

Review Article

Cystic Echinococcosis: An Impact Assessment of Prevention Programs in Endemic Developing Countries in Africa, Central Asia, and South America

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Background. Cystic echinococcosis (CE), caused by the tapeworm species, *Echinococcus granulosus sensu stricto* (G1), is one of many primary neglected zoonoses worldwide. Within endemic developing countries, CE has multiple effects on animal and human health and well-being. To address such effects, veterinary and human medical sector collaboration on prevention program delivery is essential. To begin preliminary evaluations of county specific prevention programs, a critically appraised topic (CAT) was conducted. It sought to answer: What impact do CE prevention programs have on human and animal disease prevalence, in populations living in endemic developing countries within Africa, Central Asia, and South America? **Methodology.** The aim was to assess the ability of prevention and control program outputs to produce measurable differences in health, social, and economic outcomes (e.g., improved access to medical services, positive behavioral change, or reduced treatment costs, respectively). Included articles were obtained using predefined inclusion/exclusion criteria from the four databases (CAB Abstracts and Global Health; the National Library of Medicine (PubMed); ScienceDirect; and WHO Institutional Repository of Information Sharing (IRIS)). The articles were appraised using three checklists: the Royal College of Veterinary Surgeons (RCVS), the Critical Appraisals Skills Programme (CASP), and the Joanna Briggs Institute checklists. **Results.** Ten articles were selected. Geographically, 20% of studies were conducted in South America, 30% in Africa, and 50% in Central Asia. For definitive hosts, dogs, CoproELISA antigen testing, before and after Praziquantel (PZQ) de-worming, was a primary focus. For humans, who are intermediate hosts (IH), disease surveillance methods, namely ultrasound (US), were commonly assessed. Whilst for sheep, also acting as IH, disease prevention methods, such as the EG95 livestock vaccine and de-worming farm dogs, were evaluated. Common to all studies were issues of program sustainability, in terms of regular human US screening, dog de-worming, and annual sheep vaccination. This was attributed to transient and remote human or animal populations; limited access to adequate roads or hospitals; few skilled health workers or veterinarians; an over-reliance on communities to administer preventatives; and limited resources. **Conclusion.** Despite variations in result validity and collection periods, useful comparisons of CE endemic countries produced key research and program recommendations. Future research recommendations included testing the significance of multiple program outcomes in relation to prevalence (e.g., the social outcome: behavioral change), further research on the impact of livestock vaccinations, and the CE transmission role of waterways and sanitation. Program recommendations included calculating and distinguishing between stray versus owned dog populations; formal representation of internal and external stakeholder interests through institutional organization; establishing sustainable guidelines around the frequency of PZQ and vaccination administration; improved veterinary-human medical training and resource sharing; and combined prevention methods and multiple canine disease management.

1. Introduction

Globally each year, cystic echinococcosis (CE) causes an estimated 19,300 deaths, and a loss of US\$3 billion to treatment

costs, especially within the livestock industry [1]. Within the multi complex species (*Echinococcus granulosus sensu lato*), *E. granulosus sensu stricto* (G1) causes the highest prevalence and widest global distribution of human cases ([2], p. 2).

Dogs are the definitive hosts, infected by ingesting prey or raw meat containing metacestode cysts (larvae) [3]. Although dogs remain mostly asymptomatic, they excrete proglottids or infective eggs that are ingested by multiple mammalian intermediate hosts (IH), such as sheep, cattle, wildlife, and humans [4]. IH can remain asymptomatic for years, until growing cysts rupture or cause complications in adjacent organs ([5], p.12).

For many living in low socioeconomic and/or remote areas within endemic countries, recommended medical diagnostic methods and preventatives, such as Praziquantel (PZQ) (5 mg/kg) for dogs [6] or the EG95 livestock vaccine [2, 7], are not always readily accessible. Access to social services, such as healthcare, can act as a development capability [8, 9]. That is, it presents an opportunity to enhance one's well-being or acts as a constraint, which contributes to vicious cycles of poverty [10–12]. Cost-effective preventatives, such as public health education programs, and veterinary and human medical collaboration [13–17] have been suggested to overcome resource constraints. Public health education campaigns and multi-stakeholder collaboration are essential to producing social outcomes, such as behavioural change, that can reduce disease incidence. Examples of positive behaviours include: not feeding dogs raw meat, hand washing after handling dogs, and preventing canine access to common livestock, wildlife, and human environments [18–20].

CE control and prevention programs have been broadly identified in endemic regions of Africa, South America, and Central Asia [16]. Since 2019, the progress is evident in countries, like Mongolia, where a multi-stakeholder program provided PZQ de-worming for dogs and human ultrasound (US) screening [21]. However, few studies have analyzed the effectiveness of prevention or control programs, in terms of specific outcomes. Most focus on human medical and surgical treatments or conducting cohort or case control studies to identify common risk factors. Thus, the aim of this critical appraisal was to conduct a program impact assessment to provide evidence-based recommendations for current public and animal health programs.

2. Methodology

Four online databases were searched (Table 1). These included the following: CAB Abstracts and Global Health (1973-present), the National Library of Medicine (PubMed), ScienceDirect, and the WHO Institutional Repository of Information Sharing (IRIS) [22] and “Echinococcosis” webpage [11]. PubMed and CAB abstracts produce comprehensive veterinary and human medical research [23–25], while the ScienceDirect database produces full text, peer reviewed literature on healthcare [26]. Additionally, the WHO resources were searched, as it is one of the leading international organizations conducting CE programs in endemic regions.

2.1. Screening Process. Within the ScienceDirect database, the journals were selected from two “Subject Areas”: “Veterinary Science and Veterinary Medicine” and “Medicine and

Dentistry.” Further refinement was achieved by applying inclusion/exclusion based upon relevance to the topics of “parasitology,” “public health,” “zoonoses,” and “developing countries” [26]. Additionally, within CAB abstracts, the word “veterinary” and phrases “one health” and “animal health” originally resulted in the exclusion of several relevant articles. This became evident when conducting repeat searches. Thus, these terms were excluded in the final search (Table 1) to improve sensitivity, as lower specificity could be easily corrected. For example, predefined inclusion/exclusion criteria (Table 2), synonyms, Boolean operators, parentheses, and truncation (CAB Abstracts only) were used to increase result specificity.

Furthermore, articles were refined using an ordered selection process (Table 3). The fifth exclusion criteria “non-English articles” (Table 2) presents a methodological limitation, as sensitivity is reduced. However, the aim was to avoid timely and possible inaccurate article translations. Additionally, across all databases, the words “diagnostic” and “tests” were included in search terms; as many prevention programs encompassed diagnostic tests to monitor program impact. However, studies [27] that conducted generalized evaluations of individual treatment or diagnostic tools were excluded [28].

Finally, articles were sorted based upon relevance. The article title and abstract were reviewed for key words e.g., “echinococcus,” “prevention,” and/or “control.” If relevance could not be determined, the full texts, namely, the discussion and methodology, were reviewed. Integrated prevention program assessments of multiple diseases [31–33] were excluded. Individual disease analysis is important, as each disease has its own complex transmission pathway and diagnostics. However, there was one exception [34], because CE program outputs and impacts were readily distinguished from other diseases.

Despite the described replicable criteria, methodological limitations may arise from inaccurate subjective application of inclusion/exclusion criteria or study design categorization. For example, controlled clinical trials were excluded because of a high number of false positive search results. Nevertheless, PubMed still produced a non-randomized controlled trial that fit the inclusion criteria. Differences in categorization of this study existed between this CAT, article authors, and the database.

2.2. Geographical Selection. Africa, South America, and Central Asia are listed as CE endemic regions [16], consisting of low to middle income countries [35–37]. The included studies within these regions were mostly in countries that ranked below 50/188 on the United Nations Development Programme (UNDP) multidimensional poverty index [38]. For example, Kyrgyzstan (142) and Kenya (143) are two of the lowest ranked [38], but countries like China were included, as it represents 40% of the world's CE caused disability-adjusted life years (DALYs) ([39], p.138).

2.3. Critical Appraisal Method. Applying a triangulation method, which is not reliant upon one set of appraisal criteria, reduced the probability of information bias. Checklists

TABLE 1: Search strategy for the four databases.

Database	Search terms and total results (before exclusion criteria)
CAB Abstracts via Web of Science: CAB Abstracts® and Global Health® (1973-present)	<p>1. Echinococcus* OR <i>Echinococcus granulosus</i> OR cystic echinococcosis OR hydatid OR tapeworm OR neglected zoonoses* OR zoonotic</p> <p>2. Prevention* OR preventatives OR control OR diagnostic* OR tests OR surveillance OR education OR praziquantel OR copro* OR vaccine* OR ultrasound</p> <p>3. Effectiveness* OR impact OR evaluation OR assessment* OR prevalence</p> <p>4. Animal* OR public health OR medical*</p> <p>5. South America OR Americas OR Central Asia OR Asia OR Africa OR developing OR endemic OR poverty OR impoverished OR low socioeconomic OR poor</p> <p>Total: 4991</p> <p>(<i>Echinococcus granulosus</i> OR cystic echinococcosis OR hydatid OR tapeworm OR neglected zoonoses OR zoonotic) AND (prevention OR preventatives OR control OR surveillance OR education) AND (effectiveness OR impact OR evaluation OR assessment) AND (veterinary OR animal OR public health OR medical) AND (South America OR Central Asia OR Asia OR Africa OR developing OR endemic OR poverty OR impoverished OR low socioeconomic OR poor)</p>
PubMed (National Library of Medicine)	<p>NB: using the search word “cystic,” before echinococcosis, made a difference of 2 articles, which were excluded</p> <p>Total: 4932</p> <p>(<i>Echinococcus granulosus</i> OR cystic echinococcosis OR Echinococcosis) AND (prevention OR control OR surveillance) AND (effectiveness OR impact OR evaluation)</p>
ScienceDirect	<p>Total: 276</p> <p>(<i>Echinococcus granulosus</i> OR cystic echinococcosis OR hydatid OR tapeworm OR neglected zoonoses OR zoonotic) AND (prevention OR preventatives OR control OR surveillance OR education) AND (effectiveness OR impact OR evaluation OR assessment) AND (veterinary OR animal OR public health OR medical) AND (South America OR Central Asia OR Asia OR Africa OR developing OR endemic OR poverty OR impoverished OR low socioeconomic OR poor)</p>
(i) WHO Echinococcosis Webpage (ii) Institutional Repository of Information Sharing (IRIS) Database	<p>NB: individual journals within IRIS database searched using words “echino,” “cyst,” or “helminth”</p> <p>Total: IRIS: 3535; WHO Site: 2 journal articles</p>

Search dates: Repeated 4 times over December 2020, January 11th, and February 2021.

included templates from the Royal College of Veterinary Surgeons [24], the Critical Appraisals Skills Programme [40] for health professionals, and the Joanna Briggs Institute [41] for health and medical sciences.

3. Results

3.1. Summary of Evidence. A total of ten studies (Tables 4–13) were selected using predefined selection criteria (Table 2) and the screening process outlined (Table 3). Most studies (70%) were non-randomized, non-blinded studies. This included four observational studies (cross-sectional studies: two randomized and two non-randomized), one experimental (non-randomized controlled trial), three quasi-experimental before/after studies (two non-randomized and one randomized), and two qualitative studies. Cross-sectional and before/after studies predominated (7/10 studies), as they produced direct evaluations of program outcomes and impact. There were variations in study designs, sample size, and collection periods, which complicated direct comparisons. Nevertheless, programs were all situated in endemic low to middle income countries and produced useful comparative findings. Geographically, two studies (20%)

were conducted in Argentina (South America), one (10%) in Kenya, and two (20%) in Morocco (Africa). Five (50%) were conducted in Central Asia, specifically in China, Mongolia, and Kyrgyzstan.

3.2. Study Designs. This CAT focused on evaluating program outcomes and impacts, versus disease causality and risk factors, commonly tested by several excluded cohort and case control studies. Compared to cross-sectional studies and case control studies, cohort studies are relatively expensive, which is often not suitable in low socioeconomic contexts. Nevertheless, cohort studies are superior in terms of monitoring disease incidence rates and controlling against confounding demographic or signalment variations, by consistent respondent follow-up. Whilst case control studies are usually more cost effective, within a low socioeconomic context, access to consistent human and animal health data may be limited. Respondant follow-up was a challenge across most included studies, as sample human or animal populations were often transient [42, 43, 51] and resided in remote areas [15, 34, 43], with limited access to adequate roads, hospitals, or resources [2, 6]. These challenges make selection of a control group practically difficult and may account for the few experimental studies encountered.

