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Economic evaluations of neglected tropical disease interventions in low- and middle-income countries: a systematic review protocol

Biswajit Mahapatra[1,2] · Nirmalya Mukherjee[1,2] · Sajda Khatoon[1,2] · Paramita Bhattacharya[1,2] · Pritha Das[1,2] · Omesh Bharti[3] · Denny John[2,4]

[1]Centre for Public Health Research, Manbhum Ananda Ashram Nityananda Trust (MANT), Kolkata, West Bengal, India, [2]Evidence Synthesis and Implementation for Indigenous Health: A JBI Affiliated Group, Manbhum Ananda Ashram Nityananda Trust (MANT), Kolkata, West Bengal, India, [3]State Institute of Health and Family Welfare, Department of Health and Family Welfare, Government of Himachal Pradesh, Shimla, Himachal Pradesh, India, and [4]Faculty of Life and Allied Health Sciences, M.S. Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India

ABSTRACT

Objective: The objective of this systematic review is to provide an overview of economic evaluation studies of interventions for neglected tropical diseases in low- and/or middle-income countries.

Introduction: The majority of people most susceptible to neglected tropical diseases reside in low- and middle-income countries and suffer significant economic impact due to these diseases. The World Health Organization suggests utilizing a systematic and cross-cutting approach with multiple interventions to lessen the neglected tropical disease burden.

Inclusion criteria: Studies will be eligible for inclusion if they include economic evaluations of interventions for neglected tropical diseases and are conducted in low- and/or middle-income country settings.

Methods: A preliminary search of MEDLINE (PubMed) was undertaken using MeSH terms, such as *neglected tropical disease, economic evaluation, therapeutics, low- and/or middle-income countries*. Two reviewers will screen titles and abstracts independently, followed by a full-text review against the inclusion criteria. Disagreements will be resolved by discussion or with a third reviewer. To assess methodological quality, the JBI checklist for economic evaluations will be used. For economic evaluations, data will be extracted using the standardized JBI data extraction form. The Dominance Ranking Matrix will be used to summarize and compare the results of different types of economic evaluations. Cost per quality adjusted life year gained and cost per disability adjusted life year averted will be measures for economic evaluation. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach will be used to assess the certainty of economic evidence, such as resource use and costs.

Review registration: PROSPERO CRD42017070386

Keywords: cost effectiveness; economic evaluation; low- and middle-income countries; neglected tropical disease

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Introduction

As per the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO), neglected tropical diseases (NTDs) are a group of 20 conditions of parasitic, bacterial, viral, fungal, and non-communicable origin.[1–3] According to the WHO, NTDs are a diverse group of communicable diseases that prevail in tropical and subtropical conditions, affecting more than 1 billion people and costing developing economies billions of dollars every year.[2] Although 179 nations and territories reported at least one NTD case in 2021, 16 countries accounted for 80% of the worldwide NTD burden.[4] Globally, it is anticipated that 1.65 billion individuals will require treatment for at least one NTD.[4] These diseases are also known as *diseases of poverty*[5] or *diseases of neglected populations*.[6]

More than a billion people around the world have NTDs, and these people are the most susceptible and have the least access to health care.[7–9] According to

Correspondence: Denny John, denny@cphr-mant.org
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the "Global Report on Neglected Tropical Diseases 2023," NTDs affect more than 1.7 billion people in 149 countries, causing severe illness, mortality, disability, stigma, and social isolation.[4] NTDs also have a significant economic impact on individuals, households, communities, and health care systems, with lost productivity and health care expenditure costing up to US$170 billion each year.[4] According to the World Health statistics report, there were an estimated 2.3 million disability-adjusted life years attributed to NTDs globally in 2018, with 86% occurring in low- and/or middle-income countries (LMICs).[10]

The 5 fundamental strategies that the WHO suggests to minimize the burden of NTDs (utilizing a systematic and cross-cutting approach) include preventive chemotherapy; individual disease management; vector control; veterinary public health; and water, sanitation, and hygiene. However, any strategy to lessen the burden of NTDs would require a multipronged approach due to the intricacies involved.[11] While several systematic reviews on economic evaluations of interventions have been conducted, these have focused on a single NTD, were literature reviews, or did not specifically focus on LMICs.[12–19]

It is critical to provide health economic evidence to support effective resource allocation when it comes to NTDs, as impoverished populations in LMICs are more susceptible to a wide range of NTDs due to their countries' underfunded health care systems. Clinical decision-makers and policymakers in LMICs may benefit from the insights provided by health economic evaluations regarding the financial costs and benefits of patient care options. Due to the rise in public expectations for health care and quality of life in LMICs, there are more requirements and technology solutions being applied to the health field in direct proportion to population expansion. Health administrators must simultaneously make difficult decisions due to financial and human resource limitations in such settings. In this setting, economic analyses are practical tools for enhancing decision-making and assisting governmental policy.

A preliminary search conducted on MEDLINE (PubMed), the *JBI Database of Systematic Reviews and Implementation Reports*, the Cochrane Database of Systematic Reviews, Epistemonikos, and PROSPERO identified no current or in-progress systematic review on this topic. This systematic review aims to identify and assess the economic literature on interventions to prevent, control, and eliminate NTDs in LMICs. The objective of this review is to synthesize the existing evidence on economic evaluations of interventions for NTDs in LMICs.

Review question

What is the available evidence on economic evaluations, in terms of cost effectiveness, cost utility, cost benefit, or cost minimization analysis, for interventions on NTDs in LMICs?

