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RECEIVED 16 June 2024

ACCEPTED 29 July 2024

PUBLISHED 23 August 2024

CITATION

Shirley H, Orriols AM, Hogan D,
Chimfwembe K, Bwalya A, Sibbuku K,
Lardizabal J, Tillotson S, Grifferty G,
Coombs PE and Wamai R (2024)
A scoping review of lymphatic
filariasis research in Zambia.
Front. Trop. Dis 5:1449719.
doi: 10.3389/ftd.2024.1449719

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A scoping review of lymphatic filariasis research in Zambia

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Lymphatic filariasis (LF) is a neglected tropical disease caused by microfilariae of the *Wuchereria* and *Brugia* genus and spread by mosquitoes. Chronic infection and associated morbidity leads to poor psychosocial and economic outcomes. LF elimination programs have been underway in many countries, including Zambia, a country in Sub-Saharan Africa where LF has long been endemic. Zambia has made great progress in moving towards elimination through a multipronged strategy involving mass drug administration, regular surveillance, and morbidity management and disease prevention. This scoping review aims to capture the breadth of literature published on LF in Zambia to support further research into the disease that may support ongoing elimination efforts, research gaps, and funding opportunities. PRISMA-ScR and JBI scoping review guidelines were used in the design and conduct of this scoping review, leading to 475 full-text articles screened and included in data analysis, with analyzed information including publication year, journal, study theme, study type, citation number, and funding sources. The resulting screen found many articles focused on disease epidemiology in Zambia, but less research on vectors, treatment and prevention. Therefore, we conclude there may be opportunities to better understand this disease in the Zambian context through filling in these research gaps.

Systematic review registration: <https://doi.org/10.17605/OSF.IO/7W62G>

KEYWORDS

lymphatic filariasis, neglected tropical diseases (NTDs), sub-Saharan Africa, *Wuchereria bancrofti*-parasite, vector-borne disease (VBD), mosquito borne disease

Introduction

In 1997, lymphatic filariasis (LF) became one of a handful of neglected tropical diseases (NTDs) targeted for elimination (1, 2). The Global Programme to End LF (GPELF) was initiated in 2000 with the goal of eliminating LF by 2020. While significant progress has been made over the subsequent two decades, in 2019 over 50 million people were infected with LF among the 793 million people still at risk within 72 endemic countries (3–5). Elimination is achieved and validated through a series of steps, including mapping surveys, mass drug administration (MDA), and transmission assessment surveys (TAS) (5). Bangladesh and Lao People's Democratic Republic most recently achieved elimination in 2023 following completion of multiple rounds of MDA and confirmation that the disease prevalence is below transmission thresholds (6, 7). Globally, LF causes the loss of an estimated 1.6 million disability adjusted life years (DALYs) (8).

LF is spread when *Anopheles* and *Culex* mosquitoes infected with *Wuchereria bancrofti*, *Brugia malayi*, or *B. timori filariae* bite a human (9). During this blood meal, the infected mosquitoes introduce third-stage filarial larvae into the human host's skin via the bite site. These larvae ultimately develop into adults that reside in the lymphatic system, and themselves produce sheathed microfilariae that enter the peripheral circulation. A mosquito biting an infected human host then ingests the microfilariae during a blood meal, that then matures to become an L3 larvae in the mosquito and is transmitted to another human during that mosquito's next blood meal (10). The migration of filariae to the host's lymphatic vessels results in dysfunction that can present clinically with lymphedema and hydrocele (11). Acute attacks, also referred to as secondary bacterial infections, may also occur from insufficient daily hygiene practices related to limb washing and drying and ultimately drive disease progression (12, 13). The clinical consequences of infection can be stigmatizing, resulting in social, psychological, and economic consequences beyond the health effects (14). Treatment consists of a package of morbidity management and disability prevention, which consists of antimicrobial agents for the primary filarial infection and secondary acute adenolymphangitis, topical treatments and hygiene for lymphedema, and surgical care for hydrocele (15). Antifilarial agents are selected based on co-endemicity of onchocerciasis and loiasis. In locales where onchocerciasis and loiasis are not endemic, triple therapy consisting of ivermectin, diethylcarbamazine (DEC), and albendazole is recommended (16). This triple therapy has been shown to be effective in clearing microfilariae from the blood stream (17). Where onchocerciasis is present, DEC is contraindicated due to a severe inflammatory effect, called the Mazzotti reaction (18). Ivermectin is associated with severe encephalopathy in patients with high serum Loa loa burden as is therefore avoided in regions known to be endemic with loiasis (19).

LF imparts a significant burden of disease in Africa, where the disease remains endemic in 34 countries placing an estimated 288 million people at risk of infection (5). A study estimated the prevalence of LF in Africa to be 10 million in 2018, down from 74 million in 2000 (3) While likely underestimates, over 160

thousand lymphedema patients and over 147 thousand hydrocele patients were reported to the World Health Organization (WHO) by endemic countries in Africa in 2022 (5). While almost all endemic countries have made progress towards reducing the burden of LF, Malawi and Togo were the first in Sub-Saharan Africa (SSA) to be validated as having eliminated the disease (5). Several other countries, including Zambia, have completed the necessary number of rounds of MDA, and have transitioned into an impact survey stage to assess for any evidence of ongoing disease transmission.

Zambia, a landlocked country in SSA, has made significant progress towards reducing the burden of LF (20). The country is made up of 10 provinces and 116 districts and is home to over 19 million people (21, 22). LF is endemic in 96 of those 116 districts (23). LF in Zambia was first noted in the literature by Buckley in 1946 (24), while the first definitive locally transmitted cases were described by Hira in the 1970s (25, 26). In 2003, following the establishment of the GPELF, the government of Zambia launched a program to eliminate LF. Epidemiological mapping of the disease was completed in 2011, which found an average prevalence of 7.4% across the country (27). Five rounds of MDA have since been conducted in Zambia, and despite funding challenges, the country now awaits the results of TAS to determine if MDAs are no longer needed (5). Both the challenges and successes along the road to elimination may be useful to inform similar efforts in neighboring countries (20). As Zambia steadily moves from active MDA towards disease surveillance and, eventually, elimination, we conducted a scoping review of the literature on LF in Zambia to identify general research gaps as to guide further research and elimination efforts.