TABLE 2: Article exclusion/inclusion criteria.

Exclusion:	<ol style="list-style-type: none"> 1. Date: anything outside of 2015-2021 2. PubMed and WHO IRIS only: “full text” and “abstract” selected to exclude articles with incomplete access 3. Document type: <ol style="list-style-type: none"> (i) CAB: book, book chapter, thesis, conference proceedings, correspondence, bulletin, editorial, bulletin article, miscellaneous, and annual report (ii) PubMed: books and documents (iii) WHO: publications, technical documents, advisory committees, meeting minutes, governing bodies documents, and regional director documents (iv) Science Direct: exclusion of both document and study types combined under one category: “Article Types” 4. <ol style="list-style-type: none"> (i) CAB: 13 “Research Areas” (Plant Sciences, Reproductive Biology, Marine Freshwater Biology, Meteorology Atmospheric Sciences, Anesthesiology, Forestry, Sports Science, Film Radio Television, Fisheries, Archaeology, Arts Humanities Other Topics, Materials Science, and Paleontology) All searched using “echinococcosis,” “cyst,” “tapeworm,” “control,” or “prevention,” before final exclusion. (ii) Science Direct: 8 “Subject Areas” (Immunology and Microbiology; Agricultural and Biological Sciences; Biochemistry, Genetics and Molecular Biology; Pharmacology, Toxicology, and Pharmaceutical Science; Environmental Science; Chemistry; Neuroscience; and Engineering) 5. Language: non-English 6. Study type: <ol style="list-style-type: none"> (i) PubMed: clinical study, clinical trial, controlled clinical trial, meta-analysis, clinical trial veterinary, and systemic review (ii) Manual exclusion for CAB, WHO, and ScienceDirect Reviews: systemic reviews (exception for program and country specific reviews) and narrative reviews Experimental studies: crossover trials, controlled in vitro laboratory or clinical trials (based on individualized treatment and diagnostic methods, not country or program specific) Observational studies: case control studies, opinion pieces, and meta-analysis 7. Relevance based upon “title,” “abstract,” or “full text” (if exclusion could not be made from reviewing article title or abstract)
Inclusion:	<ol style="list-style-type: none"> 1. Date: 2015-2021 2. PubMed and WHO IRIS only: “full text” and “abstract” selected 3. Document type: <ol style="list-style-type: none"> (i) CAB: journal article, conference paper, and journal issue (ii) PubMed: journal article (iii) WHO (“Communities and Collections” in IRIS: Headquarters (Journal Bulletin, Journal articles); Regional office for Africa (Country Offices, Journal articles); Regional office for the Americas (Journal articles and newsletters, publications); Regional office for Southeast Asia (Country Offices, Regional Journals, Regional Publications, Sub-Committee on Policy and Programme Development and Management); and Regional office for the Western Pacific (Regional Office for the Western Pacific Publications)) (iv) Science Direct: “article types:” review articles, research articles, data articles, case reports, mini reviews, and other 4. <ol style="list-style-type: none"> (i) CAB: all but 13 excluded “Research Areas” (ii) Science Direct: “Subject Areas”: “Veterinary Science and Veterinary Medicine,” and “Medicine and Dentistry” 5. Language: English 6. Study type: <ol style="list-style-type: none"> (i) PubMed: comparative study, evaluation study, observational study, observation study veterinary, and review (ii) No selection option for CAB, WHO, and Science Direct. Thus, manual inclusion Observational studies: cohort, cross-sectional, before and after study, and interrupted time series Descriptive studies: case series, program, and country-specific observational studies 7. Relevance based upon title, abstract, or full text review: <ol style="list-style-type: none"> (i) Addresses research question (ii) Focused on surveillance, control, or prevention programs; social, health, or economic outcomes (e.g., behavioral change and access to medical services); impact (e.g., disease prevalence) (iii) Disease: <i>Echinococcus granulosus</i> species (iv) Population: Endemic developing countries in Central Asia, Africa, or South America

In addition, ethical issues arise if an animal or human, with little access to services, is denied preventative treatment to be assigned to a control group. Indeed, Yang et al. [43] concluded that it would be ethically negligent to select a control site, after the government identified that CE was endemic in Northwest China ([43], p.357). Thus, in China [15, 43], Mongolia [15], Argentina [2, 6], and Kenya [42],

many included studies utilized non-randomized convenience sampling. The majority used cross-sectional study designs, as they are relatively cost effective and practical at sampling populations at different points in time.

Furthermore, quasi-experimental studies were suitable in comparing a pre- and post-program impact. The sample population is ideally exposed to the same program output

TABLE 3: Search outcome inclusion/exclusion strategy.

Database 1.Date (2015-2021)	2. Full text and abstract	3.Excluded document or article types	4.Excluded "Research or subject areas"	5. Non- English articles excluded	6. Excluded study types	7. Relevance to RQ: title, abstract, and full text	Duplicates Total: 17	Total Included Studies
CAB Abstracts® and Global Health® (1973-present)	No search selection available	130 4861 articles left	436 4425 articles (4861-4425) 13 "research areas"	936 (4425- 3489)	11 (1 Mathematical modeling- Bayesian 1 case control 8 narrative reviews 1 systemic review) (3489- 11 = 3,478)	3471 (3478-1-6)	1 Previous studies ex: [29, 30]. Recent article on complete 8- year program included [2]	6
PubMed	112 (4932-4820)	37 (4820-4783) Study types excluded: systemic reviews, meta-analyses, control trials, and book chapter	No search selection available	41 (4783- 4742)	15 (4742- 15 = 4,727) 1 case control 1 report 11 narrative reviews 2 systemic reviews	4716 (4727-9-2 = 4, 716)	9	2
ScienceDirect (see Appendix A for detailed selection process)	No search selection available	34	8 "subject areas"	No search selection available	34 Website: 1 website article IRIS: 957 publications 1 Meeting Report 1 narrative review	242 (5 duplicate PubMed, 6 duplicate CAB) (1 article both CAB and PubMed)	7	2
WHO Echinococcosis Webpage AND IRIS	IRIS: 3535 articles left after initial non- full text exclusion WHO Website: 2 research articles	No search selection available	No search selection available	IRIS: 578 (3535- 2957)		IRIS: 1998 WHO site: 2	0	0

Total articles included: 10.

TABLE 4: Appraisal summary of Article Meeting Inclusion Criteria [6].

Population:	Rio Negro province (Northern Patagonia), Argentina: (i) Province area: 120,013 km ² (ii) Population density: 0.88 inhabitants/km ² (iii) Dogs living on livestock (sheep and goat) farms (iv) School Children (6-14 years old) associated with 13 program areas (hospitals) and 80 Primary Health Care Centers (PHCCs)
Sample size:	(i) 1790 canine fecal samples (ii) 34,515 school children (6-14 years old)
Program outputs:	<i>Definitive hosts (dogs)</i> (i) Praziquantel (PZQ) de-wormer (5 mg/kg four times a year). Administered by 65 rural health assistants (tablets smeared in liver pate) or dog owners <i>Intermediate hosts</i> (i) Livestock: vaccination (EG95) from 2006 (ii) Children: ultrasound (US) screening by trained general physicians. All cases surveyed to identify potential exposure sites (e.g., relationship to livestock). Case follow-ups within hospitals (iii) <i>Community surveys</i> conducted by veterinarians, doctors, and surgical services (iv) <i>Sanitary education</i> : 65 rural health assistants
Study design:	Randomized prospective cross-sectional study
Program outcomes and/or impact:	<i>CE prevalence in three sampling periods (2003–2005, 2009–2010, 2017–2018):</i> <i>Dogs:</i> (i) Positive CoproELISA samples confirmed by Western blot (WB) (2003–2005; 2009–2010) and PCR (2017–2018) (ii) Samples collected using sterile methods and stored at –40 °C until processing (iii) Veterinarians ($n = 12$) provided technical and scientific support <i>Children:</i> (i) US screening across 13 public hospitals and 80 primary health centers (ii) Temporal-spatial heat mapping (QGIS 3.4.6) of human cases in areas with highest proportion of CE positive dogs
Main findings:	<i>Prevalence in dogs (definitive host):</i> (i) Canine positive fecal samples by CoproELISA: 32.0% (2003-2005), 32.9% (2009-2010), and 15.6% (2017-2018). Between 2003-2018, 16.4% decrease in prevalence (ii) Subsequent confirmation tests (WB and PCR) over three testing periods: 14.7% (95% CI, 10.7–19.5), 12.1% (95% CI, 8.1–16.2), and 7.4% (95% CI, 4–11.9). A 7.3% prevalence decrease detected from positive canine fecal samples (iii) Prevalence differences between the first (2003-2005) and third (2017-2018) period statistically significant ($P < 0.05$, $P = 0.009$), based upon Chi-squared linear (EPIDAT 3.1) trend analysis. Not significant between periods one-two or two-three <i>Prevalence in children (6-14years) (intermediate host):</i> (i) In periods 2003–2008, 2009–2016, and 2017–2018: 0.4% (95% CI, 0.3–0.6), 0.2% (95% CI, 0.1–0.3), and 0.1% (95% CI, 0.05–0.3), respectively, calculated. Between 2003-2018: 0.3% decrease, with 95 asymptomatic cases diagnosed with hepatic CE (ii) Statistically significant differences: first (2003-2008) and second period (2009-2016) ($P = 0.0004$, $P < 0.05$); not second-third ($P = 0.35$, $P > 0.05$) (iii) <i>Highest livestock farm prevalence</i> : Andean and Pre-Andean regions (program areas of Norquinco, Comallo, and Pilcaniyeu); the central plateau of the province (Ingeniero Jacobacci, Los Menucos, and Maquincha); and in the east (Valcheta and Ramos Mexia) <i>Barriers (limited access to diagnostic, treatment, and prevention services):</i> (i) Harsh or remote climatic terrain limited access or delivery of resources (ii) Infrastructure constraints: poorly structured roads limited frequent and safe travel (iii) Poor sanitation: little knowledge about sanitary practices. Minimal sanitation infrastructure to dispose of infected offal (iv) Distance between rural hospitals and primary health centers (normally >80/100 km) (v) Missed PZQ administration, causing reinfection in dogs (vi) Urbanization: increasing rural to urban transmission from dogs to children, due to increasing domestic slaughter of small ruminants in cities
Limitations:	(i) No clearly defined research question (ii) Information bias: temperature fecal samples collected not reported. Hotter summers and freezing winters can decrease CE egg lifespan, compared to ideal temperatures in Autumn or Spring

TABLE 4: Continued.

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- (iii) Result reliability: CoproELISA tests confirmed by two different methods: WB in first two study periods and PCR in the last
 - (iv) Limited sensitivity of US in detecting pulmonary cysts
 - (v) Sample size calculation: prevalence treated as a single independent proportion for each sample population (dogs and children). Comparing two independent proportions may be more suitable, as the two populations were treated as interdependent
 - (vi) Few details about community survey method (e.g., verbal, written, and electronic) or question type (open, closed, and MCQ)
 - (vii) CoproELISA results not instantaneous. Thus, control measures may be delayed
- Confounding variables*
- (i) Did not distinguish between owned and stray dogs
 - (ii) Non-standardized PZQ administration: owner and rural health workers
 - (iii) Researchers not blinded to de-worming administration method (e.g., if farmers or rural health workers de-wormed dogs)
 - (iv) List “sanitary education” as a program output, but do not measure behavioral outcomes
-

to reduce confounding bias and increase validity. Ensuring sample group similarity was an evident limitation of some studies [2, 34, 45]. For example, in Van Kesteren et al.’s [34] study, pre-intervention prevalence rates for dogs were only calculated in 4/10 communities. For the remaining six communities, post-intervention data was not comparable. Finally, a limitation common to qualitative, or mixed methods studies, was an absence of detail about questionnaires, survey or interview question type, or delivery mode [6, 15, 45].

3.3. Sample Size. Four studies did not calculate sample size and/or include confidence intervals (CI) [39, 42, 43, 46], and some provided limited information about sample collection methods [15, 39]. This may be attributed to issues of accessing remote and/or transient communities. In Yu et al.’s [39] study, all data was centrally controlled by the National Ministry of Health, China, and no information about sample collection was provided. Consideration of how political or organizational agendas align with program outcomes is important, due to the centralized control of statistical data on CE prevalence.