Inclusion criteria

Participants

This review will include studies with people, regardless of their age or gender, who are exposed to any intervention aimed to prevent, treat, control, eliminate, interrupt, or manage single or multiple NTDs.

Interventions

We will consider studies that assess interventions for NTDs, such as prevention, treatment, control, elimination, interruption of disease transmission, or any combinations of these. Examples include preventive chemotherapy; individual disease management; vector control; veterinary public health; and water, sanitation, and hygiene. These interventions can be provided at a community, household, or facility level, including public health initiatives by community health workers, volunteers, or formal health care providers to cover large populations.

For this review, NTDs include those diseases listed by the WHO, namely Buruli ulcer; Chagas disease; dengue and chikungunya; dracunculiasis; echinococcosis; foodborne trematodiases; human African trypanosomiasis; leishmaniasis; leprosy; lymphatic filariasis; mycetoma, chromoblastomycosis and other deep mycoses; onchocerciasis; rabies; scabies and other ectoparasitoses; schistosomiasis; soil-transmitted helminthiases; snakebite envenoming; taeniasis/cysticercosis; trachoma; and yaws.[19] Studies where participants may have used intervention(s) once and/or over a longer period of time will be considered, and there will not be any timeline for participants being exposed to these interventions.

Comparators

Comparators of interventions could be active (alternative) or passive (do nothing) and there will be no restrictions.

Outcomes

Outcomes will be measured in terms of estimated average cost per NTD prevented/treated, incremental cost per patient treated, incremental cost-effectiveness ratio per quality-/disability-adjusted life years, net costs, or cost-benefit ratio. We will exclude studies that report only total cost or unit cost without an evaluation of comparative effectiveness estimates.

Context

This review will consider primary studies focusing on NTD interventions involving patients, households, or communities residing in LMICs as per World Bank criteria.[20]

Types of studies

This review will consider economic evidence studies reporting cost-effectiveness, cost-benefit analysis, cost-utility analysis, or cost minimization analysis. Studies must include NTDs as listed by the WHO with 1 intervention group and at least 1 other control or comparator group. Studies conducting an economic evaluation alongside experimental designs (randomized controlled trials or quasi experimental studies), or observational designs with or without control or comparator groups, will be included. Economic evaluation studies conducted using modeling methods, such as a decision tree, Markov models, or simulation models, will also be considered.

Reviews, editorials, commentaries, or methodological studies will be excluded from this review.

Methods

The proposed systematic review will adhere to the JBI methodology for systematic reviews of economic evaluation.[21] The protocol has been conducted following the PRISMA-P guidelines and registered with PROSPERO (CRD42017070386).

Search strategy

The search strategy will include both unpublished and published studies. An initial limited search of MEDLINE (PubMed) was conducted to find relevant papers. The content of relevant publications' titles and abstracts, as well as the index terms used to characterize the articles, will be utilized to construct a preliminary search strategy on MEDLINE (PubMed; Appendix I). This search strategy will then be peer-reviewed by an author with health economics expertise (DJ) using Canada's Drug and Health Technology Agency (CADTH) 2015 Peer Review of Electronic Search Strategies (PRESS) guidelines.[22]

The search strategy will then be modified for MEDLINE (PubMed) and adapted for each included database and/or information source, taking into account all recognized index terms and keywords. The search filters for "cost" will be adapted from the CADTH search filters database and the filters for "LMIC" adapted from the School of Health and Related Research (ScHARR) LMIC filter, respectively.[23] The reference lists of all included sources of evidence will be checked for additional studies. The literature search will not have any lower or upper date limits. Studies in languages other than English will be excluded, as the majority of the economic evaluation studies published in LMICs are in English.

The following databases will be searched:

- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Systematic Reviews
- Cochrane Methodology Register
- Cost Effectiveness Analysis Registry (CEA)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCOhost)
- Database of Abstracts of Reviews of Effects (DARE)
- EconLit (EBSCOhost)
- Embase (Ovid)
- Health Economic Evaluation Database (HEED)
- Health Management Information Consortium (HMIC)
- Health Technology Assessment Database (HTA)
- Literature of the Latin American and Caribbean Health Sciences (LILACS)
- National Health Service Economic Evaluation Database (NHS EED)
- NHS Health Technology Assessment Database
- Science Direct
- US National Library of Medicine National Institutes of Health (PubMed)
- Web of Science

The search for gray literature will include:

- Asian Development Bank
- Google Scholar (limited to first 20 pages)
- New York Academy of Medicine (NYAM)
- Open Access Thesis and Dissertations (OATD.org)

- WHO
- World Development Bank
- WorldWideScience.org

Study selection

Following the search, all identified citations will be compiled and uploaded into Zotero v.6.0.10 (Corporation for Digital Scholarship and Roy Rosenzweig Center for History and New Media, VA, USA), and duplicates deleted. Titles and abstracts will be screened by 2 independent reviewers (BM and PD) for inclusion based on the eligibility criteria. The reasons for the exclusion of full-text studies will be included as an appendix in the final systematic review. Any disagreements will be handled via discussion or with a third reviewer (SK). All screening will be done using the JBI System for the Unified Management of the Assessment and Review of Information (JBI SUMARI; JBI Adelaide, Australia).[21] In the final systematic review, the search findings will be presented in a Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) flow diagram.[24]

