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Plant milks and childhood growth and nutritional status: a protocol for a systematic review

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Plant milks and childhood growth and nutritional status: a protocol for a systematic review

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ABSTRACT

Introduction: There has been much debate about the appropriateness of plant milks for supporting the nutritional requirements of growing children. This proposed systematic review aims to assess the totality of the evidence on the relationship between plant milk consumption and growth and nutritional status in childhood.

Methods and analysis: Ovid MEDLINE ALL (1946-Present), Ovid EMBASE Classic (1947-Present), CINAHL Complete (Cumulative Index to Nursing and Allied Health Literature), Scopus and the Cochrane Library (from 2000 to present; English language) alongside a search of grey literature will be searched comprehensively to find studies that describe the association between plant milk consumption and growth or nutrition in children 1-18 years of age. Two reviewers will identify eligible articles, extract data and assess the risk of bias in individual studies. If a meta-analyses is not conducted, the evidence will be synthesized narratively and the overall certainty of evidence will be rated using GRADE.

Ethics and dissemination: Ethical approval is not required for this study since no data will be collected. Results of the systematic review will be published in a peer-reviewed journal. Findings from this study may be useful in informing future evidence-based recommendations about plant milk consumption in children.

Registration: The study protocol was registered with PROSPERO (registration number: CRD42022367269).

KEYWORDS: children; plant milks; childhood growth; nutrition

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Article Summary

Strengths and limitations of this study

- The study could be limited by the number of available studies considering plant milk consumption in children is relatively new. Nonetheless, the findings of this review will fill an important knowledge gap and increase our understanding of the effects of plant milk consumption on childhood growth and nutritional status.
- Some relevant studies could potentially be missed. However, a comprehensive search strategy involving searching multiple databases alongside a search of grey literature will provide a comprehensive review of this important topic.

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1. INTRODUCTION

Cow milk has long been recommended as a good source of nutrition for children starting at one year of age [1,2]. Although cow milk has been a dietary staple for children in North America for over a century [3,4], parents are increasingly choosing plant milks (e.g., almond, soy, oat, rice) as a replacement for cow milk for children [5,6]. A recent study showed that one-third of parents of preschool-aged children purchased plant milk beverages [7]. With milk preferences shifting, understanding the nutritional effects of plant milk consumption in children is important.

While plant milks are often used as replacements for cow milk, many of these beverages are lower in nutrients than cow milk including energy, protein, fat and micronutrients such as calcium and vitamin D if not fortified [8,9]. There have been over 30 published cases of severe nutritional deficiencies (e.g., rickets, failure-to-thrive) in children between 2.5 and 22 months of age as a result of consuming rice, almond and soy milk instead of breastmilk, infant formula and cow milk [10]. These case reports have generated considerable debate about the appropriateness of plant milk consumption, particularly for young children. While most plant milk contain fewer nutrients than cow milk [8], consumption of plant milk may be common in children with allergies (e.g., to cow milk) [11] or pre-existing health conditions (e.g., atopic dermatitis) [12], which may independently influence growth and nutrient intake [13]. Furthermore, recommendations for vegetarian and vegan children state that fortified plant milks can provide children with essential nutrients such as calcium and contribute positively to children's nutrient intake [14]. Additionally, it is the position of the American Dietetic Association, Dietitians of Canada [15] and the Academy of Nutrition and Dietetics [16] that well-planned vegetarian including vegan diets (which exclude cow milk and may include plant milks) are not only nutritionally adequate but may provide

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health benefits for children. The complete avoidance of vegan in children was recommended only a decade ago, which reflects the evolution of nutrition recommendations [17].

1.1. *Objectives*

There is a great need for more research to fill the gaps in our knowledge of plant milk consumption in children. The proposed systematic review aims to synthesize the existing evidence on the effects of plant milk consumption on growth and nutritional status in children 1-18 years of age and to identify areas requiring further research.

1.2. *Rationale for the study*

To our knowledge, no systematic reviews have been done to assess the totality of the evidence on plant milk consumption in children. A literature search conducted in September 2022 in Ovid MEDLINE, Ovid Embase, PROSPERO, Open Science Framework, Google Scholar and the Cochrane Database of Systematic Reviews did not identify any ongoing or completed systematic reviews about plant milk for children. Thus, this systematic review will address an important knowledge gap providing evidence synthesis which may be helpful in informing future plant milk recommendations for children and help parents and healthcare professionals make informed decisions about plant milk for children.

