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Prevalence, incidence and etiologies of chronic leg ulcers in Africa: a systematic review and meta-analysis protocol

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Keywords:	Chronic leg ulcer, Prevalence, Incidence, Africa, Review

Prevalence, incidence and etiologies of chronic leg ulcers in Africa: a systematic review and meta-analysis protocol

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Abstract

Introduction

Chronic leg ulcers (CLU) are known as a major and snowballing threat to public health and the economy globally and in Africa. Data available mostly in developed countries show that the prevalence of this ailment seems to vary greatly, and also follows trends of associated risk factors like obesity and diabetes. In Africa, studies reporting on epidemiology of CLU are scare. The present systematic review and meta-analysis aims at determining the prevalence, incidence and etiologies of chronic leg ulcers in this continent.

Methods and design

We will include cohort studies, case–control, cross-sectional studies and case series with more than 30 participants. Electronic databases including AJOL (African Journals Online), MEDLINE through PubMed, Excerpta Medica Database (EMBASE), and ISI Web of Science (Science Citation Index), will be searched for relevant abstracts of studies published between January 1, 2000 and December 30, 2018, without language restriction. The review will be reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. After screening of abstracts, study selection, data extraction, and assessment of risk of bias, we shall assess the studies individually for clinical and statistical heterogeneity. Appropriate meta-analytic techniques will then be used to pool studies judged to be clinically homogenous. Visual inspection of Funnel-plots, and Egger's test will be used to detect publication bias. Results will be presented by country.

Ethics and dissemination

Since primary data are not collected in this study, ethical approval is not required. This review is expected to provide relevant data to help in quantifying the burden of CLU in Africa. The final report will be published in a peer-reviewed journal.

Trial registration number: CRD42018108250.

Keywords: Chronic leg ulcer; prevalence; incidence; Africa.

Strengths and limitations of the study

- This will be the first systematic review summarizing data on the epidemiology of chronic leg ulcer in Africa.
- Robust statistical methods such as a meta-analysis will be used.
- Studies included in this review will be those done between 2000 and 2018 and thus the burden reported will be contemporary.
- A limited number of studies on the subject in African countries could lead to an underestimation of the burden of this condition.

Introduction

Defined as ulcers of the leg which shows no tendency to heal after three months of appropriate treatment or still not fully healed at twelve months (1,2), chronic leg ulcers(CLU) are known as a major and snowballing threat to public health and the global economy and particularly in Africa (3). Data available mostly in developed countries show that the prevalence of this ailment seems to vary greatly, and also follows trends of associated risk factors like obesity and diabetes (4). It is estimated that the annual incidence of leg ulcer in the UK and Switzerland are 3.5 and 0.2 per 1000 individuals respectively (2).

Many conditions can be associated with CLU including sickle cell diseases, skin cancers, venous and arterial diseases, infectious diseases such as Buruli ulcers (2,5). In developed countries, the most frequent etiology is venous insufficiency which is found in 1-2% of the population (6,7). Complaints at presentation usually include pain, wound break down with foul odour and discharge. This results in social distress, which can explain the fact that CLU, particularly in the elderly, are a common cause of visits to the podiatrist, wound care specialist, primary care physician, vascular surgeon, or dermatologist (8,9).

In Africa where the number of specialists able to take care of people with CLU is low, this remains a serious health issue, which burden need to be estimated in order to help policy makers to develop strategies to curb down this pathology. The present study aims therefore to estimate by means of a systematic review and meta-analysis the prevalence, incidence and etiologies of CLU in Africa.

Review questions

1. What is the prevalence of CLU in Africa?

2. What is the incidence of CLU in Africa?
3. What are the main etiologies of CLU in Africa?

Objectives

This systematic review and meta-analysis aims to:

1. Determine the prevalence of CLU in Africa;
2. Determine the incidence of CLU in Africa;
3. Determine the etiologies of CLU in the African population.

Methods and design

The present protocol is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis for Protocol (PRISMA-P) (10). An additional file shows the PRISMA-P for protocol checklist [see Additional File 1]. The systematic review and meta-analysis will be reported in conformity with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (11).

Criteria for considering studies for the review

Types of participants

We will include all participants of African descendants and residing in African countries regardless of their age.

Types of studies

We will include cohort studies, case–control, cross-sectional studies and case series with more than 30 participants.

Narrative reviews, letters to the editor, commentaries, perspectives and editorials will be excluded.