Assessment of methodological quality

Two independent reviewers (BM and PD) will use the JBI checklist for economic assessment to evaluate the methodological quality of the studies that are selected for final inclusion.[21] Any disagreements between the reviewers will be solved through discussion or with the assistance of a third reviewer (SK). The outcomes of critical evaluation will be presented in narrative and tabular format. After screening titles and abstracts and removing duplicates, selected studies will undergo data extraction and synthesis, irrespective of the quality of their methodology. The results of the appraisal of methodological quality of the included studies will be used to inform synthesis and interpretation of the results of the study.[21]

Data extraction

A modified data extraction form based on JBI data extraction form for economic evaluation using JBI SUMARI will be first piloted using 2 to 3 studies from the included list of studies (Appendix II).[21] Two independent reviewers (BM and PD) will conduct data extraction from all included studies. Specific information about interventions, populations, economic perspectives, costs, currencies, study designs, economic evaluation methods, and outcomes that are relevant to the review question and specific objectives, including funding information, will be extracted from the data. Additionally, data on study participants, interventions, comparators and outcomes (PICO); study methodology, including type of assessment design, source of effectiveness data, analytical point (s), time and price used for cost, cost analysis, time periods of analysis, sensitivity analysis, measures of resource use, clinical and health effects, and cost effectiveness/utility/benefit/minimization; and context of the study (geographic, cultural and health care) will be extracted. We will also include results for resource consumption and/or cost and/or cost-effectiveness/utility/benefit/minimization metrics; and present the reviewers' conclusions on aspects that increase the intervention cost-effectiveness, where possible.

Total treatment expenditures will be divided into 3 categories, according to a comprehensive analysis of the economic burden of NTDs: i) direct medical costs (eg, consultation fees, test fees, medicine fees, hospitalization fees); ii) direct non-medical costs (eg, transport fees and food costs during health care visits); and iii) indirect costs (lost income) incurred at the patient and/or household level, as reported. Any disagreements between the reviewers will be resolved by discussion or with a third reviewer (DJ).

Data synthesis

Using tables and figures, the data will be narratively synthesized across all identified studies. When applicable, the results for economic evaluation indicators will be summarized based on each identified outcome for each intervention against a particular NTD. All cost data will be converted into a single year (2023) and single currency (USD) using CCEMG-EPPI Cost Converter (Campbell and Cochrane Methods Group and the EPPI Centre, London, UK). The JBI Dominance Ranking Matrix (DRM), a categorization method, will be used by the reviewers as per JBI guidelines for economic evaluations in systematic reviews.[21] We will analyze the data to see if we can draw any inferences about the types of situations in which this intervention is more (or less) cost effective than the other groups. There are 3 possible outcomes for the decision matrix when the cost of an intervention of interest is weighed against the health outcomes:

i) Strong dominance is thought to be acceptable for judgments that clearly favor either the treatment or the control intervention, from the point of view of clinical effectiveness as well as cost.

ii) Weak dominance occurs when either clinical effectiveness or costs are supported by the data, but not both.
iii) Non-dominance occurs when an intervention is less successful or more expensive.

Assessing certainty in the findings

Economic evidence for outcomes related to resource usage will be assessed for certainty using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach, and a Summary of Findings will be compiled based on the results.[25] According to GRADE, significant variations in resource consumption between different management techniques, as well as other significant results, should be included in the evidence profile and Summary of Findings. Finding evidence for the differences in resource use, making decisions regarding confidence in effect estimates using the same criteria used for health outcomes, and valuing the resource use in terms of costs for the specific setting for which the recommendation is being made are key steps in taking resources into consideration when making recommendations with GRADE. Two reviewers will independently assess studies, and a third reviewer will be consulted in the event of any disagreement.

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Declarations

Author contributions

DJ conceptualized the topic. BM developed the initial search strategy and the protocol manuscript with support from DJ. OB and DJ have previously collaborated on research related to snakebites and rabies. DJ has contributed to an evidence summary related to soil-transmitted helminths and schistosomiasis. These experiences, along with NM's work with indigenous populations, contributed to the improvement of the paper. All authors reviewed the protocol and agreed to the submission of the final protocol. DJ is Chair, Campbell and Cochrane Economic Methods Group and has contributed to methodological work on systematic reviews of economic evidence.

