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The prevalence and associated factors of preterm birth in Ethiopia: Systematic review and meta-analysis protocol

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The prevalence and associated factors of preterm birth in Ethiopia: Systematic review and meta-analysis protocol

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ABSTRACT

Introduction: Preterm birth complications are the leading cause of death among neonates globally. The reduction in neonatal mortality is not remarkable in Ethiopia. Therefore, this review is aimed at assessing the magnitude and associated factors of preterm birth in Ethiopia.

Methods and analysis: The preferred reporting items for systematic reviews and meta-analyses guideline will be followed during the systematic review. We will include all observational studies published from Jan 01, 2009 to Dec 31, 2019 that examined the level and/or associated factors of preterm birth in Ethiopia. Electronic databases such as PubMed, and Science Direct as well as Google search engine and Google Scholar will be searched. The pooled prevalence of preterm and effect size of association for associated factors will be analyzed using the Stata software version 14. The heterogeneity between studies will be measured by I^2 statistics. A random-effects model will be used to estimate if heterogeneity detected among studies. Publication bias will be assessed using a funnel plot. Forest plots will be used to present the combined estimate with 95% confidence intervals. The quality of evidence of the outcomes will be assessed with the GRADE approach.

Ethics and dissemination: No ethical approval is necessary for a systematic review. The findings will be published in a peer-reviewed journal.

PROSPERO registration number: CRD42017077356.

Keywords: Preterm birth, Prevalence, Associated Factors, Ethiopia, Systematic review, Meta-analysis

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The proposed systematic review focuses on preterm birth, the global leading cause of neonatal mortality, in Ethiopia where the reduction in neonatal mortality is not remarkable
- This proposed systematic review and meta-analysis will provide updated knowledge on the prevalence of preterm birth in Ethiopia.
- The proposed systematic review with meta-analysis will provide a comprehensive knowledge on the associated factors of preterm birth in Ethiopia.
- The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline will be followed during the proposed systematic review.
- Standard tool for critical appraisal and data extraction will be used
- Only quantitative observational studies published in English will be included.

INTRODUCTION

Preterm birth is a birth before 37 completed weeks of gestation (1). It is more prevalent in Africa and Asia. Preterm birth complications remained the leading cause of under-5 and neonatal mortalities. Preterm birth, the majority being spontaneously, occurs for a variety of reasons(2). Currently, World Health Organization (WHO) is committed to reduce the health problems and lives lost as a result of preterm births.

Globally, 14.9 million babies born preterm making a birth rate of 11.1%, ranging from 5% to 18%, in 2010 (3). The majority (60%) of these births occurred in sub-Saharan Africa and South Asia where 52% of global livebirths occur. The estimated global preterm birth rate was also 10·6%, 14·84 million live preterm births, in 2014 (4). Twelve million (81·1%) of these preterm births occurred in Asia and sub-Saharan Africa (4) showing the contribution is raised from 2010. Ethiopia is one of the low-middle incomes countries in Sub-Saharan Africa.

Preterm birth remains a crucial issue in child mortality and improving quality of maternal and newborn care(4). Complications of preterm birth is the leading cause of death among under 5 children with risk of dying ranged between 1.9 and 155.1 per 1,000 livebirths , in 2015 (5). In the same report, it had been found as the leading cause of death among neonates contributing for 0·944 million deaths. Complication of infants born preterm result in significant cost to the health sector, parents and the society in that preterm neonates take the first place for neonatal intensive care unit (NICU) admission and longer hospital stay globally (4).

Currently, WHO is committed to reduce the health problems and lives lost as a result of preterm births (6). Hence, WHO had developed new guidelines including interventions

provided to the mother and the newborn baby (6). The Every Woman Every Child movement is also aiming to intensify national and international commitment and action to ensure that women, children and adolescents are at the heart of development. The movement puts into action the global strategy (2016-2030) (7). The strategy is aimed to end all preventable deaths of women, children and adolescents within a generation and ensuring their well-being. Though Ethiopia achieved the millennium development goal 4 with 67% under-five mortality reduction from the 1990 estimate, the reduction in neonatal mortality is not remarkable (8). However, Ethiopia has planned to reduce neonatal mortality rate from 28 in 2015/16 to 10 by 2019/2020 (9). Furthermore, the country is also devoted to end preventable deaths of newborns and children under 5 years of age by 2030 (10).

There are local studies on preterm conducted in Ethiopia. The need for an accurate and reliable result (11, 12), a single study aggregating these studies is necessary for policy makers and implementers. Even though, there is a systematic review (13) done, it addressed only the effect of pregnancy induced hypertension and multiple pregnancies on preterm birth. However, literatures show that more factors affect preterm birth. Some of the identified associated factors of preterm birth in Ethiopia are pregnancy induced hypertension (14, 15), chronic illness (14, 16), obstetric complication (17), nutritional status (17), anemia (16), antenatal care follow up (15-17), substance intake during pregnancy (18), history of abortion (18), history of still birth (18), premature rapture of membrane (16, 18), hypertension during pregnancy (18), multiple gestation (15, 18), history of low birth weight (18), history of preterm birth (18), and income status (16).

