as results were presented graphically in the original article

c Starting point of moderate quality as the study is a pilot study for an RCT
1 Single-study analysis
2 ADC to detect brain swelling was used as a proxy for mild cerebral oedema
3 Not sufficiently powered to detect small differences and power calculations were not aimed at detecting between-group differences; calculations were to detect a 1.3 standard deviation change in ADC between treatment and post-recovery
4 No confidence interval was calculable as data were not normally distributed
5 MID not calculable

Table 52: Evidence profile for a slower rate of fluid administration compared with a faster rate of fluid administration in children and young people with diabetic ketoacidosis – partially randomised study

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Slower ratea,b	Faster ratea,b	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Time to resolution of acidosis, hours											
1 (Felner 2001)	30	60	NA	MD -4.10 (-5.88 to -2.32)[c]	Very low	Partially randomised cohort study	Serious[1]	No serious inconsistency[2]	No serious indirectness	Serious[3]	Yes[4]
Change in serum sodium, mmol/l											
1 (Felner 2001)	30	60	NA	MD 0.00 (-1.78 to 1.78)[c]	Very low	Partially randomised cohort study	Very serious[5,6]	No serious inconsistency[2]	Serious[7]	No serious imprecision[8]	Yes[4]
Change in serum chloride, mmol/l											
1 (Felner 2001)	30	60	NA	MD 1.95 (-0.78 to 4.68)[c]	Very low	Partially randomised cohort study	Very serious[5,6]	No serious inconsistency[2]	Serious[7]	Serious[9]	Yes[4]
Admission to ICU[d]											
1 (Felner 2001)	30	60	RR 0.95 (0.48 to 1.86)[c]	NA	Very low	Partially randomised cohort study	No serious bias	No serious inconsistency[2]	No serious indirectness	Very serious[10]	Yes[4]

CI confidence interval, ICU intensive care unit, MD mean difference, NA not applicable
a Treatment groups were assigned based on the introduction of a new treatment protocol in 1997; for the faster rate group fluid deficit was calculated based on the percentage of dehydration (7 to 10%) by weight in kg and added to 1.5 times the required maintenance rate (50% of the fluids were administered in the first 12 hours and the remaining 50% over the next 24 hours); the slower rate group received total fluids at a rate of 2.5 times the required maintenance rate regardless of the degree of dehydration (fluids were decreased to 1 to 1.5 times the maintenance rate after 24 hours of treatment)
b The total mean volumes of fluid (l/m2/24 hours) were 5.3 ±1.4 and 5.4 ±1.2 for the faster rate group, depending on whether a two- or three-bag protocol was used, and 4.1 ±1.1 for the slower rate group
c Calculated by the NCC-WCH technical team using the t-distribution due to a small sample size
d Admission to ICU was defined according to symptoms and signs including altered level of consciousness, severe acidosis (pH <7.00), haemodynamic instability, or very young age (<3 years)
1 Resolution of acidosis was not defined
2 Single-study analysis
3 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.70 calculated by the NCC-WCH technical team using sample means and standard deviations

Update 2015

4 The study authors conducted retrospective analyses on non-randomised participants to compare groups 1A and 1B due to subtle differences in the treatment protocols (three- versus two-bag rehydration); no statistically significant differences were observed therefore data were pooled by the NCC-WCH technical team
5 The amount of sodium chloride varied slightly between treatment groups (0.45% for the faster rate group and 0.675% for the slower rate group)
6 The time over which the change in serum levels of biochemical variables was assessed was not reported
7 Serum levels were reported as change scores not actual values after treatment
8 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update') based on an MID of 2.26 calculated by the NCC-WCH technical team using sample means and standard deviations
9 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.33 calculated by the NCC-WCH technical team using sample means and standard deviations
10 Confidence interval for the RR crosses all three zones related to precision (see 'Methodology for 2015 update')

Review question: What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Table 53: Evidence profile for comparison of 75 mEq/l concentration of sodium with 100 mEq/l concentration of sodium for the treatment of diabetic ketoacidosis in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (75 mEq/l)	Comparator (100 mEq/l)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Plasma sodium (corrected)											
Baseline											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.7 (-3.1 to 4.5)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[3]	None
4 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.6 (-3.0 to 4.2)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious4	None
8 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -1.5 (-5.3 to 2.3)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Serious[5]	None
16 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.2 (-2.7 to 2.3)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[6]	None
24 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.6 (-3.1 to 1.9)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[7]	None

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (75 mEq/l)	Comparator (100 mEq/l)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Plasma carbon dioxide											
Baseline											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.9 (-4.8 to 3.0)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[8]	None
4 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.2 (-4.8 to 4.4)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[9]	None
8 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.8 (-5.5 to 3.9)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[10]	None
16 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.4 (-3.5 to 4.3)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[11]	None
24 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -1.2 (-5.9 to 3.5)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[12]	None
pH											
Baseline											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.10 (-0.21 to 0.01)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Serious[13]	None
4 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.00 (-0.07 to 0.07)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[14]	None
8 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.06 (-0.13 to 0.01)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Serious[15]	None
16 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.0 (-0.7 to 0.7)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[16]	None
24 hours' follow-up											
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.0 (-0.7 to 0.7)[a]	Very low	Retrospective chart review	Serious[1]	NA[2]	No serious indirectness	Very serious[16]	None

ANOVA analysis of variance, CI confidence interval, MD mean difference, MID minimally important difference, NA not applicable
a Calculated by the NCC-WCH technical team using confidence intervals based on the t-distribution due to a small sample size

Update 2015

1 Analysis used ANOVA however there is no mention of potential confounders being accounted for in the analysis
2 Single-study analysis
3 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.48 calculated by the NCC-WCH technical team using sample means and standard deviations
4 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.37 calculated by the NCC-WCH technical team using sample means and standard deviations
5 Confidence interval crosses more than one zone related to precision (see 'Methodology for 2015 update') based on an MID of 2.42 calculated by the NCC-WCH technical team using sample means and standard deviations
6 Confidence interval spans crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 1.57 calculated by the NCC-WCH technical team using sample means and standard deviations
7 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 1.49 calculated by the NCC-WCH technical team using sample means and standard deviations
8 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.59 calculated by the NCC-WCH technical team using sample means and standard deviations
9 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.03 calculated by the NCC-WCH technical team using sample means and standard deviations
10 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.08 calculated by the NCC-WCH technical team using sample means and standard deviations
11 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.63 calculated by the NCC-WCH technical team using sample means and standard deviations
12 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') zones based on an MID of 3.19 calculated by the NCC-WCH technical team using sample means and standard deviations
13 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.09 calculated by the NCC-WCH technical team using sample means and standard deviations
14 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.05 calculated by the NCC-WCH technical team using sample means and standard deviations
15 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.05 calculated by the NCC-WCH technical team using sample means and standard deviations
16 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.46 calculated by the NCC-WCH technical team using sample means and standard deviations

Update 2015

Table 54: Evidence profile for comparison of bicarbonate with no bicarbonate for the treatment of diabetic ketoacidosis in children and young people

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (bicarbonate)	Comparator (no bicarbonate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration of hospitalisation, hours											
1 (Green 1998)	57/106 Mean duration 85 (75 to 95)	49/106 Mean duration 69 (58 to 60)	NA	Adjusted R2 0.23, p-value 0.07[a,b]	Very low	Retrospective case series	Serious[1]	NA[2]	Serious[3]	No serious imprecision[4]	Yes[5,6]

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (bicarbonate)	Comparator (no bicarbonate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Marr 1981)[c]	45	33	NA	MD 1.75 (0.04 to 3.46)[d]	Very low	Retrospective chart review	Serious[7]	NA[2]	Serious[8]	Serious[9]	Yes[5]
Risk of cerebral oedema											
1 (Lawrence 2005)	4/17 cases 1/34 controls	13/17 cases 33/34 controls	OR 10.15 (1.03 to 99.57)[e]	NA	Very low	Surveillance and retrospective case control	Serious[10]	NA[2]	No serious indirectness	Serious[11]	Yes[s5]
1 (Edge 2006)	5/43 cases 6/169 controls	38/43 cases 163/169 controls	OR 3.70 (1.02 to 13.10)	NA	Very low	Matched case control	No serious bias[12]	NA[2]	No serious indirectness	Serious[11]	None
Risk of cerebral oedema adjusted for baseline acidosis											
1 (Edge 2006)	5/43 cases 6/169 controls	38/43 cases 163/169 controls	OR 1.50 (0.39 to 5.76)[f]	NA	Very low	Matched case control	No serious bias[12]	NA[2]	No serious indirectness	Very serious[13]	None
Duration of acidosis, hours											
1 (Marr 1981)[c]	45	33	NA	MD -2.70 (-5.20 to -0.20)[d]	Very low	Retrospective chart review	Very serious[5,14]	NA[2]	Serious[6]	Serious[15]	Yes[5]

CI confidence interval, DKA diabetic ketoacidosis, MD mean difference, MID minimally important difference, NA not applicable, OR odds ratio, RR relative risk
a R^2 represents the correlation between duration of hospitalisation and the administration of bicarbonate
b Adjusted for calendar year, pH, base deficit, creatinine and haemoglobin because treatment groups were not comparable at baseline for these variables
c Comparison of children and young people who received sodium as either sodium bicarbonate, or sodium bicarbonate plus saline, or sodium bicarbonate and saline and lactate Ringers, or sodium bicarbonate and lactate Ringers with children and young people who received saline alone, lactate Ringers, or lactate Ringers with saline
d Calculated by the NCC-WCH technical team
e Crude effect estimate calculated by the NCC-WCH technical team
f The OR was also adjusted for age, sex and whether diabetes was newly diagnosed
1 Missing data were present for 124 out of 486 admissions reviewed for inclusion and these admissions were, therefore, excluded from analyses; high risk of bias
2 Single-study analysis
3 Only severe cases of DKA were included in the study; generalisability is reduced
4 MID not calculable.
5 Diabetes type not reported
6 Data from matched analyses were not used by the NCC-WCH technical team due to the high percentage of missing data (41%) generated by the matching process (49 participants per group, reduced to 29 participants per group after matching)
7 No baseline characteristics were reported; selection bias is likely
8 Treatments were grouped according to data extracted from medical records and combined by the NCC-WCH technical team to derive comparisons which best matched the review protocol
9 Confidence interval crosses more than one zone related to precision (see 'Methodology for 2015 update') based on an MID of 2.41 calculated by the NCC-WCH technical team using sample means and standard deviations
10 Results are from only 17 of 21 cases and 34 of 42 controls; loss of information is likely to have caused bias
11 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')

Update 2015

12 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets
13 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update')
14 Acidosis was not defined
15 Confidence interval crosses more than one zone related to precision (see 'Methodology for 2015 update') based on an MID of 3.48 calculated by the NCC-WCH technical team using sample means and standard deviations

Table 55: Evidence profile for the use of bicarbonate in treating diabetic ketoacidosis in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Cases (cerebral oedema)	Controls (no cerebral oedema)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Treatment with bicarbonate											
1 (Glaser 2001)	61	183	RR 4.2 (1.5 to 12.1)[a]	NA	Moderate[b]	Retrospective case control	No serious bias	NA[1]	No serious indirectness	No serious imprecision[2]	None

CI confidence interval, NA not applicable, RR relative risk
a Reported as RR by study authors based on the rare disease assumption; effect estimate actually derived from conditional multivariate logistic regression; controls were matched to cases by age, onset of diabetes, venous pH at presentation and serum glucose at presentation
b Quality upgraded due to a large effect size
1 Single-study analysis
2 Confidence interval is entirely in one zone related to precision (see 'Methodology for 2015 update')

Table 56: Evidence profile for comparison of phosphate with no phosphate for the treatment of diabetic ketoacidosis in children and young people

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (phosphate)	Comparator (no phosphate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Serum calcium											
1 (Becker 1983)	13	9	NA	MD -1.1 (-1.7 to -0.5)[a,b]	Very low	Partially randomised prospective cohort	Very serious[1,2,3,4]	NA[5]	No serious indirectness	No serious imprecision[6]	Yes[7]

CI confidence interval, MD mean difference, NA not applicable
a Calculated by the NCC-WCH technical team using confidence intervals based on the t-distribution due to a small sample size
b The intervention group received potassium replacement as mono- or di-basic phosphate salts versus controls who received no phosphate
1 Controls were not allocated using randomisation; randomisation method for the treatment groups is not described
2 Controls were less severe cases and received substantially different treatment compared with the two randomised treatment groups
3 Groups were not comparable at baseline

Update 2015

4 Data were presented graphically in the original article; numerical data were reported only for values at 12 hours' follow-up because results were significant for phosphate versus controls; high risk of reporting bias
5 Single-study analysis
6 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.29 calculated by the NCC-WCH technical team using sample means and standard deviations
7 Diabetes type is not reported

K.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Table 57: Effectiveness of intravenous osmotic agents in the treatment of cerebral oedema associated with diabetic ketoacidosis in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Mannitol	Hypertonic saline	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Adjusted odds ratio of mortality for hypertonic saline alone versus mannitol alone											
1 (DeCourcey 2013)	NA	NA	2.71 (1.01 to 7.26) [5,6]	NA	Very low	Retrospective cohort	Serious[1]	NA[2]	Serious indirectness[3]	Very serious imprecision[4]	None
Healthcare utilisation: brain imaging with CT scan (%)											
1 (DeCourcey 2013)	525/1202 (43.7)	109/299 (36.5)	NA	NA	Very low	Retrospective cohort	Serious[1]	NA[2]	Serious indirectness[3]	Very serious imprecision[4]	None
Healthcare utilisation: mechanical ventilation (%)											
1 (DeCourcey 2013)	184/1202 (15.3)	43/299 (14.4)	NA	NA	Very low	Retrospective cohort	Serious[1]	NA[2]	Serious indirectness[3]	Very serious imprecision[4]	None
Healthcare utilisation: intensive care unit admission (%)											
1 (DeCourcey 2013)	784/1202 (65.2)	269/299 (90)	NA	NA	Very low	Retrospective cohort	Serious[1]	NA[2]	Serious indirectness[3]	Very serious imprecision[4]	None

CI confidence interval, NA not applicable
1 More participants in the hypertonic saline group were admitted to intensive care unit (ICU) than those in the mannitol group
2 Single-study analysis
3 Upper age limit is slightly higher than the guideline population and a small number of participants (<1.5% total) who may not have had cerebral oedema associated with diabetic ketoacidosis (DKA) were included in the analysis
4 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')

Update 2015

5 Adjusted for discharge year, hospital clustering, gender, mechanical ventilation, brain imaging with CT scan, ICD-9 code (diabetes with hyperosmolar state (250.2) or diabetes with coma [250.3])
6 Treatment group with both hypertonic saline and mannitol was excluded from further analysis as participants treated with both agents would have been switched to the alternative agent once the initial therapy failed and the study database did not allow for the order of therapy intervention to be determined

K.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review question: When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

Table 58: Evidence profile for the effect of insulin administered within 1 hour of fluid replacement compared to insulin administered at least 1 hour after fluid administration on the risk of cerebral oedema

Number of studies	Number of patients		Effect		Quality	Design	Quality assessment				
	Cases (cerebral oedema)	Controls (no cerebral oedema)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Association between timing of insulin therapy and risk of cerebral oedema											
1 (Edge 2006)	43	169	Adjusted OR: 4.7 (1.5 to 13.9)[a,b]	NA	Moderate	Matched case control	No serious bias[1,2,3]	Not relevant	No serious indirectness	No serious imprecision[4,5]	None
Association between timing of insulin therapy and risk of cerebral oedema, adjusted for baseline biochemical measures to account for severity of acidosis											
1 (Edge 2006)	43	169	Adjusted OR: 12.7 (1.41 to 114.5)[a,b,c]	NA	Moderate	Matched case control	No serious bias[1,2,3]	Not relevant	No serious indirectness	No serious imprecision[4,5]	None

CI confidence interval, OR odds ratio, NA not applicable
a OR is for participants who received insulin therapy within 1 hour of fluid replacement compared to those who did not
b Adjusted for matching variables: age, sex and whether diabetes was newly diagnosed as well as baseline acidosis
c Baseline biochemical measures included in the multivariate model included: plasma glucose, potassium, urea, sodium and paCO2
1 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets
2 Whether controls were clearly established as not being cases was not reported
3 Standardisation of exposure measurement was not clear
4 Large effect size
5 Wide CI suggests imprecision but CI is entirely within one zone related to precision (see 'Methodology for 2015 update') therefore not downgraded

Update 2015

Review question: How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Table 59: Comparison of insulin dosage of 0.025 U/kg/hour or 0.05 U/kg/hour with a dosage of 0.1 U/kg/hour in children and young people with type 1 diabetes and DKA

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Low dosage insulin	Standard dosage insulin	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Change in blood glucose from admission (low dosage 0.05 U/kg/hour)											
Children of all ages											
1 (Al Hanshi 2011)	n=33 Median difference: -17 mmol/l (IQR: -26 to -12)	n=34 Median difference: -21 mmol/l (IQR: -52 to -15)	NA	p=0.004, adjusted R=0.62[a]	Very low	Retrospective cohort	Serious[1]	NA[5]	No serious indirectness	No serious imprecision[8]	
1 (Puttha 2010)	n=41 MD: 11.3 mmol/l (8.6 to 13.9)	n=52 MD: 11.8 mmol/l (8.4 to 15.2)	NA	MD: -0.50 (-4.75 to 3.75)[b]	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness	No serious imprecision[8]	Short follow-up period
Subgroup analysis: children aged less than 5 years											
1 (Puttha 2010)	n=6 MD: 15.9 mmol/l (2.2 to 29.5)	n=5 MD: 20.1 mmol/l (10.6 to 29.6)	NA	MD: -4.20 (-20.61 to 12.21)[b]	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness[6]	No serious imprecision[8]	Short follow-up period
Incidence of hypoglycaemia (low dosage 0.025 U/kg/hour)											
1 (Kapellen 2012)	8/23	2/41	RR: 7.13 (1.65 to 30.79)[c]	NA	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness[6]	No serious imprecision[9]	
Incidence of hypoglycaemia (low dosage 0.05 U/kg/hour)											
1 (Puttha 2010)	0/41	7/80	RR: 0.13 (0.008 to 2.22)[c]	NA	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness[6,7]	Very serious[10]	
Incidence of hypokalaemia (low dosage 0.025 U/kg/hour)											
1 (Kapellen 2012)	3/23	15/41	RR: 0.36 (0.12 to 1.10)[c]	NA	Very low	Retrospective cohort	Very serious[2,3,4]	NA[5]	No serious indirectness[6]	Serious[11]	
Change in blood pH from admission (low dosage 0.05 U/kg/hour)											
Children of all ages											
1 (Puttha 2010)	n=41 MD: 0.13 (0.09 to 0.18)	n=52 MD: 0.11 (0.07 to 0.15)	NA	MD: 0.02 (-0.04 to 0.08)[b]	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness[6]	No serious imprecision[8]	Short follow-up period

Update 2015

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Low dosage insulin	Standard dosage insulin	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Subgroup analysis: children aged less than 5 years											
1 (Puttha 2010)	n=6 MD: 0.17 (-0.01 to 0.31)	n=5 MD: 0.15 (-0.8 to 0.40)	NA	MD: 0.02 (-0.26 to 0.30)[b]	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness[6]	No serious imprecision[8]	Short follow-up period
Time to pH >7.3 (resolution of acidosis)											
1 (Puttha 2010)	n=41	n=52	NA	MD: -1.3 (-4.4 to 1.8)[b]	Very low	Retrospective cohort	Very serious[2,3]	NA[5]	No serious indirectness[6]	No serious imprecision[8]	Short follow-up period

CI confidence interval, IQR interquartile range, MD mean difference, MID minimally important difference, NA not applicable, RR relative risk
a R represents the correlation between insulin doseag and plasma glucose at 12 hours' follow-up, adjusted for the baseline value and age
b Confidence intervals calculated by the NCC-WCH technical team using a standard deviation based on the t-distribution due to small sample size
c Calculated by the NCC-WCH technical team
1 Dosages were changed from initial values in some participants
2 Failure to adequately control for confounding
3 Participants not selected from the same population
4 Differences between groups may be due to differences in treatment protocols for management of blood potassium
5 Single-study analysis
6 Population and measurement outcome match the protocol
7 Participants from 1 PICU centre were included in the analysis; this may have reduced generalisability or skewed results due to the inclusion of more severe cases
8 The guideline development group did not specify a MID for this outcome
9 Confidence interval entirely within one zone related to precision (see 'Methodology for 2015 update')
10 Confidence interval cross all three zones related to precision (see 'Methodology for 2015 update')
11 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')

Update 2015

K.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Table 60: Evidence profile for prevalence of retinopathy according to age

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age <9 years									
8 (Frank 1982, Cerutti 1989, Johansen 1994, Klein 1984, Kernell 1997, Joner 1992, Flack 1996, Donaghue 1999)	NC	0.0 to 9.0 (4.5)	Moderate	Cross sectional and prospective cohort	No serious risk of bias	No serious inconsistency	No serious indirectness	NA[1]	None
Age 9 years									
8 (Frank 1982, Cerutti 1989, Johansen 1994, Klein 1984, Kernell 1997, Joner 1992, Flack 1996, Donaghue 1999)	NC	0.0 to 9.0 (4.5)	Moderate	Cross sectional and prospective cohort	No serious risk of bias	No serious inconsistency	No serious indirectness	NA[1]	None
Age 10 years									
9 (Cerutti 1989, Massin 2007, Kernell 1997, Johansen 1994, Joner 1992, Flack 1996, Frank 1982, Donaghue 1999, Klein 1984)	NC	0.0 to 15.0 (6.7)	Low[a]	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency[2]	No serious indirectness	NA[1]	None
Age 11 years									
8 (Cerutti 1989, Massin 2007, Johansen l 1994, Cho 2011, Joner 1992, Flack 1996, Frank 1982, Klein 1984)	NC	0.0 to 15.0 (6.4)	Low[a]	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency[2]	No serious indirectness	NA[1]	None
Age 12 years									
9 (Massin 2007, Johansen 1994, Cho 2011, Joner 1992, Flack 1996, Frank 1982, Cerutti 1989, Klein 1984, Olsen l 2004)	NC	1.0 to 19.0 (7.7)	Low[a]	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency[2]	No serious indirectness	NA[1]	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age 13 years									
8 (Massin 2007, Johansen 1994, Frank 1982, Cho 2011, Klein 1984, Olsen 2004, Flack 1996, Cerutti 1989)	NC	1.0 to 25.0 (13.0)	Low[a]	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency[2]	No serious indirectness	NA[1]	None
Age 14 years									
8 (Massin 2007, Johansen 1994, Frank 1982, Cho 2011, Klein 1984, Olsen 2004, Flack 1996, Cerutti 1989)	NC	5.8 to 44.0 (13.0)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[1]	None
Age 15 years									
8 (Massin 2007, Johansen 1994, Cho 2011, Olsen 2004, Flack 1996, Cerutti 1989, Frank 1982, Klein 1984)	NC	5.8 to 54.0 (28.7)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[1]	None
Age 16 years									
6 (Cho 2011, Massin 2007, Flack 1996, Cerutti 1989, Frank 1982, Klein 1984)	NC	11.0 to 54.0 (42.8)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[1]	None
Age 17 years									
5 (Massin 2007, Cerutti 1989, Flack 1996, Frank 1982, Klein 1984)	NC	17.7 to 54.0 (45.7)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[1]	None
Age 18 years									
5 (Massin 2007, Flack 1996, Frank 1982, Klein 1984, Cerutti 1989)	NC	17.7 to 60.0 (48.0)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[1]	None

NA not applicable, NC not calculable
a Serious inconsistency between point estimates
b Very serious inconsistency between point estimates
1 Unable to comment on imprecision as no confidence intervals reported for ranges
2 Serious inconsistency as range of point estimates varies between 10 and 20 percentage points
3 Very serious inconsistency as range of point estimates varies by more than 20 percentage points

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Table 61: Evidence profile for prevalence of retinopathy according to duration of diabetes

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration <2 years									
6 (Frank 1982, Massin 2007, Kernell 1997, Flack 1996, Lobefalo 1997, Murphy 1990)	NC	1.0 to 21.0 (7.9)	Low[a]	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency[1]	No serious indirectness	NA[2]	None
Duration 2 years									
6 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990)	NC	1.0 to 21.0 (10.9)	Low[a]	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency[1]	No serious indirectness	NA[2]	None
Duration 3 years									
7 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990, Cerutti 1989)	NC	1.0 to 23.0 (10.5)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 4 years									
7 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990, Cerutti 1989)	NC	1.0 to 23.0 (10.5)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 5 years									
7 (Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Cerutti 1989, Frank 1982, Murphy 1990)	NC	6.2 to 50.0 (13.6)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 6 years									
6 (Massin 2007, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)	NC	6.2 to 50.0 (19.3)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 7 years									
6 (Massin 2007, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)	NC	6.2 to 50.0 (22.9)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 8 years									
7 (Massin 2007, Joner 1992, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)	NC	6.2 to 50.0 (20.7)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration 9 years									
6 (Massin 2007, Lobefalo 1997, Frank 1982, Goldstein 1993, Murphy 1990, Flack 1996)	NC	6.2 to 59.0 (37.0)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 10 years									
6 (Massin 2007, Lobefalo 1997, Kernell 1997, Murphy 1990, Flack 1996, Frank 1982)	NC	6.2 to 67.0 (41.0)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 11 years									
7 (Massin 2007, Lobefalo 1997, Kernell 1997, Cerutti 1989, Flack 1996, Frank 1982, Murphy 1990)	NC	13.0 to 75.0 (57.5)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 12 years									
7 (Massin 2007, Lobefalo 1997, Kernell 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990)	NC	13.0 to 75.0 (57.1)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 13 years									
6 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, 1990)	NC	13.0 to 75.0 (57.3)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 14 years									
6 (Massin 2007, Lobefalo 1997, Joner 1992, Flack 1996, Cerutti 1989, Murphy 1990)	NC	13.0 to 75.0 (53.1)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 15 years									
7 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990, Goldstein 1993)	NC	13.0 to 92.0 (57.5)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 16 years									

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
6 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990)	NC	13.0 to 75.0 (57.3)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 17 years									
5 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Murphy 1990)	NC	13.0 to 75.0 (57.1)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None
Duration 18 years									
4 (Massin 2007, Lobefalo 1997, Flack 1996, Murphy 1990)	NC	13.0 to 75.0 (38.9)	Very low[b]	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency[3]	No serious indirectness	NA[2]	None

NA not applicable, NC not calculable
a Serious inconsistency between point estimates
b Very serious inconsistency between point estimates
1 Serious inconsistency as range of point estimates varies between 10 and 20 percentage points
2 Unable to comment on imprecision as no confidence intervals reported for ranges
3 Very serious inconsistency as range of point estimates varies by more than 20 percentage points

Table 62: Evidence profile for incidence of retinopathy

Number of studies	Number of children and young people	Incidence per hundred person years	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Any sustained retinopathy									
1 (DCCT Research Group 1994)	55	18	High	RCT	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Intensive treatment group; no participant had retinopathy at baseline
1 (DCCT Research Group 1994)	70	23	High	RCT	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Conventional treatment group; no participant had retinopathy at baseline
≥ 3 step worsening of retinopathy									
1 (DCCT Research Group 1994)	55	3.2	High	RCT	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Intensive treatment group; no participant had retinopathy at baseline

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Number of studies	Number of children and young people	Incidence per hundred person years	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
1 (DCCT Research Group 1994)	70	6.3	High	RCT	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Conventional treatment group; no participant had retinopathy at baseline
Any retinopathy									
1 (Cheung 2008)	645	14.8	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
1 (Flack 1996)	182	7	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Incidence estimated by subtracting prevalence at start of study from prevalence at end of stud.
Any retinopathy in age group 0 to 9 years									
1 (Klein 1989)	26	3.85	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
1 (Klein 1997)	14	0	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
Any retinopathy in age group 10 to 12 years									
1 (Klein 1989)	42	13.7	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
Any retinopathy in age group 13 to 14 years									
1 (Klein 1989)	25	12	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
Any retinopathy in age group 10 to 14 years									
1 (Klein 1997)	47	1.08	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline

DCCT Diabetes Control and Complications Trial, NA not applicable

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K.17 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Table 63: Evidence profile for prevalence of low-level albuminuria by age (albumin:creatinine ratio ranging from >3.39 mg/mmol to >3.5 mg/mmol in males, and from >3.39 mg/mmol to >4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age <10 years									
5 (Daniels 2013; Donaghue 1999; Dunger 2014 dos Santos 2002; Yoo 2004)	NC	0 to 66.7 (0)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Age 10 years									
8 (Bognetti 1997; Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Gallego 2006; Galler 2012; Yoo 2004)	NC	0 to 9 (0)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Age 11 years									
5 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002)	NC	0 to 10 (2.4)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Age 12 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	0 to 15.4 (2.2)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age 13 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	0 to 67 (5)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	Very serious inconsistency[5]	No serious indirectness	NA[4]	None
Age 14 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	0 to 67 (4.7)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	Very serious inconsistency[5]	No serious indirectness	NA[4]	None
Age 15 years									
7 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; Dos Santos 2002; Galler 2012; Olsen 2004)	NC	0 to 75 (5)	Very low	Cross sectional and prospective	Very serious risk of bias[1,2,3]	Very serious inconsistency [6]	No serious indirectness	NA[4]	None
Age 16 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014 dos Santos 2002; Olsen 2004)	NC	3 to 75 (9.9)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	Very serious inconsistency [7]	No serious indirectness	NA[4]	None
Age 17 years									
5 (Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	5 to 67 (14)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	Very serious inconsistency[8]	No serious indirectness	NA[4]	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age 18 years									
5 (Daniels 2013; Donaghue 1999; Dunger 2014; Dos Santos 2002; Olsen 2004)	NC	5 to 67 (14)	Very low	Cross sectional and prospective cohort	Very serious risk of bias[1,2,3]	Very serious inconsistency [8]	No serious indirectness	NA[4]	None

NA not applicable, NC not calculable
1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the majority of studies
2. Small sample size (28 participants) in 1 study (dos Santos 2002)
3. Reasons for losses to follow-up (ranging from 11% to 69%) not reported in most studies
4. Not applicable as no confidence intervals were reported
5. Range of prevalence estimates varied between 0% and 67% (prevalence of 67% calculated by NCC-WCH from a study of only 28 patients)
6. Range of prevalence estimates varied between 0% and 75% (prevalence of 75% calculated by NCC-WCH from a study of only 28 patients)
7. Range of prevalence estimates varied between 3% and 75% (prevalence of 75% calculated by NCC-WCH from a study of only 28 patients)
8. Range of prevalence estimates varied between 5% and 67% (prevalence of 67% calculated by NCC-WCH from a study of only 28 patients)

Table 64: Evidence profile for prevalence of low-level albuminuria by age (albumin:creatinine ratio >4.59 in males, and >5.24 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age ≤ 10 years									
1 (Karavanaki 1999)	NC	0 to 0 (0)	Low	Prospective cohort	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None

NA not applicable, NC not calculable
1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the study
2. Not applicable as no confidence intervals were reported

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Table 65: Evidence profile for prevalence of low-level albuminuria by duration of diabetes (albumin:creatinine ratio ranging from >3.39 mg/mmol to >3.5 mg/mmol in males, and from >3.39 mg/mmol to >4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration <2 years									
5 (Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001; Yoo 2004)	NC	0 to 0 (0)	Very low	Cross sectional and prospective	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 2 years									
5 (Donaghue 1999; dos Santos . 2002; Dunger 2014; Nicoloff 2001; Yoo 2004)	NC	0 to 16.7 (1)	Very low	Cross sectional and prospective	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 3 years									
4 (Donaghue 1999; Dos Santos 2002; Dunger 2014; Nicoloff 2001)	NC	0 to 2 (0)	Very low	Cross sectional and prospective	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 4 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001)	NC	0 to 16.7 (2)	Very low	Cross sectional and prospective	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 5 years									
6 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005; Nicoloff 2001)	NC	0 to 25 (2.8)	Very low	Cross sectional and prospective	Very serious risk of bias[1,2,3]	No serious inconsistency	No serious indirectness	NA[4]	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration 6 years									
6 (Bognetti 1997; Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	0 to 50 (4.4)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	Very serious inconsistency[5]	No serious indirectness	NA[4]	None
Duration 7 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1.9 to 26.1 (5)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	Very serious inconsistency[6]	No serious indirectness	NA[4]	None
Duration 8 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Kong 2005)	NC	1.9 to 22.2 (5)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	Very serious inconsistency[6]	No serious indirectness	NA[4]	None
Duration 9 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1.9 to 29 (5)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	Very serious inconsistency[7]	No serious indirectness	NA[4]	None
Duration 10 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1.9 to 31.8 (6.9)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	Very serious inconsistency[7]	No serious indirectness	NA[4]	None
Duration 11 years									
4 (Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1 to 28.3 (20.2)	Very low	Cross sectional	Very serious risk of bias[1,2,3]	Very serious inconsistency[8]	No serious indirectness	NA[4]	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration 12 years									
2 (Dunger 2014; Kong 2005)	NC	1 to 16.3 (8.66)	Low	Cross sectional	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 13 years									
2 (Dunger 2014; Kong 2005)	NC	1 to 31.9 (16.5)	Low	Cross sectional	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 14 years									
2 (Dunger 2014; Kong 2005)	NC	1 to 35.9 (18.5)	Low	Cross sectional	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 15 years									
2 (Dunger 2014; Kong 2005)	NC	1 to 20 (10.5)	Low	Cross sectional	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[4]	None

NA not applicable, NC not calculable
1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the majority of studies
2. Small sample size (28 participants) in 1 study (dos Santos 2002)
3. Reasons for losses to follow-up (ranging from 11% to 69%) not reported in most studies
4. Not applicable as no confidence intervals were reported
5. Range of prevalence estimates varied between 0% and 50% (prevalence of 50% calculated by NCC-WCH technical team from a study of only 28 participants)
6. Range of prevalence estimates varied between 1.87% and 20% (prevalence of 20% calculated by NCC-WCH technical team from a study of only 28 participants)
7. Range of prevalence estimates varied between 1.87% and 28.6% (prevalence of 28.6% calculated by NCC-WCH technical team from a study of only 28 participants)
8. Range of prevalence estimates varied between 1.02% and 80% (prevalence of 80% calculated by NCC-WCH technical team from a study of only 28 participants)

Table 66: Evidence profile for incidence of low-level albuminuria by duration of diabetes (albumin:creatinine ratio >3.5 mg/mmol in males, and >4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of incidence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration <1 year									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None

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Number of studies	Number of children and young people	Range of incidence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration 1 year									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 2 years									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 3 years									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 4 years									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 5 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 6 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 7 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 8 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None
Duration 9 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias[1]	No serious inconsistency	No serious indirectness	NA[2]	None

NA not applicable, NC not calculable
1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for
2. Not applicable as no confidence intervals were reported

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K.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.19 Type 2 diabetes – psychological interventions

Review question: What is the effectiveness of psychological interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

Review question: What is the effectiveness of psychological interventions to improve outcomes in children and young people with type 2 diabetes?

There are no evidence profiles for these review questions because no studies were identified for inclusion.

K.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Table 67: Evidence profile for comparison of a very low calorie diet with usual care in morbidly obese African-American children and young people with type 2 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention	Comparator	Relative (95% confidence interval)	Absolute (95% confidence interval)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Change in BMI by end of diet (approximately 2 months after baseline)											
1 (Willi 2004)	15	15	NA	MD -12.4 (-17.1 to -7.7) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[5,6]	Yes[i]
Change in BMI by 6 months' follow-up											
1 (Willi 2004)	15	15	NA	MD -12.7 (-18.1 to -7.2) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[5,6]	Yes[i]

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Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention	Comparator	Relative (95% confidence interval)	Absolute (95% confidence interval)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Change in BMI by 12 months' follow-up											
1 (Willi 2004)	15	15	NA	MD -9.5 (-16.2 to -2.8) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[5,6]	Yes[i]
Change in BMI by 18 months' follow-up											
1 (Willi 2004)	15	15	NA	MD -9.1 (-16.8 to -1.4) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[5,6]	Yes[i]
Change in BMI by 24 months' follow-up											
1 (Willi 2004)	15	15	NA	MD: -9.1 (-17.8 to -0.3) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[6,7]	Yes[i]
HbA1c levels at end of diet (approximately 2 months after baseline)											
1 (Willi 2004)	15	15	NA	MD -1.6 (-3.5 to 0.3) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[6,7]	None
HbA1c levels at 6 months after baseline											
1 (Willi 2004)	15	15	NA	MD -0.9 (-3.1 to 1.4) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[6,7]	None
HbA1c levels at 12 months after baseline											
1 (Willi 2004)	15	15	NA	MD -0.5 (-2.7 to 1.7) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[6,7]	None
HbA1c levels at 18 months after baseline											
1 (Willi 2004)	15	15	NA	MD -0.4 (-2.7 to 1.9) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[6,7]	None
HbA1c levels at 24 months after baseline											
1 (Willi 2004)	15	15	NA	MD -1.0 (-3.4 to 1.4) [a,b]	Very low	Retrospective chart review	Very serious[1,2,3]	NA	Serious indirectness[4,5]	Very serious[6,7]	None

BMI body mass index, CI confidence interval, NA not applicable, MD mean difference, SDS standard deviation score, SE standard error
a Point estimate and SE derived from graphs by NCC-WCH technical team
b CI calculated using t-distribution due to small sample size
1 No randomisation used to allocate the intervention
2 Usual care for controls is unclear; likely to differ from intervention group by more than just diet as intervention group was withdrawn from oral anti-diabetic medication before treatment
3 Attrition bias is unclear; participants who adhered to the diet for less than 6 weeks were excluded from long-term follow-up analysis
4Population is narrow (morbidly obese African-American children and young people) therefore generalisability is reduced
5 Results for this outcome are based on BMI alone, not BMI SDS score
6 No CIs reported and none calculable (estimates derived from graphs by NCC-WCH technical team, see footnote a)
7 p-values reported as <critical value (for example, p <0.05 or p <0.01), not as exact values

Update 2015

K.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Table 68: Evidence profile for effectiveness of weight loss in children and young people with type 2 diabetes who are overweight or obese in improving glycaemic control

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Metformin and lifestyle intervention	Metformin only	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Number of glycaemic failure cases over 5 years[a]											
1 (TODAY Study Group 2012)	109/234 (46.6%)	120/232 (51.7%)	RR 0.90 lower (0.75 to 1.08)	52 fewer per 1000 (from 129 fewer to 41 more)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	Serious indirectness[3]	No serious imprecision[4]	None
Median time to treatment failure (months)											
1 (TODAY Study Group 2012)	234 (median=11.8 months)	232 (median=10.3 months)	NA[5]	NA[5]	Low	RCT	No serious risk of bias[1]	No serious inconsistency[2]	Serious indirectness[3]	NA[6]	None
Number of children and young people achieving a reduction of at least 7 percentage points in percent overweight											
1 (TODAY Study Group 2012)	73/234 (31.2%)	56/232 (24.3%)	RR 1.27 higher (0.95 to 1.72)	65 more per 1000 (from 12 fewer to 174 more)	Moderate	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness	Serious imprecision[7]	

CI confidence interval, NA not applicable, RR relative risk, RCT randomised controlled trial, TODAY Treatment Options for type 2 Diabetes in Adolescents and Youth
a The study defined treatment failure as a persistently elevated glycated haemoglobin level of 8% or higher over a period of 6 months or persistent metabolic decompensation (defined as either the inability to wean the participant from insulin within 3 months of its initiation for decompensation or the occurrence of a second episode of decompensation within 3 months of discontinuation of insulin)
1 The evaluation identified no serious risk of bias
2 Single-study analysis
3 The outcomes reported in the study were not strictly pertinent to the requirements of the protocol
4The 95% CI is entirely within one zone related to precision (see 'Methodology for 2015 update')
5Median values cannot be used to assess effects
6 Imprecision cannot be assessed because median values cannot be used to assess effects
7The 95% CI crosses two zones related to precision (see 'Methodology for 2015 update')

Update 2015

K.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Table 69: Evidence profile for effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with placebo

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Metformin	Placebo	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (% at endpoint)											
1 (Jones 2002)	36	36	NA	MD between the groups at endpoint 1.1 lower (1.19 lower to 1.01 lower)a	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision	None
Number needing rescue medication											
1 (Jones 2002)	4/42 (9.5%)	26/40 (65%)	RR 0.15 (0.06 to 0.4)	552 fewer per 1000 (from 390 fewer to 611 fewer)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[4]	None
Number reporting any adverse event (including number with DKA)											
1 (Jones 2002)	29/42 (69%)	24/40 (60%)	RR 1.15 (0.83 to 1.59)	90 more per 1000 (from 102 fewer to 354 more)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[5]	None
Number of dropouts											
1 (Jones 2002)	6/42 (14.3%)	4/40 (10%)	RR 1.43 (0.42 to 3.91)	43 more per 1000 (from 58 fewer to 291 more)	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[6]	None
FPG concentration (change from baseline, mmol/l)											
1 (Jones 2002)	36	36	NA	MD between the groups 3.6 lower (3.83 lower to 3.37 lower)[h]	High	RCT	No serious risk of bias[1]	No serious inconsistency[2]	No serious indirectness[3]	No serious imprecision[7]	None

DKA diabetic ketoacidosis, FPG fasting plasma glucose, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk
a Adjusted mean HbA1c at baseline (%), metformin 7.2 ±1.2, placebo 8.6 ±0.2
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Study met population, intervention and outcomes as specified in the review protocol
4 Mean difference at endpoint is greater than MID of 0.5 percentage points (5.5 mmol/mol)
5 Absolute effect is greater than default MID of 25% (250 per 1,000)
6 While the absolute effect does not meet default MID criteria, this was not considered to impact on the findings as the adverse events were spread equally across study groups

Update 2015

7 Change in FPG from baseline (mmol/l), metformin -2.4 ±0.5, placebo 1.2 ±0.5

K.23 Type 2 diabetes – HbA1c targets

Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Table 70: Evidence profile for prevalence of hypertension by age

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Median age of 13.2 years at diagnosis									
Hypertension (blood pressure values >95th percentile)									
1 (Reinehr 2008)	51	44.0% (30.1 to 57.9)a	Very low	Prospective chart review	Serious[1]	No serious inconsistency[2]	Serious[3]	No serious imprecision	None
Aged 10 to 15 years at diagnosis									
Hypertension (systolic blood pressure >130mmHg and diastolic blood pressure >85mmHg)									
1 (Urakami 2009)	112	11.6% (5.6 to 17.6)[a]	Very low	Retrospective chart review	No serious bias	No serious inconsistency[2]	Very serious[4,5,6]	No serious imprecision	None

CI confidence interval, IQR interquartile range
a Calculated by the NCC-WCH technical team.
1 Data were analysed only for participants with complete follow up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up
2 Single-study analysis
3 Prevalence estimates do not relate to a specific age; only the median age was reported (13.2 years, IQR 12.1 to 14.7)
4 Prevalence estimates do not relate to a specific age; only the mean age was reported (12.9 years ±1.5)
5 Hypertension was defined based on absolute values and not percentiles
6 The study population comprised Japanese participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

Update 2015

Table 71: Evidence profile for prevalence of hypertension by duration of diabetes

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Within 1 year of diagnosis									
Hypertension (systolic or diastolic >95th percentile)									
1 (Rodriguez 2010)	176	18.2% (12.5 to 23.9)[a]	Very low	Prospective multi-centre study	Serious[1]	No serious inconsistency[2]	No serious indirectness	No serious imprecision	None
One year after diagnosis									
Systolic hypertension (>98th percentile)									
1 (Shield 2009)	59	15.7% (6.2 to 25.2)[a]	Low	Prospective follow-up of surveillance data	No serious bias	No serious inconsistency[2]	No serious indirectness	No serious imprecision	None
Diastolic hypertension (>98th percentile)									
1 (Shield 2009)	59	34.1% (21.8 to 46.4)[a]	Low	Prospective follow-up of surveillance data	No serious bias	No serious inconsistency[2]	No serious indirectness	No serious imprecision	None
Within 2 years of diagnosis									
Hypertension (blood pressure values >90th percentile)									
1 (Copeland 2011)	704	26.3% (23.0 to 29.6)[a]	Low	Analysis of baseline data from a RCT[4]	No serious bias	No serious inconsistency[2]	Serious[3]	No serious imprecision	None
Hypertension (blood pressure values >95th percentile)									
1 (Copeland 2011)	704	13.6% (11.1 to 16.1)[a]	Low	Analysis of baseline data from a RCT[4]	No serious bias	No serious inconsistency[2]	Serious[3]	No serious imprecision	None
Two years after diagnosis									
Hypertension (blood pressure values >95th percentile)									
1 (Reinehr 2008)	51	32.0% (18.9 to 45.1)[a]	Very low	Prospective chart review	Serious[5]	No serious inconsistency[2]	No serious indirectness	No serious imprecision	None
Within 3 years of diagnosis									
Hypertension (blood pressure values ≥ 95th percentile)									
1 (Ettinger 2005)	26	58.0% (38.0 to 78.0)[a]	Very low	Prospective chart review	No serious bias	No serious inconsistency[2]	Very serious[3,6]	No serious imprecision	Yes[7]
Within 4 years of diagnosis									
Hypertension (systolic and diastolic >95th percentile)									
1 (Eppens 2006)	265	8.0% (4.7 to 11.3)[a]	Very low	Cross-sectional survey	Very serious[8,9]	No serious inconsistency[2]	Very serious[3,10]	No serious imprecision	Yes[11]
Hypertension (systolic >95th percentile)									
1 (Hotu 2004)	3	28.0% (5.6 to 50.4)[a]	Very low	Cross-sectional survey	No serious bias	No serious inconsistency[2]	Very serious[3,12,13]	No serious imprecision	None
Between 1 and 5 years after diagnosis									
Hypertension (systolic or diastolic >95th percentile)									
1 (Rodriguez 2010)	219	27.9% (22.0 to 33.8)[a]	Very low	Prospective multi-centre study	Serious[14]	No serious inconsistency[2]	No serious indirectness	No serious imprecision	None

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Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
More than 5 years after diagnosis									
Hypertension (systolic or diastolic >95th percentile)									
1 (Rodriguez 2010)	15	26.7% (2.3 to 51.1)[a]	Very low	Prospective multi-centre study	Very serious[15]	No serious inconsistency[2]	No serious indirectness	No serious imprecision	None

CI confidence interval, RCT randomised controlled trial
a Calculated by the NCC-WCH technical team
1 Data for this outcome were available for only 176 (42.9%) of the 410 participants in the study
2 Single-study analysis
3 Prevalence estimates do not relate to specific times after diagnosis
4 Starting point of moderate for quality rating as baseline analysis of an RCT
5 Data were analysed only for participants with complete follow up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up
6 The population comprised non-Hispanic black or Hispanic Latino participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
7 Children and young people who were taking anti-hypertensive medication were eligible for inclusion
8 Participants with missing data were excluded from analysis however the number of missing values was not reported
9 Hypertension was screened for in only 80% of participants
10 The majority of the population comprised Western Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
11 The minimum duration of diabetes of study participants was 12 months
12 The study population comprised Maori and Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
13 The study population comprised young people aged 18 and 19 years (age range 11 to 19 years); it is unclear at what time point after diagnosis the prevalence estimate for hypertension is based on therefore some participants may be above the age range specified in the protocol for this review
14 Data for this outcome were available for only 219 (53.4%) of the 410 participants in the study
15 Data for this outcome were available for only 15 (3.7%) of the 410 participants in the study

Update 2015

K.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Table 72: Evidence profile for prevalence of dyslipidaemia by age

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Median age of 13.2 years at diagnosis									
Prevalence of dyslipidaemia[a]									
1 (Reinehr 2008)	51	65.0% (51.6 to 78.4)[b]	Very low	Prospective chart review	Very Serious[1,2]	No serious inconsistency[3]	Serious4	No serious imprecision	None

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Aged between 10 and 15 years at diagnosis[c]									
Triglycerides >150mg/dl (1.7mmol/l)									
1 (Urakami 2009)	112	33.0% (24.2 to 41.8)[b]	Very low	Retrospective chart review	No serious bias	No serious inconsistency[3]	Serious[5,6]	No serious imprecision	None
High density lipoproteins <40mg/dl (1.0mmol/l)									
1 (Urakami 2009)	112	21.4% (13.7 to 29.1)[b]	Very low	Retrospective chart review	No serious bias	No serious inconsistency[3]	Serious[5,6]	No serious imprecision	None

CI confidence interval, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, RCT randomised controlled trial
a Dyslipidaemia was defined using the following cut-offs: total cholesterol >5.1mmol/l (200mg/dl), LDL >3.3mmol/l (130mg/dl), HDL <0.9mmol (35mg/dl) or triglycerides >1.7mmol/l (150mg/dl)
b Calculated by the NCC-WCH technical team
c Based on the age range for inclusion in the study as the actual age range of participants was not reported
1 Data were analysed only for participants with complete follow-up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up
2 The study did not report whether or not total cholesterol, LDL, HDL, and triglycerides were measured using fasting samples, and this would affect the accuracy of LDL and triglyceride measurements
3 Single-study analysis
4 Prevalence estimates do not relate to a specific age; only the median age was reported (13.2 years, IQR 12.1 to 14.7)
5 Prevalence estimates do not relate to a specific age; only the mean age was reported (12.9 years ±1.5)
6 The population comprised Japanese participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

Table 73: Evidence profile for prevalence of dyslipidaemia by duration of diabetes

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
At 1 year after diagnosis									
Prevalence of LDL >130mg/dl (3.4mmol/l)									
1 (Le 2013)	86	12.5% (5.4 to 19.6)[a]	Very low	Retrospective chart review	Serious bias[1]	No serious inconsistency[2]	No serious indirectness	No serious imprecision	
Prevalence of HDL <35mg/dl (0.9mmol/l)									
1 (Le 2013)	86	25.0% (15.8 to 34.2)[a]	Very low	Retrospective chart review	No serious bias	No serious inconsistency[2]	No serious indirectness	No serious imprecision	
Within 2 years of diagnosis									
Low density lipoproteins ≥ 160mg/dl (4.1mmol/l)									
1 (Copeland 2011)	704	0.4% (0.00 to 0.87)[a]	Low	Analysis of baseline data from a RCT[b]	No serious bias	No serious inconsistency[2]	Serious[3]	No serious imprecision	
High density lipoproteins <50mg/dl (1.3mmol/l, females) or <40mg/dl (1.0mmol/l, males)									
1 (Copeland 2011)	704	79.8% (76.8 to 82.8)[a]	Low	Analysis of baseline data from a RCT[b]	No serious bias	No serious inconsistency[2]	Serious[3]	No serious imprecision	

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Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Triglycerides ≥ 200mg/dl (2.3mmol/l)									
1 (Copeland 2011)	704	10.2% (8.0 to 12.4)[a]	Low	Analysis of baseline data from a RCT[b]	No serious bias	No serious inconsistency[2]	Serious[3]	No serious imprecision	
At 2 years after diagnosis									
Prevalence of dyslipidaemia[c]									
1 (Reinehr 2008)	51	69.0% (56.0 to 82.0)a	Very low	Prospective chart review	Very serious[4,5]	No serious inconsistency[2]	No serious indirectness	No serious imprecision	
Within 3 years of diagnosis									
Dyslipidaemia (not defined)									
1 (Ettinger 2005)	26	69.2% (50.5 to 87.9)a	Very low	Prospective chart review	Serious6	No serious inconsistency[2]	Very serious[3,7]	No serious imprecision	
Within 4 years of diagnosis									
Total cholesterol ≥ 6mmol/l									
1 (Eppens 2006)	331	12.0% (8.5 to 15.5)[a]	Very low	Cross-sectional survey	Serious[8]	No serious inconsistency[2]	Very serious[3,9]	No serious imprecision	Yes[10]
Low density lipoproteins >4mmol/l									
1 (Eppens 2006)	331	12.0% (8.5 to 15.5)[a]	Very low	Cross-sectional survey	Serious[8]	No serious inconsistency[2]	Very serious[3,9]	No serious imprecision	Yes[10]
High density lipoproteins <0.9mmol/l									
1 (Eppens 2006)	331	10.0% (6.8 to 13.2)[a]	Very low	Cross-sectional survey	Serious[8]	No serious inconsistency[2]	Very serious[3,9]	No serious imprecision	Yes[10]
Triglycerides ≥ 2.2mmol/l									
1 (Eppens 2006)	331	16.0% (12.1 to 19.9)[a]	Very low	Cross-sectional survey	Serious[8]	No serious inconsistency[2]	Very serious[3,9]	No serious imprecision	Yes[10]
Total cholesterol:high density lipoproteins molar ratio >4.5 molar units									
1 (Hotu 2004)	13	85.0% (63.4 to 1.00)[a]	Very low	Cross-sectional survey	Very serious[5, 11]	No serious inconsistency[2]	Very serious[3,12, 13]	No serious imprecision	

CI confidence interval, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, RCT randomised controlled trial
a Calculated by the NCC-WCH technical team
b Starting point of moderate for quality rating as baseline analysis of an RCT
c Dyslipidaemia was defined using the following cut-offs: total cholesterol >5.1mmol/l (200mg/dl), LDL >3.3mmol/l (130mg/dl), HDL <0.9mmol (35mg/dl) or triglycerides >1.7mmol/l (150mg/dl)
1 Due to the retrospective study design, the study could not guarantee the fasting status of lipid measures, which would affect the accuracy of LDL and triglycerides
2 Single-study analysis
3 Prevalence estimates do not relate to specific times after diagnosis
4 Data were analysed only for participants with complete follow-up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up
5 The study did not report whether or not total cholesterol, LDL, HDL, and triglycerides were measured using fasting samples and this would affect the accuracy of LDL and triglyceride measurements
6 Dyslipidaemia was not defined

Update 2015

7 The population comprised non-Hispanic black or Hispanic Latino participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
8 Participants with missing data were excluded from analysis however the number of missing values was not reported
9 The majority of the population comprised Western Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
10 The minimum duration of diabetes of study participants was 12 months (this item was not included in evidence grading)
11 Dyslipidaemia was measured in only 72.0% (13/18) of study participants
12 The study population comprised Maori and Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
13 The study population comprised young people aged 18 and 19 years (age range 11 to 19 years); it is unclear at what time point after diagnosis the prevalence estimate for dyslipidaemia is based on and, therefore, some participants may be above the age range specified in the protocol for this review

K.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Table 74: Evidence profile for prevalence of retinopathy according to age

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
12 to 16 years									
1 (Levitsky 2013)	140	5.7 (2.5 to 11.0)[a]	Moderate[b]	RCT	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None
17 to 18 years									
1 (Levitsky 2013)	137	12.4 (7.4 to 19.1)[a]	Moderate[b]	RCT	No serious risk of bias	NA	No serious indirectness	No serious imprecision	None
10.8 to 17.8 years									
1 (Shield 2009)	55	0.0 (0.0 to 6.5)[a]	Low[c]	Prospective cohort	Serious risk of bias1	No serious inconsistency	No serious indirectness	No serious imprecision	None

CI confidence interval, NA not applicable, RCT randomised controlled trial
a 95% CI calculated by NCC-WCH technical team from data reported in the article
b Although the study design was an RCT, data obtained were cross-sectional and observational in nature
c Serious risk of bias
1 Study design included postal survey of clinicians therefore at risk of selection bias

Table 75: Evidence profile for prevalence of retinopathy according to duration of diabetes

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
12 months									
1 (Shield 2009)	55	0.0 (0.0 to 6.5)[a]	Low[b]	Prospective cohort	Serious risk of bias[1]	NA	No serious indirectness	No serious imprecision	

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Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
24 to 49 months									
1 (Levitsky 2013)	170	5.3 (2.5 to 9.8)[a]	Low[c,d]	RCT	No serious risk of bias	NA	Serious indirectness[2]	No serious imprecision	
50 to 66 months									
1 (Levitsky 2013)	172	13.4 (8.7 to 19.4) [a]	Low[c,d]	RCT	No serious risk of bias	NA	Serious indirectness[2]	No serious imprecision	
67 to 101 months									
1 (Levitsky 2013)	137	22.3 (16.3 to 29.2) [a]	Low[c,d]	RCT	No serious risk of bias	NA	Serious indirectness[2]	No serious imprecision	

CI confidence interval, NA not applicable, RCT randomised controlled trial
a 95% CI calculated by NCC-WCH technical team from data reported in the article
b Serious risk of bias
c Although the study design was an RCT, data obtained were cross-sectional and observational in nature
d Serious indirectness
1 Study design included postal survey of clinicians therefore at risk of selection bias

K.27 Type 2 diabetes – nephropathy

Update 2015

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Table 76: Evidence profile for prevalence of low-level albuminuria by age in children and young people with type 2 diabetes

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age <11									
1 (Yoo. 2004)	NC	0 (NA)	Very low	Cross sectional	Very serious risk of bias[1,2]	No serious inconsistency	No serious indirectness	NA[c]	None

Low-level albuminuria defined as albumin:creatinine ratio (ACR) >3.5 mg/mmol in males and ACR >4.0 mg/mmol in females in at least 2 out of 3 urine collections
NC not calculable, NA not applicable
1 Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the study
2 Small sample size (22 participants) for type 2 diabetes
c Not applicable as confidence intervals were not reported

Table 77: Evidence profile for prevalence of low-level albuminuria by duration of diabetes in children and young people with type 2 diabetes

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration <2 years									
3 (Farah 2006; Lynch 2013; Yoo 2004)	NC	0 to 29.6 (6.3)	Very low	Cross sectional	Very serious risk of bias[1,2]	Very serious inconsistency[3]	No serious indirectness	NA[4]	None
Duration 2 years									
1 (Farah 2006)	NC	29.6 (NA)	Very low	Cross sectional	Very serious risk of bias[1,2]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 3 years									
1 (Farah 2006)	NC	32.3 (NA)	Very low	Cross sectional	Very serious risk of bias[1,2]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 4 years									
1 (Farah 2006)	NC	32.3 (NA)	Very low	Cross sectional	Very serious risk of bias[1,2]	No serious inconsistency	No serious indirectness	NA[4]	None
Duration 5 years									
1 (Farah 2006)	NC	32.3 (NA)	Very low	Cross sectional	Very serious risk of bias[1,2]	No serious inconsistency	No serious indirectness	NA[4]	None

Low-level albuminuria defined as albumin:creatinine ratio (ACR) >3.5 mg/mmol in males and ACR >4.0 mg/mmol in females in at least 2 out of 3 urine collections
NC not calculable, NA not applicable
1 Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in studies
2 Small sample sizes in studies for type 2 diabetes (40 participants in Farah 2006 and 22 in Yoo 2004)
3 Prevalence estimates ranged from 0% to 29.6%
4 Not applicable as confidence intervals were not reported

Update 2015

Appendix L: Research recommendations

L.1 2015 recommendations for research

L.1.1 Type 1 diabetes – education

L.1.1.1 What is the clinical and cost effectiveness of a programme of structured education from diagnosis for children and young people with type 1 diabetes?