Types of outcomes

We will consider studies reporting the following outcomes or with enough data to compute these estimates:

- Prevalence of chronic leg ulcers;
- Incidence of chronic leg ulcers;
- Etiologies of chronic leg ulcers.

Other criteria

- All published data between January 1, 2000 and December 30, 2018 will be considered.
- No language restriction will be applied.

For duplicates of studies published in more than one report, the one reporting the largest sample size will be considered.

- Studies with inaccessible full text either online or from the corresponding author as well as studies in which relevant data on CLU is impossible to extract even after contacting the corresponding author will be excluded.

Search strategy for identifying relevant studies

The search strategy will be conducted as follow:

Bibliographic database searches

Relevant articles published on CLU amount African populations will be identified by searching AJOL (African Journals Online), MEDLINE through PubMed, Excerpta Medica Database (EMBASE), and ISI Web of Science (Science Citation Index), between January 1, 2000 and December 30, 2018, without any language restriction. The search strategy is show in Table 1.

Searching for other sources

We will scan the references of all relevant articles for additional data sources missed during our search, and their full-texts will be retrieved. References of pertinent reviews will also be scanned.

Selection of studies for inclusion in the review

Two reviewers (CD and JNT) will independently screen the studies obtained from the searches, using an assessment form to ensure that the selection criteria are reliably applied. These reviewers will screen the titles, and abstracts of papers obtained, after which the full texts of potentially eligible papers will be retrieved. The two reviewers will independently review the full text of each potentially eligible study, compare their results, and resolve any discrepancy by consensus.

Assessment of methodological quality and reporting of data

Methodological quality, and risk of bias of included studies will be assessed using the tool of bias assessment for prevalence studies developed by Hoy *et al* (12).

Data extraction and management

All records obtained from various databases after implementation of the search strategy will be combined in a single Endnote library, and the duplicates will be removed. A data extraction form will thereafter be used to collect information on the last name of the first author, year of publication, country, study design, study area (rural versus urban), age groups (children, adolescents, adults, elders), sample size, mean or median age, gender, specific characteristics of the study population, etiology of CLU, prevalence, and incidence of CLU in the study population. For multinational studies, the prevalence, or incidence will be reported for the individual countries.

Data synthesis and analysis

We plan to do a meta-analysis after data collection. Unadjusted prevalence, and standard errors for the study-specific estimates will be recalculated based on the information of crude numerators, and denominators provided by individual studies. The variance of the study-specific prevalence will be stabilized with the Freeman-Tukey double arc-sine transformation (14), before poling the data using a random effects meta-analysis model. Heterogeneity will be assessed using the $\chi 2$ test on Cochrane's Q statistic, and quantified by calculating I_2 (15). Values of 25%, 50% and, 75%for I_2 will respectively represent low, medium and, high heterogeneity. We will assess the presence of publication bias using funnel plots inspection and, Egger's test (16). When necessary, meta-regression, and subgroup analyses will be performed to investigate the possible sources of heterogeneity using the aforementioned variables, and the study quality. In case of substantial clinical heterogeneity, a narrative summary of findings will be done. The inter-rater agreement for study inclusion between investigators will be assessed using Cohen's κ coefficient (17). Data analyses will be done using the 'meta' package of the statistical software R (version 3.2.2 [2014-08-14], The R Foundation for statistical computing, Vienna, Austria). This systematic review protocol is registered under the trial number: CRD42018108250 in the International Prospective Register of Systematic Reviews (PROSPERO).

Presentation and reporting of results

A flow diagram will be used to summarize the study selection process. Quantitative data will be presented in tables of individual studies, and in summary tables, and forest plots where appropriate. The quality scores, and risk of bias for each eligible study will be reported accordingly. This may be tabulated, and accompanied by narrative summaries.

Patient and Public Involvement

In this study, data will not be collected directly from patients, but in published studies available in main databases.

Conclusion

CLU are emerging public health threat in Africa. In western countries, its etiologies include diabetes mellitus, and venous insufficiency while in Africa, the main etiologies remain unclear. The present study aims to estimate by means of a systematic review and meta-analysis the prevalence, incidence and etiologies of CLU in Africa. This should help public health authorities in Africa in making informed decision, so as to curb the burden inflicted by this chronic pathology.

Review status:

Preliminary searches.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis.

CLU: Chronic leg ulcer.

Declarations

Acknowledgments

None to declare

Competing interests

The authors declare that they have no competing interests.

Funding

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Authors' Contributions

CD had the idea. CD designed and, conceived the protocol and, drafted the manuscript.JNT, MNT, RNN and JJB participated in the critical revision of the manuscript for methodology and, intellectual content. CD is the guarantor of the review. All authors approved the final version of this manuscript.