2. **METHODS AND ANALYSIS**

2.1. *Study registration*

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The systematic review will be conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [18]. The protocol has been structured following the PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) guidelines for systematic review protocols [19] and has been registered with PROSPERO (International Prospective Register of Systematic Reviews) (registration number: CRD42022367269). The PRISMA-P checklist is attached in *Appendix 1*.

2.2. *Inclusion and exclusion criteria for study selection*

The study will include articles reporting the association between plant milk consumption and growth in children that meet the following inclusion criteria, as described in Table 1.

Table 1: Inclusion criteria and exclusion criteria for study selection

	Inclusion criteria	**Exclusion criteria**
Exposure	Plant milk (soy, almond, rice, oat, etc.) - Fortified or non-fortified - Sweetened or unsweetened	Dairy milk beverages Breastmilk or breastmilk substitutes (e.g., infant formula)
Outcomes	*Primary outcome:* - Child growth (weight or height) *Secondary outcomes:* - Body composition - Biochemical measures - Weight status - Prevalence of short stature	No data on any of the outcomes

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Types of studies	Cross-sectional, cohort, case-control, longitudinal studies and clinical trials (randomized and non-randomized)	Case reports
Publication type	Published in the English language Published in the year 2000 or later	Published in non-English language Published before the year 2000

2.2.1. Study population

Studies examining children between the ages of 1 to 18 years. Studies conducted in children younger than one year of age will be excluded as plant milks are not recommended in the first year of life [2,20].

2.2.2. Exposure

Studies evaluating consumption of plant milk (fortified or non-fortified; sweetened or unsweetened), which will be defined as any 'milk' beverage derived from plant-based ingredients (e.g., soy, almond, coconut, cashew, oats, rice or blends of these ingredients). A list of different types of plant milks can be found in Table 2. Studies examining breastmilk, breastmilk substitutes (e.g., infant formula, follow-up formula, toddler formula) and dairy milk beverages (e.g., goat's milk) will be excluded.

Table 2: Different types of plant milk beverages and example [21]

Legume	Nut	Seed	Grain/cereal
Soy Pea protein Peanut	Almond Cashew Coconut Macadamia Hazelnut	Flax Hemp Pumpkin Sunflower Sesame	Oat Rice Quinoa Buckwheat

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2.2.3. Outcomes

Studies evaluating childhood growth (weight or height) or nutritional status (e.g., dietary intake, micronutrient status, prevalence of overweight or obesity). Studies that do not contain information on at least one of the outcome measures will be excluded.

2.2.4. Types of studies and publication type

Cross-sectional, cohort, case-control and longitudinal studies or controlled clinical trials (randomized or non-randomized) published in English in a peer-reviewed journal during or after the year 2000. Articles published before this time will be excluded as plant milk consumption in children is relatively new and food practices have changed over the past few decades [22]. Only full-text articles will be considered (i.e., abstracts will be excluded).

2.3. *Outcomes*

2.3.1. Primary outcome

The primary outcome will be child growth. These will include anthropometric measurements (weight, kg; height, cm) as well as weight and height related z-scores (i.e., weight-for-age, weight-for-length, BMI-for-age, length-for-age, height-for-age).

2.3.2. Secondary outcome

The secondary outcome will be nutritional status which will be assessed using: (i) dietary intake (e.g., food frequency questionnaire or diet records collected over multiple days); (ii) biochemical

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indicators as measures of nutrient status (e.g., serum vitamin D, ferritin, B vitamins); (iii) body composition (e.g., waist circumference, body fat mass, lean body mass, body fat percentage, skinfold thickness); (iv) prevalence of underweight, overweight and obesity defined using BMI cut-offs as defined by the WHO: World Health Organization [23], CDC: Centers for Disease Control and Prevention [24], IOTF: International Obesity Task Force [25] or those provided by the author if other growth charts were used; and (v) prevalence of short stature defined as height that falls two standard deviations below the median height for children the same age and sex or height <3rd percentile of the WHO child growth standards [23].