Hence, conducting a systematic review and meta-analysis on preterm birth is paramount important in Ethiopia by updating the latest possible evidences.

Therefore this review is aimed at assessing the magnitude and associated factors of preterm birth among in Ethiopia.

METHODS AND ANALYSIS

Development of the review method

The methods of this systematic review and meta-analysis protocol was developed based on the PRISMA Protocols (PRISMA-P) 2015 statement (19). The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline will be followed during the systematic review(20, 21). The result of the review will be reported according to the PRISMA guideline for reporting (22). The four phases that were drawn from the PRISMA flow chart (23) will be documented in the results to show the study selection process from initially identified records to finally included studies. The protocol for this systematic review and meta-analysis is registered in international prospective register of systematic reviews (PROSPERO) and obtained the registration number (CRD42017064585).

Eligibility criteria

We will include all observational studies that examined the level and/or associated factors of preterm birth in Ethiopia. Reviews, editorials, case series and case reports on preterm birth as well as studies that only reported qualitative findings on preterm birth will be excluded. In studies that reported both quantitative and qualitative results, we will only consider the quantitative findings. Studies will be considered relevant if they assessed the magnitude of preterm birth and/or examined the associated factors of preterm birth.

Search strategy

Major medical electronic databases such as PubMed, and Science Direct will be searched to identify relevant literature for the review. To cover grey literature, we will hand-search literature using the Google search engine and Google Scholar and references of electronically identified articles. Further, references list will also be considered from relevant studies considered for critical appraisal.

The literature search will be carried out by the primary author (KFM). The search will be limited to humans, and journal studies published in English from Jan 01, 2009 to Dec 31, 2020. We will apply Medical Subject Headings (MeSH) terms from PubMed, and combined key words to identify studies in the databases.

Accordingly, literatures will be retrieved using the exact search phrase *("Premature Birth/epidemiology"[Mesh] OR "Premature Birth/etiology"[Mesh] OR "Premature Birth/statistics and numerical data"[Mesh] OR premature birth* [MeSH] OR preterm birth OR premature birth OR preterm labo* OR preterm deliver* OR preterm infant OR preterm neonate* OR preterm newborn* OR birth outcome OR pregnancy outcome$ OR pregnancy complication$ OR birth outcome$ OR birth complication$) AND Ethiopia AND ((incidence OR prevalence OR magnitude OR burden) OR (predict* OR associated factor* OR risk factor* OR determinant*))* from PubMed. This will be customized for other databases.

Study selection process

The retrieved studies will be exported to the citation manager (EndNote) and then duplicates excluded. The titles and abstracts of the studies will be reviewed for screening by two authors (KFM and AML) for obvious exclusion according to the inclusion criteria.

Based on this screening, the titles and abstracts of the studies will be classified as included, excluded, and undecided. Full text of all the included and the undecided studies will be searched for further eligibility assessment.

The full texts of the included and undecided categories of the studies will be independently reviewed by two authors (KFM and AML) against the eligibility criteria for final inclusion. Studies that are not eligible based on the examination of the full-text will be excluded by stating the reasons according to the inclusion criteria. Disagreements between the two reviewers will be resolved through discussion and consensus.

Studies deemed to be appropriate will be scanned in full to determine relevance. Secondly, the references lists of all relevant studies will be reviewed to find additional studies that may have been difficult to detect in the database search due to non-reporting in the abstract (possibly due to non-significant effects). Studies published by the same team will be carefully reviewed to ensure the results of a given study are not included twice in this review.

Critical appraisal

All of the included studies will be critically appraised for their validity. The three authors (DFT, MKY, FA) will check the methodological robustness and validity of the findings using the Joanna Briggs Institute (JBI) Meta-Analysis of Statistics Assessment and Review Instrument (24). Uncertainties will be resolved by joint discussion between the reviewers. Disagreements among the reviewers will be resolved through discussion and consensus.

The JBI Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) will be used for critical appraisal (25). This tool contains a separate appraisal checklist for

each type of the study design. The reviewers will independently assess articles prior to inclusion in the final review using this instrument. Any disagreement among the reviewers will be resolved through discussion, and by involving another reviewer. A Study with quality assessment score of 50% and above and a study having a response rate of 80% and above were included in the final review.

Data extraction

The JBI data extraction form will be used to extract the characteristics of the studies and prevalence of preterm birth (primary outcome) as well as Odds ratio (secondary outcomes). A standardized excel sheet will be created and information from the standardized review forms will be transferred in order to be readily available for the systematic review. Three reviewers (KFM, MMS and AML) will extract data independently. Disagreements among the reviewers were resolved through discussion and consensus.

This tool will include information on the author, year of publication, objective, study setting, year of survey, study design, sample size, data collection method, study participants, definition used for preterm birth, prevalence of preterm, 95% CI for prevalence of preterm birth, and list of associated factors with their effect size. A quantitative data of cross-tabulation between the subject's characteristics (associated factors) and the preterm birth will also systematically abstracted.