Why is this important

The guideline development group has recommended education from diagnosis for children and young people with type 1 diabetes but not specified that this should be 'structured' because there is no evidence to support structured education delivered at diagnosis. Future research should compare a structured education programme delivered from diagnosis with a non-structured education programme delivered from diagnosis (usual care). Important outcomes will include achieving the target HbA1c after 1 year and satisfaction of the child or young person and their family members or carers (as appropriate).

L.1.1.2 What is the impact of training in teaching skills for healthcare professionals on the effectiveness of education for children and young people with type 1 diabetes?

Why this is important

The guideline development group has recommended that children and young people with type 1 diabetes should be offered education, but has not specified that the education should be delivered by healthcare professionals trained in its delivery. Future research should use RCTs to compare diabetes education delivered by healthcare professionals who have received training in teaching skills and those who have not. Different approaches to training (such as participating in training in schools) should be considered as part of the research. Important outcomes will include the child or young person achieving their target HbA1c, satisfaction of the child or young person and their family members or carers (as appropriate), and satisfaction among healthcare professionals delivering the education.

Update 2015

L.1.1.3 What is the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers?

Why this is important

Training delivered by peers is effective both in healthcare and in other settings. This research should evaluate the engagement of the child or young person with type 1 diabetes and their family members or carers (as appropriate), and outcomes for the child or young person. Outcomes could include their success in achieving their target HbA1c level, engagement with diabetes care and management (for example, attendance at clinic), satisfaction with the education programme, and quality of life. The impact on the young person delivering the training should also be evaluated (this could cover the impact on their diabetes care and the psychosocial impact of providing training for their peers). The research should be conducted using quantitative, qualitative and mixed methods.

This is a rephrasing of a 2004 research recommendation to comply with current NICE format and style as it was selected a key research recommendation by the guideline development group for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because there is evidence of the effectiveness of peer-delivered education in other healthcare and wider settings
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Lack of evidence specific to peer-delivered education in children and young people with diabetes
Equality	Research would need to take account of accessibility to and effectiveness of education for people with protected characteristics such as different age and ethnic groups
Feasibility	Feasible
Other comments	None

L.1.2 Type 1 diabetes – blood glucose targets

L.1.2.1 What is the optimal upper limit and timing for blood glucose measurements after meals for children and young people with type 1 diabetes to reach an HbA1c level of 48 mmol/mol (6.5%) without unacceptable hypoglycaemia?

Why this is important

Setting an upper limit for plasma glucose measurements 1–2 hours after meals of less than 8 mmol/litre (rather than the 9 mmol/litre recommended in this guideline) could potentially lead to an improvement in blood glucose control without an unacceptable risk of hypoglycaemia. The evidence reviewed for the guideline did not allow a precise evaluation of the upper limit for the target range, or the timing of blood glucose testing relative to meals. Future research should investigate the HbA1c levels of children and young people with type 1 diabetes who aim for blood glucose measurements after meals slightly lower (to ensure their safety) than 9 mmol/litre, to help decide whether lowering the upper limit is effective in improving long-term blood glucose control. Outcomes include the child or young person's satisfaction with treatment, their HbA1c levels, rates of hypoglycaemia, and the views of their family members or carers (as appropriate), and quality of life.

This was selected a key research recommendation by the guideline development group for the 2015 update. The justification for the selection is summarised in the table below.

Update 2015

Potential criterion	Explanation
Importance to patients or the population	This is of importance because it is of interest to know whether it is safe and acceptable to refine the target range for postprandial blood glucose measurements
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Further evidence is needed
Equality	Not applicable
Feasibility	Feasible
Other comments	None

L.1.3 Type 1 diabetes – intermittent continuous glucose monitoring compared with real-time continuous glucose monitoring

L.1.3.1 What is the clinical and cost effectiveness of real-time continuous glucose monitoring systems compared to 5 or more capillary blood glucose tests per day in children aged 5 years or younger with type 1 diabetes who use insulin pump therapy?

Why this is important

The guideline development group's recommendation was to consider ongoing real-time continuous glucose monitoring systems (CGMS) for neonates, infants and pre-school children with type 1 diabetes. This weak recommendation reflected a lack of evidence of effectiveness of CGMS in such children (only a few studies having been conducted in this age group). The guideline development group considered use of CGMS in this age group to be important because of the risk of adverse neurodevelopmental consequences of type 1 diabetes and parental anxiety (particularly in those with pre-school children). Further research in the form of a multi-centre RCT comparing CGMS with 5 or more capillary blood glucose tests per day is needed to achieve a large enough sample size. Important outcomes include HbA1c levels, incidence of hypoglycaemia, satisfaction of the child and their family members or carers (as appropriate), and quality of life. Future research should ideally monitor neurodevelopmental consequences but this would require studies with long-term follow up.

L.1.4 Type 1 diabetes – dietary advice

L.1.4.1 What is the impact of educating children and young people with type 1 diabetes and their family members or carers (as appropriate) about their glycaemic index from diagnosis?

Why this is important

Very little evidence on the effectiveness of dietary advice based on glycaemic index was identified for inclusion in the guideline review, and the evidence that was identified related mostly to twice-daily insulin regimens. Research is needed to evaluate the effectiveness of teaching children and young people with type 1 diabetes and their family members or carers (as appropriate) about glycaemic index in the context of modern, intensive insulin treatment regimens (insulin pump therapy or multiple daily injections). Important outcomes include success in achieving the target HbA1c level, blood glucose levels after meals, frequency of hypoglycaemia, quality of life, food choices, and the frequency and timing of insulin administration to lower blood glucose levels after meals.

This was selected a key research recommendation by the guideline development group for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because there is very little evidence of effectiveness of dietetic advice based on glycaemic index from diagnosis in terms of improving glycaemic control
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Lack of evidence currently other than in relation to cardiovascular health and no evidence in relation to modern intensive insulin treatment regimens

Update 2015

Potential criterion	Explanation
Equality	Research would need to take account of accessibility to and effectiveness of education for children and young people with protected characteristics such as different age and ethnic groups
Feasibility	Feasible
Other comments	None

L.1.5 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

L.1.5.1 What is the optimal dosage of intravenous insulin for managing diabetic ketoacidosis (DKA) in children and young people?

Why this is important

The evidence reviewed for the guideline did not allow evaluation of the comparative effectiveness and safety of specific dosages of intravenous insulin, such as 0.025, 0.05 and 0.1 units/kg/hour. The only relevant studies conducted to date have been small retrospective cohort studies with fewer than 100 participants. A large, multi-centre RCT is needed to undertake a comparative study of different dosages. This is because DKA is relatively uncommon and cerebral oedema (a potential adverse consequence of DKA) is rare, and there is a concern that larger dosages are associated with an increased risk of cerebral oedema. Important outcomes include rate of DKA resolution, incidence of hypoglycaemia and incidence of cerebral oedema.

This was selected a key research recommendation by the guideline development group for the 2015 update. The justification for the selection is summarised in the table below.

Update 2015

Potential criterion	Explanation
Importance to patients or the population	The guideline development group was able to make a recommendation about dosages of 0.05-0.1 units/kg/hour and further research would allow refinement of the recommendations
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs from avoiding prolonged hospitalisation and improving patient safety
National priorities	Not applicable
Current evidence base	Limited evidence was identified and there were no RCT
Equality	Not applicable
Feasibility	Feasible with a large multi-centre RCT
Other comments	None

L.1.6 Type 2 diabetes – psychological interventions

L.1.6.1 What is the clinical and cost effectiveness of psychological interventions for children and young people with type 2 diabetes?

Why this is important

The guideline development group has recommended that children and young people with type 2 diabetes and their family members or carers (as appropriate) should have access to mental health services, and this could include access to psychological interventions. However, the evidence reviewed for the guideline was insufficient to recommend any specific

psychological intervention (no evidence at all related to psychological interventions in children and young people with type 2 diabetes was identified for inclusion in the guideline review). The guideline development group recognised that for children and young people with type 2 diabetes and their family members or carers (as appropriate) lack of engagement with services (for example, non-attendance at clinic) is an important factor. Research is, therefore, needed to evaluate the effectiveness of any of the psychological interventions prioritised by the guideline development group for consideration: family therapy (including behavioural family systems therapy); cognitive behavioural therapy; motivational interviewing; counselling; mentoring; and peer support. In particular, family therapy is a priority for evaluation given the social and cultural impact of type 2 diabetes in children and young people. Other psychological interventions that are socially and culturally relevant and appropriate for children and young people with type 2 diabetes should also be evaluated. Initial research should be piloted at a local level and include process evaluation to assess cultural factors which may affect the application of interventions. Research ultimately needs to consist of multicentre, regional or national RCTs because type 2 diabetes in children and young people is still relatively rare. Any large-scale research study should include consideration of clinical and cost effectiveness.

L.1.7 Type 2 diabetes – weight loss

L.1.7.1 What is the correlation between changes in body mass index standard deviation scores and absolute HbA1c measurements or changes in HbA1c in children and young people with type 2 diabetes?

Why this is important

The guideline development group did not identify any evidence in children and young people with type 2 diabetes to indicate a correlation between weight loss or changes in body mass index standard deviation scores (BMISDS) and HbA1c. However, this form of correlation would be expected in children and young people and has already been demonstrated in adults. Studies in children and young people with type 2 diabetes are, therefore, needed. Such studies are likely to be observational in design and a prospective, register-based follow-up study covering all children and young people with type 2 diabetes in the UK would be ideal because type 2 diabetes is a relatively rarer condition in this age group. Changes in BMISDS and HbA1c over time would be of interest in such a study.

Update 2015

L.1.8 Type 2 diabetes – metformin

L.1.8.1 What is the long-term comparative clinical and cost effectiveness of different metformin preparations for treating type 2 diabetes in children and young people?

Why this is important

There is high-quality evidence for the clinical and cost effectiveness of metformin as a treatment for type 2 diabetes from diagnosis in children and young people. However, all of the relevant evidence relates to administration in tablet form and using a standard dosage, despite alternative oral preparations (including solutions and extended-release tablets) being available and having potential advantages to the standard preparation. Gastrointestinal disorders (for example, nausea, vomiting, diarrhoea, abdominal pain and loss of appetite) are very common with metformin, especially at the start of treatment, and may be reduced or avoided with alternative preparations. Extended-release tablets and oral solutions may also be easier to swallow, as standard formulation metformin consists of large tablets. Further research would preferably consist of RCTs. Outcomes should include blood glucose control (preferably using measurement of HbA1c levels) and the child or young person's satisfaction with and adherence to treatment.

This was selected a key research recommendation by the guideline development group for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because there are existing and emerging non-insulin agents (for example, metformin) which could be combined with insulin with potential benefit
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Not yet addressed in a NICE guideline
Equality	Not applicable
Feasibility	Feasible
Other comments	None

L.2 2004 recommendations for research that remain relevant in the 2015 update

Type 1 diabetes		Comments
Education	Further research is needed to evaluate the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers	This research recommendation was retained by the guideline development group but re-expressed to conform to current NICE format and style (it was also selected as a key research recommendation – see above)
Insulin regimens	Research is needed to compare the effectiveness of continuous subcutaneous insulin infusion (or insulin pump therapy) and multiple daily injection regimens in children and young people with type 1 diabetes	
Insulin preparations	Research is needed to evaluate the effectiveness of long-acting insulin analogues in children and young people with type 1 diabetes	
Methods of delivering insulin	Further research is required to evaluate the effectiveness of insulin delivery systems in children and young people with type 1 diabetes	
	Research is needed to compare the effectiveness of insulin delivery modes (for example, dermal, nasal, oral and pulmonary) in children and young people with type 1 diabetes	The guideline development group for the 2015 update noted that this research recommendation was still relevant because there is a new product to evaluate
Non-insulin agents (oral antidiabetic drugs)	What is the clinical and cost effectiveness of non-insulin agents (for example, metformin) combined with insulin treatment in children and young people with type 1 diabetes?	This research recommendation replaces the following from the 2004 guideline. Further research is needed to evaluate the effectiveness of (for example, metformin) combined with insulin treatment in children and young

Update 2015

Type 1 diabetes		Comments
		people with type 1 diabetes. The guideline development group's view was this remained an important area for research, and that non-insulin agents other than metformin could be investigated as part of the research. The guideline development group summarised the importance of the proposed research as follows. There are existing and emerging non-insulin agents which have potential for improving control in type 1 diabetes in children and young people (for example, metformin). Research comparing treatment with such agents combined with insulin and treatment with insulin alone should be conducted in the form of RCTs. Important outcomes to measure will include achieving HbA1c targets, tolerability and satisfaction with treatment
Monitoring glycaemic control	Research is needed to investigate the clinical implications of alternative site monitoring (for example, the arm as opposed to the finger) in children and young people with type 1 diabetes	
Screening for complications and associated conditions	Further research is needed to evaluate the effectiveness of screening for cardiovascular risk factors in children and young people with type 1 diabetes	
Cognitive disorders	Further research is needed to evaluate the effects of persistent hypoglycaemia and recurrent diabetic ketoacidosis on neurocognitive function	
Adolescence	Further studies are needed to evaluate the effectiveness of behavioural and social interventions on anxiety and depression, eating disorders, behavioural and conduct disorders, and adherence to therapy in children and young people with type 1 diabetes, especially in adolescence, from diagnosis and in established diabetes	
Communication between organisations	Further research is needed to evaluate the effects of low blood glucose levels on learning, attendance at school and educational attainment	
Transition from paediatric to adult care	Further research is needed to investigate young people's experiences of transition from paediatric to adult services for people with type 1 diabetes	

Update 2015

L.3 2004 recommendations for research that were deleted as part of the 2015 update

Type 1 diabetes		Explanation
Education	Further research is needed to evaluate the effectiveness of age-specific structured education programmes covering all aspects of care in children and young people with type 1 diabetes, their families and other carers	This research has been done and the intervention was ineffective. The guideline development group has, therefore, deleted this research recommendation as part of the update
	Further research is needed to determine the most effective way of training healthcare professionals to provide education about type 1 diabetes in children and young people	This research recommendation was replaced by a new research recommendation related to training of healthcare professionals as part of the update
Insulin regimens	Research is needed to compare the effectiveness of multiple daily injection regimens with twice-daily injection regimens in children and young people with type 1 diabetes	The guideline development group deleted this research recommendation because the update has addressed this topic and made recommendations in the section about multiple daily injections
Insulin preparations	Further research is needed to evaluate the effectiveness of once-daily injection regimens in children and young people with type 1 diabetes, and especially in pre-school children	The guideline development group deleted this research recommendation because the update has addressed this topic and made recommendations in the section about multiple daily injections
Monitoring glycaemic control	Research is needed to evaluate the clinical effectiveness of the routine use of invasive and non-invasive continuous glucose monitoring systems for optimising glycaemic control in children and young people with type 1 diabetes.	This research recommendation was deleted because the update has addressed this topic and recommendations have been made in the section about continuous glucose monitoring systems
Diet	Further research is needed to evaluate the effectiveness of training in flexible, intensive insulin management to enable children and young people with type 1 diabetes to adjust insulin doses to match carbohydrate intake	This research recommendation was deleted because the update has addressed this and recommendations have been made in the sections about multiple daily injections and dietary advice related to carbohydrate counting
Diabetic ketoacidosis	Further research is needed to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis in children and young people with type 1 diabetes	This research recommendation was deleted because the update has addressed this topic and made a recommendation in the section about ketone monitoring during intercurrent illness
	Further research is needed to investigate the effectiveness of different concentrations of rehydration fluid, the rate of rehydration, the use of albumin infusion and the dose of insulin infusion in the management of diabetic ketoacidosis in children and young people	This research recommendation was replaced with a research recommendation focused specifically on identifying the optimal intravenous insulin dosage during management for diabetic ketoacidosis (the other aspects of the 2004 research recommendation have been addressed as part of the update and recommendations have been made for these topics)

Update 2015

Appendix M: Young people's consultation day

A young people's consultation day was organised for this guideline in collaboration with the NCB. The objective of the consultation day was to elicit the views of young people with type

1 diabetes and their carers in relation to topics considered in the guideline. Fourteen young women aged 13 to 17 years, seven young men aged 13 to 18 years, and 20 adults (14 mothers, five fathers and one older sister) participated in the consultation day. The main conclusions were[38] [evidence level IV]

- Young people wanted to be treated as 'normal' individuals growing towards adulthood.
- Young people wanted to be well informed about diabetes and to be involved in decisions affecting their care as they became more mature and independent.
- Young people and their parents wanted healthcare to be accessible, supportive and age-banded.
- Young people and their parents wanted consistent, accessible and up-to-date information about living with type 1 diabetes.
- Young people and their parents wanted schools to have consistent, but flexible, policies that offered support to young people with type 1 diabetes without treating them differently from their peers.
- More specific points identified by the NCB are summarised below and in the relevant sections of the guideline.38 [evidence level IV]
- Young people with type 1 diabetes felt that healthcare professionals should be skilled in gaining the confidence of young people by educating them about diabetes in accessible language, treated them as individuals and with respect, and ensuring that they are given the opportunity to contribute to decisions about their diabetes care – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes and their parents felt they should have 24-hour access to a named specialist nurse with whom they could speak confidentially and whom they could contact between clinic appointments – see Section 3.2 (diabetes care teams).
- Some young women with type 1 diabetes stated a preference for a female doctor who they felt they would be more comfortable with than a male doctor – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes and their parents felt that it was important to see the same members of the diabetes care team wherever possible – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes liked age-banded clinics – see Sections 3.2 (diabetes care teams) and 7.2 (transition from paediatric to adult care).
- Young people with type 1 diabetes were happy to miss school in order to attend clinic appointments, but their parents would prefer clinic appointments to be available outside school hours – see Section 3.2 (diabetes care teams).
- Parents suggested that clinic appointments should be flexible enough to take into account school terms and timetables and examination schedules – see Section 3.2 (diabetes care teams).
- Parents of young people with type 1 diabetes felt that there should be easy access to psychology services and suggested that paediatric diabetes care teams should include a psychologist – see Sections 3.2 (diabetes care teams) and 6.7 (psychosocial support).
- At the time of diagnosis some young people with type 1 diabetes felt they were given too much information at one time – see Section 3.4 (essential education at diagnosis).
- Young people with type 1 diabetes wanted information aimed at them rather than just at their parents although they understood that their parents also needed to know how to manage type 1 diabetes – see Section 3.4 (essential education at diagnosis).
- Young people with type 1 diabetes wanted insulin regimens that were flexible and allowed for a measure of spontaneity, and they wanted to be informed about the types of insulin that are available and given up-to-date information on insulin delivery devices and blood glucose testing monitors – see Section 4.2 (insulin regimens).

- Parents suggested annual updates from staff on the new products available – see Section 4.2 (insulin regimens).
- It was mentioned that some young people with type 1 diabetes may find four injections/day too many but they wanted to be involved in the discussion about how best to fit diabetes treatment into their chosen lifestyle while maintaining optimal metabolic control – see Section 4.2 (insulin regimens).
- Young people with type 1 diabetes and their parents wanted consistent, accessible up-to-date information on many aspects of living with type 1 diabetes, including information on what happens when you have type 1 diabetes, healthy eating, what to expect at clinic visits, types of insulin, injecting insulin and injection sites, hypoglycaemia and what to do if it occurs, complications of diabetes, how to drink alcohol safely, travelling abroad and leisure activities, becoming more independent, leaving home, implications for future careers, and new products and research – see Sections 4.2 (insulin regimens) and 4.1 (universal principles of education).
- Parents felt that education should be delivered through one-to-one or group education sessions with a specialist nurse, whereas young people with type 1 diabetes were more positive about accessing information through leaflets, CD-ROMs, videos and websites – see Section 4.1 (universal principles of education).
- Young people with type 1 diabetes, in particular young women, were sensitive about body weight and wanted weighing to be carried out in a private room – see Section 5.5 (screening for complications and associated conditions).
- Young people with type 1 diabetes valued meeting other young people with type 1 diabetes and might benefit from formalised arrangements for meeting each other – see Section 7.1 (support groups).
- Some parents suggested that age of transfer of young people with type 1 diabetes from paediatric to adult services should be standardised and that clinics should be jointly run by paediatric and adult services to provide continuity of care – see Section 7.2 (transition from paediatric to adult care).
- Other parents thought that individual young people with type 1 diabetes should be involved in the decision about when transfer should occur – see Section 7.2 (transition from paediatric to adult care).

Appendix N: Superseded text from 2004 guideline

Entire sections of the 2004 guideline that have been superseded as a result of the 2015 update, and smaller sections of text that have also been deleted and replaced, are reproduced on the following pages as a record of the 2004 guideline content.

Superseded text associated with an unnumbered heading in the 2004 guideline is marked with the page number in the 2004 guideline where it appeared.

All numbered headings from the 2004 guideline have been included here for reference in the 2015 update, even those for which no associated text has been superseded in the update.

N.1 Chapter 1 Introduction

Type 1 diabetes is one of the most frequent chronic diseases in childhood. Children and young people with type 1 diabetes and their families have particular needs which differ from those of adults with type 1 diabetes.

Type 1 diabetes is a continuing hormonal deficiency disorder that has significant short-term impacts on health and lifestyle and is associated with major long-term complications and reduced life expectancy. People with type 1 diabetes require insulin-replacement therapy from diagnosis.

There are more than 1 million people with diagnosed diabetes in England and Wales (and perhaps a similar number with undiagnosed diabetes); 15–20% of these people are diagnosed as having type 1 diabetes. A recent survey showed that about 16 000 children and young people aged 0–16 years attended paediatric diabetes centres in England.1 [evidence level III] Of these, 95% had type 1 diabetes and 1% had non-type 1 diabetes (the type of diabetes was not specified in 4% of cases).1 [evidence level III]

Keeping blood glucose concentrations as close as possible to the normal range for people without diabetes is known to prevent or to delay the long-term vascular complications of diabetes. Systems of surveillance for the early detection of complications are important, as is effective management of complications when they occur.]

N.1.1 Section 1.1 Aim of the guideline

Clinical guidelines have been defined as ‘systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions’.2 This guideline addresses the diagnosis and management of children and young people with type 1 diabetes. It has been developed with the aim of providing guidance on:

- initial management at diagnosis (including consideration of admission criteria and initial insulin regimens)
- continuing care of children and young people with type 1 diabetes
- ongoing monitoring of glycaemic control (including the role of home glucose monitoring and the frequency of HbA1c measurement)
- management of hypoglycaemia (insufficient blood sugar) and hypoglycaemic coma
- prevention and management of diabetic ketoacidosis (including the management of intercurrent illness, that is, illness that occurs alongside type 1 diabetes; for example, influenza)
- peri-operative management of children and young people with type 1 diabetes

- surveillance for complications.

The guideline also addresses the special needs of young people (adolescents) and the interface between paediatric and adult services.

N.1.2 Section 1.2 Areas outside the remit of the guideline

The guideline does not address:

- the issue of contraception in young women with type 1 diabetes
- the management of young women with type 1 diabetes who wish to conceive or are pregnant
- the management of young women who develop type 1 diabetes during pregnancy
- the management of non-type 1 diabetes.

A separate guideline on diabetes in pregnancy (covering type 1 diabetes, type 2 diabetes and gestational diabetes) will be developed in the future.

N.1.3 Section 1.3 For whom is the guideline intended?

This guideline is of relevance to those who work in or use the National Health Service in England and Wales, in particular:

- primary and secondary healthcare professionals who have direct contact with and make decisions concerning the care of children and young people with type 1 diabetes (including dietitians, general practitioners, nurses, paediatricians, pharmacists, physicians and podiatrists)
- those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales commissioners, and public health and trust managers
- children and young people with type 1 diabetes, their families and other carers.

The guideline is also relevant to (but does not cover the practice of) those who work in:

- social services and the voluntary sector
- services supplied by secondary and tertiary specialties for the complications of type 1 diabetes (for example, cardiology, ophthalmology, renal and urology services) to which patients may be referred
- the education and childcare sectors.

A version of this guideline for children and young people with type 1 diabetes, their families and the public is available entitled Type 1 diabetes in children and young people. Understanding NICE guidance – information for the families and carers of children with type 1 diabetes, young people with type 1 diabetes, and the public (reproduced in Appendix A). It can be downloaded from the NICE website (www.nice.org.uk) or ordered via the NHS Response Line (0870 1555 455; quote reference number N0623 for an English version and N0560 for an English and Welsh version).[2004]

N.1.4 Section 1.4 Who has developed this guideline?

The guideline was developed by a multi-professional and lay working group (the Guideline Development Group; guideline development group) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included:

- two consumer representatives
- two paediatric diabetes nurses
- three paediatricians

- a paediatric dietitian
- a general practitioner
- a clinical psychologist
- an adult physician with an interest in adolescence.

Staff from the NCC-WCH provided methodological support for the guideline development process, undertook systematic searches, retrieval and appraisal of the evidence, and wrote successive drafts of the guideline.

All guideline development group members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry in accordance with guidance from the National Institute for Clinical Excellence (NICE).

N.1.5 Section 1.5 Other relevant documents

This guideline is intended to complement other existing and proposed work of relevance, including the Diabetes National Service Framework, the Children's National Service Framework and a guideline commissioned by NICE that relates to the diagnosis and management of type 1 diabetes in adults.