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Appendix I: Search strategy

MEDLINE (PubMed)
Search date: June 26, 2023

Search ID no.	Query/search formula	Results retrieved
#1	Ulcer[MeSH Terms] OR Ulcer[tiab] OR Mycobacterium Ulcerans[MeSH Terms] OR Mycobacterium Ulcerans[tiab] OR Mycobacterium Ulcerans Infection[MeSH Terms] OR Mycobacterium Ulcerans Infection[tiab] OR Buruli Ulcer Disease[MeSH Terms] OR Buruli Ulcer Disease[tiab] OR Buruli Ulcer[MeSH Terms] OR Buruli Ulcer[tiab] OR Ulcer Disease[MeSH Terms] OR Ulcer Disease[tiab] OR Osteomyelitis[MeSH Terms] OR Osteomyelitis[tiab] OR Osteomyelitides[MeSH Terms] OR Osteomyelitides[tiab] OR Mycobacterium Marinum[MeSH Terms] OR Mycobacterium Marinum[tiab] OR Indolent Necrotizing Disease[tiab] OR Aggressive Skin Ulcers[tiab] OR Debilitating Osteoarthritis[tiab] OR Limb Deformity[tiab] OR Necrotizing Skin Lesions[tiab] OR Buruli[tiab]	180,990
#2	American Trypanosomiasis[MeSH Terms] OR American Trypanosomiasis[tiab] OR South American Trypanosomiasis[MeSH Terms] OR South American Trypanosomiasis [tiab] OR Trypanosomiasis[MeSH Terms] OR Trypanosomiasis[tiab] OR Trypanosoma cruzi Infection[MeSH Terms] OR Trypanosoma cruzi Infection*[tiab] OR Trypanosoma cruzi[MeSH Terms] OR Trypanosoma cruzi[tiab] OR Chagas' Disease[MeSH Terms] OR Chagas' Disease[tiab] OR Cardiovascular Trypanosomiasis[MeSH Terms] OR Cardiovascular Trypanosomiasis[tiab] OR Meningoencephalitides[MeSH Terms] OR Meningoencephalitides[tiab] OR Cerebromeningitis[MeSH Terms] OR Cerebromeningitis[tiab] OR Cerebromeningitides[MeSH Terms] OR Encephalomeningitis [MeSH Terms] OR Encephalomeningitis[tiab] OR Encephalomeningitides[MeSH Terms] OR Encephalomeningitides[tiab] OR Anthropozoonosis[tiab] OR Trypanosoma Cruzi[tiab] OR Parasitic Infection[tiab] OR Tropical Vector-Borne Infection[tiab] OR Chronic Chagas Cardiomyopathy[tiab] OR Triatomine Vectors[tiab] OR Congenital Chagas Disease[tiab]	47,304
#3	Breakbone Fever[MeSH Terms] OR Breakbone Fever*[tiab] OR Classical Dengue Fever[MeSH Terms] OR Classical Dengue Fever*[tiab] OR Dengue Fever[MeSH Terms] OR Dengue Fever[tiab] OR Severe Dengues[MeSH Terms] OR Severe Dengues[tiab] OR Dengue Hemorrhagic Fever[MeSH Terms] OR Dengue Hemorrhagic Fever[tiab] OR Hemorrhagic Dengue[MeSH Terms] OR Hemorrhagic Dengue[tiab] OR Dengue Shock Syndrome[MeSH Terms] OR Dengue Shock Syndrome[tiab] OR Dengue Viruses [tiab] OR NS1 Protein[tiab] OR Nonstructural Protein 1[tiab] OR Dengue Virus Type 2[tiab] OR prM Protein[tiab] OR Dengue 3 Virus[tiab] OR DEN-3 prM Protein[tiab] OR Dengue Virus Type 3[tiab] OR E protein[tiab] OR DENV-4[tiab] OR DENV[tiab] OR Envelope Glycoprotein[tiab] OR Dengue-4 Virus[tiab] OR Dengue Virus Type 4 Glycoprotein E[tiab] OR Secondary Heterologous Dengue Infection[tiab] OR Dengue Pathogenesis[tiab] OR Arboviral Disease[tiab]	31,601
#4	Chikungunya Virus[tiab] OR Chikungunya Fevers[tiab] OR Chikungunya Virus Infection*[tiab] OR E1-Envelope Protein[tiab] OR Ns P4 Protein[tiab] OR Non-Structural Protein 4[tiab] OR Zoonotic Disease[tiab] OR Zoonotic Infections[tiab] OR Zoonotic Infectious Disease[tiab] OR Arbovirus[tiab] OR Anthropod Borne Virus[tiab] OR Chikungunya Arthritis[tiab] OR Arthralgia[tiab] OR Myalgia[tiab] OR Febrile Disease[tiab] OR Aedes Aegypti[tiab] OR Aedes Albopictus[tiab] OR Mosquito-Transmitted Alphavirus[tiab] OR CHIKF[tiab]	44,210
#5	Guinea Worm Disease[tiab] OR Dracunculosis[tiab] OR Parasitic Infection[tiab] OR Dracunculus Nematodes[tiab] OR Dracunculus Medinensis[tiab] OR Medina Worm[tiab] OR Water-Borne Anthroponosis[tiab] OR Food-Borne Zoonoses[tiab] OR Cyclops Copepods[tiab]	5003
#6	Echinococcoses[tiab] OR Echinococcus Infection[tiab] OR Cystic Echinococcosis[tiab] OR Cystic Echinococcoses[tiab] OR Hydatidosis[tiab] OR Hydatidoses[tiab] OR Cyst Hydatid[tiab] OR Hydatid Disease[tiab] OR Echinococcus Granulosus Infection [tiab] OR Echinococcus Multilocularis[tiab] OR Antigen II-3-10[tiab] OR EM10 Protein[tiab] OR Elp Protein[tiab] OR Echinococcus Surface Antigen EM10[tiab] OR Echinococcus Major Surface Antigen EM10[tiab] OR Alveolar Echinococcosis[tiab] OR Alveolar Hydatid Disease[tiab] OR Severe Helminthic Zoonoses[tiab] OR Echinococcus Ortleppi[tiab] OR Echinococcus Canadensis[tiab] OR Echinococcus Intermedius[tiab] OR Echinococcus Vogeli[tiab] OR Echinococcus Oligarthrus[tiab] OR Taenia Echinococcus [tiab] OR Impaired Immune Responsiveness[tiab] OR Helminths[tiab] OR Echinococcosis Foodborne Trematodiases[tiab] OR Helminth Infections[tiab]	22,892
#7	African Trypanosomiases[tiab] OR African Trypanosomiasis[tiab] OR African Sleeping Sickness[tiab] OR Nagana[tiab] OR Trypanosoma Brucei [tiab] OR Gambiense[tiab] OR Trypanosoma Brucei Rhodesienses[tiab] OR Brucei Rhodesiense[tiab] OR Rhodesienses[tiab] OR Hemolymphatic[tiab] OR Meningoencephalitic[tiab] OR Human African Trypanosomiasis[tiab] OR HAT [tiab] OR T Brucei Gambiense HAT[tiab] OR T Brucei Rhodesiense HAT[tiab] OR Flagellate Protozoan[tiab] OR Glossina[tiab] OR Nagana[tiab]	21,124
#8	Leishmania Infantum[tiab] OR Leishmaniases[tiab] OR Leishmania Infection[tiab] OR Leishmaniasis[tiab] OR Cutaneous Leishmaniases[tiab] OR Diffuse Cutaneous Leishmaniases[tiab] OR Visceral Leishmaniasis[tiab] OR Black Fever[tiab] OR Kala Azar [tiab] OR Leishmania Leishmania Infantum[tiab] OR Leishmania Donovani Infantum[tiab] OR Leishmania Chagasi[tiab] OR Leishmania Donovani Chagasi[tiab] OR Leishmania Infantum Chagasi[tiab] OR Lepp12 Protein[tiab] OR Mucocutaneous	179,591