Nevertheless, four studies did calculate sample size [2, 6, 34, 45]. For one before/after study [2], each expected proportion (prevalence rate) for humans, dogs, and sheep was treated independently. However, calculation based upon paired data (discordant pairs) would have been suitable, as one group of animals or humans was paired to two different prevalence values, at the start and end of the program. In addition, studies with limited population size [42, 43] could have utilized a finite population sample calculation [52].

Notably, a major issue with sample size calculation was captured in the 8/10 studies that did not specify an estimated stray dog population or sample size. This meant that only owned dogs were treated [2, 6, 39, 42] or generalized terms, such as “free roaming” dogs [34] or “dog management” [15], were used. Only three studies [43, 45, 46] clearly distinguished and treated stray dogs with PZQ. However, administration methods were not standardized, and population size was also not calculated by Yang et al. [43].

Additionally, one study [45] utilized convenience sampling of dogs caught by the local dog catcher. Although

ethics approval was obtained, the number ($n = 38$) of dogs euthanised for necropsy was not justified using a pre-defined sample size calculation. This is essential to minimise and validate the number of stray dogs necessary to test for significant differences in prevalence. Convenience sampling also reduced external validity, as selected stray dogs may have only been representative of a small area.

Furthermore, one before/after study [34] revealed the benefit of Lot Quality Assurance Sampling (LQAS) to evaluate the quality of health care programs [53]. Compared to other sampling methods, LQAS allows randomized analysis of a small community sample size, but not individual village level analysis. For countries with small, but remote or widely distributed communities, utilizing a sample size, such as nineteen, is ideal and has been proven to minimize type a and b errors [34, 54]. The LQAS enables identification of community areas that fall below average in achieving a specific program target. Indeed, Van Kesteren et al. [34] traced a transition from poor PZQ dosing coverage in 8/10 villages to improvements in reaching dosing targets (p.3). Nevertheless, LQAS may be logistically costly if researchers are required to travel to multiple program areas.

3.4. Program Outcomes and Impact. It is helpful to distinguish between program outputs, outcomes, and impacts when evaluating programs. Outputs can be defined as “the goods or services produced by programs...while outcomes are defined as the impact on social, economic, or other indicators arising from the delivery of outputs” [55]. An adapted definition of impact is when a program outcome “helps solve the problem that inspired actors to create” ([56], p.460) it.

Studies focused on health outputs and outcomes (e.g., access to medical or veterinary services) and their impact, in terms of disease prevalence. One study assessed economic outcomes (e.g., accumulated financial costs), and a few studies [34, 39] evaluated social outcomes (e.g., positive behavioral change in response to public health campaigns). While a core impact of prevention programs is to resolve the issue of rising disease prevalence, most studies failed to test the significance of prevalence changes in correlation to multiple social, health, and economic outputs and associated outcomes [2, 6, 34, 42, 43].

TABLE 5: Appraisal summary of Article Meeting Inclusion Criteria [42].

Population:	<p><i>Northwest Kenya, Turkana County (mainly migratory pastoral population): Five age groups</i></p> <ul style="list-style-type: none"> (i) (0-5 years): 15.4% (1985), 22.9% (2010-2011), and 25.7% (2011-2012) (ii) (6-11 years): 26.6% (1985), 24.6% (2010-2011), and 23.9% (2011-2012) (iii) (16-25 years): 23.2% (1985), 10.8% (2010-2011), and 11.9% (2011-2012) (iv) 26-50 years: 32.0% (1985), 29.0% (2010-2011), and 29.0% (2011-2012) (v) (>50 years): 2.8% (1985), 11.8% (2010-2011), and 9.4% (2011-2012) <p><i>Gender:</i></p> <ul style="list-style-type: none"> (i) Males: 38.2% (1985), 39.5% (2010-2011), and 39.9% (2011-2012) (ii) Females: 61.8% (1985), 60.5% (2010-2011), and 60.1% (2011-2012) <p><i>Program target areas:</i></p> <ul style="list-style-type: none"> (i) Highest surgical incidence of CE in the district (40 per 100,000); highest prevalence in dogs (63.5%); highest dog-to-human ratio; presence of wild animal reservoirs (golden and silver-backed jackals)
Sample size:	<ul style="list-style-type: none"> (i) No sample size reported (ii) Non-randomized convenience sampling
Program outputs:	<p><i>Cystic echinococcosis control program (Kenyan Ministry of Health; African Medical and Research Foundation (AMREF) Health Africa; Kenya Medical and Research Institute; Ministry of Agriculture; and local non-governmental organizations):</i></p> <ul style="list-style-type: none"> (i) <i>Health education campaigns:</i> reducing contact with dogs, not feeding infected offal, large stray dog population transmission, and anthelmintic administration. Education delivered verbally, via video and images of surgical treatments and canine CE infections (ii) Targeted women (high risk population). Initially delivered by program education officers. Subsequently, community members trained <p><i>Human ultrasound (US) screening in Lopiding, Kakuma, and Lodwar hospitals:</i></p> <ul style="list-style-type: none"> (i) Total scanned: 3,553 (1985), 3,179 (2010-2011), and 4,188 (2011-2012) (ii) World Health Organization CE cyst classification: standardized screening of the liver, spleen, and kidneys. Screening at the same time of year and same location. Video display of suspected CE lesions recorded digitally or on thermal paper (iii) Positive cases referred to closest health facility for follow-up (funding permitted) and counseled on stage of infection (iv) Positive cases treated: smaller cysts with albendazole and puncture-aspiration-injection. Larger, complex cysts (e.g., CE2-3 stages) treated surgically <p><i>Dogs:</i></p> <ul style="list-style-type: none"> (i) Arecoline (ii) Praziquantel (PZQ) de-wormer every 6 weeks (iii) Female dogs spayed
Study design:	Non-randomized cross-sectional study
Program outcomes and/or impact:	(i) <i>Prevalence</i> in patients who tested positive between 1985-2012 and 2010-2012
Main findings:	<p><i>CE prevalence:</i></p> <ul style="list-style-type: none"> (i) US diagnosed: 961 patients with 2,182 cysts (1983-2012). Overall decrease: 5.6% (1985) to 1.9% (2010-2011), and 3.8% (2011-2012) (ii) Early prevalence reductions mostly attributed to reductions in dog population and regular PZQ treatment (iii) Age: Statistically significant differences ($P = 0.005$, $P < 0.05$) in age groups (0-5, 16-25, and <50 years) between 1985 and 2012. Continuing trend of higher prevalence in females, across multiple age groups. Although a relatively smaller sample size, prevalence (>50 years) has not changed significantly when compared to other age groups. Attributed to persistent infection and lower life expectancy before program (iv) <i>Gender:</i> CE prevalence per 1000 males or females between 1985 and 2010-2011 or 2011-2012, statistically significant ($P = 0.0083$, $P < 0.05$) (v) <i>Behavioral outcomes:</i> appropriate disposal of offal and dog population control. Health education programs targeted to women, who spent most time at home with dogs, linked to behavioral changes and decreased CE prevalence. Effects of health education conclusively slow and rarely effective alone (vi) <i>Infrastructure:</i> construction of abattoirs (vii) Statistically significant changes to prevalence linked to both gender and age, using Pearson χ^2 ($P < 0.001$) and ordinal Somers' d tests ($P < 0.01$) (viii) US proved superior results (higher sensitivity) compared to serology ELISA. CE cysts detected in 198 patients using US vs. 76 using serology ELISA

TABLE 5: Continued.

	<p><i>Barriers:</i></p> <ul style="list-style-type: none"> (i) Large, young, immunologically naive dog population (ii) Human behavior facilitating transmission (iii) Limited Infrastructure and Services: no abattoirs; and limited access to medical and veterinary care (iv) Test positive patients hesitant to undergo surgical treatment (v) Low education and literacy rates (vi) Transmission-supportive customs or behaviors (vii) Environmental factors, such as open grazing or herding dogs near cattle, can reduce the impact of health education
Limitations:	<ul style="list-style-type: none"> (i) No research question (ii) No sample size reported. Due to transient nature and remoteness of the Turkana population, actual population numbers not obtained, only representative estimates (iii) Unclear when serology testing ceased (may be 1980s) (iv) Analysis of data between (1983-2010) obtained from secondary source (v) Missing serology data for 5-year-old patients (vi) Reliability: some dogs administered arecoline, and some PZQ (vii) Information bias: US screening times not standardized. Study did not control for multiple presentations (duplicate results) or specify skill set of US screeners (viii) US is not sensitive to detecting pulmonary or osseous lesions (ix) No details of ethics approval for female dogs spayed <p><i>Confounding variables:</i></p> <ul style="list-style-type: none"> (i) The introduction of unvaccinated sheep into study area (ii) Community behavioral changes not tested for correlation to health education or prevalence (iii) Did not distinguish between stray and owned dogs. Not clear if stray dogs were tested or treated. Used general term: "local dog population"

More specifically, studies identified health education campaigns as program outputs [2, 6, 34, 39, 42, 43, 50], but only three [2, 34, 42] measured campaign outcomes (e.g., social outcome: behavioral change). For example, Arezo et al. [6] identified sanitary education (e.g., adequate disposal of infected offal) as a program output, but it was not analyzed with respect to specific outcomes. Van Kesteren et al. [34] went further to measure behavior as a social outcome, in terms of dog owner PZQ administration. While semi-structured questionnaires measured CE disease knowledge, it was not linked to a specific program output (e.g., public health education) or tested for significant correlations to specific program impacts (e.g., decreased CE prevalence).

Additionally, a study in China [45] linked communities' level of knowledge to achieving high PZQ dosing rates in the previous year (p.5). However, significant correlations of de-worming behavior to a specific program output (e.g., public health campaign) or prevalence, were not tested. Thus, the final impact could not be concluded. Similarly, Yu et al. [39] measured behavioral change, by measuring pre and post-program de-worming coverage, but did not test for significant correlations to a program output or impact.

Solomon et al.'s [42] study went further, in terms of evaluating a specific health education campaign, which was targeted to women in Kenya, who spent most of the time at home with dogs. Prevalence reduction was attributed to health education producing positive behavioral change, such as appropriate offal disposal. Given that education programs targeted women and statistically significant changes in prevalence were linked to gender (Pearson χ^2 , $P < 0.001$; ordinal Somers' d tests, $P < 0.01$) ([42], p.591), this correlation

seems valid. However, confounding variables, such as literacy rates, previous reductions in dog population size, and increased PZQ treatment, introduced confounding bias.

3.5. Confounding Variables. Numerous studies did not measure behavior as an outcome of public health education outputs, which essentially introduced confounding bias. Consistent positive behavioral change is essential to minimize CE transmission. The behavior can potentially enhance or constrain the effects of animal or human health outcomes and, ultimately, the impact of disease prevalence. For example, feeding dogs infected offal is an established transmission pathway [3] that can constrain the effects of de-worming dogs. Indeed, Van Kesteren et al. [45] concluded that health education had the potential to decrease CoproELISA prevalence, by inciting positive behavioral change, such as increasing PZQ administration. Whilst Larrieu et al. [2] concluded that programs with a combined education component enhanced the positive effects of canine anthelmintic treatment and sheep vaccination coverage ([2], p.5).

In addition to behavioral change, only one study [46] accounted for seasonal climatic variations. It is essential, as at 4 °C, *E. granulosus* eggs have a lifespan of ≥ 300 days compared to 2–14 days at 37–39 °C ([3], p.438). Indeed, Amarir et al. [46] reported that calendar time and location had significant effects ($P < 0.001$) on CE prevalence in stray and owned dogs in Morocco (p.440).

Finally, there were evident disparities in skill levels when conducting diagnostic tests or administering preventive treatments, such as PZQ [6, 34, 42, 43, 46]. Van Kesteren et al. [34] acknowledged the reality that leaving dog owners

TABLE 6: Appraisal summary of Article Meeting Inclusion Criteria [43].