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Table 1: Search strategy for PubMed from January 1st, 2000 to December 30th, 2017

Search	Search terms
#1	Chronic leg ulcer OR chronic leg ulcerations OR chronic leg sores OR chronic leg wounds OR leg venous ulcers OR buruli leg ulcer OR malignant leg ulcers OR arterial leg ulcers OR diabetic leg ulcers
#2	Africa* OR Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR Cameroon OR "CanaryIslands" OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "DemocraticRepublic of Congo" OR Djibouti OR Egypt OR "Equatorial Guinea" OR Eritrea OR Ethiopia OR Gabon OR GambiaOR Ghana OR Guinea OR "Guinea Bissau" OR "Ivory Coast" OR "Cote d'Ivoire" OR Jamahiriya OR Kenya ORLesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "SaoTome" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "South Africa" OR "St Helena" OR SudanOR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR "Western Sahara" OR Zaire OR Zambia ORZimbabwe OR "Central Africa" OR "Central African" OR "West Africa" OR "West African" OR "Western Africa" OR"Western African" OR "East Africa" OR "East African" OR "Eastern Africa" OR "Eastern African" OR "North Africa" OR "North African" OR "Northern Africa" OR "Northern African" OR "South African" OR "Southern Africa" OR"Southern African" OR "sub Saharan Africa" OR "sub Saharan African" OR "subSaharan Africa" OR "subSaharanAfrican)" NOT ("guinea pig" OR "guinea pigs" OR "aspergillus niger)"
	#3 #1 AND #2 Limits: 01/01/2000 to 30/12/2017 on humans with no language

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 **5**:15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	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	☐	☒	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	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	☒	☐	10
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	☐	☒	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	9
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	9
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☐	☒	
INTRODUCTION					

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	5
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	5-6
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	☒	☐	6
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	☒	☐	6
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	7
Selection process	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)	☒	☐	7
Data collection process	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	☒	☐	7
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	☒	☐	7
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	☒	☐	7
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	7-8
	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	☒	☐	8

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
		consistency (e.g., I^2, Kendall's tau)			
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☒	☐	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	8

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Contemporary occurrence and etiology of chronic leg ulcers in Africa: a systematic review and meta-analysis protocol

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Dermatology, Surgery
Keywords:	Chronic leg ulcer, Prevalence, Africa

Contemporary occurrence and etiology of chronic leg ulcers in Africa: a systematic review and meta-analysis protocol

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Abstract

Introduction

Chronic leg ulcers (CLU) are known as a major and snowballing threat to public health and the economy globally and in Africa. Data available mostly in developed countries show that the prevalence of this ailment seems to vary greatly, and also follows trends of associated risk factors like obesity and diabetes. In Africa, studies reporting on epidemiology of CLU are scare. The present systematic review and meta-analysis aims at determining the prevalence, incidence, and etiologies of CLU in this continent.

Methods and design

We will include cohort studies, case–control, cross-sectional studies, and case series with more than 30 participants. Electronic databases including African Journals Online, MEDLINE through PubMed, Excerpta Medica Database, and Web of Science, and grey literature will be searched for relevant abstracts of studies published and unpublished between January 1, 2000 and February 28, 2019 without language restriction. The review will be reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. Each study included in this review will be assessed for methodological quality. Clinically homogenous studies will be pooled using random-effects meta-analysis. Visual inspection of funnel-plots and the Egger's test will be used to investigate publication bias.

Ethics and dissemination

The present study will be based on published data; therefore, an ethical approval is not required. The findings of this study will help to build efficient strategies to curb the burden of CLU in Africa. The findings of this review will be presented at conference and to relevant health policy makers, and will be published in a biomedical peer-reviewed journal.

Protocol registration number: PROSPERO, CRD42018108250.

Keywords: Chronic leg ulcer; prevalence; epidemiology; Africa.

Strengths and limitations of the study

- This will be the first systematic review summarizing data on the epidemiology of chronic leg ulcer in Africa.
- Robust statistical methods will be used to pool studies.
- Studies included in this review will be those done between 2000 and 2019 and thus the burden reported will be contemporary.
- A limited number of studies on the subject in African countries could lead to the weakness of evidence from this review.

