The Epidemiology of Chronic Pain in Children and Adolescents: A Protocol for a Systematic Review Update

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The Epidemiology of Chronic Pain in Children and Adolescents: A Protocol for a Systematic Review Update

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ABSTRACT

Introduction: Chronic pain, defined as persistent or recurring pain lasting longer than three months, is a common childhood problem and can profoundly impact children's physical, psychological, and social functioning. The last comprehensive systematic review estimating the prevalence of chronic pain in children and adolescents was published in 2011. Since then, the literature on pediatric chronic pain has grown substantially. This manuscript outlines a protocol for an updated systematic review to provide updated estimates of the prevalence of various forms of chronic pain in children and adolescence. The review will also examine the relationship between sociodemographic and psychosocial factors related to chronic pain prevalence.

Methods and Analysis: This review will follow PRISMA guidelines. We will search EMBASE, PubMed, CINAHL, and PsycINFO for observational studies published in English between 2009 and 2020 reporting population-based estimates of chronic non-disease-related pain prevalence in children or adolescents (age ≤ 19 years). Two independent reviewers will screen the titles and abstracts retrieved from the search based on predefined eligibility criteria. The full texts of relevant studies will then be assessed by two reviewers. Studies meeting inclusion criteria will be categorized according to the type of pain investigated: headache only, abdominal pain only, back pain only, musculoskeletal pain, combined pain, and other/general pain. Data will be extracted using customized forms and studies will be assessed for risk of bias using a 10-item tool developed by Hoy et al. (2012). A narrative synthesis will summarize the prevalence estimates of pediatric chronic pain and associated sociodemographic and psychosocial correlates. Meta-analyses and meta-regressions will be performed if the data permit.

Ethics and dissemination: Ethical approval is not required. Findings will be disseminated through publication in an academic journal, presentations at conferences, and in various media.

PROSPERO registration number: Submitted to PROSPERO on July 22, 2020. Currently awaiting registration number.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This systematic review will provide updated estimates of the prevalence of various forms of chronic pain in children and adolescents.
- A comprehensive literature search will be conducted to identify eligible studies.
- This systematic review will follow the PRISMA guidelines and will assess included articles for risk of bias using a validated quality assessment tool.
- Heterogeneity in study methods and populations may limit our ability to pool the findings across studies.
- The findings of this review will enhance our understanding of the current burden of pediatric chronic pain which may help inform the treatment and allocation of clinical resources for this population.

INTRODUCTION

Chronic pain, defined as persistent or recurring pain lasting longer than three months,[1] is a common problem in childhood. Although numerous recent population-based studies have provided estimates of the prevalence of chronic pain in children and adolescents, the reported proportions have varied considerably across studies. For example, the prevalence of primary headache disorders in children and adolescents in recent population-based studies has ranged from 19.4-66.4%,[2,3] while estimates of the prevalence of functional gastrointestinal disorders have varied from 4.6%-31.2%.[4,5] Due to the wide variability in the reported estimates, the current epidemiology of chronic pain in children and adolescents is unclear. The uncertainty regarding the number of children and adolescents impacted by chronic pain may limit the appropriate allocation of clinical services for this population, which are crucial given the pervasive and long-term consequences of chronic pain on young people.

Chronic pain can have a profound impact on children and adolescents. Children who experience chronic pain are at increased risk for depression and anxiety,[6,7] school absences,[8] social isolation,[9] and poorer quality of life.[10] Approximately 5% of children with chronic pain experience severe severe levels of pain which significantly impact their daily functioning.[11] Unfortunately, a substantial majority of children with chronic pain become adults with chronic pain. In a study of adult patients with chronic pain, 80% of participants reported their pain originated in childhood or adolescence.[12] The persistence of chronic pain from childhood to adulthood has significant social and economic consequences. For instance, children with chronic pain are at risk for opioid misuse[13] and psychiatric morbidity in adulthood,[14] and pediatric chronic pain is associated with high rates of outpatient appointments, emergency department visits, and hospitalizations all resulting in creased healthcare costs.[15–17] The total annual cost of pediatric chronic pain in the United States is estimated to be $19.5 billion.[16] The significant individual, social and economic burden of pediatric chronic pain, and its persistence into adulthood, demonstrates the importance of understanding the epidemiology of this disease in order to improve treatment and reduce the impact that chronic pain has on the lives of children and adolescents.

The most recent, comprehensive review on the epidemiology of chronic pain in children and adolescents was published 2011.[18] This review estimated that the median prevalence of chronic pain in children and adolescents ranged from 11-38% depending on body site and study. The prevalence of chronic pain was found to be higher in girls and prevalence proportions increased with age.[18] The review identified several psychosocial correlates of chronic pain in children and adolescents such as lower socio-economic status, anxiety, depression and low self-esteem.[18] However, other correlates of chronic pain in children and adolescents, such as sleep[19,20] and post-traumatic stress disorder,[21,22] have since been identified and were not consistently examined at the population level at the time of the past review. The review also identified several gaps in the understanding of the epidemiology of chronic pain in children and adolescents, including restricted age ranges and lack of longitudinal studies.[18] Furthermore, at the time of the past review the quality of included studies was generally low to moderate and methodological limitations, such as inconsistent definitions of pain between studies, made it difficult to estimate overall prevalence proportions.[18]

The literature on pediatric pain is growing exponentially; a recent bibliometric analysis revealed that there was nearly a 40-fold increase in the number of publications on pediatric pain from 1975 to 2010.[23] Since the last comprehensive systematic review on the epidemiology of chronic pain in children and adolescents,[18] numerous population-based studies estimating the prevalence of various forms of pediatric chronic pain have been published.[24–26] A few recent reviews estimating the prevlance of certain forms of chronic pain, such as functional abdominal pain[27] and headache[28,29] have also been conducted. However, in order to appropriately meet the clinical needs of children and adolescents with chronic pain, an updated review that estimates the proportion of various forms of chronic pain and examines key sociodemographic and psychosocial correlates of chronic pain in children and adolescents is needed.