Population:	(i) Location: Emin County, Xinjiang Uygur Autonomous Region, China (Xinjiang 1/5 major pastoral areas). Comprised of 11 administrative townships, with five pastures and one farm, covering 1,050 acres of natural grassland (ii) All sheep raised locally outdoors: 73.5% (12,649/17,215) males; 42.8% (7,363/17,215) aged <1 year; 91.4% (15,735/17,215) aged <3 and 1.6% >4 years old. Thus, majority male sheep (0-3 years old) (iii) Domestic and stray dogs
Sample size:	(i) 17,215 slaughtered sheep (ii) Total human population 220, 000 (iii) All domestic dogs and stray dogs in the county
Program outputs:	<i>National control program launched 2006, study commenced October 2007:</i> (i) <i>De-worming dogs with Praziquantel (PZQ):</i> dose 200 mg/<15 kg and 400 mg >15 kg. Each village appointed one resident to de-worm owned dogs (ii) Stray dogs de-wormed by auto-feeding PZQ-mixed in food and left at assigned sites (iii) Dog feces buried to prevent transmission <i>The County Department of Quarantine implemented:</i> (i) Strict management and inspection of slaughterhouses (ii) Quarantine of livestock from dogs (iii) Restrictions on feeding dogs infected offal (iv) Prohibited sale of infected meat or “sick animals” (v) Community health education to promote positive behavioral change. Village appointed one resident to de-worm dogs and deliver health education (e.g., washing hands before meals and drinking boiled water) (vi) Treatment of human patients
Study design:	Non-randomized prospective cross-sectional study
Program outcomes and/or impact:	(i) Cystic Echinococcosis (CE) prevalence in slaughtered sheep from during peak slaughter (October 2007 to November 2013) at one authorized slaughterhouse in Emin County (ii) Prevalence calculated by subjective visual inspection and palpation of hydatid cysts across multiple organs: liver, lungs, spleen, heart, and kidneys
Main findings:	(i) <i>Prevalence/infection rate:</i> Statistically significant ($X_{trend^2}=59.79, P < 0.001$) decreased 27% (1.8/6.6) (2007-2010) (ii) 2007 (6.6%); 2008 (3.9%); 2009 (2.0%); 2010 (1.8%); 2011 (1.9%); 2012 (1.7%); 2013 (2.0%); 2010-2013 not statistically significant ($P > 0.05$) (iii) Prevalence increased as sheep aged: 4.5% at the age <1, 6.7% at age 2~, and 17.9% ≥ 4 years. Decline in sheep response to control measures attributed to issues of program sustainability (e.g., missed PZQ dosing increasing dog-sheep transmission) (iv) Domestic dogs living in large populations in Northwest China (2-4 shepherding dogs per household) were primary definitive host (v) Dogs played important cultural and productive roles as shepherds of livestock. In ethnic communities in Western China, Buddhist religion forbids the killing of any animals (vi) Dogs' proximity to humans and water sources increased transmission (vii) Barriers to testing roaming stray dogs due to inaccessibility of remote and widely distributed terrain
Limitations:	(i) No sample size calculation for sheep (ii) No sample size calculation or population size for owned or stray dogs (iii) No detail about sample collection methods (iv) Mentioned community public health education, but no measures of program outcomes or correlation to significant differences in prevalence (v) PZQ administration method not standardized for domestic vs. stray dogs (vi) Each village appointed one resident to de-worm dogs and deliver health education. No mention of how resident was selected or trained (vii) Post-mortem: visual assessment could introduce subjective bias if variations in assessor skill or method (viii) The finding of increased incidence as sheep age was not clearly supported by the study's cited reference [44]

to self-monitor de-worming does not guarantee that recommended guidelines are followed. Across all studies, there was no detail of ongoing support or training of assigned community members to program tasks, which may have limited program impact.

3.6. Diagnostic Tests

3.6.1. *Canine Definitive Host: Diagnostics, Coproantigen ELISA Prevails.* Despite potential cross reactions with *Taenia hydatigena*, Arezo et al. [6] concluded that Coproantigen

TABLE 7: Appraisal summary of Article Meeting Inclusion Criteria [2].

Population:	<ul style="list-style-type: none"> (i) Study location: Rio Chico Abajo (Department Ñorquinco), Anecón Grande (Department Pilcaniyeu), Mamuel Choique (Department 25 de Mayo), and Nahuel Pan (Department Bariloche) in the Province of Rio Negro, Patagonia region, Argentina (ii) Small ruminant farmers in Rio Chico (iii) Human population: Mapuche native communities (Anecón Grande and Nahuel Pan) living on reserves, with a Lonco (cacique), common property land
Sample size:	<ul style="list-style-type: none"> (i) <i>Sheep</i>: 2009, 79 farmers (8483 sheep); 2017 (3898 sheep). Randomized farm selection (ii) <i>Dogs</i>: 2009 (309 dogs); 2017 (221). Total dogs Praziquantel (PZQ) treated: 11, 500. Non-randomized sampling of high dog population areas (judgment sampling) and voluntary dog owner participation (convenience sampling) (iii) <i>Humans</i>: non-randomized selection of 84 children from a school within vaccination area
Program outputs:	<p><i>Definitive host control (dogs)</i>: 1980 four government departments launched dog de-worming program. Health centre at each study site (except Nahuel Pan):</p> <ul style="list-style-type: none"> (i) Rio Chico and Mamuel Choique: health workers conducted home visits to administer PZQ, by combining tablets with minced meat (ii) Anecón Grande: health worker travelled by horse to deliver PZQ, but dog owners administered (iii) Nahuel Pan: dog owners collected PZQ from local health center to administer <p><i>Intermediate host control</i>:</p> <ul style="list-style-type: none"> (i) <i>Sheep</i>: 29, 323 doses of EG95 vaccine administered between December 2009 and January 2017 in Rio Chico (17, 894); Nahuel Pan (1056); Mamuel Choique (2220); and Anecón Grande (8153) (ii) Vaccination coverage: dose 1: 83.5%; 2: 80.1%; and 3: 85.7% (57.3% average vaccination coverage). Three doses over 12 months: (1) 30 days of age; (2) 60 days, before weaning; and (3) booster injection at 1-1.5 years of age (iii) Vaccine prepared and donated by the University of Melbourne (50 or 100 dose vials plus an adjuvant) (iv) Administration method: vaccine reconstituted with distilled water and injected subcutaneously (dose: 50 µg of EG95 protein in 2 ml volume). Ear tags placed on vaccinated. Veterinarians administered for one week every December and January from 2009 (v) Local health care workers and national AM radio sent reminders to ensure farmers gathered all sheep prior to vaccination weeks (vi) Animals who escaped or failure to gather not vaccinated (vii) <i>Children (6–14 years old)</i>: ultrasound screening and albendazole treatment from 1997 (viii) <i>Community education campaign</i>: health workers and veterinarians delivered. Aimed at schoolchildren and rural residents
Study design:	Quasi-experimental, non-randomized before and after study
Program outcomes and/or impact:	<p><i>Cystic Echinococcosis (CE) prevalence tested pre-program</i>:</p> <ul style="list-style-type: none"> (i) <i>Dogs</i>: CoproELISA confirmed by Western Blot (WB) of dog fecal samples and arecoline purgation test (ii) <i>Sheep</i>: ELISA test on sera from sheep confirmed by WB. Necropsies of adult sheep, confirmed by histology <p><i>Post-program (2009-2017) follow-up (100% sheep vaccination coverage expected)</i>:</p> <ul style="list-style-type: none"> (i) 2011 serology: ELISA/WB 2-year-old sheep ($n = 238$) (ii) 2015 necropsy sheep (iii) 2017 veterinarians performed arecoline purgation tests to detect <i>E. granulosus</i> worms in vomit and Coproantigen ELISA testing of fecal samples (from 2003) (iv) Serology (double diffusion 5, ELISA) initially. From 1997: US screening of children (6–14 years old) replaced ELISA. Albendazole treatment also delivered
Main findings:	<p><i>Sheep</i>:</p> <ul style="list-style-type: none"> (i) 2011 Serology-ELISA/WB 2-year-old sheep ($n = 238$): significant difference detected between baseline number originally sampled and post-program impact ($P < 0.001$) (ii) Necropsy sheep: 56.3% 6-year-old sheep (2009) reduced to 21.1% (2015). Statistically significant decrease ($P = 0.03$, $P < 0.05$). Cysts per animal decreased size < 1 cm (iii) Infected sheep: 84.2% (2009) reduced to 22.2% (2017). A statistically significant decrease (P value = 0.0002, $P < 0.05$) (iv) Important to administer 3 vaccination doses: after the third EG95 vaccine, serum IgG increased to levels higher than those observed after the second. Antibody serum levels were maintained for 5 years, ensuring coverage against slow progression of fertile cysts <p><i>Dogs</i>:</p> <ul style="list-style-type: none"> (i) Arecoline purgation test: 4.5% (2009) to 4.3% (2017) infected. No statistically significant difference (P value = 0.8, $P > 0.05$) (ii) CoproELISA Infected dogs: 9.6% infected (2009) to 3.7% (2017). Statistically significant ($P = 0.04$, $P < 0.05$)

TABLE 7: Continued.

	<p>(iii) <i>CoproELISA farms with infected dogs</i>: 20.3% (2009) to 8.9% (2017). Not statistically significant decrease ($P = 0.1, P > 0.05$)</p> <p><i>Children (6–14 years)</i>:</p> <p>(i) <i>US Rio Negro province</i>: prevalence decreased 5.6% (1984/6) to 0.12% (2015)</p> <p><i>Children and adults in high-risk regions (e.g., Rio Chico Abajo, Mamuel Choique, and Anecon Grande)</i>:</p> <p>(i) 38 new cases (1995–2015): cumulative incidence rate 7800 per 100,000 inhabitants</p> <p>(ii) 2016 only 1 (1.1%) asymptomatic CE case (10 cm lung cysts)</p> <p><i>Behavioral risk factors</i>:</p> <p>(i) Home slaughter of adult sheep and goats</p> <p>(ii) Livestock viscera fed to dogs</p> <p>(iii) Poor slaughterhouse disposal, hygiene, and standards</p> <p>(iv) Death of infected livestock in fields/poor carcass disposal</p> <p><i>Barriers</i>:</p> <p>(i) Ecological conditions suitable for <i>E. granulosus</i> lifecycle (e.g., temperature and humidity)</p> <p>(ii) Low socioeconomic conditions</p> <p>(iii) Aggregation of small productive units with home slaughter</p> <p>(iv) Poor sanitary infrastructure</p> <p>(v) Harsh climate and lack of road infrastructure limited farm access during autumn and winter</p> <p>(vi) Failure to deliver all vaccination doses attributed to poor animal handling facilities and communication gaps between control staff and residents</p> <p>(vii) Unsustainable dog de-worming programs (4–12 times per year) and sheep vaccination programs (twice yearly). Attributed to difficulties accessing remote rural areas and few skilled health or veterinary workers</p> <p>(viii) Vaccination alone not recommended. Combined program with regular de-worming and health education recommended</p>
Limitations:	<p>(i) Failed to deliver 3 vaccination doses to 40% of sheep who escaped or failed to present at vaccination times</p> <p>(ii) Selection bias: non-randomized sample selection of children from one school</p> <p>(iii) Sample size calculations for each species treated prevalence separately. However, calculation based upon paired data (discordant pairs) for each species may be more suitable for two prevalence values in a before and after study</p> <p><i>Confounding variables</i>:</p> <p>(i) No clear distinguishment between owned and stray dogs. Only reference to “roaming dogs”</p> <p>(ii) Older, unvaccinated sheep, purchased from areas outside vaccination zones, may limit program outputs</p> <p>(iii) Sheep housed in mixed ages and sexes may have affected transmission and prevalence rates</p> <p>(iv) Variation between health workers or dog owner PZQ administration</p> <p>(v) Program outcomes not tested (e.g., health education effects on behavioral change)</p> <p>(vi) Goats excluded from vaccination program, as low prevalence in goats (unpublished study) and little local slaughter. However, one CE infected dog lived on a property that exclusively housed goats</p>

ELISA tests were superior when calculating CE prevalence rates. Justifications were based upon the higher sensitivity (78%–100%) and specificity (85%) of CoproELISA, compared to arecoline purgation tests, and CoproELISA showing similar trends to confirmation tests (PCR or Western Blot (WB)) ([6], p.5). Indeed, Larrieu et al. [2] reported that the calculated prevalence rates from arecoline tests were not statistically significant (P value = 0.08, $P > 0.05$) compared to CoproELISA tests ($P = 0.04, P < 0.05$). Previous research has revealed that when the prevalence remains high, CoproELISA sensitivity, alone, may be used for accurate CE diagnosis [47]. Nevertheless, arecoline was utilized, as both a program output (e.g., a treatment or diagnostic method) and a research method [2, 42, 43, 46].