Introduction

Defined as ulcers of the leg which shows no tendency to heal after three months of appropriate treatment or still not fully healed at twelve months (1,2), chronic leg ulcers (CLU) are known as a major and snowballing threat to public health and the global economy, particularly in Africa (3). Data available mostly in developed countries show that the prevalence of this ailment seems to vary greatly between countries, and also follows trends of associated risk factors like obesity, diabetes, and age (4). It is estimated that the annual incidence of leg ulcer in the UK and Switzerland are 3.5 and 0.2 per 1000 individuals respectively , 4.5 per 1000 in India, 0.11% in Western Australia, and between 393 and 839 per 100,000 individuals per year in New Zealand (2,5).

Many conditions can be associated with CLU including sickle cell diseases, skin cancers, peripheral venous and arterial diseases, neuropathy , allergic diseases, infectious diseases such as Buruli ulcers (2,6). In developed countries, the most frequent etiology is venous insufficiency (7,8). Found as etiology of leg ulcers in 47.6%, 72%, 81% in Germany, UK and Ireland respectively (9–11). Complaints at presentation usually include pain, wound break down with foul odor and discharge. This results in social distress, which can explain the fact that CLU, particularly in the elderly, are a common cause of visits to the podiatrist, wound care specialist, primary care physician, vascular surgeon, or dermatologist (12,13).

Africa continent is facing an epidemiological transition. This region presents the highest burden of well-known risk factors for leg ulcers including sickle cell disease and infectious diseases like Buruli ulcer. In the addition, in this region, there is an increasing burden of non-communicable diseases such as diabetes, obesity, venous insufficiency, peripheral arterial diseases, and cancers that increase the risk for CLU (14–16). In this context, it would be therefore interesting to well describe the burden of CLU in Africa in order to curb the burden

in the continent. Such epidemiological estimate would help to build efficient strategies by policy makers and to orientate future research on this field.

Review questions

1. What is the prevalence and incidence of CLU in general and specific-disease/condition populations living in Africa?
2. What are the main etiologies of CLU in people living in Africa?

Objectives

This systematic review and meta-analysis aims to:

1. Determine the prevalence and incidence of CLU in people living in Africa;
2. Determine the prevalence and distribution of etiologies of CLU in people living in Africa.

Methods and design

The present protocol is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis for Protocol (PRISMA-P) (17). An additional file shows the PRISMA-P checklist [see Additional File 1]. The final report will be published according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (18). This systematic review protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the number CRD42018108250.

Criteria for considering studies for the review

Types of participants

We will include all populations residing in African countries regardless of their age and sex. We will consider both general and specific-disease/condition populations.

Types of studies

We will include cohort studies, case–control, cross-sectional studies and case series with more than 30 participants. Narrative reviews, letters to the editor, commentaries, perspectives and editorials will be excluded.

Types of outcomes

We will consider studies reporting the prevalence, incidence, or etiologies of CLU; or enough data to compute these estimates. We considered CLU as a defect in the skin below the level of knee persisting for more than six weeks and shows no tendency to heal after three or more months (2).

Other criteria

- All published data between January 1, 2000 and February 28, 2019 will be considered.
- No language restriction will be applied.
- Studies with inaccessible full text either online or from the corresponding author as well as studies in which relevant data on CLU is impossible to extract even after contacting the corresponding author will be excluded.

Search strategy for identifying relevant studies

The search strategy will be conducted as follow:

Bibliographic database searching

Relevant articles published on CLU amount African populations will be identified by searching African Journals Online (AJOL), MEDLINE through PubMed, Excerpta Medica Database (EMBASE), and Web of Knowledge between January 1, 2000 and February 28, 2019, without any language restriction. The search strategy in PubMed is shown in Table 1.

Searching for other sources

We will scan the references of all relevant articles and reviews for additional data sources missed during our database searching, and their full-texts will be retrieved. Grey literature will also be searched through Google Scholar for relevant articles eligible for this study.

Selection of studies for inclusion in the review

All records obtained from various databases after implementation of the search strategy will be combined in a single Endnote library, and the duplicates will be removed. Two reviewers (CD and JNT) will independently screen the records obtained from the searches, using an assessment form to ensure that the selection criteria are reliably applied. These reviewers will screen the titles and abstracts of records obtained, after which the full texts of potentially eligible papers will be retrieved. These two reviewers will independently review the full text of each potentially eligible study, compare their results, and resolve any discrepancy by consensus. For duplicates of studies published in more than one report, the one reporting the largest sample size will be considered.

