


BMJ Open Leishmaniasis in Cameroon: what is known and is done so far? A protocol for systematic review

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To cite: Djune Yemeli L, Domche A, Nana Djeunga HC, et al. Leishmaniasis in Cameroon: what is known and is done so far? A protocol for systematic review. *BMJ Open* 2021;**11**:e047530. doi:10.1136/bmjopen-2020-047530

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-047530>).

Received 01 December 2020
Revised 16 March 2021
Accepted 23 March 2021



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ABSTRACT

Introduction The first visceral and cutaneous leishmaniasis cases were reported in Cameroon since more than six decades. However, interest in the disease has decreased over time and data on its epidemiology across the country are scanty. This systematic review aims to update data on what is known and done so far on leishmaniasis in Cameroon.

Methods and analysis PubMed/MEDLINE, EMBASE and Web of Science will be searched from inception onwards. Grey literature will be identified through Google Scholar searches, dissertation databases and other relevant documents such as report of the National Control Program. Searches will be conducted between January and February 2021. All studies reporting endemicity, distribution, infecting species, vectors and reservoirs will be eligible. The main outcomes will be epidemiological data (infection rate, distribution, infecting species, vectors and animal reservoir), while the secondary outcomes will be the cases management (diagnostic, treatment, reporting, intervention...). Two reviewers will independently screen eligible papers, and potential conflicts will be resolved by involving a third reviewer as an adjudicator. Methodological quality including bias will be appraised using a methodological quality critical appraisal checklist proposed in the Joanna Briggs Institute systematic review methods manual. A narrative synthesis will describe quality and content of the epidemiological evidence. Data on prevalence and vectors will be used to draw thematic maps of the distribution of leishmaniasis in Cameroon.

Ethics and dissemination This study will not require ethical approval as it will be based on already published or unpublished data. The final report of this review will be published in a peer-reviewed journal, and the outcomes will be used (1) as baseline information to design further studies that will help to better refine the epidemiological situation of leishmaniasis in Cameroon, and (2) to inform both programme managers and policy-makers of the situation of leishmaniasis in the country.

Systematic review registration This protocol was registered with the International Prospective Register of Systematic reviews (PROSPERO; registration number: CRD42020211864) database.

INTRODUCTION

Leishmaniasis is a complex vector-borne zoonotic disease caused by more than 20 species of an obligate intracellular parasitic

Strengths and limitations of this study

- To our knowledge, this article will be the second review on leishmaniasis in Cameroon, the first being done since 2001. The results obtained will provide an update of the leishmaniasis situation in Cameroon, which is important for the development of better management strategy in the fight against this group of diseases.
- A narrative synthesis will be used to describe quality and content of the epidemiological evidence; a thematic map of the distribution of leishmaniasis in Cameroon will be drawn.
- A limit of this review could be the few number of published studies given that the disease is underexplored in Cameroon.
- There are often reports of suspicious cases with signs and symptoms of these diseases, but no confirmatory testing is carried out. This therefore represents a potential limitation to this study.

protozoa of the genus *Leishmania*, and transmitted by sand fly vectors of the genera *Phlebotomus* and *Lutzomyia*.¹ Humans are infected when they share the same environment with a sand fly vector and reservoir hosts. There are different types of leishmaniasis according to the infecting species and clinical presentations. According to the 2010 WHO expert committee report, the different forms of leishmaniasis encountered in the old world are (1) visceral leishmaniasis (VL, also known as kala-azar, caused by *L. donovani* and *L. infantum*), (2) cutaneous leishmaniasis (CL, most frequently caused by *L. tropica*, *L. major* and *L. aethiops*), (3) mucosal leishmaniasis (can be caused by any species), (4) diffused cutaneous leishmaniasis (caused by *L. aethiops*) and (5) post kala-azar dermal leishmaniasis (present in all areas with *L. donovani*).² While CL is the most common form of the disease, VL is the most serious and is almost always fatal if untreated.³



Leishmaniasis is highly heterogeneous in its distribution. In fact, while the incidence across a region may appear low, focal areas are intensely affected, leading to a high complexity in assessing the real incidence of the disease.^{4,5} Globally, the disease is endemic in all the six WHO regions, with 87 and 75 countries having reported at least one case of CL and VL, respectively.⁶ In 2015, an estimated 200 000 new CL and 25 000 new VL cases were reported worldwide.⁶

Both CL and VL have been described in Cameroon, and studies have revealed the presence of about 20 sand fly species.^{7,8} In fact, the first cases of CL and VL were described in 1930 and 1976 in the northern part of the country and in a hospital in Yaoundé, respectively.^{9,10} However, over time, studies on leishmaniasis are becoming scarce, and data are very scanty and poorly documented. Cameroon is currently classified among the countries with no data available on leishmaniasis.¹¹ Indeed, Cameroon is classified by WHO as endemic to CL but with no available data on the number of cases, and appears among countries with previously reported VL cases with no available data on the number of cases.⁶ Since the systematic review on the situation of leishmaniasis in Cameroon carried out in 2001,⁹ and the leishmaniasis country profile established by WHO in 2012,¹² no update has been made to allow the establishment of new management strategies against this group of diseases. There is therefore an urgent need to perform a situation analysis of leishmaniasis in Cameroon.