3.6.2. Human Intermediate Hosts: Diagnostic Ultrasound and Treatment. Assessing the impact of program surveillance, using US, was the primary focus of the four studies that measured human CE prevalence [2, 6, 39, 42]. In contrast to dogs, it was generally concluded that CoproELISA

serology was less sensitive than US, although US had limited sensitivity in detecting pulmonary cysts [6, 42]. For example, 198 CE cases were US identified compared to 76 using serology ELISA ([42], p.588). Larrieu et al. [2] substituted serology (double diffusion 5, ELISA) tests for US, due to higher sensitivity.

Surveillance measures, such as US, are essential to identifying rising incidence or prevalence rates for endemic diseases, like CE. In CE endemic countries, such as Mongolia, when programs focused more on human surgical treatment than preventative dog management, they have resulted in under reporting and under diagnosis of CE cases ([15], p.64). While complete CE eradication is difficult in endemic countries, an over emphasis on post-infection control and treatment measures may inevitably lead to missed opportunities for early disease prevention. This may lead to increased demand and costs for surgical or medical treatments.

Additionally, one study acknowledged patient hesitation to undergo surgical treatment [42]. However, no study

TABLE 8: Appraisal summary of Article Meeting Inclusion Criteria [45].

Population:	<p><i>Northwest China: Six communities in Hobukesar County, Xinjiang Uyghur Autonomous Region:</i></p> <ul style="list-style-type: none"> (i) Narenhebuke (ii) Budengjian (iii) Changan Kul (iv) Chahete (v) Bayenoma (vi) Tiebukenwusan <p><i>Ethnic groups:</i></p> <ul style="list-style-type: none"> (i) Uyghur (ii) Han Kazakh (iii) Hui (iv) Mongol <p><i>Lifestyle:</i></p> <ul style="list-style-type: none"> (i) Pastoral and semi nomadic agricultural communities (livestock farming) <p><i>Owned dogs:</i></p> <ul style="list-style-type: none"> (i) Majority adult males (78.6%) (72.2% ≤4 years old) <p><i>Stray dogs:</i></p> <ul style="list-style-type: none"> (i) 21 male (ii) 17 female (≥1 years old)
Sample size:	<ul style="list-style-type: none"> (i) <i>Stray dogs</i> ($n = 38$): convenience sampling (non-randomized) (ii) <i>Owned dogs</i> ($n = 126$): randomized sampling of ≥19 dogs per community (iii) <i>117 dog owners</i>: randomized sampling
Program outputs:	<p><i>Chinese National Echinococcosis Control Programme implemented in Xinjiang (2010):</i></p> <ul style="list-style-type: none"> (i) <i>Praziquantel (PZQ) (0.2g/tablet)</i>: 1–2 tablets for dogs >15 kg, once a month. Supervised dosing to confirm dogs swallowed tablets and dosing date recorded (ii) <i>Environmental prevention</i>: dog feces collected, buried, or burned every 5 days after de-worming (iii) <i>Dog population control</i>: culling (iv) <i>Humans</i>: ultrasound (US) screening and medical treatment
Study design:	Quasi-experimental non-randomized before and after study
Program outcomes and/or impact:	<p><i>Pre-program Cystic Echinococcosis (CE) prevalence:</i></p> <ul style="list-style-type: none"> (i) 50/139 dogs (36% sampled in Hobukesar County, Narenhebuke) <p><i>Post-program (April 2013) six communities:</i></p> <ul style="list-style-type: none"> (i) <i>Dog necropsy</i>: 38 dogs caught by local dog catcher. Euthanised by qualified animal technician using intravenous ketamine (ii) Experienced researchers used a magnifying glass to inspect small intestine for CE worm burden. Worms washed in water and stored in 70% ethanol for PCR analysis <p><i>Lot Quality Assurance Sampling (LQAS) evaluation:</i></p> <ul style="list-style-type: none"> (i) <i>CoproELISA</i>: Dog fecal samples collected from grounds surrounding each household. Stored in 0.3% PBS Tween, with 10% formalin. Transported to Salford University, UK, at room temperature. If $n = 19$ was not met, translators consulted other community areas where dogs could be sampled (ii) <i>Analysis</i>: genus-specific sandwich ELISA. Fecal samples extracted by homogenizing, shaking, and centrifuging. Supernatant collected. Conjugate antibody: hyperimmune rabbit IgG from adult <i>Echinococcus granulosus</i> worms. Capture antibody: <i>Anti-E. granulosus</i> whole worm somatic (iii) <i>Positive controls</i>: fecal supernatants of known positives (arecoline purge from Kyrgyzstan) and a sample spiked with <i>E. granulosus</i> whole worm extract (1 : 100 concentration) (iv) <i>Negative controls</i> from a low endemic area (Falkland Islands) <p><i>PCR stray dog necropsy samples:</i></p> <ul style="list-style-type: none"> (i) DNA extracted from <i>Taenia</i> spp. and <i>Echinococcus</i> spp. worms using a Qiagen® DNEasy Blood & Tissue kit (ii) DNA extracted from fecal samples (1 g) using a QIAamp® DNA Stool kit (iii) <i>Positive controls</i>: sequenced DNA from adult <i>E. multilocularis</i>/<i>E. granulosus</i>/<i>Taenia hydatigena</i> (iv) <i>Negative controls</i>: PCR grade water <p><i>Questionnaire (n = 117):</i></p> <ul style="list-style-type: none"> (i) Four communities sampled: Bayenoma, Budengjian, Changan Kul, and Tiebukenwusan (ii) Delivered in Mandarin Chinese, Mongolian, or Kazakh (iii) Age, sex, and last PZQ dosing recorded (iv) Dog owners asked to describe echinococcosis

TABLE 8: Continued.

Main findings:	<p><i>Prevalence stray dogs:</i></p> <ul style="list-style-type: none"> (i) <i>Dog necropsy</i> ($n=38$) 20 dogs (52.6%) <i>Taenia</i> spp.; 16 (42.1%) <i>Echinococcus</i> spp.; 13 (34.2%) infected with both parasites; 14 dogs (36.8%) neither (ii) PCR: 15/15 (<i>E. granulosus</i> G1) tested tapeworm positive samples ($\geq 99\%$ match) <p><i>Prevalence owned dogs:</i></p> <ul style="list-style-type: none"> (i) Range: 15% in Chahete to 70% in Budengjian; overall ($n = 41.3\%$) (ii) CoproELISA positive ground fecal samples ($n = 52$) (iii) CoproELISA positive cases ($>35\%$) in 5/6 communities (iv) Only Chahete had CoproELISA prevalence $<35\%$ threshold. However, no dog owners reported dosing their dogs with PZQ over the past 2 years prior to sampling, and Chahete was a newly established farm. Thus, it could not be concluded if Chahete's prevalence reduction was attributed to program outputs (v) PCR: 26 samples (50%) tested positive for <i>E. granulosus</i>. All negative for <i>E. multilocularis</i> DNA <p><i>Dog owners self-reported Praziquantel dosing:</i></p> <ul style="list-style-type: none"> (i) 43 (36.8%) reported never dosing; 16 (13.7%) could not recall the last dosing; 26 (22.2%) administered PZQ within 6 weeks prior to sampling; 23 (27.4%) between 6 weeks to 2 years. Great variation among six communities with dosing ranging from 5-93.3% (ii) 15/26 (57.7%) dog owners who reported dosing their dogs no earlier than 6 weeks prior were CoproELISA positive (iii) LQAS decision rule for PZQ dosing only met in Changan Kul (23 dogs dosed in year before sampling). This meant low PZQ administration ($<90\%$) in 5/6 communities (Bayenoma, Budengjian, Chahete, Narenhebuke, and Tiebukenwusan) <p><i>Questionnaire:</i></p> <ul style="list-style-type: none"> (i) Could accurately describe CE: Bayenoma 5/13 (38.5%); Budengjian 14/19 (73.7%); 18 (94.7%) in Changan Kul; and 4 people (26.7%) in Tiebukenwusan (ii) Decision rule for knowledge of echinococcosis reached in 2/6 communities (Budengjian and Changan Kul). Meaning, knowledge did not fall below average (65% threshold) in these 2 communities. Notably, Changan Kul had PZQ dosing rates $>90\%$ target threshold in the previous year <p><i>Barriers:</i></p> <ul style="list-style-type: none"> (i) Unsustainable PZQ dosing in remote and semi-nomadic communities, due to logistics (funding, time, access, climate, skilled program workers, and dogs dislike tablet taste) 	
	Limitations:	<ul style="list-style-type: none"> (i) Ethical issue: no sample size justification for stray dog euthanasia numbers (ii) Convenience sampling of stray dog population may not be representative of local population, e.g., if dogs caught from one specific area (iii) No consent obtained for 9 owned dog fecal samples collected (iv) Missing questionnaire data (v) Not guaranteed feces collected from the ground belonged to associated household owned dog (vi) Inability to accurately measure dog weights (vii) PCR test: ground collection of dog feces conducted in dry and warm environments that may have denatured or degraded DNA (viii) Pre-program CoproELISA prevalence data from secondary study. Thus, post-program sample groups not the same as pre-program. Variations in collection or analysis methods between studies can reduce reliability and internal validity (ix) Not clear why only 4/6 communities administered questionnaires (p.2), but in results, it states that 117 dog owners were sampled across 6 communities (p.4) (x) Lack of detail about questionnaire delivery, consent, participant information and question types (xi) Tapeworm samples lost in transport (xii) No detail of necropsy method used to "estimate" <i>Echinococcus</i> spp. worm burden (xiii) Recall bias: some dog owners did not regularly record PZQ administration (xiv) LQAS is limited to group vs. individual village-based analysis (confidence intervals are wider for individual villages, which reduced precision) (xv) No significance tests for CoproELISA prevalence reductions in 2/6 communities (Budengjian and Changan Kul), in relation to PZQ dosing (xvi) Study stated that PZQ dosing is only beneficial to owned dogs. Although less sustainable for stray dog populations, treatment may be beneficial in reducing environmental egg burdens. Stray dogs are likely to access intermediate hosts (e.g., livestock or wildlife carcasses) due to roaming behavior

investigated the post-operative impact of surgical treatments on human quality of life. Many remote farming populations, reliant upon physical labor for their livelihood, had little ongoing access to medical care [2, 6, 7]. This would likely

result in higher post-operative complication rates. Thus, initiating early prevention methods has potential benefits of reducing prevalence rates and associated treatment costs and/or medical complications.

TABLE 9: Appraisal summary of Article Meeting Inclusion Criteria [34].