Data synthesis and statistical analysis

The individual studies will be concisely described using a summary table. The summary table particularly describes the characteristics of the included studies and the main findings.

The data will be analyzed by the Stata software version 14. For studies which did not present a standard error (SE), it will be calculated using the formula; SE = $\sqrt{(p \times (1-p)/n)}$. The calculated standard error and prevalence rate of each study will then entered into Stata software to calculate the overall prevalence and its 95% confidence interval (CI). Similarly, the relationship between factors and preterm birth will be summarized using statistical estimates of effect sizes, odds ratio.

The level of heterogeneity among the studies will be quantified using the I^2 statistics (26). Meta-analysis using random effects model will be conducted for the I^2 value of more than 75%, considered as heterogeneity. Publication bias will be assessed using a funnel plot. Subgroup analysis will be sought based on possible characteristics of the studies. Forest plots will be used to present the combined estimate with 95% CI. The quality of evidence of the outcomes will be assessed with the GRADE approach. If no more than one study will be found for each of the objective, then the finding will be synthesized narratively.

Potential limitations

Only quantitative observational studies published in English will be included. This might excluded studies those published in other languages. Further, qualitative studies that may assessed the associated factors might be excluded. Therefore, the readers are advised to take this into account.

Patient and public involvement

It was not appropriate to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research as no individual information will be discussed.

Ethics and dissemination

The review will be based on published data, and thus there is no requirement for ethical approval. The results will be disseminated through publication in a peer reviewed journal, and through presentations at academic conferences.

DISCUSSION

It is crucial to know the importance of preterm birth and contributing factors considering the latest statistics in a country. Hence, this review will present on the country wide magnitude of preterm birth and the associated factors of preterm birth. The result will provide information to guide health professionals and health policy makers for monitoring preterm birth strategy and applying necessary preventive and appropriate measures to decrease preterm birth.

Abbreviations

ACTION: Antenatal Corticosteroids for Improving Outcomes in preterm Newborns

CI: Confidence Interval

JBI: Joanna Briggs Institute

JBI-MAStARI: JBI Meta-Analysis of Statistics Assessment and Review Instrument

KMC: Kangaroo Mother Care

LMICs: Low and Middle Income Countries

MeSH: Medical Subject Headings

NICU: Neonatal Intensive Care Unit

NMR: Neonatal Mortality Rate

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol

PROSPERO: Prospective Register of Systematic Reviews

SE: Standard Error

WHO: World Health Organization

Declarations

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests

Funding

None.

Author contributions

KFM, MKY, YAH contributed to the conception of the research protocol. KFM, AML, DFT, MMS, FAM designed the study. KFM, DFT, AML reviewed the literature, and wrote the protocol. KFM, AML, DFT, MKY, FAM, MMS, and YAH reviewed and rewrote the protocol. All authors read and approved the final manuscript.

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

Section and topic	Item No	Checklist item	(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	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2, 6
Authors:			
Contact	3a	Provide name, institutional affiliation, 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	NA
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	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
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
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	7
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	7

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-10
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)	6-9
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	9
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	9
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
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	8-9
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	10
	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)	10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	10
	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) (such as publication bias across studies, selective reporting within studies)	10
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	10

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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- Only quantitative observational studies published in English will be included.

INTRODUCTION

Preterm birth is a birth before 37 completed weeks of gestation (1). It is more prevalent in Africa and Asia. Preterm birth complications remained the leading cause of under-5 and neonatal mortalities. Preterm birth, the majority being spontaneously, occurs for a variety of reasons(2). Currently, World Health Organization (WHO) is committed to reduce the health problems and lives lost as a result of preterm births.

Globally, 14.9 million babies born preterm making a birth rate of 11.1%, ranging from 5% to 18%, in 2010 (3). The majority (60%) of these births occurred in sub-Saharan Africa and South Asia where 52% of global livebirths occur. The estimated global preterm birth rate was also 10·6%, 14·84 million live preterm births, in 2014 (4). Twelve million (81·1%) of these preterm births occurred in Asia and sub-Saharan Africa (4) showing the contribution is raised from 2010. Ethiopia is one of the low-middle incomes countries in Sub-Saharan Africa.

Preterm birth remains a crucial issue in child mortality and improving quality of maternal and newborn care(4). Complications of preterm birth is the leading cause of death among under 5 children with risk of dying ranged between 1.9 and 155.1 per 1,000 livebirths , in 2015 (5). In the same report, it had been found as the leading cause of death among neonates contributing for 0·944 million deaths. Complication of infants born preterm result in significant cost to the health sector, parents and the society in that preterm neonates take the first place for neonatal intensive care unit (NICU) admission and longer hospital stay globally (4).

