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

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-047530
Article Type:	Protocol
Date Submitted by the Author:	01-Dec-2020
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Keywords:	Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, Tropical medicine < INFECTIOUS DISEASES, PARASITOLOGY, Epidemiology < TROPICAL MEDICINE, Geographical mapping < TROPICAL MEDICINE
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Leishmaniasis in Cameroon: what is known and is done so far? A protocol for systematic review

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Abstract

Introduction: First visceral and cutaneous leishmaniasis cases were reported in Cameroon since more than six decades. However, interest in the disease has decrease 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 Buruli Ulcer, Leprosy, Yaws, and Leishmaniasis Control Program. 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 management of cases (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 (JBI) 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This proposed study will not require ethical approval as it will be based on already existing published or unpublished data.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 (i) as baseline information

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to design further studies that will help to better refine the epidemiological situation of 34 leishmaniasis in Cameroon, and (ii) to inform both program managers and policy makers of the 35 situation of leishmaniasis in the country. 36

38 Systematic review registration:

This protocol was registered with the International Prospective Register of Systematic reviews 39 (PROSPERO) database. 40

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Strengths and limitations of this study

- > To our knowledge, this article will be the second review on leishmaniasis in Cameroon, 43 the first being done since 2001. The results obtained will provide an update of the 44 leishmaniasis situation in Cameroon, which is important for the development of better 45 management strategy in the fight against this group of diseases. 46
- > A narrative synthesis will be used to describe quality and content of the epidemiological 47 evidence; a thematic map of the distribution of leishmaniasis in Cameroon will be drew. 48
 - > A limit of this review could be the few number of published studies given that the diseases 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.

Introduction 56

Leishmaniasis is a complex vector-borne zoonotic disease caused by more than 20 species of 57 an obligate intracellular parasitic protozoa of the genus Leishmania, and transmitted by sand 58 fly vectors of the genera *Phlebotomus* and *Lutzomyia* [1]. Humans are infected when they share 59 the same environment with a sand fly vector, and reservoir hosts. There are different types of 60 leishmaniasis according to the infecting species and clinical presentations. According to the 61 2010 World Health Organization (WHO) expert committee report, the different forms of 62 63 leishmaniasis encountered in the old world are (i) visceral leishmaniasis (VL also known as kala-azar, caused by L. donovani and L. infantum), (ii) cutaneous leishmaniasis (CL, most 64 frequently caused by L. tropica, L. major, and L. aethiopica), (iii) mucosal leishmaniasis (ML, 65 that can be caused by any species), (iv) diffused cutaneous leishmaniasis (DCL, caused by L. 66

aethiopica) and (v) post Kala-azar dermal leishmaniasis (PKDL, 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 sandflies 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 the 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 the WHO as endemic to CL but with no available data on the number of cases, and appears among countries with previous 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 (Ref), 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

92 This systematic review aims to document the infection rate, circulating species, vectors and 93 reservoirs of leishmaniasis as well as data on control/management strategies in Cameroon. This 94 will help updating the situation of leishmaniasis in Cameroon, and ultimately helps 95 defining/refining control strategies and reinforcing advocacy.

07 Doviou quest

Review questions

98 By documenting data on what is known and done so far on leishmaniasis in Cameroon, this99 review will help answering the following questions:

60 100

1. What are the circulating species and the clinical presentations?

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What are the vectors responsible of the transmission of leishmaniasis? .01 2. 3. What are the non-human reservoirs of leishmaniasis? .02 How is the diagnostic of leishmaniasis conducted? .03 4. What is the level of endemicity and distribution of leishmaniasis? .04 5. How is the control of leishmaniasis organized? .05 6. .06 .07 Methods and analysis .08 This systematic review protocol was written in accordance with reporting guidance provided .09

109 This systematic review protocol was written in accordance with reporting guidance provided 110 by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols 111 (PRISMA-P) statement [12] (see PRISMA-P checklist in Additional file 1). The registration 112 process of the protocol with the Prospective Register of Systematic reviews (PROSPERO) 113 database is done (registration reference number: 211864; registration process ongoing in 114 PROSPERO).