2.4. *Information sources and search strategy*

2.4.1. Databases

A comprehensive search strategy will be designed by an Information Specialist (SC) in collaboration with the team. The search will be performed in the following databases: Ovid MEDLINE ALL which includes E-pub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® (1946-Present), Ovid Embase Classic +Embase (1947-Present), EBSCOhost CINAHL Complete (Cumulative Index to Nursing and Allied Health Literature), Scopus and the Cochrane Library, both Cochrane CENTRAL and the Cochrane Database of Systematic Reviews (CDSR). The databases will be searched for studies that were published in the year 2000 onwards. After the initial search will be completed in Ovid MEDLINE ALL, the search will be peer-reviewed by another Information Specialist following CADTH's Peer Review of Electronic Search Strategies (PRESS) checklist [26]. Revisions will be made accordingly and approved by the team before being translated into the other databases. A combination of subject headings and text words will be searched as appropriate in each database.

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The search strategy will combine various terms for plant milk (i.e., plant-based milk, non-dairy milk, non-dairy beverage, milk alternative, non-cow milk, soy milk, soy beverage, almond milk, almond beverage, nut milk, etc.) and study population ages 1 to 18 years (i.e., infant, preschool, child, adolescents, youth, pediatrics) using the Ovid Expert Searches Children Filter (Broad) [27]. A preliminary search strategy in Ovid MEDLINE is provided as an example in *Appendix 2*. PRISMA-S will be used to report the search strategies [28].

2.4.2. Manual searches

To ensure comprehensiveness, grey literature will be searched to identify any missing or additional studies. We will also search the reference section of included studies to identify additional articles and will try to contact experts in the field about any unpublished or ongoing studies. The grey literature search strategy will involve searching websites of pediatric nutrition societies (e.g., Canadian Pediatric Society, American Academy of Pediatrics), government organizations (e.g., Health Canada) and nutrition databases (e.g., PEN: Practice-based Evidence in Nutrition® developed by Dietitians of Canada) for relevant documents (fact sheets, government reports) about plant milk for children. The grey literature search will reflect the same eligibility criteria as the published literature searches.

2.6. *Data management*

Upon completing the translation of the search strategy across all selected databases, the Information Specialist (SC) will collate all studies in the bibliographic software program EndNote X9 and deduplicate the results using the Bramer method [29]. The studies will then be

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imported into the screening and extraction software Covidence [30], where two stages of screening will take place.

2.7. *Study selection*

The first reviewer (IS) will screen titles and abstracts to identify eligible articles. A second reviewer (CHD) will confirm the eligibility of the identified articles. Then, the same two authors will independently review and read the full text of potentially eligible studies. Any disagreements about inclusion will be resolved by discussion or a third senior reviewer (JLM). Publications that used the same cohort but evaluated different outcomes will be included as separate studies. The excluded studies will be reported using a PRISMA flowchart [31].

2.8. *Data extraction*

Two reviewers will independently extract the data from included studies. Conflicts will be resolved by a third reviewer, if needed. The following information will be extracted from each study using a standardized data extraction form: the first author, year of publication, country, study design, sample size, age of children, details about the exposure (daily amount of plant milk consumed, type of plant milk, etc.) and study results (estimates and corresponding 95% confidence intervals for each outcome of interest and p-value). If data on the same populations were reported in multiple articles, both will be considered for analysis. If sufficient information is not available in the full text publication the study authors will be contacted via email to obtain additional data.

2.8. *Risk of bias in individual studies*

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Risk of bias will be assessed independently by two reviewers. Discrepancies will be resolved by consensus. The Newcastle-Ottawa Scale will be used to assess the risk of bias in individual observational cohort and cross-sectional studies, which expresses risk of bias on a numerical scale ranging from 0 to 9. Scores < 7 will be considered low risk. Risk of bias of included clinical trials will be assessed using the Cochrane risk of bias tool (low, high, unclear) [32].

2.9. *Data synthesis*

The evidence will be summarized narratively due to anticipated heterogeneity between studies (e.g., variability in participants studied, exposure and outcome measures). Data on each outcome will be extracted, tabulated or graphed and characteristics of the studies, heterogeneity in study participants, exposure and outcomes, strengths and limitations and key findings will be described in the text. A meta-analysis will be conducted only if the study participants, exposure and outcomes are sufficiently similar. The heterogeneity between studies will be assessed using a forest plot and with the I^2 statistic [32].

2.10. *Additional analyses*

If sufficient data are available, we will tabulate the evidence by: (i) the type of plant milk consumed (soy, almond, etc.); (ii) age of children (since younger children have a higher risk of nutritional deficiencies) [33]; and (iii) health issues (e.g., food allergies) which contribute to suboptimal nutrient intake and poor growth in children [13].