Population:	<p><i>Alay Valley, Kyrgyzstan:</i></p> <ul style="list-style-type: none"> (i) 10 communities: Kyzyl-Eshme, Kabyk, Achyk-Suu, Jaylima, Kashka Suu, Kara Kavak, Sary Mogul, Taldu Suu, Archa Bulak, and Sary Tash (ii) Small villages of 400 households (iii) Approximate population: 3,000 people <p><i>Dog population:</i></p> <ul style="list-style-type: none"> (i) Average dog density: 1.56 dogs/100m² (ii) April 2013 <ul style="list-style-type: none"> Sex: 157 (82.2%) males; 28 (14.7%) females Age: <5 years old =131 (69.3%); 10-year-old not recorded; 6 (3.1%) dogs no age or sex recorded (iii) April 2014 <ul style="list-style-type: none"> Sex: 156 (81.3%) males; 35 (18.2%) females Age: <5 years old =156 (81.3%); 5 dogs no age or sex recorded
Sample size:	<p><i>Random selection of dogs and households</i></p> <ul style="list-style-type: none"> (i) 7, 610 dogs registered under control program (a) Pre-program: 318 dogs sampled (May 2012) (b) Post-program: 191 sampled (April 2013); 192 (April 2014) (c) Total (2012-2014) = 701 dogs (ii) 25% of village households registered (149 dog owners) <p><i>Lot Quality Assurance Sampling (LQAS):</i></p> <ul style="list-style-type: none"> (i) Assess Praziquantel (PZQ) dosing and CoproELISA prevalence (ii) Random selection of 18-21 dogs sampled (target 19) from each community.
Program outputs:	<p><i>Echinococcosis Control Program 2012 (Kyrgyzstan, Ministry of Agriculture; financial support from the World Bank):</i></p> <ul style="list-style-type: none"> (i) Animal disease surveillance system (ii) National public information campaign (iii) Nationwide vaccination and testing program for eight diseases of livestock and/or dogs (foot and mouth disease, anthrax, rabies, brucellosis, sheep pox, peste des petits ruminants, echinococcosis, and tuberculosis) <p><i>Program Output Tested:</i></p> <p><i>Praziquantel (PZQ) dog de-worming:</i></p> <ul style="list-style-type: none"> (i) 109 dogs administered PZQ four months prior to prevalence sampling (2013) (ii) PZQ tablets provided to local community veterinarians at regional centers (iii) Veterinarians visited households once every season to either dose dogs or leave tablets with owners to administer. Veterinarians provided dog passports for owners to monitor monthly PZQ administration (iv) 2015-2016 PZQ de-worming ongoing: estimated 6,000 (2015) to 4,000 (2016) dogs treated <p><i>2015 Stray Dog Culling Campaign:</i></p> <ul style="list-style-type: none"> (i) Dog owners advised to tie up dogs and any dogs left roaming, euthanised (ii) Conducted randomly each year
Study design:	Quasi-experimental, randomized before/after study
Program outcomes and/or impact:	<p><i>Cystic Echinococcosis (CE) prevalence in dogs:</i></p> <p><i>Pre-program CoproELISA testing (May 2012):</i></p> <ul style="list-style-type: none"> (i) Fecal samples collected from 4 communities: Kara Kavak = 35, Kashka Suu =42, Sary Mogul =155, Taldu Suu =86 (ii) Only occupants home sampled. Otherwise, six nearest households sampled and questioned about dog ownership of unavailable households. Process continued until a sample of 50 dogs obtained (iii) <i>CoproELISA test method:</i> Decontaminated (80°C for ≥4 days) and fecal samples extracted by homogenizing, shaking, and centrifuging. Known positive and negative supernatant samples used as controls (iv) Cutoff values for ROC curve panels determined from previous data of arecoline purge samples in Alay Valley, and necropsy samples from Hobukesar County, Xinjiang China <p><i>Post-program CoproELISA sampling (April 2013 and April 2014):</i></p> <ul style="list-style-type: none"> (i) <i>Lot Quality Assurance Sampling (LQAS):</i> fecal samples collected from around dog owner's home, stored in 0.3% PBS Tween, with 10% formalin. Shipped at room temperature to the University of Salford, UK <p><i>Questionnaires:</i></p> <ul style="list-style-type: none"> (i) In 2014, dog owners (<i>n</i> = 149) asked about dogs' age, sex, and PZQ administration (ii) Open-ended questions delivered verbally in Kyrgyz, by native speaker (Bermet Mytnova) (iii) Answers to "CE causes" classified as "correct," "incorrect," or "partially correct." Correct answers based

TABLE 9: Continued.

	upon identifying the definitive host (e.g., dogs, foxes, or wolves) or direct cause (e.g., infective eggs in dog feces)
	<p><i>Pre-program prevalence: CoproELISA (May 2012): 20.1% (n = 318):</i></p> <p><i>Post-program: CoproELISA (2013; 2014):</i></p> <ul style="list-style-type: none"> (i) Prevalence decreased from 5 (2013) to 3 (2014) communities that did not meet the LQAS decision number or program target <p><i>PZQ administration (dog owners self-reported):</i></p> <ul style="list-style-type: none"> (i) In 2013, 141 (73.8%) reported dosing in last 7 months before sampling; 1 (0.5%) reported last 11 months; 39 (20.42%) reported never dosing their dogs; and 10 (5.2%) could not recall (ii) In 2014, 152 (79.2%) reported dosing in the last seven months; 4 (2.1%) dosed between 7 and 8 months; 23 (12.0%) never administered PZQ, and 13 (6.8%) could not recall (iii) Improvement in PZQ administration in 2014 across communities: 128 (66.7%) coverage. Only two communities (Kashka Suu and Kyzyl-Eshme) failed to meet the LQAS decision number (meaning they had below average PZQ administration rates) (iv) In 2013, only 4/10 communities reached the 75% PZQ dosing target compared to 8/10 in 2014 (21 months post- program) <p><i>Questionnaires:</i></p> <ul style="list-style-type: none"> (i) 149 dog owners participated (some declined to answer and some owned multiple dogs) (ii) 126 respondents (84.6%) had heard of echinococcosis (iii) 93 (78.3%) correctly identified causes of echinococcosis (iv) 13 (10.3%) partially correct responses (v) From those who had heard of echinococcosis, 20 could not identify a cause (vi) 23 (15.6%) had never heard of echinococcosis nor identified a cause (vii) Total: 43 (28.9%) could not identify the cause of echinococcosis, but the majority (78.3%) could <p><i>Barriers:</i></p> <ul style="list-style-type: none"> (i) Remoteness (communities and households scattered) (ii) Community semi-nomadic customs and lack of resources (iii) Lack of funding for diagnostic tests (iv) Free roaming dogs; and changing population numbers (v) Financial costs and human resources present challenges to sustainability of PZQ treatments every 6 weeks. It requires consistent PZQ administration to reduce environmental eggs burdens and break transmission cycles. Thus, longer-term studies were advocated
Main findings:	
	<ul style="list-style-type: none"> (i) Recall bias: owners could not recall PZQ administration (ii) Sample size calculation unclear. Reported as an “estimated” value from unpublished data from the Kyrgyz Ministry of Agriculture, Land Reclamation, and the Kyrgyz State Inspectorate for Veterinary and Phytosanitary Safety (iii) Missing signalment details for dogs (age and sex) (iv) Results on local knowledge not comparable, as no pre-program measures (v) No detail about dog culling or if humanely euthanised (vi) Minimal analysis or further testing of questionnaire results <p><i>Confounding variables:</i></p> <ul style="list-style-type: none"> (i) 4/10 communities sampled before program (2012) versus 6 post-program. Communities may have different dogs, sheep, and human population demographics (ii) Multiple sub-programs comprised the broader national program, and public health notices appeared on Kyrgyz television during the program. These program outputs were not controlled or tested (iii) No sample size calculation for stray dog population (iv) Due to logistics (time) all dogs not sampled in one community (Kashka Suu) (v) Fecal samples collected around dog owners’ homes may have belonged to stray dogs or wildlife vs. the residing dog (vi) Non-standardized PZQ administration method <ul style="list-style-type: none"> (a) Veterinarians or dog owners administered PZQ (b) In Sary Mogul, 0/19 dogs administered PZQ four months before sampling (2013), compared to 16/19 dogs in Jaylima
Limitations:	

3.6.3. *Program Sustainability.* A major finding across program evaluations was the unsustainability of six weekly PZQ treatments. Larrieu et al. [2] explained that programs using dog de-worming alone, often failed globally due to logistical constraints of sustaining 100% coverage; up to eight times per year, in remote areas (p.6). In Kyrgyzstan,

it was concluded that six weekly PZQ intervals were not practical, due to funding and human resource constraints ([34], pp. 9, 16). Two studies recommended three to four monthly intervals to reduce canine and livestock prevalence rates to $\leq 1\%$ within 10–15 years ([45], p. 6, [34]). Nearby, in northwest China, six weekly PZQ treatments were also

TABLE 10: Appraisal summary of Article Meeting Inclusion Criteria [15].

Population:	<ul style="list-style-type: none"> (i) WHO Mongolia Office (ii) Mongolian government sectors (iii) Local hospitals (iv) Veterinary institutes; (v) Laboratories (vi) Two Cystic Echinococcosis (CE) patients
Sample size:	(i) 29 private and public stakeholders
Program outputs:	<p><i>Chinese Central Communist Party (CCP). National Health Committee implemented the National Control Program on Major Parasitic Diseases (2006–2015):</i></p> <ul style="list-style-type: none"> (i) Subsidized surgeries for CE patients from 2007 (ii) November 2015 State Council created a multi-stakeholder network of 30 agencies: the National Health Commission; the United Front Work Department of the Communist Party of China (CPC) Central Committee; the Central Comprehensive Management Office; the National Development and Reform Commission; and the Ministry of Education (iii) <i>March 2017:</i> 10 Chinese government departments formed a Steering Working Group in the Tibet Autonomous Region, Sichuan Tibetan Area; Yushu and Guoluo Prefecture in Qinghai Province <p><i>Multiple CCP ministries and commissions implemented an integrated national plan for major parasitic disease control (2016–2020):</i></p> <ul style="list-style-type: none"> (i) Dog and livestock management (ii) Public health education (iii) Human patient treatment and surveillance <p><i>The Ministry of Health, Mongolia (2017):</i></p> <ul style="list-style-type: none"> (i) Issued “Technical Guidelines for Zoonotic Disease” Prevention and Control, which encompassed specific guidelines for CE
Study design:	Qualitative case study
Program outcome and impact:	<p><i>March 2018 qualitative field research:</i></p> <ul style="list-style-type: none"> (i) Focus group discussions and in-depth interviews conducted by Chinese public health practitioners (ii) Participants expressed opinions on China-Mongolia collaboration and discussed program themes: challenges, funding gaps, training, medical diagnostic methods, and presence of field controls
Main findings:	<p><i>Secondary findings Mongolia:</i></p> <ul style="list-style-type: none"> (i) Focused on treatment versus preventative dog management, which resulted in underreporting and under diagnosis (ii) Issues with Mongolian program implementation and coordination due to multiple stakeholders: The Ministry of Health, hospitals, zoonotic health centers, and veterinary departments <p><i>Primary qualitative research (interview responses, n = 15):</i></p> <ul style="list-style-type: none"> (i) 79.3% not aware of the national plan for infectious disease control (ii) 44.8% stated limited funding was a challenge for control (iii) Two participants claimed that the government and international agencies’ research funding reduced monetary constraints (iv) 58.6% concluded that there are no CE field control efforts (v) 75.9% received no training associated with CE in the last 5 years (e.g., respondents from the WHO Mongolia Office, Mongolian government sectors, local hospitals, veterinary institutes, and laboratories) (vi) Two clinical doctors stated diagnosis was based upon experience vs. following WHO-<i>Informal Working Group on Echinococcosis (IWGE)</i> ultrasound cyst staging <p><i>Proposed challenges and solutions:</i></p> <ul style="list-style-type: none"> (i) 8 proposed more government engagement (ii) 10 identified low public awareness (iii) 17 identified insufficient capacity (iv) 22 proposed establishing a national strategy, which encompassed routine disease surveillance and technical support from China <p><i>Group discussions:</i></p> <ul style="list-style-type: none"> (i) Limited nationwide disease surveillance and associated distribution mapping (ii) Poor management of stray dogs (iii) Inadequate diagnostic tools for humans and dogs (iv) Praziquantel and albendazole viewed as an obstruction to control (v) High drug costs <p><i>Recommendations:</i></p> <ul style="list-style-type: none"> (i) Mongolia led, China supported, bilateral cooperation. China prepares formal documents and aids in developing technical guidelines and standards

TABLE 10: Continued.

	<ul style="list-style-type: none"> (ii) China-Mongolia cross sector collaboration (e.g., disciplines: medicine, veterinary, parasitology, and epidemiology) and government departments (e.g., public health, quarantine, and animal health) to share technology, technical and project management skills, information, and resources (iii) Integrating CE control with other dog transmitted, neglected zoonoses (e.g., rabies), to improve efficiency and reduce costs (iv) Cross-sectional population survey to create a disease baseline (v) Dog management: de-worming and registration (vi) Financial support (vii) Public health education (viii) Strengthen existing surveillance systems (ix) Increase physical and economic access to affordable drugs
Limitations:	<ul style="list-style-type: none"> (i) No clear research question (ii) Only sampled participants from Mongolia (iii) Research bias: no information on the types of survey, focus group or interview questions (e.g., open ended or closed); number of participants in each focus group; ethics statement; or how surveys were delivered (e.g., verbal, written, and online) (iv) Unequal respondent demographics: no survey, interview, or focus group representation of health organizations, apart from the WHO Mongolia office. Only two CE patient participants (v) Research bias: authors work within research centers, government bodies, and/or for the WHO, which funds control programs (vi) Some results are not readily comparable, due to context specific nature of case study designs

unsustainable, as there were issues obtaining dogs' weight, and with dosing logistics (e.g., dogs disliked taste, funding, remoteness, and skilled worker availability). Moving to Northern African, in Morocco, it was concluded that only two monthly PZQ de-worming intervals effectively controlled infective egg shedding in stray and owned dogs ([46], p. 441).

Furthermore, Yu et al. [39] attributed failed prevalence reduction in China, and the autonomous regions of Mongolia and Tibet, to the unsustainable de-worming of domestic canines, and controlling "wild canines" (p.2), such as foxes. Although studies [34, 42, 45, 50] identified the sylvatic cycle, no program outputs were discussed, apart from surveying community knowledge of wildlife transmission pathways [45].