This manuscript outlines a protocol for a systematic review to update a prior review synthesizing the published literature on the prevalence of chronic pain in children and adolescents. Specifically, the objectives of this review are to: 1) Provide updated estimates of the prevalence of various forms of chronic pain (headache, abdominal pain, back pain, musculoskeletal pain, combined pain, and other/general pain) in children and adolescence; 2) Provide an updated examination of sociodemographic (e.g., age, sex, race) and psychosocial (e.g., anxiety, depression, sleep) factors related to the prevalence of chronic pain in children; and 3) Assess study quality and identify gaps in the literature and areas for future research.

METHODS AND ANALYSIS

This systematic review protocol was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines (see supplementary file 1).[30] The study protocol was submitted for registration with the International Prospective Register of Systematic Reviews (PROSPERO) on July 22, 2020. In the event of an amendment to this protocol, the date of the amendment, a description of the change and the rationale will be documented and recorded in PROSPERO. The dates for this review are May 14, 2020-April 1, 2021(expected).

Search strategy

We will search the following electronic databases: EMBASE, PubMed, CINAHL and PsycINFO. The search terms will be comprised of three conceptual blocks: i) Pain terms (e.g., musculoskeletal pain, back pain, headache, abdominal pain, recurrent pain); ii) Pediatric terms (e.g., child, adolescent, boy, girl); and iii) Epidemiological terms (e.g., epidemiology, prevalence, incidence, frequency). The searches will be restricted to English language articles, human studies, and manuscripts published between January 2009-June 2020 (the original systematic review[31] included studies published up until 2009).

Eligibility criteria

Studies will be eligible for inclusion if they meet the following criteria:

1. Observational studies (epidemiological, case-control, cross-sectional, retrospective and prospective cohort studies) using a population-based sampling frame to estimate the prevalence of chronic pain, defined as pain lasting 3 months or longer, in children or adolescents (study sample age ≤19 years).
2. Studies published in peer-reviewed journals in English.

Studies meeting the following criteria will be excluded:

1. Studies with sampling frames not deemed to be population-based.
2. Case studies, conference abstracts, dissertations, reviews, book chapters and qualitative studies.
3. Studies reporting on the prevalence of chronic pain in adults (sample age is exclusively ≥20 years)
4. Studies of non-human samples.

5. Studies exclusively examining the prevalence of disease- (e.g., cancer, arthritis) or condition- (e.g., cerebral palsy, muscular dystrophy) related chronic pain in children and adolescents.

Studies reporting on multiple populations (e.g., disease/condition and non-disease/condition-related chronic pain, adults and children), where data on one or more sub-populations that fit the eligibility criteria for this review can be separately identified, will be included and the relevant data will be extracted.

Screening and Data Extraction

Literature search results will be transferred to Covidence systematic review management software and duplicates will be removed. An initial title/abstract review of studies retrieved by the search will be independently conducted by two members of the study team to determine which studies potentially met the inclusion/exclusion criteria. Articles included from the title/abstract review phase will then by reviewed in full by two reviewers. The two reviewers will be blinded to each other's decisions. Discrepancies regarding the eligibility of a study will be resolved by consensus, and if necessary, through discussion with a third reviewer.

Data will be extracted from included studies using customized forms. Extracted information will include study design, location where the study was conducted, number of participants, participant demographics (e.g., age, sex, race), study sample (e.g., headache only, abdominal pain only, back pain only, musculoskeletal pain, combined pain, and other/general.), study methodology, prevalence proportion of chronic pain, and sociodemographic (e.g., age, sex, race, parent education, household income) and psychosocial (e.g., anxiety, depression, sleep, post-traumatic stress) predictors of chronic pain. In accordance with the PRISMA guidelines

[32], the number of studies meeting inclusion criteria will be recorded and the reason for exclusion of those not included will be documented.

Quality Assessment

Two independent reviewers will assess study quality using the 10-item tool developed by Hoy et al. (2012). This tool was developed to assess external and internal validity of prevalence studies.[33] Response options for each item are either “yes” (indicating low risk of bias) or “no” (indicating high risk of bias).[33] The tool will be adapted for this review if necessary. Consensus will be reached by discussion between the reviewers.

Data Synthesis

A narrative synthesis will summarize the prevalence proportions of chronic pain in children and adolescents in the following categories; headache only; abdominal pain only; back pain only; musculoskeletal pain; combined pain; and other/general pain. Additionally, the relationship between psychosocial factors (e.g., sleep, anxiety and depression) and sociodemographic factors (e.g., sex, age, race and indicators of socio-economic status such as, but not limited to, household income, parental level of education and urban versus rural area of residence) and chronic pain in children and adolescents will be reviewed.