Assessment of methodological quality

The Joanna Briggs Institute Critical Appraisal tool for prevalence studies will be used to assess the methodological quality of finally retained studies (19). The generic version of this tool will be adapted for the present review [See Additional File 2]. This is a nine-item tool. The defined questions will be scored with 0 for "No" or "Unclear" and 1 for "Yes". The total score of each article will be calculated by the sum of its points. Based on this tool, studies will be rated as low risk, moderate risk and high risk with scores 0-3, 4-6 and 7-9, respectively.

Data extraction and management

A pretested data extraction form will be used to collect information on the last name of the first author, year of publication, country, study design, study area (rural versus urban), age groups (children, adolescents, adults, elders), types of population (general population versus specific-disease population), sample size, mean or median age, sex distribution, specific characteristics of the study population, study setting, etiology of CLU, prevalence, and incidence of CLU in the study population. For multinational studies, the prevalence, or incidence will be reported for the individual countries.

Data synthesis and analysis

We plan to do a meta-analysis after data collection. Unadjusted prevalence and incidence with their standard errors for each study will be recalculated based on the information of crude numerators and denominators provided by individual studies. The variance of the study-specific prevalence will be stabilized with the Freeman-Tukey double arc-sine transformation (20), before pooling the data using a random-effects meta-analysis model. . All pooled estimate will be reported with their 95% confidence interval. Heterogeneity will be assessed using the $\chi 2$ test on Cochran's Q statistic, and quantified by calculating I^2 (21). Values of 25%, 50% and, 75%for I^2 will respectively represent low, medium and, high heterogeneity. We will assess the presence of publication bias using funnel plots inspection and Egger's test if there is three studies or more for a meta-analysis (22). When they will be enough data, meta-regression and subgroup analyses will be performed to investigate the possible sources of heterogeneity using the aforementioned variables and the study quality. In case of substantial clinical heterogeneity, a narrative summary of findings will be done. The inter-rater agreement for study inclusion between investigators will be assessed using Cohen's κ coefficient (23). Data analyses will be done using the 'meta' package of the statistical software R (version 3.2.2 [2014-08-14], The R Foundation for statistical computing, Vienna, Austria).

Presentation and reporting of results

A flow diagram will be used to summarize the study selection process. Tables and forest plots will be used to present results of meta-analysis. Data of individual studies will be presented and summarized in tables accompanied with narrative synthesis. Moreover, studies will be classified according to their level of evidence (GRADE).

Patient and Public Involvement

Patients and the public were not involved in the conception and design of this protocol.

Ethics and dissemination

Since data will not be collected directly from patients but from already published studies, ethical approval is not required. The findings of this study will help to build efficient strategies to curb the burden of CLU in Africa. The findings of this review will be presented at conference and to relevant health policy makers, and will be published in a biomedical peer-reviewed journal.

Review status:

Preliminary searches.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis.

CLU: Chronic leg ulcer.

Acknowledgments

None to declare

Competing interests

The authors declare that they have no competing interests.

Funding

This review received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Authors' Contributions

CD had the idea. CD and JNT designed and conceived the protocol, and drafted the manuscript. JNT,MNT, RNN, and JJB participated in the critical revision of the manuscript for methodology and, intellectual content. CD is the guarantor of the review. All authors approved the final version of this manuscript.

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Table 1: Search strategy for PubMed

Search	Search terms
#1	"Chronic leg ulcer" OR "chronic foot ulcers" OR "foot ulcer" OR "leg ulcer" OR "leg ulceration" OR "varicose ulceration" OR "varicose ulcer" OR "chronic varicose ulcers" OR "chronic leg ulcerations" OR "chronic leg sores" OR "chronic leg wounds" OR "leg wound" OR "leg venous ulcers" OR "venous ulcers" OR "Buruli leg ulcer" OR "Buruli ulcer" OR "foot ulcer" OR "malignant leg ulcers" OR "arterial leg ulcers" OR "diabetic leg ulcers" OR "diabetic foot"
#2	Africa* OR Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR Cameroon OR "Canary Islands" OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Democratic Republic of Congo" OR Djibouti OR Egypt OR "Equatorial Guinea" OR Eritrea OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR "Guinea Bissau" OR "Ivory Coast" OR "Cote d'Ivoire" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "South Africa" OR "St Helena" OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe OR "Central Africa" OR "Central African" OR "West Africa" OR "West African" OR "Western Africa" OR "Western African" OR "East Africa" OR "East African" OR "Eastern Africa" OR "Eastern African" OR "North Africa" OR "North African" OR "Northern Africa" OR "Northern African" OR "South African" OR "Southern Africa" OR "Southern African" OR "sub Saharan Africa" OR "sub Saharan African" OR "sub-Saharan Africa" OR "sub-Saharan African") NOT ("guinea pig" OR "guinea pigs" OR "aspergillus niger)"
#3	#1 AND #2 Limits: 01/01/2000 to 02/28/2019