(*Continued*)

Search ID no.	Query/search formula	Results retrieved
	Leishmaniasis[tiab] OR Vector-Borne Infection Disease[tiab] OR Obligate Intracellular Pathogen[tiab] OR Phlebotamine Sand Flies[tiab] OR Leishmania Spp[tiab] OR Tegumentary Leishmaniasis[tiab] OR VL[tiab] OR CL[tiab] OR Canine Leishmaniasis[tiab] OR Canine Visceral Leishmaniasis[tiab] OR CVL[tiab] OR MCL[tiab]	
#9	Hansen Disease*[tiab] OR Leprosies[tiab] OR Multibacillary Leprosies[tiab] OR Midborderline Lepromatous[tiab] OR Multibacillary Leprosy[tiab] OR Borderline Lepromatous[tiab] OR Borderline Leprosy*[tiab] OR Paucibacillary Leprosies[tiab] OR Paucibacillary[tiab] OR Indeterminate Tuberculoid*[tiab] OR Paucibacillary Leprosy[tiab] OR Borderline Tuberculoid*[tiab] OR Tuberculoid Leprosy*[tiab] OR Neural Leprosy*[tiab] OR Macular Leprosy*[tiab] OR Lepromatous[tiab] OR Lepromatous Leprosy*[tiab] OR Cutaneous Leprosy*[tiab] OR Nodular Leprosy*[tiab] OR Dimorphous Leprosy*[tiab] OR Mycobacterium Leprae Bacillus[tiab] OR Hypoesthetic Skin Lesions[tiab] OR Nodular Skin Lesions[tiab] OR Mycobacterium Leprae[tiab] OR Chronic Infectous Disease[tiab] OR HD[tiab] OR Skin Lesions[tiab] OR Neuropathic Sequelae[tiab] OR Anthropophylic[tiab] OR M. Leprae[tiab]	93,285
#10	Elephantiases[tiab] OR Filarial Elephantiases*[tiab] OR Lymphatic Filariasis*[tiab] OR Bancroftian Filariasis*[tiab] OR Bancroftian Elephantiasis*[tiab] OR Malayi Filariasis*[tiab] OR Malayi Elephantiasis*[tiab] OR LF[tiab] OR Filarial Parasites[tiab] OR Parasitic Helminth Diseases[tiab] OR Filarial Nematodes[tiab] OR Endosymbionts[tiab] OR Lymphedema[tiab] OR Hydrocele[tiab]	37,283
#11	Maduromycosis[tiab] OR Madura Foot[tiab] OR Actinomycetoma[tiab] OR Eumycetoma[tiab] OR Madurella mycetomatis[tiab] OR Madurella mycetomi[tiab] OR TCTP protein[tiab] OR Streptomyces somaliensis[tiab] OR Actinomadura madurae[tiab] OR Actinomadura pelletieri[tiab] OR Nocardia brasiliensis[tiab] OR Nocardia asteroids[tiab] OR Madurella grisea[tiab] OR Pseudoallescheria boydii[tiab] OR Leptosphaeria senegalensis[tiab] OR aerobic actinomycetes[tiab] OR Filamentous Fungi[tiab] OR Filamentous Bacteria[tiab] OR Eumycotic[tiab] OR Actinomycetes[tiab] OR Eumycetes[tiab] OR N. Brasiliensis Mycetoma [tiab]	15,700
#12	Chromoblastomycoses[tiab] OR Dermatitis Verrucosa[tiab] OR Chromomycosis[tiab] OR Invasive Fungal Infection[tiab] OR Disseminated Fungal Infection[tiab] OR Invasive Mycoses[tiab] OR Mycoses[tiab] OR Chromomycosis[tiab] OR gamut of mycoses[tiab] OR Melanised Fungi[tiab] OR brown-pigmented fungi[tiab] OR CBM[tiab] OR Microabscesses[tiab] OR Nonprotective T Helper Type 2[tiab] OR Th2[tiab] OR Muriform Cells[tiab] OR Sclerotic Cells[tiab] OR Polymorphic[tiab] OR Granulomatous Mycosis[tiab] OR Suppurative Mycosis [tiab] OR Dematiaceous Fungi[tiab] OR Dematiaceous Saprophytic Moulds[tiab] OR Herpotrichiellaceae[tiab] OR Fonsecaea pedrosoi[tiab] OR Fonsecaea compactum[tiab] OR Cladophialophora carrionii[tiab] OR Phialophora verrucosa[tiab] OR Cladosporium carrionii[tiab] OR Rhino-cladiella aquaspersa polymorphous verrucous[tiab] OR verrucose plaques nodular[tiab] OR tumoral[tiab] OR atrophic[tiab] OR phaeohyphomycosis[tiab] OR mycetoma[tiab]	176,732