Currently, WHO is committed to reduce the health problems and lives lost as a result of preterm births (6). Hence, WHO had developed new guidelines including interventions

provided to the mother and the newborn baby (6). The Every Woman Every Child movement is also aiming to intensify national and international commitment and action to ensure that women, children and adolescents are at the heart of development. The movement puts into action the global strategy (2016-2030) (7). The strategy is aimed to end all preventable deaths of women, children and adolescents within a generation and ensuring their well-being. Though Ethiopia achieved the millennium development goal 4 with 67% under-five mortality reduction from the 1990 estimate, the reduction in neonatal mortality is not remarkable (8). However, Ethiopia has planned to reduce neonatal mortality rate from 28 in 2015/16 to 10 by 2019/2020 (9). Furthermore, the country is also devoted to end preventable deaths of newborns and children under 5 years of age by 2030 (10).

There are local studies on preterm births conducted in Ethiopia. The need for an accurate and reliable result (11, 12), a single study aggregating these studies is necessary for policy makers and implementers. Even though, there is a systematic review (13) done, it addressed only the effect of pregnancy induced hypertension and multiple pregnancies on preterm birth. However, literatures show that more factors affect preterm birth. Among some of the identified associated factors of preterm birth in Ethiopia are obstetric complication during the current pregnancy (14) specifically including pregnancy induced hypertension (15, 16), premature rapture of membrane (17, 18) and hypertension during pregnancy (17); history of obstetric complications including history of abortion (17), history of still birth (17), history of low birth weight (17) and history of preterm birth (17); chronic illness (15, 18), nutritional status (14), anemia (18), antenatal care follow up (14, 16, 18), substance intake during pregnancy (17), multiple gestation (16, 17), and income status

(18). Hence, conducting a systematic review and meta-analysis on preterm birth is paramount important in Ethiopia by updating the latest possible evidences.

Therefore this review is aimed at assessing the magnitude and associated factors of preterm birth (births before 37 gestational weeks) in Ethiopia.

METHODS AND ANALYSIS

Development of the review method

The methods of this systematic review and meta-analysis protocol was developed based on the PRISMA Protocols (PRISMA-P) 2015 statement (19). The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline will be followed during the systematic review(20, 21). The result of the review will be reported according to the PRISMA guideline for reporting (22). The four phases that were drawn from the PRISMA flow chart (23) will be documented in the results to show the study selection process from initially identified records to finally included studies. The protocol for this systematic review and meta-analysis is registered in international prospective register of systematic reviews (PROSPERO) and obtained the registration number (CRD42017064585). The initial anticipated or actual start date as well as anticipated completion date were updated with brief details on PROSPERO records. We would like to disclose that the update was not related to any problem to the present study.

Eligibility criteria

We will include all observational studies that examined the level and/or associated factors of preterm birth (births before 37 weeks of gestational period) in Ethiopia. Reviews, editorials, case series and case reports on preterm birth as well as studies that only reported qualitative findings on preterm birth will be excluded. In studies that reported

both quantitative and qualitative results, we will only consider the quantitative findings. Studies will be considered relevant if they assessed the magnitude of preterm birth and/or examined the associated factors of preterm birth. Regarding magnitude, only those studies that reported percentages out of livebirths will be eligible.

Search strategy

Major medical electronic databases such as PubMed, and Science Direct will be searched to identify relevant literature for the review. To cover grey literature, we will hand-search literature using the Google search engine and Google Scholar and references of electronically identified articles. Further, references list will also be considered from relevant studies considered for critical appraisal.

The literature search will be carried out by the primary author (KFM). The search will be limited to humans, and journal studies published in English from Jan 01, 2009 to Dec 31, 2019. We will apply Medical Subject Headings (MeSH) terms from PubMed, and combined key words to identify studies in the databases.

Accordingly, literatures will be retrieved using the exact search phrase *("Premature Birth/epidemiology"[Mesh] OR "Premature Birth/etiology"[Mesh] OR "Premature Birth/statistics and numerical data"[Mesh] OR premature birth* [MeSH] OR preterm birth OR premature birth OR preterm labo* OR preterm deliver* OR preterm infant OR preterm neonate* OR preterm newborn* OR birth outcome OR pregnancy outcome$ OR pregnancy complication$ OR birth outcome$ OR birth complication$) AND Ethiopia AND ((incidence OR prevalence OR magnitude OR burden) OR (predict* OR associated factor* OR risk factor* OR determinant*))* from PubMed. This will be customized for other databases.

Study selection process

The retrieved studies will be exported to the citation manager (EndNote) and then duplicates excluded. The titles and abstracts of the studies will be reviewed for screening by two authors (KFM and AML) for obvious exclusion according to the eligibility/inclusion criteria. Based on this screening, the titles and abstracts of the studies will be classified as included, excluded, and undecided. Full text of all the included and the undecided studies will be searched for further eligibility assessment.

The full texts of the included and undecided categories of the studies will be independently reviewed by two authors (KFM and AML) against the eligibility criteria for final inclusion. Studies that are not eligible based on the examination of the full-text will be excluded by stating the reasons according to the inclusion criteria. Disagreements between the two reviewers will be resolved through discussion and consensus.