Objective

This systematic review aims to document the infection rate, circulating species, vectors and reservoirs of leishmaniasis as well as data on control/management strategies in Cameroon. This will help in updating the situation of leishmaniasis in Cameroon, and ultimately helps defining/refining control strategies and reinforcing advocacy.

Review questions

By documenting data on what is known and done so far on leishmaniasis in Cameroon, this review will help in answering the following questions:

1. What are the circulating species and the clinical presentations?
2. What are the vectors responsible of the transmission of leishmaniasis?
3. What are the non-human reservoirs of leishmaniasis?
4. How is the diagnostic of leishmaniasis conducted?
5. What is the level of endemicity and distribution of leishmaniasis?
6. How is the control of leishmaniasis organised?

METHODS AND ANALYSIS

This systematic review protocol was written in accordance with reporting guidance provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement¹³ (see

PRISMA-P checklist as online supplemental file 1). The registration process of the protocol with the Prospective Register of Systematic reviews (PROSPERO) database is done (registration process ongoing in PROSPERO). The review process will be conducted between January and February 2021.

Eligibility criteria

There will be no restrictions regarding the date of the study. Any type of study, either published or not, on *Leishmania* species, endemicity, distribution, clinical presentation, co-infection (HIV or any other infection), vectors and reservoirs in Cameroon will be eligible for this review. Since leishmaniasis belongs to case management Neglected Tropical Diseases group, case reports and health facilities' data will also be considered in this review. In addition, study or reports on control/management as well as surveillance will be of interest. However, systematic reviews or meta-analyses will be excluded. The search languages will be English and French, the Cameroon official languages in which almost all publications are done.

Information sources and search strategies

PubMed/MEDLINE, EMBASE and Web of Science will be searched, from their inception onwards, to identify relevant articles. Grey literature will be identified through search in Google Scholar and other relevant documents such as dissertation databases and government/control programme reports. The combination of keywords to use in the search strategy will be "leishmaniose" OR "leishmaniasis" OR "Kala-azar" OR "black fever" OR "fièvre noire" OR "Leishmania" OR "sandflies" OR "mouche du sable" OR "phlebotomine" OR "Phlebotomus" AND "Cameroon" OR "Cameroon" (online supplemental file 2). Authors of primary publications or aggregated data and stakeholders involved in research and/or control of leishmaniasis in Cameroon (National Buruli Ulcer, Leprosy, Yaws and Leishmaniasis Control Program) will be contacted to request for unpublished data and/or resources (reports, datasets) relevant for this study.

Study selection

Two independent reviewers will first screen titles and abstracts against eligibility criteria to identify studies that can be potentially included in this review. Studies whose titles and abstracts will give indication that they contain any relevant information on the topic will be included. Full texts of articles deemed potentially relevant will then be retrieved and assessed by the two independent reviewers for the compliance with eligibility criteria. Finally, data will be extracted using a purpose-built Microsoft Office Excel spreadsheet. In case of disagreements between the two independent reviewers, a third one will be involved as an adjudicator, either by consensus or by discussion.

Data extraction and management

A reference manager software (EndNote/Zotero) will be used to manage the retrieval of literature and to screen for

and exclude duplicates. This will be done first automatically using the “find duplicate” or “de-duplication” function under EndNote or Zotero, respectively, by comparing the title or various combinations of the author(s), year, secondary title, volume, issue and page numbers. In the second instance, the records of suspected duplicates will be visually inspected.

Full texts will be read, and Excel spreadsheet will be used for data extraction. The following items will be extracted: (a) title, (b) years of publication, (c) author names, (d) location of the study (regions, health areas, communities), (e) type of environment (forest, savannah, forest–savannah mosaic, type of vegetation), (f) place of report (communities, school or hospital for case report), (g) date of data collection, (h) type of study (is the study on human, vectors or animal reservoirs?), (i) study design, (j) diagnostic methods, (k) *Leishmania* species, (l) vector species, (m) potential reservoirs, (n) treatment provided and (o) geographical coordinates (latitude, longitude and altitude).

Outcomes

The main outcomes will be (1) the prevalence of leishmaniasis, (2) the distribution throughout the country, (3) the infecting species and their distribution, (4) the vectors responsible of transmission and (5) the animal reservoir species. In addition, the secondary outcomes will be the management of cases (diagnostic, treatment, reporting, intervention...). We therefore expected at the end of this study to demonstrate that although data on leishmaniasis are scanty in Cameroon, the disease is a public health concern. This will further serve (1) as a basis to design studies that will help to better refine the epidemiological situation of leishmaniasis in Cameroon, and (2) to inform both programme managers and policy-makers of the situation of leishmaniasis in the country.

Data analysis

Data will be recorded as prevalence with 95% CIs.¹⁴ Prevalence of infection estimates will be stratified according to gender, age, geographical location and year of publication. Chi-square test will be used to compare the prevalence of leishmaniasis between different data collection time points/periods. Data on prevalence and vectors will be used to draw a thematic map of the distribution of leishmaniasis in Cameroon using a geographical information system (GIS) software (ArcGIS, V.10.2; ESRI)

Assessment of risk of bias

The risk of bias of primary observational studies will be evaluated using a methodological quality critical appraisal checklist proposed in the Joanna Briggs Institute systematic review methods manual.¹⁵ We will also not include studies with aggregated data by community/village.

