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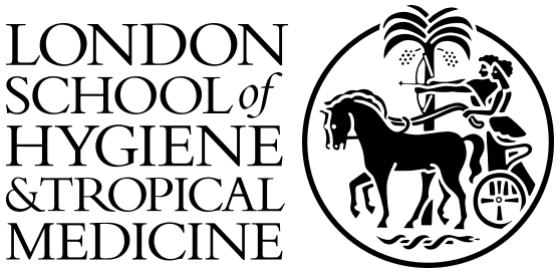

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Spatio - temporal modelling assessing the burden of malaria in affected low and middle-income countries: a scoping review

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ABSTRACT

Introduction Spatio - temporal modelling of malaria has proven to be a valuable tool for forecasting as well as control and elimination activities. This has been triggered by an increasing availability of spatially indexed data, enabling not only the characterisation of malaria at macrospatial and microspatial levels but also the development of geospatial techniques and tools that enable health policy planners to use these available data more effectively. However, there has been little synthesis regarding the variety of spatio - temporal approaches employed, covariates employed and 'best practice' type recommendations to guide future modelling decisions. This review will seek to summarise available evidence on the current state of spatio - temporal modelling approaches that have been employed in malaria modelling in low and middle-income countries within malaria transmission limits, so as to guide future modelling decisions.

Methods and analysis A comprehensive search for articles published from January 1968 to April 2018 will be conducted using of the following electronic databases: PubMed, Web of Science, JSTOR, Cochrane CENTRAL via Wiley, Academic Search Complete via EBSCOhost, MasterFILE Premier via EBSCOhost, CINAHL via EBSCOhost, MEDLINE via EBSCOhost and Google Scholar. Relevant grey literature sources such as unpublished reports, conference proceedings and dissertations will also be incorporated in the search. Two reviewers will independently conduct the title screening, abstract screening and, thereafter, a full-text review of all potentially eligible articles. Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols guidelines will be used as the standard reporting format. A qualitative thematic analysis will be used to group and evaluate selected studies around their aim, spatio - temporal methodology employed, covariates used and model validation techniques.

Ethics and dissemination Ethical approval is not applicable to this study. The results will be disseminated through a peer-reviewed journal and presented in conferences related to malaria and spatial epidemiology.

PROSPERO registration number CRD42017076427.

Strength and limitations of this study

- The review will summarise and compare existing approaches and develop a consolidated 'best practice' conceptual model of the methods and covariates to be incorporated in malaria modelling for control and elimination activities in low and middle-income countries.
- The results of the review may inform future malaria spatio - temporal modelling decisions.
- The review will evaluate the methodological rigour of included studies.

INTRODUCTION

Malaria is a global public health problem and a leading cause of morbidity and mortality in low and middle-income countries (LMICs). It is estimated that 3.2 billion of the world population are living in malaria-prone regions in 91 countries and territories. Global efforts towards sustaining and accelerating the reduction of malaria have been prioritised in endemic regions of Sub-Saharan Africa (SSA), the Americas, Western Pacific, Eastern Mediterranean and Southeast Asia. Studies conducted between 2000 and 2016 have reported substantial progress towards the control and elimination of malaria in endemic countries in the world.[1–4] However, an estimated 216 million clinical episodes of malaria and 445 000 deaths were reported worldwide in 2016,[4] with the burden being disproportionately high in children under 5 and pregnant women in LMICs.[4]

The Global Technical Strategy for Malaria (2016–2030) seeks to sustainably reduce malaria-attributable cases and deaths by 90% in 2030, by incorporating surveillance as a core intervention strategy.[5] Surveillance encompasses disease tracking, programmatic responses and data analysis, geared towards assessing the disease trends for optimal response.[6] According to a study conducted by the Global Burden of Disease (2016), delivering targeted interventions may be the most cost-effective strategy for improving health

outcomes.[7] Thus, identifying the burden of malaria in its geographical heterogeneity has been a priority for research in endemic regions of LMICs.[8–11] This has been boosted by advances in geographic information systems (GIS), remotely sensed satellite data and renewed interest in establishing precise estimates of morbidity and mortality in both space and time.[12] A recent study, covering the period between 1900 and 2015, reported a disproportionate geographic decline in malaria transmission intensity within countries in SSA,[13] highlighting the need for interventions to be commensurate with the unequal burden of disease within a country.[14] According to Kazembe *et al*, evidence-based resource utilisation is an important avenue for the control and elimination of malaria in high-burden countries.[15] Growing evidence has made a persuasive case for the incorporation of comprehensive baseline risk maps to help guide malaria control strategies.[16] This has been further fueled by the increasing availability of digital topographical, climatic and population data in LMICs.[17]