Studies deemed to be appropriate will be scanned in full to determine relevance. Secondly, the references lists of all relevant studies will be reviewed to find additional studies that may have been difficult to detect in the database search due to non-reporting in the abstract (possibly due to non-significant effects). Studies published by the same team will be carefully reviewed to ensure the results of a given study are not included twice in this review.

Critical appraisal

All of the included studies will be critically appraised for their validity. The three authors (DFT, MKY, FA) will check the methodological robustness and validity of the findings using the Joanna Briggs Institute (JBI) Meta-Analysis of Statistics Assessment and Review Instrument (24). Uncertainties will be resolved by joint discussion between the

reviewers. Disagreements among the reviewers will be resolved through discussion and consensus.

The JBI Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) will be used for critical appraisal (25). This tool contains a separate appraisal checklist for each type of the study design. The reviewers will independently assess articles prior to inclusion in the final review using this instrument. Any disagreement among the reviewers will be resolved through discussion, and by involving another reviewer. A Study with quality assessment score of 50% and above and a study having a response rate of 80% and above were included in the final review.

Data extraction

The JBI data extraction form will be used to extract the characteristics of the studies and prevalence of preterm birth (primary outcome) as well as Odds ratio (secondary outcomes). A standardized excel sheet will be created and information from the standardized review forms will be transferred in order to be readily available for the systematic review. Three reviewers (KFM, MMS and AML) will extract data independently. Disagreements among the reviewers were resolved through discussion and consensus.

This tool will include information on the author, year of publication, objective, study setting, year of survey, study design, sample size, data collection method, study participants, definition used for preterm birth, prevalence of preterm, 95% CI for prevalence of preterm birth, and list of associated factors with their effect size. A quantitative data of cross-tabulation between the subject's characteristics (associated factors) and the preterm birth will also systematically abstracted.

Data synthesis and statistical analysis

The individual studies will be concisely described using a summary table. The summary table particularly describes the characteristics of the included studies and the main findings.

The data will be analyzed by the Stata software version 14. For studies which did not present a standard error (SE), it will be calculated using the formula; SE = $\sqrt{(p \times (1-p)/n)}$. The calculated standard error and prevalence rate of each study will then entered into Stata software to calculate the overall prevalence and its 95% confidence interval (CI). Similarly, the relationship between factors and preterm birth will be summarized using statistical estimates of effect sizes, odds ratio. Subgroup analysis will be sought based on possible characteristics of the studies.

The level of heterogeneity among the studies will be quantified using the I^2 statistics (26). Meta-analysis using random effects model will be conducted for the I^2 value of more than 75%, considered as heterogeneity. Publication bias will be assessed using a funnel plot and Egger's test of small study bias. Symmetric funnel plot as well as insignificant Egger's test will be taken as evidence for no serious small study bias (publication bias). Trim and fill technique will be considered for substantial publication bias. Further, sensitivity analysis will be used to assess the influential studies on the pooled estimate.

Forest plots will be used to present the combined estimate with 95% CI. The quality of evidence of the outcomes will be assessed with the GRADE approach. If no more than one study will be found for each of the objective, then the finding will be synthesized narratively.

Potential limitations

Only quantitative observational studies published in English will be included. This might exclude studies those published in other languages. Further, qualitative studies that assessed the associated factors might be excluded. Therefore, the readers are advised to take this into account.

Patient and public involvement

It was not appropriate to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research as no individual information will be discussed.

Ethics and dissemination

The review will be based on published data, and thus there is no requirement for ethical approval. The results will be disseminated through publication in a peer reviewed journal, and through presentations at academic conferences.

DISCUSSION

It is crucial to know the importance of preterm birth and contributing factors considering the latest statistics in a country. Hence, this review will present on the country wide magnitude of preterm birth and the associated factors of preterm birth. The result will provide information to guide health professionals and health policy makers for monitoring preterm birth strategy and applying necessary preventive and appropriate measures to decrease preterm birth.

Abbreviations

ACTION: Antenatal Corticosteroids for Improving Outcomes in preterm Newborns

CI: Confidence Interval

JBI: Joanna Briggs Institute

JBI-MAStARI: JBI Meta-Analysis of Statistics Assessment and Review Instrument

KMC: Kangaroo Mother Care

LMICs: Low and Middle Income Countries

MeSH: Medical Subject Headings

NICU: Neonatal Intensive Care Unit

NMR: Neonatal Mortality Rate

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol

PROSPERO: Prospective Register of Systematic Reviews

SE: Standard Error

WHO: World Health Organization

Declarations

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests

Funding

None.

Author contributions

KFM, MKY, YAH contributed to the conception of the research protocol. KFM, AML, DFT, MMS, FAM designed the study. KFM, DFT, AML reviewed the literature, and wrote the protocol. KFM, AML, DFT, MKY, FAM, MMS, and YAH reviewed and rewrote the protocol. All authors read and approved the final manuscript.

