Appendix D: Clinical evidence tables

For Abbott, Glanton and Merion, see “USRDS”

Study	Amaral 2016[15]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=7527)
Countries and setting	Conducted in USA; Setting: USA
Line of therapy	1st line
Duration of study	Follow up (post intervention): Median 5.2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	<18, from USRDS, entered Medicare between 2000 and 2012
Exclusion criteria	Previous renal transplant, multiorgan transplant
Recruitment/selection of patients	All incident patients from USRDS meeting inclusion criteria
Age, gender and ethnicity	Age - Mean (SD): 10.8 (5.3. Gender (M:F): 59:41. Ethnicity: 50% white, 20% hispanic, 20% black

Further population details	
Indirectness of population	No indirectness
Interventions	(n=1668) Intervention 1: Transplant - Pre-emptive. Transplant with no history of dialysis. Duration Median follow-up 5.2 years. Concurrent medication/care: Usual care (n=5859) Intervention 2: Transplant - Not pre-emptive. Transplant after dialysis. Duration Median follow-up 5.2 years . Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PRE-EMPTIVE versus NOT PRE-EMPTIVE Protocol outcome 1: Time to failure of RRT form - Actual outcome for General population: Graft failure at Median follow-up 5.2 years; Group 1: n=1668 ; Group 2: n=5859; HR 0.75; Lower CI 0.64 to Upper CI 0.91 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	ANZDATA (dialysis) trial: Johnson 2009[183]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=21935)
Countries and setting	Conducted in Australia, New Zealand; Setting: All centres in Australia or New Zealand
Line of therapy	1st line
Duration of study	Intervention time: Up to 10 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	18 years or older, starting dialysis for CKD between 1995 and 2005 in a centre in Australia or New Zealand
Exclusion criteria	Nil recorded
Recruitment/selection of patients	ANZDATA registry data 1995-2005
Age, gender and ethnicity	Age - Mean (SD): PD 62.7(51.0-71.3), HD 60.4(47.8-70.8). Gender (M:F): 41:59. Ethnicity: White 74%
Further population details	1. Age: Not applicable (Ave 61). 2. BMI: Not applicable 3. DM: Not applicable (Prev 38%). 4. Ethnicity: Not applicable (White 74%).
Extra comments	Paper reports significant difference between PD and HD in age (HD younger), gender (HD less women), late referral (HD more), smoking (HD more), DM (PD more) and residence (HD less likely new zealand). Pt characteristics (PD/HD): BMI - underweight 4/5%, obese 20/24% Late referral - 17/28% Current smoker - 12/14% IHD - 41/40% DM - 40/37%

	Dialysis features: Started 1995-97 23/20%, started 1998-2000 27/27%, started 2001-03 31/31%, 2004-2005 18/21%. Centre in NZ 26/15%. Centre size <340pt 20/28%, size >740 29/28%
Indirectness of population	No indirectness: Inclusion criteria mean most pts will be RRT naive
Interventions	(n=15916) Intervention 1: Haemodialysis - HD (generic). Received haemodialysis as first dialysis therapy. Duration Up to 10y (mean 2.4y). Concurrent medication/care: Not controlled, observational study Comments: Proportion switching to PD was 21.1% at 6 months, 24.7% at 2 years, and 26.9% at 6 years; proportion receiving transplant 14%; recovery 0.29%, lost to FU 0.1% (n=6020) Intervention 2: Peritoneal dialysis - PD (generic). Received peritoneal dialysis as first modality of dialysis. Around 15.7% received automated PD. Duration Up to 10y (ave 3.2y). Concurrent medication/care: Not controlled, observational study Comments: Switched to HD 8.5% at six months, 27.9% at 2y, 63.6% at 6y; received transplant 10%; recovered 0.04%; lost to FU 0.1%
Funding	Principal author funded by industry (Johnson is a consultant for Baxter, and has received funds from Fresenius. Bannister is a consultant for Baxter. McDonald has received speak honoraria and travel grants from AMGEN, Fresenius, Solvay, Genzyme and Jansen-Cilag)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC)

Protocol outcome 1: AEs - infections
- Actual outcome for General population: Death from infection (after 6 months) at 6 months - 2 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Imbalance at baseline, care not standardised between groups, not clear how dealt with switching; Indirectness of outcome: Serious indirectness, Comments: Adjusted HR for overall deaths (not censored for time of occurrence) not available. There were also values for before 6m, and between 2y and 6y, and more than 6 years - which are statistically different from this result; Baseline details: Multiple indicators of imbalance, inc age, ethnicity, DM status and late referral; Key confounders: age, ethnicity, comorbidities, health at baseline (late referral used as proxy); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ;

	Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	ANZDATA registry trial: Milton 2008[293]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=2603)
Countries and setting	Conducted in Australia, New Zealand; Setting: As recorded in ANZDATA, a registry of residents in Aus and NZ who receive chronic renal replacement therapy
Line of therapy	1st line
Duration of study	Follow up (post intervention): Up to 10 years post-transplant
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients in Australia or New Zealand who received a first kidney transplant from a live donor
Exclusion criteria	Not defined
Recruitment/selection of patients	April 1991 - December 2005
Age, gender and ethnicity	Age - Mean (SD): 35y (34-36) PreT, 38y (37-38) Non-PreT. Gender (M:F): Not stated. Ethnicity: Non-indigenous 94%, Aboriginal/Torres Strait Islander 2%, Maori/Islander 4%
Further population details	1. Age: Not applicable (Ave 36). 2. BMI: Not applicable (Ave 24). 3. DM: Not applicable (Ave type1 4%, type2 5%). 4. Ethnicity: Not applicable (94% non-indigenous).
Extra comments	Demographics in the two groups are said to vary, and particularly for age (PreT younger), GFR (PreT higher), ethnicity (PreT less indigenous), heart disease (PreT less), hypertension (PreT less) and smoking (PreT less). There were no statistically significant differences in donor characteristics. Demographics between the two

	groups (PreT v Non): Age 35v38, GFR at RRT 13.1v9.9, Non-indigenous 97v93%, Hx IHD 3v7%, DM type1 3v4%, DM type2 2v5%, HTN 91v95%, BMI 23.7v23.9, current smoker 5v10%, late referral 3v18%
Indirectness of population	Serious indirectness: The distinction between pre-emptive and not has been made by the presence or absence of preceding dialysis, therefore most are not naive to RRT. Those in non-PreT started RRT an average of 1.6 years prior to transplant
Interventions	(n=578) Intervention 1: Transplant - Pre-emptive. Received a first kidney transplant without a prior period of dialysis from a living donor (related or unrelated). Duration Up to 10 years. Concurrent medication/care: Not controlled (observational study) (n=2025) Intervention 2: Transplant - Not pre-emptive. Received a first kidney transplant from a living donor (related or unrelated) after starting dialysis. Duration Up to 10 years. Concurrent medication/care: Not controlled (observational study)
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PRE-EMPTIVE versus NOT PRE-EMPTIVE

Protocol outcome 1: Time to failure of RRT form
- Actual outcome for General population: Risk of graft failure at Up to 10 years; Group 1: n=578 ; Group 2: n=2025; HR 0.8; Lower CI 0.64 to Upper CI 0.99; Test statistic: p=0.036
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Younger and healthier at baseline, confounders addressed with Cox multivariate analysis, background treatment not controlled and may be different; Indirectness of outcome: No indirectness, Comments: Corrected as reported; Baseline details: Younger, healthier; Key confounders: Age, ethnicity, comorbidity, health at commencement (variable "late referral" used as proxy); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Balasubramanian 2011[36]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=372)
Countries and setting	Conducted in United Kingdom; Setting: Single centre (Barts and The London Hospital)
Line of therapy	1st line
Duration of study	Intervention time: Ave 2.2y
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients starting peritoneal dialysis
Exclusion criteria	Define
Recruitment/selection of patients	Pts starting PD June 2003 to June 2006 had data reviewed January 2003 to January 2008
Age, gender and ethnicity	Age - Mean (SD): APD 51.2(14.5) v CAPD 57.6(15.3). Gender (M:F): 62:38. Ethnicity: White 44%, Afro-Caribbean 17%, Indian SC 33%, Other 6%
Further population details	1. Age: Not applicable (ave 55). 2. BMI: Not stated / Unclear 3. DM: Not applicable (Prev 40%). 4. Ethnicity: Not applicable (White 44%, Indian sub-Continent 33%).
Extra comments	. Prev diabetes 40%, Independent for dialysis 75%, eGFR at start 6.9, Hb at start 9.5
Indirectness of population	No indirectness: Incident dialysis pts, so most will be RRT naive

Interventions	(n=194) Intervention 1: Peritoneal dialysis - APD/CCPD. APD preferred method of dialysis. Duration Ave 2.2y (up to 4.5y). Concurrent medication/care: The same pre-dialysis team saw all patients, they received pre-PD training, and were seen at three months and at one year routinely (n=178) Intervention 2: Peritoneal dialysis - CAPD. CAPD preferred modality of dialysis. Duration Ave 2.18y (max 4.5y). Concurrent medication/care: The same pre-dialysis team saw all patients, they received pre-PD training, and were seen at three months and at one year routinely
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: APD/CCPD versus CAPD Protocol outcome 1: Quality of life - Actual outcome for General population: SF36 mental composite score at 1 year; MD; -1.5 (p-value: 0.66) pt SF36 MCS 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear what statistical methods used and whether appropriate; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Key confounders: age, ethnicity, comorbidity score, Karnofsky score (for health at baseline); Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: SF36 physical composite score at 1 year; MD; -2.2 (p-value: 0.47) pt SF36 PCS 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear what statistical methods used and whether appropriate; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Key confounders: age, ethnicity, comorbidity score, Karnofsky score (for health at baseline); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to failure of RRT form - Actual outcome for General population: Failure of technique at Ave 2.2y; HR; 0.751 (SE (of coefficient): 0.182)); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear what statistical methods used and whether appropriate; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, comorbidity score, Karnofsky score (for health at baseline); Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource

	use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	BRAZPD II trial: Beduschi gde 2015[43]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=2890)
Countries and setting	Conducted in Brazil; Setting: Centres recruited into the study
Line of therapy	1st line
Duration of study	Intervention time: Up to 7 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Attending dialysis centre, received at least 90 days' PD which was exclusively APD or CAPD (not mixture of both)
Exclusion criteria	Less than 90 days' treatment
Recruitment/selection of patients	December 2004 to January 2011, 9,905 pts identified, 4198 did not receive 90 days of PD, 1308 received more than one modality
Age, gender and ethnicity	Age - Mean (SD): 59. Gender (M:F): 55:45. Ethnicity: white 50%
Further population details	1. Age: Not applicable (ave 59y). 2. BMI: Not applicable (Ave BMI 25). 3. DM: Not applicable (Prev 43%). 4. Ethnicity: Not applicable (White 50%).
Extra comments	Etiology: HTN 18%, DM 36%, G'nephritis 9%, unknown 18% BMI >25Kg/m2 41% IHD 21%, DM 43%, HTN 77%

Indirectness of population	Serious indirectness: 36% had a history of prior haemodialysis
Interventions	(n=1334) Intervention 1: Peritoneal dialysis - APD/CCPD. Received APD. Duration Up to 7 years. Concurrent medication/care: No detail given Comments: - paper does not say how decision on modality was reached (n=1556) Intervention 2: Peritoneal dialysis - CAPD. Received CAPD. Duration Up to 7 years. Concurrent medication/care: Not detailed Comments: paper does not say how decision on modality is reached
Funding	Study funded by industry (Baxter healthcare)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CAPD versus APD/CCPD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Overall mortality at Up to 7 years; Group 1: Observed events 245 ; Group 2: Observed events 305; HR 1.44; Lower CI 1.21 to Upper CI 1.71
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Indication of allocation unstated, standard of care not stated; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Group 1 Number missing: , Reason: possible that no loss as registry-type study; Group 2 Number missing:

Protocol outcome 2: Time to failure of RRT form
- Actual outcome for General population: Technique failure at Up to 7 years; HR 0.83; Lower CI 0.69 to Upper CI 1.02
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Indication of allocation unstated, standard of care not stated; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Group 1 Number missing: , Reason: possible that no loss as registry-type study; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection

episodes

Study	Bro 1999[53]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=34)
Countries and setting	Conducted in Denmark; Setting: Three Danish CAPD units
Line of therapy	1st line
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18 or over, at least 1 month CAPD treatment judged to be adequate (creatinine clearance at least 50L/wk/1.73m3), recent peritoneal equilibration test showing high or high-average peritoneal transport characteristics and judged to be able to learn the APD technique
Exclusion criteria	Pregnancy, lactation, mental retardation or dementia, psychiatric illness, inability to speak Danish, major medical or surgical event in the last 3 months or malignancy
Recruitment/selection of patients	Total population of units 118. 34 met criteria and agreed to take part. 25 completed protocol
Age, gender and ethnicity	Age - Mean (SD): 50 (5) amongst completers. Gender (M:F): 16:9 (amongst completers). Ethnicity: Not stated
Further population details	1. Age: Not applicable (ave 52). 2. BMI: Not stated / Unclear 3. DM: Not applicable 4. Ethnicity: Not stated / Unclear
Extra comments	. Baseline characteristics for completers: Primary kidney disease (n for CAPD/ n for APD) Diabetes 3/4, HTN 1/1 glomerulonephritis 5/3 other 4/4