0 116 Eligibility criteria

There will be no restriction regarding the date of the study. Any type of study, either published 17 or not, on Leishmania species, endemicity, distribution, clinical presentation, co-infection (HIV 18 19 or any other infection), vectors and reservoirs in Cameroon will be eligible for this review. Since leishmaniasis belongs to case management Neglected Tropical Diseases (NTDs) group, 20 case reports and health facilities' data will also be considered in this review. In addition, study 21 or reports on control/management, as well as surveillance will be of interest. However, 22 systematic reviews or meta-analyses will be excluded. The search languages will be English 23 and French, the Cameroon official languages in which almost all publications are done. 24

Information sources and search strategies

PubMed/MEDLINE, EMBASE and Web of Science will be searched, from their inception 27 onwards, to identify relevant articles. Grey literature will be identified through search in Google 28 Scholar and other relevant documents such as dissertation databases and government/control 29 program reports. The combination of keywords to use in the search strategy will be .30 "leishmaniose" OR "leishmaniasis" OR "Kala-azar" OR "black fever" OR "fièvre noire" OR 31 "Leishmania" OR "sandflies" OR "mouche du sable" OR "phlebotomine" OR "Phlebotomus" 32 AND "Cameroun" OR "Cameroon". Authors of primary publications or aggregated data and 133 59 60

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.

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138 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-build 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.

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148 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) authors 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, (o) geographical coordinates (latitude, longitude and altitude).

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57 165 **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

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transmission and (5) the animal reservoir species. In addition, the secondary outcomes will bethe management of cases (diagnostic, treatment, reporting, intervention...).

171 Data analysis

Data will be recorded as prevalence with 95% confidence intervals [13]. 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 thematic map of the distribution of leishmaniasis in Cameroon using a geographical information system (GIS) software (ArcGIS, version 10.2, ESRI Inc.)

179 Assessment of risk of bias

180 The risk of bias of primary observational studies will be evaluated using a methodological 181 quality critical appraisal checklist proposed in the Joanna Briggs Institute (JBI) systematic 182 review methods manual [14]. We will also not include studies with aggregated data by 183 community/village.

² 185 **Confidence in cumulative evidence**

The quality of the evidence will be judged using the Grading of Recommendations Assessment, 6 Development and Evaluation (GRADE) approach [15]. Evidence quality assessment will be 7 performed for each outcome. The grades of evidence will be defined into four categories and 8 adjudicated as "high" (further research is unlikely to change our confidence in the estimate of 9 effect), "moderate" (further research is likely to have an important impact on our confidence in 0 the estimate of effect and may change the estimate), "low" (further research is very likely to 1 have an important impact on our confidence in the estimate of effect and is likely to change the 2 estimate) and "very low" (any estimate of effect is very uncertain) [15]. The confidence in 3 evidence will be discussed among authors, and a narrative synthesis of the results will be 4 provided as some degree of heterogeneity is expected. 5

197 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

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3 4	200	species and vectors will be used to draw thematic map of the distribution of leishmaniasis in
5	201	Cameroon.
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8 9	203	Amendments to protocol
10 11 12	204	Any necessary amendment to the protocol will be registered with PROSPERO and documented
	205	in the final publication, by indicating the date, description and rationale of each amendment.
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15	207	Ethics and dissemination
16 17	208	This proposed study will not require ethical approval as it will be based on already existing
18 19	209	published or unpublished data. The final report of this review will be published in a peer-
20 21	210	reviewed journal, and the outcomes will be used (i) as baseline information to design further
22	211	studies that will help to better refine the epidemiological situation of leishmaniasis in
23 24	212	Cameroon, and (ii) to inform both program managers and policy makers of the situation of
25 26	213	leishmaniasis in the country.
27	214	
28 29	215	Author affiliation
30 31	216	¹ Centre for Research on Filariasis and other Tropical Diseases (CRFilMT), Yaoundé,
32 33	217	Cameroon
34	218	² Molecular Diagnosis Research Group, Biotechnology Centre-University of Yaoundé I (BTC-
35 36	219	UY-I), Yaoundé Cameroon
37 38	220	³ Parasitology and Ecology Laboratory, Department of Animal Biology and Physiology, Faculty
39	221	of Sciences, University of Yaoundé 1, Yaoundé Cameroon
40 41	222	⁴ National Buruli Ulcer, Leprosy, Yaws and Leishmaniasis Control Program, Ministry of Public
42 43	223	Health, Yaoundé, Cameroon
44 45	224	⁵ National Neglected Tropical Diseases Coordination Unit, Ministry of Public Health, Yaounde,
46	225	Cameroon
47 48	226	⁶ Department of Public Health, Faculty of Medicine and Biomedical Sciences, University of Vacundá L Vacundá Cameroon
49 50	227	Yaoundé I, Yaoundé, Cameroon
51	228 229	Author's contributions
52 53	230	All study authors contributed intellectually to the development of the present protocol. LDY,
54 55 56	230	AD and HND prepared the first draft of the manuscript. All authors reviewed and approved this
57 58	232	version of this manuscript. HND and JK are the study guarantors.
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3 4	234	Fu	Inding
5	235	No	o financial support is available for this publication.
6 7	236		
8 9	237	Co	ompeting interests
10 11	238	Th	e authors declare that they have no competing interests.
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20 21	244	Ac	lditional file 1: Text S1. PRISMA-P checklist
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25 26	247	RI	EFERENCES
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55	266		sand flies of the Mokolo leishmaniasis focus, northern Cameroon, with description of new
56 57	267		Sergentomyia taxa (Diptera: Psychodidae). Acta Tropica 2019;194:172-80.
58	268		doi:10.1016/j.actatropica.2019.04.006
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2 3 4 5	269 270	9	Dondji B. Leishmaniasis and Phlebotomus of Cameroon: review of current data. <i>Bulletin de la Societe de pathologie exotique (1990)</i> 2001; 94 :277–9.
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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-Preporting 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.

