

# Scoping review protocol on control strategies for *Echinococcus granulosus*

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# ABSTRACT

**Introduction** Cystic echinococcosis (CE), previously known as hydatidosis, is one of the most important zoonotic parasitic diseases of humans and livestock caused by the larval stage of the canine tapeworm *Echinococcus granulosus sensu lato*. Cystic echinococcosis has great economic and public health significance with a worldwide distribution. It is listed among the most severe parasitic diseases in humans, representing one of the 17 neglected diseases prioritised by the World Health Organisation.

**Methods and analyses** This study will review the literature on *Echinococcus granulosus* control strategies until 2022. This will be achieved by searching for English, Spanish, and Portuguese peer-reviewed articles in the following electronic databases MEDLINE (via PubMed), EMBASE, SCOPUS, Web of Science, and Global Index Medicus to locate the relevant articles. We will perform a grey literature search including the American Society of Tropical Medicine Annual Conference Abstract Book from 2017 to 2022, the World Association of Echinococcosis Congress Abstract Book from 2017 to 2022, Google Scholar (first 200 hits), and review the references of the selected articles. No restrictions on study design will be applied. We will develop a systematic search strategy using a combination of keywords and Boolean operators AND/OR. Eligibility screening and data extraction will be conducted by two independent reviewers, and disagreements resolved by a third independent reviewer.

**Ethics and dissemination** Ethical review is not required as scoping reviews are a form of secondary data analysis that synthesises data from publicly available sources. Review findings will be shared with researchers, public health authorities, and other relevant stakeholders and disseminated through a peer-reviewed publication and conference presentations. This protocol is registered on the Open Science Framework ([www.osf.io](http://www.osf.io)) with DOI [10.17605/OSF.IO/48AZR](https://doi.org/10.17605/OSF.IO/48AZR).

# INTRODUCTION

Cystic echinococcosis (CE) is a neglected zoonosis caused by *Echinococcus granulosus sensus lato*, a cestode that represents a public health priority due to its worldwide distribution and human health repercussions. CE is most prevalent in the Mediterranean area, Eurasia, South America, and North and East Africa (1,2). CE affects livestock, producing financial losses and impacting rural livelihoods, as well as humans with 2-4% of mortality reported and more than 20,000 new cases reported in countries of South America in a 5-year period (3,4). The approximate economic losses related to CE human infection total 760 million US\$ and annual livestock production losses amount to at least US\$ 3 billion (5,6).

The complex life cycle of *Echinococcus granulosus s.l.* includes definitive, intermediate, and accidental intermediate hosts. Herbivorous animals act as intermediate hosts, infected by ingesting the parasite eggs in contaminated pasture or water, developing the larval cysts in internal organs, mainly in livers and lungs. The definitive host, usually wild or domestic canids (dogs), are infected through the consumption of cyst-containing organs of intermediate hosts. Humans are accidental intermediate hosts, acquiring the infection by accidentally swallowing *Echinococcus granulosus s.l.* eggs. The most common intermediate hosts are sheep, though other domestic animals may also act as intermediate hosts, including goats, swine, cattle, camels, and yaks (7,8).

Control of CE has the objective of reducing the incidence of the disease in both humans and animals. Common interventions to prevent infection focus on the interruption of the biological cycle through canine deworming, management of dog populations, vaccination of sheep, development of health infrastructure, and epidemiological surveillance, among others (9,10). In 2017, Craig et. al. compiled successful interventions in New Zealand, Tasmania, Cyprus, and Chile, focusing on the consecutive treatment of dogs with Praziquantel (11). Nonetheless, this type of strategy presents operative challenges, such as underdosage and dog owners' approval (or compliance). Educational programs could be necessary to improve the understanding of the disease and increase the acceptance of other interventions such as sheep chemotherapy, dog population management through sterilisation, and overall sustainability of long-term interventions (12,13). Other integrative alternatives for CE management that have been suggested are task forces focusing on education, One Health, surveillance, and diagnostics activities (14-16).

Despite social, environmental, and economical differences across countries impacted by CE, a shared characteristic is the inadequate reporting of cases produced by poor surveillance impeding advances in disease control. It is necessary to review the literature on field interventions and control strategies for *E. granulosus s.l.* with a view to recognizing initiatives that could enhance epidemiological surveillance and other control measures. Systematizing and documenting implemented strategies worldwide will allow extracting insights and identifying gaps that can lead to the creation of new interventions, control-centred guidelines, and public health policies.

We propose a comprehensive revision of the literature using the methodology of a scoping review. We aim to identify the scientific rationale, objectives, and efficacy/effectiveness of various

interventions, and provide a full and accurate picture of the current state of *E. granulosus* s.l. control interventions worldwide, to gain new insights for future research and public health work in this field.

## METHODS

We will carry out a scoping review as we want to map all available evidence on interventions for *E. granulosus* s.l. control. As echinococcosis is a neglected disease, instead of specific/pointed questions, we consider it best to keep a broad scope so that we can access as much of the available information as possible. To do this, a scoping review is deemed more appropriate.