Depending on the heterogeneity of included studies the prevalence proportions of chronic pain will be calculated using median prevalence proportions and/or meta-analysis. When at least two or more studies are comparable in terms of the study sample (e.g., category of chronic pain), and methodology (e.g., operationalization of chronic pain), we will pool the effects to determine the prevalence proportion of chronic pain across studies. Similarly, if studies have used similar methods to examine the relationship between certain sociodemographic and/or psychosocial variables in comparable chronic pain samples, we will conduct separate meta-regressions to examine the relationship between these variables and chronic pain across studies.

Reporting of this systematic review will follow PRISMA guidelines.[34] A PRISMA flow diagram will be included in the final manuscript of this review.

Ethics and Dissemination

Ethical approval will not be sought for this study, as no human subject participants will be involved. A manuscript outlining the results of this review will be submitted for publication in a peer-reviewed academic journal and for presentation at relevant academic conferences. Results will be publicly disseminated through social media, news and media outlets, and newsletters and blog posts, as appropriate.

IMPLICATIONS OF THE REVIEW

We anticipate that the results from this review will enhance our understanding of the current burden of pediatric chronic pain which may help inform treatment and allocation of clinical resources for this population. Furthermore, findings from this study will identify priority areas for research on the epidemiology of chronic pain to guide future research efforts. Through our planned knowledge translation efforts, findings of the review will be disseminated not only to clinicians and scientists, but also to patients and families, which may aid in public awareness and advocacy efforts.

PATIENT AND PUBLIC INVOLVEMENT

This protocol was designed in collaboration with a patient partner and co-author, JM. JM will remain involved as a patient partner throughout all steps of the review.

CONTRIBUTORS

CTC conceived the study idea. CL, PRT and JAP designed the study protocol, data extraction, and statistical analysis and wrote the first draft of the manuscript. DC, GAF, GTJ, GJM and JM provided critical insights. All authors approved and contributed to the final manuscript.

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COMPETING INTERESTS

None declared.

PATIENT CONSENT FOR PUBLICATION

Not required.

REFERENCES

1 Treede R-D, Rief W, Barke A, *et al.* A classification of chronic pain for ICD-11. *PAIN* 2015;**156**:1. doi:10.1097/j.pain.0000000000000160

2 Al-Hashel JY, Ahmed SF, Alroughani R. Prevalence and burden of primary headache disorders in Kuwaiti children and adolescents: A community based study. *Front Neurol* 2019;**10**:793. doi:10.3389/fneur.2019.00793

3 Malik AH, Shah PA, Yaseen Y. Prevalence of primary headache disorders in school-going children in Kashmir Valley (North-west India). *Ann Indian Acad Neurol* 2012;**15**:100–3. doi:10.4103/0972-2327.100030

4 Zheng S, Fu W, Zhou J, *et al.* Prevalence and related factors of irritable bowel syndrome among middle-school students in areas affected by Wenchuan earthquake: An epidemiological study. J. Clin. Gastroenterol. 2012;**46**:345–6. doi:10.1097/MCG.0b013e31824712d0

5 Demirceken FG, Kurt G, Dulkadir R, *et al.* Functional dyspepsia in children: A Turkish prospective survey in Kirikkale province. 2010.

6 Shelby GD, Shirkey KC, Sherman AL, *et al.* Functional abdominal pain in childhood and long-term vulnerability to anxiety disorders. *Pediatrics* 2013;**132**:475–82. doi:10.1542/peds.2012-2191

7 Simons LE, Sieberg CB, Claar RL. Anxiety and impairment in a large sample of children and adolescents with chronic pain. *Pain Res Manag* 2012;**17**:93–7. doi:10.1155/2012/420676

8 Logan DE, Gray LS, Iversen CN, *et al.* School Self-Concept in Adolescents With Chronic Pain. *J Pediatr Psychol* 2017;**42**:892–901. doi:10.1093/jpepsy/jsx063

9 Maes M, Van den Noortgate W, Fustolo-Gunnink SF, *et al.* Loneliness in Children and Adolescents With Chronic Physical Conditions: A Meta-Analysis. *J Pediatr Psychol* 2017;**42**:622–35. doi:10.1093/jpepsy/jsx046

10 Gold JI, Yetwin AK, Mahrer NE, *et al.* Pediatric Chronic Pain and Health-Related Quality of Life. *J Pediatr Nurs* 2009;**24**:141–50. doi:10.1016/j.pedn.2008.07.003

11 Huguet A, Miró J. The Severity of Chronic Pediatric Pain: An Epidemiological Study. *J Pain* 2008;**9**:226–36. doi:10.1016/j.jpain.2007.10.015

12 Hassett AL, Hilliard PE, Goesling J, *et al.* Reports of chronic pain in childhood and adolescence among patients at a tertiary care pain clinic. *J Pain* 2013;**14**:1390–7. doi:10.1016/j.jpain.2013.06.010

13 Groenewald CB, Law EF, Fisher E, *et al.* Associations Between Adolescent Chronic Pain and Prescription Opioid Misuse in Adulthood. *J Pain* 2019;**20**:28–37. doi:10.1016/j.jpain.2018.07.007

14 Noel M, Groenewald CB, Beals-Erickson SE, *et al.* Chronic Pain in Adolescence and Internalizing Mental Health Disorders: A Nationally Representative Study. *Pain* 2016;**157**:1333–8. doi:10.1097/j.pain.0000000000000522

15 Ho IK, Goldschneider KR, Kashikar-Zuck S, *et al.* Healthcare Utilization and Indirect Burden among Families of Pediatric Patients with Chronic Pain. *J Musculoskelet Pain* 2008;**16**:155–64. doi:10.1080/10582450802161853