Methods

Article screening

We conducted a scoping review of the existing literature on LF in Zambia. The full protocol is published here (28). PRISMA-Scoping Review (ScR) and Joanna Briggs Institute (JBI) scoping review guidelines were used in the design and conduct of this scoping review (29–31) The PRISMA Scoping Review checklist can be found in Table 1. In brief, a search was conducted with the goal of collecting articles that may include a discussion of LF in Zambia. The search strings used for each database are detailed in Table 2. Following de-duplication, 6363 primary records were uploaded into Rayyan (32). Primary and secondary inclusion criteria and exclusion criteria were formulated and are described below. The overall screening strategy across title-abstract and full-text screens is visualized in Figure 1.

Prior to initiation of the screening phase, a test batch of 20 articles was used to train all screeners. Screening was not initiated until reviewers achieved >90% concordance with the results of a senior author (HS) on the same set of 20 articles. The title-abstract screen was conducted by 8 reviewers (HS, AO, DH, KC, AB, KS, JL, ST). Each article was analyzed by two independent reviewers, and a third senior author (HS, AO) resolved any disagreements. Articles were screened-in if they explicitly mention lymphatic filariasis in

TABLE 1 PRISMA-Scoping Review (ScR) checklist.

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	Title (page 1)
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	Pg. 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	Pg. 2
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	Pg. 2
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	Pg. 2, Ref. 28
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	Pg. 2, 4
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	Pg. 2, 4; Table 2
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Pg. 2, 4; Table 2
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	Pg. 2, 4
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	Pg. 4
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Pg. 4
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Pg. 4
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	Pg. 4
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Pg. 5-6
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Pg. 5-6, Table 5-7
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not done
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Pg. 5-6, Table 3-8
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	Pg. 5-6, Table 5-8

(Continued)

TABLE 1 Continued

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	Pg. 6, 7, 13
Limitations	20	Discuss the limitations of the scoping review process.	Pg. 6, 7, 13
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	Pg. 14
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	Pg. 14

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.

JB1, Joanna Briggs Institute; PRISMA-ScR, Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where sources of evidence (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with information sources (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018;169:467–473. doi: 10.7326/M18-0850 (29).

the Zambian context in their title or abstract or if they mentioned categories of which LF or Zambia were a part (i.e. NTDs, Sub-Saharan Africa, etc.) and there was a reasonable possibility that the full text would include a discussion of LF in Zambia, specifically. Articles were excluded if not in English.

A total of 513 articles were screened in from the title-abstract phase while 5850 articles were excluded. Of those 513, the full text of 38 articles was unretrievable. The remaining 475 full text articles were then screened by 6 reviewers (HS, AO, DH, AB, JL, ST). At this stage, articles were included in the next stage of analysis if their full text included a thorough discussion of LF in Zambia. Thorough was operationalized for LF to mean "containing LF-related discussion or data, including incidence, prevalence, GIS data, etc." Thorough was operationalized for Zambia to mean "containing discussion or data that is specific to Zambia or includes Zambia among a set of data or discussions of multiple countries/contexts". Additionally, included articles must discuss LF in Zambia specifically; separate thorough discussions of each subject were not sufficient. Exclusion criteria included articles that were unretrievable, were not published in peer-reviewed journals or by government and international regulatory bodies, were published as part of conference proceedings or poster abstracts or were published as part of a book. Reference lists from screened-in articles were reviewed and cross-referenced with the list of articles acquired from the screening process when the title was suggestive of possible relevance. Articles that were absent from the list of screened articles but were deemed possibly relevant were screened using the same criteria for possible inclusion in the final set of articles. Expert opinion was sought on the inclusion of official government literature, as many of these articles are not indexed in searchable databases.

For relevant articles that have been published as part of a series of regular updates, for example the annual Global Programme to Eliminate LF (GPELF) updates published in the Bulletin of the WHO, only the most recent was included to avoid diluting results with similar or equivalent articles.

Data extraction

Article information, including publication year, journal, study theme, study type, citation number, and funding sources, was extracted into Microsoft Excel for further analysis. Study theme describes the article's core focus as it relates to LF, for example, LF epidemiology or LF health policy. Study type describes the methodology used to carry out the study, such as secondary or clinical research. The study themes included general epidemiology, diagnostics, treatment, health systems/policy, vectors, and co-infections, as well as a general topics category aimed at articles that touch on multiple themes equally or that focused on themes that were not well captured by the existing framework. Study types included clinical research, epidemiological research, secondary research, and institutional or government reports. A codebook was adapted from Grifferty et al. to capture the expected study themes and types relevant to LF research (33). General epidemiology was defined as "studies that aimed to describe the prevalence, distribution, or other epidemiological indicators of disease." The study type, epidemiological research, was defined as "studies that collected and/or independently analyzed epidemiological data." Two authors (HS, AO) independently assigned labels to each article then collaboratively reviewed and resolved any disagreements. These data were analyzed by two

TABLE 2 Search strings, results, date of search and filters used for 7 databases for article retrieval.

