

BMJ Open Forecasting models for leprosy cases: a scoping review protocol

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ABSTRACT

Introduction Leprosy is a neglected tropical disease caused by *Mycobacterium leprae* that mainly affects the skin, the peripheral nerves, the mucosa of the upper respiratory tract and the eyes. Mathematical models and statistical methodologies could play an important role in decision-making and help maintain the gains in elimination programmes. Various models for predicting leprosy cases have been reported in the literature, but they have different settings and distinct approaches to predicting the cases. This study describes the protocol for a scoping review to identify and synthesise information from studies using models to forecast leprosy cases.

Methods and analysis A scoping review methodology will be applied following the Joanna Briggs Institute methodology for scoping reviews and will be reported according to Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews. We will perform a systematic search from when each database started until April 2022 and we will include the following electronic databases: MEDLINE via PubMed, Embase, Cochrane Library and Latin American and Caribbean Health Science Literature Database. Data will be extracted and recorded on a calibrated predefined data form and will be presented in a tabular form accompanied by a descriptive summary. The Prediction Model Study Risk of Bias Assessment Tool (PROBAST) will be used.

Ethics and dissemination No ethical approval is required for this study. This scoping review will identify and map the methodological and other characteristics of modelling studies predicting leprosy cases. We hope that the review will contribute to scientific knowledge in this area and act as a basis for researchers designing and conducting leprosy models. This information can also be used to enhance national surveillance systems and to target specific policies. The protocol and consequent publications of this scoping review will be disseminated through peer-reviewed publications and policy briefs.

Systematic review registration This scoping review was registered in the Open Science Framework (<https://doi.org/10.17605/OSF.IO/W9375>).

INTRODUCTION

Leprosy or Hansen's disease, a neglected tropical disease (NTD), is an infectious disease caused by *Mycobacterium leprae*, which mainly affects the skin, the peripheral nerves, the mucosa of the upper respiratory tract and the eyes.¹ Leprosy has physical and psychological

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We aim to undertake the first scoping review evaluating the main characteristics of leprosy forecast modelling studies.
- ⇒ We will use rigorous methodology in accordance with the framework proposed by Arksey and O'Malley and the refinements made by the Joanna Briggs Institute.
- ⇒ The present protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Protocols.
- ⇒ The inclusion of studies with various modelling methods and the data extraction based on descriptive information may cause potential heterogeneity in this scoping review.
- ⇒ Risk of bias will be evaluated through the Prediction Model Study Risk of Bias Assessment Tool, but it may be limited due to anticipated data incompleteness.

consequences that can lead to activity limitations, economic and physical dependence, social exclusion and stigma.²

The WHO estimated that there were 202 256 new patients with leprosy globally only in 2019, with Brazil, India and Indonesia being responsible for 79% of the burden.³ The WHO Global Leprosy Strategy 2021–2030 aims to eliminate leprosy and is aligned to the WHO roadmap for NTD 2021–2030 and the Sustainable Development Goal targets.⁴

Many of the countries that achieved a substantial reduction in incidence over recent decades used strategies such as BCG vaccination, active case finding, ensuring adherence to multidrug therapy and continued surveillance following treatment.⁵ Alongside these efforts, there has been an increasing role for quantitative analysis and modelling to better evaluate the impact of these interventions and identify factors that might reduce their effectiveness, as well as to assess the role of new diagnostics and treatments in reducing transmission.⁶

Mathematical models and statistical methodologies could play an important role in supporting decision-making to help maintain

the gains achieved through elimination programmes.⁷ However, some countries face challenges in developing mathematical models that provide accurate estimates of undetected incident cases.^{4 8} Failure to detect leprosy cases and the subsequent under-reporting of the disease can occur for a variety of reasons, including the low capacity of healthcare services or health professionals to diagnose and register new cases of the disease, lack of specific leprosy programmes and policies, absent or inadequate national disease registries and deficiencies in national or local leprosy programmes.⁹ Models predicting the incidence or prevalence of cases of leprosy can facilitate the identification of new or undetected cases and inform health decision-making in respect of the target population for treatment and disease control and prevention actions.⁷ Various prognostic modelling studies of leprosy cases have been reported in the literature, but they have been undertaken in a diverse range of settings using distinct approaches to predict cases.^{9–13}

A study by Blok *et al* identified three mathematical models of leprosy transmission and control, two compartmental models and one individual-based model, and highlighted their main methodological characteristics, mechanisms and related mathematical issues.¹⁴ The literature also contains other types of models using back-calculation, linear mixed methods and autoregressive integrated moving average (ARIMA) modelling, among other techniques.¹⁵ However, there is no published study evaluating all available prognostic modelling studies as well as the impact of the application of the models in clinical settings, or that considers the sources of the data used (hospital, national database and regional database) or what type of outcome is being predicted (new cases detection rate, disease elimination, under-reporting, etc.). Furthermore, there is a lack of information about the risk of bias in these studies. It is also important to assess the methodological rigour of the models as this can affect the quality of the evidence generated. The purpose of this study, therefore, will be to complete a scoping review to identify and synthesise prognostic modelling studies of leprosy cases. Specifically, we aimed to (1) chart the characteristics and range of the methodologies used in the identified studies, (2) identify if under-reporting of cases has been addressed by the models, (3) uncover gaps and limitations in the research field and (4) propose recommendations to enhance the applicability and consistency of modelling studies of leprosy cases.