16 Groenewald CB, Essner BS, Wright D, *et al.* The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. *J Pain* 2014;**15**:925–33. doi:10.1016/j.jpain.2014.06.002

17 Tumin D, Drees D, Miller R, *et al.* Health Care Utilization and Costs Associated With Pediatric Chronic Pain. *J Pain* 2018;**19**:973–82. doi:10.1016/j.jpain.2018.03.012

18 King S, Chambers CT, Huguet A, *et al.* The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain* 2011;**152**:2729–38. doi:10.1016/j.pain.2011.07.016

19 Evans S, Djilas V, Seidman LC, *et al.* Sleep Quality, Affect, Pain, and Disability in Children With Chronic Pain: Is Affect a Mediator or Moderator? *J Pain* 2017;**18**:1087–95. doi:10.1016/j.jpain.2017.04.007

20 Murphy LK, Palermo TM, Tham SW, *et al.* Comorbid Sleep Disturbance in Adolescents with Functional Abdominal Pain. *Behav Sleep Med* 2020;**0**:1–10. doi:10.1080/15402002.2020.1781634

21 Noel M, Wilson AC, Holley AL, *et al.* Posttraumatic stress disorder symptoms in youth with vs without chronic pain. *Pain* 2016;**157**:2277–84. doi:10.1097/j.pain.0000000000000642

22 Stahlschmidt L, Rosenkranz F, Dobe M, *et al.* Posttraumatic stress disorder in children and adolescents with chronic pain. *Health Psychol* 2020;**39**:463–70. doi:10.1037/hea0000859

23 Caes L, Boerner KE, Chambers CT, *et al.* A comprehensive categorical and bibliometric analysis of published research articles on pediatric pain from 1975 to 2010. Pain. 2016;**157**:302–13. doi:10.1097/j.pain.0000000000000403

24 Oswari H, Alatas FS, Hegar B, *et al.* Functional abdominal pain disorders in adolescents in Indonesia and their association with family related stress. *BMC Pediatr* 2019;**19**:342–5. doi:10.1186/s12887-019-1682-5 [doi]

25 Aartun E, Hartvigsen J, Wedderkopp N, *et al.* Spinal pain in adolescents: prevalence, incidence, and course: a school-based two-year prospective cohort study in 1,300 Danes aged 11–13. *BMC Musculoskelet Disord* 2014;**15**:187. doi:10.1186/1471-2474-15-187

26 Arruda MA, Arruda R, Guidetti V, *et al.* Psychosocial adjustment of children with migraine and tension-type headache - a nationwide study. *Headache* 2015;**55 Suppl 1**:39–50. doi:10.1111/head.12510

27 Korterink JJ, Diederen K, Benninga MA, *et al.* Epidemiology of Pediatric Functional Abdominal Pain Disorders: A Meta-Analysis. *PLOS ONE* 2015;**10**:e0126982–e0126982. doi:10.1371/journal.pone.0126982

28 Albers L, von Kries R, Heinen F, *et al.* Headache in School Children: Is the Prevalence Increasing? *Curr Pain Headache Rep* 2015;**19**:4. doi:10.1007/s11916-015-0477-0

29 Wöber-Bingöl Ç. Epidemiology of migraine and headache in children and adolescents topical collection on childhood and adolescent headache. *Curr Pain Headache Rep* 2013;**17**:1–11. doi:10.1007/s11916-013-0341-z

30 Moher D, Shamseer L, Clarke M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Rev Espanola Nutr Humana Diet* 2016;**20**:148–60. doi:10.1186/2046-4053-4-1

31 King S, Chambers CT, Huguet A, *et al.* The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain* 2011;**152**:2729–38. doi:10.1016/j.pain.2011.07.016

32 Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009;**6**. doi:10.1371/journal.pmed.1000097

33 Hoy D, Brooks P, Woolf A, *et al.* Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012;**65**:934–9. doi:10.1016/j.jclinepi.2011.11.014

34 Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009;**6**. doi:10.1371/journal.pmed.1000097

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

PRISMA Protocol Checklist

Section and topic	**Item No**	**Checklist**	**Reporting. Page No**
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	1,3
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	12
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	7
Support:			
Sources	5a	Indicate sources of financial or other support for the review	12
Sponsor	5b	Provide name for the review funder and/or sponsor Role of sponsor/ funder	N/A
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5-7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7
METHODS			
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years	8-9

		considered, language, publication status) to be used as criteria for eligibility for the review	
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	7,8
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	To be included in final manuscript
Study Records			
	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9
	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	9-11
	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9-11
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	9,10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	9-11
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	10
Data synthesis			
	15a	Describe criteria under which study data will be quantitatively synthesized	10,11
	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 (e.g., I 2 , Kendall's tau)	10,11
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	10,11
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10

Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., 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 (e.g., GRADE)	N/A

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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For peer review only

The Epidemiology of Chronic Pain in Children and Adolescents: A Protocol for a Systematic Review Update

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ABSTRACT

Introduction: Chronic pain, defined as persistent or recurring pain or pain lasting longer than three months, is a common childhood problem and can profoundly impact children's physical, psychological, and social functioning. The last comprehensive systematic review estimating the prevalence of chronic pain in children and adolescents was published in 2011. Since then, the literature on pediatric chronic pain has grown substantially. This manuscript outlines a protocol for an updated systematic review to provide updated estimates of the prevalence of various forms of chronic pain in children and adolescence. The review will also examine the relationship between sociodemographic and psychosocial factors related to chronic pain prevalence.