Some aspects of the adult guideline are relevant to the diagnosis and management of type 1 diabetes in children and young people. The developers of the children's and adults' guidelines worked in parallel and communication between the two development groups was maintained at project and advisory levels. [from 2004]

N.2 Chapter 2 Summary of recommendations and practice algorithm

N.2.1 Section 2.1 Summary of recommendations

Chapter 3 Diagnosis and initial management

3.1 Diagnosis

The diagnosis of type 1 diabetes in children and young people should be based on the criteria specified in the 1999 World Health Organization report on the diagnosis and classification of diabetes mellitus. [D]

Children and young people with suspected type 1 diabetes should be offered immediate (same day) referral to a multidisciplinary paediatric diabetes care team that has the competencies needed to confirm diagnosis and to provide immediate care. [GPP]

Consideration should be given to the possibility of other types of diabetes (such as early-onset type 2 diabetes, other insulin resistance syndromes, maturity-onset diabetes in the young and molecular/enzymatic abnormalities) in children and young people with suspected type 1 diabetes who:

- have a strong family history of diabetes
- are obese at presentation
- are of Black or Asian origin
- have an insulin requirement of less than 0.5 units/kg body weight/day outside a partial remission phase
- have no insulin requirement

- rarely or never produce ketone bodies in the urine (ketonuria) during episodes of hyperglycaemia
- show evidence of insulin resistance (for example, acanthosis nigricans)
- have associated features, such as eye disease, deafness, or another systemic illness or syndrome. [GPP]

Children and young people with type 1 diabetes should be entered on a population-based, practice-based and/or clinic-based diabetes register. [GPP]

3.2 Management from diagnosis

Children and young people with type 1 diabetes should be offered an ongoing integrated package of care by a multidisciplinary paediatric diabetes care team. To optimise the effectiveness of care and reduce the risk of complications, the diabetes care team should include members with appropriate training in clinical, educational, dietetic, lifestyle, mental health and foot care aspects of diabetes for children and young people. [GPP]

Children and young people with type 1 diabetes and their families should be offered 24-hour access to advice from the diabetes care team. [GPP]

Children and young people with type 1 diabetes and their families should be involved in making decisions about the package of care provided by the diabetes care team. [GPP]

At the time of diagnosis, children and young people with type 1 diabetes should be offered home-based or inpatient management according to clinical need, family circumstances and wishes, and residential proximity to inpatient services. Home-based care with support from the local paediatric diabetes care team (including 24-hour telephone access to advice) is safe and as effective as inpatient initial management. [A]

Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. [D]

Children with type 1 diabetes who are younger than 2 years of age and children and young people who have social or emotional difficulties, or who live a long way from hospital should be offered inpatient initial management. [GPP]

Children and young people with type 1 diabetes and their families should be offered appropriate emotional support following diagnosis, which should be tailored to emotional, social, cultural and age-dependent needs. [GPP]

3.3 Natural history of type 1 diabetes

Children and young people with newly diagnosed type 1 diabetes should be informed that they may experience a partial remission phase (or 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 7%. [D]

Children and young people with type 1 diabetes should be informed that the use of multiple daily insulin injection regimens or continuous subcutaneous insulin infusion (or insulin pump therapy) will not prolong the partial remission phase, although these forms of therapy may be appropriate for optimising glycaemic control, especially in young people. [A]

3.4 Essential education at diagnosis

Children and young people with newly diagnosed type 1 diabetes should be offered a structured programme of education covering the aims of insulin therapy, delivery of insulin, self-monitoring of blood glucose, the effects of diet, physical activity and intercurrent illness on glycaemic control, and the detection and management of hypoglycaemia. [D]

Chapter 4 Ongoing management

4.1 Education

Children and young people with type 1 diabetes and their families should be offered timely and ongoing opportunities to access information about the development, management and effects of type 1 diabetes. The information provided should be accurate and consistent and it should support informed decision making. [GPP]

Children and young people with type 1 diabetes and their families should be offered opportunities to discuss particular issues and to ask questions at each clinic visit. [GPP]

The method of delivering education and content will depend on the individual and should be appropriate for the child's or young person's age, maturity, culture, wishes and existing knowledge within the family. [GPP]

Particular care should be given to communication and the provision of information when children and young people with type 1 diabetes and/or their parents have special needs, such as those associated with physical and sensory disabilities, or difficulties in speaking or reading English. [GPP]

4.2 Insulin regimens

Pre-school and primary school children with type 1 diabetes should be offered the most appropriate individualised regimens to optimise their glycaemic control. [C]

Young people with type 1 diabetes should be offered multiple daily injection regimens to help optimise their glycaemic control. [A]

Multiple daily injection regimens should be offered only as part of a package of care that involves continuing education, dietary management, instruction on the use of insulin delivery systems and blood glucose monitoring, emotional and behavioural support, and medical, nursing and dietetic expertise in paediatric diabetes, because this improves glycaemic control. [C]

Children and young people using multiple daily injection regimens should be informed that they may experience an initial increase in the risk of hypoglycaemia and short-term weight gain. [B]

Children and young people with type 1 diabetes and their families should be informed about strategies for the avoidance and management of hypoglycaemia. [C]

Young people who do not achieve satisfactory glycaemic control with multiple daily injection regimens should be offered additional support and, if appropriate, alternative insulin therapy (once-, twice- or three-times daily mixed insulin regimens or continuous subcutaneous insulin infusion using an insulin pump). [GPP]

Young people with type 1 diabetes who have difficulty adhering to multiple daily injection regimens should be offered twice-daily injection regimens. [GPP]

Continuous subcutaneous insulin infusion (or insulin pump therapy) is recommended as an option for people with type 1 diabetes provided that:

- multiple-dose insulin therapy (including, where appropriate, the use of insulin glargine) has failed;* and
- those receiving the treatment have the commitment and competence to use the therapy effectively.

*People for whom multiple-dose therapy has failed are considered to be those for whom it has been impossible to maintain an HbA1c level no greater than 7.5% (or 6.5% in the

presence of microalbuminuria or adverse features of the metabolic syndrome) without disabling hypoglycaemia occurring, despite a high level of self-care of their diabetes. 'Disabling hypoglycaemia', for the purpose of this guidance, means the repeated and unpredicted occurrence of hypoglycaemia requiring third-party assistance that results in continuing anxiety about recurrence and is associated with significant adverse effect on quality of life. [NICE TA]

Continuous subcutaneous insulin infusion therapy should be initiated only by a trained specialist team, which should normally comprise a physician with a specialist interest in insulin pump therapy, a diabetes specialist nurse and a dietitian. [NICE TA]

All individuals beginning continuous subcutaneous insulin infusion therapy should be provided with specific training in its use. Ongoing support from a specialist team should be available, particularly in the period immediately following the initiation of continuous subcutaneous insulin infusion. It is recommended that specialist teams should agree a common core of advice appropriate for continuous subcutaneous insulin infusion users. [NICE TA]

Established users of continuous subcutaneous insulin infusion therapy should have their insulin management reviewed by their specialist team so that a decision can be made about whether a trial or a switch to multiple-dose insulin incorporating insulin glargine would be appropriate. [NICE TA]

4.3 Insulin preparations

Children and young people with type 1 diabetes should be offered the most appropriate insulin preparations (rapid-acting insulin analogues, short-acting insulins, intermediate-acting insulins, long-acting insulin analogues or biphasic insulins) according to their individual needs and the instructions in the patient information leaflet supplied with the product with the aim of obtaining an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and maximising quality of life. [GPP]

Children and young people with type 1 diabetes using multiple daily insulin regimens should be informed that injection of rapid-acting insulin analogues before eating (rather than after eating) reduces postprandial blood glucose levels and thus helps to optimise blood glucose control. [B]

For pre-school children with type 1 diabetes it may be appropriate to use rapid-acting insulin analogues shortly after eating (rather than before eating) because food intake can be unpredictable. [GPP]

Children and young people with type 1 diabetes who use insulin preparations containing intermediate-acting insulin should be informed that these preparations should be mixed before use according to the instructions in the patient information leaflet supplied with the product. [GPP]

4.4 Methods of delivering insulin

Children and young people with type 1 diabetes should be offered a choice of insulin delivery systems that takes account of their insulin requirements and personal preferences. [GPP]

Children and young people with type 1 diabetes using insulin injection regimens should be offered needles that are of an appropriate length for their body fat (short needles are appropriate for children and young people with less body fat; longer needles are appropriate for children and young people with more body fat). [GPP]

4.5 Non-insulin agents (oral antidiabetic drugs)

Children and young people with type 1 diabetes should not be offered acarbose or sulphonylureas (glibenclamide, gliclazide, glipizide, tolazamide or glyburide) in combination with insulin because they may increase the risk of hypoglycaemia without improving glycaemic control. [A]

Metformin in combination with insulin is suitable for use only within research studies because the effectiveness of this combined treatment in improving glycaemic control is uncertain. [A]

4.6 Monitoring glycaemic control

Children and young people with type 1 diabetes and their families should be informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and that their care package should be designed to attempt to achieve this. [A]

Children and young people with type 1 diabetes should be offered testing of their HbA1c levels two to four times per year (more frequent testing may be appropriate if there is concern about poor glycaemic control). [D]

Current HbA1c measurements should be made available in outpatient clinics because their availability can lead to immediate changes in insulin therapy and/or diet and so reduce the need for follow-up appointments. [D]

Children and young people with type 1 diabetes and their families should be informed that aiming to achieve low levels of HbA1c can lead to increased risks of hypoglycaemia and that high levels of HbA1c can lead to increased risks of long-term microvascular complications. [A]

Children and young people with HbA1c levels consistently above 9.5% should be offered additional support by their diabetes care teams to help them improve their glycaemic control because they are at increased risk of developing diabetic ketoacidosis and long-term complications. [B]

Children and young people with type 1 diabetes should be encouraged to use blood glucose measurements for short-term monitoring of glycaemic control because this is associated with reduced levels of glycated haemoglobin. Urine glucose monitoring is not recommended because it is less effective and is associated with lower patient satisfaction. [A]

Children and young people with type 1 diabetes and their families should be informed that the optimal targets for short-term glycaemic control are a preprandial blood glucose level of 4–8 mmol/l and a postprandial blood glucose level of less than 10 mmol/l. [D]

Children and young people with type 1 diabetes and their families should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care teams. [C]

Children and young people with type 1 diabetes and their families should be offered a choice of appropriate equipment for undertaking monitoring of capillary blood glucose to optimise their glycaemic control in response to adjustment of insulin, diet and exercise. [GPP]

Children and young people using multiple daily injection regimens should be encouraged to adjust their insulin dose if appropriate after each preprandial, bedtime and occasional night-time blood glucose measurement. [D]

Children and young people using twice-daily injection regimens should be encouraged to adjust their insulin dose according to the general trend in preprandial, bedtime and occasional night-time blood glucose measurements. [D]

Children and young people with type 1 diabetes who are trying to optimise their glycaemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day. [GPP]

Children and young people with type 1 diabetes and their families should be informed that blood glucose levels should be interpreted in the context of the 'whole child', which includes the social, emotional and physical environment. [GPP]

Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems. [B]

Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction. [B]

Children and young people with type 1 diabetes should be encouraged to use a diary in conjunction with a blood glucose monitor because recording food intake and events such as intercurrent illness can help to reduce the frequency of hypoglycaemic episodes. [GPP]

4.7 Diet

Children and young people with type 1 diabetes should be offered appropriate dietetic support to help optimise body weight and glycaemic control. [C]

Children and young people with type 1 diabetes and their families should be informed that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows:

- carbohydrates – more than 50%
- protein – 10–15%
- fat – 30–35%. [D]

The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs. [D]

Children and young people with type 1 diabetes should be encouraged to develop a good working knowledge of nutrition and how it affects their diabetes. [GPP]

Children and young people with type 1 diabetes and their families should be informed of the importance of healthy eating in reducing the risk of cardiovascular disease (including foods with a low glycaemic index, fruit and vegetables, and types and amounts of fats), and means of making appropriate nutritional changes in the period after diagnosis and according to need and interest at intervals thereafter. [GPP]

Children and young people with type 1 diabetes should be encouraged to consider eating a bedtime snack. The nutritional composition and timing of all snacks should be discussed with the diabetes care team. [B]

Children and young people using multiple daily injection regimens should be offered education about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake. [C]

Children and young people with type 1 diabetes should be offered education about the practical problems associated with fasting and feasting. [GPP]

4.8 Exercise

All children and young people, including those with type 1 diabetes, should be encouraged to exercise on a regular basis because this reduces the risks of developing macrovascular disease in the long term. [B]

Children and young people with type 1 diabetes and their families should be informed that they can participate in all forms of exercise, provided that appropriate attention is given to changes in insulin and dietary management. [GPP]

Children and young people with type 1 diabetes wishing to participate in restricted sports (such as scuba diving) should be offered comprehensive advice by their diabetes care teams. Additional information may be available from local and/or national patient support groups and organisations. [GPP]

Children and young people with type 1 diabetes and their families should be informed about the effects of exercise on blood glucose levels and about strategies for preventing exercise-induced hypoglycaemia during and/or after physical activity. [C]

Children and young people with type 1 diabetes should be encouraged to monitor their blood glucose levels before and after exercise so that they can:

- identify when changes in insulin or food intake are necessary
- learn the glycaemic response to different exercise conditions
- be aware of exercise-induced hypoglycaemia
- be aware that hypoglycaemia may occur several hours after prolonged exercise. [D]

Children and young people with type 1 diabetes, their parents and other carers should be informed that additional carbohydrate should be consumed as appropriate to avoid hypoglycaemia and that carbohydrate-based foods should be readily available during and after exercise. [D]

Children and young people with type 1 diabetes, their parents and other carers should be informed that additional carbohydrate should be consumed if blood glucose levels are less than 7 mmol/l before exercise is undertaken. [GPP]

Children and young people with type 1 diabetes and their families should be informed that changes in their daily exercise patterns may require insulin dose and/or carbohydrate intake to be altered. [GPP]

Children and young people with type 1 diabetes, their parents and other carers should be informed that exercise should be undertaken with caution if blood glucose levels are greater than 17 mmol/l in the presence of ketosis. [GPP]

4.9 Alcohol, smoking and recreational drugs

Young people with type 1 diabetes should be informed about the specific effects of alcohol consumption on glycaemic control, particularly the risk of (nocturnal) hypoglycaemia. [C]

Young people with type 1 diabetes should be offered alcohol education programmes. [GPP]

Young people with type 1 diabetes who drink alcohol should be informed that they should:

- eat food containing carbohydrate before and after drinking
- monitor their blood glucose levels regularly and aim to keep the levels within the recommended range by eating food containing carbohydrate. [GPP]

Children and young people with type 1 diabetes and their families should be informed about general health problems associated with smoking and in particular the risks of developing vascular complications. [B]

Children and young people with type 1 diabetes should be encouraged not to start smoking. [GPP]

Children and young people with type 1 diabetes who smoke should be offered smoking cessation programmes. [GPP]

Children and young people with type 1 diabetes and their families should be informed about the general dangers of substance misuse and the possible effects on glycaemic control. [GPP]

4.10 Long-distance travel

Children and young people with type 1 diabetes and their families should be offered education about the practical issues related to long-distance travel, such as when best to eat and inject insulin when travelling across time zones. [GPP]

4.11 Immunisation

Children and young people with type 1 diabetes and their families should be informed that the Department of Health recommends annual immunisation against influenza for children and young people with diabetes over the age of 6 months. [D]

Children and young people with type 1 diabetes and their families should be informed that the Department of Health recommends immunisation against pneumococcal infection for children and young people with diabetes over the age of 2 months. [D]

Chapter 5 Complications and associated conditions

5.1 Hypoglycaemia

Children and young people with type 1 diabetes, their parents and other carers should be informed that they should always have access to an immediate source of carbohydrate (glucose or sucrose) and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. [D]

Children and young people, their parents, schoolteachers and other carers should be offered education about the recognition and management of hypoglycaemia. [D]

Children and young people with type 1 diabetes should be encouraged to wear or carry something that identifies them as having type 1 diabetes (for example, a bracelet). [D]

Children and young people with mild to moderate hypoglycaemia should be treated as follows.

- Take immediate action.
- The first line of treatment should be the consumption of rapidly absorbed simple carbohydrate (for example, 10–20 g carbohydrate given by mouth).
- The simple carbohydrate should raise blood glucose levels within 5–15 minutes.
- Carbohydrate given in liquid form may be taken more easily.
- It may be appropriate to give small amounts of rapidly absorbed simple carbohydrate frequently because hypoglycaemia may cause vomiting.
- As symptoms improve or normoglycaemia is restored additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels unless a snack or meal is imminent.
- Additional complex long-acting carbohydrate is not required for children and young people using continuous subcutaneous insulin infusion.

- Blood glucose levels should be rechecked within 15 minutes. [GPP]

Children and young people with severe hypoglycaemia should be treated as follows.

- In a hospital setting, 10% intravenous glucose should be used when rapid intravenous access is possible (up to 500 mg/kg body weight – 10% glucose is 100 mg/ml).
- Outside hospital, or where intravenous access is not practicable, intramuscular glucagon or concentrated oral glucose solution (for example, Hypostop®) may be used.
- Children and young people over 8 years old (or body weight more than 25 kg) should be given 1 mg glucagon.
- Children under 8 years old (or body weight less than 25 kg) should be given 500g glucagon.
- Blood glucose levels should respond within 10 minutes.
- As symptoms improve or normoglycaemia is restored, in children and young people who are sufficiently awake, additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels.
- Some children and young people may continue to have reduced consciousness for several hours after a severe hypoglycaemic episode, and repeat blood glucose
- measurements will be required to determine whether further glucose is necessary.
- Medical assistance should be sought for children and young people whose blood glucose levels fail to respond and those in whom symptoms persist for more than 10 minutes. [GPP]

Parents and, where appropriate, school nurses and other carers should have access to glucagon for subcutaneous or intramuscular use in an emergency, especially when there is a high risk of severe hypoglycaemia. [D]

Parents and, where appropriate, school nurses and other carers should be offered education on the administration of glucagon. [D]

Children and young people with type 1 diabetes and their families should be informed that when alcohol causes or contributes to the development of hypoglycaemia, glucagon may be ineffective in treating the hypoglycaemia and intravenous glucose will be required. [GPP]

5.2 Diabetic ketoacidosis

Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. [D]

Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. [D]

Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. [D]

Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit. [D]

Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/l), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose. [D]

5.3 Surgery

Children and young people with type 1 diabetes should be offered surgery only in centres that have dedicated paediatric facilities for the care of children and young people with diabetes. [D]

Careful liaison between surgical, anaesthetic and diabetes care teams should occur before children and young people with type 1 diabetes are admitted to hospital for elective surgery and as soon as possible after admission for emergency surgery. [D]

All centres caring for children and young people with type 1 diabetes should have written protocols concerning the safe management of children and young people during surgery. The protocols should be agreed between surgical and anaesthetic staff and the diabetes care team. [D]

5.4 Intercurrent illness

Children and young people with type 1 diabetes and their families should be offered clear guidance and protocols ('sick-day rules') for the management of type 1 diabetes during intercurrent illness. [D]

Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness. [GPP]

5.5 Screening for complications and associated conditions

Children and young people with type 1 diabetes should be offered screening for:

- coeliac disease at diagnosis [C]
- and at least every 3 years thereafter until transfer to adult services [GPP]
- thyroid disease at diagnosis and annually thereafter until transfer to adult services [C]
- retinopathy annually from the age of 12 years [C]
- microalbuminuria annually from the age of 12 years [C]
- blood pressure annually from the age of 12 years. [C]

Routine screening for elevated blood lipid levels and/or neurological function is not recommended for children and young people with type 1 diabetes. [C]

Children and young people with type 1 diabetes should be offered:

- annual foot care reviews [GPP]
- investigation of the state of injection sites at each clinic visit. [C]

Children and young people with type 1 diabetes and their families should be informed that, as for other children, regular dental examinations and eye examinations (every 2 years) are recommended. [D]

Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. [GPP]

Children and young people with type 1 diabetes should have their height and weight measured in a private room. [D]

The following complications, although rare, should be considered at clinic visits:

- juvenile cataracts
- necrobiosis lipoidica
- Addison's disease. [GPP]

Chapter 6 Psychological and social issues

6.1 Emotional and behavioural problems

Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than other children and young people. [C]

6.2 Anxiety and depression

Diabetes care teams should be aware that children and young people with type 1 diabetes may develop anxiety and/or depression, particularly when difficulties in self-management arise in young people and children who have had type 1 diabetes for a long time. [B]

Children and young people with type 1 diabetes who have persistently poor glycaemic control should be offered screening for anxiety and depression. [GPP]

Children and young people with type 1 diabetes and suspected anxiety and/or depression should be referred promptly to child mental health professionals. [GPP]

6.3 Eating disorders

Diabetes care teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. [C]

Diabetes care teams should be aware that children and young people with type 1 diabetes who have eating disorders may have associated problems of persistent hyperglycaemia, recurrent hypoglycaemia, and/or symptoms associated with gastric paresis. [C]

Children and young people with type 1 diabetes in whom eating disorders are identified by their diabetes care team should be offered joint management involving their diabetes care team and child mental health professionals. [GPP]

6.4 Cognitive disorders

Parents of pre-school children with type 1 diabetes should be informed that persistent hypoglycaemia, in particular in association with seizures, is associated with a small but definite risk of long-term neurocognitive dysfunction. [C]

Diabetes care teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. [GPP]

6.5 Behavioural and conduct disorders

Children and young people with type 1 diabetes who have behavioural or conduct disorders, and their families, should be offered access to appropriate mental health professionals. [GPP]

6.6 Non-adherence

Non-adherence to therapy should be considered in children and young people with type 1 diabetes who have poor glycaemic control, especially in adolescence. [B]

Non-adherence to therapy should be considered in children and young people with established type 1 diabetes who present with diabetic ketoacidosis, especially if the diabetic ketoacidosis is recurrent. [B]

Young people with 'brittle diabetes' (that is, those who present with frequent episodes of diabetic ketoacidosis over a relatively short time) should have their emotional and psychological wellbeing assessed. [GPP]

The issue of non-adherence to therapy should be raised with children and young people and their families in a sensitive manner. [GPP]

6.7 Psychosocial support

Diabetes care teams should be aware that poor psychosocial support has a negative impact on a variety of outcomes of type 1 diabetes in children and young people, including glycaemic control and self-esteem. [C]

Children and young people with type 1 diabetes, especially young people using multiple daily injection regimens, should be offered structured behavioural intervention strategies because these may improve psychological wellbeing and glycaemic control. [A]

Young people with type 1 diabetes should be offered specific support strategies, such as mentoring and self-monitoring of blood glucose levels supported by problem solving, to improve their self-esteem and glycaemic control. [A]

Families of children and young people with type 1 diabetes should be offered specific support strategies (such as behavioural family systems therapy) to reduce diabetes-related conflict between family members. [A]

Children and young people with type 1 diabetes and their families should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and wellbeing. [GPP]

Diabetes care teams should have appropriate access to mental health professionals to support them in the assessment of psychological dysfunction and the delivery of psychosocial support. [GPP]

6.8 Adolescence

Diabetes care teams should be aware that adolescence can be a period of worsening glycaemic control, which may in part be due to non-adherence to therapy. [B]

Chapter 7 Continuity of care

7.1 Communication between organisations

Children and young people with type 1 diabetes and their families should be offered information about the existence of and means of contacting local and/or national diabetes support groups and organisations, and the potential benefits of membership. This should be done in the time following diagnosis and periodically thereafter. [GPP]

Diabetes care teams should liaise regularly with school staff involved in supervising children and young people with type 1 diabetes to offer appropriate diabetes education and practical information. [GPP]

Teaching staff should be informed about the potential effects of type 1 diabetes on cognitive function and educational attainment. [GPP]

Children and young people with type 1 diabetes and their families should be advised how to obtain information about benefits in relation to government disability support. [GPP]

7.2 Transition from paediatric to adult care

Young people with type 1 diabetes should be encouraged to attend clinics on a regular basis (three or four times per year) because regular attendance is associated with good glycaemic control. [D]

Young people with type 1 diabetes should be allowed sufficient time to familiarise themselves with the practicalities of the transition from paediatric to adult services because this has been shown to improve clinic attendance. [GPP]

Specific local protocols should be agreed for transferring young people with type 1 diabetes from paediatric to adult services. [GPP]

The age of transfer to the adult service should depend on the individual's physical development and emotional maturity, and local circumstances. [GPP]

Transition from the paediatric service should occur at a time of relative stability in the individual's health and should be coordinated with other life transitions. [D]

Paediatric diabetes care teams should organise age-banded clinics for young people and young adults jointly with their adult specialty colleagues. [D]

Young people with type 1 diabetes who are preparing for transition to adult services should be informed that some aspects of diabetes care will change at transition. The main changes relate to targets for short-term glycaemic control and screening for complications. [GPP]

N.2.2 Section 2.2 Future research recommendations

Chapter 4 Ongoing management

4/1 Education

Further research is needed to evaluate the effectiveness of age-specific structured education programmes covering all aspects of care in children and young people with type 1 diabetes, their families and other carers.

Further research is needed to evaluate the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers.

Further research is needed to determine the most effective way of training healthcare professionals to provide education about type 1 diabetes in children and young people.

4.2 Insulin regimens

Research is needed to compare the effectiveness of multiple daily injection regimens with twice-daily injection regimens in children and young people with type 1 diabetes.

Research is needed to compare the effectiveness of continuous subcutaneous insulin infusion (or insulin pump therapy) and multiple daily injection regimens in children and young people with type 1 diabetes.

4.3 Insulin preparations

Research is needed to evaluate the effectiveness of long-acting insulin analogues in children and young people with type 1 diabetes.

Further research is needed to evaluate the effectiveness of once-daily injection regimens in children and young people with type 1 diabetes, and especially in pre-school children.

4.4 Methods of delivering insulin

Further research is required to evaluate the effectiveness of insulin delivery systems in children and young people with type 1 diabetes.

Research is needed to compare the effectiveness of insulin delivery modes (for example, dermal, nasal, oral and pulmonary) in children and young people with type 1 diabetes.

4.5 Non-insulin agents (oral antidiabetic drugs)

Further research is needed to evaluate the effectiveness of metformin combined with insulin treatment in children and young people with type 1 diabetes.

4.6 Monitoring glycaemic control

Research is needed to investigate the clinical implications of alternative site monitoring (for example, the arm as opposed to the finger) in children and young people with type 1 diabetes.

Research is needed to evaluate the clinical effectiveness of the routine use of invasive and non-invasive continuous glucose monitoring systems for optimising glycaemic control in children and young people with type 1 diabetes.

4.7 Diet

Further research is needed to evaluate the effectiveness of training in flexible, intensive insulin management to enable children and young people with type 1 diabetes to adjust insulin doses to match carbohydrate intake.

Chapter 5 Complications and associated conditions

5.2 Diabetic ketoacidosis

Further research is needed to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis in children and young people with type 1 diabetes.

Further research is needed to investigate the effectiveness of different concentrations of rehydration fluid, the rate of rehydration, the use of albumin infusion and the dose of insulin infusion in the management of diabetic ketoacidosis in children and young people.

5.3 Screening for complications and associated conditions

Further research is needed to evaluate the effectiveness of screening for cardiovascular risk factors in children and young people with type 1 diabetes.

Chapter 6 Psychological and social issues

6.4 Cognitive disorders

Further research is needed to evaluate the effects of persistent hypoglycaemia and recurrent diabetic ketoacidosis on neurocognitive function.

6.8 Adolescence

Further studies are needed to evaluate the effectiveness of behavioural and social interventions on anxiety and depression, eating disorders, behavioural and conduct disorders, and adherence to therapy in children and young people with type 1 diabetes, especially in adolescence, from diagnosis and in established diabetes.

Chapter 7 Continuity of care

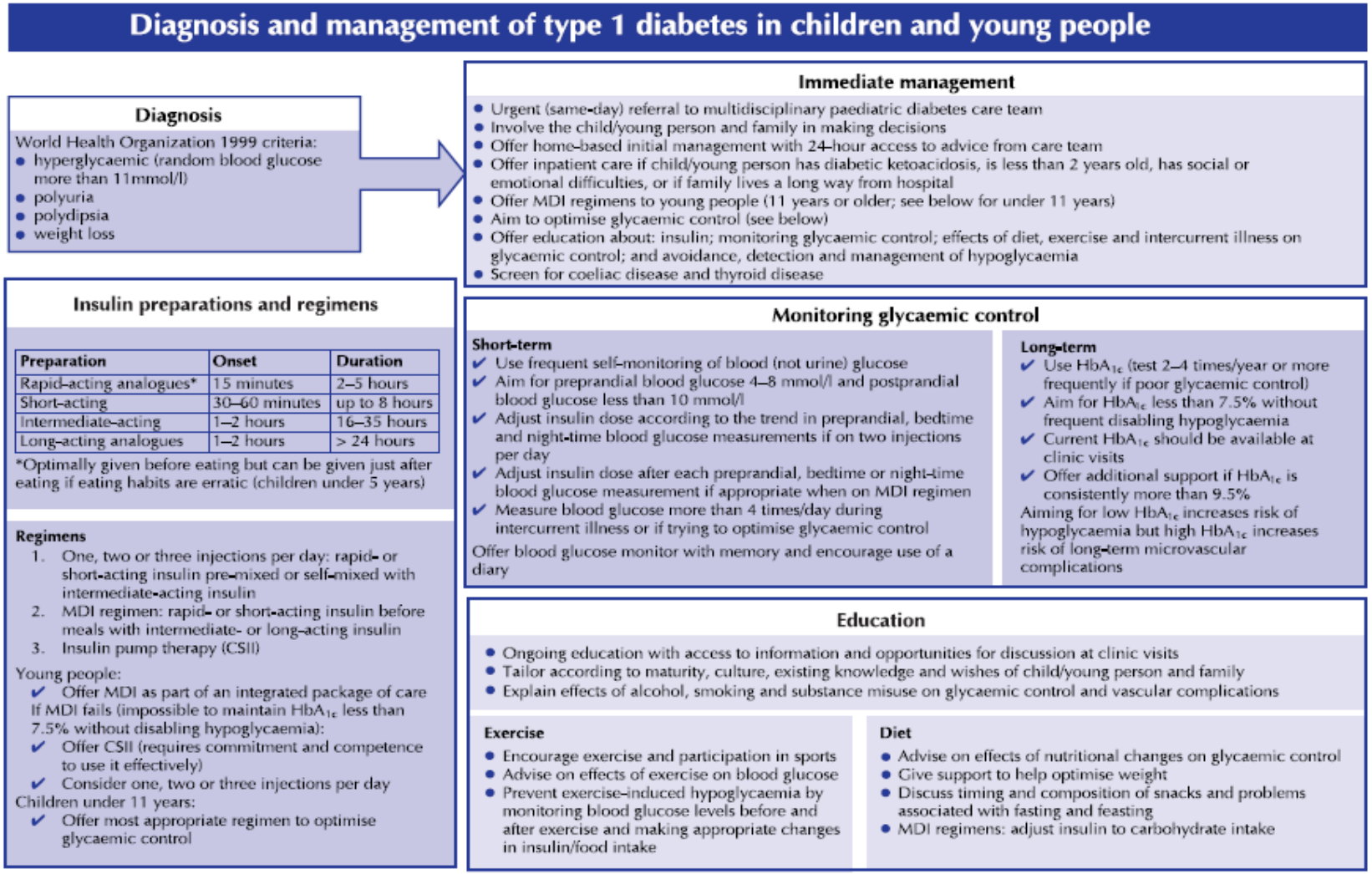
7.1 Communication between organisations

Further research is needed to evaluate the effects of low blood glucose levels on learning, attendance at school and educational attainment.