	Time on PD (months) 13, previous transplant 2/2, in work 1/4 Comorbidity HTN 8/7, IHD 1/2, DM 1/0* (* this appears to be incorrect, but is what is written in the paper)
Indirectness of population	Serious indirectness: Not RRT naive. Required to be stable on CAPD
Interventions	(n=17) Intervention 1: Peritoneal dialysis - APD/CCPD. Automated peritoneal dialysis. Trained by skilled PD nurse. Prescription changed for APD process based on pre-study PET, and would usually consist of nightly intermittent PD, with an added bag in the morning and an additional manual exchange in the afternoon if necessary. Duration 6 months. Concurrent medication/care: Seen monthly. Dialysis adequacy tested every 3 months (PET). Biochemical data monitored Comments: 5 patients dropped out (1 transplant, 1 request, 2 disliked APD, 1 other) (n=17) Intervention 2: Peritoneal dialysis - CAPD. Continued with previous regimen. Prescription altered during trial if necessary to maintain adequacy. Duration 6 months. Concurrent medication/care: Seen monthly. Dialysis adequacy tested every 3 months (PET). Biochemical data monitored Comments: 4 pts dropped out (1 transplant 2 decision to start HD 1 other)
Funding	Other (Danish Society of Nephrology Research Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: APD/CCPD versus CAPD

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: Physical discomfort at 6 months; Group 1: mean 1.9 pt (SD 1); n=12, Group 2: mean 2.2 pt (SD 1.3); n=13; Treatment-Specific Questionnaire 1-5 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - More in APD group working, discomfort at baseline not given, unvalidated scale; Indirectness of outcome: No indirectness, Comments: One dimension of 11-item/5-dimension treatment-specific questionnaire. Appears to be author's own scale with no published validation; Baseline details: Age 54/50, female 5/4, HTN 1/1, DM 3/4, time on CAPD 15/12, yrs education 10/13, working 1/4; Group 1 Number missing: 5, Reason: dropped out; Group 2 Number missing: 4, Reason: dropped out

Protocol outcome 3: AEs - infections
- Actual outcome for General population: Peritonitis at 6 months; Group 1: 1/12, Group 2: 2/13
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - More in APD group working (not felt to be large threat, hence not downgraded twice); Indirectness of outcome: No indirectness ; Baseline details: Age 54/50, female 5/4, HTN 1/1, DM 3/4, time on CAPD 15/12, yrs

education 10/13, working 1/4; Group 1 Number missing: 5, Reason: dropped out; Group 2 Number missing: 4, Reason: dropped out - Actual outcome for General population: Exit-site infection at 6 months; Group 1: 1/12, Group 2: 1/13 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - More in APD group working (not felt to be large threat, hence not downgraded twice); Indirectness of outcome: No indirectness ; Baseline details: Age 54/50, female 5/4, HTN 1/1, DM 3/4, time on CAPD 15/12, yrs education 10/13, working 1/4; Group 1 Number missing: 5, Reason: dropped out; Group 2 Number missing: 4, Reason: dropped out	
Protocol outcomes not reported by the study	Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Chandna 2011[65]
Study type	Non randomised study
Number of studies (number of participants)	183 >75s (n=844)
Countries and setting	Conducted in United Kingdom; Setting: Nephrology clinic, Lister hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: Up to 18 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Planned starters: Late starters unlikely to be captured in this database
Subgroup analysis within study	Not applicable: Over 75s analysed separately, made up 78% of incident conservative management, and 11% of incident dialysis
Inclusion criteria	Attended nephrology clinics with chronic progressive kidney disease who registered an eGFR10-15ml/min/1.73m² (MDRD-4 equation) with all subsequent eGFR measurements <15.
Exclusion criteria	Patients presenting for the first time in advanced stage 5 CKD (eGFR<10)
Recruitment/selection of patients	Retrospective ascertainment through hospital database 1990-2008
Age, gender and ethnicity	Age - Mean (SD): age at stage 5 CKD: 60(15) overall. Gender (M:F): 65:35 (overall) 64:36 (>75s). Ethnicity: Non-white 14% (overall) 6.5% (>75s)
Further population details	1. Age: >80 (results given for >75s). 2. BMI: Not stated / Unclear 3. DM: Not applicable (51% of all pts have diabetes, 28% in over 75s). 4. Ethnicity: Not applicable (non-white 16% overall, 7% in >75s).
Extra comments	No age restriction, but >75s analysed in more detail. Characteristics of >75 cohort: Comorbidity high 39%, diabetes 28%

Indirectness of population	No indirectness: All RRT naive
Interventions	(n=689) Intervention 1: Haemodialysis - HD (generic). Following progression into stage 5 CKD they commenced haemodialysis or peritoneal dialysis, or received kidney transplant, or had intervention suggesting preparation for dialysis (such as creation of A-V fistula) but died before dialysis commenced. Duration Up to 18 years. Concurrent medication/care: Uncontrolled (n=155) Intervention 2: Conservative management. Did not receive RRT during the progression of their kidney disease (or prepared for dialysis and die before it could commence). Duration Up to 18 years. Concurrent medication/care: Patients opting for conservative management were offered ongoing support by the MDT in liaison with community, primary care and hospice services. Full medical treatment continued, which included the use of erythropoietin as appropriate to treat or prevent anaemia
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RRT (GENERIC) versus CONSERVATIVE MANAGEMENT

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for Planned starters: Mortality in over 75s at up to 18y; Group 1: n=106 ; Group 2: n=77; HR 0.85; Lower CI 0.569 to Upper CI 1.271; Test statistic: p=0.428
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference at baseline, unclear comparability of care, unclear if subgroup a priori but unlikely to compromise results; Indirectness of outcome: No indirectness ; Baseline details: Differed in age (68v82); Key confounders: age, diabetes, comorbidity score, ethnicity; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	CONvective TRAnsport STudy (CONTRAST) trial: Grooteman 2012[140] (Den Hoedt 2014[97], Den Hoedt 2015[98], Mazairac 2013[276])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=714)
Countries and setting	Conducted in Canada, Netherlands, Norway; Setting: Multi-centre trial recruited 597 in the Netherlands, 102 in Canada, 15 in Norway
Line of therapy	1st line
Duration of study	Intervention time: Study stopped early due to results Dec 2010. Follow-up range 0.4-6.6 years, median 2.9 years, mean 3.0 years.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults, treated by low-flux HD 2 or 3 times a week for at least two months, able to understand the study procedures and willing to provide written consent
Exclusion criteria	Age <18y, treatment with HDF or high-flux HD in the preceding 6 months, severe incompliance, life expectancy <3m due to non-renal disease, participation in other clinical intervention trials evaluating cardiovascular outcomes
Recruitment/selection of patients	June 2004 - December 2009
Age, gender and ethnicity	Age - Mean (SD): HDF 64.1(14.0) HD 64.0(13.4). Gender (M:F): 270:444. Ethnicity: Caucasian 84%, Afro-Caribbean 8%, Asian 6%, Other 2%
Further population details	1. Age: Not applicable (ave age 64). 2. BMI: Not applicable (ave BMI 25). 3. DM: Not applicable (DM in 24%).

	4. Ethnicity: Not applicable (84% Caucasian).
Extra comments	Baseline characteristics: Years on dialysis 2.9; vascular access AVF 80%, graft 14%, catheter 6%; 3xwk 94%; blood flow 300ml/min; residual renal function 52%. Clinical factors: CV disease 44%, diabetes 24%, Hb 11.9g/dl, BMI 25kg/m2, Albumin 40g/L Prescribed med: B-blockers 52%, ACE-ARB 49%, statin 50%
Indirectness of population	Serious indirectness: Not naive to RRT. Protocol requires 2 months stability on low-flux HD prior to commencement (6 months if new patient)
Interventions	(n=358) Intervention 1: Haemodialysis - HDF. Online HDF. Treated with a target post-dilution dose of 6 l/h (~100 ml/min) and a high-flux synthetic dialyser (UF-coefficient > 20 ml/mmHg/h). Blood flow will be set at >300 ml/min, if possible, in order to achieve a substitution volume of 100 ml/min. If the blood flow is less than 300 ml/min, the post-dilution volume will be decreased accordingly (filtration and post-dilution <25–33% of blood flow). If necessary, the dose of LMWH will be increased and given in two separate doses. Treatment times will be fixed according to the prescription in the stabilisation period and adjusted only when spKt/V urea is < 1.2 / treatment. Duration Ave 3y (total 1085 person-yr). Concurrent medication/care: Metabolic control will be performed according to the guidelines of the Quality of Care Committee of the Dutch Federation of Nephrology. Anti-hypertensive medication, lipid lowering therapy, platelet aggregation inhibitors and medication to treat renal anaemia and renal osteodystrophy will also be prescribed according to these guidelines, and, if not available, according to usual care. Comments: 121 stopped HDF, mainly due to transplant (n=356) Intervention 2: Haemodialysis - HD (generic). Low-flux haemodialysis. Low-flux synthetic dialysers (UF-coefficient < 20 ml/mmHg/h). Blood flow will be maintained at 250–400 ml/min. Anticoagulation is performed with low molecular weight heparin (LMWH) before HD. Patients on coumarins receive 50% of the LMWH dose. Treatment times will be adapted to a target dialysis spKt/V urea of ≥ 1.2 per treatment. Duration Ave 3y (total 1085 person-yrs). Concurrent medication/care: Metabolic control will be performed according to the guidelines of the Quality of Care Committee of the Dutch Federation of Nephrology. Anti-hypertensive medication, lipid lowering therapy, platelet aggregation inhibitors and medication to treat renal anaemia and renal osteodystrophy will also be prescribed according to these guidelines, and, if not available, according to usual care. Comments: 118 stopped, mainly due to transplant
Funding	Other (Dutch Kidney Foundation and Fresenius Medical Care, Netherlands, and Gambro Lundia AB, Sweden. Additional support was received from the Dr. E.E. Twiss Fund, Roche Netherlands, the International Society

	of Nephrology/Baxter Extramural Grant Program, and the Netherlands Organization for Health Research and Development.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD Protocol outcome 1: Quality of life - Actual outcome for General population: EQ5D at Ave 3y; Group 1: mean 0.74 (SD 0.19); n=205, Group 2: mean 0.73 (SD 0.38); n=204 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Mortality at >/= 6 months - Actual outcome for General population: All-Cause Mortality at Ave 3y; Group 1: Observed events 131 n=358 ; Group 2: Observed events 137 n=356; HR 0.95; Lower CI 0.75 to Upper CI 1.2 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: All-Cause Mortality at Ave 3y; Group 1: 131/358, Group 2: 138/356 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: AEs - infections - Actual outcome for General population: All infections at Ave 3y; Group 1: 118/358, Group 2: 106/356 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures, adjudication by blind committee; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant

rejection episodes

Study	De Fijter 1994[92]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=97)
Countries and setting	Conducted in Netherlands; Setting: Single university hospital
Line of therapy	1st line
Duration of study	Intervention time: Up to 30 months (723 patient-months)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable:
Inclusion criteria	Patients referred to peritoneal dialysis for end-stage renal failure
Exclusion criteria	Absolute contraindications to peritoneal dialysis
Recruitment/selection of patients	From January 1988 - August 1991, all previously untreated patients considered, 97 randomised (50 CAPD and 47 APD), 82 started allocated intervention (41 CAPD and 41 APD)
Age, gender and ethnicity	Age - Median (range): 55 (18-86). Gender (M:F): 52:45. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 55, 42% over 60y). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	Stratified by age and sex. Primary renal disease (CAPD/APD)%: glomerulonephritis 16/23, interstitial nephritis 10/17, diabetes 16/17. nephrosclerosis 30/15, PKD 6/11, other 14/15, unknown 8/2
Indirectness of population	No indirectness

Interventions	(n=41) Intervention 1: Peritoneal dialysis - CAPD. Continuous ambulatory peritoneal dialysis with a Y-connector. Pts used the Y set without disinfectant and performed three to five daily 2-L exchanges. Duration 6-30 months. Concurrent medication/care: Standardised training for home peritoneal dialysis (on an outpatient basis) usually began within two weeks after the insertion of the peritoneal catheter. Median 8.5 days training (range 3 to 26 days) Comments: By the end of the follow-up, 11 pts still receiving. Reason for stopping: death 2, recovery 1, transplant 13, method failure 14 (n=41) Intervention 2: Peritoneal dialysis - APD/CCPD. Continuous cyclic peritoneal dialysis, using an automated cycler (PAC-X) that provided four or five nocturnal cycles and one diurnal cycle (2-L volume per cycle). Duration 6-30 months. Concurrent medication/care: Standardised training for home peritoneal dialysis (on an outpatient basis) usually began within two weeks after the insertion of the peritoneal catheter. Median 8.5 days training (range 3 to 26 days) Comments: At the end of follow-up, 16 were still using CCPD. Reasons for dropout: death 4, renal transplant 13, method failure 8
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CAPD versus APD/CCPD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death at during follow-up (6-30 months, 1411 pt months in total); Group 1: 2/41, Group 2: 4/41
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail on randomisation, limited baseline details (no ethnicity or comorbidities), background care not described, high dropout due to transplantation; Indirectness of outcome: No indirectness ; Baseline details: Female 27/25, median age 55.5/54, %>60y 42/42.5, median duration CKD tx 17.5/19.5, caused by diabetes 8/8; Group 1 Number missing: 14, Reason: 1 recovery, 13 transplant; Group 2 Number missing: 13, Reason: 13 transplant

Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations at during follow-up (6-30 months, 1411 pt months in total); rate ratio: 1.67 hospital admissions per patient per year);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail on randomisation, limited baseline details (no ethnicity or comorbidities), background care not described, high dropout due to transplantation; Indirectness of outcome: No indirectness ; Baseline details: Female 27/25, median age 55.5/54, %>60y 42/42.5, median duration CKD tx 17.5/19.5, caused by diabetes 8/8; Group 1 Number missing: 16, Reason: 2

death, 1 recovery, 13 transplant; Group 2 Number missing: 17, Reason: 4 death, 13 transplant Protocol outcome 4: AEs - infections - Actual outcome for General population: Method failure due to peritonitis at during follow-up (6-30 months, 1411 pt months in total); Group 1: 6/23, Group 2: 2/24; Comments: Number analysed calculated from patients randomised x (actual patient-months)/(potential patient-months if all randomised completed 30 months) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail on randomisation, limited baseline details (no ethnicity or comorbidities), background care not described, high dropout due to transplantation; Indirectness of outcome: No indirectness ; Baseline details: Female 27/25, median age 55.5/54, %>60y 42/42.5, median duration CKD tx 17.5/19.5, caused by diabetes 8/8; Group 1 Number missing: 16, Reason: 2 death, 1 recovery, 13 transplant; Group 2 Number missing: 17, Reason: 4 death, 13 transplant	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Estudio de Supervivencia de Hemodiafiltración On-Line (ESHOL) trial: Maduell 2013[262]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=906)
Countries and setting	Conducted in Spain; Setting: All haemodialysis units of Catalonia, either in hospital or out-hospital units
Line of therapy	1st line
Duration of study	Intervention time: Ave 1.9y (Median{IQR} 2.1 {0.86-3.00}y)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients older than 18 years with end-stage renal disease receiving thrice-weekly standard haemodialysis for more than 3 months
Exclusion criteria	Exclusion criteria consisted of active systemic diseases, liver cirrhosis, malignancies, immunosuppressor treatment, infradialysis dose (Kt/V <1.3), unipuncture dialysis and temporal nontunnelized catheter
Recruitment/selection of patients	May 2007 - September 2008. 939 identified in 27 centres. Exclusions: 18 did not meet the inclusion criteria, 5 refused to provide informed consent and 10 for logistical reasons
Age, gender and ethnicity	Age - Mean (SD): 65(14). Gender (M:F): 606:300. Ethnicity: Not stated
Further population details	1. Age: Not applicable (ave 65). 2. BMI: Not stated / Unclear 3. DM: Not applicable (Prev 25%). 4. Ethnicity: Not stated / Unclear
Extra comments	Baseline characteristics: %diabetes 24.9, Charlson comorb 6.6(2.3), time on dialysis 48.8(64) months

	Dialysis: AVF 85.8%, Catheter 10.5%, high flux 93.7%, Kt/V 1.66(0.36)
Indirectness of population	Serious indirectness: Not RRT naive, recruited people on conventional HD
Interventions	(n=456) Intervention 1: Haemodialysis - HDF. Online haemodiafiltration with post dilution, receiving a minimum of 18 litres/session replacement volume. Other aspects of HD prescription kept the same, all 3 x wk. Utilised synthetic high-flux dialyser with ultrapure dialysis fluids, the composition of which was specified in the protocol. Duration Ave 1.9y. Concurrent medication/care: Every 3 months the doses of erythropoiesis-stimulating agents, iron supplements, antihypertensive drugs and phosphate binders will be recorded Comments: 265 completed protocol, discontinuation most commonly for transplant (101/191) (n=450) Intervention 2: Haemodialysis - HD (generic). Haemodialysis to continue as previously (92% high flux, 8% low flux) using ultrapure dialysis fluid, composition specified, 3 x wk. Duration Ave 1.9y. Concurrent medication/care: Every 3 months the doses of erythropoiesis-stimulating agents, iron supplements, antihypertensive drugs and phosphate binders will be recorded Comments: 286 completed protocol, most common reason for discontinuation was transplant (79/164)
Funding	Other (Partly supported by grants from Fresenius Medical Care and Gambro Healthcare)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death at Ave 1.9y;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete (less of a problem for HR); Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study
- Actual outcome for General population: Death at Ave 1.9y; Group 1: 85/265, Group 2: 122/286
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete; Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study
- Actual outcome for People and children with diabetes: Death at Ave 1.9y; Group 1: n=104 ; Group 2: n=122; HR 0.75; Lower CI 0.46 to Upper CI 1.21; Test statistic: p-value interaction between diabetes status and survival = 0.776

Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete (less of a problem for HR), appears to be post-hoc sg analysis; Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: All-cause hospitalisation (count) at Ave 1.9y; RR; Rate ratio 0.78 (95%CI 0.67 to 0.9) (p-value: 0.001) ; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete; Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	Frequent Hemodialysis Network (Daily) trial: F. H. N. Trial Group 2010[110] (Chertow 2016[70], Hall 2012[145], Kurella Tamura 2013[220], Suri 2013[408], Unruh 2013[426])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=245)
Countries and setting	Conducted in USA; Setting: 11 university-based and 54 community-based haemodialysis facilities
Line of therapy	1st line
Duration of study	Intervention + follow up: 12m intervention, with selected outcomes in sub-set after follow-up of 3y
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with renal disease requiring chronic renal replacement therapy, aged >12 years (elsewhere says 18 or over), achieved mean eKt/V ≥ 1.0 for last two baseline HD sessions, weight ≥ 30kg
Exclusion criteria	Unable or unwilling to follow the study protocol, or not consenting. Requiring HD > 3xwk (not just occasional HDF), unable to attend for HD 6xwk, or history of poor compliance. Pregnant or expecting to become so. Expecting to move such that would be unable to attend any participating HD centre. Problems with heparin, or use of any experimental drugs that may interact with treatment. Expectation that there would be kidney recovery or transplant in the next 14 months. Life expectancy < 6 month or disorder that might limit ability to complete the 12 month trial [examples listed]. Unable to undergo MRI [examples listed]. Inability to communicate verbally in English or Spanish. Vascular access is a non-tunnelled catheter.
Recruitment/selection of patients	January 2006 - March 2009, 378 identified, 133 excluded for: 6xwk not feasible (38), residual renal function (27), no MRI (18), adherence judged unlikely (13), other (37)
Age, gender and ethnicity	Age - Mean (SD): Int 49(14) Control 52(14), Gender (M:F): 38:62, Ethnicity: % Black 44, White 38, Native 9,

	Asian 6, other/mixed 10
Further population details	1. Age: Not applicable (Ave 50y. Unclear minimum age). 2. BMI: Not applicable (Ave 27.5). 3. DM: Not applicable (41% had DM 1/2). 4. Ethnicity: Not applicable (Over 50% non-white).
Extra comments	Baseline characteristics: BMI 27.5, serum creatinine 10.5(0.3), Kt/Vurea equilibrated 1.43(0.25). Etiology%: Diabetes 35, Glomerulonephritis 19, HTN 21, PKD 4. Time on dialysis: <2y 16%, >5y 45%. Comorbidities%: HTN 90, DM 41, HF 20, prev MI 10.
Indirectness of population	Serious indirectness: Not RRT naive, needed to have been on haemodialysis at time of enrolment
Interventions	(n=125) Intervention 1: Haemodialysis - HD >3x a week. Haemodialysis six times a week in a centre. The target equilibrated Kt/Vn was 0.9, with the length of the session between 1.5 and 2.75 hours. Duration 12 months. Concurrent medication/care: Prescriptions for dialysis were determined centrally and were transmitted to each clinical centre. Non-dialysis treatment that forms the minimum expected for both arms detailed in full protocol Comments: 77.7% participants attended >80% sessions (n=120) Intervention 2: Haemodialysis - HD 3x a week. Haemodialysis three times a week in-centre continued their usual dialysis prescriptions, which included a minimum target equilibrated Kt/Vurea of 1.1 and a session length of 2.5 to 4.0 hours. Duration 12 months. Concurrent medication/care: Prescriptions for dialysis were determined centrally and were transmitted to each clinical centre. Non-dialysis treatment that forms the minimum expected for both arms detailed in full protocol Comments: 94.9% participants attended >80% of sessions
Funding	Other (National Institute of Diabetes and Digestive and Kidney Diseases and National Institute of Health Research Foundation (contributors the NIH Foundation in support of the FHN trials included Amgen, inc; Baxter, inc; and Dialysis Clinics, Inc))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD >3X A WEEK versus HD 3X A WEEK

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical composite score at 12m; Group 1: mean 3.4 pt (SD 0.8); n=100, Group 2: mean 0.4 pt (SD 0.8); n=90; SF-36 PHC 0-100 Top=High is good outcome; Comments: Adjusted mean differences
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. Subjective.; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 21, Reason: Death (5), transplant (11), did not complete (5); Group 2 Number missing: 27, Reason: Death (9) transplant (13) did not complete (5)
- Actual outcome for General population: SF-36 mental health composite at 12m; Group 1: mean 3.7 pt (SD 0.9); n=100, Group 2: mean 0.2 pt (SD 1); n=89; SF-36 MHC 0-100 Top=High is good outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. Subjective.; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 21, Reason: Death (5), transplant (11), did not complete (5); Group 2 Number missing: 27, Reason: Death (9) transplant (13) did not complete (5)

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: Short physical performance score at 12m; Group 1: mean -0.2 pt (SD 0.19); n=96, Group 2: mean -0.4 pt (SD 0.21); n=81; Short Physical Performance Battery (SPPB) 0-12 Top=High is good outcome; Comments: Involves gait speed, sit to stand x5, and standing balance
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 21, Reason: Death (5), transplant (11), did not complete (5); Group 2 Number missing: 27, Reason: Death (9) transplant (13) did not complete (5)

Protocol outcome 3: Mortality at >/= 6 months
- Actual outcome for General population: Death at 3y; Group 1: 20/122, Group 2: 34/118; Comments: Breakdown by time: during trial 5v10, 1-2y 5v6, 2y+ 10v18
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness ; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 2, Reason: ltfu; Group 2 Number missing: 3, Reason: ltfu

Protocol outcome 4: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations (count) at 12m; Rate ratio: 1.09);
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover

- Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness ; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%). 6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 1, Reason: lost to follow up; Group 2 Number missing: 1, Reason: lost to follow up Protocol outcome 7: AEs - vascular access issues - Actual outcome for General population: Underwent vascular access procedure at 12m; Group 1: 47/125, Group 2: 29/120; Comments: No of events: 65 vs 95 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness ; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%). 6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 1, Reason: lost to follow up; Group 2 Number missing: 1, Reason: lost to follow up	
Protocol outcomes not reported by the study	Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Preferred location of death ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	Frequent Hemodialysis Network Nocturnal trial: Rocco 2011[365] (Rocco 2015[364])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=87)
Countries and setting	Conducted in USA; Setting: University and community haemodialysis centres
Line of therapy	1st line
Duration of study	Intervention + follow up: 12 month intervention, with survival also followed over three years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	ESRD requiring chronic RRT. Age ≥ 18. Achieved mean eKt/V ≥ 1.0 for last two baseline HD sessions. Willing to perform dialysis at home.
Exclusion criteria	Unable or unwilling to carry out protocol, or give informed consent, or train to carry out HD at home. Requires >3 x wk HD or currently on daily or nocturnal HD. Expected to move to an area with no trial centres. Currently in hospital. Contraindication to Heparin, currently on any investigational drugs that could interfere, or less than three months since returned to HD due to rejected transplant. Scheduled to receive transplant within 12 months, life expectancy less than six months, or medical condition that could interfere with completing the 12 month protocol. Inability to communicate verbally in English or Spanish. Current access is temporary non-tunneled catheter.
Recruitment/selection of patients	March 2006 - May 2009. Originally aiming to recruit 250 participants, struggled to recruit, and recruitment stopped early. 118 pts identified, 31 excluded.
Age, gender and ethnicity	Age - Mean (SD): 52.8 (13.6). Gender (M:F): 30:57. Ethnicity: Black 26%, White 55%, Native 5%, Asian 14%

Further population details	1. Age: Not applicable (ave 53). 2. BMI: Not applicable (ave 29). 3. DM: Not applicable (prev 45). 4. Ethnicity: Not applicable (White 55).
Extra comments	Baseline characteristics: BMI 29, ESRD vintage <2y 55%, anuric 28%, equilibrated Kt/V 1.38, dialysis access through fistula 47%. Etiology: diabetes 35%, glomerulonephritis 36%, HTN 8%, PKD 22%. Comorbidities: HTN 90%, DM 43%, prev MI 10%, HF 14%
Indirectness of population	Serious indirectness: Not RRT naive, as have all been receiving 3xwk HD
Interventions	(n=45) Intervention 1: Haemodialysis - HD >3x a week. 6 nights per week at home dialysis following dialysis prescriptions subject to a stdKt/Urea of ≥4.0 and a treatment time of ≥6h . Duration 12m. Concurrent medication/care: All study participants were dialyzed using single-use high-flux dialyzers. A committee on standards of care, blinded to intervention, periodically reviewed and reported to clinical centres results of prespecified measures (phosphate, haemoglobin, bicarbonate, normalized protein nitrogen appearance, and blood pressure relative to achieved target post-dialysis weight) that were outside of values recommended in published guidelines. Comments: 72.7% participants dialysed at least 4.8 time per week (80% concordance) (n=42) Intervention 2: Haemodialysis - HD 3x a week. 3 days per week haemodialysis in home or at centre (depending on when recruited into study) target eKt/V ≥ 1.1/session, time ≤ 2.75h. Duration 12m. Concurrent medication/care: All study participants were dialyzed using single-use high-flux dialyzers. A committee on standards of care, blinded to intervention, periodically reviewed and reported to clinical centres results of prespecified measures (phosphate, haemoglobin, bicarbonate, normalized protein nitrogen appearance, and blood pressure relative to achieved target post-dialysis weight) that were outside of values recommended in published guidelines. Comments: 98% attended at least 2.4 treatments a week
Funding	Other (Supported by national Institute for Diabetes and Digestive and Kidney Diseases. Received some industry funding via donations to the NIH Research Foundation (Amgen, Baxter, Dialysis Clinics and Fresenius Medical Center) and through funding of authors (DaVita, Satellite Healthcare, Baxter, Eli Lilly, Amgen, Cormedix, Keryx, Nephrogenex, Merck, Sigma Tau and DCI))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD NOCTURNAL >3X WK versus HD 3X A WEEK