2.10. *Confidence in cumulative evidence*

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The certainty of evidence will be assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation) [34,35]. The grade of the evidence will be downgraded based on study limitations (risk of bias as assessed by the Newcastle-Ottawa Scale or Cochrane risk of bias tool), inconsistency of results, imprecision (small sample size, wide confidence intervals), indirectness of evidence (presence of factors that limit the generalizability of the findings) and publication bias.

2.11. *Patient and public involvement*

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

DISCUSSION

Plant milk consumption is becoming increasingly popular among children. Despite this, it is unclear whether plant milks are beneficial for children. To address this, the aim of this review is to synthesize the available evidence on the association between plant milk consumption and growth and nutritional status in children up to 18 years of age. The findings of this review could also help identify gaps in the literature and areas that require further research. The certainty of the evidence in this systematic review may be limited by the number of studies available and the quality of individual studies. Nonetheless, it is expected that the findings will help strengthen the evidence that informs evidence-based recommendations about plant milk for children and may be of interest to parents, dietitians, paediatricians and other healthcare professionals when considering plant milk for children.

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Author Contributions: IS and JLM conceptualized and designed the research study and were major contributors in writing the protocol. SC developed and conducted the systematic review search, generated the initial search results and was a major contributor in writing the methods section. All authors critically reviewed and revised the protocol.

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Disclaimer: The funding agency had no role in study design, in the writing of the protocol or in the decision to submit the article for publication.

Competing Interests: JLM received an unrestricted research grant for a completed investigator-initiated study from the Dairy Farmers of Canada (2011-2012) and D-drops provided non-financial support (vitamin D supplements) for an investigator initiated study on vitamin D and respiratory tract infections (2011–2015).

Ethics Approval: This study does not involve human participants and ethical approval was not required.

Data availability: Not applicable.

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Appendix 1: PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol[17]

Section and topic	Item #	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,4
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1, 13
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	13
Sponsor	5b	Provide name for the review funder and/or sponsor	13
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	13
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8-9

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Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	8-9, Appendix 2
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	n/a
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7-8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	11
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	11
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11
Meta-bias(es)	16	Specify any planned assessment of meta-biases (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

From: Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg.* 2010;8(5):336-3

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Appendix 2: Final Ovid MEDLINE Search Strategy (October 6, 2022)

No.	Searches	Results
1	milk substitutes/ or soy milk/	1091
2	(milk* adj3 (noncow* or non cow* or substitut* or alternat* or plant* or vegan or vegeta*)).tw,kf.	3575
3	((milk* or beverage* or drink*) adj3 (soy* or oat* or almond* or nut or nuts or coconut* or macadamia* or hemp* or quinoa or rice or cashew* or corn or spelt or pea or peas or peanut* or pecan or pecans or banana* or lupin or cowpea* or hazelnut* or pistachio* or walnut* or sesame or flax* or sunflower* or teff or amaranth or pumpkin* or buckwheat or seed or seeds or legume*)).tw,kf.	4882
4	(nondairy or non dairy).tw,kf.	618
5	or/1-4	9230
6	exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young). in. [OVID broad children filter]	5517123
7	5 and 6	3820
8	limit 7 to english language	3415
9	limit 8 to yr="2000 -Current"	2637

Database: Ovid MEDLINE® ALL 1946 to October 5, 2022

This search used the Ovid Expert Searches Children Filter (Broad) – MEDLINE on line 6: https://tools.ovid.com/ovidtools/expertsearches.html

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-Preporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,4
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1,13

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Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	#5a	Indicate sources of financial or other support for the review	13
Sponsor	#5b	Provide name for the review funder and / or sponsor	13
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	13
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is already known	5
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
Methods			
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8-9
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	8-9, Appendix 2
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10

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Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
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Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

Notes:

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- 10: 8-9, Appendix 2 The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist was completed on 02. February 2023 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

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The effect of plant milk consumption on childhood growth: protocol for a systematic review

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Manuscripts

The effect of plant milk consumption on childhood growth: protocol for a systematic review

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ABSTRACT

Introduction: There has been much debate about the appropriateness of plant milks for supporting the nutritional requirements of growing children. This proposed systematic review aims to assess the totality of the evidence on the relationship between plant milk consumption and growth and nutritional status in childhood.