#13	Onchocerciases[tiab] OR Onchocerciasis[tiab] OR Ocular Onchocerciases*[tiab] OR River Blindness[tiab] OR Onchocerca Volvulus[tiab] OR O. Volvulus[tiab] OR O. Volvulus Infection[tiab] OR Filarial Nematodes[tiab] OR Onchocerciasis-Associated Epilepsy[tiab] OR OAE[tiab] OR Onchocerca Volvulus Microfilarial[tiab] OR Hyperendemic Foci[tiab] OR Visual Handicap[tiab] OR S. Damnosum S.L. Species[tiab] OR Savanna Cytospecies[tiab] OR S. Damnosum S.S[tiab] OR S. Sirbanum[tiab] OR Onchocerca-Simulium Complexes[tiab] OR Blindness[tiab] OR Dermatitis[tiab] OR Atonic Neck Seizures[tiab] OR Myoclonic Neck Seizures [tiab] OR Nakalanga Syndrome[tiab] OR Nodding Syndrome[tiab]	113,953
#14	Lyssa*[tiab] OR Hydrophobia[tiab] OR Encephalitic Rabies[tiab] OR Paralytic Rabies[tiab] OR Furious Rabies[tiab] OR Furious Raby[tiab] OR Rabies Viruses[tiab] OR P Protein*[tiab] OR Rv L Protein[tiab] OR Large Protein[tiab] OR Rabies Virus Glycoprotein G [tiab] OR Rabies G[tiab] OR Rabies G[tiab] OR N Protein[tiab] OR G Protein[tiab] OR Antigen Vap21[tiab] OR G Glycoprotein [tiab] OR Bat Rabies Virus[tiab] OR Acute Neurological Infection[tiab] OR Encephalitic Rabies[tiab] OR Hyperexcitability[tiab] OR Lethal Zoonotic Disease[tiab] OR Lyssaviruses[tiab] OR Acute Encephalitis[tiab] OR RABV[tiab] OR Rhabdoviridae[tiab] OR Zoonotic Pathogen[tiab] OR Dog Rabies[tiab]	97,440
#15	Sarcoptic Mange[tiab] OR Scabies[tiab] OR Streptomyces scabies[tiab] OR Oospora scabies[tiab] OR Actinomyces scabies[tiab] OR Virulence protein nec1[tiab] OR Thread-Like Papules[tiab] OR Burrows[tiab] OR Intense Pruritus[tiab] OR Dermatitis [tiab] OR Ectoparasitic dermatosis[tiab] OR Sarcoptes scabiei var. hominis[tiab] OR Skin Disease[tiab] OR Obligate Human Parasite Mite[tiab] OR Erythematous Papular Eruption[tiab] OR Serpiginous Burrows[tiab] OR Highly Contagious Parasitic Cutaneous Disease[tiab] OR Staphylococcal Bacteraemia[tiab] OR Streptococcal Bacteraemia[tiab] OR Sarcoptes scabiei[tiab] OR Streptococcus aureus[tiab] OR Staphylococcus aureus[tiab] OR Itch [tiab] OR Ectoparasites[tiab] OR Ectoparasitoses[tiab] OR Boophilus microplus[tiab] OR Pediculosis[tiab] OR Pediculosis Capitis[tiab] OR Cutaneous Larva Migrans[tiab] OR Tungiasis[tiab] OR Pediculus humanus capitis*[tiab] OR Ectoparasitic Arthropods[tiab] OR Intestinal Helminths[tiab] OR Columba livia domestica[tiab] OR C. l. domestica[tiab] OR Harami pigeons[tiab] OR Columbiformes[tiab] OR Columbidae[tiab] OR Menopon gallinae[tiab] OR Phthiraptera[tiab] OR Menoponidae[tiab] OR Pseudolynchia canariensis[tiab] OR Diptera[tiab] OR Hippoboscidae[tiab] OR Goniodes dissimilis[tiab] OR Psocodea[tiab] OR Philopteridae[tiab] OR Raillietina spp.[tiab] OR Cyclophyllidea[tiab] OR Davaineidae[tiab] OR Ascaridia sp.[tiab] OR Ascaridida[tiab] OR Ascaridiidae[tiab] OR Lucilia cuprina [tiab] OR Rat-Borne Ectoparasite[tiab] OR Head lice[tiab] OR Mites[tiab] OR Fleas[tiab] OR Ticks[tiab] OR Lice[tiab] OR	297,729

(*Continued*)