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical health composite at 12m; Group 1: mean 2.7 pt (SD 1.4); n=39, Group 2: mean 2.1 pt (SD 1.5); n=38; SF-36 PHC 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died
- Actual outcome for General population: SF-36 mental health composite at 12m; Group 1: mean 3 pt (SD 1.6); n=38, Group 2: mean -0.7 pt (SD 1.6); n=39; SF-36 MHC 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: Short Physical Performance Battery at 12m; Group 1: mean -0.92 pt (SD 0.44); n=34, Group 2: mean -0.41 pt (SD 0.43); n=37; SPPB score 0-12 Top=High is good outcome
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died

Protocol outcome 3: Mortality at >/= 6 months
- Actual outcome for General population: Deaths at 3y; Group 1: 14/45, Group 2: 5/42
Risk of bias: All domain - ; Indirectness of outcome: No indirectness

Protocol outcome 4: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations (count) at 12m; rate ratio: 1.34);
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37;

Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died Protocol outcome 7: AEs - vascular access issues - Actual outcome for General population: Vascular access procedures at 12m; Group 1: 23/45, Group 2: 15/42; Comments: Numbers of events 43v30 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died	
Protocol outcomes not reported by the study	Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Preferred location of death ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Grams 2013[139]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=120,753)
Countries and setting	Conducted in USA; Setting: Public and private insurance, with data from the Organ Procurement and Transplantation Network
Line of therapy	1st line
Duration of study	Follow up (post intervention): 3 years (average)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population: Adults
Subgroup analysis within study	Not applicable
Inclusion criteria	First-time kidney-only adult deceased donor kidney transplant recipients
Exclusion criteria	Live-donor recipients
Recruitment/selection of patients	Transplant recipients from January 1, 1995 to May 31, 2011 were identified through the scientific registry of Transplant Recipients (SRTR) n=121,853
Age, gender and ethnicity	Age - Mean (SD): pre 52.7(12.5), early 50.6(13.2), late 50.9(13.0). Gender (M:F): Given as % of males/females receiving pre-emptive, early and late: 8.3/10.2, 12.0/11.6, 79.7/78.3. Ethnicity: % of the Caucasian, African American and Other ethnicities in each treatment category given but not numbers overall, i.e. 13% of Caucasians received pre, 16% received early and 70% received late; for AAs 5%, 7% and 89%; for others 5%, 9% and 86%.

Further population details	1. Age: Not applicable (Adults). 2. BMI: Not applicable (Ave BMI 27 kg/m2). 3. DM: Not applicable (Mixed). 4. Ethnicity: Not applicable (Mixed).
Extra comments	Not described in this study. Factors associated with pre-emptive transplant were zero-antigen mismatch, older recipient age, female sex, hepatitis C infection, private insurance (OR 3.2), and negatively associated with African American ethnicity (OR 0.44). Multivariable model adjusts for Recipient factors (age, sex, ethnicity, impaired functional status, reactive antibody >40%, hepatitis C virus, previous non-kidney transplant, private insurance, aetiology of kidney disease) and Transplant factors (transplant year, expanded criteria donor, non-heart-beating donor, HLA zero-mismatch, donor age, cold ischaemia time, centre)
Indirectness of population	No indirectness
Interventions	(n=10992) Intervention 1: Transplant - Pre-emptive. Transplant not preceded by dialysis. Duration up to 15 years. Concurrent medication/care: Not controlled (n=14428) Intervention 2: Transplant - Not pre-emptive. "Early" deceased donor transplant, within one year from starting dialysis. Duration Up to 15 years. Concurrent medication/care: Not controlled (n=96433) Intervention 3: Transplant - Not pre-emptive. Deceased donor transplant after more than one year on dialysis. Duration Up to 15 years. Concurrent medication/care: Not controlled Comments: Not extracted as evidence presented only in terms of statistical significance
Funding	Academic or government funding (This work was funded by the National Kidney Foundation of Maryland, National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases Grant and National Institutes of Health Grants cofunded by the American Federation of Aging Research)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY TRANSPLANT versus PRE-EMPTIVE

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death, recipient under 65y at up to 15y;
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness. Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent

	associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: Death, recipient 65y or older at up to 15y; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness, Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: Graft loss, recipient 65y or older at up to 15y; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No definition of graft loss given. Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness, Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to failure of RRT form - Actual outcome for General population: Graft loss, recipient under 65y at up to 15y; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No definition of graft loss given. Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness, Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Jaar 2005[172]
Study type	Non randomised study
Number of studies (number of participants)	(n=)
Countries and setting	Conducted in USA; Setting: 81 dialysis clinics in 19 US states
Line of therapy	1st line
Duration of study	--:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	>17, starting dialysis in 1995-1998 in 81 participating dialysis clinics, oversampled for peritoneal dialysis
Exclusion criteria	None specified
Recruitment/selection of patients	None further specified
Age, gender and ethnicity	Age - Mean (SD): ~55 (14.9). Gender (M:F): Define. Ethnicity:
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	No indirectness
Interventions	(n=1041) Intervention 1: Haemodialysis - HD (generic). Generic HD, no further details provided, 5% switched type of dialysis. Duration Mean follow-up 2.4 years . Concurrent medication/care: Usual care (n=609) Intervention 2: Peritoneal dialysis - PD (generic). Generic HD, no further details provided but included

	CAPD and CCPD, 25% switched type of dialysis. Duration Mean follow-up 2.4 years . Concurrent medication/care: Usual care
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: <65 subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 1.67; Lower CI 1.01 to Upper CI 2.75
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: >65 subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 1.66; Lower CI 0.93 to Upper CI 2.97
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome for People and children without diabetes: No DM subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 2.78; Lower CI 1.36 to Upper CI 5.68
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome for People and children with diabetes: DM subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 1.23; Lower CI 0.79 to Upper CI 1.94
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome for General population: residual urine output subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=860 ; Group 2: n=502; HR 1.15; Lower CI 0.8 to Upper CI 1.64; Test statistic: P.interaction (residual urine output) x (PDvHD) >0.2
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Concern over baseline comparability and consistency of care; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, coexistent disease score, albumin level; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: no residual urine output subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=181 ; Group 2: n=107; HR 3.78; Lower CI 1.33 to Upper CI 10.7
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Concern over baseline comparability and consistency of care; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, coexistent disease score, albumin level; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Jain 2009[173]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=755)
Countries and setting	Conducted in United Kingdom; Setting: Four NHS units in West Midlands of UK
Line of therapy	1st line
Duration of study	Intervention + follow up: mean 4.6y
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population:
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults starting dialysis at one of four centres
Exclusion criteria	Previous transplant, died or recovered in first 90 days of dialysis
Recruitment/selection of patients	Consecutive pts from 1996 until the centre had fulfilled its allocated study slots (between 1998 and 2000)
Age, gender and ethnicity	Age - Median (range): 62 (16-86). Gender (M:F): 1.7:1. Ethnicity: White 85%, Black 3%, SE Asian 11%
Further population details	1. Age: Not applicable (18-86y). 2. BMI: Not stated / Unclear 3. DM: Not applicable (25% had DM). 4. Ethnicity: Not applicable (RR given for survival in Blacks and SE Asian, but not in interaction with treatment).
Extra comments	. Proportion starting dialysis on temporary access 39% Comorbidity score 0 - 43%, 1-2 - 48%, >2 - 9%
Indirectness of population	No indirectness: All pt naive at start of study, although those who get transplants later will have received dialysis

Interventions	(n=598) Intervention 1: Haemodialysis - HD (generic). Undifferentiated dialysis for >90 days, with no transplantation before follow-up finished. Duration mean 4.6y +/- 3.1y. Concurrent medication/care: Uncontrolled Comments: Ratio HD:PD overall 2.6:1 (n=157) Intervention 2: Transplant - Transplant (generic). Received dialysis for at least 90 days, and went on to receive a kidney transplant. Duration mean 4.6y +/- 3.1y. Concurrent medication/care: Uncontrolled
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIALYSIS (GENERIC) versus TRANSPLANT (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Death (adjusted) at 4.6y; RR; 0.20 (95%CI 0.11 to 0.34); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Differences at baseline, no comparability of care; Indirectness of outcome: No indirectness ; Baseline details: Differences reached stat sig for age, ethnicity, presence of diabetes, glomerulonephritis; Key confounders: age, individual comorbidity, comorbidity score, ethnicity; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Kantartzi 2013[192]
Study type	RCT (Patient randomised; Crossover: Adequate, according to protocol)
Number of studies (number of participants)	1 (n=24)
Countries and setting	Conducted in Greece; Setting: Appears to be performed at one university hospital
Line of therapy	1st line
Duration of study	Intervention time: Four blocks of treatment, of three months each
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Anuric pts, receiving HD through AVF or graft
Exclusion criteria	Nil listed
Recruitment/selection of patients	Unclear
Age, gender and ethnicity	Age - Mean (SD): 62(13)y. Gender (M:F): 19:5. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 62). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	Etiology CKD: diabetes 2 (although only 1 currently has DM), glomerulonephritis 5, HTN 6, pylenephritis 4, unknown 7. Average time on dialysis 31(23) months
Indirectness of population	Serious indirectness: Not RRT naive, existing HD pt

Interventions	(n=24) Intervention 1: Haemodialysis - HDF. Haemodiafiltration, postdilutional, one block being online HDF and one block using prepared bags (results combined), with blood flow 250-350ml/min, diasylate flow rate 500-700ml/min and substitution fluid 3.75-5litres/h, with prescription using Daugirdas formula to calculate Kt/V. Duration 3 months. Concurrent medication/care: Protocol alternates 3 months HDF with 3 months HD for 12 months total, with order randomised. Other treatment not specified (n=24) Intervention 2: Haemodialysis - HD (generic). Low-flux haemodialysis with blood flow 250-350ml/min and diasylate flow rate 500-700ml/min, with prescription using Daugirdas formula to calculate Kt/V. Duration 3 months. Concurrent medication/care: Protocol alternates 3 months HDF with 3 months HD for 12 months total, with order randomised. Other treatment not specified
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 Physical Health Composite at 3 months; Mean; HDF 40.7 (30.2-62.8), HD 36.1 (26.7-45.7) - statistics based on 44 independent ratings, which may be inappropriate (p-value: 0.029) pt 0-100 SF-36 Top=High is good outcome;
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - High, Other 2 - Low, Other 3 - Low, Comments - Unblind, no statement re comparability of care, no detail re where pt come from or how selected; Indirectness of outcome: No indirectness ; Baseline details: Age: 62/62, years on dialysis 2.5/3.7, female 2/3, DM 0/1; Group 1 Number missing: 1, Reason: unstated; Group 2 Number missing: 1, Reason: unstated

Protocol outcomes not reported by the study	Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Katopodis 2009[196]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=18)
Countries and setting	Conducted in Greece; Setting: One haemodialysis unit in university hospital
Line of therapy	1st line
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	People and children without diabetes
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults, stable 6 months on HD through an AVF/AV graft with minimal (<5%) recirculation. All had residual diuresis <100ml
Exclusion criteria	Diabetes, uncured malignancy, active inflammation, liver or severe heart failure (NYHA IV), malnutrition and medications affecting urea metabolism
Recruitment/selection of patients	All eligible pts informed
Age, gender and ethnicity	Age - Mean (SD): 53.6(15.1) int, 60.1(10.1) control. Gender (M:F): 12:6. Ethnicity: Not stated
Further population details	1. Age: Not applicable 2. BMI: Not stated / Unclear 3. DM: Not applicable (All non-diabetic). 4. Ethnicity: Not stated / Unclear
Extra comments	Body weight (kg): 69.7(9.1) int, 70.1(9.1) control. Etiology: Glomerulonephritis 11, HTN 2, other 5

Indirectness of population	Serious indirectness: Not RRT naive, required to have been stable on HD for six months prior to entry
Interventions	(n=8) Intervention 1: Haemodialysis - HD >3x a week. HD every other day (eod), with equal intervals of 44 hours between sessions, with other aspects of the dialysis prescription being carried over from their conventional dialysis, and amended as needed every three months. Duration 12 months. Concurrent medication/care: Protocol given for blood pressure, Hb and PTH management Comments: All pts completed (n=8) Intervention 2: Haemodialysis - HD 3x a week. HD on a conventional schedule, with 2 x 44h and 1 x 72h intervals between sessions. Dialysis prescriptions remained unchanged on entry, and were reviewed every three months for necessary changes. Duration 12 months. Concurrent medication/care: Protocol given for blood pressure, Hb and PTH management Comments: All pts completed
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD >3X A WEEK versus HD 3X A WEEK

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for People and children without diabetes: Death at 12 months; Group 1: 0/8, Group 2: 0/8
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Inadequate randomisation (alphabetic-alternate) and limited baseline stats; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Korevaar 2003[211]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=38)
Countries and setting	Conducted in Netherlands; Setting: 38 Dutch dialysis centres
Line of therapy	1st line
Duration of study	Intervention + follow up: Median 2.5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	>18, dialysis as first form of RRT, no medical/social/logistic objections against HD or PD
Exclusion criteria	Nil else
Recruitment/selection of patients	Nil specified
Age, gender and ethnicity	Age - Range of means: 55-62. Gender (M:F): 22:16. Ethnicity:
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	No indirectness
Interventions	(n=18) Intervention 1: Haemodialysis - HD (generic). HD, nil else specified, of 18 randomised to HD: 1 started with PD, 5 received a kidney transplant, 1 changed to PD after starting with HD . Duration Median follow-up 2.5 years . Concurrent medication/care: Usual care