Methods and analysis: Ovid MEDLINE ALL (1946-Present), Ovid EMBASE Classic (1947-Present), CINAHL Complete (Cumulative Index to Nursing and Allied Health Literature), Scopus and the Cochrane Library (from 2000 to present; English language) alongside a search of grey literature will be searched comprehensively to find studies that describe the association between plant milk consumption and growth or nutrition in children 1-18 years of age. Two reviewers will identify eligible articles, extract data and assess the risk of bias in individual studies. If a meta-analyses is not conducted, the evidence will be synthesized narratively and the overall certainty of evidence will be rated using GRADE.

Ethics and dissemination: Ethical approval is not required for this study since no data will be collected. Results of the systematic review will be published in a peer-reviewed journal. Findings from this study may be useful in informing future evidence-based recommendations about plant milk consumption in children.

Registration: The study protocol was registered with PROSPERO (registration number: CRD42022367269).

KEYWORDS: children; plant milks; childhood growth; nutrition

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Article Summary

Strengths and limitations of this study

- A search strategy involving multiple databases and grey literature will provide a comprehensive overview of the existing literature on plant milk consumption in childhood.

- The study may be limited by few available studies because plant milk consumption in children is a relatively new dietary trend.

- Pooling data on various types of plant milks that differ in nutritional content may increase the sample size but potentially limits interpretation of findings.

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1. INTRODUCTION

Cow milk has long been recommended for children as it contains important nutrient such as calcium and vitamin D that are necessary for growth [1-3]. However, with plant milks such as almond and oat milk becoming more widely available in recent years many parents are choosing these beverages instead of cow milk for their children [4-6]. A recent Canadian study found that one-third of parents of preschool-aged children purchased plant milks [7]. With milk preferences shifting, understanding the nutritional effects of plant milk consumption in children is important.

Although plant milks are gaining popularity among children, it is not clear whether these beverages offer nutritional benefits for children [8-11]. International guidelines such as those from the American Academy of Pediatrics and Canadian Pediatric Society advise against plant milk consumption in early childhood [12,13]. While plant milks may be fortified with essential micronutrients such as calcium and vitamin D, they are generally lower in energy, protein and fat compared to cow milk [14,15]. There have been over 30 published cases of severe nutritional deficiencies (e.g. rickets, failure-to-thrive) reported in children between 2.5 and 22 months of age who consumed rice, almond and soy milk instead of breastmilk, infant formula and cow milk [16]. While these case reports have generated considerable debate about the appropriateness of plant milks for children, it is worth noting that in most of these studies children were given plant milk because of an allergy to cow milk [17] or a pre-existing health condition (e.g. atopic dermatitis) [18], which may independently affect growth and nutrient intake [19].

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Several recently published viewpoints and commentaries have challenged the current guidelines suggesting that children avoid plant milks, claiming that they are misguided and poorly supported, and that plant milks could be beneficial for children (e.g. due to their lower saturated content) [20,21]. Furthermore, some children may be allergic to dairy, lactose intolerant or follow a vegan diet that may prevent them from consuming cow milk [22]. Several studies have emphasized the important role of fortified plant milks in supporting nutritional requirements (e.g. calcium) of children who do not consume cow milk [19,23,24]. Moreover, results of the German Vechi Youth Study have shown that children who follow a vegetarian and vegan diet and consume some or no plant milk still meet their nutritional requirements and attain normal growth [25].

1.1. *Objectives*

There is a need for more research to fill the gaps in our knowledge of plant milk consumption in children. The proposed systematic review aims to synthesize and evaluate the existing evidence on the effects of plant milk consumption on growth and nutrition in children 1 to 18 years of age.

1.2. *Rationale for the study*

To our knowledge, no systematic reviews have been done to assess the totality of the evidence on plant milk consumption in children. A literature search conducted in September 2022 in Ovid MEDLINE, Ovid Embase, PROSPERO, Open Science Framework, Google Scholar and the Cochrane Database of Systematic Reviews did not identify any ongoing or completed systematic

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reviews about plant milk for children. Thus, this systematic review will address an important knowledge gap providing evidence synthesis which may be helpful in informing future plant milk recommendations for children and help parents and healthcare professionals make informed decisions about plant milk for children.