PubMed	("Elephantiasis, Filarial" [Mesh] OR "Lymphatic filariasis" OR "neglected tropical diseases" OR "Wuchereria bancrofti" OR "elephantiasis" OR "Lymphedema"[Mesh : NoExp] OR "lymphoedema" OR "lymphedema" OR "Testicular Hydrocele" [Mesh] OR "hydrocele" OR "nchofu" OR "nthumbo" OR "pholo") AND ("Zambia" [Mesh] OR "Zambia" OR "Zambian" OR "Africa South of the Sahara" [Mesh] OR "sub-Saharan Africa" OR "Southern Africa" OR "Africa") Results: 2265 Date searched: 2/27/23 Filters: None
Embase	('Lymphatic filariasis'/exp OR 'Lymphatic filariasis' OR 'neglected tropical diseases' OR 'Wuchereria bancrofti'/exp OR 'Wuchereria bancrofti' OR 'elephantiasis' OR 'lymphedema'/exp OR 'lymphoedema' OR 'lymphedema' OR 'hydrocele'/exp OR 'hydrocele' OR 'nchofu' OR 'nthumbo' OR 'pholo') AND ('Zambia'/exp OR 'Zambia' OR 'Zambian' OR 'Africa south of the Sahara'/exp OR 'sub-Saharan Africa' OR 'Southern Africa' OR 'Africa') AND ('article'/it OR 'article in press'/it OR 'preprint'/it OR 'review'/it) Results: 4203 Date searched: 2/27/23 Filters: None
Web of Science	("Lymphatic filariasis" OR "neglected tropical diseases" OR "Wuchereria bancrofti" OR "elephantiasis" OR "lymphedema" OR "lymphoedema" OR "hydrocele" OR "nchofu" OR "nthumbo" OR "pholo") AND ("Zambia" OR "Zambian" OR "Africa South of the Sahara" OR "sub-Saharan Africa" OR "Southern Africa" OR "Africa") Results: 4376 Date searched: 2/27/23 Filters: Document Type: Exclude: Meeting, Editorial Material, Letter, Biography, Books, News, Patent
Cochrane CENTRAL	#1 MeSH descriptor: [Elephantiasis, Filarial] explode all trees #2 MeSH descriptor: [Lymphedema] this term only #3 MeSH descriptor: [Testicular Hydrocele] explode all trees #4 "Lymphatic filariasis" OR "neglected tropical diseases" OR "Wuchereria bancrofti" OR "elephantiasis" OR "lymphoedema" OR "lymphedema" OR "hydrocele" OR "nchofu" OR "nthumbo" OR "pholo" #5 MeSH descriptor: [Zambia] explode all trees #6 MeSH descriptor: [Africa South of the Sahara] explode all trees #7 "Zambia" OR "Zambian" OR "sub-Saharan Africa" OR "Southern Africa" OR "Africa" #8 #1 OR #2 OR #3 OR #4 #9 #5 OR #6 OR #7 #10 #8 AND #9 Results: 191 Date searched: 2/27/23 Filters: None
WHO's Global Index Medicus	("Lymphatic filariasis" OR "neglected tropical diseases" OR "Wuchereria bancrofti" OR "elephantiasis" OR "lymphedema" OR "lymphoedema" OR "hydrocele" OR "nchofu" OR "nthumbo" OR "pholo") AND ("Zambia" OR "Zambian" OR "Africa South of the Sahara" OR "sub-Saharan Africa" OR "Southern Africa" OR "Africa") Results: 35 Date searched: 2/27/23 Filters: None

(Continued)

TABLE 2 Continued

WHO's ICTRP	Lymphatic filariasis = Condition Recruiting country = Zambia Recruitment status = All Results: 0 Date searched: 2/27/23
ClinicalTrials.gov	Condition or disease = lymphatic filariasis Locations - Country = Zambia Results: 0 Date searched: 2/27/23
Total Results	11,070 prior to deduplication 6,363 after deduplication

A total of 11,070 articles were retrieved, with 6,363 articles following de-duplication.

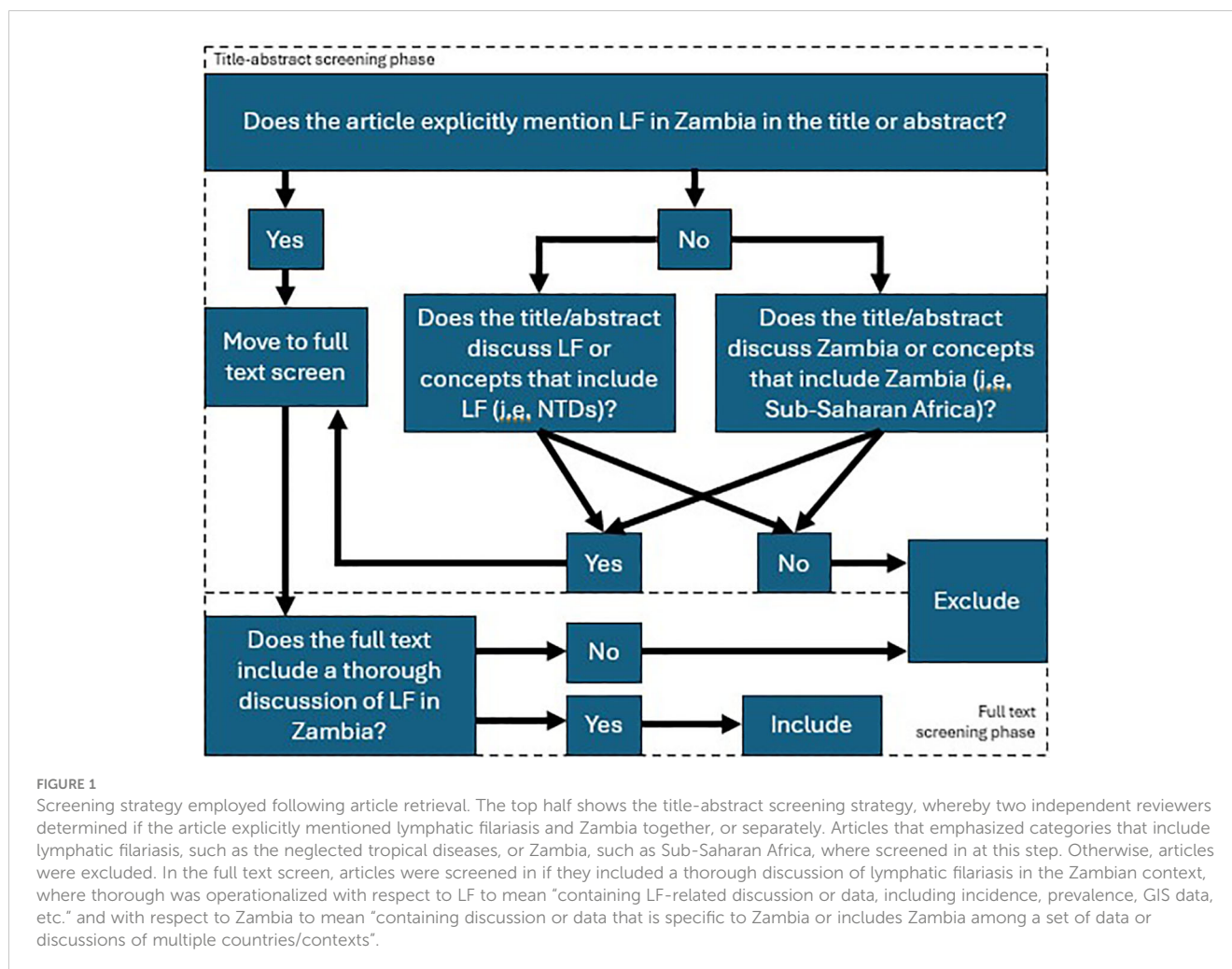
authors (HS, GG) to generate summary statistics and data visualizations. Citation numbers were drawn from Google Scholar citation estimates.