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

Section and topic	Item No	Checklist item	(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	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2, 6
Authors:			
Contact	3a	Provide name, institutional affiliation, 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	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	NA
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	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-6
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	7
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	7

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-10
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)	8-9
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	9
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	9
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
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	8-10
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	10
	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)	10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	10
	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) (such as publication bias across studies, selective reporting within studies)	10
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	10

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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The prevalence and associated factors of preterm birth in Ethiopia: Systematic review and meta-analysis protocol

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Global health
Keywords:	PUBLIC HEALTH, NEONATOLOGY, GYNAECOLOGY, OBSTETRICS

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The prevalence and associated factors of preterm birth in Ethiopia: Systematic review and meta-analysis protocol

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ABSTRACT

Introduction: Preterm birth (PTB) complications are the leading cause of death among neonates globally. The reduction in neonatal mortality is not remarkable in Ethiopia. Therefore, this review will assess the magnitude and associated factors of PTB in Ethiopia.

Methods and Analysis: The preferred reporting items for systematic reviews and meta-analyses guideline will be followed during the systematic review. We will include all observational studies published from Jan 01, 2009 to Dec 31, 2019 that examined the level and/or associated factors of any type of PTB among livebirths in Ethiopia. Inclusion criteria will be all livebirths, PTB defined as delivery before 37 weeks' gestation. The primary outcome will be PTB < 37 weeks, and secondary outcomes including PTB < 34, < 32 and <28 weeks will be analyzed. PubMed, and Science Direct databases as well as Google search engine and Google Scholar will be searched. The pooled prevalence of preterm and effect size of association for associated factors will be analyzed using the Stata software version 14. The heterogeneity between studies will be measured by I^2 statistics. A random-effects model will be used to estimate if heterogeneity detected. Publication bias will be assessed using a funnel plot. Subgroup analysis will be sought based on possible characteristics of the studies, specific morbidity (like pre-eclampsia, hypertension), type of PTB (spontaneous or iotrogenic), and quality of study (high quality or low risk). Meta-regression will be considered for major covariates (maternal age and maternal body mass index) related to PTB. Forest plots will be used to present the combined estimate with 95% confidence intervals. The quality of evidence of the outcomes will be assessed with the GRADE approach.

Ethics and dissemination: No ethical approval is necessary for this systematic review. The findings will be published in a peer-reviewed journal.

PROSPERO registration number: CRD42017077356.

Keywords: Preterm birth, Prevalence, Associated Factors, Ethiopia, Systematic review, Meta-analysis

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The proposed study will provide updated knowledge on the prevalence of preterm birth, leading cause of neonatal death, in Ethiopia where reduction in neonatal mortality is no remarkable.
- The proposed study will provide a comprehensive knowledge on the associated factors of preterm birth in Ethiopia.
- The PRISMA guideline will be followed during the proposed systematic review.
- Standard tool for critical appraisal and data extraction will be used
- Only quantitative observational studies published in English will be included.

INTRODUCTION

Preterm birth (PTB) is a birth before 37 completed weeks of gestation (1). It is more prevalent in Africa and Asia. PTB complications remained the leading cause of under-5 and neonatal mortalities. PTB, the majority being spontaneously, occurs for a variety of reasons(2). Currently, World Health Organization (WHO) is committed to reduce the health problems and lives lost as a result of preterm births.

Globally, 14.9 million babies born preterm making a birth rate of 11.1%, ranging from 5% to 18%, in 2010 (3). The majority (60%) of these births occurred in sub-Saharan Africa and South Asia where 52% of global livebirths occur. The estimated global PTB rate was also 10·6%, 14·84 million live PTBs, in 2014 (4). Twelve million (81·1%) of these PTBs occurred in Asia and sub-Saharan Africa (4) showing the contribution is raised from 2010. Ethiopia is one of the low-middle incomes countries in Sub-Saharan Africa.

Preterm birth remains a crucial issue in child mortality and improving quality of maternal and newborn care(4). Complications of PTB is the leading cause of death among under 5 children with risk of dying ranged between 1.9 and 155.1 per 1,000 livebirths , in 2015 (5). In the same report, it had been found as the leading cause of death among neonates contributing for 0·944 million deaths. Complication of infants born preterm result in significant cost to the health sector, parents and the society in that preterm neonates take the first place for neonatal intensive care unit (NICU) admission and longer hospital stay globally (4).

Currently, WHO is committed to reduce the health problems and lives lost as a result of PTBs (6). Hence, WHO had developed new guidelines including interventions provided to the mother and the newborn baby (6). The Every Woman Every Child movement is

also aiming to intensify national and international commitment and action to ensure that women, children and adolescents are at the heart of development. The movement puts into action the global strategy (2016-2030) (7). The strategy is aimed to end all preventable deaths of women, children and adolescents within a generation and ensuring their well-being. Though Ethiopia achieved the millennium development goal 4 with 67% under-five mortality reduction from the 1990 estimate, the reduction in neonatal mortality is not remarkable (8). However, Ethiopia has planned to reduce neonatal mortality rate from 28 in 2015/16 to 10 by 2019/2020 (9). Furthermore, the country is also devoted to end preventable deaths of newborns and children under 5 years of age by 2030 (10).

