

Forecasting Modeling Studies For Predicting New Leprosy Cases: Protocol For A Scoping Review

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Protocol

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Abstract

Background: Leprosy is a neglected tropical disease caused by *Mycobacterium leprae* that mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract, and the eyes. Mathematical models and statistical methodology could have a role to play in decision-making for maintaining the gains in elimination programs. Diverse forecasting modeling studies of leprosy cases have been reported in the literature, but there are distinct approaches and settings for predicting the cases being proposed. The purpose of this study is to complete a scoping review to identify and synthesize forecasting modeling studies of leprosy cases.

Methods: A scoping review methodology will be applied following the Joanna Briggs Institute methodology for scoping reviews and will be reported according to PRISMA-ScR. We will perform a systematic search from inception until June 2021 and we will include the following electronic databases: MEDLINE via PubMed, Embase, Cochrane Library, and Lilacs. 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.

Discussion: This scoping review will identify and map the methodological characteristics and further evidence from modeling studies for predicting leprosy cases. Thereby contributing to a scientific basis for researchers to inform, design, and conduct appropriate models for predicting cases of leprosy. This information could be used to enhance national surveillance systems and to target specific policies.

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

Background

Leprosy or Hansen's disease, a neglected tropical disease (NTD), is an infectious disease caused by *Mycobacterium leprae* that mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract, and the eyes (1). Leprosy has physical and psychological consequences that can lead to activity limitations, economic and physical dependence, social exclusion, and stigma (2).

The World Health Organization (WHO) has estimated 202.256 new leprosy patients globally only in 2019. Brazil, India, and Indonesia are responsible for 79% of the burden (3). The WHO Global Leprosy Strategy 2021–2030 aims to eliminate leprosy and is aligned to advancing progress on 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 as *Bacillus Calmette–Guérin* (BCG) vaccination, active case finding, adherence to multidrug therapy, and continued surveillance following treatment (5). Alongside these efforts, there has been an increasing role for quantitative analysis and modeling to support the achievement of these goals through

evaluation of the desirable impact of interventions, the factors that could undermine these achievements and the role of new diagnostics and treatments in reducing transmission (6).

Mathematical models and statistical methodology could have a role to play in decision-making for maintaining the gains in elimination programs (7). Nonetheless, some countries are still facing some challenges in developing a mathematical model that provides an estimate of undetected incident cases that can approximate the reality of cases (4, 8). Undetected cases or underreporting cases of leprosy can occur for many reasons, including the low capacity of health care services or health professionals to diagnose and register new cases of the disease, lack of specific leprosy programs and policies, absence or poor national disease registries, or deficiencies of national or local leprosy programs (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 regarding the target population for treatment and disease control, and prevention actions (7). Several forecasting modeling studies of leprosy cases have been reported in the literature, however, there are distinct approaches and settings for predicting the cases (9-13).

As there is no information regarding studies that mapped the main methodological characteristics of the modeling studies for prediction of leprosy cases, the purpose of this study was therefore to complete a scoping review to identify and synthesize forecasting modeling studies of leprosy cases. Specifically, we aimed to: (1) chart the characteristics and range of methodologies used in the identified studies, (2) map out the main predictions made by the identified studies (3) uncover gaps and limitations of the research field, and (4) propose recommendations for advancing the approach and enhancing the applicability and consistency of modeling studies of leprosy cases.

Methods

Study design

We chose a scoping review methodology to map how modeling studies for predicting cases of leprosy are being designed and conducted (type of statistical approach; mathematical modeling applied; extension of prediction; variables included in the model; quality and robustness of the models), and what are the main predictions and conclusions reported in these studies. This scoping review was developed using the methodological framework proposed by Arksey and O'Malley (14) and refinements by the Joanna Briggs Institute (15). The present protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for protocols (PRISMA-P) (16) (**Additional File 1**). This scoping review has been registered with the Open Science Framework (<https://doi.org/10.17605/OSF.IO/W9375>).

Research Question

The research question for this scoping review is "What are the main methodological characteristics and results of modeling studies for prediction of cases of leprosy?". A structured question with inclusion and exclusion criteria was developed following the acronym PCC - Population, Concept, and Context.

Population

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 subsidize the decision-making process regarding neglected tropical diseases, there is a need to know what the estimate for new cases of leprosy in the future is, mainly in endemic areas like Brazil, India, and Southeast Asia (WHO, 2021b). Thus, it is of paramount importance to understand the methodological characteristics of all modeling studies developed for predicting cases of leprosy (forecasting models), and the main model assumptions and conclusions reported by these studies. We will include studies evaluating or predicting new future cases or underreporting/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 known that nowadays we work with underreporting estimates for leprosy, which makes it difficult for the decision-making process. Thus, there is a need for mapping the methodological characteristics of studies that predict cases of leprosy to provide robust evidence that can be used to support health system planning and surveillance and implementation of leprosy health policies. We will include studies with no restriction regarding the study context (eg, health care settings) or data source (e.g. primary data or secondary data).

Evidence sources

We have adopted an extension to the PRISMA statement for Reporting Literature Searches in Systematic Reviews (PRISMA-S)(17). A comprehensive search of general electronic databases and a manual search will be done to identify relevant studies (from inception up to 16 June 2021). We will include the following electronic databases: Medline via PubMed, Embase, Cochrane Library, and Latin American and Caribbean Health Science (LILACS). A detailed description of the search strategy is available in **the Additional File 02**. A manual search in the references of all included studies will be done. Also, 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 was performed independently by two reviewers (BOA and HAOJ).