This scoping review will follow the guidance of the JBI Manual for Evidence Synthesis for scoping reviews (17), and further recommendations (18-21), in order to explore all evidence available systematically. The content of this protocol was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols Extension for Scoping Reviews (PRISMA-ScR) (22), furthermore, the content of the methodology of this review follows the Arksey and O'Malley Framework (18) consisting of five stages.

### Stage 1: Identifying the research questions

This review aims to (i) map all evidence available regarding field interventions looking to control, reduce or eliminate Echinococcosis in endemic areas and, (ii) identify research gaps that can lead to future successful interventions. The following questions were formulated to guide this review:

1. What strategies have been implemented, piloted, or tested to reduce, control, or eliminate *Echinococcosis granulosus* infection in animals and/or humans?
  - a. What was the rationale for the study/intervention?
  - b. Who were the targets? (e.g. rural/urban, animals/human, older vs younger sheep)
  - c. What barriers/facilitators were encountered?
2. For each intervention found in question 1
  - a. What was the efficacy/effectiveness outcome?
  - b. Was there any safety outcome? (e.g., adverse effect, increased mortality)
  - c. How long has the program/intervention worked? Is it still in place?
  - d. What kind of modifications/changes has the intervention undergone over time?

### Stage 2: Identifying relevant studies

To locate the relevant studies, we will develop a search strategy in stages. We will initially outline a search strategy for databases and search engines for published data, followed by reference scanning and grey literature search for unpublished or difficult-to-find studies.

We will search in MEDLINE (via PubMed), EMBASE, SCOPUS, AGRICOLA, Web of Science, and Global Index Medicus. An initial search will be carried out in MEDLINE and later adapted for other databases. The search strategy will be outlined by the research team with the support of a librarian. The full strategy is available in Appendix 2.

The review will be conducted according to the Peer Review of Electronic Search Strategies (PRESS) guidelines to improve quality and reduce errors (23). The search will include all studies until December 2022. We will scan the reference lists of included studies to identify additional relevant sources. Authors of primary sources will be contacted should any further information be required.

We will perform a grey literature search including the American Society of Tropical Medicine Annual Conference Abstract Book from 2017 to 2022, the World Association of Echinococcosis Congress Abstract Book from 2017 to 2022, Google Scholar (first 200 hits), and review the references of the selected articles. The results from all searches will be imported and organised in the Covidence software□.

### **Stage 3: Study selection**

In stage 3, we will use a two-step approach to filter the studies found in stage 2:

- 1) Screening by title and abstract
- 2) Full-text screening.

The team will use the eligibility criteria to select the studies:

- Studies evaluating interventions to reduce, control, or eliminate echinococcosis by *Echinococcus granulosus s.l.* infections in animals/humans.
- Studies containing descriptions of or suggested interventions.

Studies that include vaccines as components of field interventions will be included; however, studies whose primary endpoint is to evaluate the efficacy of vaccines will be excluded.

Because our objective is to include all evidence available, we will not restrict studies by date or region. We will consider publications in English, Spanish, and Portuguese. Publications written in other languages will be excluded.

#### *Titles and abstracts screening*

Titles and abstracts imported to Covidence software□ will be evaluated by two pairs of independent reviewers, who will check eligibility and filter out duplicates.

A random sample of 10 titles and abstracts will be piloted and screened by all four reviewers using the eligibility criteria. The results of both teams will be compared, discrepancies will be discussed, and if necessary, the eligibility criteria and definitions/elaboration document/terms will be refined. The team will only start the actual screening after disagreements are discussed and a consensus is reached. If a consensus is not reached, an additional reviewer will be consulted.

### *Full-text screening*

The final list of screened studies for full-text review will be reviewed by two pairs of reviewers for eligibility. A sample of 10 studies will be piloted to assess reviewers' agreement, following the same previous methodology.

The process of full-text review will be conducted by four reviewers grouped in pairs. The inclusion of the article and data extraction from it must obtain the agreement of at least two reviewers. If an agreement is not reached, discrepancies will be resolved by a third reviewer. We will use an electronic form for reviewers referencing and tracking, and documentation of excluded studies. For critical appraisal, we will use the Risk of Bias 2 (RoB 2) tool for RCT studies (24) and the Mixed methods appraisal tool (MMAT) (25) for non-RCT studies.

### **Stage 4: Data charting**

Studies included will be charted and coded in an Excel<sup>®</sup> sheet developed by the research team. Key information recorded will include (but not be limited to): author(s), year of publication, and methodology. Following the established methodology for scoping reviews, we will begin the charting with a pilot study test of five (05) articles using the data extraction template to assess consistency between reviewers and to ensure that their approach is aligned with the objectives of the scoping review. If there are inconsistencies, the research team will review, discuss and make changes to the data abstraction template as necessary.

### **Stage 5: Collating, synthesis, and reporting results**

The data found will be first divided into types of intervention and will be classified according to the associated pathophysiology mechanism (elimination of parasites, population control of hosts, management of sick human/animal population, among others) and their target population.