There are local studies on PTBs conducted in Ethiopia. The need for an accurate and reliable result (11, 12), a single study aggregating these studies is necessary for policy makers and implementers. Even though, there is a systematic review (13) done, it addressed only the effect of pregnancy induced hypertension and multiple pregnancies on preterm birth. However, literatures show that more factors affect PTB. Among some of the identified associated factors of PTB in Ethiopia are obstetric complication during the current pregnancy (14) specifically including pregnancy induced hypertension (15, 16), premature rapture of membrane (17, 18) and hypertension during pregnancy (17); history of obstetric complications including history of abortion (17), history of still birth (17), history of low birth weight (17) and history of PTB (17); chronic illness (15, 18), nutritional status (14), anemia (18), antenatal care follow up (14, 16, 18), substance intake during pregnancy (17), multiple gestation (16, 17), and income status (18). Hence, conducting a systematic review and meta-analysis on PTB is paramount important in Ethiopia by updating the latest possible evidences.

Therefore this review is aimed at assessing the magnitude and associated factors of PTB in Ethiopia.

METHODS AND ANALYSIS

Development of the review method

The methods of this systematic review and meta-analysis protocol was developed based on the PRISMA Protocols (PRISMA-P) 2015 statement (19). The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline will be followed during the systematic review(20, 21). The result of the review will be reported according to the PRISMA guideline for reporting (22). The four phases that were drawn from the PRISMA flow chart (23) will be documented in the results to show the study selection process from initially identified records to finally included studies. The protocol for this systematic review and meta-analysis is registered in international prospective register of systematic reviews (PROSPERO) and obtained the registration number (CRD42017064585). The initial anticipated or actual start date as well as anticipated completion date were updated with brief details on PROSPERO records. We would like to disclose that the update was not related to any problem to the present study.

Eligibility criteria

We will include all observational studies that examined the level and/or associated factors of any type of PTB among livebirths in Ethiopia. Inclusion criteria will be all livebirths, PTB defined as delivery before 37 weeks' gestation. The primary outcome will be PTB, with PTB defined as a delivery occurring before 37 completed weeks of gestation. Other relevant secondary outcomes to PTB will be considered including PTB < 34, < 32 or < 28 weeks. Reviews, editorials, case series and case reports on PTB as well as studies that

only reported qualitative findings on PTB will be excluded. In studies that reported both quantitative and qualitative results, we will only consider the quantitative findings. Studies will be considered relevant if they assessed the magnitude of PTB and/or examined the associated factors of preterm birth. Regarding magnitude, only those studies that reported percentages out of livebirths will be eligible.

Search strategy

Major medical electronic databases such as PubMed, and Science Direct will be searched to identify relevant literature for the review. To cover grey literature, we will hand-search literature using the Google search engine and Google Scholar and references of electronically identified articles. Further, references list will also be considered from relevant studies considered for critical appraisal.

The literature search will be carried out by the primary author (KFM). The search will be limited to humans, and journal studies published in English from Jan 01, 2009 to Dec 31, 2019. We will apply Medical Subject Headings (MeSH) terms from PubMed, and combined key words to identify studies in the databases.

Accordingly, literatures will be retrieved using the exact search phrase *("Premature Birth/epidemiology"[Mesh] OR "Premature Birth/etiology"[Mesh] OR "Premature Birth/statistics and numerical data"[Mesh] OR premature birth* [MeSH] OR preterm birth OR premature birth OR preterm labo* OR preterm deliver* OR preterm infant OR preterm neonate* OR preterm newborn* OR birth outcome OR pregnancy outcome$ OR pregnancy complication$ OR birth outcome$ OR birth complication$) AND Ethiopia AND ((incidence OR prevalence OR magnitude OR burden) OR (predict* OR associated*

factor OR risk factor* OR determinant*))* from PubMed. This will be customized for other databases.

Study selection process

The retrieved studies will be exported to the citation manager (EndNote) and then duplicates excluded. The titles and abstracts of the studies will be reviewed for screening by two authors (KFM and AML) for obvious exclusion according to the eligibility/inclusion criteria. Based on this screening, the titles and abstracts of the studies will be classified as included, excluded, and undecided. Full text of all the included and the undecided studies will be searched for further eligibility assessment.

The full texts of the included and undecided categories of the studies will be independently reviewed by two authors (KFM and AML) against the eligibility criteria for final inclusion. Studies that are not eligible based on the examination of the full-text will be excluded by stating the reasons according to the inclusion criteria. Disagreements between the two reviewers will be resolved through discussion and consensus.

Studies deemed to be appropriate will be scanned in full to determine relevance. Secondly, the references lists of all relevant studies will be reviewed to find additional studies that may have been difficult to detect in the database search due to non-reporting in the abstract (possibly due to non-significant effects). Studies published by the same team will be carefully reviewed to ensure the results of a given study are not included twice in this review.

Critical appraisal

All of the included studies will be critically appraised for their validity. The three authors (DFT, MKY, FA) will check the methodological robustness and validity of the findings

using the Joanna Briggs Institute (JBI) Meta-Analysis of Statistics Assessment and Review Instrument (24). Uncertainties will be resolved by joint discussion between the reviewers. Disagreements among the reviewers will be resolved through discussion and consensus.