2. METHODS AND ANALYSIS

2.1. *Study registration*

The study protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRIMSA-P) guidelines [26] and has been registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42022367269). The PRISMA-P checklist is attached in *Appendix 1*. The findings of the systematic review will be reported according to the PRISMA statement [27].

2.2. *Inclusion and exclusion criteria*

The study will include articles reporting the association between plant milk consumption and growth in children that meet the following inclusion criteria (as described in Table 1):

2.2.1. **Study population**

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Studies that include children aged 1-18 years of age will be considered. Studies in children <1 year of age will be excluded as plant milks are not recommended during the first year of life [28].

2.2.2. **Exposure**

Studies that report the amount of plant milk consumed (fortified or non-fortified, sweetened or unsweetened) will be included. Plant milk will be defined as any 'milk' beverage derived from plant-based ingredients (e.g. soy, almond, coconut, cashew, oats, rice or blends of these ingredients). Studies examining plant-based infant and toddler formulas (e.g. soy-based formula) will be excluded as these are specifically formulated to meet the nutritional needs of children and differ from plant milks [28].

2.2.3. **Outcomes**

Studies evaluating growth (weight or height) or nutritional status (e.g. dietary intake, micronutrient status) will be eligible. Studies that do not contain information on at least one of the outcome measure will be excluded.

2.2.4. **Types of studies and publication type**

Cross-sectional, cohort, case-control, longitudinal studies and clinical trials (randomized or non-randomized) published in English in a peer-reviewed journal during or after the year 2000 will be included. Articles published before this time will be excluded as plant milk consumption in

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children is a recent dietary trend and food fortification practices have changed over the past few decades [29]. Only studies available in full text will be considered (i.e. abstracts will be excluded).

Table 1: Inclusion and exclusion criteria for study selection

	Inclusion criteria	Exclusion criteria
Population	Children aged 1-18 years	Children <1 year
Exposure	*Plant milk consumption* · Soy, almond, rice, oat, etc. · Fortified or non-fortified · Sweetened or unsweetened	Plant-based infant or toddler formula
Outcomes	*Primary outcome* · Growth (weight or height) *Secondary outcome* · Nutritional status (e.g. dietary intake, biochemical measures)	No data on any of the outcomes
Types of studies	Cross-sectional, cohort, case-control, longitudinal studies and clinical trials	Case reports
Publication type	English language Published in the year 2000 or later	Non-English language Published before the year 2000

2.3. *Outcomes*

2.3.1. **Primary outcome**

The primary outcome will be child growth. These will include anthropometric measurements (weight, kg; height, cm) as well as weight and height related z-scores (i.e. weight-for-age, weight-for-length, BMI-for-age, length-for-age, height-for-age).

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2.3.2. **Secondary outcome**

The secondary outcome will be nutritional status which will be assessed using the following methods: (i) dietary intake (e.g. mean calcium intake assessed using a food frequency questionnaire or diet records collected over multiple days); (ii) biochemical measures of nutrient status (e.g. serum levels of vitamin D or ferritin); (iii) body composition (e.g. waist circumference, body fat mass, lean body mass, body fat percentage, skinfold thickness); (iv) bone health (e.g. bone mineral density, peak bone mass); and (v) prevalence of underweight, overweight and obesity measured according to BMI cut-offs as defined by the WHO: World Health Organization [30], CDC: Centers for Disease Control and Prevention [31], IOTF: International Obesity Task Force [32] or those provided by the author if other growth charts were used; and (v) prevalence of short stature defined as height that falls two standard deviations below the median height for children the same age and sex or height <3rd percentile of the WHO child growth standards [30].

2.4. *Information sources and search strategy*

2.4.1. **Databases**

A comprehensive search strategy will be designed by an Information Specialist (SC) in collaboration with the team. The search will be performed in the following databases: Ovid MEDLINE ALL which includes E-pub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® (1946-Present), Ovid Embase Classic