43 44 45			Reporting Item	Page Number
46 47 48 49	Title			
50 51 52 53 54 55 56 57 58 59 60	Identification	<u>#1a</u>	Identify the report as a protocol of a systematic review	1
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1 2 3	Registration			
4 5		<u>#2</u>	If registered, provide the name of the registry (such as	2
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9 10 11	Authors			
12 13 14	Contact	<u>#3a</u>	Provide name, institutional affiliation, e-mail address of	7
15 16			all protocol authors; provide physical mailing address	
17 18			of corresponding author	
19 20	Contribution	#3b	Describe contributions of protocol authors and identify	7
21 22 23	Contribution	<u></u>	the guarantor of the review	,
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44 45			review	
46 47	Sponsor	#5b	Provide name for the review funder and / or sponsor	n/a; this
48 49 50				publication is not
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55 56	Role of sponsor	<u>#5c</u>	Describe roles of funder(s), sponsor(s), and / or	n/a; this
57 58	or funder		institution(s), if any, in developing the protocol	publication is not
59 60		For pe	eer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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2 3 4 5 6 7 8 9 10 11 12 13 14 15	Introduction			
	Rationale	<u>#6</u>	Describe the rationale for the review in the context of	2
			what is already known	
	Objectives	<u>#7</u>	Provide an explicit statement of the question(s) the	3
			review will address with reference to participants,	
16 17 18			interventions, comparators, and outcomes (PICO)	
19 20 21	Methods			
22 23 24	Eligibility criteria	<u>#8</u>	Specify the study characteristics (such as PICO, study	4
24 25 26			design, setting, time frame) and report characteristics	
27 28			(such as years considered, language, publication	
29 30 31 32 33 34 35 36 37 38 39 40 41			status) to be used as criteria for eligibility for the review	
	Information	<u>#9</u>	Describe all intended information sources (such as	4
	sources		electronic databases, contact with study authors, trial	
			registers or other grey literature sources) with planned	
			dates of coverage	
41 42 43	Search strategy	<u>#10</u>	Present draft of search strategy to be used for at least	4
44 45			one electronic database, including planned limits, such	
46 47			that it could be repeated	
48 49			·	
50 51	Study records -	<u>#11a</u>	Describe the mechanism(s) that will be used to	5
52 53 54	data		manage records and data throughout the review	
55 56	management			
57 58 59 60	Study records -	<mark>#11b</mark> For pe	State the process that will be used for selecting studies er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	5

1	selection process		(such as two independent reviewers) through each	
3 4			phase of the review (that is, screening, eligibility and	
5 6			inclusion in meta-analysis)	
7 8 9	Study records -	<u>#11c</u>	Describe planned method of extracting data from	5
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30	data collection		reports (such as piloting forms, done independently, in	
	process		duplicate), any processes for obtaining and confirming	
			data from investigators	
18	Data items	<u>#12</u>	List and define all variables for which data will be	5
20			sought (such as PICO items, funding sources), any	
21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44			pre-planned data assumptions and simplifications	
	Outcomes and	<u>#13</u>	List and define all outcomes for which data will be	5-6
	prioritization		sought, including prioritization of main and additional	
			outcomes, with rationale	
	Risk of bias in	<u>#14</u>	Describe anticipated methods for assessing risk of bias	6
	individual studies		of individual studies, including whether this will be done	
38			at the outcome or study level, or both; state how this	
39 40 41			information will be used in data synthesis	
43	Data synthesis	<u>#15a</u>	Describe criteria under which study data will be	6
45 46 47			quantitatively synthesised	
48 49	Data synthesis	<u>#15b</u>	If data are appropriate for quantitative synthesis,	6
50 51 52			describe planned summary measures, methods of	
52 53 54			handling data and methods of combining data from	
55 56			studies, including any planned exploration of	
57 58			consistency (such as I2, Kendall's τ)	
59 60		For pe	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