Efficient implementation and targeting of healthcare interventions for a disease are anchored on a better understanding of its spatio - temporal dynamics.[18] The dynamic global landscape of malaria and enhanced computational power has led to an urgent demand for more reliable, elaborate and refined representation of the ever-changing malaria risk pattern[19 20] as well quantifying the sustainability and impact of antimalaria interventions.[1] This has led to the advent of malaria health data indexed at a fine geographical resolution[21] necessitating the incorporation of robust statistical methodology to capture the emerging trends in space and time.[22] A multitude of descriptive to advanced spatio - temporal methods have since been employed to provide not only a comprehensive characterisation of uncertainty but also offer substantive insights into the major factors influencing the changes.[22] Increased abundance and diversity of potential malaria covariate layers necessitates the need for robust variables selection techniques to be used so as to maximise the predictive power of the spatio - temporal models.[22–24]

There is a growing body of literature regarding spatio - temporal analytical techniques employed in malaria modelling as well as growth in the availability of georeferenced data. The variety and strengths/limitations of approaches and covariates employed require a comprehensive review to identify the best methods and compare results to inform future studies.

In order to achieve this, the review primarily seeks to:

i. Identify and describe current spatio - temporal approaches used in malaria modelling.
ii. Identify and evaluate useful covariates that have been employed in spatio - temporal modelling of malaria.
iii. To develop a consolidated 'best practice' conceptual model of the methods and covariates to be incorporated in malaria modelling.

METHODS OF ANALYSIS

The title and synopsis of this proposed scoping review have been registered on the International Prospective Register of Systematic Reviews database (http://www.crd.york.ac.uk/PROSPERO), registration number CRD42017076427.

The scoping review will be conducted in different stages as suggested by Arksey and O'Malley[25] and advanced further by Levac *et al*.[26 27] This framework entails articulating the research question to guide the scope of inquiry, methodologically identifying relevant studies using spatio-temporal approaches, iteratively selecting the studies, comprehensively extracting the data, distinctly collating, summarising and reporting the results.

Identifying the research question

What types of spatio - temporal analysis approaches have been employed for assessing the burden of malaria in endemic settings of LMICs?

The research subquestions are:

1. Which analysis techniques have been employed to assess the space–time burden of malaria?
2. How are primary data integrated from multiple sources and study designs?
3. Which covariates have been most used/useful for the spatial-temporal modelling of malaria?
4. Which methods have been used to identify spatial variation?
5. What validation tools have been used to verify the predictive accuracy of a given modelling approach?

Eligibility of the research question

The study will employ the Population, Concept and Context (PCC) framework to determine the eligibility of the research question.[28] The following table defines the criteria related to each component in more detail (table 1):

Table 1 Population, Concept and Context framework for determination of eligibility of review question

Criteria	Determinant
Population	Empirical studies utilising spatio - temporal modelling approaches
Concept	Geographic information systems, spatial visualisation techniques, spatio - temporal modelling, cluster detection techniques, covariate selection
Context	Time frame: All publications from 1968 to 2018 are to be included. The starting year of 1968 has been tentatively chosen as this was when the first global audit of malaria endemicity was undertaken.[8 22 33] Geography: low/middle-income countries with current or past malaria transmission The language of publication: No language restrictions

Table 2 Electronic search preliminary results

Database	Date of search	Keywords	Number of publications retrieved
PubMed	28 March 2018	(malaria OR plasmodium)	97 492
		(malaria OR plasmodium) AND (map* OR geographic information systems OR GIS OR global positioning system OR GPS)	1078
		(malaria OR plasmodium) AND (map* OR geographic information systems OR GIS OR global positioning system OR GPS) AND (spatial OR space-time OR space* OR spatio-temporal OR spatio* OR spatial cluster OR small area OR small-area OR bayesian OR geo statistical OR modelling)	352
		Limit publication year from 1968 to 2018	352

Identifying relevant studies

Eligible studies/reports will be identified through a primary keyword search in the following electronic databases: PubMed, Web of Science, JSTOR, Cochrane CENTRAL via Wiley. Academic Search Complete via EBSCOhost, MasterFILE Premier via EBSCOhost, CINAHL via EBSCOhost, MEDLINE via EBSCOhost and Google Scholar. Grey literature sources will also be searched for missing publications. Combinations of MeSH terms in MEDLINE and other indexed keywords will be used when conducting the primary search in different databases so as to improve the sensitivity and specificity of the search.