Methods and Analysis: This review will follow PRISMA guidelines. We will search EMBASE, PubMed, CINAHL, and PsycINFO for observational studies published in English between 2009 and 2020 reporting population-based estimates of chronic non-disease-related pain prevalence in children or adolescents (age ≤ 19 years). Two independent reviewers will screen the titles and abstracts retrieved from the search based on predefined eligibility criteria. The full texts of relevant studies will then be assessed by two reviewers. Studies meeting inclusion criteria will be categorized according to the type of pain investigated: headache only, abdominal pain only, back pain only, musculoskeletal pain, combined pain, general pain, and other pain. Data will be extracted using customized forms and studies will be assessed for risk of bias using a 10-item tool developed by Hoy et al. (2012). A narrative synthesis will summarize the prevalence estimates of pediatric chronic pain and associated sociodemographic and psychosocial correlates. Meta-analyses and meta-regressions will be performed if the data permit.

Ethics and dissemination: Ethical approval is not required. Findings will be disseminated through publication in an academic journal, presentations at conferences, and in various media.

PROSPERO registration number: CRD42020198690

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This systematic review will provide updated estimates of the prevalence of various forms of chronic pain in children and adolescents.
- A comprehensive literature search will be conducted to identify eligible studies.
- This systematic review will follow the PRISMA guidelines and will assess included articles for risk of bias using a validated quality assessment tool.
- Heterogeneity in study methods and populations may limit our ability to pool the findings across studies.
- The findings of this review will enhance our understanding of the current burden of pediatric chronic pain which may help inform the treatment and allocation of clinical resources for this population.

INTRODUCTION

Chronic pain, often defined as persistent or recurring pain or pain lasting longer than three months,[1] is a common problem in childhood. Although numerous recent population-based studies have provided estimates of the prevalence of chronic pain in children and adolescents, the reported proportions have varied considerably across studies. For example, the prevalence of primary headache disorders in children and adolescents in recent population-based studies has ranged from 19.4-66.4%,[2,3] while estimates of the prevalence of functional gastrointestinal disorders have varied from 4.6%-31.2%.[4,5] Due to the wide variability in the reported estimates, the current epidemiology of chronic pain in children and adolescents is unclear. The uncertainty regarding the number of children and adolescents impacted by chronic pain may limit the appropriate allocation of clinical services for this population, which are crucial given the pervasive and long-term consequences of chronic pain on young people.

Chronic pain can have a profound impact on children and adolescents. Children who experience chronic pain are at increased risk for depression and anxiety,[6,7] school absences,[8] social isolation,[9] and poorer quality of life.[10] Approximately 5% of children with chronic pain experience severe levels of pain which significantly impact their daily functioning.[11] Unfortunately, many children with chronic pain become adults with chronic pain. In a prospective study of pediatric patients with functional abdominal pain, 35% continued to report recurrent abdominal symptoms when reassessed in adulthood.[12] Similarly, in 14-year follow up study of adolescents with frequent headaches, 19% continued to report weekly headaches in young adulthood.[13] These rates are similar to retrospective reports of chronic pain in childhood by adults with chronic pain. In a study of adult patients with chronic pain, 17% of participants reported their pain originated in childhood or adolescence. [14]

The persistence of chronic pain from childhood to adulthood has significant social and economic consequences. For instance, children with chronic pain are at risk for opioid misuse[15] and psychiatric morbidity in adulthood,[16] and pediatric chronic pain is associated with high rates of outpatient appointments, emergency department visits, and hospitalizations all resulting in creased healthcare costs.[17–19] The total annual cost of pediatric chronic pain in the United States is estimated to be $19.5 billion.[18] The significant individual, social and economic burden of pediatric chronic pain, and its persistence into adulthood, demonstrates the importance of understanding the epidemiology of this disease in order to improve treatment and reduce the impact that chronic pain has on the lives of children and adolescents.

The most recent, comprehensive review on the epidemiology of chronic pain in children and adolescents was published 2011.[20] This review estimated that the median prevalence of chronic pain in children and adolescents ranged from 11-38% depending on pain type and varied substantially across studies. The prevalence of chronic pain was found to be higher in girls and prevalence proportions increased with age.[20] The review identified several psychosocial correlates of chronic pain in children and adolescents such as lower socio-economic status, anxiety, depression and low self-esteem.[20] However, other correlates of chronic pain in children and adolescents, such as sleep[21,22] and post-traumatic stress disorder,[23,24] have since been identified and were not consistently examined at the population level at the time of the past review. The review also identified several gaps in the understanding of the epidemiology of chronic pain in children and adolescents, including restricted age ranges and lack of longitudinal studies.[20] Furthermore, at the time of the past review the quality of included studies was generally low to moderate and methodological limitations, such as inconsistent definitions of pain between studies, made it difficult to estimate overall prevalence proportions.[20]

The literature on pediatric pain is growing exponentially; a recent bibliometric analysis revealed that there was nearly a 40-fold increase in the number of publications on pediatric pain from 1975 to 2010.[25] Since the last comprehensive systematic review on the epidemiology of chronic pain in children and adolescents,[20] numerous population-based studies estimating the prevalence of various forms of pediatric chronic pain have been published.[26–28] A few recent reviews estimating the prevlance of certain forms of chronic pain, such as functional abdominal pain[29] and headache[30,31] have also been conducted. However, in order to appropriately meet the clinical needs of children and adolescents with chronic pain, an updated review that estimates the proportion of various forms of chronic pain and examines key sociodemographic and psychosocial correlates of chronic pain in children and adolescents is needed.