Confidence in cumulative evidence

The quality of the evidence will be judged using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.¹⁶ Evidence

quality assessment will be performed for each outcome. The grades of evidence will be defined into four categories and adjudicated as “high” (further research is unlikely to change our confidence in the estimate of effect), “moderate” (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), “low” (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate) and “very low” (any estimate of effect is very uncertain).¹⁶ The confidence in evidence will be discussed among authors, and a narrative synthesis of the results will be provided as some degree of heterogeneity is expected.

Presentation and reporting of results

A flow chart will be used to demonstrate the study selection process. Table or plots will be used to represent qualitative/quantitative variables when appropriate. Data on prevalence, infective species and vectors will be used to draw a thematic map of the distribution of leishmaniasis in Cameroon.

Patient and public involvement

No patient involved.

Amendments to protocol

After approval of the protocol, any important amendments will be documented in the final publication. The date, rationale and description of each change will be provided. If necessary, these amendments will be registered with PROSPERO.

ETHICS AND DISSEMINATION

This proposed study will not require ethical approval as it will be based on already existing published or unpublished data. The final report of this review will be published in a peer-reviewed journal, and the outcomes will be used (1) as baseline information to design further studies that will help to better refine the epidemiological situation of leishmaniasis in Cameroon, and (2) to inform both programme managers and policy-makers of the situation of leishmaniasis in the country.

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Contributors LDY, AD, HCND, CGLN, ENT, GBN and JK contributed intellectually to the development of the present protocol. LDY, AD and HCND prepared the first draft of the manuscript. LDY, AD, HCND, CGLN, ENT, GBN and JK reviewed and approved the final version of the manuscript. HCND and JK are the study guarantors.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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Reporting checklist for protocol of a systematic review.

Based on the PRISMA-P guidelines.

Instructions to authors

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

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

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

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

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

	Reporting Item	Page Number
Title		
Identification	#1a Identify the report as a protocol of a systematic review	1
Update	#1b If the protocol is for an update of a previous systematic review, identify as such	n/a; this is the initial protocol, not an update.
Registration		
	#2 If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors		
Contact	#3a Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b Describe contributions of protocol authors and identify	8

the guarantor of the review

Amendments

[#4](#) If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments 7

Support

Sources [#5a](#) Indicate sources of financial or other support for the review 8

Sponsor [#5b](#) Provide name for the review funder and / or sponsor n/a; this publication is not funded.

Role of sponsor or funder [#5c](#) Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol n/a; this publication is not funded.

Introduction

Rationale [#6](#) Describe the rationale for the review in the context of what is already known 3

Objectives [#7](#) Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) 4

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 4-5

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 5

Search strategy [#10](#) Present draft of search strategy to be used for at least 5

		one electronic database, including planned limits, such that it could be repeated	
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5-6
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	5
Study records - 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	5-6
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	6
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
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 synthesised	6
Data synthesis	#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)	6
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a; meta-analyses will not be performed.
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n/a; meta-analyses will not

be performed.

Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	7
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	7

None The PRISMA-P checklist is distributed under the terms of the Creative Commons Attribution License CC-BY 4.0. This checklist can be completed online using <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)

Table S1. Example of search strategy used in PubMed/Medline

Search #	PubMed search terms
#6	(((((Leishmaniose) OR (Leishmania)) OR (Fièvre noir)) OR (Mouche du sable)) OR (Phlebotome)) AND (Cameroun)
#5	((((((Leishmaniasis) OR (Kala-azar)) OR (Black fever)) OR (Leishmania)) OR (Sandflies)) OR (Phlebotomus)) OR (Phlebotomine)) AND (Cameroon)
#4	(((((Leishmaniose[Title/Abstract]) OR (Fièvre noir[Title/Abstract])) OR (Leishmania[Title/Abstract])) OR (Mouche du sable[Title/Abstract])) OR (Phlebotome[Title/Abstract])) AND (Cameroun[Title/Abstract])
#3	((((((Leishmaniasis[Title/Abstract]) OR (Kala-azar[Title/Abstract])) OR (Black fever[Title/Abstract])) OR (Leishmania[Title/Abstract])) OR (Sandflies[Title/Abstract])) OR (Phlebotomus[Title/Abstract])) OR (Phlebotomine[Title/Abstract])) AND (Cameroon[Title/Abstract])
#2	(((((Leishmaniose[Title]) OR (Fièvre noir[Title])) OR (Leishmania[Title])) OR (Mouche du sable[Title])) OR (Phlebotome[Title])) AND (Cameroun[Title])
#1	((((((leishmaniasis[Title]) OR (Kala-azar[Title])) OR (Black fever[Title])) OR (Leishmania[Title])) OR (Sandflies[Title])) OR (Phlebotomine[Title])) OR (Phlebotomus[Title])) AND (Cameroon[Title])