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

Celestin Danwang,[1] Joel Noutakdie Tochie,[2] Temgoua Ngou Mazou,[3] Rolf Nyah Tuku Nzalie,[4] Jean Joel Bigna[5]

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For numbered affiliations see end of article.

Correspondence to
Dr Celestin Danwang; danram07@yahoo.fr

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 synthesising the prevalence, incidence and aetiologies 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. Electronical databases including African Journals Online, MEDLINE, Excerpta Medica Database and Web of knowledge, and grey literature will be searched for relevant abstracts of studies published and unpublished between 1 January, 2000, and 28 February, 2019, without language restriction.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 CRD42018108250.

Strengths and limitations of the study

- This will be the first systematic review summarising 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 show no tendency to heal after 3 months of appropriate treatment or still not fully healed at 12 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, neuropathies, atopic disorders and infectious diseases such as Buruli ulcers.[2 6] In high-income countries, the most frequent aetiology of CLU is venous insufficiency,[7 8] occurring at a prevalence rate of 47.6%, 72% and 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 limb mutilation or amputation. These results in the economy lost to all affected societies and social stigmatisation of patients. In addition to expenditures incurred on treating the aetiology 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 westernisation of cultures, the prevalence of the aforementioned CLUs' aetiologies has sharply increased.[14–16] Hence, confronted with this epidemiological transition, it is important to summarise 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 aetiologies 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 aetiologies 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 online supplementary 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 analysed 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 aetiologies 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 6 weeks and showing no tendency to heal after a minimum period of 3 months of treatment.[2]

Other criteria

- All published data between 1 January, 2000, and 28 February, 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 follows:

Bibliographical database searching

Relevant articles published on CLU among African populations will be identified by searching African Journals Online (AJOL), MEDLINE (via PubMed), Excerpta Medica Database (EMBASE) and Web of Knowledge between 1 January, 2000, and 28 February, 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 organisations 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 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, moderate and high risks with scores of 0 to 3, 4 to 6 and 7 to 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

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

of publication, country, study design, study area (rural vs urban), age groups (children, adolescents, adults, elders), types of population (general population vs specific-disease population), sample size, mean or median age, gender distribution, study setting, aetiology 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 stabilised with the Freeman-Tukey double arcsine transformation,[20] before pooling the data using a random-effects meta-analysis model. All pooled estimates will be reported with their 95% CIs. 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] if there is 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 (V.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 summarise 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 summarised in tables accompanied by narrative synthesis.

Patient and public involvement

Patients and the public were not 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.

Author affiliations
[1]School of Public Health, Université Libre de Bruxelles, Bruxelles, Belgium
[2]Department of Surgery and specialities, Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales, Yaounde, Cameroon
[3]Department of Internal Medicine and Specialities, Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales, Yaounde, Cameroon
[4]Department of Public Health and Hygiene, University of Buea, Buea, Cameroon
[5]Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon

Contributors 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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