METHODS AND ANALYSIS

Study design

We will use a scoping review methodology to map how modelling studies for predicting cases of leprosy are designed and conducted (type of statistical approach, method of mathematical modelling applied, predicted time horizon, variables included in the model and the quality and robustness of the models, among other factors). This scoping review will be developed using

the methodological framework proposed by Arksey and O'Malley¹⁶ and the refinements made by the Joanna Briggs Institute.¹⁷ The present protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Protocols¹⁸ (online supplemental appendix I). This scoping review has been registered in the Open Science Framework (<https://doi.org/10.17605/OSF.IO/W9375>).

Research question

The research question for this scoping review will be 'What are the main methodological characteristics of modelling studies used to predict cases of leprosy?' A structured question with inclusion and exclusion criteria will be developed following the acronym PCC, which denotes population, concept and context.

Population

The population includes patients with leprosy with no restrictions regarding age, gender, health condition and any other key demographic features.

Concept

To deal with health planning and to support the decision-making process regarding leprosy, there is a need to estimate the number of future cases of the disease, particularly in endemic areas such as Brazil, India and Southeast Asia.⁴ Thus, it is of paramount importance to understand the methodological characteristics of all modelling studies developed for predicting cases of leprosy (prognostic models), and the main model assumptions and the conclusions reported by these studies. We will include studies evaluating or predicting new future cases or under-reporting/hidden cases of leprosy (absolute or relative rates). No restriction will be made regarding the country or period of study. We will exclude studies that evaluated only crude incidence and prevalence rates during a specific period.

Context

It is generally accepted that future leprosy estimates tend to under-report its prevalence, which undermines decision-making processes. Thus, there is a need to ensure that studies whose objective is to predict cases of leprosy use rigorous methodologies so that the evidence they produce is robust and can be used to support health system planning, disease surveillance and the implementation of leprosy health policies. We will include studies with no restriction regarding the study context (eg, healthcare settings) or data source (eg, primary data or secondary data).

Evidence sources

We have adopted an extension to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA-S), for Reporting Literature Searches in Systematic Reviews.¹⁹ A comprehensive search of general electronic databases and a manual search will be undertaken to identify relevant studies (from all dates up to April

2022). We will include the following electronic databases: MEDLINE via PubMed, Embase, the Cochrane Library, and the Latin American and Caribbean Health Science Literature Database (LILACS). A detailed description of the search strategy is available in online supplemental appendix II. A manual search in the references of all included studies will also be performed. In addition, a validation search of included studies will be undertaken in Google Scholar (<https://scholar.google.com.br/>) and Epistemonikos (<https://www.epistemonikos.org/>) to guarantee completeness. In these last sources, the first 20 results will be selected and screened. The search will be performed independently by two reviewers (BOA and HAOJ).

Search strategies

To build the search strategies, we will use controlled vocabulary such as Medical Subject Headings for PubMed and Cochrane, Embase Subjects Headings (Emtree) for Embase and ‘Descritores em saúde’ for LILACS. We will also use uncontrolled vocabulary such as keywords, entry terms, synonyms and relevant related terms. We will perform a systematic search from when each database started until April 2022.

Screening and selection process

All studies identified in the search will be exported to EndNote to manage the records and to identify and remove duplicates. All records will then be imported to Rayyan to recheck duplicates and perform the blinded selection process.²⁰

As we expect to retrieve a considerable number of records in our search, one reviewer (BOA) will independently screen the titles and abstracts and another reviewer (HAOJ) will rescreen a random sample of 10% of the excluded articles.²¹ The full-length articles will be downloaded, and one reviewer (BOA) will assess the eligibility of each study. A second reviewer (HAOJ) will assess the eligibility of a sample of 50% of the excluded articles.²¹ Any disagreements will be resolved through a consensus of the two reviewers. In the case of frequent and/or substantial disagreements, a verification process for any excluded articles is planned. If no disagreements are found, the verification process will not be employed. The main reasons for excluding studies will be recorded.

Charting the data, summarising and reporting the results

A data charting form was developed by one reviewer (BOA) and validated by the other authors (HAOJ, CRFC and GLAO) (table 1). The Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS) checklist will be used to develop the data charting form.²² One reviewer (BOA) will independently extract and record data on the predefined data charting on Excel and all data extracted will be validated by another reviewer (HAOJ). The Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews²¹ and its extensions¹⁹ will be used to report this scoping review.