	(n=20) Intervention 2: Peritoneal dialysis - PD (generic). PD generic, majority CAPD, of 20 randomised to PD: 3 started with HD instead of PD, 3 received a kidney transplant during follow-up and 4 changes to HD after receiving PD . Duration Median follow-up 2.5 years. Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC) Protocol outcome 1: Quality of life - Actual outcome for General population: EuroQol VAS mean over 2 years (0-100, higher is better) at 2 years; Group 1: mean 59.2 (SD 11.8); n=18, Group 2: mean 54.4 (SD 21.9); n=20 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Mortality at >/= 6 months - Actual outcome for General population: Mortality, time to event (up to 5 year follow-up) at Median follow-up 2.5 years; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Lafrance 2012[224]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=1820)
Countries and setting	Conducted in Canada
Line of therapy	1st line
Duration of study	Intervention time:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	None
Exclusion criteria	Less than 90 days dialysis. Kidney transplant
Age, gender and ethnicity	Age - Mean (SD): HD 58.5 (16.4) PD 58.8 (15.5). Gender (M:F): 41% female. Ethnicity: > 86% white
Further population details	
Extra comments	Patients on long term dialysis between Jan 2001 and Dec 2007
Indirectness of population	No indirectness
Interventions	(n=910) Intervention 1: Haemodialysis - HD (generic). Home and in-centre combined. Duration At least 90 days. Concurrent medication/care: No details

	(n=910) Intervention 2: Peritoneal dialysis - PD (generic). No details. Duration At least 90 days. Concurrent medication/care: No details
Funding	Academic or government funding (Fonds de la recherche en sante du Quebec)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC) Protocol outcome 1: Hospitalisation - length of stay at >/= 6 months - Actual outcome for General population: Length of stay at Median 2 yrs; ; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Age HD 58.5 PD 58.8; Key confounders: Age, ethnicity, baseline health, comorbidities; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Locatelli 1996[254]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in Italy; Setting: Part of multi-centre trial, in a stratum of 30 centres
Line of therapy	1st line
Duration of study	Intervention time: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18-70y, 'very stable' clinical condition - including on RRT for at least two months - with regular thrice weekly haemodialysis
Exclusion criteria	Malignant disease (ascertained or suspected), MI within 12 months, stroke or TIA in last 6 months or severe heart failure (NYHA III-IV)
Recruitment/selection of patients	May 1991 - November 1992
Age, gender and ethnicity	Age - Mean (SD): 52.7(12.9) HDF, 54.8(12.6) HD. Gender (M:F): 71:29. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 54y). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	. Prev. diabetic nephropathy 2.0% HDF, 5.5% HD
Indirectness of population	No indirectness

Interventions	(n=50) Intervention 1: Haemodialysis - HDF. High-flux polysulfone hemodiafiltration (8 to 12 litre/session in post-dilution). The dialysate was to be carefully handled to ensure its high quality and prevent pyrogen. Session time and blood flow being scheduled in order to obtain a Kt/V of at least 1 and an ultrafiltration rate < 2% body wt/hr, adjusted according to the actual value obtained from the domain map. Duration 24 months. Concurrent medication/care: All other treatments to be continued. If treatment was deemed inadequate, physician was free to adjust as necessary Comments: Drop-outs: 12 technical, 3 inadequacy, 8 transplant (n=105) Intervention 2: Haemodialysis - HD (generic). Mix of high-flux and low-flux polysulfone haemodialysis (8 to 12 litre/session in post-dilution). Session time and blood flow being scheduled in order to obtain a Kt/V of at least 1, adjusted according to the actual value obtained from the domain map. Duration 24 months. Concurrent medication/care: All other treatments to be continued. If treatment was deemed inadequate, physician was free to adjust as necessary Comments: Dropouts: 26 technical, 4 acute clinical, 3 fistula-related, 6 inadequacy, 10 transplant
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Deaths at 24 months;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HD has more men and diabetics, high numbers not completing; Indirectness of outcome: No indirectness ; Baseline details: HD has more men and diabetics; Group 1 Number missing: 23, Reason: up to 23; Group 2 Number missing: 49, Reason: up to 49

Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations at 24 months; rate ratio: 1.5);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HD has more men and diabetics, high numbers not completing; Indirectness of outcome: No indirectness ; Baseline details: HD has more men and diabetics; Group 1 Number missing: 23, Reason: up to 23; Group 2 Number missing: 49, Reason: up to 49

Protocol outcome 3: AEs - vascular access issues
- Actual outcome for General population: Fistula-related reason for withdrawal from study at 24 months; Group 1: 0/50, Group 2: 3/105

Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HD has more men and diabetics, high numbers not completing; Indirectness of outcome: No indirectness ; Baseline details: HD has more men and diabetics; Group 1 Number missing: 23, Reason: up to 23; Group 2 Number missing: 49, Reason: up to 49	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	**Locatelli 2010[252]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=146)
Countries and setting	Conducted in Italy; Setting: Italian dialysis centres
Line of therapy	1st line
Duration of study	Intervention time: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	At the time of randomization, patients must have been on thrice weekly HD for at least 6 months. Other inclusion criteria will be: age between 18 and 80 years, body weight not higher than 90 kg, and stable clinical

	conditions.
Exclusion criteria	Patients with clinically relevant infections, malignancies, active systemic diseases, active hepatitis or cirrhosis, unstable diabetes, diuresis >200ml/24 h or a malfunction of vascular access with a blood flow rate <300ml/min will be excluded from the study. Follow-up monitoring and data registration Patients will be asked to sign a detailed informed consent. All relevant anamnestic and clinical data will be recorded. Particular attention will be paid to nutritional and cardiovascular parameters and to general co-morbid conditions. Registration of all data will be performed by one or two nephrologists and one or two nurses, appointed as study monitors in each collaborative centre. Laboratory parameters The pre-dialysis levels of the following parameters will be registered monthly: haemoglobin, leukocytes, platelets, serum electrolytes (sodium, potassium, bicarbonate, calcium, phosphorus), BUN, creatinine, total protein and albumin. BUN, sodium, potassium, bicarbonate, calcium, phosphorus and total proteins will also be evaluated at the end of session. The following parameters will be determined every 3 months: iron, ferritin and transferrin. Cholesterol, triglyg
Age, gender and ethnicity	Age - Median (IQR): 67.4 (58.1 to 73.3). Gender (M:F): 84 male, 62 female. Ethnicity:
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	Very serious indirectness: All on RRT previously
Interventions	(n=70) Intervention 1: Haemodialysis - HD (generic). HD was performed with a low-flux membrane and with a dialysate flow rate of 500 ml/min. . Duration 24 months. Concurrent medication/care: HD, HF, and HDF machines all were provided by a dialysis fluid UF system for the production of ultrapure dialysate and sterile nonpyrogen substitution fluid, checked at monthly intervals. Dialysate/infusate conductivity, dialysate/infusate calcium and bicarbonate concentrations and the dialysate/infusate temperatures, food ingestion habits during the study, and the use of

	antihypertensive drugs before the dialysis session were kept constant according to the centre's policy, to follow everyday clinical practice as much as possible. Blood flow was between 300 and 400 ml/min, and the treatment time was between 3.0 and 4.5 hours for each session. Dialysate/infusate compositions were sodium 133 to 152 mEq/L, potassium 1 to 3 mEq/L, calcium 2.5 to 4.0 mEq/L, acetate 4 mEq/L, bicarbonate 26 to 38mEq/L, and glucose 1 g/L. . Indirectness: No indirectness (n=40) Intervention 2: Haemodialysis - HDF. HDF was performed with a synthetic high-flux membrane with an infusate/blood flow ratio of 0.6 and a dialysate plus infusate rate of 700 ml/min. . Duration 24 months . Concurrent medication/care: HD, HF, and HDF machines all were provided by a dialysis fluid UF system for the production of ultrapure dialysate and sterile nonpyrogen substitution fluid, checked at monthly intervals. Dialysate/infusate conductivity, dialysate/infusate calcium and bicarbonate concentrations and the dialysate/infusate temperatures, food ingestion habits during the study, and the use of antihypertensive drugs before the dialysis session were kept constant according to the centre's policy, to follow everyday clinical practice as much as possible. Blood flow was between 300 and 400 ml/min, and the treatment time was between 3.0 and 4.5 hours for each session. Dialysate/infusate compositions were sodium 133 to 152 mEq/L, potassium 1 to 3 mEq/L, calcium 2.5 to 4.0 mEq/L, acetate 4 mEq/L, bicarbonate 26 to 38mEq/L, and glucose 1 g/L. . Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus HDF

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Mortality at 24 months at 24 months; Group 1: 8/66, Group 2: 2/39
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in diabetes and dialysis technique before study; 87.1% on HD in HD group, 77.5% on HD before study
17.1% diabetic in HD group, 27.5% diabetic HDF group; Group 1 Number missing: 4, Reason: Dropped out during 3 month adaptation period; Group 2 Number missing: 1, Reason: Dropped out during 3 month adaptation period

Protocol outcome 2: AEs - infections at Define
- Actual outcome for General population: Infection at 24 months at 24 months; Group 1: 1/66, Group 2: 0/39
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in diabetes and dialysis technique before study;

87.1% on HD in HD group, 77.5% on HD before study 17.1% diabetic in HD group, 27.5% diabetic HDF group; Group 1 Number missing: 4, Reason: Dropped out during 3 month adaptation period; Group 2 Number missing: 1, Reason: Dropped out during 3 month adaptation period Protocol outcome 3: AEs - vascular access issues at Define - Actual outcome for General population: Thrombosis or vascular access infection at 24 months at 24 months; Group 1: 2/66, Group 2: 0/39 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in diabetes and dialysis technique before study; 87.1% on HD in HD group, 77.5% on HD before study 17.1% diabetic in HD group, 27.5% diabetic HDF group; Group 1 Number missing: 4, Reason: Dropped out during 3 month adaptation period; Group 2 Number missing: 1, Reason: Dropped out during 3 month adaptation period	
Protocol outcomes not reported by the study	Quality of life at Define; Symptom scores/functional measures at Define; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form at Define; Psychological distress and mental wellbeing at Define; Preferred location of death at Define; Cognitive impairment at Define; Patient/family/carer experience of care at Define; Growth at Define; Malignancy at Define; AEs - dialysis access issues at Define; AEs - acute transplant rejection episodes at Define

Study (subsidiary papers)	Manns 2009[271] (Culleton 2007[87], Klarenbach 2013[204])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=52)
Countries and setting	Conducted in Canada; Setting: 10 dialysis centres at two universities in Alberta, Canada.
Line of therapy	1st line
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 18y or older, receiving conventional haemodialysis three times weekly, interested and willing to train for and commence nocturnal haemodialysis
Exclusion criteria	Lacked physical or mental capacity to train to carry out procedure independently
Recruitment/selection of patients	Recruitment started August 2004 and study completed in December 2006, six months after the enrolment of the last participant
Age, gender and ethnicity	Age - Mean (SD): int 55.1(12.4) control 53.1(13.4). Gender (M:F): 32:20. Ethnicity: 86% Caucasian
Further population details	1. Age: Not applicable (Adults, ave 54y). 2. BMI: Not applicable (Mixed, ave 25). 3. DM: Not applicable (41% diabetic). 4. Ethnicity: Not applicable (86% white race).
Extra comments	Baseline characteristics for int/control: White race% 69/56, BMI 26/24, year on dialysis 5.5/4.8, prior transplant% 27/36, already home/self-care HD% 31/48, AVF% 58/56, comorbid diabetes% 38/44, serum albumin 3.7/3.6, ferritin 427/493 , aetiology of CKD: diabetic 30%, Gnephritis 25%, urologic 12%, PKD 8%,

	vascular 8%. medication use: aspirin 40%, ACE/ARB 60%, CaCB 45%, Bblocker 37%, phosphate binder 72%.
Indirectness of population	Serious indirectness: Not RRT naive, moving from their existing modality to a related sub-modality
Interventions	(n=27) Intervention 1: Haemodialysis - HD at home >3x a week. Nocturnal home haemodialysis, for or six times per week. Trained in-centre 4 to 5 times per week, for 2 to 6 weeks, with direct nursing supervision and monitoring of biochemical parameters. Upon completion of training, nocturnal haemodialysis was performed at home by the patient, without remote monitoring, 5 to 6 nights per week for a minimum of 6 hours per night. Dialysis was performed using Bellco Formula (Mississauga, Ontario, Canada) machines using polysulfone synthetic membranes. Bloodflow rates up to 250 mL/min were prescribed and dialysate flow rates of 300mL/min were used in all patients. Water was purified using reverse osmosis and ultrapure dialysate was not used. Dialysate calcium was 5.0 to 7.0 mg/dL(1.25-1.75 mmol/L) and phosphate was added to the dialysate bath as needed to prevent hypophosphatemia. Duration 6 months. Concurrent medication/care: Blood pressure was managed by haemodialysis physicians according to a published algorithm targeting a goal post-dialysis blood pressure of less than 130/80 mm Hg. Anaemia management was carried out according to a standardized nursing-led anaemia protocol with a target haemoglobin of 11.0 to 12.5 g/dL using intravenously administered erythropoietic-stimulating proteins and iron supplements as necessary. Mineral metabolism was managed to achieve local treatment goals of 8.0 to 10.2mg/dL (2.00-2.55 mmol/L) for serum calcium, less than 5.6 mg/dL (1.80 mmol/L)for serum phosphate, and 150 to 300 pg/mL (150-300 ng/L) for intact parathyroid hormone. Comments: 26 received intervention, 3 discontinued before six months (n=25) Intervention 2: Haemodialysis - HD 3x a week. Usual haemodialysis: Patients continued their prerandomization dialysis modality with thrice-weekly haemodialysis and a dialysis prescription to target a single-pool Kt/V (normalized clearance by time product, a derived quantity related to treatment-related changes in urea concentrations) of greater than 1.2. Dialysate calcium was adjusted between 4.0 and 7.0 mg/dL (1.00-1.75 mmol/L)depending on the serum calcium level. Duration 6 months. Concurrent medication/care: Blood pressure was managed by haemodialysis physicians according to a published algorithm targeting a goal postdialysis blood pressure of less than 130/80 mm Hg. Anaemia management was carried out according to a standardised nursing-led anaemia protocol with a target haemoglobin of 11.0 to 12.5 g/dL using intravenously administered erythropoietic-stimulating proteins and iron supplements as necessary. Mineral metabolism was managed to achieve local treatment goals of 8.0 to 10.2mg/dL (2.00-2.55 mmol/L) for serum calcium, less than 5.6 mg/dL (1.80 mmol/L) for serum phosphate, and 150 to 300 pg/mL (150-300 ng/L) for intact parathyroid hormone. Comments: 25 received intervention, 2 discontinued before six months