The keywords will be developed thematically to cover the following aspects of the review:

1. Malaria (eg, incidence, prevalence, morbidity, mortality)
2. Geographic tools (eg, remote sensing, GIS, mapping)
3. Malaria risk factors/covariates/predictors
4. Spatial, spatio - temporal models and cluster analysis
5. Surveillance and monitoring

The search strategy will be developed and piloted to identify the optimal combination of keywords to be used (table 2). Identified studies will then be exported into EndNote reference manager V.X7 (Clarivate Analytics, Philadelphia, Pennsylvania, USA). An EndNote database will be created and will also be used to remove duplicate articles.

Study selection

Preliminary eligibility criterion has been developed to select studies that used spatiotemporal approaches for assessing the burden of malaria (table 3).

The review team will be guided by a librarian based at University of KwaZulu-Natal to help retrieve articles from the selected databases. The reviewers will also contact corresponding authors for clarification on missing information and/or unpublished data.

Two reviewers will independently conduct title and abstract screening to identify potentially publications. All publications identified where at least one reviewer deemed eligible will enter into the full-text review stage. A full-text review of all eligible articles will again be conducted by two independent reviewers. A third reviewer (arbitrator) will be used to resolve any discrepancies. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart (figure 1) will be used to highlight the study selection procedure.[29]

Data extraction

A standardised and pilot tested data extraction form will be used to ensure standardised and consistent extraction of metadata from selected publications. A data extraction form indicating the study's bibliographic information, the study aims, methodology, results, discussion, conclusion and recommendation will be used (box 1). Descriptive analytical methods will also be used to summarise the study findings.[25]

Table 3 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Studies will be included if they explicitly meet the following criteria:	**The following exclusion criteria will be applied:**
1. Use of at least one visualisation and/or modelling technique (with or without covariates) for assessing malaria burden in space and time. 2. Published between 1 January 1968 and 31 December 2018. Our selection of 1968 is guided by the year that the first global audit of malaria endemicity was undertaken.	1. Studies that focus on other diseases other than malaria. 2. Studies based on qualitative expert reviews.

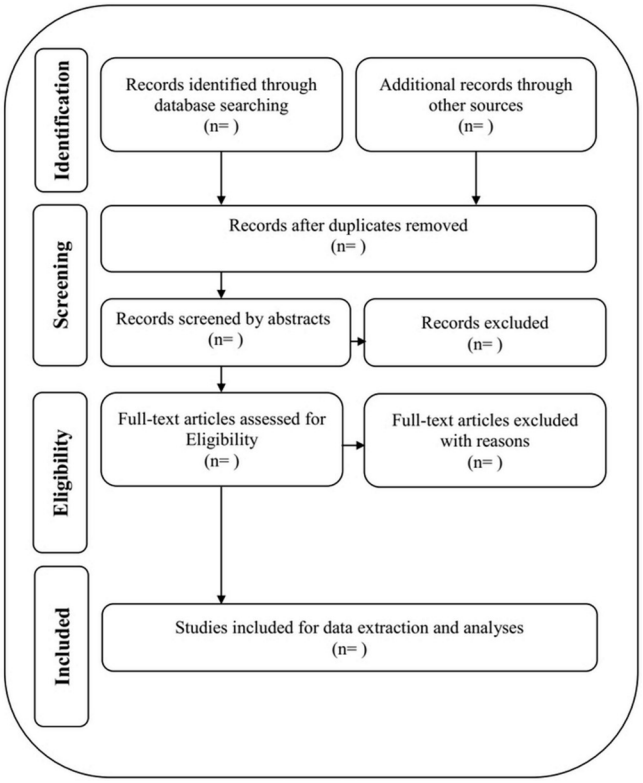

Figure 1 Study selection based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 flow diagram.

Collating, summarising and reporting results

This stage will entail three distinct steps namely analysis, reporting of results and applying meaning to the results. The analytical approach will entail a descriptive numerical summary of the total number of studies included, study design, publication year, type of covariates, study setting and the characteristics of the study population. Additionally, a qualitative thematic analysis will be used to group selected studies around their aim, spatiotemporal methodology employed, covariates used and model diagnostics/validation. Results will be reported in line with the purpose of the review. Tables showing the different data sources, visualisation techniques, covariates, cluster detection techniques and spatiotemporal methods will be developed.