Search ID no.	Query/search formula	Results retrieved
	Listrophorids[tiab] OR Myobiids[tiab] OR Immunological reactions[tiab] OR Arthropods[tiab] OR Myiasis[tiab] OR Mange[tiab] OR Blood-Sucking Arthropods[tiab] OR Ixodid Ticks[tiab] OR Trombidioses[tiab] OR Cercarial Dermatitis[tiab]	
#16	Schistosomiases[tiab] OR Bilharziasis*[tiab] OR Katayama Fever[tiab] OR Schistoma Infection*[tiab] OR Schistosoma Mansoni Infection*[tiab] OR Intestinal Schistosomiasis[tiab] OR Schistosomiasis Japonicum[tiab] OR Schistosoma Japonicum Infection*[tiab] OR Schistosomiasis Haematobium[tiab] OR Schistosoma Haematobia Infection*[tiab] OR Urogenital Schistosomiasis*[tiab] OR Urinary Schistosomiasis[tiab] OR Central Nervous System Schistosomiasis[tiab] OR Schistosomal Myeloradiculopathy* [tiab] Schistosomal Myelitis[tiab] OR Schistosomal Myelopathy[tiab] OR S. Japonicum[tiab] OR S. Haematobium[tiab] OR Helminthiasis[tiab] OR Schistosoma[tiab] OR Hepatosplenic Schistosomiasis[tiab] OR Acute Schistosomiasis[tiab] OR Flulike Syndrome[tiab] OR Trematode Flatworms[tiab] OR Hepatointestinal Schistosomiasis[tiab] OR Schistosoma Malayensis[tiab] OR Hepatic Fibrosis[tiab] OR Portal Hypertension[tiab] OR Esophageal Varices[tiab] OR Splenomegaly[tiab] OR Paediatric Schistosomiasis[tiab] OR Immunopathology[tiab] OR Type 2 Immunity[tiab] OR Tissue Scarring[tiab] OR Fibrosis[tiab] OR Organ Impairment[tiab]	301,011
#17	Soil-Transmitted Helminths[tiab] OR Ascaris lumbricoides[tiab] OR Hookworm[tiab] OR Ancylostoma duodenale[tiab] OR Necator americanus[tiab] OR Trichuris trichiura[tiab] OR Strongyloides stercoralis[tiab] OR Soil-Transmitted Helminth Infections [tiab] OR Ascariasis[tiab] OR Trichuriasis[tiab] OR STH[tiab] OR Roundworms[tiab] OR Whipworms[tiab] OR Autoimmune Disorders[tiab] OR Allergic Disorders[tiab] OR Metabolic Disorders[tiab] OR Human Parasitic Disease[tiab] OR Intestinal Nematode Infections[tiab] OR Schistosomiasis[tiab] OR SCH[tiab] OR Worm Infections[tiab] OR Enterobiasis[tiab]	85,272
#18	Snake Bite*[tiab] OR Snakebite Envenomation*[tiab] OR Snake Envenoming*[tiab] OR Exotic Venomous Snakes[tiab] OR Snake Venoms[tiab] OR Immunogens[tiab]	10,289
#19	Taeniases*[tiab] OR Taenia Infection*[tiab] OR Taenia serialis Infection*[tiab] OR Taenia brauni Infection*[tiab] OR Taenia multiceps Infection*[tiab] OR Taenia solium Infection*[tiab] OR Taenia glomeratus Infection*[tiab] OR Cysticercoses[tiab] OR Coenuri Infection*[tiab] OR Coenurus Infection*[tiab] OR Coenurosis*[tiab] OR Coenurus cerebralis Infection*[tiab] OR Cysticercus cellulosae Infection*[tiab] OR Taenia solium Cysticercosis*[tiab] OR Taenia solium neurocysticercosis[tiab] OR NCC [tiab] OR Taeniasis[tiab] OR Porcine Cysticercosis[tiab] OR Human Cysticercosis[tiab] OR Taenia solium[tiab] OR Cestode[tiab] OR tapeworm[tiab] OR Disseminated cysticercosis[tiab] OR Vesicular Cystic Lesions[tiab] OR Brain Parasite Disease[tiab] OR Pork Tapeworm[tiab] OR Seizures[tiab] OR Hydrocephalus[tiab] OR Focal Deficits[tiab] OR Chronic Meningitis[tiab] OR Cerebral Cysticercosis[tiab] OR Intestinal Tape Worm[tiab] OR Meningeal Racemose[tiab] OR Parenchymatous Ventricular[tiab] OR Meningo-Encephalitis[tiab] OR Granulomatous Meningitis[tiab] OR Ependymitis[tiab] OR Focal Granulomas[tiab] OR Parenchymatous Cysts[tiab] OR Oral Lesions[tiab] OR Oral Cysticercosis[tiab] OR Cysticerci[tiab] OR Neurocysticercosis[tiab] OR Taenia asiatica[tiab] OR Taenia saginata[tiab] OR Food-Borne Zoonoses[tiab] OR T. solium cysticercosis[tiab]	158,153
#20	Trachoma*[tiab] OR Egyptian Ophthalmia[tiab] OR Conjunctival Strains[tiab] OR Chlamydia trachomatis[tiab] OR Blindness[tiab] OR Chronic Processes[tiab] OR Trichiasis[tiab] OR C. trachomatis[tiab] OR Conjunctival Inflammation[tiab] OR Ocular Secretions [tiab] OR Chronic Infection[tiab] OR Tarsal Conjunctiva[tiab] OR Inversion Of The Eyelashes[tiab] OR Corneal Opacity[tiab] OR Keratoconjunctivitis[tiab] OR Ocular Infection[tiab] OR Chlamydia[tiab] OR Intracellular Epithelial Gram-Negative Bacterium [tiab] OR Chlamydial Infections[tiab] OR Entropion[tiab]	90,201
#21	Frambesia*[tiab] OR Frambesia Tropica[tiab] OR Yaws[tiab] OR Treponema pallidum Ssp. pertenue[tiab] OR Non-Venereal Endemic Treponemal Infection[tiab] OR Spirochaete Bacterium[tiab] OR Venereal Syphilis[tiab] OR Endemic Treponematoses [tiab] OR Contagious Lesions[tiab] OR Treponema pallidum pertenue[tiab] OR Cutaneous Ulcer Disease[tiab] OR CUD[tiab] OR T. pallidum[tiab]	3826
#22	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	1,783,830
#23	Cost Benefit Analysis[tiab] OR Cost Benefit Analyses[tiab] OR Cost-Utility Analysis*[tiab] OR Cost Benefit[tiab] OR Marginal Analysis*[tiab] OR Cost Benefit Data*[tiab] OR Economic Evaluation*[tiab] OR Cost Analysis[tiab] OR Cost Comparison*[tiab] OR Affordability*[tiab] OR Cost-Minimization Analysis*[tiab] OR Pricing[tiab] OR Cost Measure*[tiab] OR Illness Cost[tiab] OR Cost Of Sickness[tiab] OR Sickness Cost*[tiab] OR Burden Of Illness[tiab] OR Illness Burden*[tiab] OR Disease Burden*[tiab] OR Costs Of Disease[tiab] OR Disease Cost*[tiab] OR Economic Burden Of Disease[tiab] OR Burden Of Disease*[tiab] OR Cost Effectiveness Analysis[tiab] OR Cost Effectiveness[tiab] OR Cost Effectiveness Ratio*[tiab] OR Cost-Outcome Description[tiab] OR CEA[tiab] OR Cost Per Disability-Adjusted Life Years[tiab] OR DALYs[tiab] OR Cost-Per-DALY[tiab] OR COI[tiab] OR Incremental Cost-Effectiveness Ratios[tiab] OR ICERs[tiab] OR Incremental Cost-Effectiveness Ratio[tiab] OR Quality-Adjusted Life Years[tiab] OR QALYs[tiab] OR Incremental Cost-Effectiveness Ratios[tiab] OR ICERs[tiab]	193,846
#24	Developing countries[MeSH Terms] OR less developed countries[Mesh] OR third-world countries[Mesh] OR under-developed countries[Mesh] OR less developed nations[Mesh] OR third world nations[Mesh] OR under developed nations[Mesh] OR developing nations[Mesh] OR Developing countries[tiab] OR less developed countries[tiab] OR third-world countries[tiab] OR	148,156

