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INPLASY

Descriptive analysis of epidemiologic and clinical trends in Leprosy in the US: A systematic review protocol

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202540016

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 April 2025 and was last updated on 6 April 2025.

INTRODUCTION

Review question / Objective This systematic review examines trends of HD cases in the U.S.(Including Hawaii and Alaska before US statehood), evaluates the role of zoonotic and locally acquired infections, and provides insights to support early diagnosis and public health strategies.
This systematic review aims to:
1. Characterize the epidemiology of leprosy in the U.S.(Including Hawaii and Alaska before US statehood) over time by analyzing case counts, demographic factors, geographic distribution, and reported modes of transmission from published data.
2. Assess diagnostic methods and treatment patterns in the U.S.(Including Hawaii and Alaska before US statehood) over time.
3. Provide insights for public health and clinical practice by summarizing trends, challenges, and potential areas for improved HD surveillance and management in the U.S. (Including Hawaii and Alaska before US statehood).

Rationale The WHO's current leprosy control strategy focuses on interrupting transmission; however, this goal remains unattainable without a clearer understanding of zoonotic and autochthonous cases in the U.S.(Including Hawaii and Alaska before US statehood). Findings from this review are expected to have implications beyond national borders, informing global HD surveillance and mitigation strategies.

Condition being studied Prevalence and incidence, transmission, presentation, and management of leprosy.

METHODS

Search strategy The following electronic databases(complete list in information sources below) without publication status restrictions will be searched:
Scopus search was within Article title; Abstract, and Keywords. Emabase search included the following mapping options: Map to preferred term

in Emtree, Search also as free text in all fields, Explode using narrower Emtree terms, Search as broadly as possibles
Search Terms
((“Leprosy”) OR (“Hansen's disease”)) AND (“United States”)
Grey Literature Sources
– Conference abstracts (if unique and not duplicated in peer-reviewed studies)
– Public health surveillance reports.

Participant or population All patients reported in selected studies with a suspected or confirmed leprosy diagnosis without gender, ethnicity, age, or other personal restrictions.

Intervention The review does not primarily focus on evaluation of interventions but as a temporal review of leprosy in the US, diagnosis and treatment practices were reviewed.

Comparator Not applicable.

Study designs to be included Case reports, case series, observational studies, and surveillance data.

Eligibility criteria
-Full-text articles published in English
-Studies reporting on human cases of Hansen’s Disease diagnosed in the U.S. or its territories.
-Case reports, case series, observational studies, and surveillance data.

Information sources Medline(via Pubmed), Emabase, Scopus, Web of Science.

Main outcome(s) Primary outcomes: Case counts, study type, publication year, study period, age, sex, race, ethnicity, U.S. city or state of diagnosis, place of residence at diagnosis, country of birth, family origin, mode of transmission, family history of leprosy.

Additional outcome(s)
Secondary outcomes:
Initial diagnoses
Duration of onset to diagnosis
Duration of onset to diagnosis units
WHO classification
Ridley Jopling classification
PCR performance
PCR result
Slit skin smear performance
Biopsy performance
Case confirmation method
Medications/treatments prescribed, and strength of evidence
Disability/deformity at diagnosis
Reports of adverse events, side effects
Leprosy reaction
Neuropathy
Deformities of hands and feet
Functional impairment
Eye involvement
WHO disability grading
Symptoms.

Data management The Covidence platform will be used to sort the data and eliminate records that do not meet inclusion criteria or fulfill exclusion criteria. This process will be summarized in a Prisma flowchart. Thereafter, the researcher(s) performing the sorting will record a complete list in an Excel document and later assign the articles to the extraction team. Extraction data will be recorded in predefined rubrics(specified in the protocol) of an Excel data collection document. Each extractor will submit their portion of extracted data periodically via email to the analyzing team. Since the data does not include any protected information, no additional precautions were taken during the manipulation and sharing of this data. R software was also used in the processing and sorting of the data.

Quality assessment / Risk of bias analysis This systematic review primarily focuses on observational studies, and thus, does not require the evaluation of risk of reporting bias through standardized tools, such as the Cochrane Collaboration tool. Thus, we will use a study-specific assessment of bias, such as the presence of confirmatory testing, to assess the strength of diagnosis and to account for potential reporting bias.

Strategy of data synthesis
The data will be analyzed via quantitative and qualitative synthesis as described below:
Quantitative Synthesis
-Descriptive statistics summarizing demographic and clinical features.
-Aggregation of case counts from non-overlapping studies to assess national trends.
-Temporal trend analysis using R statistical software (v.4.2.2).

Qualitative Synthesis
-Thematic synthesis of emerging trends (e.g., zoonotic transmission, shifting case demographics).

Subgroup analysis The following subgroup analyses may be performed to clarify underlying trends. Analyses may be disaggregated by age, sex, country of birth, country of origin, state of clinical presentation, mode of transmission, decade or other temporal grouping.

Sensitivity analysis A sensitivity analysis will be conducted to guarantee the robustness of study conclusions and to verify that findings remain stable after excluding lower-quality studies. Excluded studies may include those of lower-study quality, studies lacking rigorous case definitions. Studies to be excluded may also include case reports and case series, those not meeting a sample size threshold, n >5, or grey literature. Studies before Multi-Drug Therapy availability may also be excluded for sensitivity analysis. Additionally, studies missing key variables including transmission mode or geographic location may be excluded.

Language restriction English only articles.

Country(ies) involved Unites States of America.