7.2 Transition from paediatric to adult care

Further research is needed to investigate young people's experiences of transition from paediatric to adult services for people with type 1 diabetes.

N.2.3 Section 2.3 Algorithm



N.3 Chapter 3 Diagnosis and initial management

N.3.1.1 Section 3.1 Diagnosis

Where uncertainty exists, additional support for the type of diagnosis can be made by measuring specific immunological markers of beta-cell damage: abnormal levels of islet cell antibodies, insulin auto-antibodies and glutamic acid decarboxylase antibodies usually signify type 1 diabetes.15 [evidence level IV]

N.3.1.2 Section 3.2 Management from diagnosis

N.3.1.3 Section 3.3 Natural history of type 1 diabetes

N.3.1.4 Section 3.4 Essential education at diagnosis

N.4 Chapter 4 Ongoing management

N.4.1 Section 4.1 Education

N.4.2 Section 4.2 Insulin regimens

Continuous subcutaneous insulin infusion (insulin pump therapy; page 44 of the 2004 guideline)

The NICE TA identified two RCTs that compared CSII therapy with multiple daily injection therapy in young people and young adults up to the age of 20 years with type 1 diabetes. In one of the studies there was a significant improvement in glycated haemoglobin at 4 months for patients on CSII therapy compared with multiple daily injection therapy, and significantly less insulin was required (glycated haemoglobin 8.8% versus 9.6%, no CIs given; insulin dosage 44 units/day, SD 12 units/day versus 60 units/day, SD 16 units/day, n=20).[122] [evidence level Ib] In the second study, glycated haemoglobin improved from baseline with both CSII and multiple daily injection therapy, but there was no difference between treatments (8.5% versus 8.7%, not significant, n=10).123 [evidence level Ib]

Two further RCTs that compared CSII therapy with multiple daily injection therapy in young people were excluded from the NICE TA. In one early crossover RCT there was no significant difference in glycated haemoglobin at 4 months for patients on CSII therapy compared with multiple daily injection therapy (n=19, glycated haemoglobin levels not reported).[124] [evidence level Ib] A second early RCT that included children and young people with type 1 diabetes found a significantly reduced mean glycated haemoglobin over the 12-month treatment period in the CSII treatment group compared with intensive conventional treatment (9.1%, SD 0.9% versus 10.4%, SD 0.2%, p <0.001, n=13). This study found elevated rates of moderate to severe hypoglycaemia and diabetic ketoacidosis. However, the numbers were not large enough to perform reliable statistical analysis (episodes of hypoglycaemia: 7 versus 4; episodes of diabetic ketoacidosis: 6 versus 0).125 [evidence level Ib]

In the absence of published RCTs comparing CSII and multiple daily injection therapy in children and young people at the time of the NICE TA, the NICE TA reviewed information from case series. The case series review concluded that CSII had a place in treatment for children with type 1 diabetes, but that better evidence was needed because of the potential for bias in case series.[121]

The NICE TA identified an abstract that reported a reduction in severe hypoglycaemic events from 0.55 to 0.25/child/year on transfer from multiple daily injections to CSII therapy.[121,128] This study was published in full after the NICE TA had been published and it reported a lower level of HbA1c after treatment with CSII than multiple daily injections (8.0 ±0.7% versus 8.1 ±0.8%, p=0.03). There were no differences in the level of fructosamine (362 ±43 µmol/l versus 354 ±56 µmol/l), frequency of severe hypoglycaemia (0.13 rate/patient year, 95% CI 0.0 to 0.4 rate/patient year versus 0.39 rate/patient year, 95% CI 0.0 to 0.84 rate/patient year) or frequency of symptomatic hyperglycaemia (7.9 ±7 mean/patients/trial period versus 6.7 ±7.3 mean/patients/trial period). Body mass index standard deviation scores after CSII treatment were lower than after treatment by multiple daily injections (0.35 ±0.83 versus 0.37 ±0.85, p=0.012). The study found higher treatment satisfaction (30.6 ±3.7 versus 21.9 ±3.8, p <0.001), but no difference in quality of life (satisfaction with quality of life: 74.8 ±13.5 versus 73.5 ±14.0; impact of quality of life: 73.2 ±9.6 versus 73.5 ±9.7; worry about quality of life: 81.6 ±12.4 versus 79.8 ±12.8) with CSII therapy compared with multiple daily injection therapy.129 [evidence level Ib]

The NICE TA also provided a background economic appraisal of the economic evidence for children, young people and adults of CSII therapy versus multiple daily injections.[121] The health economics systematic review conducted for the NICE TA found no full economic evaluation studies that addressed this question, and the clinical systematic review found no published data on the costs of intensive therapy. Therefore the costs were derived from manufacturers, patient groups and experts from two diabetes centres. Based on estimates of cost only, the NICE TA concluded that the additional costs of CSII compared with multiple daily injections would be around £3,600 to £3,900 for the first year and between £11,000 and £14,000 for 8 years depending on the life span of the pump (see Table 27).

Since the proportion of people with type 1 diabetes who used CSII pumps was not known, the NICE TA estimated that the annual costs to the National Health Service in England and Wales would be around £3.5 million if 1% of people with type 1 diabetes used CSII, £10.5 million if 3% of people with type 1 diabetes used CSII, and £17.5 million if 5% of people with type 1 diabetes used CSII. The costs of providing diabetes specialist nurses to provide education to young patients starting CSII are not included in these costs but were expected to be high.

To calculate the lifetime costs for children and young people of CSII versus multiple daily injections requires empirical data from the UK since it is not clear what the consequences for children and young people might be, given the longer time period at risk of complications associated with poor management, and potentially different impacts of hypoglycaemia and other adverse events on the quality of life of a child.

Table 78: Estimated additional costs associated with continuous subcutaneous insulin infusion (CSII) versus multiple daily injections for different types of insulin pump (source: NICE Technology Appraisal[121]; Table 4.1 in the 2004 guideline)

Total net cost for CSII	Disetronic D-Tron	Disetronic H-Tron	MiniMed 508
Year 1	£3,878	£3,571	£3,602
Assuming 4-year pump life			
Years 1–4 (discounted)	£7,081 (£6,722)	£6,569 (£6,242)	£6,058 (£5,790)
Years 1–8 (discounted)	£13,941 (£11,871)	£12,917 (£11,011)	£11,894 (£10,201)
Assuming 8-year pump life			
Years 1–8 (discounted)	£12,178 (£10,429)	£11,272 (39,663)	£10,096 (£8,728)

Summary of multiple daily injection regimens compared with other insulin regimens (page 46 of the 2004 guideline)

- Multiple daily injections as part of an intensive package of care improve glycaemic control in young people with type 1 diabetes. [evidence level Ia]
- Improved glycaemic control decreases the risk of retinopathy, nephropathy and macrovascular events. [evidence level Ia]
- Multiple daily injections increase the risk of hypoglycaemia, weight gain and possibly diabetic ketoacidosis. [evidence level Ia] These risks can be minimised with increased experience of using multiple daily injections. [evidence level Ib]

Multiple daily injections do not affect mortality, quality of life or neuropsychological impairment. [evidence level Ia]

N.4.3 Section 4.3 Insulin preparations

N.4.4 Section 4.4 Methods of delivering insulin

N.4.5 Section 4.5 Non-insulin agents (oral antidiabetic drugs)

N.4.6 Section 4.6 Monitoring glycaemic control

Glycaemic targets relevant to age (page 70 of the 2004 guideline)

The optimal level of glycaemic control for children and young people with type 1 diabetes is an area of considerable discussion, with a need to balance the long-term benefits of low blood sugar reducing risks of long-term complications with the short-term risk of hypoglycaemia and the ability to cope with an intensive approach to insulin therapy which has an impact on daily lifestyle.

Evidence relating to long-term effects of hypoglycaemia on cognitive function is presented in Section 9.3.

One study has suggested that targets for clinical care that are set in the absence of normative data and local feasibility assessment should be treated with caution.[324] [evidence level III] A second study compared DCCT glycaemic control levels with classification of glycaemic control according to numbers of SDs from the mean for a local population without diabetes. The study found that the local population without diabetes method may overestimate the glycaemic control required to reduce microvascular complications in patients with type 1 diabetes.[325] [evidence level III]

A 2001 audit of the care of children and young people with diabetes recorded HbA1c levels in 7074 of the 15 437 children and young people aged 0–16 years in England known to have diabetes. In all age groups, fewer than 20% of children and young people managed to achieve an HbA1c level of 7.5% or lower.[1] [evidence level III]

We found no other studies that specifically looked at glycaemic targets for HbA1c, urinary glucose, urinary ketones or blood ketones. However, several consensus-based recommendations exist in this area.

Summary

Lower HBA1c levels have been shown to be associated with fewer and delayed microvascular complications in young people over the age of 13 years.[91] [evidence level Ib]

Frequency and timing of measuring glycaemic parameters (page 71 of the 2004 guideline)

Frequency of self-monitoring of blood glucose testing

In a systematic review that looked at the effectiveness of self-monitoring in people with type 1 diabetes, the frequency of self-monitoring was not discussed directly.[291] [evidence level Ia] However, we found three studies that examined the frequency of self-monitoring of blood glucose.

One RCT investigated three blood glucose monitoring regimens over three 12-week periods (n=25 adults). The study compared a four-point profile on any two non-consecutive days/week versus one four-point profile on any day of the week versus two blood glucose measurements on each day for 7 days/week. There was no significant difference in glucose control or patient preference among the different regimens. However, the frequency of insulin regimen changes was increased when a four-point profile on any two nonconsecutive days/week was compared with one four-point profile on any day of the week ($p < 0.02$).[317] [evidence level Ib]

An RCT involving young people (n=30) performing self-monitoring of blood glucose compared young people who were paid to attend the study clinic with young people who were paid to attend the clinic in relation to how many days they had performed two or more blood glucose tests. The study lasted 16 weeks and showed an increase in the percentage of days blood glucose was monitored twice with the patient being paid in relation to how many days they had performed two blood glucose tests (~80% versus 58%). However, the study did not report any significant changes in mean blood glucose concentrations, mean SD of blood glucose concentrations, or mean glycated haemoglobin concentration.[326] [evidence level Ib]

A non-randomised intervention study looked at blood glucose testing four or more times/day compared with twice/day for patients using CSII, multiply daily injections and a combination of CSII and multiple daily injections for a period of 1 year (n=21, age range 15–36 years). The mean blood glucose concentration did not change significantly in any of the treatment groups. HbA1 was significantly lower when the patients performed glucose testing four or more times/day compared with twice/day. This was seen in the groups who used CSII, multiply daily injections and a combination of CSII and multiple daily injections (CSII group who previously tested at least four times/day: 7.9 ±0.4% versus 10.3 ±0.5%, $p < 0.0001$; CSII group who previously tested two times/day: 8.2 ±0.4% versus 10.2 ±0.5%, $p=0.0476$; multiple daily injection group who previously tested at least four times/day: 8.1 ±0.4% versus 10.0 ±0.9%, $p=0.0008$; CSII and multiple daily injections combined: 8.2 ±0.3% versus 10.3 ±0.3%, $p < 0.0001$).[327] [evidence level IIb]

Summary (page 72 of the 2004 guideline)

Frequent daily blood glucose monitoring as part of a package of care has been shown to be associated with improved glycaemic control.

N.4.7 Section 4.7 Diet

Page 79 of the 2004 guideline: Specific advice about food choices is an essential part of multiple daily injection approaches to treating type 1 diabetes to achieve optimal glycaemic control. Adjustment of the pre-meal insulin dose in a multiple daily injection regimen requires detailed knowledge of the carbohydrate content of food.[83] [evidence level Ib] Healthcare professionals should therefore maintain an up-to-date knowledge of carbohydrate and glycaemic indices to help them provide children and young people with type 1 diabetes and their families with adequate education in relation to appropriately maintaining multiple daily injection regimens.

Page 80 of the 2004 guideline: An RCT involving children and young people with type 1 diabetes compared dietary advice relating to low glycaemic index with dietary advice relating to carbohydrate exchange (n=104). Twelve months after giving dietary advice, the group who received advice relating to low glycaemic index had lower HbA1clevels (8.05 ±0.95% versus 8.61 ±1.37%, p=0.05) and a lower average number of hypoglycaemic episodes (11.2 ±9.8 episodes/patient/month versus 16.8 ±11.8 episodes/patient/month, p=0.06) than the group who received advice relating to carbohydrate exchange. However, there was no difference in average number of hyperglycaemic episodes (6.9 ±6.8 episodes/patient/month versus 5.8 ±5.5 episodes/patient/month, p=0.37) or macronutrient intake recorded in 3-day food diaries (dietary fat: 34.2 ±6.7% versus 33.5 ±5.6% of energy, p=0.65; carbohydrate: 48.6 ±6.5% versus 48.8 ±5.4% of energy, p=0.86; protein: 17.3 ±3.7% versus 17.6 ±2.5% of energy, p=0.61; total sugar: 19.5 ±6.1% versus 17.7 ±5.6% of energy; total fibre: 22.5 ±6.5 g/day versus 20.2 ±5.0 g/day).[434,435] [evidence level Ib]

Page 81 of the 2004 guideline: Several medium-sized RCTs in adults with poorly controlled type 1 diabetes evaluated training in flexible, intensive insulin management to improve dietary freedom in adults with poorly controlled type 1 diabetes. The aim of the training was to enable patients to adjust insulin dose to match carbohydrate intake. An improvement in HbA1 was seen in the intervention group compared with the group who received normal care. Quality of life and total wellbeing were also improved. However, no improvement was seen in the incidence of severe hypoglycaemia, weight gain or total cholesterol.[95] [evidence level Ib]

N.4.7.1 Section 4.8 Exercise

N.4.7.2 Section 4.9 Alcohol, smoking and recreational drugs

N.4.7.3 Section 4.10 Long-distance travel

N.4.7.4 Section 4.11 Immunisation

Page 87 of the 2004 guideline: The Department of Health has recommended selective immunisation to protect those who are at most risk of serious illness or death should they develop influenza. Annual influenza immunisation is strongly recommended for children and young people with diabetes.[473] [evidence level IV]

Page 88 of the 2004 guideline: Immunisation against pneumococcal infection is recommended by the Department of Health for all children and young people with diabetes, for whom pneumococcal infection is likely to be more common and/or dangerous. The Department of Health has advised that children younger than about 2 years show little antibody response to immunisation with the pneumococcal polysaccharide vaccine. However, the pneumococcal conjugate vaccine is immunogenic in infants and children over 2 months of age. Re-immunisation within 3 years of the previous dose of pneumococcal polysaccharide vaccine is not normally advised.[479] [evidence level IV]

N.5 Chapter 5 Complications and associated conditions

N.5.1 Section 5.1 Hypoglycaemia

N.5.2 Section 5.2 Diabetic ketoacidosis

N.5.2.1 Incidence

In the UK during 2001, at least 4.5% of 0–16 year-olds with previously diagnosed diabetes had one or more overnight admissions to hospital due to diabetic ketoacidosis (53.2% had no

admissions and the remaining 42.3% had no recorded overnight admissions, n=10 029).[1] [evidence level III] Among children and young people admitted to hospital at least once for diabetic ketoacidosis, 19.3% had more than one admission.[1] There is increased likelihood ofNew evidence and recommendations for 2015 update to be inserted admission for diabetic ketoacidosis in the first year of diagnosis compared with later years.[1]

Diabetic ketoacidosis is the most common cause of diabetes-related deaths in children and young people. Diabetic ketoacidosis or hyperglycaemia was implicated in 83% of deaths caused by diabetes in patients under the age of 20 years between 1990 and 1996 (n=116).[496] [evidence level III]

Diabetic ketoacidosis may be complicated by cerebral oedema. It has been reported that cerebral oedema causes 69% of deaths in children and young people with diabetes under the age of 12 years.496 [evidence level III] The risk of patients with diabetic ketoacidosis developing cerebral oedema has been reported to be between 0.2%497 and 0.9%.498,499 [evidence level III]

The risk is higher in patients with newly diagnosed diabetes (1.2%) as opposed to patients with established diabetes (0.4%).[499] [evidence level III] Twenty-four per cent of the children and young people with cerebral oedema died.[499] [evidence level III]

The cause of diabetic ketoacidosis was identified as insulin error or manipulation in 42% (20/48 episodes) of patients aged 14–24 years. It is thought that abnormal insulin treatment is likely to be a major cause of diabetic ketoacidosis in this age group.[500] [evidence level III] A further study in people aged under 30 years showed that 28% of admissions for diabetic ketoacidosis were associated with decreased adherence to treatment (25/89 of the patients had obtained less insulin than required under their prescribed insulin regimen).[501] [evidence level III]

N.5.2.2 What is the definition of diabetic ketoacidosis in children and young people with type 1 diabetes?

Acidosis (decreased pH), ketosis (abnormal amounts of ketones) and hyperglycaemia are different and can exist independently from each other. Diagnosis of diabetic ketoacidosis usually contains the following clinical findings:

- hyperglycaemia (blood glucose >15 mmol/l)
- acidosis (pH <7.3, hydrogen ion concentration >50 nmol/l, or bicarbonate <15 mmol/l)
- heavy glycosuria (>55 mmol/l) and ketonuria
- 5% or more dehydrated
- may or may not include vomiting, drowsiness and abdominal pain.

Ketonuria (or ketonaemia) without acidosis (pH >7.3, hydrogen ion concentration <50 nmol/l) in an otherwise well child with established diabetes suggests that the child has probably not received enough insulin. Administration of additional insulin should be considered in the short term with frequent re-evaluation and an increased insulin dose, and a change in regimen should be considered in the longer term.

If ketonuria is found in the presence of vomiting and/or abdominal pain, the child should be referred to emergency services immediately with probable diabetic ketoacidosis. Children and young people who are <5% dehydrated and not clinically unwell usually tolerate oral rehydration and subcutaneous insulin.15,[502] [evidence level IV] The level of care needs to be re-evaluated frequently and care should be supervised by an experienced diabetes team.503 [evidence level IV]

N.5.2.3 What is the ideal treatment of diabetic ketoacidosis?

General

Guidelines for the treatment of children and young people with diabetic ketoacidosis have been published by the British Society for Paediatric Endocrinology and Diabetes (available at http://www.bsped.org.uk/BSPEDDKAApr04.pdf).[502] [evidence level IV] These guidelines, which are which are reproduced in Appendix D, are an updated version of earlier guidelines for the treatment of diabetic ketoacidosis in children and young people that were published jointly by Diabetes UK and the British Society for Paediatric Endocrinology and Diabetes. The current guidelines take account of recently published consensus statements developed by the European Society for Paediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society.[503] [evidence level IV] The guidelines highlight the need for further research to investigate the effectiveness of different concentrations of rehydration fluid, the rate of rehydration and the concentration of insulin infusion in the management of diabetic ketoacidosis.

A Department of Health Expert Advisory Group has proposed guidelines for the provision of high dependency care for children and young people (available at www.dh.gov.uk/assetRoot/04/03/ 42/73/04034273.pdf).[505] [evidence level IV]

Monitoring

A consensus statement on monitoring diabetic ketoacidosis in children and young people has recommended that hour-by-hour clinical observations, intravenous and oral medication, fluids and laboratory results should be documented throughout the treatment period.503 [evidence level IV]

Monitoring should include:[503] [evidence level IV]

- hourly heart rate, respiratory rate and blood pressure
- hourly, or more frequent, fluid input and output (with the possibility of urinary catheterisation where there is impaired consciousness)
- electrocardiogram monitoring to assess T-waves for evidence of hyperkalaemia/ hypokalaemia in severe diabetic ketoacidosis
- hourly capillary blood glucose monitoring (to be cross-checked against laboratory venous glucose)
- laboratory testing of electrolytes, urea, haematocrit, blood glucose and blood gases every 2–4 hours (with hourly monitoring of electrolytes in more severe cases)
- hourly, or more frequent, neurological observations for warning signs and symptoms of cerebral oedema, including headache, inappropriate slowing of heart rate, recurrent vomiting, changes in neurological status (restlessness, irritability, increased drowsiness, incontinence) or specific neurological signs (such as cranial nerve palsies and papillary response), rising blood pressure and decreased oxygen saturation.

It may be difficult to discriminate cerebral oedema from other causes of altered mental status and so those who perform monitoring should be instructed to alert the physician should any of the warning signs and symptoms be thought to have occurred.503 [evidence level IV]

Fluid and salt

A retrospective study showed that decreasing the amount of fluid given in the first 24 hours, from 5.1 l/m2/24 hours to 4.35 l/m2/24 hours increased the time taken for acidosis to be resolved (16.7 **±**8.4 hours versus 12.6 **±**4.1 hours, p=0.01), although the rate of cerebral oedema was not affected.[506] [evidence level III]

A consensus statement on diabetic ketoacidosis in children and young people concerning water and salt replacement made the following recommendations.503 [evidence level IV]

- Water and salt deficiencies should be replaced, taking into account intravenous or oral fluids that may have been given before treatment and prior to assessment.
- Initial intravenous fluid administration and, if required, volume expansion, should start immediately with an isotonic solution (0.9% saline or balanced salt solutions such as Ringer-Lactate solution), the volume and rate of administration depending on circulatory status. The volume is typically 10–20 ml/kg over 1–2 hours, repeated if necessary.
- Crystalloid (not colloid) should be used.
- Subsequent fluid management should be with a solution with a tonicity equal to or greater than 0.45% saline (by administering 0.9% saline, Ringer-Lactate solution or 0.45% saline with added potassium). The rate of intravenous fluid should be calculated to rehydrate evenly over at least 48 hours.
- In addition to clinical assessment of dehydration, calculation of effective osmolality may help to guide fluid and electrolyte therapy.
- Fluid should be infused each day at a rate not usually exceeding 1.5–2 times the usual daily requirement according to age, weight, or body surface area. Urinary losses should not be added to the calculation of replacement fluids.

Insulin therapy

Insulin administered by an initial bolus as well as continuous insulin infusion has been compared with continuous insulin infusion only in an RCT involving children and young people (n=38, 58 episodes). There was no significant difference in serum glucose concentration after 1 hour of treatment.[507] [evidence level Ib]

Continuous versus intermittent insulin therapy for diabetic ketoacidosis was evaluated in a study involving adults (n=26). Insulin was administered as bolus injections (50 units/2 hours), compared with high-dose continuous insulin infusion (10 units/hour), and low-dose continuous insulin infusion (2 units/hour) after an initial loading dose (3 units). There was no significant difference between high-dose continuous infusion and bolus injection in the time to diabetic ketoacidosis recovery (measured by normalisation of blood glucose, bicarbonate, ketone bodies and pH). However, low-dose continuous infusion resulted in a higher blood glucose level after 6 hours of treatment compared with bolus injections and high-dose continuous insulin infusion (serum glucose: 284 ±36 mg/100 ml with bolus injections; 297 ±34 mg/100 ml with continuous insulin infusion; 392 ±84 mg/100 ml with low-dose continuous infusion; $p < 0.05$).[508] [evidence level Ib]

Continuation of insulin administration past the usual cut-off point of near-normoglycaemia was investigated in adults in one study (n=22). Continuation of insulin was shown to decrease the time taken for resolution of ketosis (measured as duration of elevated blood 3-hydroxybutyrate levels: 5.9 ±0.8 hours versus 21.8 ±3.4 hours, RR 0.30, 95% CI 0.16 to 0.54, p=0.0004).[509] [evidence level Ib]

Human and porcine insulins were compared in an RCT involving adults (n=21). No significant differences in recovery rates were seen following the administration of human and porcine insulins for treatment of diabetic ketoacidosis.[510] [evidence level Ib]

Insulin therapy routes

Intramuscular administration of insulin (0.1 units/kg body weight every 2 hours) was compared with a combination of subcutaneous and intravenous administration (0.05 units/kg body weight given subcutaneously every 4 hours and 0.05 units/kg body weight given intravenously every 4 hours in a small study involving children and young people, n=10).

There was no significant difference between the treatment groups in terms of the time needed to achieve serum glucose <6.46 mmol/l.511 [evidence level IIa]

Insulin administration routes were also evaluated in an RCT involving adults (n=45). No significant differences were seen for time to metabolic recovery or total insulin dose or fluid replacement requirements in intravenous, intramuscular and subcutaneous insulin administration. A significantly higher rate of decrease in glucose and ketone bodies was observed in the first 2 hours following intravenous insulin, but this difference was not maintained over the rest of the recovery period.[512] [evidence level Ib]

Administration routes of low doses of insulin were evaluated in an RCT involving adults (n=30).The RCT showed that low doses of insulin given by intermittent intramuscular injection or by constant intravenous infusion after an initial intravenous loading dose were similarly effective in controlling diabetic ketoacidosis. Time to recovery from diabetic ketoacidosis and total insulin dose required did not differ between the two treatment groups.[513] [evidence level Ib]

Insulin dose

Clinical consensus has suggested a starting dose of 0.1 units/kg/hour.502 [evidence level IV] Some health professionals have expressed the opinion, not substantiated by clinical evidence, that a lower dose (0.05 units/kg/hour) may be safer, reducing the risk of cerebral oedema. It may therefore be prudent to consider a low dose of insulin in pre-school children and consider reducing from a high to a low dose of insulin if there is a rapid fall in blood glucose.

A consensus statement on diabetic ketoacidosis in children and young people concerning insulin therapy recommends the following.[503] [evidence level IV]

- Insulin should be delivered intravenously. If this is not possible, the intramuscular or subcutaneous route of insulin administration can be used, but poor perfusion may impair absorption of insulin.
- Intravenous insulin should be commenced at 0.1 units/kg/hour.
- The dose of insulin should be adjusted thereafter with the resolution of ketoacidosis (pH >7.30, HCO3>15 mmol/l and/or closure of anion gap) and with the optimisation of blood glucose.

An unduly rapid decrease in plasma glucose concentration and possible development of hypoglycaemia can be prevented by adding glucose to the intravenous fluid when plasma glucose falls to approximately 14–17 mmol/l (250–300 mg/dl).

If there is no improvement in biochemical parameters of ketoacidosis (pH, anion gap), the patient should be reassessed, insulin therapy should be reviewed, and other causes of impaired response to insulin (such as infection, errors in insulin preparation, and adhesion of insulin to tubing with very dilute solutions) should be considered.

Bicarbonate

The use of intravenous bicarbonate together with insulin therapy for treatment of diabetic ketoacidosis was investigated in an RCT involving adults (n=20). The study showed that intravenous sodium bicarbonate therapy increased recovery of arterial pH and bicarbonate levels in the first 2 hours (7.24 ±0.04 versus 7.11 ±0.09, p <0.02, 95% CI 0.06 to 0.19), but did not affect pCO2 or blood glucose levels. All patients in the bicarbonate group developed hypokalaemia.[514] [evidence level Ib]

The effects on diabetic ketoacidosis recovery rates of two different intravenous bicarbonate doses, adjusted to initial arterial pH, and a placebo were investigated in a study involving adults (n=21). There were no significant differences between patients treated with

bicarbonate and placebo in terms of the rates of decline of glucose and ketone levels in blood and cerebrospinal fluid, or in the times required for plasma glucose to reach <13.9 mmol/l (converted from 250 mg/dl reported in the study), blood pH to reach 7.3 (hydrogen ion concentration 50 nmol/l), and bicarbonate levels to reach 15 mmol/l.515 [evidence level Ib]

A consensus guideline suggested that bicarbonate is rarely, if ever, necessary. Continuing acidosis usually means insufficient resuscitation. Bicarbonate should only be considered in children who are profoundly acidotic (pH <7.0) and shocked with circulatory failure. Its only purpose is to improve cardiac contractility in severe shock.[502] [evidence level IV]

A consensus statement on diabetic ketoacidosis in children and young people concerning bicarbonate therapy concluded that treatment with bicarbonate provided no clinical benefit and that although resuscitation fluids containing various buffering agents (bicarbonate, acetate, lactate) have been used, the efficacy and safety of these agents have not been established.[503] [evidence level IV]

Potassium

A consensus statement on diabetic ketoacidosis in children and young people concluded that potassium replacement is required and that replacement therapy should be based on serum potassium measurements. Potassium replacement should begin immediately in patients who are hypokalaemic, although it should be started at the same time as insulin therapy in other patients. In hyperkalaemic patients, potassium replacement should be delayed until urine output is documented. An initial concentration of potassium in the infusate of 40 mmol/l should be used and potassium replacement should continue throughout intravenous fluid therapy.[503] [evidence level IV]

Phosphate therapy

Two RCTs have examined the addition of phosphate therapy to insulin treatment for diabetic ketoacidosis.

The first RCT involved adults (n=30) and showed no significant differences in the rates of decline of glucose and ketone bodies after phosphate treatment. A protective effect against hypophosphataemia was observed, but only on the first day of treatment.[516] [evidence level Ib]

The second RCT involved patients aged 14–58 years (n=44) and provided no evidence of a clinical benefit of phosphate therapy.[517] [evidence level Ib]

A consensus statement on diabetic ketoacidosis in children and young people concluded that: there was no evidence for a clinical benefit of phosphate replacement, but that severe hypophosphataemia should be treated; potassium phosphate salts may be used with or instead of potassium chloride/acetate; and administration of phosphate may induce hypocalcaemia.

Provided that careful monitoring is performed to avoid hypocalcaemia, potassium phosphate may be safely used in combination with potassium chloride or acetate to avoid hyperchloraemia. [503] [evidence level IV]

Somatostatin therapy

An RCT investigated the addition of the somatostatin analogue octreotide to low-dose insulin therapy in adults (n=23). This study showed that octreotide reduced the time taken for correction of ketonuria. However, there were no such effects on the recovery rates from hyperglycaemia and acidosis.[518] [evidence level Ib]

N.5.2.4 What are the ways of preventing cerebral oedema in association with diabetic ketoacidosis?

We found no evidence relating to the prevention of cerebral oedema. However, two studies investigated factors associated with cerebral oedema.

A retrospective study compared three groups of children and young people: the first group had diabetic ketoacidosis and cerebral oedema (n=61); the second did not have diabetic ketoacidosis or cerebral oedema but they were matched to the first group (n=181); and the third group had diabetic ketoacidosis but not cerebral oedema (n=174). Factors associated with increased risk of cerebral oedema were: lower initial partial pressure of arterial carbon dioxide (for each decrease of 7.8 mmHg, 1.0 kPa: RR 3.4, 95% CI 1.9 to 6.3, p <0.001); higher initial serum urea nitrogen concentration (for each increase of 9 mg/dl, 25 mmol/l: RR 1.7, 95% CI 1.2 to 2.5, p=0.003); and treatment with bicarbonate (RR 4.2, 95% CI 1.5 to 12.1, p=0.008).[498] [evidence level III] The outcome of cerebral oedema was also examined in the study: 28% of people with cerebral oedema died or were left in a persistent vegetative state, whereas 13% survived with mild to moderate neurological disability. Factors associated with poor outcomes were: neurological depression at the time of diagnosis of cerebral oedema (coefficient 2.2, 95% CI 1.06 to 3.37, p <0.001); high initial serum urea nitrogen concentration (coefficient 0.086, 95% CI 0.01 to 0.16, p=0.02); and intubation with hyperventilation to a pCO2<22 mmHg (65% versus 11%, coefficient 2.1, 95% CI 0.29 to 3.84, p=0.02).519 [evidence level III] A small case–control study that compared pre-school children with diabetic ketoacidosis and cerebral oedema (n=4) with age-matched children and young people who had diabetic ketoacidosis without cerebral oedema (n=10) found that cerebral oedema was associated with increased initial weight (13.0 ±3.7 kg versus 9.1 ±2.2 kg, p <0.05) and decreased serum glucose (26.3 ±3.3 mmol/l versus 43.1 ±19.7 mmol/l, p <0.05). Pre-school children with cerebral oedema initially had relatively normal serum sodium and osmolality, but later developed lower minimum serum sodium (128.8 ±4.4 mmol/l versus 142.2 ±8.9 mmol/l, p <0.02) and lower minimum serum osmolality (265.5 ±10 Osm/kg versus 296.7 ±15.3 Osm/kg, p <0.01).[520] [evidence level III]

N.5.2.5 Treatment of cerebral oedema

A consensus statement on diabetic ketoacidosis in children and young people concerning treatment of cerebral oedema recommended the following.[503] [evidence level IV]

- Treatment should begin as soon as the condition is suspected.
- The rate of fluid administration should be reduced.
- Intravenous mannitol should be given (0.25–1.09 g/kg body weight over 20 minutes) in patients with signs of cerebral oedema before impending respiratory failure. Hypertonic saline (3%) 5–10 ml/kg body weight over 30 minutes may be an alternative to mannitol.
- Repeat intravenous mannitol after 2 hours if there is no initial response.
- Intubation and ventilation may be needed.

N.5.2.6 What is the acceptable reference range for ketones in children and young people with type 1 diabetes?

We found no studies that examined the acceptable reference range for ketones in children and young people with type 1 diabetes.

It has been suggested that a hand-held ketone sensor beta-hydroxybutyrate reading ≥ 1 mmol/l requires further action, and that levels >3 mmol/l necessitate medical review. Falling beta-hydroxybutyrate levels during treatment of diabetic ketoacidosis can indicate adequacy of treatment. The median time taken, from initiation of treatment, for beta-hydroxybutyrate concentrations to fall to below 1 mmol/l was 8.46 hours (range 5–58.33 hours).521 [evidence level IV] Laboratory enzymatic assays have been shown to have good correlation with

bedside (r=0.97, p <0.05) and hand-held blood ketone monitoring for measurement of beta-hydroxybutyrate.522,523 [evidence level III]

In a study of children and young people measuring beta-hydroxybutyrate eight times/day for two weeks, 6.0% of the beta-hydroxybutyrate measurements were ≥ 0.2 mmol/l (n=45).524 [evidence level III]

Urine ketone dip tests can be used to screen for ketonuria in ketoacidosis and ketosis. A study using urine ketone dip tests in which screening of patients with diabetic ketoacidosis or ketosis was recorded in medical notes detected 97% of patients with diabetic ketoacidosis (95% CI 94% to 99%, 96 out of 99 cases of diabetic ketoacidosis) and 98% of those with diabetic ketosis (95% CI 95% to 99%, 46 out of 47 cases of diabetic ketosis).525 [evidence level III] A further study showed that the anion gap and serum bicarbonate level were less sensitive but more specific than the urine ketone dip test for the detection of diabetic ketoacidosis and diabetic ketosis.526 [evidence level III]

N.5.2.7 What is the ideal frequency for measuring ketones in children and young people with type 1 diabetes?

We found no studies that looked at the ideal frequency for measuring ketones.

N.5.2.8 What are the indications for measuring ketones in children and young people with type 1 diabetes?

It has been recommended that children and children with diabetes measure beta-hydroxybutyrate when symptoms such as nausea or vomiting occur (to differentiate ketoacidosis from gastroenteritis), during infections, during periods with high blood glucose (>15 mmol/l), and when they are aware of ketonuria.524 [evidence level IV]

N.5.2.9 Recommendations

Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.

Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children’s ward.

Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.

Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.

Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/l), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.

N.5.2.10 Research recommendations

Further research is needed to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis in children and young people with type 1 diabetes.

Further research is needed to investigate the effectiveness of different concentrations of rehydration fluid, the rate of rehydration, the use of albumin infusion and the dose of insulin infusion in the management of diabetic ketoacidosis in children and young people.

N.5.3 Section 5.3 Surgery

N.5.4 Section 5.4 Intercurrent illness

N.5.5 Section 5.5 Screening for complications and associated conditions

N.5.5.1 Retinopathy (page 105 of the 2004 guideline)

Young people with long-standing type 1 diabetes and/or poor glycaemic control are at risk of developing retinopathy. A cohort study of 937 patients aged 6–20 years found that 9% of children under the age of 11 years had retinopathy (mean age 9.5 years, n=110), whereas 29% of young people over the age of 11 years were found to have retinopathy (mean age 14.0 years, n=827). The odds of developing retinopathy increased with increased duration of diabetes (OR 1.22, 95% CI 1.16 to 1.29), increased age (OR 1.13, 95% CI 1.06 to 1.21), and increased HbA1c levels (OR 1.26, 95% CI 1.11 to 1.43).[536] [evidence level IIb] These findings were supported by results of a study of 90 children and young people (mean age 14.7 years) attending an outpatient clinic in Wales, in which 14% of the children and young people developed retinopathy.[537] [evidence level IIb] The children and young people who developed retinopathy attended the clinic less frequently than those who did not develop retinopathy (1.7 visits/year versus 2.9 visits/year, p <0.05).

The NICE clinical guideline on the management of type 1 diabetes in adults states that eye surveillance should start at diagnosis in post-pubertal new onset patients. Screening should continue at 1-year intervals unless otherwise indicated, in which case referral to an ophthalmologist is appropriate.[538] Digital retinal photography should be used for population surveillance, and tropicamide should used to achieve mydriasis for photography. Routine eye surveillance should also include visual acuity testing.

Evidence suggests that screening for retinopathy should be undertaken annually.[9,15,539–543] [evidence level III–IV] However, recommendations differ with respect to the age at which to start screening. Several advisory panels, consensus groups and national recommendations have suggested various retinal screening programmes (see Table 79).

Table 79: Guidance on the age at which to start retinal screening.

When to start screening	Evidence level
After age 15 years, or 5 years after onset	III–IV[539]
Age 12 years	IV[9]
Age 11 years, 5 years after pre-pubertal onset, or 2 years after post-pubertal onset	IV[15]
Age 12 years, or at post-pubertal onset	IV[543]
Within 3–5 years of diagnosis in children and young people older than 9 years	IV[541]
5 years after diagnosis if onset occurs before the age of 30 years	IV[544]
5 years after onset but not before puberty unless otherwise indicated	IV[542,545]

A 1998 survey of consultant paediatricians who provide care for children and young people with diabetes aged under 16 years in the UK found that 87% of respondents indicated that retinopathy screening was performed on an annual basis. Of those screening for retinopathy, 31% reported screening all children, 59% reported screening patients over the age of 12 years and 40% reported screening if patients were over the age of 12 years or if they had had diabetes for more than 5 years.[18] [evidence level III]

N.5.5.2 Nephropathy (page 105 of the 2004 guideline)

Early detection of microalbuminuria aims to minimise morbidity and mortality associated with nephropathy and end-stage renal failure in people with type 1 diabetes. Accepted predictors of nephropathy are elevated levels of timed urine albumin excretion rate, albumin:creatinine ratio, and albumin concentration.[546,547] [evidence level III] A population-based study in Oxford estimated a 40% cumulative probability of developing microalbuminuria for children and young people (<16 years old) 11 years after diagnosis.[548] [evidence level IIb]

A cohort study of 937 patients aged 6–20 years found that no children under the age of 11 years had an albumin excretion rate ≥ 20 µg/min (mean age 9.5 years, n=110), whereas 5% of children over the age of 11 years had an albumin excretion rate ≥ 20 µg/min (mean age 14.0, n=827). The odds of developing an albumin excretion rate ≥ 20 µg/min increased with increased duration of diabetes (OR 1.19, 95% CI 1.06 to 1.33) and increased age (OR 1.37, 95% CI 1.16 to 1.62).[536] [evidence level IIb] Similar results were obtained in a second study (age of patients not reported).[548] [evidence level IIb]

A consensus guideline has defined persistent microalbuminuria (two out of three successive samples) in children and young people with type 1 diabetes as follows:[15] [evidence level IV]

- albumin excretion rate of 20–200 µg/min in timed overnight collection
- albumin excretion rate of 30–300 mg/24 hours in 24-hour collection
- albumin:creatinine ratio of 2.5–25 mg/mmol (spot urine)
- albumin:creatinine ratio of 30–300 mg/g (spot urine)
- albumin concentration of 30–300 mg/l (early morning).

Evidence-based and consensus guidelines have advised that annual nephropathy screening should be undertaken in children and young people with type 1 diabetes.[9,15] [evidence level IV] Recommendations for screening methods include:

- 24-hour albumin excretion rate
- morning albumin:creatinine ratio testing
- early morning urine albumin concentration
- spot urine albumin:creatinine ratio
- timed urine collection.

Various times for starting microalbuminuria screening have been proposed:

- 5 years after onset, or at the age of 11 years, or at puberty in the case of pre-pubertal onset[15]
- 2 years after onset of diabetes in the case of post-pubertal onset[15]
- at the age of 12 years.[9]

Clinically based reviews recommend annual timed urine albumin excretion rate screening to start at puberty or after having diabetes for 3–5 years,[539] or annual random microalbuminuria spot checks (<30 µg/mg creatinine) and 24-hour collection (<30 mg/24 hours).[540] [evidence level IV]

A 1998 survey of consultant paediatricians who provide care for children and young people with diabetes aged under 16 years in the UK found that 66% of respondents measured urinary microalbumin regularly at clinic, although 26% reported that this was limited to certain age groups and/or durations of diabetes (n=163 respondents).[18] [evidence level III]

The NICE clinical guideline for the management of type 1 diabetes in adults recommends that all people with type 1 diabetes bring in an annual first-passed morning urine specimen, which will be tested for an albumin:creatinine ratio. Abnormal results require repeat

screening at each clinic visit or every 3–4 months. Implications of detected abnormal albumin excretion rates should be discussed with children and young people and their families.[538]

Healthcare professionals should be made aware of other risk factors for microalbuminuria (elevated blood pressure and smoking) and other causes of microalbuminuria (such as urinary tract infections, glomerulonephritis, menstrual bleeding and strenuous exercise).[15] [evidence level IV]

N.6 Chapter 6 Psychological and social issues

N.6.1 Section 6.1 Emotional and behavioural problems

N.6.2 Section 6.2 Anxiety and depression

N.6.3 Section 6.3 Eating disorders

N.6.4 Section 6.4 Cognitive disorders

N.6.5 Section 6.5 Behavioural and conduct disorders

N.6.6 Section 6.6 Non-adherence

N.6.7 Section 6.7 Psychosocial support

Given that psychological and social issues have a substantial influence on acceptance of, coping with and outcome of type 1 diabetes in children and young people and their families, explicit psychological components of management to support the acceptance of therapy have been investigated.

A recent UK systematic review identified a lack of good-quality evidence on the effectiveness of structured behavioural support for young people with type 1 diabetes; the limited amount of evidence that was available was drawn from studies conducted in the USA. The review highlighted the following issues.[72] [evidence level Ia]

- Educational and psychosocial interventions have small to medium beneficial effects on various diabetes management outcomes.
- Interventions are more likely to be effective if they show the interdependence of the different aspects of diabetes management, and interventions should be evaluated by assessing outcomes that the intervention is specifically designed to change.
- There is no systematic understanding of whether interventions should be targeted (for example, modified for different disease stages, different types of diabetes management problems, or the different age groups subsumed by adolescence).

A 1998 survey of consultant paediatricians who provide care for children and young people with diabetes aged under 16 years in the UK found that just over 25% reported that there was some form of ‘counsellor’ regularly attending the children’s diabetes clinic (n=17 192 children and young people).[18] [evidence level III] Most of the counsellors were psychologists (75.8%), with other clinics supported by psychiatrists (11.3%), nurse therapists (6.5%) or other counsellors (6.5%) such as psychotherapists.

The young people’s consultation day organised for this guideline in collaboration with the NCB found that the parents of young people with type 1 diabetes felt that there should be easy access to psychology services and suggested that paediatric diabetes care teams should include a psychologist.[38] [evidence level IV]

Associations between support and diabetes outcomes

An evidence-based guideline for children and young people with type 1 diabetes advised regular assessment for psychological problems and recommended cognitive coping strategies for diabetes-specific problems.[9] [evidence level IV]

Seventy-four young people (mean age 15.2 years) were surveyed about various psychosocial aspects of dealing with diabetes.[636] [evidence level III] Perceived impact of diabetes and peer support were significant predictors of depression ($p < 0.002$ and $p < 0.02$, respectively). Family support was significantly associated with all self-management measures ($p < 0.05$) and perceived efficacy of control-mediated dietary self-management ($p < 0.001$). After 6 months of follow-up (70% of the original sample), young women reported higher levels of depression and anxiety ($p < 0.02$ and $p < 0.001$), and more peer support ($p < 0.05$) than young men.[637]

These gender differences are supported by an observational study of 74 young people (mean age 14.2 years).[638] Young women reported more emotional support and support for blood glucose monitoring from peers than did young men ($p < 0.01$). When controlled for age, support from friends was related to adherence to blood glucose monitoring ($p < 0.0001$).

A descriptive study asked 13 families of children and young people with newly diagnosed type 1 diabetes about the psychology service offered and whether it met the demands and needs of children and young people and their parents.[639] [evidence level III] Two families indicated a positive need for a psychology service, while the rest of the sample expressed reluctance in seeking and receiving psychological support. This reluctance might reflect a perceived stigma associated with receiving psychological support.

Psychosocial interventions to enhance support

General behavioural interventions

A systematic review of 18 behavioural interventions (education or skills training) compared with standard care found that theoretical behavioural interventions had a small to moderate beneficial effect (effect size 0.47 ±0.60) in improving psychosocial, self-management and metabolic outcomes.[640] [evidence level Ia–IIa]

More specifically, an RCT has shown a beneficial effect of coping skills training combined with intensive insulin therapy compared with intensive insulin therapy regimen alone on quality of life, coping with diabetes, wellbeing and monthly HbA1c in people aged 12–20 years. Outcomes were measured at study entry and after 3, 6 and 12 months of follow-up (n=65, 77 and 75, respectively).[641–643] [evidence level Ib] Coping skills training aimed to retrain inappropriate or non-constructive coping styles and form more positive behaviour patterns. Over a 12-month period, intensive insulin therapy improved glycaemic control ($p < 0.01$). Intensive therapy combined with coping skills training, however, was more effective than intensive therapy alone (HbA1c at 12 months: 7.5% versus 8.5%, $p = 0.011$).

Another RCT compared the effectiveness of behavioural family systems therapy (n=38) with an education and support group (n=40) and a control group of current therapy (n=41) in young people with type 1 diabetes and their families.[644,645] [evidence level Ib] Metabolic control, parent–adolescent relationship, parent–child conflict and teen adjustment to diabetes were assessed at study entry and after 3, 6 and 12 months of follow-up (n=119 families). Baseline differences in family structure were evident between groups and 73% of the participants had HbA1clevels above 10%.[644] [evidence level Ib] After receiving behavioural family systems therapy, education and support, or current therapy for 3 months, there was evidence of a significant effect for all groups on mean change in family composite scores (overt conflict and skills deficits) in parent–adolescent relationship assessment. Composite scores favoured behavioural family systems therapy recipients in decreasing diabetes-specific conflict between children and young people and their parents ($p = 0.05$). Total HbA1c

values increased significantly over the study period for all groups (p <0.05). The behavioural family systems therapy group had a lasting improvement in the extreme beliefs scale of parent–adolescent relationship (p <0.01), while overt conflict and skills deficits between parents and teenagers showed improvement for the behavioural family systems therapy group compared with the current therapy group post-treatment (p <0.03) and at 6 months follow-up (p <0.05). Composite behavioural family systems therapy scores in parent–child conflict measurement differed from the other groups at post-treatment (p <0.04) and 6 months (p <0.05). This difference only remained when compared with the current therapy group (p <0.05) at 12 months follow-up. There were no significant between-group differences for teenagers' adjustment to diabetes outcomes.

Family support

A consensus-based guideline has stated that the diabetes care team or a healthcare professional trained in child/family therapy should provide support for explicit psychological problems or psychiatric disorders among young patients or their family members.[15] [evidence level IV] An evidence-based guideline has encouraged parental support and family communication, with psychological intervention targeting family disruption and stress.[9] [evidence level IV]

RCTs have studied interventions employed to improve outcomes associated with the disruptive effects that diabetes has on family life. Interventions that have been tested include family-to-family networks, community-based family support, behavioural family systems therapy, teamwork intervention, attention control, education and support groups. Outcome measures that have been studied are glycaemic control, diabetes-related conflict, parental involvement in management, children's and young people's adjustment to diabetes care, and parents' anxiety levels.[646–649]

Families participating in an attention control and teamwork group trial (n=57) reported a greater decrease in diabetes-specific conflict than did recipients of standard care (n=24) after 24 months of follow-up (p <0.03).[646] [evidence level Ib] However, glycaemic control was not improved significantly in the intervention group (p <0.07). The intervention group had less parental involvement in the administration of insulin (p <0.03).

Young people and their families reporting conflict were randomised into a behavioural family systems therapy group (n=39), an education/support group (n=40), or a control group (n=40). Diabetes conflict scores decreased more in mothers whose children received behavioural family systems therapy compared with other groups (p <0.05). However, there were no significant changes in diabetes conflict scores in any of the treatment groups.[647] [evidence level Ib]

Mothers of chronically ill children (aged 7–11 years, 40% of whom had type 1 diabetes) were randomised into a community-based family support group (n=73) or a control group (n=66) to examine changes in their wellbeing over 15 months.[648] [evidence level Ib] Community-based family support improved wellbeing in mothers with elevated baseline anxiety and poor health status (p <0.001 and p <0.01). Community-based family support reduced maladjustment scores in the children from 19% to 10%, whereas maladjustment scores increased from 15% to 21% in the control group. However, community-based family support had no effect on children's anxiety, depression, or self-esteem.

A cohort study examined the effectiveness of 10 half-hour sessions of home-based behavioural family systems therapy on general psychological functioning of young people, family functioning, and mothers' diabetes-associated conflict scores.[650] [evidence level IIb] Inclusion criteria for participants were a history of two or more missed clinic appointments and chronically poor metabolic control. This small study (n=18, age range 13–18 years) found significant improvements in psychological and family functioning.

An observational study described helpful and non-helpful forms of support as reported by 16 young people (age range 11–18 years) and their parents.[651] [evidence level III] Parents defined responses of helpful support as directive guidance, non-directive support, positive social interaction and forms of physical assistance. Young people described helpful support as that which related to parents giving or not giving tangible assistance and non-helpful support as directive guidance.

Peer support

Social support systems aim to foster positive and informed health-related choices for young people with chronic conditions. A narrative review examined 32 studies that assessed the types of social support used to enhance metabolic control in young people with type 1 diabetes.[652] [evidence level IV] The types of support were qualitative family support (18 studies), regimen-specific support (11 studies), sibling and peer support (6 studies), and communication (2 studies).

An RCT aimed at improving adolescent diabetes management by implementing mentoring/sponsorship programmes for young people aged 12–16 years consisted of a range of social and educational activities (n=54). The young people were randomised to receive bimonthly contact from adult mentors with type 1 diabetes or no mentoring.[653] [evidence level Ib] Young people with mentors were less likely to agree with statements such as 'I wish I didn't have diabetes' and demonstrated significant increases in self-esteem in relation to social acceptance and romantic appeal ($p < 0.05$). Mean glycosylated haemoglobin levels decreased in young people with mentors compared with those without.[653] [evidence level Ib]

The effect on glycaemic control of self-monitoring of blood glucose supported by problem solving was assessed in an RCT: 30 young people (aged 11–14 years) with type 1 diabetes who received the problem solving support were compared with 30 young people with type 1 diabetes who did not receive the problem solving support.[654] [evidence level Ib] HbA1 levels followed over 18 months were lower in the intervention group than in the control group (10.1 ±2.0% versus 11.0 ±2.3%, $p=0.04$). The intervention group used self-monitored blood glucose measurements more often when exercising than the young people with type 1 diabetes who did not receive the problem solving support (60.0% versus 33.3%, $p=0.04$).

Home-based intervention was assessed in 21 children and young people (age range 8–17 years) over 15 months.[655] [evidence level IIb] Children and young people in the intervention group chose three people from their family, peers, neighbourhood or school to participate in a support scheme. Children and young people with lower glycaemic levels received more support from team peers ($r=-0.50$, $p < 0.05$). Perceptions of peer support were not correlated with glycaemic control, self-reported adherence, or the number of support team peers participating in the intervention.

Another study paired 21 young people with diabetes with their best friends and invited them to attend a 4-week intervention programme.[656] [evidence level IIb] The study reported higher levels of diabetes knowledge and support ($p < 0.0001$) and a higher ratio of peer-to-family support ($p < 0.05$) compared with pre-intervention measurements. Friends reported improved self-perception post-intervention ($p < 0.0001$), and parents reported a decrease in diabetes-related conflict at home ($p < 0.05$). Peers provided more support than family members.

N.6.8 Section 6.8 Adolescence

N.7 Chapter 7 Continuity of care

N.7.1 Section 7.1 Communication between organisations

N.7.2 Section 7.2 Transition from paediatric to adult care

Page 127 of the 2004 guideline: In particular the NICE guideline for the diagnosis and management of type 1 diabetes in adults recommends the following.[538]

- Preprandial and postprandial blood glucose targets of 4–7 mmol/l and less than 9 mmol/l, respectively, apply to adults because it becomes easier to attain glycaemic control as maturity increases.
- Adults should not be offered routine screening for coeliac disease or thyroid disease because these conditions are rare in adults.
- Adults should be offered routine screening for cardiovascular risk factors and neuropathy because these are complications of type 1 diabetes that arise in adulthood.
- Healthcare professionals may use the term ‘A1C’ instead of ‘HbA1c’ when communicating with adults with type 1 diabetes.

N.8 Chapter 8 Auditable standards

Table 80: Suggested audit criteria

Recommendation	Criterion	Exception	Definition of terms
Children and young people with type 1 diabetes should be offered an ongoing integrated package of care care by a multidisciplinary paediatric diabetes care team. To optimise the effectiveness of care and reduce the risk of complications, the diabetes care team should include members with appropriate training in clinical, educational, dietetic, lifestyle, mental health and foot care aspects of diabetes for children and young people	a. A paediatric team providing care for a child or young person with type 1 diabetes should include members with specialist training in clinical, educational, dietetic, lifestyle, mental health and foot care aspects of diabetes appropriate for children and young people	None	
At the time of diagnosis, children and young people with type 1 diabetes should be offered home-based or inpatient management according to clinical need, family circumstances and wishes, and residential proximity to inpatient services. Home-based care with support from the local paediatric diabetes care team (including 24-hour	a. A newly diagnosed child or young person with type 1 diabetes has an offer of home-based or inpatient initial management documented in their notes	Children and young people with diabetic ketoacidosis Children and young people with social or emotional difficulties Children under the age of 2 years Children and young people who live a long way	Initial – treatment received starting from diagnosis continuing for the first 2 weeks Social and emotional difficulties – a situation judged by the paediatric diabetes care team to indicate that home-based or

Recommendation	Criterion	Exception	Definition of terms
telephone access to advice) is safe and as effective as inpatient initial management		from inpatient facilities	outpatient initial management would not be in the best interests of the child or young person or their family
	b. A child or young person with newly diagnosed type 1 diabetes who receives home-based or inpatient initial management should have it documented in their notes	None	
Children and young people with type 1 diabetes and their families should be offered timely and ongoing opportunities to access information about the development, management and effects of type 1 diabetes. The information provided should be accurate and consistent and it should support informed decision making	a. A child or young person with type 1 diabetes has it documented in their notes that an offer of timely and ongoing opportunities to access information about development, management and effects of type 1 diabetes in relation to care has been made. The information should be accurate and consistent and it should support informed decision making	None	
Children and young people with type 1 diabetes and their families should be informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and that their care package should be designed to attempt to achieve this	a. A child or young person with type 1 diabetes has it documented in their notes that they have been informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia	None	HbA1c is measured with a DCCT-standardised assay
	b. A child or young person with type 1 diabetes has it documented in their notes that they have been offered testing of their HbA1c levels two to four times per year	None	
	c. A child or young person with type 1 diabetes has an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia	Children and young people with haemoglobinopathies or abnormalities of erythrocyte turnover	Haemoglobinopathies that interfere with glycated haemoglobin measurement – see www.missouri.edu/~diab

Recommendation	Criterion	Exception	Definition of terms
			etes/ngsp/factors.htm
	d. A child or young person with type 1 diabetes has an HbA1c level of less than 7.5% with frequent disabling hypoglycaemia	None	
Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes	a. A child or young person with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes	None	
	b. A child or young person with diabetic ketoacidosis recovers without complications	None	Complications – death, cerebral oedema with permanent neurological disability
Children and young people with type 1 diabetes should be offered screening for: coeliac disease at diagnosis and at least every 3 years thereafter until transfer to adult servicesa thyroid disease at diagnosis and annually thereafter until transfer to adult services retinopathy annually from the age of 12 years microalbuminuria annually from the age of 12 years blood pressure annually from the age of 12 years	a. A child or young person with type 1 diabetes has it documented in their notes that an offer of a coeliac disease test at diagnosis *and at least every three years has been made* [*Following the development of 'Coeliac disease: recognition and assessment of coeliac disease' (NICE clinical guideline 86, 2009) NICE updated its guidance on screening for coeliac disease in children and young people with type 1 diabetes. Specifically, the recommendation to re-test for coeliac disease at least every 3 years after diagnosis was removed.]*	Children and young people who are known to have coeliac disease	
	b. A child or young person with type 1 diabetes has it documented in their notes that an offer of a thyroid disease test at	Children and young people who are known to have thyroid disease	

[a] We have updated our guidance on screening for other conditions in children and young people with type 1 diabetes; we have removed the recommendation to re -test for coeliac disease at least every 3 years after diagnosis. This update follows the development of 'Coeliac disease: recognition and assessment of coeliac disease' (NICE clinical guideline 86, 2009).

Recommendation	Criterion	Exception	Definition of terms
	diagnosis and every year subsequently has been made		
	c. A child or young person with type 1 diabetes has it documented in their notes that an offer of a retinopathy test every year from the age of 12 years, has been made	None	
	d. A child or young person with type 1 diabetes has it documented in their notes that an offer of a microalbuminuria test every year from the age of 12 years has been made	None	
	e. A child or young person with type 1 diabetes has it documented in their notes that an offer of blood pressure measurement every year from the age of 12 years has been made	None	
Children and young people with type 1 diabetes should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and wellbeing	a. A child or young person with type 1 diabetes or their family referred to a mental health specialist should be seen as soon as possible	None	

N.9 Appendix A Understanding NICE guidance – information for the families and carers of children with type 1 diabetes, and the public

N.9.1 About this information

This information describes the guidance that the National Institute for Clinical Excellence (called NICE for short) has issued to the NHS on the diagnosis and management of type 1 diabetes in children and young people in the community and in hospitals. It is based on ‘Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults’, which is a clinical guideline produced by NICE for doctors, nurses and others working

in the NHS in England and Wales. NICE has also issued information describing the guidance on the diagnosis and management of type 1 diabetes in adults.

N.9.1.1 Clinical guidelines

Clinical guidelines are recommendations for good practice. The recommendations in NICE guidelines are prepared by groups of health workers, lay representatives with experience or knowledge of the condition being discussed, and scientists. The groups look at the evidence available on the best way of treating or managing a condition and make recommendations based on this evidence.

There is more about NICE and the way that the NICE guidelines are developed on the NICE website (www.nice.org.uk). You can download the booklet The Guideline Development Process – An Overview for Stakeholders, the Public and the NHS from the website, or you can order a copy by phoning the NHS Response Line on 0870 1555 455 (quote reference number N0472).

N.9.1.2 What the recommendations cover

NICE clinical guidelines can look at different areas of diagnosis, treatment, care, self-help or a combination of these. The areas that a guideline covers depend on the topic.

The recommendations in 'Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults' (NICE Clinical Guideline number 15), which are also described here, cover the care that should be available from the NHS to children and young people with type 1 diabetes. In this information, a child is someone younger than 11 years of age, a young person is 11 or older and younger than 18, and an adult is 18 or older. The recommendations include how the diagnosis should be made and the options that should be offered at different times.

The information that follows tells you about the NICE guideline on type 1 diabetes. It doesn't attempt to explain diabetes or its management in detail. NHS Direct is a starting point to find out more. Phone NHS Direct on 0845 46 47 or visit the website at www.nhsdirect.nhs.uk

If you have questions about the specific options covered, talk to a member of your diabetes care team.

N.9.1.3 How guidelines are used in the NHS

In general, health workers in the NHS are expected to follow NICE's clinical guidelines. But there will be times when the recommendations won't be suitable for someone because of his or her specific medical condition, general health, wishes or a combination of these. If you think that the care you or your child receives does not match what's described in the pages that follow, talk to a member of the diabetes care team.

If you want to read the other versions of this guideline

There are four versions of this guideline:

- this one
- the NICE guideline, 'Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults' (NICE Clinical Guideline 15)
- the quick reference guide, which is a summary of the main recommendations in the NICE guideline; NICE has sent copies of the quick reference guide to doctors and other health professionals working in the NHS
- the full guideline, which contains all the details of the guideline recommendations, how they were developed and information about the evidence on which they were based.

All versions of the guideline are available from the NICE website (www.nice.org.uk). This version and the quick reference guide are also available from the NHS Response Line – phone 0870 1555 455 and give the reference number(s) of the booklets you want (N0623 for this version, N0560 for this version in English and Welsh, and N0622 for the quick reference guide).

N.9.1.4 Explanation of medical words and terms

Short explanations of some of the medical words and terms used in this booklet are provided on pages 147 to 148.

N.9.2 Type1 diabetes

Type 1 diabetes happens when the cells in the pancreas that produce insulin are damaged by the body's immune system. Insulin is the main substance that coordinates how the body handles glucose (sugar) after it enters the blood from digested food. Without enough insulin, the amount of glucose in the blood becomes higher than normal.

There are two groups of problems that can happen as a result of type 1 diabetes. First, a sudden, severe lack of insulin can cause immediate problems, including one kind of coma. Second, having blood glucose levels that are too high for long periods can damage the blood vessels, heart, nerves, feet, kidneys and eyes.

Type 1 diabetes is managed by putting insulin into the body – this is sometimes called 'insulin replacement' because you are replacing the insulin that would normally be made in the body. There are different types of insulin, and insulin is usually given by injection or using what's known as an insulin pump (see pages 137 to 139).

N.9.3 Diagnosis

Doctors should follow the advice of the World Health Organization when they are deciding on a diagnosis of type 1 diabetes in children and young people (the document with this advice can be found on the Internet at http://whqlibdoc.who.int/hq/1999/WHO_NCD_NCS_99.2.pdf). The advice is outlined in the next paragraph.

Type 1 diabetes in children and young people is nearly always simple to diagnose. Usually the person has high levels of glucose in their blood and urine, and chemicals known as ketones in their urine (sometimes they are very ill with ketoacidosis – see page 143). Occasionally, symptoms may be very mild: even so, blood glucose levels are always higher than they should be.

If it's thought that a child or young person may have type 1 diabetes, they should be able to see a children's diabetes care team that same day. The health professionals in this team should be able to confirm whether it is type 1 diabetes and to start to look after the child or young person if it is. There is more information on children's diabetes care teams on page 135.

Sometimes, it's possible that a child or young person may have another type of diabetes (different types of diabetes need different treatments). Doctors should think about this if the child or young person:

- has several close relatives with diabetes
- is overweight
- is Black or Asian (or has a Black or Asian background)
- needs quite a small amount of insulin to control their blood glucose levels, even when they're not in a partial remission phase (this is an initial period when a person's body is

still able to make some insulin so they don't need to have the full pattern of insulin replacement straight away)
- does not need insulin at all
- hardly ever or never has ketones in their urine when they have high levels of glucose in their blood
- has signs that their body doesn't use insulin normally (for example, they may have brown markings on their skin – this is known as acanthosis nigricans)
- has other conditions at the time the diabetes is diagnosed, such as eye problems or deafness.

Children and young people diagnosed with type 1 diabetes should have their details kept on a register, for example at their clinic or doctor's practice, so that their diabetes care team knows who they are and can make sure they get the care they need.

N.9.4 Straight after diagnosis

N.9.4.1 The children's diabetes care team

A team of health professionals called a children's (paediatric) diabetes care team should be involved in confirming the diagnosis of type 1 diabetes in a child or young person. From that time onwards, it's this team that the child or young person should see for treatment and care.

A children's diabetes care team is what's known as a multidisciplinary team: it's made up of different types of health professional with specialist knowledge and up-to-date training of, in this case, treating and caring for children and young people with diabetes. Between them, the team members should know about:
- teaching people about or giving information on diabetes, or both
- nutrition for children and young people with diabetes
- how diabetes affects a child or young person's life and how the effects can be managed
- mental health problems (such as anxiety) that may affect a child or young person with diabetes
- looking after the feet of a child or young person with diabetes

The team should offer the child or young person a 'package' of care that brings all these things together. And this should continue to be on offer as the child or young person gets older. The child or young person and their family should be involved in the decisions made about the package of care.

N.9.4.2 Staying at home or going into hospital

At the time of diagnosis, a child or young person should be offered care at home or in hospital, depending on:
- how likely they are to need medical help quickly (for example, if they are poorly at diagnosis they are likely to need to be in hospital)
- their family's circumstances and wishes
- how far they live from the hospital.

Normally, being cared for at home is as good as being cared for in hospital, as long as the diabetes care team is involved and the person or their family can get advice when they need it. But a short time in hospital should be offered for:
- young children (under 2 years)
- children and young people with social or emotional problems
- children and young people who live a long way from the hospital.

N.9.4.3 Diabetic ketoacidosis

If the first sign of type 1 diabetes is that the child or young person has diabetic ketoacidosis, they should be treated in hospital (see page 143).

N.9.4.4 Dealing with the diagnosis

After the diagnosis, children, young people and their families should be given the chance to talk about their feelings and any worries. They should be offered support that's suited to their individual needs (for example, it should be suited to their age, how upset they feel, their background and their culture). They should also be told about support groups for people with diabetes (see page 146).

N.9.4.5 24-hour advice

Children and young people with type 1 diabetes and their families should be able to get advice from their diabetes care team 24 hours a day.

Learning about type 1 diabetes and how to manage it

Soon after the diagnosis, children and young people should be given the chance to learn:

- the aims of insulin therapy
- how insulin is given
- how and when to check their blood glucose levels
- how glucose levels are affected by food and drink, exercise, and being unwell
- the signs of a hypoglycaemic episode and what to do if this happens (this is known as having a 'hypo', where blood glucose drops to a low level).

These things should be covered in a structured education programme rather than being discussed informally.

N.9.4.6 Starting insulin

In most cases, insulin is started straight away in the first day or two of diagnosis (see page 137 for more information about insulin).

N.9.5 Ongoing care

The following sections describe the ongoing care you should receive, including the information you should be offered, day-to-day management of diabetes and dealing with problems that can happen because of diabetes.

N.9.6 Education about type 1 diabetes

Children and young people with type 1 diabetes, and their families, should be offered information about the development, management and effects of type 1 diabetes as and when they need it. Things should be explained in such a way that the information can be understood, so each person feels able to take part in the discussions and decisions about how the diabetes should be managed. It's also important that children, young people and their families aren't told different things by different members of the care team, and that the information they are given is right. There should be an opportunity to ask questions and to discuss different issues about diabetes at every clinic visit.

The way in which a child or young person is given information should be matched to their age and maturity, culture, and their wishes and those of their family. How much the family already knows about type 1 diabetes should also be taken into account. Health professionals

should be particularly careful that useful information is available for children, young people and parents with special needs. These include people with disabilities and people who find it difficult to speak or read English.

Children's diabetes care teams should be in regular contact with school staff who look after children and young people with type 1 diabetes. They should offer staff education and practical information about diabetes and its management.

Children and young people with type 1 diabetes and their families should be told how to find out about government disability benefits that they may be able to claim.

N.9.6.1 Information for an emergency

It's a good idea for children and young people to wear or to carry something, such as a bracelet, that tells people that they have type 1 diabetes, just in case they need help while they're out.

N.9.7 Using insulin

Type 1 diabetes happens when the body doesn't make the insulin it needs to control the amount of glucose in the blood. So insulin needs to be put into the body to do this. At first, a person may only need a low dose of insulin to control their blood glucose because their body is still making some insulin itself – this period is called a partial remission phase (or 'honeymoon period'). This period does not last, and it can't be made to last longer by having more than two daily insulin injections or by using an insulin pump.

If the balance of insulin and food is not quite right, the person can become hypoglycaemic – too much insulin means that the blood glucose level becomes so low that there isn't enough to supply the body. Children, young people and their families should be told how to reduce the likelihood of a hypo and what to do if it happens.

The main types of insulin are described in the box below.

Types of insulin

In people without diabetes, there's normally a low level of insulin in the blood. After a meal, the level of insulin increases to deal with the sudden increase of glucose in the blood that comes from the food or drink.

Different types of insulin are available for people with type 1 diabetes. They work for different lengths of time. By matching the type of insulin to a person's needs, it's usually possible to get a pattern of glucose control that is either similar to the normal pattern or that gives the same overall control of glucose levels. The main categories of insulin are:

- **rapid-acting insulin analogues**: (an insulin analogue is a synthetic form of insulin made to be similar to human insulin, but with characteristics that affect how long it lasts in the body) rapid-acting insulin analogues aim to work like the insulin normally produced to cope with a meal; their effect falls away quickly
- **short-acting insulins**: these work more slowly than rapid-acting insulin analogues, and their effect may last up to 8 hours
- **intermediate-acting insulins**: these have an effect that lasts longer, and can even last through the night
- **long-acting insulin analogues**: these have an effect that can last for a longer period, even a whole day.

A **biphasic insulin** is a mixture of rapid-acting insulin analogue or short-acting insulin together with intermediate-acting insulin.

It's not possible to have insulin in a tablet form because it is destroyed by the juices in the stomach and intestine. So insulin has to be put into the body in a way that bypasses these, using injections or a pump.

Children and young people with type 1 diabetes should be offered the insulins that are likely to suit them best. The choice depends on the child or young person's individual needs and

what's appropriate for them according to the instructions in the patient information leaflet supplied with the insulin.

N.9.7.1 Insulins containing intermediate-acting insulin

Insulin products that contain intermediate-acting insulin should be mixed before being used (following the instructions in the patient information leaflet supplied with the insulin).

N.9.7.2 Insulin timings

There are different patterns for taking insulin. The number of times each day and the exact times of the day that the person has to take insulin will depend on the types of insulin being taken. The more common daily patterns for taking insulin are shown in the box below.

Insulin timings

One, two or three insulin injections per day: these are usually injections of short-acting insulin or rapid-acting insulin analogue mixed with intermediate-acting insulin.

Multiple daily injection regimen: the person has injections of short-acting insulin or rapid-acting insulin analogue before meals, together with one or more separate daily injections of intermediate-acting insulin or long-acting insulin analogue.

Insulin pump therapy: a pump worn on the body gives a regular or continuous feed of insulin into the skin (see below) – the medical name is continuous subcutaneous insulin infusion.

Pre-school and primary school children

For a pre-school or primary school child, the insulin pattern should be individually designed to suit the specific needs of the child.

Multiple daily injection regimens

A young person or child who is using a multiple daily injection regimen should be warned that, at first, they may find that they become hypoglycaemic more often, put on a bit of weight, or both.

Young people (11 or older) should be able to try a multiple daily injection regimen (see box above) to keep their glucose levels under control. But they should only try this as part of a 'package' of care, because having the whole package improves glucose control. This package should include:

- continuing education about diabetes
- help with diet
- being taught how to use insulin delivery systems and how to monitor their own blood glucose levels (known as 'self-monitoring')
- support for emotional problems or to overcome difficult behaviour patterns
- help from doctors, nurses and dietitians with expert knowledge about diabetes in young people.

If a young person finds it hard to keep their blood glucose levels under control with a multiple daily injection regimen, they should be offered extra help from the diabetes care team and, if it is appropriate, they should be offered a different insulin regimen (one, two or three times a day or insulin pump therapy).

If a young person finds it difficult to keep to the multiple injection regimen, they should be able to change to two insulin injections a day.

Using rapid-acting analogues

For children and young people using multiple daily insulin injections, injecting a rapid-acting insulin analogue before eating helps with glucose control. For pre-school children, it may be better to inject it shortly after they've eaten, just in case they don't actually eat their food.

Insulin pumps

Sometimes it's impossible to keep to the target HbA1cwithout having problems with hypoglycaemia, even with multiple daily injections (see 'Checking blood glucose' on page 139 for more information on HbA1c). In this case, a child or young person should be offered the option of trying an insulin pump (a system that puts a regular or continuous amount of insulin into the body), if the diabetes care team and the child or young person and their family feel that that they are able, and want, to use the system.

If a child or young person is going to try a pump, they should be trained how to use it. A trained specialist team should be involved in starting them off with the pump, and should provide advice if it's needed once the pump is being used. After a person has been using a pump for a while, the specialist team should see whether it might be a good idea to try a switch to multiple daily injections that include insulin glargine (a long-acting insulin analogue).

N.9.7.3 Insulin delivery systems

Children and young people should be able to choose the insulin delivery system they want to use to give themselves their insulin, although the options (for example, syringes or pens) will depend on the type of insulin they have and what's suitable for them.

If needles are used for injections, the needles should be the right length for the child or young person (short needles for children and young people with less body fat and longer needles for children and young people with more body fat).

N.9.8 Other medicines for diabetes

Children and young people with type 1 diabetes should not be prescribed acarbose, glibenclamide, gliclazide, glipizide, tolazamide, or glyburide to help with their diabetes (these are not brand names, they are the general or generic names). These medicines wouldn't be expected to improve glucose control and they may increase the risk of hypoglycaemia.

Another medicine, metformin, should be prescribed for a child or young person with type 1 diabetes only as part of a research study. Not enough is currently known about its effect on blood glucose for it to be used routinely.

N.9.9 Checking blood glucose

It is important to keep blood glucose levels under control. The diabetes care team should explain that if the glucose level is too high, there's a risk of developing problems with the eyes, kidneys, nerves, feet and heart later in life. But if their glucose level gets too low, a child or young person can become hypoglycaemic – feeling dizzy and faint, and even possibly blacking out.

When there's a high amount of glucose in the blood, some of it gets attached to a part of the blood called the haemoglobin. At any particular time, the amount that's attached shows the amount of glucose that has been in the blood over the last 6 to 12 weeks. The part with the glucose is called HbA1c, and this is what should be measured in the clinic's test for blood glucose. The diabetes care team should talk to the child or young person about the level of HbA1c to aim for – normally the aim is a level that's under 7.5%. The child or young person's care package should aim to help the child or young person to reach this target, while at the same time making sure that they don't have problems with hypoglycaemia too often. The

person shouldn't be having repeated hypos that put them in the position of needing help from someone else – not only is this unpleasant but it can make the person worry about the next time it's going to happen.

Children and young people who continue to have a very high HbA1c(over 9.5%) should be offered extra help to improve their glucose control.

N.9.9.1 At the clinic

At the clinic, the diabetes team should check how a child's or young person's blood glucose control has been over the previous few months. This is best done using a test that measures a substance in the blood called HbA1c. Tests for HbA1c should be carried out two to four times a year, and team members should have the up-to-date results when they see the child or young person in the clinic, so that they can decide whether any immediate changes are needed to the person's insulin or diet.

N.9.9.2 Self-monitoring of blood glucose

When a person checks their own blood glucose, it's known as 'self-monitoring' – the test is different from the HbA1c test that's done in the clinic because it measures the amount of glucose in the blood at that moment. People who self-monitor their blood glucose control properly are more likely to get to and keep to their target HbA1c because their overall awareness of their blood glucose is better. The diabetes team should explain how and when to self-monitor (blood is used, not urine, because urine doesn't give such reliable results).

Children and their families, and young people should be able to choose the type of equipment for self-monitoring that suits them best. The diabetes team should explain that the best way to keep a check on glucose levels is to use a glucose monitor with a memory that stores results, together with a diary to write down the results as well as other things that happen (such as, food eaten and hypos) as this helps reduce the frequency of hypoglycaemia.

Children and young people should be offered a system that monitors their glucose levels all the time if either or both of the following continues to happen.

- They don't realise when they are becoming hypoglycaemic.
- Their blood glucose often becomes too low (hypoglycaemia) or too high (hyperglycaemia).

Regular self-monitoring should be part of children and young people's care packages, together with diet management, and having continuing opportunities to learn about diabetes and regular contact with members of the diabetes care team.

What to aim for

Self-monitoring of blood glucose measures the amount of glucose in the blood as 'mmol/litre' (mmol/litre is pronounced 'milli mole per litre'). The diabetes care team should explain that the aim of self-monitoring is to get a blood glucose level of 4–8 mmol/litre before a meal, and less than 10 mmol/litre after a meal. Remember, this is different from the HbA1c test – self-monitoring of blood glucose is a measure of how much glucose there is in the blood at the moment, whereas HbA1c is a measure of how well blood glucose has been controlled in the last few months.

To try to keep to the targets, children and young people should be taught how to adjust their insulin and diet. How often someone should check their blood glucose depends on their individual circumstances.

Diabetes care teams should encourage children and young people who have multiple daily insulin injections to check their blood glucose before meals, at bedtime and occasionally at

night-time and to adjust their insulin if they need to. Children and young people who have two insulin injections a day should be encouraged to take measurements before meals, at bedtime and occasionally at night-time and to look at the general pattern ('trend') and adjust their insulin dose if they need to.

For someone who is trying to work out the best way to control their blood glucose, it's a good idea to check the levels more than four times a day. If a child or young person is unwell, they should also check their blood glucose more than four times a day.

Glucose results need to be thought about in the light of what's going on in the child or young person's world at that time, and diabetes care teams should explain this. Many different things can affect glucose control – for example, stress because of exams or moving schools can have an effect.

N.9.10 Diet

In general, children and young people with type 1 diabetes need the same balance of foods as other people of their age, and diabetes care teams should talk about this. Very young children (newborns, infants and pre-school children) should have their individual dietary needs worked out by their diabetes team.

Sometimes, using insulin can make a person put on weight. Children and young people should be offered advice and support with their diet so that they can keep to or reach a healthy weight while, at the same time, they achieve good glucose control.

Children and young people should be encouraged to learn what different foods provide to the body and how they affect glucose levels. As part of their package of care, a child or young person who has multiple daily insulin injections should have the chance to learn in depth how to change their insulin dose and timing according to what they eat. Information and advice should also be available to children and young people to help them cope with the practicalities of managing their diabetes during special times like religious fasts and feasts.

Together with their families, children and young people with type 1 diabetes should have the chance to learn about healthy eating and how they can reduce the risk of having problems such as heart disease or stroke when they're older. For example, they should be encouraged to eat five portions of fruit and vegetables a day as part of a healthy lifestyle. They should also have help to make changes in their diet after type 1 diabetes is diagnosed and at different times from then on if changes are needed.

N.9.10.1 Bedtime snacks

It's a good idea for most children and young people with type 1 diabetes to eat a snack at bedtime. The team should talk about this with the child and their family, or the young person. They should agree on the best things to have as a snack and exactly when to have them.

N.9.11 Exercise

Regular exercise at any level is good for all children and young people because it can lower the chance of having problems such as heart disease or stroke in later life.

Diabetes isn't a barrier to taking part in any sort of sport or exercise, as long as the child or young person makes the right changes in their insulin and diet. Their diabetes care team should help with this. For some sports, such as scuba diving, a lot of advice will be needed from the team. Information may also be available from local and national diabetes support groups and organisations.

One of the things it's important to know about is the effect of exercise on blood glucose. The diabetes care team should advise on checking glucose levels before and after exercising.

This is so the child or young person can see how the glucose levels change and can work out how to manage their insulin and diet to allow for the effects of the exercise. The diabetes team should also explain how exercise can cause hypoglycaemia during or after exercise – a long period of exercise can result in hypoglycaemia several hours later. They should advise on how to reduce the chance of a hypo; this should include advice to:

- have an extra carbohydrate-based snack before exercise, as needed (for example, if blood glucose is under 7 mmol/litre before exercise)
- make sure that there's a carbohydrate-based snack close by during and after exercise.

If a child or young person's daily routine changes so that they exercise more or less often (for example, if they start training for an event), their insulin dose, carbohydrate intake or both may need to be changed.

If blood glucose is above 17 mmol/litre and there are signs of ketosis, the child or young person should be especially careful when exercising. Ketosis is the medical name for a build-up of ketones – the signs are a feeling of, or actual, sickness and stomach pain. The diabetes care team should discuss this.

N.9.12 Drinking, smoking and using recreational drugs

N.9.12.1 Alcohol

The particular problems that alcohol can cause people with type 1 diabetes (for example, nighttime hypoglycaemia) should be explained to young people (11 years or older) with type 1 diabetes. They should also be offered an alcohol education programme to help them learn more.

Young people who choose to drink should be advised:

- to eat a carbohydrate-based snack or meal before and after drinking
- to check their blood glucose regularly and to try to keep their glucose levels in the right range by eating foods containing carbohydrate.

N.9.12.2 Smoking

Smoking causes all sorts of health problems. For example, it increases the risk of problems such as heart disease and stroke. Diabetes care teams should talk about this with children, young people and their families. Children and young people should be encouraged not to smoke. If they smoke, they should be helped to stop and should be offered a programme designed to stop people smoking (this is called a smoking cessation programme).

N.9.12.3 Recreational drugs and substance abuse

The dangerous effects of recreational drugs and other substances that can be misused should be explained – both the general problems and the ones that can specifically affect someone with diabetes.

N.9.13 Problems that can happen because of diabetes

N.9.13.1 Hypoglycaemia

Hypoglycaemia is when the blood glucose dips too low so there's not enough glucose going to the different parts of the body. It can make a person feel dizzy and, if it gets bad, they can black out.

Diabetes care teams should explain what to do if there are signs of hypoglycaemia. Children and young people should, for example, always have a carbohydrate-based snack or drink

close by, and their glucose monitor should be handy so that their glucose levels can be checked easily. Parents, other carers and schoolteachers should also be given the chance to learn about the signs of hypoglycaemia and what to do if the child or young person becomes hypoglycaemic.

If a child or young person is feeling dizzy and weak with hypoglycaemia, the advice is:

- do something straight away (don't wait to see how it goes)
- the child or young person should eat or drink something containing sugary carbohydrate that will quickly get sugar into the bloodstream (sometimes it will be easier to drink something than to eat it; if the person is being sick they may have to have several lots of small amounts) – blood glucose should start to rise in 5 to 15 minutes
- once they feel better or their blood glucose returns to the usual level, they should eat starchy carbohydrate foods that will keep the glucose levels up (unless they are just about to have a meal or are using an insulin pump)
- re-check blood glucose within 15 minutes.

If a child or young person has severe hypoglycaemia and becomes unconscious, the advice for the people who treat them is shown in the box below.

Advice when a child or young person has severe hypoglycaemia

- If in hospital, medical staff should inject glucose (10%) into a blood vessel (vein) if this is possible.
- If not in hospital or if it isn't possible to inject into a blood vessel, inject glucagon (a hormone that raises blood sugar levels) into a muscle or get the person to swallow a concentrated dose of glucose. If alcohol has caused or added to the hypoglycaemia, glucagon is unlikely to work, and intravenous glucose will have to be used.
- If the child is over 8 years old or weighs more than 25 kg, use 1 mg glucagon (all the injection); use 500 micrograms (half the injection) for younger or lighter children.
- Blood glucose should start to get back to usual levels within 10 minutes.
- Providing they are awake, give starchy carbohydrate food to eat as they start to get better or their blood glucose gets back to the usual level.
- The child or young person may not be properly awake for several hours afterwards. If this is the case, their blood glucose should be checked regularly to see if further glucose is needed.
- Get medical help if the child or young person does not seem any better or their blood glucose levels haven't increased after 10 minutes.

Parents, school nurses and other carers should have glucagon available to use if there's an emergency, especially if severe hypoglycaemia is quite likely. They should also be given the opportunity to learn how to give glucagon.

N.9.13.2 Diabetic ketoacidosis

Diabetic ketoacidosis happens if the body becomes unusually stressed (during an illness, for example) and there's not enough insulin to cope with the effects; for example, if the person has not been eating or drinking properly and perhaps has been sick as well. The body starts to break down fat for energy, and ketones build up in the blood and urine. Blood glucose levels are very high (hyperglycaemia) and the person is dehydrated. What's known as a metabolic acidosis develops (the body's natural acid levels become disturbed). Diabetic ketoacidosis is a medical emergency. The person may go into a coma if they aren't treated.

A child or young person who has diabetic ketoacidosis should be treated following the guidelines published by a professional body (the British Society for Paediatric Endocrinology and Diabetes).

At first, a child or young person who has ketoacidosis should go into a hospital high-dependency unit or should be in a high-dependency bed on a children's ward. If they're under 2, they should go into a children's intensive care unit. An older child should be moved

to the children's intensive care unit if their condition is getting worse, a problem is suspected or if they are not recovering as expected.

If the child or young person seems well but their acid level is still abnormal (pH less than 7.3), they may be given fluids and insulin injections (which should be given frequently). Their blood glucose should be checked regularly.

N.9.13.3 Checking for other medical problems

There's a chance that children and young people with type 1 diabetes can develop other conditions linked with type 1 diabetes. There are also problems that can develop as a result of having too much glucose in the blood over a long period of time. Because of these risks, children and young people should be checked for certain things at regular times.

- When they are first being diagnosed with diabetes, the child or young person should be tested for signs of coeliac disease, a condition that affects the digestive system. *This test should be repeated at least every 3 years until the person moves to an adult clinic. [Following the development of 'Coeliac disease: recognition and assessment of coeliac disease' (NICE clinical guideline 86, 2009) NICE updated its guidance on screening for coeliac disease in children and young people with type 1 diabetes. Specifically, the recommendation to re-test for coeliac disease at least every 3 years after diagnosis was removed.]*
- They should be tested for signs of thyroid disease when they're diagnosed and then every year after that until they move to an adult clinic. The thyroid is a gland in the neck that produces hormones. The important effects of these hormones include metabolic regulation (the metabolism is the balance of chemical reactions in the body).
- Once a child is 12 years old, they should be tested every year for:
  - signs of eye disease linked to diabetes, known as retinopathy
  - the presence of a protein, called albumin, in their urine (this can be a sign of kidney problems)
  - high blood pressure.
- They should be offered a foot check every year.
- At every clinic visit, a member of the diabetes care team should ask if they can look at the injection sites to check they're OK.
- Regular dental check-ups and eye tests are recommended as for other children and young people.