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 **5**:15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	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	☐	☒	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	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	☒	☐	10
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	☐	☒	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	9
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	9
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☐	☒	
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	5
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	5-6
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	☒	☐	6
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	☒	☐	6
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	7
Selection process	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)	☒	☐	7
Data collection process	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	☒	☐	7
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	☒	☐	7
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	☒	☐	7
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	7-8
	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)	☒	☐	8
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-	☒	☐	8

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
		regression)			
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	8

BMJ Open

Contemporary occurrence and etiology of chronic leg ulcers in Africa: a systematic review and meta-analysis protocol

Journal:	*BMJ Open*
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Date Submitted by the Author:	22-Apr-2019
Complete List of Authors:	Danwang, Celestin; Universite Libre de Bruxelles, School of Public Health Tochie, Joel Noutakdie; Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales, Mazou, Temgoua Ngou ; Faculty of Medecine and Biomedical Sciences, Internal medicine and specialities Nzalie, Rolf ; Ngong District Hospital, North Region, Cameroon Bigna, Jean Joel; Centre Pasteur of Cameroon, Department of Epidemiology and Public Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Dermatology, Surgery
Keywords:	Chronic leg ulcer, Prevalence, Africa

Contemporary occurrence and etiology of chronic leg ulcers in Africa: a systematic review and meta-analysis protocol

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Abstract

Introduction

Chronic leg ulcers are known as a major and snowballing threat to public health and the global economy. In Africa, there is controversy on the dearth of studies reporting the epidemiology of chronic leg ulcers. The present systematic review and meta-analysis aim at synthesizing the prevalence, incidence, and etiologies of this ailment in this continent from contemporary data.

Methods and design

We will include cohort studies, case–control, cross-sectional studies, and case series with more than 30 participants. Electronic databases including African Journals Online, MEDLINE, Excerpta Medica Database, and Web of Science, and grey literature will be searched for relevant abstracts of studies published and unpublished between January 1, 2000, and February 28, 2019, without language restriction. The review will be reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. Each study included in this review will be assessed for methodological quality. Clinically homogenous studies will be pooled using random-effects meta-analysis. Visual inspection of funnel-plots and the Egger's test will be used to investigate publication bias. Meta-regression and subgroup analyses will be performed to investigate the possible sources of heterogeneity.

Ethics and dissemination

The present study will be based on published data; therefore, ethical approval is not required. Result of the review will be presented at conferences, to relevant health authorities, and will be published in a biomedical peer-reviewed journal.

Protocol registration number: PROSPERO, CRD42018108250.

Keywords: chronic leg ulcer; prevalence; epidemiology; Africa.

Strengths and limitations of the study

- This will be the first systematic review summarizing data on the epidemiology of chronic leg ulcer in Africa.
- Robust statistical methods will be used to pool studies.
- Studies included in this review will be those carried out between the years 2000 and 2019, hence, the burden reported will be contemporary.
- A limited number of studies on the topic in African countries could lead to underestimation of the true epidemiology of this pathology.

Introduction

Defined as ulcers of the leg which shows no tendency to heal after three months of appropriate treatment or still not fully healed at twelve months (1,2), chronic leg ulcers (CLU) are known as a major and snowballing threat to public health and the global economy. This pathology disproportionately affects Africa (3). The prevalence of CLU varies greatly between countries, and also follows the trends of its risk factors such as obesity, diabetes, and advanced age (4). It is estimated that the annual incidence of CLU in the UK, Switzerland, and India ranges between 0.2 to 4.5 per 1000 inhabitants, while it occurs at a prevalence rate of 0.11% in Western Australia, and an incidence varying between 393 and 839 per 100,000 population per year has been reported in New Zealand (2,5).

Many underlining pathologies are associated with CLU, namely; sickle cell diseases, skin cancers, peripheral venous and arterial diseases, neuropathy, atopic disorders, and infectious diseases such as Buruli ulcers (2,6). In high-income countries, the most frequent etiology of CLU is venous insufficiency (7,8), occurring at a prevalence rate of 47.6%, 72%, 81% in Germany, UK, and Ireland respectively (9–11). CLU may cause severe leg pain, long-standing and foul-smelling infected wounds, physical handicaps and even lower limp mutilation or amputation. These results in the economy lost to all affected societies and social stigmatization of patients. In addition to expenditures incurred on treating the etiology of CLU, affected patients also pay considerable expenses to podiatrists, wound care specialists, primary care physicians, vascular surgeons, or dermatologists (12,13).