This manuscript outlines a protocol for a systematic review to update a prior review synthesizing the published literature on the prevalence of chronic pain in children and adolescents. Specifically, the objectives of this review are to: 1) Provide updated estimates of the prevalence of various forms of chronic pain (headache, abdominal pain, back pain, musculoskeletal pain, combined pain, general pain, and other pain) in children and adolescents; 2) Provide an updated examination of sociodemographic (e.g., age, sex, race) and psychosocial (e.g., anxiety, depression, sleep) factors related to the prevalence of chronic pain in children and adolescents; and 3) Assess study quality and identify gaps in the literature and areas for future research.

METHODS AND ANALYSIS

This systematic review protocol was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines (see supplementary file 1).[32] The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on September 3, 2020. In the event of an amendment to this protocol, the date of the amendment, a description of the change and the rationale will be documented and recorded in PROSPERO. The dates for this review are May 14, 2020-April 1, 2021(expected).

Search strategy

We will search the following electronic databases: EMBASE, PubMed, CINAHL and PsycINFO. The search terms will be comprised of three conceptual blocks: i) Pain terms (e.g., musculoskeletal pain, back pain, headache, abdominal pain, recurrent pain); ii) Pediatric terms (e.g., child, adolescent, boy, girl); and iii) Epidemiological terms (e.g., epidemiology, prevalence, frequency). The searches will be restricted to English language articles, human studies, and manuscripts published between January 2009-June 2020 (the original systematic review[20] included studies published up until 2009).

Eligibility criteria

Studies will be eligible for inclusion if they meet the following criteria:

1. Observational studies using a population-based sampling frame to estimate the prevalence of chronic pain in children or adolescents (study sample age ≤19 years).
2. Studies examining the prevalence of chronic pain in children and adolescents, defined as pain with a minimum duration of at least 3 months or pain that is described as chronic, persistent, or recurrent. This definition was selected to align with current conceptualizations of chronic pain [1] while allowing for flexibility to accommodate

established diagnostic criteria for common childhood chronic pain conditions (e.g., functional abdominal pain [33] and migraine [34]).

3. Studies published in peer-reviewed journals in English.

Studies meeting the following criteria will be excluded:

1. Studies with sampling frames not deemed to be population-based.
2. Case studies, conference abstracts, dissertations, reviews, book chapters and qualitative studies.
3. Studies reporting on the prevalence of chronic pain in adults (sample age is exclusively ≥20 years)
4. Studies of non-human samples.
5. Studies examining the prevalence of chronic pain in specific sub-populations, such as children and adolescents with chronic illnesses (e.g., cancer, arthritis) or other health conditions (e.g., cerebral palsy, muscular dystrophy).

Studies reporting on multiple populations (e.g., adults and children), where data on one or more sub-populations that fit the eligibility criteria for this review can be separately identified, will be included and the relevant data will be extracted.

Screening and Data Extraction

Literature search results will be transferred to Covidence systematic review management software and duplicates will be removed. An initial title/abstract review of studies retrieved by the search will be independently conducted by two members of the study team to determine which studies potentially met the inclusion/exclusion criteria. Articles included from the title/abstract review phase will then be reviewed in full by two reviewers. The two reviewers will be blinded to each other's decisions. Discrepancies regarding the eligibility of a study will be resolved by consensus, and if necessary, through discussion with a third reviewer.

Data will be extracted from included studies using customized forms. Extracted information will include study design, location where the study was conducted, number of participants, participant demographics (e.g., age, sex, race), study sample (e.g., headache only, abdominal pain only, back pain only, musculoskeletal pain, combined pain, general pain, and other pain), study methodology, prevalence proportion of chronic pain, and sociodemographic (e.g., age, sex, race, parent education, household income) and psychosocial (e.g., anxiety, depression, sleep, post-traumatic stress) predictors of chronic pain. In accordance with the PRISMA guidelines [35], the number of studies meeting inclusion criteria will be recorded and the reason for exclusion of those not included will be documented.

Quality Assessment

Two independent reviewers will assess study quality using the 10-item tool developed by Hoy et al. (2012). This tool was developed to assess external and internal validity of prevalence studies.[36] Response options for each item are either "yes" (indicating low risk of bias) or "no" (indicating high risk of bias).[36] The tool will be adapted for this review if necessary. Consensus will be reached by discussion between the reviewers.

Data Synthesis

A narrative synthesis will summarize the prevalence proportions of chronic pain in children and adolescents in the following categories; headache only; abdominal pain only; back pain only; musculoskeletal pain; combined pain; general pain; and other pain. Additionally, the relationship between psychosocial factors (e.g., sleep, anxiety, and depression) and sociodemographic factors (e.g., sex, age, race and indicators of socio-economic status such as, but not limited to, household income, parental level of education and urban versus rural area of residence) and chronic pain in children and adolescents will be reviewed.

Depending on the heterogeneity of included studies the prevalence proportions of chronic pain will be calculated using median prevalence proportions and/or meta-analysis. When at least two or more studies are comparable in terms of the study sample (e.g., category of chronic pain), and methodology (e.g., operationalization of chronic pain), we will pool the effects to determine the prevalence proportion of chronic pain across studies. Similarly, if studies have used similar methods to examine the relationship between certain sociodemographic and/or psychosocial variables in comparable chronic pain samples, we will conduct separate meta-regressions to examine the relationship between these variables and chronic pain across studies.