Results

From an initial search that obtained over 6,000 unique articles, the yield following the screening process was approximately 0.6%, or 40 articles. An additional 4 articles were included for analysis, 2 government documents and 2 screened-in article references, for a total of 44 articles. Figure 2 shows the PRISMA flow diagram of this scoping review, which describes the number of articles at each step of the review process (34). The final article list is included in Table 3.

Generally, there has been a slight increase in the number of articles published about LF in Zambia over time; with most articles being published after 2010 and relatively few before that point. Figure 3 depicts the number and proportion of articles published per half decade, with the greatest share being published in the period between 2015-2019.

The most frequently noted study theme was general epidemiology (n = 16; 37%) followed by health policy/systems (n = 9; 21%) (Figure 4). The next most common study themes were general topics (n = 8; 18%), vectors (n = 5; 11%), and diagnostics (n = 4; 9%), respectively. There was limited research coverage of co-infections with LF and diagnostics in Zambia, each with only one article, 2% of the total number of articles. There were no articles focused on disease prevention or pathophysiology. The most frequent study type was secondary research (n = 19; 43%) followed closely by epidemiological research (n = 17; 39%). There were relatively few clinical research articles published on LF in Zambia (n=4; 9%). There were no basic science articles found during this review. One article by Shawa et al., 2013 was found to fit into two thematic categories, general epidemiology, and vectors. Researchers took community serum samples to assess anti-filarial antibody and filarial antigen seropositivity and conduct vector assessments with light traps. On reviewer discussion, we determined that this paper would be given its own mixed category of general epidemiology/vectors, rather than be double counted in each category. Table 4 depicts the study theme per half decade, highlighting trends in article focus over time. Study theme



by study type and study type by decade can be found in [Tables 5, 6](#), respectively, and in addition to [Figure 4](#).

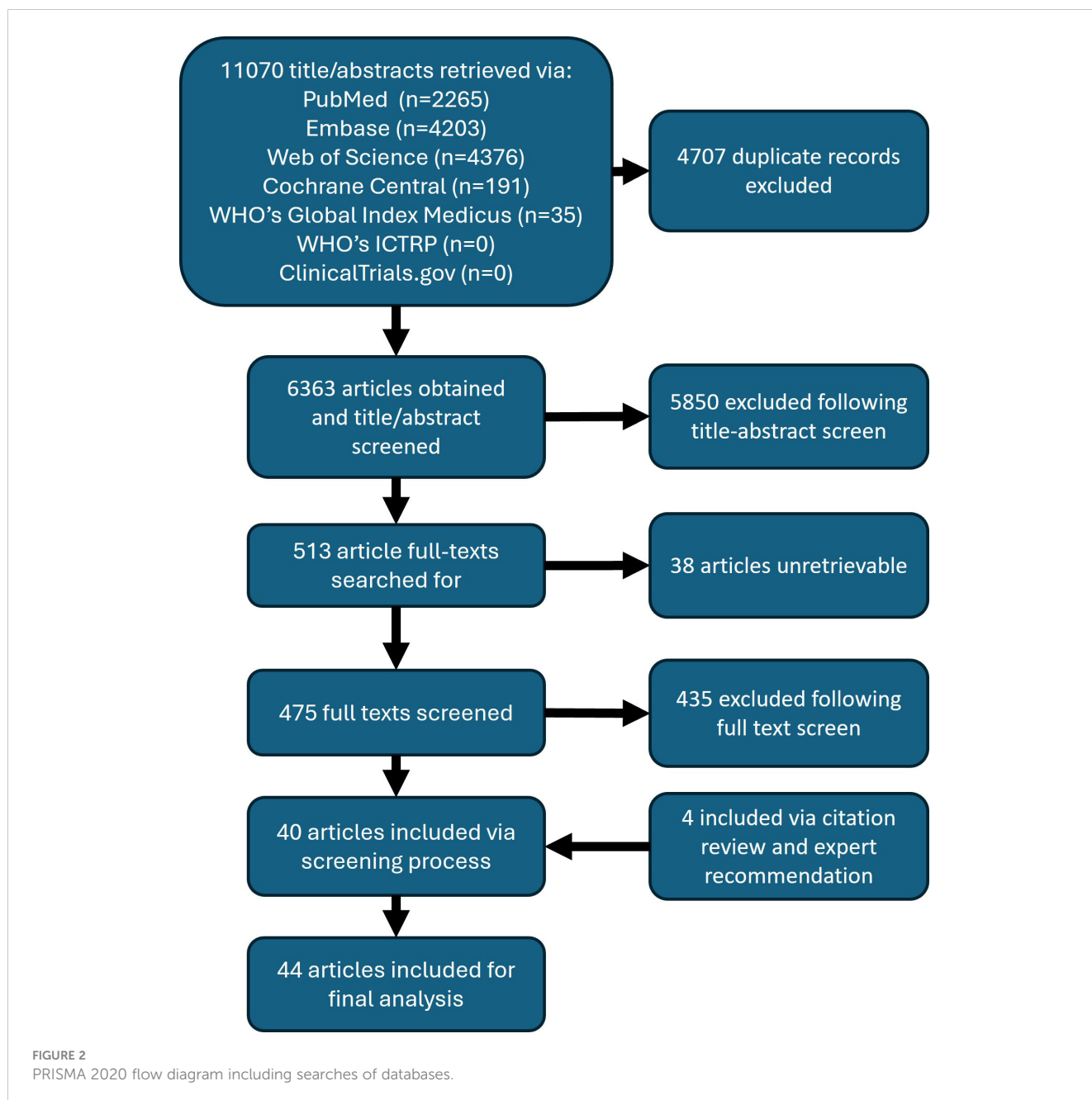
The full list of funding organizations acknowledged by articles are detailed in [Table 7](#). The Bill and Melinda Gates Foundation provided funding to the greatest number of articles ($n = 9$; 20%). The Department of International Development, United Kingdom, and the Wellcome Trust contributed to the second greatest number of articles, at 4 each. No funders were reported in 16 articles, which is the largest collection of articles included for final analysis. In total, 24 unique funding organizations were identified across 44 articles.

In reviewing the most cited articles that include a thorough discussion of LF in Zambia, which are detailed in [Table 8](#), the 2015 Global Burden of Disease Study has the greatest number of citing articles at 5221. This is followed by "Re-assessing the global prevalence and distribution of lymphatic filariasis," at 637. The most cited article that focuses exclusively on LF in Zambia was "Mapping the geographical distribution of lymphatic filariasis in Zambia," at 29 citing articles, and was the 26th most cited article included in the analysis. Articles were published in 26 unique peer-reviewed journals. Only 6 journals published more than one article on LF in Zambia. The journals in which articles were most frequently published were PLoS NTD ($n = 7$; 16%), Parasites & Vectors ($n = 5$; 11%), and Trends in Parasitology ($n = 3$; 6.8%).

Discussion

This article is, to our knowledge, the first scoping review of LF in Zambia, or of LF research generally. Our goal was to capture and describe the body of literature at this intersection as completely as possible. We found that most studies focused on the epidemiology of LF as a theme and used secondary research methodologies, such as systematic reviews. There were no articles that fit the study themes of prevention or pathophysiology or the study type of basic science research. The absence of prevention focused articles was especially surprising, and potentially a reflection of limitations inherent in this study. Prevention as a research focus may be captured by those articles that were labeled as vector studies, given research into host-vector interactions may be targeted at preventing future infections.

A significant number of studies were published with maps of the distribution and prevalence of LF globally or in Africa, which included information on Zambia, but beyond these maps, did not further conversation around LF in Zambia specifically. These studies were included in our analysis as they met our inclusion criteria and definition for a 'thorough' discussion of LF in Zambia. The greatest number of studies were published in the 2010s, which corresponds to the completion of the initial LF mapping studies



conducted prior to the initiation of MDAs (27). Prior to this, there was relatively little knowledge about the disease in Zambia published in the literature. Many of the subsequent epidemiological studies draw from the paper published by Mwase et al. which outlines the results of those initial surveys (27). Those papers that referenced epidemiological information about LF in Zambia but did not perform a primary analysis of previously collected epidemiological data, were considered secondary research for the purposes of this scoping review. There were 8 articles fitting this description. There is another subset of 9 articles that gathered primary epidemiological data or independently analyzed existing data, for example (35, 36). Information about the epidemiology of LF in Zambia is helpful in determining where MDAs are necessary and continued monitoring needs to occur.

There were relatively few studies that focused on the vectors of LF in Zambia. However, the *Anopheles* mosquito that spreads the disease similarly spreads malaria. There were a number of studies screened out that focused on the vectors of malaria, but made no explicit mention of lymphatic filariasis, while a much smaller number did reference their co-endemicity in the region (37). Malaria researchers may consider the impact of their work on *Anopheles* mosquitoes on LF, thereby allowing the scientific community to better understand how to control both diseases, perhaps even synergistically.

There was only one study that focused on co-infections with LF (38). Given LF co-endemicity has important implications for selecting therapeutics and that infrastructure needed to deploy LF programming could be coopted for other disease target, further research into co-endemic infections could be useful in Zambia. Additionally, there were

TABLE 3 Final list of articles following full text screening.

Title	Publication Date	Journal	Study theme	Study type	Citations	Funder(s)
Mapping the geographical distribution of lymphatic filariasis in Zambia	2010-2014	PLoS NTD	General Epidemiology	Epidemiological Research	29	Ministry of Health, Zambia; WHO-Afro' Liverpool Centre for Neglected Tropical diseases' Danida Research Council, Denmark
Significant decline in lymphatic filariasis associated with nationwide scale-up of insecticide-treated nets in Zambia	2015-2019	Parasite Epidemiology and Control	Vectors	Epidemiological Research	27	Department of International Development,UK
Lymphatic filariasis in Luangwa District, South-East Zambia	2010-2014	Parasites and Vectors	General Epidemiology; Vectors	Epidemiological Research	22	Danida Research Council. Denmark
How community engagement strategies shape participation in mass drug administration programmes for lymphatic filariasis: The case of Luangwa District, Zambia	2015-2019	Plos NTD	Health Systems/ Policy	Clinical Research	26	None reported
Predicting the current and future potential distributions of lymphatic filariasis in Africa using maximum entropy ecological niche modeling	2010-2014	PLoS One	General Epidemiology	Epidemiological Research	153	Natural Environment Research Council, UK; Grantham Institute for Climate Change at Imperial College London; NIH, USA
Mapping, bayesian geostatistical analysis and spatial prediction of lymphatic filariasis prevalence in Africa	2010-2014	PLoS ONE	General Epidemiology	Epidemiological Research	53	Natural Environment Research Council, UK; Grantham Institute for Climate Change at Imperial College London; NIH
Mapping and monitoring for a lymphatic filariasis elimination program: a systematic review	2015-2019	Research and Reports in Tropical Medicine	General Epidemiology	Secondary Research	18	None reported
Community views on mass drug administration for filariasis: a qualitative evidence synthesis	2020+	Cochrane Database of Systemic Reviews	Health Systems/Policy	Secondary Research	7	Liverpool School of Tropical Medicine, UK
Unlocking Trust in Community Health Systems: Lessons From the Lymphatic Filariasis Morbidity Management and Disability Prevention Pilot Project in Luangwa District, Zambia	2020+	International Journal of Health Policy and Management	Health Systems/Policy	Clinical Research	8	Coalition for Operational Research on Neglected Tropical Diseases (COR-NTD)
The Current Status of Molecular Xenomonitoring for Lymphatic Filariasis and Onchocerciasis	2015-2019	Trends in Parasitology	Vectors	Secondary Research	35	None reported
Can Lymphatic Filariasis Be Eliminated by 2020?	2015-2019	Trends in Parasitology	General Topics	Secondary Research	54	None reported
The distribution of human filariasis throughout the world. Part III. Africa	1975-1979	Tropical Diseases Bulletin	General Epidemiology	Secondary Research	86	None reported
BANCROFTIAN FILARIASIS AN AUTOCHTHONOUS CASE IN ZAMBIA	1975-1979	Medical Journal of Zambia	Diagnostics	Clinical Research	3	None reported
What Is Needed to Eradicate Lymphatic Filariasis? A Model-Based Assessment on the Impact of Scaling Up Mass Drug Administration Programs	2015-2019	PLoS NTD	Treatment	Epidemiological Research	34	Eradication Investment Case of Onchocerciasis, Lymphatic Filariasis, and Human African Trypanosomiasis; Bill and Melinda Gates Foundation

(Continued)

TABLE 3 Continued

Title	Publication Date	Journal	Study theme	Study type	Citations	Funder(s)
Can malaria vector control accelerate the interruption of lymphatic filariasis transmission in Africa; capturing a window of opportunity?	2010-2014	Parasites and Vectors	Vectors	Epidemiological Research	76	Department of International Development, UK; GlaxoSmithKline
Health beliefs and health seeking behavior towards lymphatic filariasis morbidity management and disability prevention services in luangwa district, zambia: Community and provider perspectives	2020+	PLoS NTD	Health Systems/Policy	Clinical Research	13	Coalition for Operational Research on Neglected Tropical Diseases (COR-NTD)
Re-assessing the global prevalence and distribution of lymphatic filariasis	1995-1999	Parasitology	General Epidemiology	Secondary Research	637	Wellcome Trust
Continental-scale, data-driven predictive assessment of eliminating the vector-borne disease, lymphatic filariasis, in sub-Saharan Africa by 2020	2015-2019	BMC Medicine	General Epidemiology	Epidemiological Research	29	Eck Institute for Global Health, Notre Dame' Office of the vice President for Research, Notre Dame; Bill and Melinda gates Foundation
Sustainable Surveillance of Neglected Tropical Diseases for the Post-Elimination Era	2020+	Clinical Infectious Diseases	General Epidemiology	Secondary Research	18	Bill and Melinda Gates Foundation
Filariasis in Africa—treatment challenges and prospects	2010-2014	Clinical Microbiology and Infection	Treatment	Secondary Research	164	EU FP6; EU FP7; Volkswagen Foundation; DFG; DAAD' A-WOL; DOLF
Disease Eradication	2010-2014	New England Journal of Medicine	General Topics	Secondary Research	155	None reported
Complex emergencies and the control and elimination of neglected tropical diseases in Africa: developing a practical approach for implementing safe and effective mapping and intervention strategies	2020+	Conflict and Health	Health Systems/Policy	Epidemiological Research	12	None reported
The monetary value of human lives lost due to neglected tropical diseases in Africa	2015-2019	Infectious Diseases of Poverty	General Topics	Epidemiological Research	28	None reported
Mapping and estimating the population at risk from lymphatic filariasis in Africa	2000-2004	Transactions of the Royal Society of Tropical Medicine and Hygiene	General Epidemiology	Secondary Research	121	None reported
A research agenda for helminth diseases of humans: the problem of helminthiasis	2010-2014	PLoS NTD	General Topics	Secondary Research	410	Special Programme for Research and Training in Tropical Diseases;
Modeling the distribution and transmission intensity of lymphatic filariasis in sub-Saharan Africa prior to scaling up interventions: integrated use of geostatistical and mathematical modeling	2015-2019	Parasites and Vectors	General Epidemiology	Secondary Research	72	Coalition for Operational Research on the NTDs (COR-NTD); The Wellcome Trust; Bill and Melinda Gates Foundation, GlaxoSmithKline, Department for International Development (UK)
Lymphatic filariasis	2000-2004	WHO Weekly Epidemiological Record	General Topics	Institutional Report	81	None reported

(Continued)

TABLE 3 Continued

Title	Publication Date	Journal	Study theme	Study type	Citations	Funder(s)
Global program to eliminate lymphatic filariasis: progress report, 2014	2015-2019	WHO Weekly Epidemiological Record	General Topics	Institutional Report	5	None reported
The global distribution and transmission limits of lymphatic filariasis: past and present	2010-2014	Parasites and Vectors	General Epidemiology	Secondary Research	150	Bill and Melinda Gates Foundation; Department for International Development (UK); Wellcome Trust
An Operational Framework for Insecticide Resistance Management Planning	2015-2019	Emerging Infectious Diseases	Vectors	Secondary Research	43	President's Malaria Initiative
African regional progress and status of the programme to eliminate lymphatic filariasis: 2000-2020	2020+	International Health	General Topics	Secondary Research	16	Mectizan Donation Program; Global Alliance for LF Elimination; Wellcome Trust
The global distribution of lymphatic filariasis, 2000–18: a geospatial analysis	2020+	Lancet Global Health	General Epidemiology	Epidemiological Research	106	Bill and Melinda Gates Foundation
Potential Value of Triple Drug Therapy with Ivermectin, Diethylcarbamazine, and Albendazole (IDA) to Accelerate Elimination of Lymphatic Filariasis and Onchocerciasis in Africa	2015-2019	PLoS NTD	Treatment	Secondary Research	78	Bill and Melinda Gates Foundation
Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015	2015-2019	Lancet	General Epidemiology	Epidemiological Research	5221	European Commission; German Ministry of Education and Research; US National Institute on Aging
Understanding cultural and logistical contexts for urologists in low-income countries	1905-1909	BJUI International	Treatment	Secondary Research	4	None reported
The effects of climate change on human health in Africa, a dermatologic perspective: a report from the International Society of Dermatology Climate Change Committee	2020+	International Journal of Dermatology	General Topics	Secondary Research	33	None reported
Monitoring equity in universal health coverage with essential services for neglected tropical diseases: an analysis of data reported for five diseases in 123 countries over 9 years	2015-2019	Lancet Global Health	Health Systems/Policy	Clinical Research	27	None reported
Zambia Neglected Tropical Diseases Masterplan 2022-2026	2020+		Health Systems/Policy	Institutional Report		
Global Programme to Eliminate Lymphatic Filariasis: The Processes Underlying Programme Success.	2010-2014	PLoS NTD	Health Systems/Policy	Secondary Research	167	None reported
A Helminthological Survey in Northern Rhodesia	1945-1949	Journal of Helminthology	General Epidemiology	Epidemiological Research	49	None reported
2022-2026 National Health Strategic Plan	2020+		Health Systems/Policy	Institutional Report		None reported
Global trends in the use of insecticides to control vector-borne diseases	2010-2014	Environmental Health Perspectives	Vectors	Epidemiological Research	286	Bill and Melinda Gates Foundation

(Continued)

TABLE 3 Continued

Title	Publication Date	Journal	Study theme	Study type	Citations	Funder(s)
Global mapping of lymphatic filariasis	1995-1999	Trends in Parasitology	General Epidemiology	Epidemiological Research	319	Special Programme for Research and Training in Tropical Diseases;
Identifying co-endemic areas for major filarial infections in sub-Saharan Africa: seeking synergies and preventing severe adverse events during mass drug administration campaigns	2015-2019	Parasites and Vectors	Co-infections	Epidemiological Research	33	Bill and Melinda Gaates Foundation

Article titles, publication date, journal, study theme and type, citation as indexed on Google Scholar, and author-reported funding organization. 40 articles were included following screening.

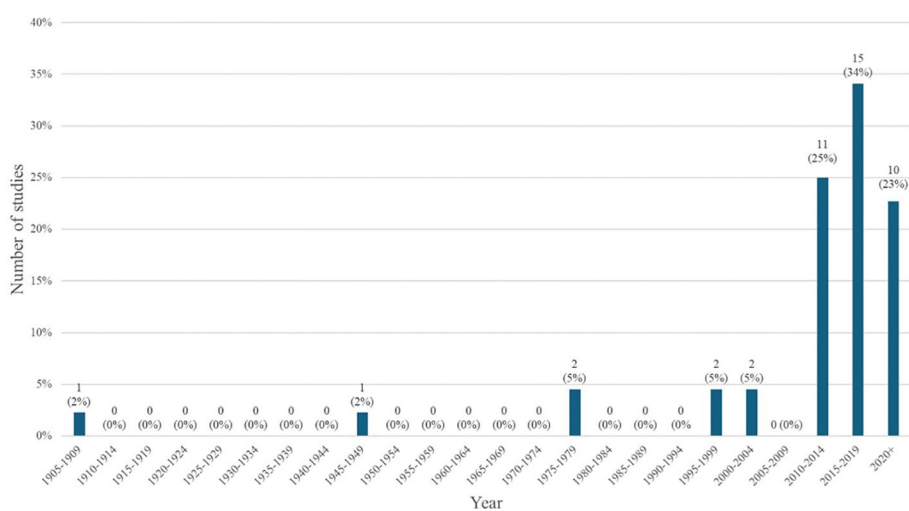


FIGURE 3
Number of articles published per half decade.

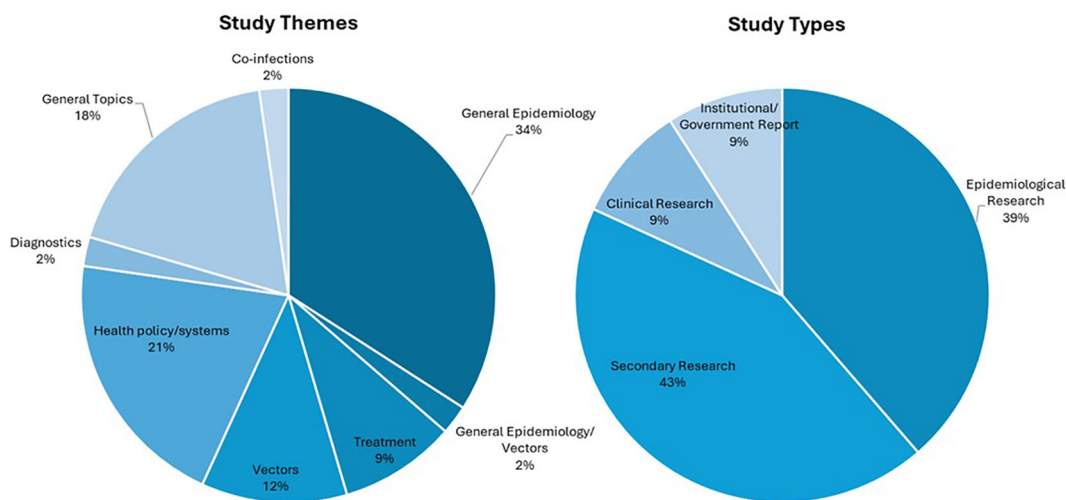


FIGURE 4
Number of articles per study theme and per study type.

TABLE 4 Number of articles in each study theme by half decade, excluding half decades in which no articles were published.

Year	Co-infections	Diagnostics	General Epidemiology	General Epidemiology; Vectors	General Topics	Health Systems/Policy	Treatment	Vectors	Total per Year
1905-09							1		1
1945-49			1						1
1975-79		1	1						2
1995-99			2						2
2000-04			1		1				2
2010-14			4	1	2	1	1	2	11
2015-19	1		4		3	2	2	3	15
2020+			2		2	6			10
Total per Theme	1	1	15	1	8	9	4	5	44

Color coding corresponds to half decades in which the most articles were published.

TABLE 5 Study type by half decade and total articles published per half decade.

Year	Clinical Research	Epidemiological Research	Institutional Report	Secondary Research	Grand Total per Half Decade
1905-1909				1	1
1945-1949		1			1
1975-1979	1			1	2
1995-1999		1		1	2
2000-2004			1	1	2
2010-2014		6		5	11
2015-2019	2	6	1	6	15
2020+	2	2	2	4	10
Grand Total per Study Type	5	16	4	19	44

The most frequently seen study types were epidemiological research in the 2010s, and secondary research between 2015-2019. Significance of the coloring within the table indicates frequency, with darker colors drawing attention to higher frequency.

TABLE 6 Study theme by study type, color gradient indicates most common intersection between theme and type.

	Clinical Research	Epidemiological Research	Institutional Report	Secondary Research	Total per Study Theme
Co-infections		1			1
Diagnostics	1				1
General Epidemiology		8		7	15
General Epidemiology; Vectors		1			1
General Topics		1	2	5	8

(Continued)

TABLE 6 Continued

	Clinical Research	Epidemiological Research	Institutional Report	Secondary Research	Total per Study Theme
Health Systems/Policy	4	1	2	2	9
Treatment		1		3	4
Vectors		3		2	5
Total per Study Type	5	16	4	19	44

Total study type and total study theme are also reported. The most commonly seen study types and themes were general epidemiology and epidemiological research, general epidemiology and secondary research, and general topics and secondary research. Significance of the coloring within the table indicates frequency, with darker colors drawing attention to higher frequency.

TABLE 7 List of organizations and donors acknowledged by articles as providing support in order from most frequently reported.

Reported Funding Organization	Reported Frequency
None Reported	16
Bill and Melinda Gates Foundation	9
Department of International Development, UK	4
Wellcome Trust	4
Coalition for Operational Research on Neglected Tropical Diseases (COR-NTD)	3
Liverpool Centre of NTDs	2
Danida Research Council, Denmark	2
Natural Environment Research Council, Grantham Institute for Climate Change at Imperial College London	2
GlaxoSmithKline	2
Special Programme for Research and Training in Tropical Diseases;	2
Ministry of Health, Zambia	1
WHO-Afro	1
Eradication Investment Case of Onchocerciasis, Lymphatic Filariasis, and Huma African Trypanosomiasis	1
Eck Institute for Global Health, Notre Dame' Office of the vice President for Research, Notre Dame	1
EU FP6; EU FP7	1
Volkswagen Foundation	1
DAAD' A-WOL	1
DFG	1
DOLF	1
President's Malaria Initiative	1
Mectizan Donation Program	1
Global Alliance for LF Elimination	1
European Commission	1
German Ministry of Education and Research	1
US National Institute on Aging	1

None reported was most frequently seen.

no basic science studies or articles that focused on the pathophysiology of lymphatic filariasis in Zambia, however there's no clear reason that research into LF pathophysiology conducted in Zambia specifically would yield novel results. Articles that specifically focused on Zambia had relatively few citations, suggesting the limited impact of the field, while those studies that had a broader focus than specifically LF or Zambia on their own, such as the 2015 Global Burden of Disease study, had significantly more citations, the vast majority likely from papers that are unrelated to this study's focus. Given our inclusive approach, we retained these broadly encompassing articles. Most articles were concentrated around a select few journals that had scopes that focused on either NTDs or parasitology.

There are several limitations in the design and conduct of this study. There were several older studies, for example those by Hira (25, 26), that were not included in the analysis despite their significant contribution to the understanding of LF in Zambia, as the full text for these articles could not be located and thus could not be carefully analyzed. It is possible that articles that should have been included in this scoping review were missed. However, we attempted to mitigate this by being as inclusive as possible during the title-abstract screening process to ensure that any article that may have reasonably contained a thorough discussion of LF in Zambia was included in the full-text screen. Additionally, efforts were made to ensure that screeners were properly trained and had achieved a high level of inter-reviewer concordance prior to the initiation of the title-abstract screening phase. While we performed a review of the relevant government and institutional literature that discusses LF in Zambia, these articles are often less readily accessible than those published in peer-reviewed journals, thus we may have missed some of these articles during our search.

Interestingly, the most prevalent funding status for published articles was 'None reported'. Some articles explicitly stated that no funding was obtained for the purposes of that research, while others made no mention of funding in any explicit way. These were described the same way in this study. This suggests that much of the work that has been done on LF in Zambia has been unfunded and serves to highlight the neglected status of this neglected tropical disease.

Conclusions

Global efforts to eliminate LF are making progress worldwide. In Zambia, following 5 rounds of MDA, the country is awaiting

TABLE 8 Article title, number of citations as indexed by Google Scholar, study theme, type and year of publication for the 10 most highly cited articles found in this scoping review.

Article	Number of times cited	Study Theme	Study Type	Year of Publication
Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015	5221	General Epidemiology	Epidemiological Research	2016
Re-assessing the global prevalence and distribution of lymphatic filariasis	637	General Epidemiology	Secondary Research	1996
A research agenda for helminth diseases of humans: the problem of helminthiasis	410	General Topics	Secondary Research	2012
Global mapping of lymphatic filariasis	319	General Epidemiology	Epidemiological Research	1997
Global trends in the use of insecticides to control vector-borne diseases	286	Vectors	Epidemiological Research	2012
Global Programme to Eliminate Lymphatic Filariasis: The Processes Underlying Programme Success.	167	Health Systems/ Policy	Secondary Research	2014
Filariasis in Africa—treatment challenges and prospects	164	Treatment	Secondary Research	2011
Disease Eradication	155	General Topics	Secondary Research	2013
Predicting the current and future potential distributions of lymphatic filariasis in Africa using maximum entropy ecological niche modeling	153	General Epidemiology	Epidemiological Research	2012
The global distribution and transmission limits of lymphatic filariasis: past and present	150	General Epidemiology	Secondary Research	2014

verification that no further rounds are necessary. On this backdrop, we conducted a scoping review of the literature on LF in Zambia to describe and contextualize the existing body of knowledge. Through an analysis of 44 records that discuss LF in Zambia, we found that the most frequent articles focus was on the epidemiology of LF, while the most frequently used methodology was secondary research. Consolidating the body of knowledge on LF in Zambia may be helpful in several ways, including to support the efforts other countries that aim to follow the same path Zambia has taken toward elimination and to guide future research efforts in Zambia through the identification of potential gaps. Those gaps include further research into the vectors of LF and co-infections, given the *Anopheles* mosquito that spreads the disease is also a principal vector for malaria.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

HS: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization,

Writing – original draft, Writing – review & editing. AO: Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. DH: Data curation, Writing – original draft, Writing – review & editing. KC: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. AB: Data curation, Writing – review & editing. KS: Data curation, Writing – review & editing. JL: Data curation, Writing – review & editing. ST: Data curation, Writing – review & editing. GG: Formal analysis, Methodology, Visualization, Writing – review & editing. PC: Data curation, Methodology, Project administration, Software, Supervision, Writing – review & editing. RW: Conceptualization, Investigation, Methodology, Supervision, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Acknowledgments

The authors would like to acknowledge the institutional support of the College of Social Sciences and Humanities at

Northeastern University and the support of the Northeastern University Library.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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