With the epidemiological transition faced by Africa, due to westernization of cultures, the prevalence of the aforementioned CLUs' etiologies has sharply increased (14–16). Hence, confronted with this epidemiological transition, it is important to summarize existing data reporting on the occurrence of CLU in Africa, in order to curb the burden of this debilitating pathology in this continent. Such epidemiological estimate may help to build efficient and

sustainable strategies by policymakers. Furthermore, this will help to orientate future research on CLU.

Review questions

1. What is the prevalence and incidence of CLU in Africa?
2. What are the main etiologies of CLU in people living in Africa?

Objectives

This systematic review and meta-analysis aim to:

1. Determine the prevalence and incidence of CLU in people living in Africa;
2. Determine the etiologies of CLU in people living in Africa.

Methods and design

The present protocol is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis for Protocol (PRISMA-P) (17). An additional file shows the PRISMA-P checklist [see Additional File 1]. The final report will be published according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (18). This systematic review protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42018108250.

Criteria for considering studies for the review

Population

We will include all populations residing in African countries regardless of their age and sex. We will consider studies that recruited, investigated or analyzed data concerning CLU in all populations.

Types of studies

We will include cohort studies, case–control, cross-sectional studies and case series with more than 30 participants. Narrative reviews, letters to the editor, commentaries, perspectives, and editorials will be excluded.

Types of outcomes

We will consider studies reporting the occurrence (prevalence and/or incidence) or etiologies of CLU or research articles with enough data to compute these estimates. CLU will be defined as a defect in the skin below the level of knee persisting for more than six weeks and showing no tendency to heal after a minimum period of three months of treatment (2).

Other criteria

- All published data between January 1, 2000, and February 28, 2019, will be considered.
- No language restriction will be applied.
- Studies with inaccessible full text either online or from the corresponding author will be excluded.
- Studies in which relevant data on CLU is impossible to extract even after contacting the corresponding author will be excluded.

Search strategy for identifying relevant studies

The search strategy will be conducted as follow:

Bibliographic database searching

Relevant articles published on CLU amongst African populations will be identified by searching African Journals Online (AJOL), MEDLINE (via PubMed), Excerpta Medica Database (EMBASE), and Web of Knowledge between January 1, 2000, and February 28, 2019, without any language restriction. The search strategy in PubMed is shown in Table 1.

Searching for other sources

We will scan the references of all relevant articles and reviews for additional data sources missed during our database search, and their full-texts will be retrieved. Grey literature will

also be searched through book chapters, theses, conference proceedings, governmental and non-governmental organizations reports.

Selection of studies for inclusion in the review

All records obtained from various databases after implementation of the search strategy will be combined in a single Endnote library, and the duplicates will be removed. Two reviewers (CD and JNT) will independently screen the records obtained from the search, using an assessment form to ensure that the selection criteria are reliably applied. These reviewers will screen the titles and abstracts of records obtained, after which the full texts of potentially eligible papers will be retrieved. These two reviewers will independently review the full text of each potentially eligible study, compare their results, and resolve any discrepancy by consensus. For duplicates of studies published in more than one report, the one reporting the largest sample size will be considered. We will contact the corresponding author to request the full text if it is not accessible.

Assessment of methodological quality

The Joanna Briggs Institute Critical Appraisal tool (a nine-item tool) for prevalence studies will be used to assess the methodological quality of retained studies (19). The generic version of this tool will be adapted for the present review. The defined questions will be scored with zero for "No" or "Unclear" and 1 for "Yes". The total score of each article will be calculated by the sum of its points. Based on this tool, studies will be rated as low, moderate and high risks with scores of 0-3, 4-6 and 7-9 respectively.

Data extraction and management

A pretested data extraction form will be used to collect information on the last name of the first author, year of publication, country, study design, study area (rural versus urban), age groups (children, adolescents, adults, elders), types of population (general population versus specific-disease population), sample size, mean or median age, gender distribution, study

setting, etiology of CLU, prevalence, and incidence of CLU in the study population. For multinational studies, the prevalence, or incidence will be reported for the individual countries.