Table 1 Charting data form

Charting dimensions	Aspects
General study information	
General information	Year of publication Aim of study
Methodological characteristics of included studies	
Data source	Data source category: systematic reviews, clinical trial, prospective cohort; retrospective cohort, cross-sectional study, databases registries, medical records Description of the data source Period
Study population	Participants description Total study sample size
Location	Country and regions
Prediction modelling	Number of models used
Model development	Modelling method (eg, back-calculation, individual-based, hierarchical Poisson models and other available models)
Period of prediction	For example, years, days
Type of prediction modelling studies	Prediction model development without external validation in independent data Prediction model development with external validation in independent data External model validation, possibly with model updating
Number and type of predictors	Variables evaluated for their association with the outcome of interest (eg, demographics and disease characteristics)
Predicted outcome	New cases; under-reporting cases; new confirmed cases Study description: description of the cases that will be assessed
Missing data	Number of participants with missing data for each predictor Handling of missing data (eg, complete case analysis, imputation or other methods)
Was under-reporting considered?	Yes, no or unclear How was it considered in the model (predictor or outcome)
Statistical approaches	Types of statistical approaches
Model predictive performance	Calibration (calibration plot, calibration slope and Hosmer-Lemeshow test) and discrimination (C-statistic, D-statistic and log-rank) measures with CIs, if applicable
Formats of presenting models	Formats including tables, figures, formulas and multiple formats
Software	Any software used to build the model
Limitations	Limitations reported by authors
Conclusion	Main conclusion

After finalising the data charting forms and elucidating the evidence, the two reviewers (BOA and HAOJ) will elaborate a narrative summary and present the summarised findings in tables or using interactive visual representations.

Systematic reporting of the results will consider details of the selection process and the inclusion and exclusion criteria; tabulation of the studies’ characteristics, the participants, the modelling technique and the main conclusions;



qualitative synthesis of the available evidence and study characteristics according to the charting data form (location, model type, prediction period, number and type of predictors and model report); independent assessment of the risk of bias through use of the Prediction Model Study Risk of Bias Assessment Tool, reporting the decision for each domain and the relevant reasons. We will establish the presence of any potential gaps in respect of model type, predictors, prediction period, missing data, outcomes predicted validity and model robustness using the data chart described earlier. Figures and graphs will be used whenever necessary.

Modelling technique identification, reporting and assessment

Transmission models adopted in selected studies will be registered and assessed independent of the modelling technique. Based on a preliminary search, we anticipate finding the following models in the context of leprosy forecasting: SIMLEP, ARMA, ARIMA, mixed-linear and Simcolep, among others. Furthermore, models will be evaluated in respect of the number of participants and completeness, the appropriateness of handling with continuous and categorical predictors, dealing with missing data, the predictor selection mode, model performance measures and other factors. A number of evaluated outcomes are expected in the modelling studies (ie, new case detection rate, under-reporting, evidence of disease elimination, selection of specific subgroups, etc). We intend to aggregate similar outcomes predicted when dealing with the body of evidence and to identify the influence of the model technique on outcome distribution. Some exploratory analysis may be undertaken if data are available and may consider factors such as the country of origin/endemic area, database extension and leprosy classification among others. Data will be deployed and discussed narratively as, due to the anticipated heterogeneity (different countries, outcomes, prediction periods, etc), we do not expect that there will be enough data of sufficient quality to perform a quantitative assessment.

Critical appraisal of included studies

Two reviewers (BOA and HAOJ) will perform the critical appraisal of included studies. Disagreements will be solved by consensus. The Prediction Model Study Risk of Bias Assessment Tool, which includes 20 questions divided into four domains (participants, predictors, outcome and analysis) will be used, if applicable. We will classify risk of bias as low risk, high risk or unclear for each domain.²³

Patient and public involvement

This is a scoping review study with no primary data collection. There was no direct involvement by patients or the general public.

ETHICS AND DISSEMINATION

As there is a wide range of literature on modelling studies for predicting leprosy cases, a comprehensive and robust scoping review is the best approach to identify and map these studies. The findings of this pioneer scoping review

are expected to provide a better understanding of how modelling studies have been designed and conducted, and what are the main limitations and challenges reported in these studies. This knowledge will help to provide a scientific basis for researchers designing and conducting models for predicting leprosy cases. Additionally, the insights of this scoping review could be used to enhance national surveillance systems and target specific policies that indirectly help detect and control leprosy worldwide. The protocol and consequent publications originating from this scoping review will be disseminated through peer-reviewed publications and policy briefs. We will report relevant amendments to this protocol with the results of the scoping review.

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Contributors BOA, HAOJ, CRFC GLAO conceived and designed the study and drafted the manuscript, which was edited and revised by all authors. BOA and HAOJ created electronic search strategies and customised the form for charting data. BOA and HAOJ conducted the study screening and selection, extraction data and risk of bias assessment. CRFC and GLAO provided methodological advice on leprosy disease and made important intellectual contributions to the manuscript. HAOJ, CRFC and GLAO provided supervision. All authors read and approved the final version of the manuscript.

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Competing interests None declared.

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