Search Strategies

To build the search strategies, we have used controlled vocabulary as Medical Subjects Headings (MeSH) for PubMed and Cochrane, Embase Subjects Headings (Emtree) for Embase, and "*Descritores em saúde*"

(Decs) for LILACS. We also used uncontrolled vocabulary as keywords, entry terms, synonyms, and relevant related terms. No restrictions on the publication year were made.

Screening and selection process

All studies identified in the search will be export to EndNote® to manage the records and to identify and remove duplicates. Afterward, we will import all records to Rayyan® to re-check duplicate and then, perform the blinded selection process (18).

Our comprehensive search retrieved a considerable amount of records, for this reason, 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 (19). The full-length articles will be downloaded, and one reviewer (BOA) will assess the eligibility of each pre-selected study. A second reviewer (HAOJ) will assess the full eligibility of a sample of 50% of the excluded articles (19). 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 reason for excluding studies will be recorded.

Charting the Data, Summarizing and Reporting the Results

A data charting form was developed for one reviewer (BOA) and validated by the other members (**HAOJ, CRFC, GLAO**) (**Table 1**). The Critical appraisal and data extraction for systematic reviews of prediction modeling studies (the CHARMS checklist) was used to develop the data charting form (20). 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). A descriptive analysis of the data will be conducted. The Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) (19) and its extensions (17) will be used to report this scoping review.

Table 1. Charting data form.

Charting dimensions.	Aspects
General study information	
General information	<i>Year of Publication</i> <i>Aim of study</i>
Methodological characteristics of included studies	
Data source	<i>Data source category: systematic reviews, clinical trial, prospective cohort; retrospective cohort, cross-sectional study, databases registries, medical records;</i> <i>Description of the data source</i> <i>Period</i>
Study Population	<i>Participants eligibility</i> <i>Participants description</i> <i>Total Study Sample Size</i>
Location	<i>Country and regions</i>
Prediction Modeling	<i>Number of models used</i>
Model development	<i>Modeling method (e.g., back-calculation, individual-based, hierarchical Poisson models)</i>
The time of prediction	<i>Period of prediction (e.g. years, days.)</i>
Type of prediction modeling studies	<i>Prediction model development without external validation in independent data;</i> <i>Prediction model development with external validation in independent data</i> <i>External model validation, possibly with model updating</i>
Number and type of predictors	<i>Variables evaluated for their association with the outcome of interest (e.g., demographics, disease characteristics)</i>
The outcome to be predicted	<i>New cases; underreporting cases; confirmed cases;</i> <i>Study description: description of the cases that will be assessed.</i>
Missing data	<i>Number of participants with missing data for each predictor</i> <i>Handling of missing data (e.g., complete-case analysis, imputation, or other methods)</i>
Underreporting was considered?	<i>Yes, no, or unclear</i>

Charting dimensions.	Aspects
Statistical Approaches	<i>Types of statistical approaches</i>
Model Predictive Performance	<i>Calibration (calibration plot, calibration slope, Hosmer-Lemeshow test) and Discrimination (C-statistic, D-statistic, log-rank) measures with confidence intervals</i>
Formula presented	<i>Formula available</i>
Softwares	<i>Any software used to build the model</i>
Relevant results of the included studies	
Predictions	<i>Prediction for each model and population</i>
Interpretations	<i>Interpretation of presented model</i>
Limitations	<i>Limitations reported by authors</i>
Conclusion	<i>Main conclusion</i>

Critical appraisal of included studies

Two reviewers (BOA, HAOJ) will perform the risk of bias assessment. Disagreements will be solved by consensus. The Prediction model study Risk of Bias Assessment Tool (PROBAST), which includes 20 questions divided into four domains (participants, predictors, outcome, and analysis) will be used. We will classify as low risk, high risk, or unclear each domain of risk of bias (21).

Discussion

Since there is a broad literature of modeling studies for predicting leprosy cases, a comprehensive and robust scoping review of the literature 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 modeling studies have been designed and conducted, what are the main predictions and conclusions made, and what are the main limitations and challenges reported in these studies. This knowledge would give a scientific basis for researchers to inform, design, and conduct appropriate models for predicting leprosy cases. Additionally, the insights of this scoping review could be used to enhance national surveillance systems and to target specific policies, and indirectly, to help to detect and control leprosy worldwide. The protocol and consequent publications of this scoping review will be disseminated through peer-reviewed publications and policy brief. We will report relevant amendments to this protocol with the results of the scoping review.

Abbreviations

PCC: Population, Concept, and Context;

NTD: Neglected Tropical Disease

WHO: World Health Organization

BCG: Bacillus Calmette–Guérin

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for protocols

LILACS: Latin American and Caribbean Health Science

MESH: Medical Subjects Headings

Emtree: Embase Subjects Headings

Decs: Descritores em saúde

CHARMS: Critical appraisal and data extraction for systematic reviews of prediction modelling studies

PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews

PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews

PROBAST: Prediction model study Risk of Bias Assessment Tool

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Additional file 1. PRISMA for systematic review protocols (PRISMA-P) Checklist. Source: Moher et al. (16).

Additional file 2. Search Strategies of electronic databases.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

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

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