Funding	Other (Funded entirely by the Kidney Foundation of Canada)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NOCTURNAL HD versus HD 3X A WEEK

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical composite score at 6 months; MD; 1.24 (95%CI -3.59 to 6.07) (p-value: 0.61) pt SF-36 physical composite score mean difference of change score Top=High is good outcome, Comments: Using difference in quality of life (nocturnal haemodialysis-conventional haemodialysis) comparing pre-randomisation and 6 months after start;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: SF-36 mental composite score at 6 months; MD; 0.71 (95%CI -5.85 to 7.26) (p-value: 0.61) pt SF-36 mental composite score mean difference in change score Top=High is good outcome, Comments: Using difference in quality of life (nocturnal haemodialysis-conventional haemodialysis) comparing pre-randomisation and 6 months after start.;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: EQ5D at 6 months; Group 1: mean 0.6 (SD 0.28); n=27, Group 2: mean 0.6 (SD 0.29); n=25
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: KDQOL symptom score at 6 months; MD; -1.04 (95%CI -8.31 to 6.23) (p-value: 0.77) pt KDQOL symptom score mean difference in change score Top=High is good outcome, Comments: Using difference in quality of life (nocturnal haemodialysis-conventional haemodialysis) comparing pre-randomisation and 6 months after start;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Hospitalisation - length of stay at >/= 6 months
- Actual outcome for General population: Death at 6 months; Group 1: 1/26, Group 2: 0/25
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal). No mention of baseline rate of hospitalisations; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 6: AEs - infections - Actual outcome for General population: Bacteraemia at 6 months; Group 1: 4/26, Group 2: 4/25; Comments: No events: nHD 5 vs cHD 4 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal). No mention of baseline rate of hospitalisations; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: AEs - vascular access issues - Actual outcome for General population: Insertion or replacement of tunneled dialysis catheter at 6 months; Group 1: 7/26, Group 2: 5/25; Comments: Numbers of events: nHD 7 vs cHD 7 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal). No mention of baseline rate of hospitalisations; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Hospitalisation or other healthcare resource use at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Growth ; Malignancy ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	McDonald 2009[278]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=25287)
Countries and setting	Conducted in Australia, New Zealand; Setting: Australia and New Zealand
Line of therapy	1st line
Duration of study	Follow up (post intervention): Maximum follow-up 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients commencing dialysis from 1991 to 2005 in Australia and New Zealand
Exclusion criteria	Survived less than 90 days from commencement of dialysis
Recruitment/selection of patients	Retrospective cohort analysis from ANZDATA
Age, gender and ethnicity	Age - Median (IQR): 60 (48 to 70). Gender (M:F): 55:45. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=14733) Intervention 1: Haemodialysis - HD (generic). Including hospital, satellite and home based. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care

	(n=10554) Intervention 2: Peritoneal dialysis - PD (generic). Including CAPD and APD . Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care
Funding	Principal author funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality, HR, general population, median age ~60 at From 1 year onwards, median duration of follow-up ~2.5 years; Group 1: n=10554 ; Group 2: n=14733; HR 1.35; Lower CI 1.27 to Upper CI 1.42 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Mehrotra 2011[284]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=252961)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up: Median follow-up ~2.5years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients from US renal data system 1996-2004, recorded as on dialysis modality as specified 90 days after service date, continuous treatment for 60 days
Exclusion criteria	-
Recruitment/selection of patients	Retrospective cohort analysis
Age, gender and ethnicity	Age - Other: >18, results stratified by age. Gender (M:F): Define. Ethnicity:
Further population details	
Extra comments	Latest of 3 3 year cohorts extracted to avoid overlap with other publications
Indirectness of population	No indirectness

Interventions	(n=233082) Intervention 1: Haemodialysis - HD in centre. In centre HD only. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care (n=19879) Intervention 2: Peritoneal dialysis - PD (generic). CAPD or APD but not other forms of PD. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care
Funding	Study funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD IN CENTRE Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for People and children without diabetes: Mortality, HR, 18-64, with at least one comorbidity and no DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Mortality, HR, 65 and older, with at least one comorbidity and DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children without diabetes: Mortality, HR, 65 and older, with at least one comorbidity and no DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Mortality, HR, 18-64, with at least one comorbidity and DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Mesaros-Devcic 2013[290]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=85)
Countries and setting	Conducted in Croatia; Setting: Three dialysis centres in Croatia
Line of therapy	1st line
Duration of study	Intervention time: 36 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Unclear: A number of subgroup comparisons presented in paper, only overall analysed here
Inclusion criteria	Aged over 18, with established renal failure, on chronic program at HD centre for at least three months
Exclusion criteria	Blood flow <250ml/min in more than 30% treatments in the three months before enrolment
Recruitment/selection of patients	Selected by centres for the trial
Age, gender and ethnicity	Age - Mean (SD): HDF 58(11), HD 62(12). Gender (M:F): 50:35. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Does present results separately for older than 65y vs not). 2. BMI: Not applicable 3. DM: Not applicable (Does present results separately for diabetic nephropathy vs not, but not by current DM status). 4. Ethnicity: Not applicable
Extra comments	Pt Characteristics: vascular access via AVF 87%, catheter 13%, time on dialysis 90 months, SBP 140mmHg, on antiHTN 72%, Hb 108g/L Etiology: G.nephritis 32%, diabetes 12%, N.sclerosis 8%, P.nephritis 7%, PKD 5%, unknown 5%

Indirectness of population	Serious indirectness: Not RRT naive, chosen on basis had at least 3 months on HD
Interventions	(n=42) Intervention 1: Haemodialysis - HDF. Online haemodiafiltration performed in the postdilution mode, with the filtration rates were adjusted to be between 25 and 30% of the achieved blood flow rate and substitution volume was targeted to be above 19 L per session. The electrolyte composition of the infusate was the same as the composition of the dialysis fluid. The intended HD treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min, as registered in a single haemodialysis treatments. The dialysate flow rate was kept at 500mL/min in both groups. The same high-flux dialyser was used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 36 months. Concurrent medication/care: In keeping with good practice guidelines Comments: Unclear how many completed protocol (n=43) Intervention 2: Haemodialysis - HD (generic). Low flux haemodialysis referred to as "standard dialysis". The intended HD treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min, as registered in a single haemodialysis treatments. The dialysate flow rate was kept at 500mL/min in both groups. The same high-flux dialyser was used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 36 months. Concurrent medication/care: In keeping with good clinical practice guidelines
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Death at 36 months; Group 1: 5/42, Group 2: 14/43 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail re randomisation, missing data not mentioned (high in other studies); Indirectness of outcome: No indirectness ; Baseline details: Female 17v18, age 62v58, time on RRT 85v100; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress

	and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Morena 2017[296]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=381)
Countries and setting	Conducted in France; Setting: Dialysis facilities
Line of therapy	1st line
Duration of study	Intervention + follow up: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged ≥65 years, with no significant diuresis and/or residual kidney function, on HFHD for ≥3 months, and considered stabilised, with 3-times-weekly HD sessions and haemoglobin within 9-13g/dl.
Exclusion criteria	Patients with severe malnutrition, unstable clinical condition, unipuncture or failed vascular access flow, or known problems of coagulation.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): 76.2 (4.9). Gender (M:F): 229/152. Ethnicity: Not reported
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	No indirectness
Interventions	(n=190) Intervention 1: Haemodialysis - HDF. Online hemodiafiltration (OLHDF) 3 time a week, 3 to 4 hours per sessions, with blood flow of 350 to 400 ml/min and a dialysate flow of 500 to 600 ml/min. Duration 24

	months. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=191) Intervention 2: Haemodialysis - HD 3x a week. High-flux haemodialysis (HFHD) 3 time a week, 3 to 4 hours per sessions, with blood flow of 350 to 400 ml/min and a dialysate flow of 500 to 600 ml/min. Duration 24 months. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Academic or government funding (Supported by a grant from the French Ministry of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OLHDF versus HFHD Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Deaths at 24 months; Group 1: 36/190, Group 2: 43/191 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 47; Group 2 Number missing: 58 Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: Hospitalisation at 24 months; Group 1: 309/190, Group 2: 346/191 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 47; Group 2 Number missing: 58	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Murtagh 2007[301]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=129)
Countries and setting	Conducted in United Kingdom; Setting: Four major renal units in South Thames Region
Line of therapy	1st line
Duration of study	Intervention time: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 75-79y 28%, 80-84y 46%, 85-89y 23%, >89y 4%
Stratum	Planned starters: "Late starters" would not be captured, as different pathway
Subgroup analysis within study	Not applicable
Inclusion criteria	Age >75 receiving routine pre-dialysis care - that is, under the care of dedicated multidisciplinary team for people expected to need renal replacement therapy in the next 18 months, who had chosen to prepare for dialysis or receive conservative care
Exclusion criteria	"Late starters" would not be captured, as different pathway, and those with incurable solid organ cancers were excluded
Recruitment/selection of patients	September 2003 to August 2004
Age, gender and ethnicity	Age - Range: . Gender (M:F): 85:44. Ethnicity: White 83%, black 11%, Asian 5%, other 1%
Further population details	1. Age: >80 (Age >75). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear (total comorbidity score given). 4. Ethnicity: Not applicable (83% white).
Extra comments	Analysis of prognosis by comorbidity performed. Proportion dialysis/conservative. Age <80y: 46/16%, 80-84y: 44/47%, >85y: 10/37%

	Etiology: uncertain 23/35%, GN 4/3%, diabetes 25/23%, renovascular 16%. Comorbidity (Davies) score 0: 15/13%, 1: 65/69%, 2: 19/18%
Indirectness of population	No indirectness
Interventions	(n=52) Intervention 1: Haemodialysis - HD (generic). After assessment and support, chose to start dialysis when indicated (HD or PD), whether or not started during the time of study. Duration 2 years. Concurrent medication/care: Multidisciplinary pre-dialysis care (n=77) Intervention 2: Conservative management. After assessment and support, chose not to receive dialysis. Duration 2 years. Concurrent medication/care: Multi-disciplinary pre-dialysis care
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIALYSIS versus CONSERVATIVE MANAGEMENT

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for Planned starters: Mortality in age >75 at 2 years; Group 1: Observed events 14 ; Group 2: Observed events 40; HR 2.94; Lower CI 1.56 to Upper CI 5.53; Test statistic: p=0.001
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Only 6 events per covariate, comparability of care unclear; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Baseline details: Difference seen in age (not comorbidity, ethnicity, aetiology or comorbidity score); Key confounders: age (not significant in multivariate model), ethnicity (not significant in univariate model), comorbidity (only vascular disease significant in multivariate model), aetiology (not significant in univariate model); Group 1 Number missing: , Reason: believable for registry trial; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Park 2013[330]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=26)
Countries and setting	Conducted in South Korea; Setting: Single university hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: 24 months, with selected 7 year follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	End-stage renal disease, receiving regular chronic haemodialysis at least three months, three times a week, using high flux
Exclusion criteria	Any of the following medical events: MI, CVA, surgical procedure in last 2 months, CHF >NYHA2 or valvular or congenital heart defect, AF, pacemaker, COPD, severe hepatic disease, malignant neoplasm, or other physical or mental problems that limit normal daily activities
Recruitment/selection of patients	2005-6 from HD outpatients
Age, gender and ethnicity	Age - Mean (SD): HD 59.8(6.5) HDF 55.7(18.5). Gender (M:F): 11:15. Ethnicity: Not stated
Further population details	
Extra comments	. Baseline characteristics: HD duration 36 months, cause diabetic 65%, cause HTN 19%, comorbid diabetes 65%, comorbid HTN 54%, ave SBP 145mmHg

Indirectness of population	Serious indirectness: Not naive to RRT - all receiving HD prior to randomisation
Interventions	(n=20) Intervention 1: Haemodialysis - HDF. Online haemodiafiltration with postdilution, 4h, 3 x week with bicarbonate dialysis fluid and heparin as an anticoagulant. Used the AK200 ULTRA S with nonreprocessed polyamide membrane. Blood flow was maintained at 250ml/minute, dialysate flow was 600ml/minute, and the temperature of the dialysate was approximately 36 degrees. Duration 24 months. Concurrent medication/care: Not stated Comments: 11 completed trial, with 3 of drop-outs switching to HD (n=20) Intervention 2: Haemodialysis - HD (generic). conventional HD (4-hour sessions, three times a week, high-flux). Duration 24 months. Concurrent medication/care: Not stated Comments: 15 completed trial, with one drop-out switching to HDF
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Death at 24 months; Group 1: 1/20, Group 2: 1/20 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear randomisation/concealment, no statement re comparability of care, unclear whether those who left study were followed for mortality; Indirectness of outcome: No indirectness ; Group 1 Number missing: , Reason: unclear ? 4 that transferred hospital; Group 2 Number missing: , Reason: unclear ? 2 that transferred hospital	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Schiffl 2007[386]
Study type	RCT (Patient randomised; Crossover: Adequate according to protocol)
Number of studies (number of participants)	1 (n=76)
Countries and setting	Conducted in Germany; Setting: Unclear
Line of therapy	1st line
Duration of study	Intervention time: Two blocks of two years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Clinically stable, CKD on 3 x wk conventional HD for at least 6 months and a permanent vascular access capable of a blood flow of at least 250ml/min
Exclusion criteria	Malignancy, severe comorbidity (e.g. heart failure NYHA III-IV) or infectious disease
Recruitment/selection of patients	Unclear
Age, gender and ethnicity	Age - Mean (range): 62 (32-78). Gender (M:F): 42:34. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 62). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	At entry, pts had completed between 9 and 280 months of HD, mean 25. Etiology: glomerulonephritis (22) HTN (18) diabetes (22) PKD (8) chronic tubulointerstitial (7) unknown (6)
Indirectness of population	Serious indirectness: Not RRT naive, required to have been on HD for six months prior to entry