Reporting of this systematic review will follow PRISMA guidelines.[37] A PRISMA flow diagram will be included in the final manuscript of this review.

Ethics and Dissemination

Ethical approval will not be sought for this study, as no human subject participants will be involved. A manuscript outlining the results of this review will be submitted for publication in a peer-reviewed academic journal and for presentation at relevant academic conferences. Results will be publicly disseminated through social media, news and media outlets, and newsletters and blog posts, as appropriate.

IMPLICATIONS OF THE REVIEW

We anticipate that the results from this review will enhance our understanding of the current burden of pediatric chronic pain which may help inform treatment and allocation of clinical resources for this population. Furthermore, findings from this study will identify priority areas for research on the epidemiology of chronic pain to guide future research efforts. Through our planned knowledge translation efforts, findings of the review will be disseminated not only to clinicians and scientists, but also to patients and families, which may aid in public awareness and advocacy efforts.

PATIENT AND PUBLIC INVOLVEMENT

This protocol was designed in collaboration with a patient partner and co-author, JM. JM will remain involved as a patient partner throughout all steps of the review.

CONTRIBUTORS

CTC conceived the study idea. CL, PRT, and JAP designed the study protocol, data extraction, and statistical analysis and wrote the first draft of the manuscript. CTC, DC, GAF, GTJ, GJM and JM provided critical insights at all stages. All authors approved and contributed to the final manuscript.

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COMPETING INTERESTS

None declared.

PATIENT CONSENT FOR PUBLICATION

Not required.

DATA AVAILABILITY STATEMENT

Data sharing not applicable as no datasets were generated and/or analysed for this protocol.

REFERENCES

1 Treede R-D, Rief W, Barke A, *et al.* A classification of chronic pain for ICD-11. *PAIN* 2015;**156**:1. doi:10.1097/j.pain.0000000000000160

2 Al-Hashel JY, Ahmed SF, Alroughani R. Prevalence and burden of primary headache disorders in Kuwaiti children and adolescents: A community based study. *Front Neurol* 2019;**10**:793. doi:10.3389/fneur.2019.00793

3 Malik AH, Shah PA, Yaseen Y. Prevalence of primary headache disorders in school-going children in Kashmir Valley (North-west India). *Ann Indian Acad Neurol* 2012;**15**:100–3. doi:10.4103/0972-2327.100030

4 Zheng S, Fu W, Zhou J, *et al.* Prevalence and related factors of irritable bowel syndrome among middle-school students in areas affected by Wenchuan earthquake: An epidemiological study. J. Clin. Gastroenterol. 2012;**46**:345–6. doi:10.1097/MCG.0b013e31824712d0

5 Demirceken FG, Kurt G, Dulkadir R, *et al.* Functional dyspepsia in children: A Turkish prospective survey in Kirikkale province. 2010.

6 Shelby GD, Shirkey KC, Sherman AL, *et al.* Functional abdominal pain in childhood and long-term vulnerability to anxiety disorders. *Pediatrics* 2013;**132**:475–82. doi:10.1542/peds.2012-2191

7 Simons LE, Sieberg CB, Claar RL. Anxiety and impairment in a large sample of children and adolescents with chronic pain. *Pain Res Manag* 2012;**17**:93–7. doi:10.1155/2012/420676

8 Logan DE, Gray LS, Iversen CN, *et al.* School Self-Concept in Adolescents With Chronic Pain. *J Pediatr Psychol* 2017;**42**:892–901. doi:10.1093/jpepsy/jsx063

9 Maes M, Van den Noortgate W, Fustolo-Gunnink SF, *et al.* Loneliness in Children and Adolescents With Chronic Physical Conditions: A Meta-Analysis. *J Pediatr Psychol* 2017;**42**:622–35. doi:10.1093/jpepsy/jsx046

10 Gold JI, Yetwin AK, Mahrer NE, *et al.* Pediatric Chronic Pain and Health-Related Quality of Life. *J Pediatr Nurs* 2009;**24**:141–50. doi:10.1016/j.pedn.2008.07.003

11 Huguet A, Miró J. The Severity of Chronic Pediatric Pain: An Epidemiological Study. *J Pain* 2008;**9**:226–36. doi:10.1016/j.jpain.2007.10.015

12 Walker LS, Dengler-Crish CM, Rippel S, *et al.* Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood. *PAIN* 2010;**150**:568–572. doi:10.1016/j.pain.2010.06.018

13 Larsson B, Sigurdson JF, Sund AM. Long-term follow-up of a community sample of adolescents with frequent headaches. *J Headache Pain* 2018;**19**:79. doi:10.1186/s10194-018-0908-5

14 Hassett AL, Hilliard PE, Goesling J, *et al.* Reports of chronic pain in childhood and adolescence among patients at a tertiary care pain clinic. *J Pain* 2013;**14**:1390–7. doi:10.1016/j.jpain.2013.06.010

15 Groenewald CB, Law EF, Fisher E, *et al.* Associations Between Adolescent Chronic Pain and Prescription Opioid Misuse in Adulthood. *J Pain* 2019;**20**:28–37. doi:10.1016/j.jpain.2018.07.007

