

Prevalence of leptospirosis in goats in Brazil: systematic review and meta-analysis protocol

1. Registration and Authorship Information

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- **Conflict of Interest:** The authors declare no conflict of interest.

2. Introduction (Rationale/Background)

Leptospirosis is an infectious and contagious zoonotic disease caused by spirochetes of the genus *Leptospira* spp., with a cosmopolitan distribution and a major impact on One Health (Adler & de la Peña Moctezuma, 2010). In goat farming, the infection results in direct economic losses due to reproductive failures, such as abortions, stillbirths, the birth of weak animals, and a drop in milk production (Ellis, 2015).

Brazil has one of the largest goat herds in the world, predominantly concentrated in the Northeast region (IBGE, 2022). The territorial extent, diversity of biomes, and management systems (extensive, semi-intensive, and intensive) create a complex epidemiological scenario for maintaining the agent in the environment (Martins & Lilenbaum, 2013).

Although there are primary studies evaluating the prevalence of caprine leptospirosis in different Brazilian states and regions, there is, to date, no pooled estimate representing the national scenario (Araújo Neto et al., 2010). This review aims to fill this gap by providing consolidated data to guide epidemiological surveillance and prophylaxis strategies in preventive veterinary medicine.

Accurate mapping of the circulating serovars in the field is something that must be elucidated. Currently, the available commercial vaccines are mostly formulated for cattle or swine and often do not confer cross-protection against the specific strains affecting small ruminants in different regional realities (Ellis, 2015; Martins & Lilenbaum, 2013). Thus, by estimating the global prevalence of *Leptospira* spp. infection in goats in Brazil, this review will provide an epidemiological foundation to justify the need for vaccination and guide the formulation of strategic vaccine protocols, encompassing the incentive to develop vaccines targeted at the herd's specific needs.

3. Objectives

- **Primary Objective:** To estimate the global prevalence of *Leptospira* spp. infection in goats in Brazil.
- **Secondary Objectives:**
 1. To identify the most frequent serogroups/serovars in the Brazilian goat herd.
 2. To investigate sources of heterogeneity through subgroup analyses, such as geographic region, biome, season, diagnostic method, herd size, and the existence of a vaccination protocol.

4. Methods

4.1. Eligibility Criteria (Condition, Context, and Population - CoCoPop)

- **Condition (Co):** Infection by *Leptospira* spp., where the prevalence of the infection will be evaluated, defined by the proportion of positive animals in relation to the total number of tested animals.
- **Context (Co):** Herds located in Brazilian territory, seeking to represent the epidemiological scenario in Brazil.
- **Population (Pop):** Goats (*Capra hircus*), regardless of breed, age, or aptitude (meat/milk).
- **Study Design:** Descriptive and analytical observational studies (cross-sectional).
Diagnostic Tests: Studies using validated reference methods, specifically Microscopic Agglutination Test (MAT) and/or molecular biology tests, such as PCR.

4.1.2. Exclusion Criteria

- **Exclusion Criteria:** Isolated case reports, case series without a defined population base, literature reviews, studies with animals outside of Brazil, controlled animal experimentation (challenges), and studies with a sample size of fewer than 30 animals.

4.2. Search Strategies and Information Sources

The bibliographic search will be conducted in the following electronic databases, with no publication date restriction: PubMed, Scopus, Web of Science, SciELO, and LILACS. The grey literature search will be performed in the Brazilian Digital Library of Theses and Dissertations (BDTD) and Google Scholar (first 200 results).

The retrieval of metadata (titles, abstracts, and publication information) will be stratified according to the availability of native and free integrations. In the PubMed and SciELO databases, extraction will be automated through scheduled routines programmed in the Python language (Python Software Foundation, 2021).

For PubMed, the Entrez module from the Biopython library (Cock et al., 2009) will be used to access the NCBI API, while for SciELO, the platform's native and open ArticleMeta API will be used. The metadata retrieved from these databases will be structured into dataframes using the Pandas library (McKinney, 2010).

Conversely, due to automation blocks, the lack of official public APIs, or commercial subscription restrictions for mass use, for the Scopus, Web of Science, LILACS, BDTD, and Google Scholar databases, the search and export of citation files will be conducted manually, using the native export features of each interface.