(*Continued*)

Search ID no.	Query/search formula	Results retrieved
	under-developed countries[tiab] OR poor countries[tiab] OR less developed nations[tiab] OR third world nations[tiab] OR under developed nations[tiab] OR developing nations[tiab] OR poor nations[tiab] OR poor economies[tiab] OR third world economies [tiab] OR developing economies[tiab] OR under developed economies[tiab] OR less developed economies[tiab] OR Developing countries[ad] OR less developed countries[ad] OR third-world countries[ad] OR under-developed countries[ad] OR poor countries[ad] OR less developed nations[ad] OR third world nations[ad] OR under developed nations[ad] OR developing nations [ad] OR poor nations[ad] OR poor economies[ad] OR third world economies[ad] OR developing economies[ad] OR under developed economies[ad] OR less developed economies[ad]	
#25	Asia [MeSH Terms] OR West Indies [MeSH Terms] OR Polynesia [MeSH Terms] OR Micronesia [MeSH Terms] OR Middle East [MeSH Terms] OR Africa [MeSH Terms] OR Latin America [MeSH Terms] OR Central America [MeSH Terms] or South America [MeSH Terms] OR Caribbean [MeSH Terms] OR West Indies region [MeSH Terms] OR Southeast Asia [MeSH Terms] OR Sub-Saharan Africa [MeSH Terms] OR Eastern Europe [MeSH Terms] OR Balkans [MeSH Terms]	1,736,175
#26	#24 OR #25	1,810,979
#37	#22 AND #23 AND #26	2437

Appendix II: Draft data extraction instrument

Author's name	
Year of publication	
Name of the journal	
Method of the economic evaluation	☐ CEA ☐ CBA ☐ CMA ☐ CUA
Interventions	
Comparator	
Geographical location/country	
Participants	
Source of effectiveness data	
Authors' conclusion	
Reviewers' comments	
Economic effectiveness results	
Dates of economic data	
Modeling used	
Measure of benefits used in economic evaluation	
Screening costs	
Statistical analysis	
Estimated benefits used in economic evaluation	
Cost results	
Synthesis of costs and results	
Clinical effectiveness results (for full economic evaluation)	
Study design	
Year range of primary studies	
Analysis used	
Clinical outcome results	
Economic study design	CEA/CUA/CBA/CMA/screening cost/screening associated cost/health outcomes only/others
Perspectives of the analysis	☐ Individual/newborn ☐ Societal ☐ Patient and patient family ☐ Health care system ☐ Health care provider ☐ Others
Cost included in the analysis	☐ Screening cost ☐ Lab/pathological test/screening associated cost ☐ Others

Converted into utilities?	☐ Yes ☐ No If Yes, report value set:
Utility values combined with survival to form QALYs?	☐ Yes ☐ No
Cost-effectiveness results	Point estimate: Probabilistic results (probability of being cost-effective):
Study conclusions	
Any others	

Clinical effectiveness

Cost	+	0	–
+	**O** A	O B	O C
0	O D	O E	O F
–	O G	O H	O I

Key	Effectiveness	Cost
+	Better	Lower
0	Equal	Equal
–	Poorer	Higher

CBA, cost-benefit analysis; CEA, cost-effectiveness analysis, CMA, cost-minimization analysis; CUA, cost-utility analysis; QALY, quality-adjusted life years.