The JBI Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) will be used for critical appraisal (25). This tool contains a separate appraisal checklist for each type of the study design. The reviewers will independently assess articles prior to inclusion in the final review using this instrument. Any disagreement among the reviewers will be resolved through discussion, and by involving another reviewer. A Study with quality assessment score of 50% and above and a study having a response rate of 80% and above were included in the final review.

Data extraction

The JBI data extraction form will be used to extract the characteristics of the studies and prevalence of preterm birth (primary outcome and secondary outcomes) as well as Odds ratio. A standardized excel sheet will be created and information from the standardized review forms will be transferred in order to be readily available for the systematic review. Three reviewers (KFM, MMS and AML) will extract data independently. Disagreements among the reviewers were resolved through discussion and consensus.

This tool will include information on the author, year of publication, objective, study setting, year of survey, study design, sample size, data collection method, study participants, definition used for preterm birth, prevalence of preterm, 95% CI for prevalence of preterm birth, and list of associated factors with their effect size. A

quantitative data of cross-tabulation between the subject's characteristics (associated factors) and the preterm birth will also systematically abstracted.

Data synthesis and statistical analysis

The individual studies will be concisely described using a summary table. The summary table particularly describes the characteristics of the included studies and the main findings.

The data will be analyzed by the Stata software version 14. For studies which did not present a standard error (SE), it will be calculated using the formula; SE = $\sqrt{(p \times (1-p)/n)}$. The calculated standard error and prevalence rate of each study will then entered into Stata software to calculate the overall prevalence and its 95% confidence interval (CI). Similarly, the relationship between factors and preterm birth will be summarized using statistical estimates of effect sizes, odds ratio. Subgroup analysis will be sought based on possible characteristics of the studies, specific morbidity (like pre-eclampsia, hypertension), type of PTB (spontaneous or iotrogenic), and quality of study (high quality or low risk). Meta-regression will be considered for major covariates (maternal age and maternal body mass index) related to PTB. Meta-regression will be considered for major covariates (maternal age and maternal body mass index) related to PTB.

The level of heterogeneity among the studies will be quantified using the I^2 statistics (26). Meta-analysis using random effects model will be conducted for the I^2 value of more than 75%, considered as heterogeneity. Publication bias will be assessed using a funnel plot and Egger's test of small study bias. Symmetric funnel plot as well as insignificant Egger's test will be taken as evidence for no serious small study bias (publication bias). Trim and

fill technique will be considered for substantial publication bias. Further, sensitivity analysis will be used to assess the influential studies on the pooled estimate.

Forest plots will be used to present the combined estimate with 95% CI. The quality of evidence of the outcomes will be assessed with the GRADE approach. If no more than one study will be found for each of the objective, then the finding will be synthesized narratively.

Potential limitations

Only quantitative observational studies published in English will be included. This might exclude studies those published in other languages. Further, qualitative studies that assessed the associated factors might be excluded. Therefore, the readers are advised to take this into account.

Patient and public involvement

It was not appropriate to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research as no individual information will be discussed.

Ethics and dissemination

The review will be based on published data, and thus there is no requirement for ethical approval. The results will be disseminated through publication in a peer reviewed journal, and through presentations at academic conferences.

DISCUSSION

It is crucial to know the importance of preterm birth and contributing factors considering the latest statistics in a country. Hence, this review will present on the country wide magnitude of preterm birth and the associated factors of preterm birth. The result will provide information to guide health professionals and health policy makers for monitoring

preterm birth strategy and applying necessary preventive and appropriate measures to decrease preterm birth.

Abbreviations

ACTION: Antenatal Corticosteroids for Improving Outcomes in preterm Newborns

CI: Confidence Interval

JBI: Joanna Briggs Institute

JBI-MAStARI: JBI Meta-Analysis of Statistics Assessment and Review Instrument

KMC: Kangaroo Mother Care

LMICs: Low and Middle Income Countries

MeSH: Medical Subject Headings

NICU: Neonatal Intensive Care Unit

NMR: Neonatal Mortality Rate

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol

PROSPERO: Prospective Register of Systematic Reviews

PTB: Preterm Birth

SE: Standard Error

WHO: World Health Organization

Declarations

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests

Funding

None.

Author contributions

KFM, MKY, YAH contributed to the conception of the research protocol. KFM, AML, DFT, MMS, FAM designed the study. KFM, DFT, AML reviewed the literature, and wrote the protocol. KFM, AML, DFT, MKY, FAM, MMS, and YAH reviewed and rewrote the protocol. All authors read and approved the final manuscript.

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

Section and topic	Item No	Checklist item	(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	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3, 7
Authors:			
Contact	3a	Provide name, institutional affiliation, 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	14
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	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	14
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5-6
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 (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	7-8
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
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

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-10
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)	7-10
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	10-11
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	10-11
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
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	11-12
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	12
	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)	11-12
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11-12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	11-12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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