Finally, to assess CE prevalence rates in sheep, postmortems within slaughterhouses [2, 43], serology ELISA, and WB were conducted [2]. Sustainability issues were identified in remote communities in Argentina ([2], p.5) and China ([45], p.6), in relation to EG95 sheep vaccinations. In Argentina, the issues were attributed to difficulties accessing remote areas, funding, and few skilled health or veterinary workers [14]. In China, statistically significant increases in infection (IF) rates among older sheep (>4 years, IF = 17.9%), compared to younger sheep (<1 years, IF = 4.5%) ([43], pp.357-8), were mostly attributed to unsustainable de-worming intervals, practices (e.g., burying dog feces), and health education delivery.

To address sustainability and a lag in vaccination flock effects, Larrieu et al. [2] and Van Kesteren et al. [45] suggested a combined program, which includes sheep vaccination, canine PZQ de-worming, and health education. Qian et al. [15] also recommended integrating CE with other neglected canine zoonotic diseases, such as rabies, to improve efficiency and reduce costs. Although excluded from this review, integrated zoonotic disease programs have

potential cost-effective benefits, in terms of access to multiple health technologies ([7, 57], p.18, [58]). Indeed, it has been calculated that it would cost 30% more per dog treated separately for rabies, cystic echinococcosis, and visceral leishmaniasis, compared to an integrated program ([31], p.7).

4. Discussion and Recommendations

4.1. Measure Multiple Program Outcomes. Cross-disciplinary research that focuses on measuring multiple social, health, and economic program outputs and outcomes, in correlation to changes in disease prevalence, is essential. Most studies concentrated on measuring disease prevalence without obtaining an understanding of the specific program outputs and outcomes that caused changes. Without this understanding, future programs may fail to reproduce successful outputs or improve upon existing ones.

Failure to assess the link between social outcomes, such as positive behavioral change, with disease prevalence may be a disciplinary issue, as behavioral studies are often confined to the psychological and social sciences. Measuring behavior, pre- and post-health education campaigns is essential. However, consistently measuring sanitary practices, such as hand hygiene, may be difficult in remote communities. Additionally, identifying if access to clean water is a location specific constraint is essential. This would also highlight an area in need of program development and funding.

4.2. Regular Training: Standardized Administration and Measurement of Program Outputs (PZQ de-worming). Stratified sampling and, if funding permitted, engaging an external statistician to analyze data may have improved the methodological reliability of studies. For example, separating dogs based upon owner versus health worker PZQ administration would control for confounding bias and increase the

TABLE 11: Appraisal summary of Article Meeting Inclusion Criteria [39].

Population:	(i) <i>China</i> : pastoral regions of project counties in ten provinces and autonomous regions: Inner Mongolia, Sichuan, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, Xinjiang, and the Xinjiang Production and Construction Corps (ii) <i>Humans</i> : 56.7–79.7 million inhabitants at the county level. 19.3–39.1 million inhabitants at the township level (2004–2014) (iii) <i>Dogs registered</i> : 96, 000 (2004) and 2.69 million (2014)
Sample size:	(i) No sample size provided
Program outputs:	<i>National Cystic Echinococcosis (CE) Control Program (2005)</i> : (i) Launched by the Chinese Central Government, National Ministry of Health, in collaboration 13 other ministries (ii) <i>Human patients</i> : ultrasound (US) screening and surgical or medical treatment (albendazole) (iii) <i>Registered dogs</i> : Praziquantel (PZQ) de-worming (8 times per year) (iv) Health education (v) Sanitation improvement
Study design:	Randomized, retrospective cross-sectional study
Program outcomes and/or impact:	<i>Statistical analysis (National Ministry of Health Database 2004–2014)</i> : (i) Program economic outcomes: financial costs and working hours to deliver human treatments (ii) Prevalence: human US screening (iii) Human medical and surgical treatment coverage (iv) Behavioral outcomes: de-worming dogs (oral PZQ) coverage
Main findings:	<i>Accumulated financial costs (2004–2014)</i> : (i) Total USD\$110.67 million: USD\$27.0 million for human treatment and registered dog de-worming. 24.4% or 1/4 of the total financial input (ii) Human medical (drug: albendazole) and surgical treatment costs (2004–2014): USD \$12.3 million (iii) Dog de-worming (oral PZQ) costs (2004–2014) (after discount): USD \$15.8 million (iv) Budgets not keeping pace with increasing demand for human treatments and dog de-worming; 2006–2014 annual and accumulated program costs increased 2840 times for human treatments and 21.8 times for dog de-worming <i>Human work hours to deliver CE surgical and medical treatments</i> : (i) 74, 145 hours (since 2010); 29, 469 unclassified hours (since 2008) (ii) Accumulated total (2011–2012): >10, 000 hours <i>Work hours per patient highest for CE cases</i> : (i) County level hours: 10.2 (CE); 3.9 alveolar echinococcosis (AE); 0.3 (co-infection); 4.4 (unclassified) (ii) Township level hours: 21.8 (CE); 8.5 (AE); 0.6 (co-infection); 7.4 (unclassified) (iii) Treatment (hours): cumulative cases increased 5.7 times for CE cases (2009–2014) (iv) Increased US screening: patient numbers increased 18 times (2004–2014). 1.5 times as many cases diagnosed, which reflected increased surgical operations (3.8× for CE) <i>Human prevalence</i> : (i) CE was responsible for the highest number of cases (2004–2014), compared to AE and co-infection (ii) Most cases were in Western China, in pastoral farming areas with domestic animal populations (e.g., dog feces infect livestock) and sylvatic lifecycles (e.g., foxes or wolves' feces infect livestock) (iii) Prevalence decreased: 1.08% (2004) to 0.24% (2012). However, prevalence per 100, 000 population rate increased (17× at county level; 10.8x township level) (iv) Total human cases identified by annual US screening (2004–2014) (a) Range 4.8% (959/20, 168) to 18.2% (318/1749) (v) Average rate of patient treatment Increased (2004–2014) (a) 32.4% increase for surgical treatment (b) 81.3% increase for medical treatment <i>Average rate of surgical operations</i> : (i) <i>Pre-program (2005–2006)</i> : >10% (ii) <i>Post-program</i> : decreased and remained stable at 5.7% (2007–2012) (95% CI: 5.0–6.9%); 7.4% (2013); 7.6% (2014) <i>Average medical treatments (albendazole)</i> : (i) <i>Pre-program</i> : 46.7% (2004) (ii) <i>Post-program</i> : 69.4% (95% CI: 56.8–82.0%) (2007) to 69.1% (2014) <i>Grand total treatment coverage</i> : (i) 64.9% (2004) to 76.7% (95% CI: 67.5–87.9%) (2014). Overall, both surgical and medical treatment coverage

TABLE 11: Continued.

	<p>increased after program launched</p> <p>(ii) Patients with coinfection (CE and AE) and unclassified cases displayed an annual decreasing trend</p> <p><i>Dog de-worming:</i></p> <p>(i) Number of registered dogs de-wormed: 9.6 (2004) increased to 269 (2014); median value 115.0 (95% CI: 83.779–226.0)</p> <p>(ii) De-worming cases ($\times 10,000$) (2004–2014): 3.7 (2004); 178 (2014). Increased 48 times</p> <p>(iii) Pre-control: 38.2% coverage (2004)</p> <p>(iv) Post-control: 66.2% (2014). Increased coverage 28% (2004–2014)</p> <p>(v) Number of registered dogs increased 28 times (269/9.6) (2004–2014), but de-worming coverage only increased 8 times (2005–2011) or 1.7 times (66.2/38.2) (2004–2014)</p> <p>(vi) Positive correlation ($R = 0.97, P < 0.01$) between registered dogs and human cases (Spearman's correlation)</p> <p><i>Recommendations:</i></p> <p>(i) Improved control measures for sylvatic cycle (wild canines)</p> <p>(ii) Human clinical case follow-up: patient information and treatment records regularly updated</p> <p>(iii) Improve stray dog management and acknowledge cultural acceptability of culling for population control</p>
Limitations:	<p>(i) Annual number of de-wormed dogs (2012–2014) missing data. Estimation calculation (expectation-maximization (EM) method) used to calculate missing data: only method description/reference was a Wikipedia link, not associated with a webpage</p> <p>(ii) Data only authorized by the National Ministry of Health until 2014</p> <p>(iii) No information about sample size or collection methods</p> <p>(iv) No distinguishment between stray versus owned dogs</p> <p>(v) No information about de-worming administration methods</p> <p>(vi) Cannot conclude if pre-program and post-program populations similar</p> <p>(vii) In text results stated that de-worming coverage increased 73% (2005–2014). However, data (10.2% (2005) and 66.2% (2014) = 58% increase)</p> <p>(viii) Data reliability: disease surveillance was not performed evenly across endemic regions due to the uneven launching of control programs</p> <p>(ix) Prevalence for human patients and dogs only available from two national surveys (2004 and 2012). However, data was presented outside these dates (e.g., canine cases (2004–2014) and “mean human prevalence” (2008–2014)</p> <p>(x) No controls or significance testing for prevalence changes in correlation to program outputs (e.g., education programs) and outcomes (e.g., behavioral change: improved sanitation methods; PZQ de-worming)</p>

validity of reported changes in disease prevalence. To illustrate potential confounding effects, dog owners reported PZQ dosing in the previous four months, but over 50% of dogs tested positive for CE and 13.7% of dog owners could not recall the last de-worming ([45], p.3). In Yang et al.'s [43] study, one village resident was assigned to de-worm dogs and deliver health education, which resulted in difficulties sustaining program measures. Similarly, two other studies identified that both health workers and dog owners provided sanitary education and administered PZQ ([2], p. 6 [6]). Finally, Solomon et al. [42] specified that a health education campaign was initially delivered by organizational officers, but community members were subsequently trained (p.588).

Common to all these studies was that resident skill set level was unclear and ongoing supportive training was not regularly provided. Variations in skill set compromised program sustainability and study reliability, due to the increased likelihood of incorrect PZQ administration, irregular dosing intervals, dog owner recall bias, and potential inaccuracies in health information. Additionally, an absence of regular training may extend to professional program workers. Qian et al. [15] revealed that 75.9% of surveyed respondents from the WHO Mongolia Office, Mongolian government sectors,

local hospitals, veterinary institutes, and laboratories reported not receiving CE training in the last 5 years (p.63). Thus, all included programs would benefit from ongoing training support for both local communities and organizational program workers.

4.3. Distinguish Between Stray and Owned Dog Populations. The OIE recommends distinguishing between owned and stray dogs to accurately calculate and trace population size [59]. Although the role of stray dogs in disease transmission was considered [2, 15, 42, 43], 70% of studies did not clearly make this distinction and/or administer PZQ to stray dogs. Only 20% calculated stray dog population size [45, 46]. The importance of this distinction was captured in Morocco, where photographic records tracked the number of stray dogs, who were 14 times as likely to be infected with *E. granulosus* compared to owned dogs (odds ratio = 14, 95% CI: 6–30; $P < 0.001$) ([46], p.439).

While the population of owned dogs is more readily calculated, using registration records or household surveys, measuring stray dog populations is essential to minimizing CE transmission. Roaming stray dogs may access common livestock, wildlife, and human environments [18–20]. A single dog can be the source of infection for 30,000 ha ([3],

TABLE 12: Appraisal summary of Article Meeting Inclusion Criteria [46].