For each type of intervention, we will describe the efficacy or effectiveness and the safety outcome, also the associated variables, and the barriers/facilitators found. The results will be presented in figures and tables respectively. For studies with qualitative results, a synthesis of the main variables will be presented. The general characteristics of included studies will be summarised.

**Patient and public involvement**

Patients or the public were not involved in the development of this protocol.

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**Contributors:** All authors contributed to conceptualising, designing, writing, and reviewing this protocol.

**Competing interests:** None declared.

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# APPENDICES

## APPENDIX 1: RECOMMENDED ITEMS TO ADDRESS IN A SCOPING REVIEW PROTOCOL

Section and topic	Item No	Checklist item	Page#
<b>ADMINISTRATIVE INFORMATION</b>			
Identification	1a	Identify the report as a protocol of a scoping review	
Update	1b	If the protocol is an update of a previous scoping review, identify it as such	
Registration	2	If registered, provide the name of the registry (such as JBI) and the registration number.	
<b>Authors:</b>			
Contact	3a	Provide name, institutional affiliation, email address of all protocol authors; provide physical mailing address of corresponding author	
Contributions	3b	Describe the contributions of the protocol authors and identify the guarantor of the review	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	
<b>Support:</b>			
Sources	5a	Indicate sources of financial or other support for the review	
Sponsor	5b	Provide the name of the review funder and/or sponsor	
Role of sponsor or funder	5c	Describe the roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known (Note: Consider providing a rationale for the choice of conducting a scoping review as compared to other evidence synthesis approaches)	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to the inclusion/ exclusion criteria	
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, timeframe) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other gray literature sources) with planned dates of coverage	

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility, and inclusion)	
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any preplanned data assumptions and simplifications (Note: Scoping reviews may not use PICO and instead may use JBI's Population, Concept, and Context [PCC] or another approach to reporting eligibility criteria)	
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (Note: Scoping reviews may not extract outcome data, so this can refer to whichever data items are extracted)	
Risk of bias in individual studies	14	If this is to occur, describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis (Note: Scoping reviews typically do not include risk of bias assessment, but this information should be described if it will occur)	
Data synthesis	15a	Describe criteria under which study data will be presented (Note: Scoping reviews do not typically include quantitative synthesis of study data, but should still describe in advance how extracted data are anticipated to be presented in the resulting review)	
	15b	Describe the planned approach to how extracted data will be presented (such as figures, tables, evidence gaps maps)	
	15c	Describe any proposed additional analyses (such as thematic analyses) (Note: The JBI methodological guidance does not recommend undertaking thematic analysis as this synthesis of data should ideally occur following methodological appraisal of the included sources)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias (es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) (Note: Scoping reviews typically do not include assessment of meta-bias[es], but this information should be described if it will occur)	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	

## APPENDIX 2. SEARCH STRATEGY

### Search Concepts

Echinococcus Granulosus	Strategies
Echinococcus	Prevention
Echinococcosis	Control
Echinococcoses	Preventive therapy
Echinococcus Infection	Preventive measures
Echinococcus Infections	Prophylaxis
Infection, Echinococcus	Therapeutic
Cystic Echinococcosis	Therapy
Cystic Echinococcoses	Treatment
Hydatidosis	Treatments
Hydatidoses	Elimination
Hydatid Cysts	Intervention
Hydatid Cyst	Early intervention
Hydatid Disease	Late intervention
Hydatid Diseases	Drug therapy
Echinococcus Granulosus Infection	Drug Therapies
	Drug Therapies
	Pharmacotherapy
	Pharmacotherapies
	Vaccine
	Health Promotion
	Health Campaign
	Pest control
	Pest management

## **MEDLINE Search strategy:**

1. Echinococcus Granulosus
2. Echinococcus
3. Echinococcosis
4. Echinococcoses
5. Echinococcus Infection
6. Echinococcus Infections
7. Infection, Echinococcus
8. Cystic Echinococcosis
9. Cystic Echinococcoses
10. Hydatidosis
11. Hydatidoses
12. Hydatid Cysts
13. Hydatid Cyst
14. Hydatid Disease
15. Hydatid Diseases
16. Echinococcus Granulosus Infection
17. 1-16 OR
18. Strategies
19. Prevention
20. Control
21. Preventive therapy
22. Preventive measures
23. Prophylaxis
24. Therapeutic
25. Therapy
26. Treatment
27. Treatments
28. Elimination
29. Intervention
30. Early intervention
31. Late intervention
32. Drug therapy
33. Drug Therapies
34. Drug Therapies
35. Pharmacotherapy
36. Pharmacotherapies
37. Vaccine
38. Health Promotion
39. Health Campaign
40. Pest control
41. Pest management
42. 18-41 OR

43. 17 AND 42

**For MEDLINE and EMBASE we will use MeSH subject heading.**

Search terms used are centred on the concepts of 'Echinococcus Granulosus infection' and 'strategy'. The 'Echinococcus Granulosus' concept was built around synonyms (eg, Hydatid disease, Hydatid cyst). The "strategy" concept was broad and included terms covering all types of interventions (eg, Pest control, Therapy, Prevention). Qualified academic librarian support will be requested for identification of key words on the different databases and search strategy refinement.