Data synthesis and analysis

We plan to do a meta-analysis after data collection. Un-adjusted prevalence and incidence with their standard errors for each study will be recalculated based on the information of crude numerators and denominators provided by individual studies. The variance of the study-specific prevalence will be stabilized with the Freeman-Tukey double arc-sine transformation (20), before pooling the data using a random-effects meta-analysis model. All pooled estimates will be reported with their 95% confidence intervals. Heterogeneity will be assessed using the $\chi 2$ test on Cochran's Q statistic, and quantified by calculating I^2 (21). Values of 25%, 50% and, 75% for I^2 will respectively represent low, medium and, high heterogeneity. We will assess the presence of publication bias using funnel plots inspection and Egger's test if there are three studies or more for a meta-analysis (22). When they will be enough data, meta-regression and subgroup analyses will be performed to investigate the possible sources of heterogeneity using the aforementioned variables and the study quality. In case of substantial clinical heterogeneity, a narrative summary of findings will be done. The inter-rater agreement for study inclusion between investigators will be assessed using Cohen's κ coefficient (23). Data analyses will be done using the 'meta' package of the statistical software R (version 3.2.2 [2014-08-14], The R Foundation for statistical computing, Vienna, Austria).

Presentation and reporting of results

A flow diagram will be used to summarize the study selection process. Tables and forest plots will be used to present the results of the meta-analysis. Data of individual studies will be presented and summarized in tables accompanied by narrative synthesis.

Patient and Public Involvement

Patients and the public will not be involved in the conception and design of this protocol. Data will be collected directly from published articles available in main databases and unpublished studies.

Ethics and dissemination

Since data will not be collected directly from patients but from already published studies, ethical approval is not required. The findings of this study will help to build sustainable strategies to curb the burden of CLU in Africa. The findings of this review will be presented at conferences, to relevant health policymakers, and will be published in a biomedical peer-reviewed journal.

Review status:

Preliminary searches.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis.

CLU: Chronic leg ulcer.

Acknowledgments

None to declare

Competing interests

The authors declare that they have no competing interests.

Funding

This review received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Authors' Contributions

CD had the idea. CD and JNT designed and conceived the protocol, and drafted the manuscript. JNT, MNT, RNN, and JJB participated in the critical revision of the manuscript for methodology and, intellectual content. CD is the guarantor of the review. All authors approved the final version of this manuscript.

References

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12. González-Consuegra RV, Verdú J. Quality of life in people with venous leg ulcers: an integrative review. J Adv Nurs 2011 ;67:926–44.

13. Sasanka CS. Venous ulcers of the lower limb: Where do we stand? Indian J Plast Surg 2012 ;45:266.

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Table 1: Search strategy for PubMed

Search	Search terms
#1	((((("Leg Ulcer"[Mesh]) OR "Foot Ulcer"[Mesh]) OR "Varicose Ulcer"[Mesh]) OR "Diabetic Foot"[Mesh]) OR "plantar ulcer*" OR "foot ulcer*" OR "varicose ulcer*" OR "stasis ulcer*" OR "venous ulcer*" OR "venous hypertension ulcer*" OR "venous stasis ulcer*" OR "leg sores" OR "leg wounds" OR "diabetic leg ulcer*" OR "Buruli ulcer*" OR "neuro* leg ulcer*"
#2	Africa* OR Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR Cameroon OR "Canary Islands" OR "Cape Verde" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Democratic Republic of Congo" OR Djibouti OR Egypt OR "Equatorial Guinea" OR Eritrea OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR "Guinea Bissau" OR "Ivory Coast" OR "Cote d'Ivoire" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "South Africa" OR "St Helena" OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe OR "Central Africa" OR "Central African" OR "West Africa" OR "West African" OR "Western Africa" OR "Western African" OR "East Africa" OR "East African" OR "Eastern Africa" OR "Eastern African" OR "North Africa" OR "North African" OR "Northern Africa" OR "Northern African" OR "South African" OR "Southern Africa" OR "Southern African" OR "sub Saharan Africa" OR "sub Saharan African" OR "sub-Saharan Africa" OR "sub-Saharan African") NOT ("guinea pig" OR "guinea pigs" OR "aspergillus niger)"
#3	#1 AND #2 Limits: 01/01/2000 to 02/28/2019

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 **5**:15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	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	☐	☒	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	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	☒	☐	10
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	☐	☒	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	9
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	9
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☐	☒	
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	5
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	5-6
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	☒	☐	6
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	☒	☐	6
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	7
Selection process	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)	☒	☐	7
Data collection process	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	☒	☐	7
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	☒	☐	7
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	☒	☐	7
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	7-8
	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)	☒	☐	8
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-	☒	☐	8

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
		regression)			
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	8