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+Embase (1947-Present), EBSCOhost CINAHL Complete (Cumulative Index to Nursing and Allied Health Literature), Scopus and the Cochrane Library, both Cochrane CENTRAL and the Cochrane Database of Systematic Reviews (CDSR). The databases will be searched for studies that were published in the year 2000 onwards. After the initial search will be completed in Ovid MEDLINE ALL, the search will be peer-reviewed by another Information Specialist following CADTH's Peer Review of Electronic Search Strategies (PRESS) checklist [33]. Revisions will be made accordingly and approved by the team before being translated into the other databases. A combination of subject headings and text words will be searched as appropriate in each database. The search strategy will combine various terms for plant milk (i.e. plant-based milk, non-dairy milk, non-dairy beverage, milk alternative, non-cow milk, soy milk, soy beverage, almond milk, almond beverage, nut milk, etc.) and study population ages 1 to 18 years (i.e. infant, preschool, child, adolescents, youth, pediatrics) using the Ovid Expert Searches Children Filter (Broad) [34]. A preliminary search strategy in Ovid MEDLINE is provided as an example in *Appendix 2*. PRISMA-S will be used to report the search strategies [35].

2.4.2. **Manual searches**

To ensure comprehensiveness, grey literature and reference lists of included studies will be searched to identify any missing or additional articles. We will also try to contact experts in the field about any unpublished or ongoing studies. The grey literature search strategy will involve searching websites of nutrition and pediatric associations (e.g. Canadian Pediatric Society, American Academy of Pediatrics), government organizations (e.g. Health Canada) and nutrition databases (e.g. PEN: Practice-based Evidence in Nutrition® developed by Dietitians of Canada)

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for relevant documents (i.e. fact sheets, government reports) about plant milk consumption in children. The grey literature search will reflect the same eligibility criteria as the published literature searches.

2.6. *Data management*

Upon completing the translation of the search strategy across all selected databases, the Information Specialist (SC) will collate all studies in the bibliographic software program EndNote X9 and deduplicate the results using the Bramer method [36]. The studies will then be imported into the screening and extraction software Covidence [37], where two stages of screening will take place.

2.7. *Study selection*

The first reviewer (IS) will screen titles and abstracts to identify eligible articles. A second reviewer (CHD) will confirm the eligibility of the identified articles. Then, the same two authors will independently review and read the full text of potentially eligible studies. Any disagreements about inclusion will be resolved by discussion or a third senior reviewer (JLM). Publications that used the same cohort but evaluated different outcomes will be included as separate studies. Excluded studies will be reported using a PRISMA flowchart [38].

2.8. *Data extraction*

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Two reviewers will independently extract the data from included studies. Conflicts will be resolved by a third reviewer, if needed. The following information will be extracted from each study using a standardized data extraction form: the first author, year of publication, country, sample size, age of children, amount of plant milk consumed (number of cups per day, daily mean intake, etc.), type of plant milk (soy, almond, rice, coconut, etc.), confounders adjusted for and results (estimates and corresponding 95% confidence intervals for each outcome of interest and p-value). If data on the same populations were reported in multiple articles, both will be considered for analysis. If sufficient information is not available in the full text publication the study authors will be contacted via email to obtain additional data.

2.8. *Risk of bias in individual studies*

Risk of bias will be assessed independently by two reviewers. Discrepancies will be resolved by consensus. The Newcastle-Ottawa Scale will be used to assess the risk of bias in individual observational cohort and cross-sectional studies, which expresses risk of bias on a numerical scale ranging from 0 to 9. Scores < 7 will be considered low risk. Risk of bias of included clinical trials will be assessed using the Cochrane risk of bias tool (low, high, unclear) [39].

2.9. *Data synthesis*

The evidence will be summarized narratively due to anticipated heterogeneity between studies (e.g. variability in participants studied, exposure and outcome measures). Data on each outcome will be extracted, tabulated or graphed and characteristics of the studies, heterogeneity in study

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participants, exposure and outcomes, strengths and limitations and key findings will be described in the text. A meta-analysis will be conducted only if the study participants, exposure and outcomes are sufficiently similar. The heterogeneity between studies will be assessed using a forest plot and with the I^2 statistic [39].

2.10. *Additional analyses*

If sufficient data are available, we will tabulate the evidence:

(i) For each type of plant milk since the nutritional content can vary between the different types of products (e.g. soy milk is higher in protein content than almond milk) [15]. A list of different types of plant milks can be found in Table 2.

(ii) By the age of children since younger children have a higher risk of nutritional deficiencies [6,40]

(iii) Separately for children with food allergies (e.g. to cow milk) which can contribute to suboptimal nutrient intake and poor growth in children [19].