Interventions	(n=76) Intervention 1: Haemodialysis - HDF. Online HDF utilising high-flux polysulfone dialysers performed thrice per week for 4 to 5 hours, blood flow rates ranged from 250-350ml/min, with dialysis flow rate 500ml/min and substitution fluid at 4.5litres/hour, with prescription adapted to the individual and reviewed intermittently. Study involves 24 months on HDF and 24 months on HF-HD in random order. Duration 24 months. Concurrent medication/care: Protocol for management of other aspects of CKD (n=76) Intervention 2: Haemodialysis - HD (generic). High-flux conventional haemodialysis utilising high-flux polysulfone dialysers performed thrice per week for 4 to 5 hours, blood flow rates ranged from 250-350ml/min, with dialysis flow rate 500ml/min, and prescription adapted to the individual and reviewed intermittently. Study involves 24 months on HDF and 24 months on HF-HD in random order. Duration 24 months. Concurrent medication/care: Protocol for managing other aspects of CKD
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD Protocol outcome 2: Symptom scores/functional measures - Actual outcome for General population: Physical symptoms at 24 months; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unblinded and query selective reporting (only dimension of QoL measure that is reported well enough to analyse); Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 Protocol outcome 3: Mortality at >/= 6 months - Actual outcome for General population: Death at 24 months; Group 1: 3/73, Group 2: 3/72 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Snyder 2002[402]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=22776)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	First started therapy between 1995 and 1998 and had been on the same dialysis modality for at least 60 days on day 90 of therapy
Exclusion criteria	Not reported
Age, gender and ethnicity	Age - Other: 80% between 30 and 64 yrs. Gender (M:F): 48%. Ethnicity:
Further population details	
Extra comments	Patients who had been on PD or HD prior to transplantation
Indirectness of population	No indirectness
Interventions	(n=22776) Intervention 1: Transplant - Living donor. Not reported. Duration Not relevant. Concurrent medication/care: Not reported

	(n=22776) Intervention 2: Transplant - Deceased donor. Not reported. Duration Not applicable. Concurrent medication/care: Not reported
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LIVING DONOR versus DECEASED DONOR Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality at Up to 5 yrs; RR; 0.71 (95%CI 0.6 to 0.83) (p<0.05) ; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: Unclear number of confounders and events; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to failure of RRT form - Actual outcome for General population: Graft failure at Up to 5 yrs; RR; 0.88 (95%CI 0.79 to 0.98) (p<0.05) ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: Unclear number of confounders and events; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Stefansson 2012[407]
Study type	RCT (Patient randomised; Crossover: None)
Number of studies (number of participants)	1 (n=20)
Countries and setting	Conducted in Sweden; Setting: Single HD unit in a university hospital
Line of therapy	1st line
Duration of study	Intervention time: 2 months in each treatment
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults aged >18 years, in a clinically stable condition, receiving HD or HDF for last three months
Exclusion criteria	Acute inflammation, infection or cardiovascular disease
Recruitment/selection of patients	Recruited twenty, then another five to replace dropouts
Age, gender and ethnicity	Age - Mean (SD): 60.6(13.6). Gender (M:F): 14:6. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 61y). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	Scant baseline information given. Etiology of kidney disease - diabetic (7), glomerulonephritis (4), nephrosclerosis (4), PCKD (2) and chronic interstitial nephritis (3)
Indirectness of population	Serious indirectness: Not naive to RRT. All had received HD or HDF for at least 3 months.

Interventions	(n=20) Intervention 1: Haemodialysis - HDF. Haemodiafiltration, on-line post-dilution, with replacement volume standardised to 25-30% total blood treated. All treatments were carried out on AK 200 ULTRA dialysis machines (Gambro, Lund, Sweden) and with BL 200B blood tubing. Polyamide dialysis membranes were used in all treatments. All treatments were patient-blinded; the dialysis machine was concealed behind a screen, making it impossible for the patient to identify which treatment was given. Anticoagulation was performed with tinzaparin sodium (Innohep , Leo Pharma, Bellerup, Denmark). For each patient, the dialysis prescription was kept constant throughout the study (total dialysis time, dialysate flow = 500 ml/min, dialysate temperature and dialysate composition) and the blood flow was kept as stable as possible. Duration 60 days. Concurrent medication/care: Individual ESA and iron prescription as indicated (n=20) Intervention 2: Haemodialysis - HD (generic). Conventional low-flux haemodialysis. All treatments were carried out on AK 200 ULTRA dialysis machines (Gambro, Lund, Sweden) and with BL 200B blood tubing. Polyamide dialysis membranes were used in all treatments. All treatments were patient-blinded; the dialysis machine was concealed behind a screen, making it impossible for the patient to identify which treatment was given. Anticoagulation was performed with tinzaparin sodium (Innohep , Leo Pharma, Bellerup, Denmark). For each patient, the dialysis prescription was kept constant throughout the study (total dialysis time, dialysate flow = 500 ml/min, dialysate temperature and dialysate composition) and the blood flow was kept as stable as possible. Duration 60 days. Concurrent medication/care: ESA and iron prescriptions as indicated
Funding	Other (The Swedish Medical Research Council 9898, the Inga-Britt and Arne Lundberg Research Foundation, the John and Brit Wennerström Research Foundation, the Medical Association of Gothenburg, and the Sahlgrenska University Hospital Grant LUA/ALF)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical composite score at 60 days; Group 1: mean 46 pt (SD 17); n=20, Group 2: mean 47 pt (SD 14); n=20; SF-36 PCS 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - 5 people dropped out and were replaced, unclear how chosen, unclear randomisation, little baseline data, no washout period but uncertain would be carry-over at 60 days; Indirectness of outcome: No indirectness ; Baseline details: Crossover, and scant detail; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for General population: SF-36 mental composite score at 60 days; Group 1: mean 63 pt (SD 10); n=20, Group 2: mean 65 pt (SD 11); n=20; SF-36 MCS 0-100 Top=High is good outcome Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - 5 people dropped out and were replaced, unclear how chosen, unclear randomisation, little baseline data, no washout period but uncertain would be carry-over at 60 days; Indirectness of outcome: No indirectness ; Baseline details: Crossover, and scant detail; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Termorshuizen 2003[416]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=1222)
Countries and setting	Conducted in Netherlands; Setting: Netherlands
Line of therapy	1st line
Duration of study	Intervention + follow up: Median follow-up ~2.5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	>18 years of age, begin chronic dialysis as first form of RRT, survived first 3 months of dialysis, modality classified at 3 months
Exclusion criteria	Nil else
Recruitment/selection of patients	From NECOSAD
Age, gender and ethnicity	Age - Range: 52-62. Gender (M:F): 60:40. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=742) Intervention 1: Haemodialysis - HD (generic). Nil else specified. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care

	(n=480) Intervention 2: Peritoneal dialysis - PD (generic). Nil else specified. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for People and children without diabetes: Death, RR, <60, no DM, ITT censoring at 3 to 24 month follow-up; RR; 0.77 (95%CI 0.34 to 1.73, Comments: n = 488); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Death, RR, <60, with DM, ITT censoring at 3 to 24 month follow-up; RR; 6.35 (95%CI 1.42 to 28.36, Comments: n = 108); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children without diabetes: Death, RR, >60, no DM, ITT censoring at 3 to 24 month follow-up; RR; 1.03 (95%CI 0.62 to 1.72, Comments: n = 479); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Death, RR, >60, with DM, ITT censoring at 3 to 24 month follow-up; RR; 1.28 (95%CI 0.65 to 2.52); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Turkish HDF study trial: Ok 2013[322]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=782)
Countries and setting	Conducted in Turkey; Setting: 10 HD centres operated by Fresenius Medical Care in south and southeast Turkey
Line of therapy	1st line
Duration of study	Intervention time: Ave 23 months (1-39 months)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	January 2007 - March 2008 (extended due to initial slow recruitment) 899 identified, 117 did not meet inc/exc
Age, gender and ethnicity	Age - Mean (SD): 56.5(13.9). Gender (M:F): Define. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 57). 2. BMI: Not applicable (Ave 25). 3. DM: Not applicable (prev 35%). 4. Ethnicity: Not stated / Unclear
Extra comments	Extensive baseline info: Etiology - unknown 37%, diabetes 30%, HTN 10%, chronic g'nepritis 3.5%, other 19% Comorbidities - Diabetes 34.7%, smoking 24.9%, CV disease 26.4% Clinical - BMI 25, SBP 128, antihypertensive 13.6%, phosphate binder 83%, IV iron 57.7%, EPO 57.3%

	Vascular access - AV fistula 95.5%, ave blood flow 294 ml/min
Indirectness of population	Serious indirectness: Not RRT naive. Required to already be on HD
Interventions	(n=391) Intervention 1: Haemodialysis - HDF. OL-HDF procedure was performed in the postdilution mode using Fresenius 4008S dialysis machines, incorporating the ONLINEplus. The filtration rates were adjusted to be between 25 and 30% of the achieved blood flow rate and substitution volume was targeted to be above 15 L per session. The electrolyte composition of the infusate was the same as the composition of the dialysis fluid. The effective substitution volume (without the ultrafiltrate volume) used in analyses was calculated as mean of substitution volumes recorded in all sessions. The intended dialysis treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min. The dialysate flow rate was kept at 500 mL/min in both groups. The same high-flux dialysers, either FX60 or FX80 (Polysulfone-based Helixone Membrane) were used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 24 months. Concurrent medication/care: Not stated Comments: 110 dropped out due to - moved (58), switched (1), transplant (11), vascular access (40) (n=391) Intervention 2: Haemodialysis - HD (generic). High-flux haemodialysis using standard dialysate. The intended dialysis treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min. The dialysate flow rate was kept at 500 mL/min in both groups. The same high-flux dialysers, either FX60 or FX80 (Polysulfone-based Helixone Membrane) were used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 24 months. Concurrent medication/care: Not stated Comments: 90 dropped out - moved (81), switched (3), transplant (6)
Funding	Academic or government funding (European nephrology and dialysis institute)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Overall mortality at ave 23 months ; Group 1: 52/391, Group 2: 65/391
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98
- Actual outcome for General population: Overall mortality at ave 23 months ; Group 1: Observed events 52 n=391 ; Group 2: Observed events 65 n=391;

HR 1.04; Lower CI 1.02 to Upper CI 1.06 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98 - Actual outcome for People and children with diabetes: Death or non-fatal cardiovascular event at ave 23 months ; RR; 0.74 (95%CI 0.47 to 1.18) (n: 142 (HDF) 130 (HD)) ; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, missing data unknown (will be high), summary data only reported; Indirectness of outcome: Serious indirectness, Comments: Not just mortality - includes myocardial infarction, stroke, coronary revascularisation and unstable angina pectoris; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: Hospitalisation (count rate) at ave 23 months ; rate ratio: 1.10); Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98 Protocol outcome 3: AEs - vascular access issues - Actual outcome for General population: Withdrew due to VA issues at ave 23 months ; Group 1: 40/391, Group 2: 0/391 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	USRDS (transplant and dialysis data) trial: Merion 2005[288] (Abbott 2004[1], Glanton 2003[133])
Study type	Non randomised study
Number of studies (number of participants)	3 overlapping studies (n=Up to 157,969)
Countries and setting	Conducted in USA; Setting: USA using USRDS and CMS databases
Line of therapy	1st line
Duration of study	Other: 4-7y data: Glanton 1995-1999, Abbott 1995-2000, Merion 1995-2002
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with CKD entered onto kidney transplant list who also received dialysis through medicare or medicaid schemes
Exclusion criteria	Previous kidney transplant, waiting for another organ transplant, received transplant before starting dialysis
Recruitment/selection of patients	Retrospective
Age, gender and ethnicity	Age - Range: Merion - 0-17y 2.4%, 18-39y 25%, 40-59y 52%, >59y 21%. Gender (M:F): Merion - 59:41. Ethnicity: Using Merion - White 60%, African American 32%, Asian 5%, Other 2%
Further population details	1. Age: Not applicable (0-60+y age included). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not applicable (White 60% (of which 14% Hispanic), African American 32%, Asian 5%).
Extra comments	. Etiology: GN 22%, Diabetes 29%, HTN 24%
Indirectness of population	No indirectness