Juvenile cataract (where the lens in the eye becomes cloudy), necrobiosis lipoidica (which is skin changes, usually on the legs), and Addison's disease (where the body produces only very low amounts of steroid hormones) are some conditions that can be linked with type 1 diabetes, but they are rare. The diabetes care team should bear them in mind, though, when they see children and young people with type 1 diabetes.

Finally, every time a child or young person goes to the clinic, their height and weight should be measured in a private room. The readings should be put on a growth chart. This will show how their weight and height are changing as they get older, so it's easy to see whether they are growing normally and have a normal weight. Unexpected changes in a person's height or weight can be a sign of problems with their glucose control. The child or young person's body mass index should also be worked out at every clinic visit. Body mass index (or BMI for short) is a standard way of working out a person's weight in relation to their height.

It is **not** recommended that children or young people with type 1 diabetes have regular checks of:

- their blood lipid levels (lipids are fat-like substances, and the amount in the blood can be linked with the risk of heart disease and stroke), or

- their nerve function (older people with diabetes can develop problems with their nerves and their ability to feel things).

When a young person transfers to an adult diabetes clinic, they should be offered regular checks for blood lipid levels and nerve function.

Emotional problems and difficult behaviour

Having type 1 diabetes can make a child or young person more likely to have an emotional problem or to behave in a way that's difficult to manage than others of their age. The diabetes care team should be aware of this and should look out for signs that problems might be developing.

If a child or young person has a disorder that's making them behave in a difficult way, they and their families should be able to see mental health professionals who can help them.

Anxiety and depression

Children and young people with type 1 diabetes can suffer from anxiety, depression or both. This may happen if, for example, they've had type 1 diabetes for a while but suddenly seem to have problems keeping their glucose levels under control. The diabetes care team should know the signs of anxiety and depression and should watch out for them in the children and young people they look after. Also, if a child or young person has problems keeping their blood glucose levels under control, their team should discuss anxiety and depression with them and should offer them the chance to be checked for signs of these.

If the diabetes team thinks a child or young person may have anxiety or depression, they should arrange without delay for them to see one or more health professionals who specialise in helping children and young people with mental health problems.

Eating disorders

Children and young people with type 1 diabetes, especially young women, are more likely to develop an eating disorder than others. If a child or young person does have an eating disorder, they may also have problems with hyperglycaemia, repeated spells of hypoglycaemia, and symptoms linked with a condition called gastric paresis, which is where the stomach doesn't empty food into the intestine properly. The diabetes care team should be aware of these things. If they think a child or young person has an eating disorder, they should arrange for them to see one or more health professionals who specialise in helping children and young people with mental health problems. These health professionals should then work with the diabetes care team to help the child or young person.

Problems with memory and thoughts

Young (pre-school) children who have very frequent severe hypoglycaemia have a chance of developing problems with their memory and thought processes. This risk is small, but is especially linked to children who have hypoglycaemia that causes seizures. The diabetes care team should discuss this with parents. They may recommend having an assessment of the child's ability to think clearly and to remember things (this ability is called cognitive function).

Teachers should be aware of the links between type 1 diabetes and possible problems with cognitive function.

N.9.14 Advice if a child or young person is unwell

Children, young people and their families should be told what changes to make to their insulin and their diet if they're unwell. This advice is sometimes called 'sick-day rules'. The diabetes care team should talk about using short-acting insulin or rapid-acting insulin analogues to help control blood glucose during the illness. These should be available to the child or young person, as should test strips for checking ketones in the blood, urine or both.

A child or young person who is unwell should try to check their blood glucose more than four times a day (see page 139).

N.9.15 Immunisations

Children and young people with type 1 diabetes and their families should be told about the Department of Health recommendations that apply to people with diabetes.

- Children (over 6 months) and young people with diabetes should have a yearly flu jab.
- Immunisation against pneumococcal infection is recommended for those over 2 months. Pneumococcal infection is a bacterial infection that can cause pneumonia, meningitis and septicaemia (infection in the blood).

N.9.16 Having an operation

If a child or young person needs an operation, it should only be done at a hospital that has special facilities for children and young people with diabetes. The surgeon and anaesthetist should talk to the diabetes care team before the child or young person goes into hospital or, if they've gone in for an emergency operation, as soon as possible afterwards.

All medical centres and hospitals that look after children and young people with diabetes should have sets of written instructions about the care of children and young people with diabetes who are having an operation.

N.9.17 Long-distance travel

Children, young people and their families should have education about when to take their insulin and when to eat when travelling across time zones during long-distance travel. They should have the chance to learn about any problems that might happen during the journey and while they are away, and how to deal with them.

N.9.18 Coping with diabetes

Some people find it particularly difficult to use their insulin properly and to have the right food and drinks all the time. Teenagers, in particular, may want to rebel against their therapy. The diabetes care team should be alert to signs of this. For example, the team should think about whether this could be a problem if someone is having trouble keeping their glucose levels under control or if someone who has had type 1 diabetes for a while suddenly has one or more episodes of diabetic ketoacidosis (see page 143). If they suspect there could be a problem, they should raise it sensitively with the child, young person or their family.

If a young person (11 or older) keeps having episodes of ketoacidosis over quite a short time, they should have a check to make sure that they are feeling OK emotionally and that they aren't having problems with their behaviour.

If a young person is feeling frustrated and is having problems coping with the routine of diabetes, their diabetes care team should try to help them get through the bad patch. Diabetes care teams should be aware that children and young people with type 1 diabetes are more likely to have emotional and behavioural problems than other youngsters.

N.9.19 Help and support

Children and young people should be given the chance to learn ways of coping with their feelings and the consequences of having diabetes. This is especially important for those who have multiple daily insulin injections. Young people should also be able to have some other specific help so they can feel more in control and able to cope. For example, they may have a mentor to talk to (a mentor is someone other than a parent or carer who gets to know the child or young person and gives guidance and advice). Or they may be taught how to use self-monitoring so they can make changes to their diet or insulin to help themselves to control their glucose better.

Children and young people with type 1 diabetes, and their families, should be able to get help from health professionals who specialise in mental health as and when they need it. This is because problems with mental health (such as anxiety and depression, and problems in the family) can affect how well a person manages their diabetes.

Diabetes care teams should understand how important it is to encourage families to help children and young people deal with the day-to-day practicalities of diabetes and with the wider effects on their lives. Family life may also be affected by the child or young person's diabetes, and family members should have the chance to learn some specific ways of dealing with and preventing these effects so problems can be avoided.

A diabetes care team should be able to get advice and help from professionals who work in mental health if they need it to help them care for a child or young person with type 1 diabetes.

N.9.20 Diabetes support groups

The diabetes care team should tell a child or young person, and their parents or carers, about local and national groups for people with diabetes. They should have the contact details for the groups and should know what they have to offer and how people can join and become involved with the groups. This information should be given to the child, young person or parents soon after the diagnosis has been made, and then the team should discuss support groups with them again from time to time.

N.9.21 Moving to an adult diabetes clinic

Young people should be encouraged to carry on going to the diabetes clinic regularly (three or four times a year). Children's and adults' diabetes care teams should make arrangements for special joint clinics for older teenagers and young adults.

When the time comes to move to an adult clinic, the young person should have time to get used to the idea of the move and any changes in their care. They should be told that some things will change – for example, the self-monitoring targets and the routine checks they have for medical problems.

The specific arrangements for moving to the adult clinic will depend on what's done in the local area, although the timing of the change depends on the individual. For example, the move shouldn't be made at a time when other things are changing in the teenager's life.

N.9.22 Where you can find more information

If you need further information about any aspects of type 1 diabetes or the care that you or your child is receiving, please ask a member of the diabetes care team. You can discuss this information with them if you wish, especially if you aren't sure about anything. They will be able to explain things to you. NHS Direct may also be helpful – phone 0845 46 47 or visit the NHS Direct website at www.nhsdirect.nhs.uk

For further information about the National Institute for Clinical Excellence (NICE), the Clinical Guidelines Programme or other versions of this guideline (including the sources of evidence used to inform the recommendations for care), you can visit the NICE website at www.nice.org.uk. On the NICE website you can also find information for the public about other guidance in the following areas. These can also be ordered from the NHS Response Line (phone 0870 1555 455):

- type 1 diabetes in adults, reference number N0559 (based on NICE Clinical Guideline No. 15)
- the use of long-acting insulin analogues for the treatment of diabetes – insulin glargine, reference number N0181 (based on NICE Technology Appraisal Guidance No. 53)
- the use of continuous subcutaneous insulin infusion for diabetes, reference number N0196 (based on NICE Technology Appraisal Guidance No. 57)
- patient education models in diabetes, reference number N0251 (based on NICE Technology Appraisal Guidance No. 60).

N.9.23 Explanation of medical words and terms

Albumin: a blood protein that can leak into the urine – if it's there persistently, it can be a sign of kidney problems.

Body mass index (BMI): a measure of a person's weight in relation to their height, showing if they are overweight or underweight.

Child: in this booklet, a child means someone younger than 11 years.

Diabetes care team: see also 'multidisciplinary team'; for children and young people, the team members should have particular skills and training in looking after children and young people with diabetes. In particular, the team should have members who have specific training in:

- the treatment and care of children and young people with diabetes
- teaching people about or giving information on diabetes, or both
- nutrition for children and young people with diabetes
- how diabetes affects a child or young person's life and how the effects can be managed
- mental health problems (such as anxiety) that may affect a child or young person with diabetes
- looking after the feet of a child or young person with diabetes.

Gastric paresis: where the stomach doesn't empty properly into the intestine.

HbA1c: the abbreviation for glycated haemoglobin: this is a measure of the average level of blood glucose over 6–12 weeks. Children without diabetes have an HbA1c less than 6%. The recommended target for children and young people with type 1 diabetes is less than 7.5%.

Heart attack: where part of the heart is damaged because the heart artery is blocked and blood has been unable to get through to the heart muscle.

High-dependency bed or unit: places in a hospital for children who need to be watched and checked more closely than children on an ordinary children's ward.

Hyperglycaemia: where there is too much glucose in the blood.

Hypoglycaemia: where there is too little glucose in the blood.

Infant: in this booklet, an infant means a baby older than 4 weeks but younger than 1 year.

Insulin analogue: a synthetic form of insulin manufactured to be similar to human insulin, but with new characteristics that can make it shorter-acting (for meal-time use) or longer-acting (as a background insulin).

Ketoacidosis: a condition where the person has raised blood glucose levels and is dehydrated so that a metabolic acidosis develops (where the body's natural acid–base balance becomes disturbed).

Ketones: substances that occur in the body under certain conditions of low blood insulin.

Multidisciplinary team: a team of different types of health professional who work together to make sure that people have the care they need, at the time they need it; for children with diabetes, these are known as children's (paediatric) diabetes care teams.

Multiple daily injection regimen: this is a pattern of taking insulin where the person has injections of short-acting insulin or rapid-acting insulin analogue before meals, together with one or more separate daily injections of intermediate-acting insulin or long-acting insulin analogue.

Newborn baby: in this booklet, a newborn baby (neonate) is a baby up to 4 weeks old.

Pre-school child: in this booklet, a pre-school child is 1 year or older, but younger than 5 years.

Primary school child: in this booklet, a primary school child is 5 years or older, but younger than 11 years.

Retinopathy: disease involving the blood vessels of the inside back wall of the eye (the retina).

Stroke: where the blood stops getting through to an area of the brain.

Young person: in this booklet, a young person is 11 years or older, but younger than 18.

N.10 Appendix D Management of diabetic ketoacidosis

Guidelines for the treatment of children and young people with diabetic ketoacidosis have been published by the British Society for Paediatric Endocrinology and Diabetes (available at http://www.bsped.org.uk/professional/guidelines/docs/DKAGuideline.pdf).[502] [evidence level IV] These guidelines are reproduced below with permission from the British Society for Paediatric Endocrinology and Diabetes. The Glasgow Coma Scale[685] is reproduced with permission from Elsevier.

N.10.1 BSPED Recommended DKA Guidelines

These guidelines for the management of Diabetic Ketoacidosis were originally produced by a working group of the British Society of Paediatric Endocrinology and Diabetes. Modifications have been made in the light of the guidelines produced by the International Society for Pediatric and Adolescent Diabetes (2000) and the recent ESPE/LWPES consensus statement on diabetic ketoacidosis in children and adolescents (Archives of Disease in Childhood, 2004, 89: 188–194).

We believe these guidelines to be as safe as possible in the light of current evidence. However, no guidelines can be considered entirely safe as complications may still arise. In particular the pathophysiology of cerebral oedema is still poorly understood.

Three aspects of the guidelines deserve further mention as being still subject to controversy:

- There is increasing (but not overwhelming) evidence that a fall in plasma sodium concentration during fluid treatment may be associated with the development of cerebral oedema. Hypotonic saline solutions should therefore not be used, and 0.45% saline with dextrose is now the fluid of choice once the initial phase of treatment with normal saline is complete.
- There is some consensus that fluid rehydration should be delivered evenly over 48 hours, and that this practice may reduce the incidence of cerebral oedema. There is no direct evidence for this, and there may be disadvantages such as slowing down correction of the dehydration and acidosis. However, the international consensus group most recently recommended this rate of rehydration.
- The initial intravenous insulin infusion dose is given as 0.1 units/kg/hour. There are some who believe that younger children (especially the under 5's) are particularly sensitive to insulin and therefore require a lower dose of 0.05 units/kg/hour. There is no scientific evidence to alter the recommended larger dose which has proven efficacy in correcting hyperglycaemia and reversing ketosis.

Any information relating to the use of these guidelines would be very valuable. Please address any comments to:

Dr. Julie Edge, Consultant Paediatric Endocrinologist, Department of Paediatrics, Level 4, John Radcliffe Hospital, Headington, Oxford, OX3 9DU.

N.10.2 General

Always accept any referral and admit children in suspected DKA.

Always consult with a more senior doctor on call as soon as you suspect DKA even if you feel confident of your management.

Remember: children can die from DKA.

They can die from -

- Cerebral oedema. This is unpredictable, occurs more frequently in younger children and newly diagnosed diabetes and has a mortality of around 25%. The causes are not known, but this protocol aims to minimise the risk by producing a slow correction of the metabolic abnormalities. The management of cerebral oedema is covered on page 165.
- Hypokalaemia. This is preventable with careful monitoring and management
- Aspiration pneumonia. Use a naso-gastric tube in semi-conscious or unconscious children.

These are general guidelines for management. Treatment may need modification to suit the individual patient and these guidelines do not remove the need for frequent detailed reassessments of the individual child's requirements.

These guidelines are intended for the management of the children who have:

- hyperglycaemia (BG >11 mmol/l)
- pH <7.3
- Bicarbonate <15 mmol/l

and who are

- more than 5% dehydrated
- and/or vomiting
- and/or drowsy
- and/or clinically acidotic

Children who are 5% dehydrated or less and not clinically unwell usually tolerate oral rehydration and subcutaneous insulin. Discuss this with the senior doctor on call.

N.10.3 Emergency management in A & E

N.10.3.1 General Resuscitation: A, B, C

Airway	Ensure that the airway is patent and if the child is comatose, insert an airway. If comatose or has recurrent vomiting, insert N/G tube, aspirate and leave on open drainage.
Breathing	Give 100% oxygen by face-mask.
Circulation	Insert IV cannula and take blood samples (see below). Cardiac monitor for T waves (peaked in hyperkalaemia) If shocked (poor peripheral pulses, poor capillary filling with tachycardia, and/or hypotension) give 10 ml/kg 0.9% (normal) saline as a bolus, and repeat as necessary to a maximum of 30 ml/kg.

Note: (There is no evidence to support the use of colloids or other volume expanders in preference to crystalloids)

N.10.3.2 Confirm the Diagnosis

History:	polydipsia, polyuria
Clinical:	acidotic respiration dehydration drowsiness abdominal pain/vomiting
Biochemical:	high blood glucose on finger-prick test glucose and ketones in urine

Initial Investigations

- blood glucose
- urea and electrolytes (electrolytes on blood gas machine give a guide until accurate results available)
- blood gases (preferably arterial or capillary, but venous gives similar pH)
- PCV and full blood count (leucocytosis is common in DKA and does not necessarily indicate sepsis)

±other investigations only if indicated e.g. CXR, CSF, throat swab, blood culture, urinalysis, culture and sensitivity etc..

(DKA may rarely be precipitated by sepsis, and fever is not part of DKA.)

N.10.3.3 Full clinical assessment and observations

Assess and record in the notes, so that comparisons can be made by others later.

N.10.3.4 Degree of Dehydration

3% dehydration is only just clinically detectable

mild, 5%	**–** dry mucous membranes, reduced skin turgor
moderate, 7.5%	– above with sunken eyes, poor capillary return
severe, 10% (±shock)	– severely ill with poor perfusion, thready rapid pulse, (reduced blood pressure is not likely and is a very late sign)

N.10.3.5 Conscious Level

Institute hourly neurological observations whether or not drowsy on admission.

If in coma on admission, or there is any subsequent deterioration,

- record Glasgow Coma Score (see Appendix 1)
- transfer to PICU
- consider instituting cerebral oedema management (page 165)

N.10.3.6 Full Examination

Looking particularly for evidence of –

Cerebral oedema	Headache, irritability, slowing pulse, rising blood pressure, reducing conscious level N.B. Examine fundi but papilloedema is a late sign.
infection	
ileus	
WEIGH THE CHILD.	If this is not possible because of the clinical condition, use the most recent clinic weight as a guideline, or an estimated weight from centile charts.

N.10.3.7 Does the child need to be on PICU?

YES	**If:** • severe acidosis pH<7.1 with marked hyperventilation • severe dehydration with shock (see below) • depressed sensorium with risk of aspiration from vomiting • very young (under 2 years) • staffing levels on the wards are insufficient to allow adequate monitoring.

N.10.4 Observations to be carried out

Ensure full instructions are given to the senior nursing staff emphasising the need for:

- strict fluid balance
- measurement of volume of every urine sample, and testing for ketones
- hourly BP and basic observations
- capillary blood ketone levels may be available and may be a more sensitive measure of suppression of ketogenesis during treatment
- hourly capillary blood glucose measurements (these may be inaccurate with severe dehydration/acidosis but useful in documenting the trends. Do not rely on any sudden changes but check with a venous laboratory glucose measurement)
- twice daily weight; can be helpful in assessing fluid balance
- hourly or more frequent neuro observations initially
- reporting immediately to the medical staff, even at night, symptoms of headache or any change in either conscious level or behaviour
- reporting any changes in the ECG trace, especially T wave changes suggesting hyperkalaemia

N.10.5 Management

N.10.5.1 Fluids

N.B. It is essential that all fluids given are documented carefully, particularly the fluid which is given in Casualty and on the way to the ward, as this is where most mistakes occur.

a) Volume of fluid

By this stage, the circulating volume should have been restored. If not, give a further 10 ml/kg 0.9% saline (to a maximum of 30 ml/kg) over 30 minutes. (discuss with a consultant if the child has already received 30 ml/kg).

Otherwise, once circulating blood volume has been restored, calculate fluid requirements as follows

Requirement=Maintenance + Deficit

Deficit (litres)=% dehydration × body weight (kg)

Ensure this result is then converted to ml.

Never use more than 10% dehydration in the calculations.

Age	Maintenance requirements
0–2 yrs	80 ml/kg/24 hrs
3–5	70 ml/kg/24 hrs
6–9	60 ml/kg/24 hrs
10–14	50 ml/kg/24 hrs
adult (>15)	30 ml/kg/24 hrs

Add calculated maintenance (for 48 hrs) and estimated deficit, subtract the amount already given as resuscitation fluid, and give the total volume evenly over the next 48 hours. i.e.

$$\text{Hourly rate} = \frac{\text{48 hr maintenance} + \text{deficit} - \text{resuscitation fluid already given}}{48}$$

Example:

A 20 kg 6 year old boy who is 10% dehydrated, and who has already had 20 ml/kg saline, will require

- $10\% \times 20\,\text{kg}$ = 2000 mls deficit
- **plus** $60\,\text{ml} \times 20\,\text{kg}$ = 1200 mls maintenance each 24 hours

  1200 mls

  = 4400 mls
- **minus** $20\,\text{kg} \times 20\,\text{ml}$ = 400 mls resus fluid

  4000 mls over 48 hours=83 mls/hour

Do not include continuing urinary losses in the calculations

b) Type of fluid

Initially use 0.9% saline.

Generally once the blood glucose has fallen to 14–17 mmol/l add glucose to the fluid.

If this occurs within the first 6 hours, the child may still be sodium depleted. Discuss this with consultant, who may wish to continue with Normal saline and added dextrose.

If this occurs after the first 6 hours and the child's plasma sodium level is stable, change the fluid type to 0.45% saline/5% dextrose.

Check U & E's 2 hours after resuscitation is begun and then at least 4 hourly

Electrolytes on blood gas machine can be helpful for trends whilst awaiting laboratory results.

c) Oral Fluids

In severe dehydration, impaired consciousness & acidosis do not allow fluids by mouth. A NG tube may be necessary in the case of gastric paresis.

Oral fluids (e.g. fruit juice/oral rehydration solution) should only be offered after substantial clinical improvement and no vomiting

When good clinical improvement occurs before the 48hr rehydration calculations have been completed, oral intake may proceed and the need for IV infusions reduced to take account of the oral intake.

N.10.6 Potassium

Once the child has been resuscitated, potassium should be commenced immediately with rehydration fluid unless anuria is suspected. Potassium is mainly an intracellular ion, and there is always massive depletion of total body potassium although initial plasma levels may be low, normal or even high. Levels in the blood will fall once insulin is commenced.

Therefore initially add 20 mmol KCl to every 500 ml bag of fluid (40 mmol per litre).

Check U & E's 2 hours after resuscitation is begun and then at least 4 hourly, and alter potassium replacements accordingly. There may be standard bags available; if not, strong potassium solution may need to be added, but always check with another person.

Use a cardiac monitor and observe frequently for T wave changes.

N.10.7 Insulin

Once rehydration fluids and potassium are running, blood glucose will already be falling. However, insulin is essential to switch off ketogenesis and reverse the acidosis.

Continuous low-dose intravenous infusion is the preferred method. There is no need for an initial bolus.

Make up a solution of 1 unit per ml. of human soluble insulin (e.g. Actrapid) by adding 50 units (0.5 ml) insulin to 50 ml 0.9% saline in a syringe pump. Attach this using a Y-connector to the IV fluids already running. Do not add insulin directly to the fluid bags.

The solution should then run at 0.1 units/kg/hour (0.1ml/kg/hour).

- If the rate of blood glucose fall exceeds 5 mmol/l per hour, or falls to around 14–17 mmol/l, add dextrose (5–10% equivalent) to the IV fluids running (see "fluids" above). The insulin dose needs to be maintained at 0.1 units/kg/hour to switch off ketogenesis.
- Do not stop the insulin infusion while dextrose is being infused, as insulin is required to switch off ketone production. If the blood glucose falls below 4 mmol/l, give a bolus of 2 ml/kg of 10% dextrose and increase the dextrose concentration of the infusion.

- If needed, a solution of 10% dextrose with 0.45% saline can be made up by mixing 250 ml 20% glucose with 250ml N.Saline by withdrawing 250 ml from each 500 ml bag & mixing the residual amounts with each other.
- Once the pH is above 7.3, the blood glucose is down to 14–17 mmol/l, and a dextrose-containing fluid has been started, consider reducing the insulin infusion rate, but to no less than 0.05 units/kg/hour.
- If the blood glucose rises out of control, or the pH level is not improving after 4–6 hours consult senior medical staff, re-evaluate (possible sepsis, insulin errors or other condition), and consider starting the whole protocol again.

N.10.8 Bicarbonate

This is rarely, if ever, necessary. Continuing acidosis usually means insufficient resuscitation or insufficient insulin. Bicarbonate should only be considered in children who are profoundly acidotic (pH<6.9) and shocked with circulatory failure. Its only purpose is to improve cardiac contractility in severe shock.

Before starting bicarbonate, discuss with senior staff, and the quantity should be decided by the paediatric resuscitation team or consultant on-call.

N.10.9 Phosphate

There is always depletion of phosphate, another predominantly intracellular ion. Plasma levels may be very low. There is no evidence in adults or children that replacement has any clinical benefit and phosphate administration may lead to hypocalcaemia.

Continuing management

- Urinary catheterisation should be avoided but may be useful in the child with impaired consciousness.
- Documentation of fluid balance is of paramount importance. All urine needs to be measured accurately and tested for ketones. All fluid input must be recorded (even oral fluids).
- If a massive diuresis continues fluid input may need to be increased. If large volumes of gastric aspirate continue, these will need to be replaced with 0.45% saline plus 10 mmol/l KCl.
- Check biochemistry, blood pH, and laboratory blood glucose 2 hours after the start of resuscitation, and then at least 4 hourly. Review the fluid composition and rate according to each set of electrolyte results.
- If acidosis is not correcting, resuscitation may have been inadequate or sepsis or inadequate insulin activity. Check infusion lines, doses of insulin and consider giving more insulin, antibiotics and/or normal saline.

N.10.10 Insulin management

Continue with IV fluids until the child is drinking well and able to tolerate food. Do not expect ketones to have disappeared completely before changing to subcutaneous insulin.

Discontinue the insulin infusion 60 minutes (if using soluble or long-acting insulin) or 10 minutes (if using Novorapid or Humalog) after the first subcutaneous injection to avoid rebound hyperglycaemia. Subcutaneous insulin should be started according to local protocols for the child with newly diagnosed diabetes, or the child should be started back onto their usual insulin regimen at an appropriate time (discuss with senior staff).

N.10.11 Cerebral oedema

The signs and symptoms of cerebral oedema include

- headache & slowing of heart rate
- change in neurological status (restlessness, irritability, increased drowsiness, incontinence)
- specific neurological signs (e.g.. cranial nerve palsies)
- rising BP, decreased O2 saturation
- abnormal posturing

More dramatic changes such as convulsions, papilloedema, respiratory arrest are late signs associated with extremely poor prognosis

N.10.12 Management

If cerebral oedema is suspected inform senior staff immediately.

The following measures should be taken immediately while arranging transfer to PICU–

- exclude hypoglycaemia as a possible cause of any behaviour change
- give Mannitol 1 g/kg stat (=5 ml/kg Mannitol 20% over 20 minutes) or hypertonic saline (5 –10 mls/kg over 30 mins). This needs to be given as soon as possible if warning signs occur.
- restrict IV fluids to 2/3 maintenance and replace deficit over 72 rather than 48 hours
- the child will need to be moved to PICU (if not there already)
- discuss with PICU consultant (if assisted ventilation is required maintain pCO_2 above 3.5 kPa)
- once the child is stable, exclude other diagnoses by CT scan – other intracerebral events may occur (thrombosis, haemorrhage or infarction) and present similarly
- a repeated dose of Mannitol should be given after 2 hours if no response
- document all events (with dates and times) very carefully in medical records

Other complications

- Hypoglycaemia and hypokalaemia – avoid by careful monitoring and adjustment of infusion rates
- Systemic Infections – Antibiotics are not given as a routine unless a severe bacterial infection is suspected
- Aspiration pneumonia – avoid by nasogastric tube in vomiting child with impaired consciousness

Other associations with DKA require specific management:

Continuing abdominal pain is common and may be due to liver swelling, gastritis, bladder retention, ileus. However, beware of appendicitis and ask for a surgical opinion once DKA is stable. A raised amylase is common in DKA.

Other problems are pneumothorax **±**pneumo-mediastinum, interstitial pulmonary oedema, unusual infections (e.g. TB, fungal infections), hyperosmolar hyperglycaemic non–ketotic coma, ketosis in type 2 diabetes.

Discuss these with the consultant on-call.

N.11 APPENDIX 1 Glasgow Coma Scale (page 167 of the 2004 guideline)

Best Motor Response	1=none
	2=extensor response to pain
	3=abnormal flexion to pain
	4=withdraws from pain
	5=localises pain
	6=responds to commands
Eye Opening	1=none
	2=to pain
	3=to speech
	4=spontaneous
Best Verbal Response	1=none
	2=incomprehensible sounds
	3=inappropriate words
	4=appropriate words but confused
	5=fully orientated

Maximum score 15, minimum score 3

Modification of verbal response score for younger children:

2–5 years	**<2 years**
1=none	1=none
2=grunts	2=grunts
3=cries or screams	3=inappropriate crying or unstimulated screaming
4=monosyllables	4=cries only
5=words of any sort	5=appropriate non-verbal responses (coos, smiles, cries)

N.11.1 APPENDIX 2 Algorithm for the Management of Diabetic Ketoacidosis (page 168 of the 2004 guideline)