1						
2	Data synthesis	<u>#15c</u>	Describe any proposed additional analyses (such as	n/a; meta-		
3 4 5 6 7 8 9 10 11 12 13			sensitivity or subgroup analyses, meta-regression)	analyses will not		
				be performed.		
	Data synthesis	<u>#15d</u>	If quantitative synthesis is not appropriate, describe the	n/a; meta-		
			type of summary planned	analyses will not		
13 14				be performed.		
15 16						
10 17 18	Meta-bias(es)	<u>#16</u> <	Specify any planned assessment of meta-bias(es)	6		
19 20			(such as publication bias across studies, selective			
21 22			reporting within studies)			
23						
24 25	Confidence in	<u>#17</u>	Describe how the strength of the body of evidence will	6		
26 27	cumulative		be assessed (such as GRADE)			
28 29 30 31 32 33 34 35	evidence					
	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					
36 37	made by the EQUATOR Network in collaboration with Penelope.ai					
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Leishmaniasis in Cameroon: what is known and is done so far? A protocol for systematic review

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-047530.R1
Article Type:	Protocol
Date Submitted by the Author:	16-Mar-2021
Complete List of Authors:	Djune Yemeli, Linda; Centre for Research on Filariasis and other Tropical Diseases (CRFiIMT), Molecular Parasitology and Genetic Epidemiology; University of Yaounde I, Molecular Diagnosis Research Group, Biotechnology Centre Domche, André; Centre for Research on Filariasis and other Tropical Diseases (CRFiIMT), Entomology and Vector-Borne Diseases; University of Yaounde I, Department of Animal Biology and Physiology, Faculty of Science Nana Djeunga, Hugues Clotaire; Centre for Research on Filariasis and other Tropical Diseases (CRFiIMT), Molecular Parasitology and Genetic Epidemiology (MPGE); University of Yaounde I, Department of Animal Biology and Physiology, Faculty of Science Lenou Nanga, Cédric; Centre for Research on Filariasis and other Tropical Diseases (CRFiIMT), Epidemiology and Biostatistics Njih Tabah, Earnest; Ministry of Public Health, National Buruli Ulcer, Leprosy, Yaws and Leishmaniasis Control Program Nko'Ayissi, Georges; Ministry of Public Health, National Neglected Tropical Diseases Coordination Unit Kamgno, Joseph; Centre for Research on Filariasis and other Tropical Diseases (CRFiIMT), Epidemiology and Biostatistics; University of Yaounde I, Department of Public Health, Faculty of Medicine and Biomedical Sciences
Primary Subject Heading :	Infectious diseases
Secondary Subject Heading:	Diagnostics
Keywords:	Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, Tropical medicine < INFECTIOUS DISEASES, Epidemiology < TROPICAL MEDICINE, Geographical mapping < TROPICAL MEDICINE, PARASITOLOGY
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2 3 4	1	Leishmaniasis in Cameroon: what is known and is done so far? A protocol
5 6	2	for systematic review
7	3	Linda Djune-Yemeli ^{1,2} , André Domche ^{1,3} , Hugues C. Nana-Djeunga ^{1,3,*} , Cédric G. Lenou-
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41 42	23	
43 44	24	Abstract
45 46	25	Abstract
47	26	Introduction: First visceral and cutaneous leishmaniasis cases were reported in Cameroon
48 49	27	since more than six decades. However, interest in the disease has decreased over time and data
50 51	28	on its epidemiology across the country are scanty. This systematic review aims to update data
52 53	29	on what is known and done so far on leishmaniasis in Cameroon.
54	30	
55 56	31	Methods and analysis: PubMed/MEDLINE, EMBASE and Web of Science will be searched
57 58	32	from inception onwards. Grey literature will be identified through Google Scholar searches,
59	33	dissertation databases and other relevant documents such as report of the National Control
60	34	Program. Searches will be conducted between January and February 2021. All studies reporting

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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 (JBI) 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.