Table 2: Different types of plant milks [41]

Legume	Nut	Seed	Grain/cereal
Soy	Almond	Flax	Oat
Pea protein	Cashew	Hemp	Rice
Peanut	Coconut	Pumpkin	Quinoa
	Macadamia	Sunflower	Buckwheat
	Hazelnut	Sesame	

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2.11. *Confidence in cumulative evidence*

The certainty of evidence will be assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation) [42,43]. The grade of the evidence will be downgraded based on study limitations (risk of bias as assessed by the Newcastle-Ottawa Scale or Cochrane risk of bias tool), inconsistency of results, imprecision (small sample size, wide confidence intervals), indirectness of evidence (presence of factors that limit the generalizability of the findings) and publication bias.

2.11. *Patient and public involvement*

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

DISCUSSION

Plant milk consumption is becoming increasingly popular among children. Despite this, it is unclear whether plant milks are beneficial for children. To address this, the aim of this review is to synthesize the available evidence on the effect of plant milk consumption on child growth and nutrition. The certainty of the evidence may be limited by the number and quality of studies. Nonetheless, it is expected that the findings of this review will provide valuable insight into what is known about plant milk consumption in children, help to identify gaps and inconsistencies in the existing literature and areas that require further research. In addition, even with limited

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studies it may still be possible to draw some conclusions or make recommendations about plant milk intake in childhood which may help parents, dietitians, paediatricians and other healthcare professionals make informed decisions when considering plant milk for children.

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Author Contributions: IS and JLM conceptualized and designed the study and were major contributors in writing the protocol. SC developed the systematic review search, generated the initial search results and was a major contributor in writing the methods section. BRC, DLC, DJA, CSB, CDG and CDH critically reviewed and revised the protocol for important content.

Funding: This work was supported by the Canadian Institutes of Health Research (CIHR) Strategy for Patient Oriented Research (SPOR) Innovative Clinical Trial Grant number 162962.

Disclaimer: The funding agency had no role in study design, in the writing of the protocol or in the decision to submit the article for publication.

Competing Interests: IS (the first author) has been a vegetarian for over 10 years. DJA is a vegan. JLM received an unrestricted research grant for a completed investigator-initiated study from the Dairy Farmers of Canada (2011-2012) and D-drops provided non-financial support (vitamin D supplements) for an investigator initiated study on vitamin D and respiratory tract infections (2011–2015). The other authors have no competing interests to disclose.

Ethics Approval: The study does not involve human participants and ethical approval was not required.

Data availability: Not applicable.

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Appendix 1: PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol[17]

Section and topic	Item #	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,4
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1, 13
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	13
Sponsor	5b	Provide name for the review funder and/or sponsor	13
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	13
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8-9

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Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	8-9, Appendix 2
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	n/a
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7-8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	11
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	11
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11
Meta-bias(es)	16	Specify any planned assessment of meta-biases (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

From: Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg.* 2010;8(5):336-3

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Appendix 2: Final Ovid MEDLINE Search Strategy (October 6, 2022)

No.	Searches	Results
1	milk substitutes/ or soy milk/	1091
2	(milk* adj3 (noncow* or non cow* or substitut* or alternat* or plant* or vegan or vegeta*)).tw,kf.	3575
3	((milk* or beverage* or drink*) adj3 (soy* or oat* or almond* or nut or nuts or coconut* or macadamia* or hemp* or quinoa or rice or cashew* or corn or spelt or pea or peas or peanut* or pecan or pecans or banana* or lupin or cowpea* or hazelnut* or pistachio* or walnut* or sesame or flax* or sunflower* or teff or amaranth or pumpkin* or buckwheat or seed or seeds or legume*)).tw,kf.	4882
4	(nondairy or non dairy).tw,kf.	618
5	or/1-4	9230
6	exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young). in. [OVID broad children filter]	5517123
7	5 and 6	3820
8	limit 7 to english language	3415
9	limit 8 to yr="2000 -Current"	2637

Database: Ovid MEDLINE® ALL 1946 to October 5, 2022
This search used the Ovid Expert Searches Children Filter (Broad) – MEDLINE on line 6:
https://tools.ovid.com/ovidtools/expertsearches.html

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-Preporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,4
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1,13

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Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	#5a	Indicate sources of financial or other support for the review	13
Sponsor	#5b	Provide name for the review funder and / or sponsor	13
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	13
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is already known	5
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Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10

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Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

Notes:

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- 10: 8-9, Appendix 2 The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist was completed on 02. February 2023 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

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