Other relevant information
Data extraction rubrics (these rubrics may be adjusted or updated during the course of the study):
Case reports & case series
Authors
Title
Publication year
Is Covidence link correct (Y/N. If incorrect, highlight row in red and a PDF file will be shared)
Study start/end day, month, and year (if available)
Reviewer
Case count = 1 (to represent 1 case per row)
Study type (case report, case series)
Age
Sample size (1 for case report, n for case series sample size)
Sex (assigned at birth assumed, M or F)
Race (White, Black or African American, Asian, Asian/Pacific Islander, Native Hawaiian or Other Pacific Islander, or Not stated)
Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not stated)
Setting..U.S..city.or.state.of.diagnosis (Two letter state abbreviation, e.g. LA, TX)
Place of residence at time of diagnosis (Two letter state abbreviation, e.g. LA, TX)
Country of birth
Family origin (Yes, No, Not stated)
Mode of transmission (Military service abroad, community human contact, zoonoses, not stated)
Family hx of leprosy (Yes, no)
Initial diagnosis (Syphilis, Inflammatory disease, Mycosis fungoides, ringworm, and other drop-down options added. Free text available too)
Duration of onset to diagnosis (numeric value)
Duration of onset to diagnosis units (Years, months, weeks, days)
WHO classification (PB, MB, Not applicable, Not stated)
Ridley Jopling classification (Lepromatous, Tuberculoid, Borderline tuberculoid, borderline lepromatous, borderline (non-specified), Not applicable, Not stated)
Leprosy reaction (Yes, No, Not applicable, NA)
Neuropathy (Y/N)
Deformities of hands and feet (Y/N)
Functional impairment (Y/N)
WHO disability grading: hands and feet (G0, G1, G2)
Eye involvement (Y/N)
WHO disability grading: eyes (G0, G1, G2)
Adverse events (Y/N)
What symptoms?
If other(s) [text]
PCR performed (Y, N, NA, Not applicable)
PCR result (M.leprae, M. lepromatosis, Negative M. leprae, Positive, Positive M. lepromatosis, Unknown, etc.)
Slit skin smear performed (Y or N)
Biopsy performed (Y or N)
Confirmed case defined by: (lab exam, non-specific mention of lab exam)
Adverse effects from treatments (Immune-mediated reactions, drug induced toxicities, neurological and sensory complications, severe systemic effects, corticosteroid-related complications, Infectious and wound-related complications, NA)
Disabilities.deformities.at. diagnosis.Y.N. (Y, N, Not stated)
If.yes..description.of.disabilities.deformities (Neurological impairments, Sensory loss, Deformities, Ulceration, Systemic Complications, Non-specific/Unstated, NA, Not applicable)
Strength of evidence (Level 4, Level 5)
Meds (list of n = 40, insert 1 = Yes, 0 = No)

Population-based “epi” studies
Authors (count data not necessary, used for study ID confirmation)
Title (count data not necessary, used for study ID confirmation)
Publication year (count data not necessary, used for study ID confirmation)
Is Covidence link correct (Y/N. If incorrect, highlight row in red and a PDF file will be shared)
Study start/end day, month, and year (if available)
Reviewer

Case count (can put N sample size here. In some retrospective reviews that present individual-level data, case count = 1)
Study type (Retrospective cohort study, epidemiological report, historical review, Cross-sectional study, etc.)
Sample size (N)
Male (n, %)
Female (n, %)
Mean age (if available)
Median age (if available)
Age (=60 yrs)
Race category (you may need to create new race category columns to populate with n and/or %. I've included a few to start)
Ethnicity category (n, you may need to create a new ethnicity or descent category column to populate with n and/or %. I've included a few to start)
Country of birth (you may need to create new country of birth columns to populate with n and/or %. I included some to start)
Family origin (n, you may need to add separate columns/variables for each country if the country mentioned is not available)
Place of residence at time of diagnosis (n, you may need to create a new U.S. state place of residence column if needed. I included some to start)
Mode of transmission (separate variables for military service abroad, community human contact, zoonoses, and not stated. Enter n and or % if available)
Initial diagnosis besides leprosy (initial_dx)
Setting..U.S..city.or.state.of.diagnosis (Some state columns have been added, but more are needed)
WHO Classification
Ridley Jopling Classification (more columns may need to be created. Previous reviewers listed additional entries including "dimorphous", "lepra tuberosa", "lepra maculo anesthetic", etc.)
Leprosy reaction (Yes, No, NA)
Neuropathy (Y/N)
Deformities of hands and Feet (Y/N)
Functional impairment (Y/N)
WHO disability grading: hands and feet (G0, G1, G2)
Eye involvement (Y/N)
WHO disability grading: eyes (G0, G1, G2)
Adverse events (Y/N)
Family history of leprosy (Y/N/NA)
PCR performed (Y or N)
PCR result (M.leprae, M. lepromatosis, Negative M. leprae, Positive, Positive M. lepromatosis, Unknown, etc.)
Slit skin smear (Y or N)
Biopsy performed (Y or N)
Resolved (Y or N)
Strength of evidence
Treatments prescribed.

Keywords Leprosy, Hansen's disease, HD, US, USA, United States, Zoonotic transmission, Military.

Dissemination plans Publication Plan: Submission to peer-reviewed journals, and conference presentations.
Policy Implications: Recommendations for leprosy surveillance and intervention strategies in the U.S.

Contributions of each author

Author 1 - Will Eaton - Contributions include: review conception and design, review protocol writing, review coordination, data collection, data extraction, data analysis and interpretation, manuscript writing.
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