46 Ethics and dissemination: This study will not require ethical approval as it will be based on 47 already published or unpublished data. The final report of this review will be published in a 48 peer-reviewed journal, and the outcomes will be used (i) as baseline information to design 49 further studies that will help to better refine the epidemiological situation of leishmaniasis in 50 Cameroon, and (ii) to inform both program managers and policy makers of the situation of 51 leishmaniasis in the country.

53 Systematic review registration:

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

- 57 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 drew.
 - A limit of this review could be the few number of published studies given that the diseases is underexplored in Cameroon.
- 66 > There are often reports of suspicious cases with signs and symptoms of these diseases,
 58 67 but no confirmatory testing is carried out. This therefore represents a potential limitation
 60 68 to this study.

71 Introduction

Leishmaniasis is a complex vector-borne zoonotic disease caused by more than 20 species of an obligate intracellular parasitic 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 World Health Organization (WHO) expert committee report, the different forms of leishmaniasis encountered in the old world are (i) visceral leishmaniasis (VL also known as kala-azar, caused by L. donovani and L. infantum), (ii) cutaneous leishmaniasis (CL, most frequently caused by L. tropica, L. major, and L. aethiopica), (iii) mucosal leishmaniasis (ML, that can be caused by any species), (iv) diffused cutaneous leishmaniasis (DCL, caused by L. aethiopica) and (v) post Kala-azar dermal leishmaniasis (PKDL, 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 sandflies 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 the 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 the WHO as endemic to CL but with no available data on the number of cases, and appears among countries with previous 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

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3 4	102	leishmaniasis country profile established by WHO in 2012 [12] no update has been made to
5	103	allow the establishment of new management strategies against this group of diseases. There is
6 7	104	therefore an urgent need to perform a situation analysis of leishmaniasis in Cameroon.
8 9	105	
10	106	Objective
11 12	107	This systematic review aims to document the infection rate, circulating species, vectors and
13 14 15 16	108	reservoirs of leishmaniasis as well as data on control/management strategies in Cameroon. This
	109	will help updating the situation of leishmaniasis in Cameroon, and ultimately helps
17	110	defining/refining control strategies and reinforcing advocacy.
18 19	111	
20 21	112	Review questions
22 23	113	By documenting data on what is known and done so far on leishmaniasis in Cameroon, this
24	114	review will help answering the following questions:
25 26	115	1. What are the circulating species and the clinical presentations?
27 28	116	2. What are the vectors responsible of the transmission of leishmaniasis?
29	117	3. What are the non-human reservoirs of leishmaniasis?
30 31 32 33 34 35	118	4. How is the diagnostic of leishmaniasis conducted?
	119	5. What is the level of endemicity and distribution of leishmaniasis?
	120	6. How is the control of leishmaniasis organized?
36	121	
37 38	122	
39 40 41	123	Methods and analysis
42	124	This systematic review protocol was written in accordance with reporting guidance provided
43 44	125	by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols
45 46	126	(PRISMA-P) statement [13] (see PRISMA-P checklist as Supplementary file 1). The
47 48	127	registration process of the protocol with the Prospective Register of Systematic reviews
49	128	(PROSPERO) database is done (registration number: CRD42020211864; registration process
50 51	129	ongoing in PROSPERO). The review process will be conducted between January and February
52 53	130	2021.
54 55	131	
56	132	Eligibility criteria
57 58	133	There will be no restriction regarding the date of the study. Any type of study, either published
59 60	134	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 (NTDs) 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 program 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 "Cameroun" OR "Cameroon" (Supplementary 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-build 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

169 comparing the title or various combinations of the author(s), year, secondary title, volume,
170 issue, and page numbers. In the second instance, the records of suspected duplicates will be
171 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) authors 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, (o) geographical coordinates (latitude, longitude and altitude).

24 181

182 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 (i) as basis to design studies that will help to better refine the epidemiological situation of leishmaniasis in Cameroon, and (ii) to inform both program managers and policy makers of the situation of leishmaniasis in the country.

43 192

Data analysis

Data will be recorded as prevalence with 95% confidence intervals [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 thematic map of the distribution of leishmaniasis in Cameroon using a geographical information system (GIS) software (ArcGIS, version 10.2, ESRI Inc.)

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 (JBI) systematic review methods manual [15]. We will also not include studies with aggregated data by community/village.

207 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.

219 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 thematic map of the distribution of leishmaniasis in
Cameroon.