Base Search String (PubMed Example):

("Leptospira"[Mesh] OR "Leptospirosis"[Mesh] OR leptospir* OR "doença de weil") AND ("Goats"[Mesh] OR goat* OR caprine* OR caprino*) AND ("Brazil"[Mesh] OR brazil* OR brasil*)

4.3. Study Management and Selection

The retrieved references, both via automated and manual search, will be exported to the Mendeley Desktop manager (Elsevier) for duplicate removal. The screening will be performed in two phases using the Rayyan software (Ouzzani et al., 2016):

1. Reading of titles and abstracts by two independent reviewers.
2. Full-text reading of the pre-selected articles to confirm eligibility criteria.

Disagreements will be resolved by consensus or by the intervention of a third reviewer.

4.4. Data Extraction

Data will be extracted into a standardized spreadsheet containing the following domains:

Domínio	Variáveis a Extrair
Identification	First author, DOI, Publication year, Data collection period.
Local Characteristics	State, Region (N, NE, CW, SE, S), Biome, Season, Farming system.
Population Characteristics	Sample size (n), Aptitude (milk, meat, mixed), Category.
Diagnostic Tests	Method used (MAT, PCR, ELISA).
Outcomes	Number of positive animals, Apparent prevalence, Main serovars/serogroups identified.

4.5. 4.5. Methodological Quality Assessment (Risk of Bias)

The quality of cross-sectional studies will be assessed independently by two reviewers using the Joanna Briggs Institute (JBI) critical appraisal tool for prevalence studies. Studies will not be excluded based on the risk of bias, but this metric will be used for sensitivity analysis.

4.6. Data Synthesis and Statistical Meta-Analysis

- **Model:** Prevalences will be grouped (pooled prevalence) using a random-effects model, assuming high heterogeneity among populations and management in different regions of Brazil.
- **Transformation:** The Freeman-Tukey double arcsine transformation or Logit transformation will be applied to stabilize variances, which is especially useful for prevalences close to 0% or 100%.
- **Heterogeneity:** Statistical heterogeneity will be quantified using the I^2 statistic and Cochran's Q test.
- **Subgroup Analysis and Meta-regression:** Conducted to identify sources of variability.
- **Publication Bias:** Will be assessed visually through funnel plots and statistically by Egger's test (for a number of studies ≥ 10).

- **Software:** The analyses will be processed in the R language, using the *meta* and *metafor* packages.

5. 5. Bibliographic References

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6. Appendix A - Complete Search Strategies

1. PubMed

The PubMed database uses MeSH (Medical Subject Headings) descriptors combined with free-text search fields.

("Leptospira"[Mesh] OR "Leptospirosis"[Mesh] OR leptospir* OR "doença de weil" OR "doença de weil") AND ("Goats"[Mesh] OR goat* OR caprine* OR caprino*) AND ("Brazil"[Mesh] OR brazil* OR brasil*)

2. Scopus (Elsevier)

The Scopus database does not use MeSH. The standard and most sensitive search strategy focuses on the Title, Abstract, and Keyword fields, represented by the TITLE-ABS-KEY code. TITLE-ABS-KEY (("Leptospira" OR "Leptospirosis" OR leptospir* OR "doença de weil" OR "doença de weil") AND ("Goats" OR goat* OR caprine* OR caprino* OR "Capra hircus") AND ("Brazil" OR brazil* OR brasil*))

3. Web of Science

In Web of Science, topic searches (Title, Abstract, Author Keywords, and Keywords Plus) are triggered by the TS= field tag.

TS=("Leptospira" OR "Leptospirosis" OR leptospir* OR "doença de weil" OR "doença de weil") AND TS=("Goats" OR goat* OR caprine* OR caprino* OR "Capra hircus") AND TS=("Brazil" OR brazil* OR brasil*)

4. SciELO

SciELO has a simplified search interface. To ensure comprehensive retrieval, direct insertion of terms into free fields is recommended, allowing automatic scanning in titles, abstracts, and keywords.

(leptospira OR leptospirose OR leptospirosis OR leptospir* OR "doença de weil" OR "doença de weil") AND (goat* OR caprine* OR caprinos OR caprino) AND (brazil* OR brasil*)

5. LILACS (via VHL Regional Portal)

LILACS uses DeCS (Health Sciences Descriptors), which are equivalent to MeSH. The mh: tag searches for the exact descriptor, while tw: searches for the word in any text field (text word).

(mh:"Leptospira" OR mh:"Leptospirose" OR tw:leptospir* OR tw:"doença de weil" OR tw:"doença de weil") AND (mh:"Caprinos" OR tw:goat* OR tw:caprine* OR tw:caprino*) AND (mh:"Brasil" OR tw:brazil* OR tw:brasil*)

This protocol follows the recommendations of the PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) guidelines.