16 Noel M, Groenewald CB, Beals-Erickson SE, *et al.* Chronic Pain in Adolescence and Internalizing Mental Health Disorders: A Nationally Representative Study. *Pain* 2016;**157**:1333–8. doi:10.1097/j.pain.0000000000000522

17 Ho IK, Goldschneider KR, Kashikar-Zuck S, *et al.* Healthcare Utilization and Indirect Burden among Families of Pediatric Patients with Chronic Pain. *J Musculoskelet Pain* 2008;**16**:155–64. doi:10.1080/10582450802161853

18 Groenewald CB, Essner BS, Wright D, *et al.* The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. *J Pain* 2014;**15**:925–33. doi:10.1016/j.jpain.2014.06.002

19 Tumin D, Drees D, Miller R, *et al.* Health Care Utilization and Costs Associated With Pediatric Chronic Pain. *J Pain* 2018;**19**:973–82. doi:10.1016/j.jpain.2018.03.012

20 King S, Chambers CT, Huguet A, *et al.* The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain* 2011;**152**:2729–38. doi:10.1016/j.pain.2011.07.016

21 Evans S, Djilas V, Seidman LC, *et al.* Sleep Quality, Affect, Pain, and Disability in Children With Chronic Pain: Is Affect a Mediator or Moderator? *J Pain* 2017;**18**:1087–95. doi:10.1016/j.jpain.2017.04.007

22 Murphy LK, Palermo TM, Tham SW, *et al.* Comorbid Sleep Disturbance in Adolescents with Functional Abdominal Pain. *Behav Sleep Med* 2020;**0**:1–10. doi:10.1080/15402002.2020.1781634

23 Noel M, Wilson AC, Holley AL, *et al.* Posttraumatic stress disorder symptoms in youth with vs without chronic pain. *Pain* 2016;**157**:2277–84. doi:10.1097/j.pain.0000000000000642

24 Stahlschmidt L, Rosenkranz F, Dobe M, *et al.* Posttraumatic stress disorder in children and adolescents with chronic pain. *Health Psychol* 2020;**39**:463–70. doi:10.1037/hea0000859

25 Caes L, Boerner KE, Chambers CT, *et al.* A comprehensive categorical and bibliometric analysis of published research articles on pediatric pain from 1975 to 2010. Pain. 2016;**157**:302–13. doi:10.1097/j.pain.0000000000000403

26 Oswari H, Alatas FS, Hegar B, *et al.* Functional abdominal pain disorders in adolescents in Indonesia and their association with family related stress. *BMC Pediatr* 2019;**19**:342–5. doi:10.1186/s12887-019-1682-5 [doi]

27 Aartun E, Hartvigsen J, Wedderkopp N, *et al.* Spinal pain in adolescents: prevalence, incidence, and course: a school-based two-year prospective cohort study in 1,300 Danes aged 11–13. *BMC Musculoskelet Disord* 2014;**15**:187. doi:10.1186/1471-2474-15-187

28 Arruda MA, Arruda R, Guidetti V, *et al.* Psychosocial adjustment of children with migraine and tension-type headache - a nationwide study. *Headache* 2015;**55 Suppl 1**:39–50. doi:10.1111/head.12510

29 Korterink JJ, Diederen K, Benninga MA, *et al.* Epidemiology of Pediatric Functional Abdominal Pain Disorders: A Meta-Analysis. *PLOS ONE* 2015;**10**:e0126982–e0126982. doi:10.1371/journal.pone.0126982

30 Albers L, von Kries R, Heinen F, *et al.* Headache in School Children: Is the Prevalence Increasing? *Curr Pain Headache Rep* 2015;**19**:4. doi:10.1007/s11916-015-0477-0

31 Wöber-Bingöl Ç. Epidemiology of migraine and headache in children and adolescents topical collection on childhood and adolescent headache. *Curr Pain Headache Rep* 2013;**17**:1–11. doi:10.1007/s11916-013-0341-z

32 Moher D, Shamseer L, Clarke M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Rev Espanola Nutr Humana Diet* 2016;**20**:148–60. doi:10.1186/2046-4053-4-1

33 Hyams JS, Di Lorenzo C, Saps M, *et al.* Childhood Functional Gastrointestinal Disorders: Child/Adolescent. *Gastroenterology* 2016;**150**:1456-1468.e2. doi:10.1053/j.gastro.2016.02.015

34 Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018;**38**:1–211. doi:10.1177/0333102417738202

35 Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009;**6**. doi:10.1371/journal.pmed.1000097

36 Hoy D, Brooks P, Woolf A, *et al.* Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012;**65**:934–9. doi:10.1016/j.jclinepi.2011.11.014

37 Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009;**6**. doi:10.1371/journal.pmed.1000097

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

PRISMA Protocol Checklist

Section and topic	**Item No**	**Checklist**	**Reporting. Page No**
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	1,3
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	12
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	8
Support:			
Sources	5a	Indicate sources of financial or other support for the review	12
Sponsor	5b	Provide name for the review funder and/or sponsor Role of sponsor/ funder	N/A
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5-7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7
METHODS			
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years	8-9

		considered, language, publication status) to be used as criteria for eligibility for the review	
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	8
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	To be included in final manuscript
Study Records			
	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9
	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	9-11
	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9-11
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	9,10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	9-11
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	10
Data synthesis			
	15a	Describe criteria under which study data will be quantitatively synthesized	10,11
	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 (e.g., I 2 , Kendall's tau)	10,11
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	10,11
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10,11

Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., 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 (e.g., GRADE)	N/A

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.