Practical implications of the scoping review for malaria research, policy and modelling practices will be discussed against the gaps in the current state of spatio - temporal methodological approaches identified in this proposed review.

Quality appraisal

The quality of studies included in the review will be assessed using a mixed method appraisal tool.[30] The appraisal will be undertaken by two independent reviewers. Screening questions will be developed to evaluate the appropriateness of the study design, methodological approach, data analysis, presentation of findings and the authors' discussions. An adapted scoring system will be used for the aforementioned process to group studies in low-quality, medium-quality and high-quality study strata as provided in table 4.[31 32]

Box 1 Data extraction form

1. Bibliographic information
   - Study ID
   - Author, year
   - Country
   - Article title
   - Language
   - Study period (start–end)
   - Data source (medical records, multiple sources, programme data, clinical data for the study, others)
   - Type of publication (journal article, book chapter, grey literature).
   - Primary unit of analysis (cluster, individual, more than one unit, other)
   - Study population/spatial unit (household, national, province, district facility, malaria case, census tract, other)
2. Aims
   - Study aims and objectives
3. Methodology
   - Data sources used, multiples sources employed, different study designs and sampling frames employed
   - Visualisation techniques
   - Cluster detection techniques
   - Covariate(s) selection
   - Spatio- temporal modelling approach
4. Results (Does the paper report data relating to the following?)
   - Key findings
   - Unexpected results
5. Discussion
   - Key findings
   - Unexpected results
   - Modelling gap(s)
   - Limitations
6. Conclusions and recommendations
   - Modelling issues requiring further attention
   - Suggestions for improved analytical approaches for future studies

Patient and public involvement

Patients are not to be involved in the study.

DISCUSSION

Spatio-temporal modelling is relevant to any disease with elements of environmental causation. The enhanced computational ability has created an ideal environment for the upsurge of spatiotemporal epidemiological applications incorporating space, time and large data sets. With these advances, numerous studies have used diverse data sources, adopted various visualisation techniques for basic visualisation/data exploratory techniques to advanced Bayesian geostatistical modelling as well as leverage various covariates in these spatio - temporal models to improve fit and predict at unsampled locations. Despite the development and utilisation of diverse spatio - temporal methods in malaria epidemiology, limited

Table 4 Quality appraisal of individual studies

Quality appraisal was assessed using a 10-point scoring system quality assessment tool for cross-sectional studies
The total quality score varied between 0 and 10 where 1–4=low, 5–7=moderate and 8–10=high

Introduction	Methods					Results		Discussions		Total
Author/year/ country language/ study period stated	(1) Clear definition of objectives/aims/ research questions	(2) Study design appropriate for the stated aims	(3) Data management (data type/sources/ collection methods/ preprocessing/ misalignment) well defined.	(4) Cluster detection/ visualisation techniques sufficiently mentioned to enable replicability?	(5) Malaria outcome measures and covariates clearly defined (eg, malaria incidence), valid (eg, from remote sensing) and reliable.	(6) Analytic methods (variable selection, model validation) sufficiently described to enable replicability?	(7) Results clearly specified (point estimate, CI, SE)	(8) Authors discussions and conclusions justified by results	(9) Important findings/ limitations of the study/unexpected results discussed	(10) Reported modelling issues requiring further attention.	Scores (0–10)

appraisal has been done of the multitude of spatial methodologies that have been employed, the covariates leveraged and an assessment of robustness and operational practicality of implementing these complex techniques in resource-limited settings.

The catalogue and appraisal of spatio - temporal malaria modelling approaches will thus provide conceptual clarity, methodological rigour and transparency and build a recommendation framework for future research in this domain and help guide 'best practice' with regard to spatio-temporal modelling techniques in a given context. This review will also attempt to synthesise the range of techniques that have been employed and thus help to improve the understanding of spatio - temporal methods for health applications among researchers. We anticipate the review to also benefit policy makers, epidemiologists and ecologists who are involved in malaria research.

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Contributors JNO conceptualised the study and prepared the draft review under the supervision of BS. Both JNO and BS contributed to the development of the background and planned output of the research as well as the design of the review protocol. BS contributed to the development of the methods relating to the review and synthesis of data including the sifting and data extraction process. JNO prepared the manuscript, and BS reviewed it. Both authors contributed to the reviewed draft version of the manuscript and approved the final version.

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Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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