225 Patient and Public Involvement

226 No patient involved.

228 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.

2		
3 4	233	Ethics and dissemination
5	234	This proposed study will not require ethical approval as it will be based on already existing
6 7	235	published or unpublished data. The final report of this review will be published in a peer-
8 9	236	reviewed journal, and the outcomes will be used (i) as baseline information to design further
10	237	studies that will help to better refine the epidemiological situation of leishmaniasis in
11 12	238	Cameroon, and (ii) to inform both program managers and policy makers of the situation of
13 14	239	leishmaniasis in the country.
15	240	
16 17	241	Author's contributions
18 19	242	LDY, AD, HCND, CGLN, ENT, GBN and JK contributed intellectually to the development of
20 21	243	the present protocol. LDY, AD and HCND prepared the first draft of the manuscript. LDY, AD,
22	244	HCND, CGLN, ENT, GBN and JK reviewed and approved the final version of the manuscript.
23 24	245	HCND and JK are the study guarantors.
25 26	246	
20 27 28	247	Funding
29	248	Not applicable.
30 31	249	
32 33	250	Competing interests
34 35	251	The authors declare that they have no competing interests.
36	252	
37 38	253	Word count
39 40	254	1725
41 42	255	
43 44	256	
45	257	Additional files
46 47	258	Supplementary file 1: Text S1. PRISMA-P checklist
48 49	259	Supplementary file 2: Table S1. Example of search strategy used in PubMed/Medline
50	260	
51 52	261	
53 54	262	References
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Reporting checklist for protocol of a systematic review.

Based on the PRISMA-P guidelines.

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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.

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32 33			Reporting Item	Page Number
34 35	Title			
36 37 38	Identification	<u>#1a</u>	Identify the report as a protocol of a systematic review	1
39 40 41 42 43	Update	<u>#1b</u>	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.
44 45 46 47 48 49	Registration	<u>#2</u>	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
50 51	Authors			
52 53 54 55 56 57	Contact	<u>#3a</u>	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
57 58 59 60	Contribution	<u>#3b</u> For pee	Describe contributions of protocol authors and identify er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	8

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1			the guarantor of the review	
2	Amendments			
3 4 5 6 7 8 9 10	Amenaments			
		<u>#4</u>	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
11 12	Support			
13 14 15 16	Sources	<u>#5a</u>	Indicate sources of financial or other support for the review	8
17 18 19 20 21 22	Sponsor	<u>#5b</u>	Provide name for the review funder and / or sponsor	n/a; this publication is not funded.
22 23 24 25 26 27	Role of sponsor or funder	<u>#5c</u>	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	n/a; this publication is not funded.
28 29	Introduction			
30 31 32 33 34 35 36 37 38 39	Rationale	<u>#6</u>	Describe the rationale for the review in the context of what is already known	3
	Objectives	<u>#7</u>	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
40	Methods			
41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56	Eligibility criteria	<u>#8</u>	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	<u>#9</u>	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
57 58	Search strategy	<u>#10</u>	Present draft of search strategy to be used for at least	5
59 60		For pee	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

Page	13	of	14	
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1 2 3			one electronic database, including planned limits, such that it could be repeated	
4 5 6	Study records - data management	<u>#11a</u>	Describe the mechanism(s) that will be used to manage records and data throughout the review	5-6
7 8 9 10 11 12 13	Study records - selection process	<u>#11b</u>	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
14 15 16 17 18 19 20	Study records - data collection process	<u>#11c</u>	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
21 22 23 24 25	Data items	<u>#12</u>	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
26 27 28 29 30 31	Outcomes and prioritization	<u>#13</u>	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
32 33 34 35 36 37	Risk of bias in individual studies	<u>#14</u>	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
38 39 40 41	Data synthesis	<u>#15a</u>	Describe criteria under which study data will be quantitatively synthesised	6
42 43 44 45 46 47 48 49	Data synthesis	<u>#15b</u>	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 I2, Kendall's T)	6
50 51 52 53 54 55	Data synthesis	<u>#15c</u>	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a; meta- analyses will not be performed.
56 57 58 59	Data synthesis	<u>#15d</u>	If quantitative synthesis is not appropriate, describe the type of summary planned	n/a; meta- analyses will not
60		For pee	r review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es)	7
		(such as publication bias across studies, selective	
		reporting within studies)	

#17 Describe how the strength of the body of evidence will be assessed (such as GRADE)

evidence

Confidence in

cumulative

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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])