Interventions	(n=45082) Intervention 1: Haemodialysis - HD (generic). On the transplant waiting list, receiving dialysis. Duration 2-7y. Concurrent medication/care: Uncontrolled Comments: PD:HD not stated (n=64045) Intervention 2: Transplant - Transplant (generic). Received dialysis while on transplant waiting list, and received a transplant within five years. Duration 2-7y. Concurrent medication/care: Uncontrolled Comments: 14% live donor, 38% deceased donor, 7% extended-criteria donor
Funding	Academic or government funding (USRDS is supported by US dept Health Resources and Service Administration)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSPLANT (GENERIC) versus DIALYSIS (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death - deceased (non-extended criteria donor) transplant vs remain on waiting list - adjusted (Merion 2005) at Ave 3y; RR; 0.28 (95%CI 0.27 to 0.3);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern; Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: Death - deceased donor transplant vs remain on waiting list - adjusted (Abbott 2004) at Ave 3y; Group 1: n=16495 ; Group 2: n=17044; HR 0.47; Lower CI 0.44 to Upper CI 0.5
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern; Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: Death aged 65 and over - deceased donor transplant vs remain on waiting list - adjusted (Abbott 2004) at Ave 3y;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern; Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: Death for BMI≥30 kg/m² - deceased donor transplant vs remain on waiting list - adjusted (Glanton 2003) at Ave 2.5y; Group 1: n=1719 ; Group 2: n=5172; HR 0.39; Lower CI 0.33 to Upper CI 0.47
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern;

Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Vonesh 2004[438]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=398940)
Countries and setting	Conducted in USA; Setting: US, Medicare patients, from CMS
Line of therapy	1st line
Duration of study	Intervention + follow up: 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	Medicare patients starting dialysis between 1995 and 2000, survived first 90 days of ESRD, on modality for at least 60 days
Exclusion criteria	Nil else
Recruitment/selection of patients	Retrospective cohort analysis from CMS database
Age, gender and ethnicity	Age - Other: ~50% >65, 35% 45-64. Gender (M:F): 54:46. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=352706) Intervention 1: Haemodialysis - HD (generic). Nil else specified. Duration Maximum follow-up 3 years. Concurrent medication/care: Usual care

	(n=46234) Intervention 2: Peritoneal dialysis - PD (generic). Nil else specified. Duration Maximum follow-up 3 years. Concurrent medication/care: Usual care
Funding	Study funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for People and children without diabetes: RR, one or more comorbidities, aged 45-64, without diabetes at 3 year follow-up; RR; 1.01 (95%CI 0.92 to 1.11);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: RR, one or more comorbidities, aged 45-64, with diabetes at 3 year follow-up; RR; 0.96 (95%CI 0.91 to 1.01);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children without diabetes: RR, one or more comorbidities, aged at least 65, without diabetes at 3 year follow-up; RR; 0.82 (95%CI 0.77 to 0.87);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: RR, one or more comorbidities, aged at least 65, with diabetes at 3 year follow-up; RR; 0.80 (95%CI 0.76 to 0.85);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Ward 2000[447]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=45)
Countries and setting	Conducted in Germany; Setting: Neuried KfH dialysis centre
Line of therapy	1st line
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants had previously been treated by conventional HD of high-flux HD and were stable on thrice weekly regimen for two months, with permanent vascular access
Exclusion criteria	Vascular access not capable of delivering a blood flow of at least 250ml/min
Recruitment/selection of patients	45 pts recruited. Protocol allowed for further pts to be recruited to replace any person dropping out before six months, which led to six more being recruited
Age, gender and ethnicity	Age - Mean (SD): HDF 61+/-3, HFH 52+/-3. Gender (M:F): 29:16. Ethnicity: Not stated
Further population details	1. Age: Not applicable (ave 56y). 2. BMI: Not applicable (ave 23). 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	All participants were paired on the basis of body size, existing treatment time and blood flow rate, and predialysis serum beta2-microglobulin concentration, and pair were allocated to different treatments. Baseline characteristics: Cause of ESRD - glomerulonephritis 6/9, PCKD 2/5, diabetes 3/3, HTN 4/0; Duration of

	dialysis (mo) 47/68; BMI 23/23.
Indirectness of population	Serious indirectness: Patients not RRT naive, as needed to be stabilised on HD prior to commencement
Interventions	(n=24) Intervention 1: Haemodialysis - HDF. Postdilution hemodiafiltration was performed using a specifically designed system incorporating on-line preparation. blood is passed through a high-flux filter, where it is subjected to dialysis with ultrafiltration at a rate in excess of that required to achieve the patient's dry weight. Fluid balance is maintained by infusing sterile, nonpyrogenic substitution solution into the venous blood line. The substitution solution is derived from ultrapure dialysate by passing it through a single-use ultrafilter immediately before its infusion into the venous blood line. The dialysate is prepared by proportioning ultrafiltered water, liquid acid concentrate, and liquid bicarbonate concentrate made on-line from a dry powder cartridge. This dialysate is then rendered ultrapure by passage through a second untrafilter. At entry to the study, the ultrafiltration rate for each patient was set at 25% of the patient's blood flow rate. The ultrafiltration rate was then increased until the rate that provided a stable transmembrane pressure of 200 mmHg was found. Typical substitution solution flow rates ranged from 65 to 85 ml/min, and actual dialysate flow rates during hemodiafiltration ranged from 415 to 435 ml/min. Duration 12 months. Concurrent medication/care: Other aspects of the patients' therapy prescription did not differ between the two groups. Anticoagulation was achieved using a loading dose and constant infusion of heparin. Net fluid removal was set on an individual basis according to the patient's clinical need. (n=21) Intervention 2: Haemodialysis - HD (generic). High-flux haemodialysis was performed using a dialyzer containing polyamide membrane and a dialysate flow rate of 500ml/min . Duration 12 months. Concurrent medication/care: Other aspects of the patients' therapy prescription did not differ between the two groups. Anticoagulation was achieved using a loading dose and constant infusion of heparin. Net fluid removal was set on an individual basis according to the patient's clinical need.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD

Protocol outcome 1: Symptom scores/functional measures
- Actual outcome for General population: KDQ Physical symptoms at 12 months: Group 1: mean 4.8 pt (SD 0.3); n=24, Group 2: mean 4.8 pt (SD 0.4);

n=21; Kidney Disease Questionnaire, Physical symptoms dimension 1-7 Top=High is good outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HDF group older, shorter time on dialysis, more hypertensive kidney disease; difficult to understand why analysis of 45pts when the drop outs were replaced; Indirectness of outcome: No indirectness ; Baseline details: Age 61/52 (sd 3), aetiology HTN 4/0, duration of dialysis 47(sd9)/68(sd16); Group 1 Number missing: 1, Reason: 1 ?; Group 2 Number missing: 4, Reason: 3 hypertension worsened, 1 ? Protocol outcome 2: Psychological distress and mental wellbeing - Actual outcome for General population: KDQ Depression at 12 months; Group 1: mean 5.8 pt (SD 0.2); n=24, Group 2: mean 5.6 pt (SD 0.3); n=21; Kidney Disease Questionnaire, depression dimension 1-7 Top=High is good outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HDF group older, shorter time on dialysis, more hypertensive kidney disease; difficult to understand why analysis of 45pts when the drop outs were replaced; Indirectness of outcome: No indirectness ; Baseline details: Age 61/52 (sd 3), aetiology HTN 4/0, duration of dialysis 47(sd9)/68(sd16); Group 1 Number missing: 1, Reason: 1 ?; Group 2 Number missing: 4, Reason: 3 hypertension worsened, 1 ?	
Protocol outcomes not reported by the study	Quality of life ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Weinhandl 2010[451]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=12674)
Countries and setting	Conducted in USA; Setting: USA
Line of therapy	1st line
Duration of study	Follow up (post intervention): Mean follow-up 2.3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Adult patients, started dialysis in US in 2003, started with HD/PD, in CMS database
Exclusion criteria	Nil else
Recruitment/selection of patients	Propensity score matched cohorts used for analysis
Age, gender and ethnicity	Age - Range of means: 59-64. Gender (M:F): 54:46. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=6337) Intervention 1: Haemodialysis - HD (generic). Nil else provided . Duration Mean follow-up 2.3 years . Concurrent medication/care: Usual care

	(n=6337) Intervention 2: Peritoneal dialysis - PD (generic). Nil else provided . Duration Mean follow-up 2.3 years. Concurrent medication/care: Usual care
Funding	Study funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality, HR at Mean follow-up of 2.3 years; Group 1: n=6337 ; Group 2: n=6337; HR 0.92; Lower CI 0.86 to Upper CI 1 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Winkelmayer 2002[455]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=2539)
Countries and setting	Conducted in USA; Setting: New Jersey
Line of therapy	1st line
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	>65, began RRT between 1991 and 1996, either Medicare or Medicaid in New Jersey, renal insufficiency at least 1 year before starting dialysis, dialysis duration >1 month
Exclusion criteria	Transplantation within 1 month of starting RRT
Recruitment/selection of patients	Retrospective analysis of Medicare/Medicaid database
Age, gender and ethnicity	Age - Other: >65. Gender (M:F): 55:45. Ethnicity: ~80% white, ~15% black
Further population details	
Indirectness of population	No indirectness
Interventions	(n=1966) Intervention 1: Haemodialysis - HD (generic). HD as first mode of dialysis, no exclusion for switching but no detail provided on numbers switching, no other details specified (as entered on database). Duration 1

	year of follow-up. Concurrent medication/care: Usual care (n=537) Intervention 2: Peritoneal dialysis - PD (generic). PD as first mode of dialysis, no exclusion for switching but no detail provided on numbers switching, no other details specified (as entered on database). Duration 1 year . Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality at 1 year; Group 1: n=537 ; Group 2: n=1966; HR 1.24; Lower CI 1.09 to Upper CI 1.41; Comments: Principally driven by first and last 90 days of the year, violated proportional hazards assumption Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Wizemann 2000[457]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=44)
Countries and setting	Conducted in Germany; Setting: Appears to be from one HD centre
Line of therapy	1st line
Duration of study	Intervention time: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	"Chronic patients" not preselected according to disease status, nutritional status or anaemia
Exclusion criteria	Nil described
Recruitment/selection of patients	Not described
Age, gender and ethnicity	Age - Mean (SD): HDF 60(12)y, HD 61(11)y. Gender (M:F): 25:19. Ethnicity: not stated
Further population details	1. Age: Not applicable (Ave around 60y). 2. BMI: Not applicable (Unselected). 3. DM: Not applicable (prev 18%). 4. Ethnicity: Not stated / Unclear
Extra comments	Sparse baseline data: DM 8/44, IHD 27/44
Indirectness of population	Serious indirectness: Not RRT naive as recruited from HD programme

Interventions	(n=23) Intervention 1: Haemodialysis - HDF. Received on-line haemodiafiltration. The HDF system differed in the use of an additional filter (total surface area 3.6m2) and substitution fluid running about a target of 60litre/pt/session. The dialysate flow was kept low in order to match the Kt/V of HD, and treatment duration was kept the same. Duration 24 months. Concurrent medication/care: Both processes used bicarbonate dialysate, with blood flow 400-500ml/min and dialysate flow 500ml/min. Biochemical and clinical parameters were reviewed every two months, and prescription altered if appropriate. Non-dialysis care not described Comments: Seven pt dropped out over 24m (n=21) Intervention 2: Haemodialysis - HD (generic). Low flux haemodialysis using polysulfone filter. Duration 24 months. Concurrent medication/care: Both processes used bicarbonate dialysate, with blood flow 400-500ml/min and dialysate flow 500ml/min. Biochemical and clinical parameters were reviewed every three months, and prescription altered if appropriate. Non-dialysis care not described
Funding	Funding not stated (One of the author's affiliation is to Fresnius MC)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death at 24 months; Group 1: 1/23, Group 2: 2/21
Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No info re selection bias, high differential drop-out; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7, Reason: 2 transplant, 4 personal reasons, 1 febrile episode; Group 2 Number missing: 3, Reason: 3 personal reasons

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Woods 1996[463]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=3172)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up: Max follow up 4 years (median not stated)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Started treatment for ESRD between 1986 and 1987, Medicare entitled, data contained in USRDS,
Exclusion criteria	Patients receiving home HD within 30 days of onset of ESRD as likely to be nurse provided and worse prognosis
Recruitment/selection of patients	Retrospective cohort analysis, randomly sampled after weighting for size of centres
Age, gender and ethnicity	Age - Range: 49-59. Gender (M:F): Define. Ethnicity: ~60% white
Further population details	
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Haemodialysis - HD at home. HD at home, nil else specified. Duration Max follow-up 4 years. Concurrent medication/care: Usual care

	(n=3102) Intervention 2: Haemodialysis - HD in centre. HD in centre, nil else specified . Duration Max follow-up 4 years . Concurrent medication/care: Usual care
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD AT HOME versus HD IN CENTRE Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality, HR, median duration of follow-up not specified at Max follow-up 4 years; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Yeates 2012[468]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=35265)
Countries and setting	Conducted in Canada; Setting: Canada
Line of therapy	1st line
Duration of study	Intervention + follow up: Maximum follow-up 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	On dialysis (PD or HD) for at least 60 days, started dialysis in Canada between 1991 and 2007
Exclusion criteria	Died or censored within 90 days of starting dialysis
Recruitment/selection of patients	Retrospective cohort analysis from CORR
Age, gender and ethnicity	Age - --: >18. Gender (M:F): 58:42. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=32531) Intervention 1: Haemodialysis - HD (generic). Including hospital, community or home. Duration Maximum follow-up 5 years. Concurrent medication/care: Usual care

	(n=14308) Intervention 2: Peritoneal dialysis - PD (generic). Including home, satellite and hospital. Duration Maximum follow-up 5 years. Concurrent medication/care: Usual care
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for People and children without diabetes: Mortality, HR, age 45 to 64, no DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: Mortality, HR, age 45 to 64, with DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children without diabetes: Mortality, HR, age at least 65, no DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: Mortality, HR, age at least 65, with DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: All-cause hospitalisation rate ratio (Quebec only) at Maximum follow-up 5 years; Rate ratio: 0.99, Comments: Length of stay = HD 37.5 days per 1000 pt/days of follow-up, PD 39.7 days per 1000 pt/days of follow-up);
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Based on LaFrance 2012; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes