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Towards global elimination of lymphatic filariasis: a systematic review of the application of spatial epidemiological methods to enhance surveillance and support elimination programmes

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ABSTRACT

Background In recent decades, spatial epidemiology has increasingly been used to study neglected tropical diseases (NTDs). Spatial methods are particularly relevant when transmission is strongly driven by sociodemographic and environmental factors, resulting in heterogeneous disease distribution. We use lymphatic filariasis (LF)—an NTD targeted for global elimination—as a case study to examine how spatial epidemiology has been used to enhance NTD surveillance.

Methods We conducted a systematic literature review of spatial analytical studies of LF published in English across PubMed, Embase, Web of Science and Scopus databases, before 15 November 2022. Additional papers were identified from experts' suggestions. Studies that employed spatial analytical methods were included, but those that applied only visualisation tools were excluded.

Findings Sixty-one eligible studies published between 1997 and 2023 were identified. The studies used a wide range of spatial methods. Thirty-one (50.8%) studies used spatial statistical modelling, with model-based geostatistics being the most common method. Spatial autocorrelation and hotspot analysis were applied in 30 studies (49.2%). The most frequent model outputs were prevalence maps (17 studies, 27.9%), followed by risk maps based on environmental suitability (7 studies, 11.5%) and maps of the odds of seroprevalence being above a predetermined threshold (7 studies, 11.5%).

Interpretation By demonstrating the applicability of spatial methods for investigating transmission drivers, identifying clusters and predicting hotspots, we highlight innovative ways in which spatial epidemiology has provided valuable evidence to support LF elimination. Spatial analysis is particularly useful in low-prevalence settings for improving hotspot detection and enhancing postelimination surveillance.

PROSPERO registration number CRD42022333804.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In countries where neglected tropical diseases (NTDs), such as lymphatic filariasis (LF), are endemic, control and elimination programmes have been implemented, aiming to interrupt transmission and alleviate suffering.
⇒ As these interventions take effect, the decrease in disease prevalence is characteristically associated with increased clustering, making it difficult to identify residual pockets of infection.

WHAT THIS STUDY ADDS

⇒ In this systematic review, we demonstrated that spatial epidemiology has contributed to a better understanding of the LF burden and distribution and contributed to enhanced informed decision-making for elimination strategies.
⇒ Here, we highlight innovative ways in which spatial epidemiology has provided valuable evidence to support LF elimination.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Spatial epidemiology approaches may be particularly useful in low-prevalence areas and postelimination settings where hotspot detection can help enhance surveillance strategies.
⇒ The valuable insights of these approaches into operational decision-making for LF elimination could be also adapted in the efforts against other NTDs.
⇒ The small number of studies that met our inclusion criteria and the variety of methods adopted by these studies limits the power to provide standard recommendations for the implementation of spatial analysis for LF.

BACKGROUND

Elimination, control and prevention of neglected tropical diseases (NTDs) are key priorities in global health.[1] Spatial epidemiology can be used to combine technologies such as geographic information systems, global position systems and remote sensing with geospatial statistical methods to identify

areas of high disease prevalence, analyse risk factors and drivers of transmission and predict prevalence across regions based on multiple sources of data.[2] As a result, public health policymakers have greater access to tools that can improve surveillance, facilitate the implementation of targeted public health interventions and help with monitoring and evaluation.[3]

Spatial epidemiology can be particularly beneficial for diseases that are strongly driven by sociodemographic and environmental factors, leading to heterogeneous distribution. In recent decades, significant progress towards control and elimination of NTDs has been made due to the identification of high-prevalence areas and the implementation of mass drug administration (MDA) and other strategies based on WHO guidelines.[1] The reduction in prevalence can be associated with an increase in spatial heterogeneity of remaining infections, meaning that transmission is concentrated in focal geographic areas or subpopulations, and potentially more difficult to identify.[4 5] The challenge of identifying areas of ongoing transmission could cause setbacks for elimination programmes. Acknowledging this risk, the 2030 WHO roadmap for NTDs emphasises the importance of strengthening post-MDA and postvalidation surveillance.[1]

Here, we use lymphatic filariasis (LF) as an example of how spatial epidemiology can be used to better identify and monitor areas of high risk of transmission compared with traditional, non-spatial methods. LF is an NTD caused by the mosquitoborne filarial nematodes *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*. Infection can cause damage to the lymphatic system, resulting in chronic pain, progressive lymphoedema and permanent disability.[6 7] Despite the substantial achievements of the WHO Global Programme to Eliminate LF (launched in 2000), LF remains endemic in 44 countries in 2023, with 882 million people at risk of infection.[6]

This systematic review aimed to investigate the diverse range of spatial analytical methods employed to investigate LF epidemiology and improve our understanding of transmission dynamics to optimise the success of elimination programmes. Thus, the objectives of this systematic review were to describe and compare spatial analytical methods that have been used to examine the geographic distribution of LF, identify risk factors driving geographical distribution and assess the impact of elimination and control programmes.

METHODS

Study design

The design of this systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol.[8] The protocol for this study was registered with the international prospective register of systematic reviews (PROSPERO CRD42022333804).

Data source and search strategy

A search was conducted on PubMed, Embase, Web of Science and Scopus databases on 15 November 2022 using a combination of keywords and medical subject headings associated with two main topics: LF and spatial epidemiology. The search strategy for each database is shown in online supplemental appendix 1. Additional papers were identified through hand searching the bibliographies of retrieved articles and from suggestions from experts.

Eligibility, and inclusion and exclusion criteria

This systematic review included peer-reviewed studies that applied spatial methods to describe the distribution of human cases of LF and/or to identify the determinants of higher infection prevalence in geographic regions. Studies were also included if spatial methods were used to assess the impact of interventions such as MDA. Studies were included if they reported human cases of LF diagnosed clinically (presence of lymphoedema or elephantiasis of limbs, and/or hydrocele) or using laboratory diagnostic tests.

Although mapping is part of the spatial epidemiology framework, studies that only included a graphical representation, without any spatial analyses, were excluded. Only studies published in English were included. There was no restriction to geographical regions of reported cases and year of publication. Studies that only included mosquito monitoring were excluded. Studies that reported other causes of lymphoedema were excluded.

Screening and selection were conducted using COVIDENCE (Veritas Health Innovation, Melbourne, Victoria, Australia).[9] After the exclusion of duplicates, two researchers (BMM and ACR) independently screened the titles and abstracts to identify potentially eligible studies. The full text of the records identified from initial screening were then screened by the same two researchers to determine if the inclusion criteria were met, and any disagreements were resolved by an independent third reviewer (HJM).

Data extraction and synthesis

Three researchers (BMM, ACR and HJM) independently performed data extraction using pretested data extraction forms in Microsoft Excel (Microsoft, Redmond, Washington, USA). Disagreements were resolved by consensus. Data extracted from each publication included study characteristics (year of publication, location), LF context (vector and pathogen species, and occurrence of MDA), study design (data source, sampling design, diagnostic test, spatial scale), study aims and spatial methods and outputs. Table 1 summarises the data extracted from publications, and a description of data extraction methods can be found on the online supplemental appendix 1.

In this study, the term *hotspots* was used to describe high-risk areas or locations with significantly higher levels of infection compared with the surrounding area. *Hotspot*

Table 1 Summary of the data extracted from each paper reporting spatial methodological approaches to analyse LF included in the systematic review

Data extracted	Categories
Study characteristics	
Year of publication	1997–2023
Location	Country WHO region
LF context	
Vector species	*Aedes* sp *Anopheles* sp *Culex* sp *Mansonia* sp Multiple species
Pathogens species	*Wuchereria bancrofti* *Brugia* sp Multiple species
Previous rounds of MDA	1–5 rounds 6–10 rounds over 10 rounds
Surveys design	
Data source	Survey (community or school-based) Secondary data (filariasis report, data previously published)
Sampling design	Systematic sampling Randomised sampling Convenience sampling Mass screening Multiple stage sampling Combined sampling design
Diagnostic test	CFA (ICT, FTS, Og4C3) Antibodies (IgG4, Bm33, Bm14, BmR1, Wb123) Parasitological (microfilariae) Clinical
Spatial scale	National level Districts or regions Villages or communities Household or individual level
Study aims	
Aims	Describe geographical distribution of prevalence Identify spatial autocorrelation Identify high-risk areas or hotspots Identify explanatory factors Analyse the impact of interventions Model transmission or elimination accounting for spatial dependence Demonstrate and compare spatial methods for LF
Spatial methods and outputs	
Methods*	Spatial dependence analysis Smoothing and interpolation Spatial statistical modelling Spatial mathematical modelling
Outputs	Identification of spatial dependence Identification of high-risk areas or hotspots Identification of explanatory risk factors Predicted locations of hotspots Predicted prevalence or created a prevalence map Predicted probability of occurrence of LF Predicted environmental suitability Predicted transmission Assessed the odds of elimination

*The specific tools and techniques adopted by each study are detailed in the 'Results' section.
CFA, circulating filarial antigens; FTS, Alere Filariasis Test Strip; ICT, immunochromatographic test; LF, lymphatic filariasis; MDA, mass drug administration.

analysis is considered a subtype of spatial dependence or autocorrelation methods, in which the location of the high-risk areas is identified.

Risk of bias and quality assessment

The risk of bias and quality assessment was conducted using the risk of bias in systematic reviews (ROBIS) tool.[10] As the aim of the systematic review was to identify methodological approaches used in the spatial analysis of LF, the individual assessment of risk of bias would not impact our results.

Role of the funding source

This study did not received any specific funding.

Patient and public involvement statement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Study characteristics

The initial search identified 3096 records; after excluding duplicates, 1618 papers were retained. Title and abstract screening excluded 1436, and the 182 remaining papers went through full-text review, of which 129 were excluded for not meeting inclusion criteria. Seven papers were suggested by experts and/or through hand-searching the bibliographies of retrieved articles, resulting in 61 papers being included (figure 1). The full collection of papers included in this systematic review can be found in online supplemental appendix table 1.

Included studies were published between 1997 and 2023. Although our initial search was finalised in November 2022, an additional paper published in early 2023 was included because it met the inclusion criteria. Figure 2 shows a timeline of years of publication of the studies, with an increasing trend in the number of papers during the study period. When comparing spatial methods categories, *spatial statistical modelling* and *spatial dependence analysis* approaches were implemented more constantly than other spatial methods and *spatial mathematical modelling* has been used in more recent years. However, no clear trend on spatial methods adopted through the years could be observed due to the small sample size (online supplemental appendix figure 1).

Except for the WHO European region (where LF is not endemic) and the Eastern Mediterranean region, where two (Egypt and Yemen) of the three LF-endemic countries have been validated as having eliminated the infection as a public health problem,[7] all other WHO regions were represented in this study. Three studies (4.9%) analysed data at the global level, 8 (13.1%) analysed data from multiple countries in Africa and 50 studies (82.0%) were conducted at national or subnational levels. Among the studies reporting national and subnational data, 16 (26.2%) analysed data from Africa, 15 (24.6%) from South-East Asia, 12 (19.7%) from the Western Pacific

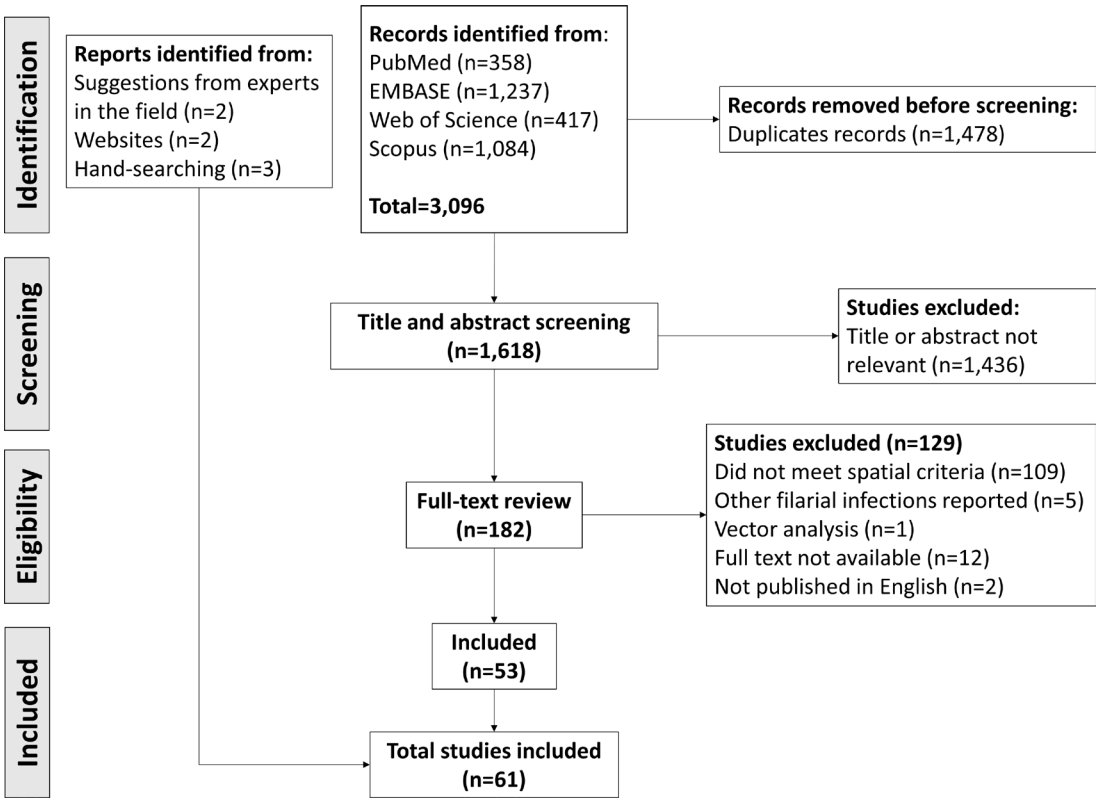

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart showing search and selection of studies procedure.

region and 9 (14.8%) from the Americas. India was the country with the highest number of studies (six, 9.7%) followed by American Samoa, Haiti and Indonesia, with five (8.1%) studies each. Online supplemental appendix table 2 shows the global distribution of the studies included in this systematic review.

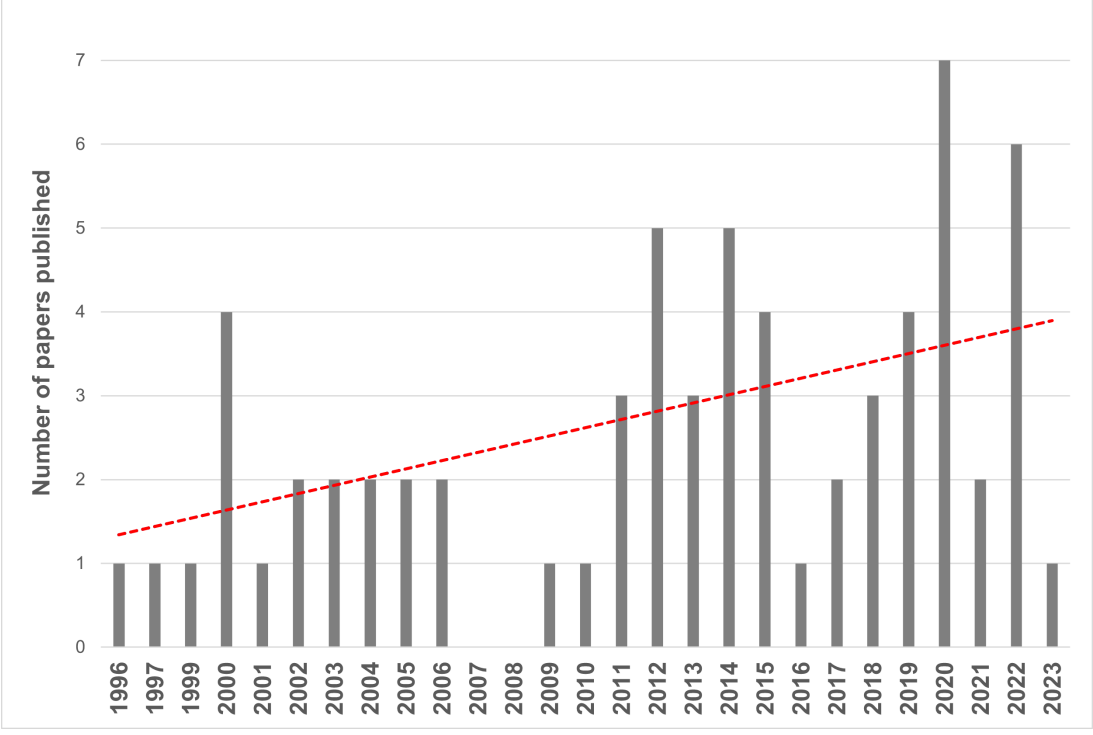

Figure 2 Number of studies that reported spatial methodological approaches to analyse lymphatic filariasis by year, for the period between 1997 and 2023. The red line shows the trend over the period.

Lymphatic filariasis context

Among the 43 papers (70.5%) that reported on vector genera, *Anopheles* was reported in 15 studies (34.9%), *Culex* sp in 10 studies (23.3%), *Aedes* sp in 8 (18.6%), *Mansonia* sp in 1 (2.3%) and multiple vector species in 9 studies (20.9%). Pathogen species were reported in 45 studies (73.8%); *W. bancrofti* in 38 studies (84.5%), *Brugia* sp in 2 studies (4.5%) and co-circulation of both species in 5 studies (11.1%).

Regarding the occurrence of MDA, 23 studies (37.7%) analysed data before the intervention, 21 (34.4%) analysed data from a post-MDA period and 2 (3.3%) papers compared data from both periods. Among the studies that included data from the post-MDA period, 6 (26.1%) reported 1–5 MDA rounds, 14 studies (60.9%) from 6 to 10 and 1 study (4.3%) over 10 rounds. Two studies that reported data after MDA were not clear about the number of rounds implemented before data collection.

Survey design

Diagnostic test

LF diagnosis was determined by the detection of microfilariae in a blood smear in 38 studies (62.3%), by the detection of antigen in blood or urine samples in 38 studies (62.3%), and by the detection of antibodies in 7 studies (11.5%). Among the studies that reported antigen results, ICT was adopted in 26 studies (68.4%), FTS in 12 studies (31.6%) and Og4C3 in 5 studies (13.2%). Among the studies that reported in antibodies results, IgG4 antibodies were reported in four studies (57.1%), anti-Wb123 in six studies (85.7%), anti-Bm14 in five studies (71.4%) and anti-Bm33 in three studies (42.9%). Three studies reported diagnosis by clinical evaluation (4.9%).

Data source and spatial scale

Forty-one (67.2%) studies reported on data obtained from surveys and 20 (32.8%) studies used secondary data (online supplemental appendix table 1). All studies that used secondary data and reported using geolocation obtained from original publications reported at the subnational level (villages or communities), except one study[11] that reported having household locations.

Analysis at the national level was conducted by 1 study (2.5%), subnational level by 10 studies (16.4%), communities/villages by 24 studies (39.3%) and at the household or individual level was reported by 26 studies (42.6%).

Study aims

We only reported study aims associated with a spatial approach; 30 studies (49.2%) aimed to describe the spatial distribution of LF, 21 (34.4%) to identify risk factors, 17 (27.9%) to identify spatial autocorrelation, 15 (24.6%) to identify hotspots or high-risk areas, 9 (14.8%) to assess the impact of an intervention, 6 (9.8%) to demonstrate the application of a model or to compare outputs of different models and 5 (8.2%) to model transmission or the odds of elimination while accounting for spatial dependence.

Spatial methods and outputs

Methods

Spatial techniques and tools are detailed in table 2. Thirty-one studies (46.8%) used techniques that identified or measured spatial structure, 42 (64.5%) used statistical modelling to examine the effect of explanatory risk factors on disease distribution and 6 (9.7%) used mathematical models to estimate disease prevalence, transmission or environmental suitability. Twenty-five studies (41.0%) used more than one technique.

Intracluster correlation is an indicator of the degree of agreement between measurements (eg, infection status) within defined groups (eg, regions, communities or households).[12] When the hierarchical level of the multilevel regression corresponds to the spatial levels of data aggregation, it reflects the spatial structure of the dataset and therefore can be used to assess spatial clustering. Table 2 summarises the range of methods used in the studies of LF. The technique adopted was not described in four studies, although it was possible to observe that one study[13] quantified spatial variation, two studies[14 15] applied spatial models to estimate the probability of disease presence and one study[16] described testing the model for spatial dependence using Moran's Index and applied spatial models to estimate the probability of disease spread, but the method was unclear.

The association between study aims, the spatial method applied and the frequency in which each association occurred is summarised in table 3. Studies could report more than one aim and/or apply more than one technique. Studies that used spatial regression models to describe disease distribution were the most frequent, followed by studies that used global spatial dependence to investigate spatial autocorrelation.

Outputs

Thirty-eight studies (62.3%) reported a prediction output, most frequently predicted prevalence by location reported as a prevalence map (17 studies, 27.9%). LF occurrence was also predicted based on the probability of environmental suitability, and of seroprevalence above a threshold, reported in seven (11.5%) studies each.

Eight studies (13.1%) assessed the impact of interventions and control programmes on disease distribution; four (50.0%) conducted in the African Region, two (25.0%) in the Western Pacific Region, one (12.5%) in the Region of Americas and one (12.5%) in the South-East Asian Region. Five studies (62.5%) investigated the impact of MDA on LF prevalence, and four studies (50.0%) assessed the odds of LF elimination by MDA and other interventions.

Five studies (8.2%) reported negative results for spatial dependence. Two studies[17 18] examined but did not identify any spatial dependence in their dataset. One study[19] did not identify spatial autocorrelation, but identified weak spatial heterogeneity. Based on these results, the authors decided to incorporate spatial terms in the model to predict LF prevalence. In two studies, the presence of

Table 2 Spatial methods used in spatial analysis of lymphatic filariasis (n=64)

Method	N (%)	References
Spatial dependence analysis	30 (49.2)	
Multilevel regression+ICC coefficient	4 (6.6)	12 21 41 42
Global		
Variogram/Semi-variogram	11 (18.0)	4 12 20 23 30 34 43–48
Moran's Index	7 (11.5)	12 16 17 19 20 35 49 50*
Others	5 (8.2)	18 51–54
Local		
Getis Ord G local statistic	3 (4.9)	12 49 55
Kulldorffs Spatial Scan Stats	3 (4.9)	12 28 56
Others†	2 (3.3)	32 57
Smoothing and interpolation	10 (16.4)	
Kernel density estimation	3 (4.9)	33 57 58
Kriging	6 (9.8)	31 44 46 48 59 60
Spatial statistical methods	31 (50.8)	
Conditional autorregressive models	2 (3.3)	30 43
Model-based geostatistics	15 (24.6)	11 20 22 23 26 35 38 44 45 48 50 61–64
Geographically weighted regression	1 (1.6)	19
Machine learning‡	10 (16.4)	25 27 34 36–38 40 49 65 66
Other	8 (13.1)	28 39 67 68
Spatially explicit mathematical modelling	6 (9.8)	
Agent-based model	2 (3.3)	69 70
APBCM	2 (3.3)	11 29
SIR (transmission model)	1 (1.6)	63
Data-driven Bayesian melding	1 (1.6)	71

*Purhadi *et al*[19] used Moran's Index to identify spatial dependence and Koenker-Basset to identify spatial heterogeneity.
†Rahman *et al*[57] used local indicators of spatial association and Brandão *et al*[32] used k-means.
‡MaxEnt was used in three studies, Eneanya *et al*[37]; Mwase *et al*[66] and Slater and Michael[36]; boosted tree regression was used in two studies, Cano *et al*[65] and Eneanya *et al*[37]; regression forest in two studies, Eneanya *et al*[34] and Kwarteng *et al*[40] and generalised additive model was used in three studies, Bisanzio *et al*[49]; Srividya *et al*[20] and Kwarteng *et al.*[40]
APBCM, adaptive approximate Bayesian computational model; ICC, intracluster correlation; SIR, susceptible (S), infected (I), and recovered (R).

spatial autocorrelation varied based on the adoption of different spatial scale[20] (spatial dependence was present at a large scale but not at a small scale) and on the diagnostic test incorporated into the model[21] (spatial dependence was identified for antigen, but not for antibodies).

Twenty-two studies (36.1%) reported the occurrence of hotspots as an output; 16 studies (26.2%) identified hotspots and 6 (9.8%) predicted the location of hotspots. Among those studies, eight (13.1%) were conducted in the Western Pacific Region, five (8.2%) in the Region of the Americas, four (6.6%) in the African Region and four (6.6%) in the South-East Asian Region. Four (6.6%) studies were conducted after MDA rounds and investigated the impact of treatment on LF prevalence and distribution.

Six studies (9.8%) presented and discussed model performance. Here, we focus on the results of comparison between spatial and non-spatial models. One study[22] compared the results of spatial and non-spatial models using national data for malaria and LF, with spatial models performing better than non-spatial models. One study[23] built and compared four models, including a spatial Bayesian geostatistical approach. The authors identified issues with the definition of neighbours and the application of spatial smoothing but highlighted that the comparison between models illustrated the importance of accounting for spatial autocorrelation, and that the spatial model was more flexible for modelling spatially correlated diseases, such as LF. A Geographically Weighted Zero-Inflated Poisson Model (GW-ZIP) was developed in one study[19] and compared with the results from a non-spatial ZIP model, finding similar results in both models, but statistically significant variables were different in each model and statistically significant variables from the spatial model were opposite to initial expectations, with health households life style, trash can and wastewater management increasing the risk of LF.

Table 3 Heatmap of the frequency in which each spatial method was employed to address each aim and to produce outputs among the studies that reported the use of spatial methods to the study of LF

	Spatial methods					
	Spatial dependence			Spatial statistical model	Spatial mathematical model	
	Global	Local	Interpolation			
Total studies*	**29**	**5**	**10**	**32**	**5**	**Total***
Studies aims†						
Describe distribution	11	0	9	18	1	30
Identify risk factors	8	0	3	15	0	21
Identify autocorrelation	14	4	1	7	0	17
Identify hotspots	11	4	2	6	0	15
Assess the impact of an intervention	3	1	1	4	4	9
Compare spatial models	3	0	0	4	2	6
Model transmission/elimination	0	1	1	4	2	5
Study outputs†						
Identified dependence	24	4	5	16	0	30
Identified risk factors	8	1	3	19	2	27
Predicted prevalence	6	0	5	10	2	17
Identified hotspots	11	5	1	7	0	16
Mapped other‡	5	0	2	8	0	10
Predicted environmental suitability	1	0	0	6	0	7
Predicted location of hotspots	4	0	1	4	0	6
Predicted risk of transmission	0	1	2	2	1	5
Assessed the impact of MDA	2	1	1	3	0	5
Assessed the odds of elimination	1	0	0	1	3	4

Frequently associated (≥20), 19–15, 14–10, 9–5, 4–1, not associated (0).
*Rows: total studies that reported each aim or output. Columns: total studies that reported each method.
†Some studies reported more than one aim or outputs.
‡Two studies mapped the standardised parasite density ratio,[30 43] one study mapped the density of microfilaremia distribution[58] and seven studies mapped the risk of LF occurrence (based on having a seromarker above a threshold).[16 27 35 36 48 64 66]
LF, lymphatic filariasis; MDA, mass drug administration.

Table 4 summarises the variables included in the statistical models with spatial terms. Eighteen studies (29.5%) investigated the relationship between LF and explanatory variables using spatial models. Among those, 10 studies (55.6%) focused on risk-factor analysis, and 7 studies (38.9%) used explanatory variables to predict disease distribution, and reported the variables incorporated into the spatial model.

DISCUSSION

Our study showed that the use of spatial analysis in LF epidemiological studies has progressively increased in recent decades. The expanded use of spatial methods has contributed to a better understanding of disease burden and distribution and contributed to enhanced informed decision-making for elimination strategies. A wide range of spatial methods have been used by researchers, with specific methods applied to address different objectives. Our review provides a helpful framework to guide others working in this field regarding choice of spatial methods when addressing questions regarding prevalence, distribution, hotspots, risk factors or odds of elimination.

Importantly, most studies included in this review demonstrated spatial dependence of LF occurrence, suggesting that spatial models may provide more accurate estimates of disease distribution and association with determinants of infection.[2 24] Additionally, the incorporation of spatial structure into complex mathematical models and machine learning models provided important insights into the impact of MDA and the odds of disease elimination.

The uptake of spatial methods varied between LF-endemic regions. Southeast Asia is under-represented compared with the LF burden in region. Among all WHO regions, Southeast Asia presents the highest LF burden, with ~60% of cases between 2000 and 2018,[25] yet only 20% of studies identified by our review was from this region. Spatial methods have been widely used for the

Table 4 Summary of variables included in the lymphatic filariasis statistical models with spatial terms

Explanatory variable	References
Sociodemographic and behaviour	
Age	22 28
Male	49
Living or studying in a specific location	23 68
Population density	36 40 62 65
Household members	49
Proxy of lower economic activity	37 38 40 66 68
Sewage treatment and waste management	15 19
Distance to an index case	28
Treatment	28
Use of bed nets	49
Environmental	
Temperature	34–37 39 62
Land cover	22 35
Water	22 38 39 62
Altitude	22 23 36 37 40 62

study of malaria,[3] which may have promoted the use of spatial methods in Africa, where endemic areas for both diseases often overlap.[26 27] Moreover, spatial methods might have greater value in low prevalence settings, when spatial heterogeneity of LF might intensify.[18 28 29] Even though spatial epidemiology can benefit areas of high or low prevalence,[2 24] the analytical options that may provide cost-effective high-quality information in low prevalence areas are more limited, justifying the computational and technological demands of spatial methods. Regions that have made significant progress towards LF elimination, such as the Pacific Islands and the Americas[7] were over-represented in our review, frequently reporting techniques to identify hotspots of LF, especially in the post-MDA setting.

The spatial modelling studies included in this systematic review demonstrated that careful selection of variables and spatial scale are needed for the models to appropriately represent spatial relationships. Environmental and sociodemographic factors incorporated into the models were initially chosen based on biological and historical plausibility.[24] For LF, models focused primarily on gender (males),[4 21 29] age (older groups),[22 28 30 31] socioeconomics (proxy of poverty),[32 33] temperature,[34–37] humidity[22 38 39] and altitude.[22 34 36 37] However, the ability of these variables to predict LF occurrence depends on how variables were represented in the model (ie, temperature may be included as mean minimum temperature, annual mean temperature, day or night land surface temperature, etc), quality of the dataset available and spatial scale of inputs and outputs. Strength and direction of association between variables in models differed when data were analysed at different spatial scales.[40] More detailed reports about the spatial data used (eg, spatial resolution, period encompassed), and the process of variable selection, are important to allow comparison and reproducibility of the model and to enable appropriate interpretation of results. This information could benefit future researchers when considering the most suitable variables for their models, and the spatial scale relevant to their study.

The importance of transmission drivers may vary within the same community, between communities and among communities within areas at subnational, national, regional and global scales.[34] It is important to understand the impact of this variation when planning public health interventions at different administrative levels. Studies that describe the global distribution of disease burden may benefit from broader analysis, for example, at the national level,[25] despite the risk that fine-scale heterogeneity will be missed. Conversely, national or regional programmes that investigate areas of residual transmission would benefit from fine-scale data inputs at the household and/or individual levels to identify small areas to be targeted for action.[30 38]

Our systematic review has several limitations. First, we only identified a small number of LF studies considering the worldwide distribution of LF, the variety of natural environment and sociodemographic settings with multiple parasite and vectors species and the different stage of elimination programme for each country where LF is endemic. The countries that are represented in the literature are not representative of LF global burden distribution. This highlight the underutilisation of spatial epidemiological methods for LF in areas where they could potentially provide valuable insights into operational decision-making. Second, we found a wide range of spatial methods compared with the low number of papers included in the review and multiple analytical techniques within the same group of methods, possibly because spatial analytics are still being explored for LF. Third, most studies reported the methods employed, but some provided only an incomplete description of how the methods were used or did not provided specific details about the spatial data. Inconsistent and incomplete reporting of methods limited the ability of this systematic review to make standard recommendations for spatial analysis for LF. Lastly, only studies published in English were included.

The strengths of this systematic review include the exhaustive and transparent review search strategy in accordance with the current methodological guidelines, input from experts and included studies that provided a comprehensive depiction of spatial methods used to study LF distribution and elimination efforts. Additionally, we explored the benefits of employing a broad range of spatial methods in the study of LF, especially on low prevalence settings.

In conclusion, our study showed that for LF, spatial analyses and models have provided valuable information and evidence to better define endemic zones, provide more precise estimates of population at risk and enable the stratification of areas by probability of transmission and infection. There are still needs for better quality of remote sensing data, especially in small or remote areas (eg, Pacific Islands), better consensus regarding definition of spatial scale related to population at risk and areas of residual transmission. As countries approach elimination, and LF prevalence continues to decline, identifying hotspots will require more robust surveillance strategies and analytical methodologies. The use of metrics that accurately describe changes in transmission intensity across space and time will be important for the design and implementation of evidence-based control and elimination strategies. The spatial methods identified by this study are also applicable for elimination of other globally important diseases.

Contributors CLL conceptualised and is the guarantor of the study. BMM did a comprehensive search of databases according to the study protocol. BMM and ACR independently screened the titles and abstracts of articles retrieved from the literature search. Full-text screening was independently conducted by BMM and ACR, data extraction was independently conducted by BMM, ACR and HJM. BMM aggregated data, did the formal analysis and drafted the first version. All authors reviewed, edited and commented on the interpretation of study findings. All authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

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