Population:	<ul style="list-style-type: none"> (i) Middle Atlas, Morocco, North Africa (locality of Had Oued Ifrane) (ii) Total area: 27, 550 km²; 15% of Morocco's mountain area (iii) Climate: mountainous continental; Mediterranean: cold, rainy, and snowy in winter; hot and dry in summer (iv) Agropastoral zone: livestock (sheep breeding: Timahdit breed or cattle of similar herd size) <p><i>Sample population:</i></p> <ul style="list-style-type: none"> (i) Owned dogs (2-3 dogs per household) or stray (>1 years old) from three douars (villages), 20-30 km from each other (ii) Located near a weekly market (souk) and slaughterhouse
Sample size:	(i) 225 owned and stray dogs
Program outputs:	<p><i>Dog Praziquantel (5 mg/kg) de-worming (December 2016 to August 2017):</i></p> <p><i>3 groups:</i></p> <ul style="list-style-type: none"> (i) <i>Group A Douar Assaka:</i> 2-month treatment interval and sampling three times (Dec, Feb, April) (ii) <i>Group B Douar Sanoual:</i> 3-month treatment interval and sampling (Dec, March, June) (iii) <i>Group C Douar Sidi Bel Khir:</i> 4-month treatment interval and sampling (Dec, April, August) (iv) All groups composed of owned (60–75%) and stray dogs (25–40%) (v) Stray dogs identified from images and owned dogs by owners (vi) Dogs who missed any sample sessions were excluded
Study design:	Non-randomized controlled trial
Program outcomes and/or impact:	<p><i>Prevalence of Cystic Echinococcosis (CE) (December 2016-August 2017):</i></p> <p><i>Owned Dogs:</i></p> <ul style="list-style-type: none"> (i) Arecoline hydrobromide (4 mg/kg body weight or 2 mg/kg for a second dose) fed in meat balls to induce defecation and egg expulsion <p><i>Stray dogs:</i></p> <ul style="list-style-type: none"> (i) Levomepromazine (25 mg orally) for sedation before arecoline administration <p><i>Fecel sample tests:</i></p> <ul style="list-style-type: none"> (ii) <i>Fecel flotation</i> (iii) <i>Microscopic examination</i> of worms and eggs <ul style="list-style-type: none"> (a) Positive samples confirmed with <i>CoproPCR</i> (b) After sample collection, feces disinfected with alcohol for at least 5 minutes and burned
Main findings:	<p><i>Pre-program prevalence:</i></p> <ul style="list-style-type: none"> (i) <i>Owned Dogs:</i> range 23.5% to 38.8% (ii) <i>Stray Dogs:</i> range 51.3% to 68.5% <p><i>Post-program (December 2016 to August 2017):</i> prevalence decreased in stray and owned dogs across all groups, but more significantly in owned dogs:</p> <ul style="list-style-type: none"> (i) <i>Group A:</i> owned dogs (0.24-0); stray dogs (0.5-0.05) (ii) <i>Group B:</i> owned dogs (0.4-0); stray dogs (0.63-0.18) (iii) <i>Group C:</i> owned dogs (0.35-0.05); stray dogs (0.76-0.5) (iv) Stray dogs were 14 times as likely to be CE infected compared to owned dogs (odds ratio = 14; 95% CI: 6-30; $P < 0.001$). Higher prevalence in stray dogs attributed to free access to condemned organs from slaughterhouses and weekly markets (v) Monthly risk was lowest in group A (2 monthly intervals) compared to B (3 monthly) and C (4 monthly intervals). Infection risk highest in group C (vi) 2 monthly PZQ intervals for owned and stray dogs can effectively control shedding of infective eggs (vii) <i>Season significantly ($P < 0.001$) associated with prevalence;</i> <ul style="list-style-type: none"> (a) Reduced risk of infection during second sampling period, as dry and warm summer conditions decrease environmental survival of CE eggs (b) During colder, winter months, higher risk of infection, due to extended lifecycle of eggs. Increase also attributed to increased livestock slaughter during winter (c) Interactions between time and dog type (stray or owned), and time and site not significant ($P = 0.9$, $P > 0.05$) <p><i>Barriers:</i></p> <ul style="list-style-type: none"> (i) Primary transmission cycle: stray dogs in urban areas; roaming or shepherding dogs in rural areas (ii) Dogs are kept as house and livestock guards, often in close contact with owners; especially women and children (high risk demographic) (iii) Home slaughtered livestock primary source of infection for owned dogs (iv) Condemned offal from slaughterhouses or weekly markets (souk) source of transmission for stray or roaming dogs

TABLE 12: Continued.

Limitations:	<ul style="list-style-type: none"> (i) No sample size calculation (ii) Study design and methods unclear: a self-identified longitudinal study, which used odds ratio to identify risk factors, such as being a stray vs. owned dog. However, unlike case control studies that focus on pre-existing disease cases, odds ratio seemed to be applied like a relative risk ratio within a prospective cohort study, to calculate disease incidence. This made reported measurements of incidence vs. prevalence confusing (iii) Ethical issue: arecoline can cause adverse reactions in young or old dogs and is generally prohibited in pregnant dogs. No signalment details for dog ages or sex (iv) Difficult to identify exact prevalence values (v) Pre-program prevalence ranges: unclear if this was an average across all three sites (vi) Could not source cited articles for fecal floatation or microscopic tests. However, use of fecal flotation to detect <i>E. granulosus</i> is not highly sensitive, as <i>Taenia</i> and <i>Echinococcus</i> eggs are morphologically indistinguishable using fecal float ([47], p.123) (vii) PCR methodology described in reference to several secondary studies. Difficult to identify which parts of each methodology were utilized, especially in reference to PBS and DNA extraction methods from Mathis et al. [48] and Abbassi et al. [49] <p><i>Confounding variables:</i></p> <ul style="list-style-type: none"> (i) Different exposure times for groups A, B, and C, due to different administration interval periods (e.g., variable time spans from 4-8 months at three sites). Instead, having three different interval groups per site, sampled at the same time, would have controlled for seasonal variation (ii) Research bias: researchers or statisticians not blinded to de-worming intervals for each group (iii) Not clear if dog owners or skilled worker administered PZQ (iv) No specification about whether skilled or unskilled personnel collected fecal samples, analyzed them for CoproPCR, fecal flotation, or microscopy (v) Does not distinguish between stray versus owned dogs
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p. 438). Although labor-intensive, the OIE [59] recommends using a refined marking method or a wildlife biology, mark-recapture method, to calculate stray dog populations. The marking method entails accounting for daily differences in dogs' distribution (e.g., variations in weather, access to food, shelter, and human activity). Dogs are temporarily captured and marked using a standardized method (e.g., a distinctive collar, paint smudge, or ear tag). After a few days, plotting the daily number of marked dogs against the accumulated total of marked dogs produces a representative value for population size. The second wildlife biology method entails initially marking and releasing dogs within a defined area. The number of marked and unmarked dogs is then calculated by distant re-observation of the same area. To calculate a total population estimate, the number of dogs initially marked and released is multiplied by the total number of re-observed dogs [59]. This is all divided by the number of marked dogs identified during re-observation. Notably, there is an increased risk of zoonotic disease transmission to researchers, and ethical concerns, in terms of the stress caused during the capture and marking process.

4.4. Coproantigen ELISA Tests: An Efficient All Rounder for Canine Prevalence. As identified, Coproantigen ELISA was commonly used to diagnose prevalence in both stray and domestic dogs [2, 6, 34, 45]. It has reported advantages, such as the ability to detect antigen 5-10 days post-infection and treatment, when >100 parasites are present ([3], p. 437 [60]). In the context of endemic low to middle income countries, this test is suitable in terms of achieving adequate sensitivity and affordability. In addition, CoproPCR [45, 46] was utilized to calculate canine CE prevalence, as a stand-

alone verification test or sometimes coupled with WB [6] or arecoline tests [2]. Although more costly, and limited to research, CoproPCR tests offer a higher sensitivity and, unlike CoproELISA, can differentiate *taeniid* spp. from *E. granulosus* or *E. multilocularis* species ([3], p. 437).

Furthermore, arecoline purgation tests were only utilized by four studies [2, 42, 43, 46]. In addition to a comparatively lower sensitivity [6], arecoline tests can be labor-intensive, present a zoonotic risk, and cause "adverse reactions (vomiting, diarrhoea, hypersalivation)" ([3], p.437 [60]). Amarir et al. [46] fed owned and sedated stray dogs, with arecoline hydrobromide (4 mg/kg; 2 mg/kg second dose) to induce defecation and egg expulsion ([46], p.438). As signalment was not recorded, ethical issues arise, because potential adverse effects may result from contraindicated use in pregnant, young, or elderly dogs ([3], p.437). Necropsy of dogs' small intestine is considered the most accurate diagnostic method among CoproELISA, CoproPCR, and arecoline purgation tests ([3], p. 437). However, across all studies, CoproELISA was relatively precise, economically practical, and an ethically sound option for CE diagnosis in stray and owned dogs.

4.5. Livestock Intermediate Hosts: More Studies on Vaccination Efficacy. Only two studies [2, 43] evaluated programs in reference to livestock vaccinations within endemic countries. Future longitudinal research is necessary to clearly establish the effectiveness of vaccination programs, in terms of multiple outcomes and significant differences in prevalence, not only in sheep, but other susceptible species, such as goats and cattle. However, relative cost constraints and the cited [2, 45] unsustainability of booster and annual

TABLE 13: Appraisal summary of Article Meeting Inclusion Criteria [50].

Population:	<p><i>Morocco: seven regions sampled:</i></p> <ul style="list-style-type: none"> (i) Rabat (administrative capital ministries location) (ii) Bel Ksiri (high Cystic Echinococcus (CE) prevalence in humans and animals) (iii) Khenifra (high human CE incidence) (iv) Agadir (high CE in humans and animals) (v) Laayoune (vi) Tantan (vii) Guelmim regions (low CE incidence in humans) <p><i>Internal stakeholders:</i></p> <ul style="list-style-type: none"> (i) Ministries of Health, Agriculture, and Interior (ii) Public hospitals <p><i>Intermediate stakeholders:</i></p> <ul style="list-style-type: none"> (i) Collaborate with internal stakeholders e.g. The Ministries of Education (teachers), Islamic Affairs, and the media (disseminate messages concerning CE) <p><i>External stakeholders:</i></p> <ul style="list-style-type: none"> (i) Researchers (ii) Private physicians (iii) Veterinarians (iv) Elected politicians (v) WHO (World Health Organization) or World Organization for Animal Health (OIE) (vi) Slaughterhouse workers; breeders; industry associations (e.g., National Association of Cattle, Sheep, or Goat breeders)
Sample size:	<ul style="list-style-type: none"> (i) Focus group: 22 (ii) Semi-structured interviews: 164 (iii) Total: 186
Program outputs:	<p><i>National Hydatidosis Control Programme (NHCP), Morocco (2007):</i></p> <p><i>Dogs:</i></p> <ul style="list-style-type: none"> (i) Population control (ii) De-worming (iii) Improving slaughterhouse sanitary standards: CE surveillance at slaughterhouse. Infected offal disposal managed by the Ministry of Agriculture via the National Office for Food Safety (ONSSA) <p><i>Humans:</i></p> <ul style="list-style-type: none"> (i) Surveillance and treatment (managed by the Ministry of Health via local health delegations and public hospitals) <p><i>Public health education:</i></p> <ul style="list-style-type: none"> (i) All government ministries, but the Ministry of Education prepared an awareness brochure for children (ii) The Ministry of Islamic Affairs delivered awareness campaigns in mosques
Study design:	Qualitative case study
Program outcomes and/or impact:	<p><i>Multi-stakeholder analysis (2016-2018):</i></p> <p><i>One day focus group (face to face in Rabat):</i></p> <ul style="list-style-type: none"> (i) Preliminary interview results presented, and groups (4-7 participants) formed to discuss result topics (obstacles, stakeholder coordination, and proposed improvements). One researcher moderated and one took notes (ii) <i>Participants</i> <ul style="list-style-type: none"> (a) Civil servants from the Ministries of Health ($n=2$), Agriculture ($n=2$), Interior ($n=1$), Education ($n=2$), and Islamic Affairs ($n=1$) (b) Researchers: The Faculty of Medicine ($n=3$); National Institute of Hygiene ($n=1$); National School of Public Health ($n=2$); Hassan II Agronomic and Veterinary Institute ($n=5$); the Institute of Tropical Medicine Antwerp (Belgium) ($n=3$) <p><i>Semi-structured interviews (face to face, $n=164$):</i></p> <ul style="list-style-type: none"> (i) 91 internal and intermediate stakeholders and 22-51 external selected from focus group (ii) Interviews transcribed into Arabic or Berber language and translated into French (common language to all researchers) or English (iii) Interviews recorded (20-45 min), transcribed, and checked for quality assurance (iv) Software-assisted textual analysis (RQDA-R software) <p><i>Interviews structured and coded (six categories):</i></p> <ul style="list-style-type: none"> (i) Stakeholder activities: priority, interests, importance (ii) Stakeholder role: involvement, influence, and power

TABLE 13: Continued.

	<p><i>Multi-stakeholder analysis (three criteria incorporated into six categories):</i></p> <p>1. <i>Appropriation:</i></p> <ul style="list-style-type: none"> (i) Stakeholders stated interests and felt involved in offal seizure, slaughterhouse development, and treatment of human cases (ii) Neglected measures (actors did not feel involved in decision making): dog population control, dog de-worming, and raising awareness. Mostly veterinary preventative and health education measures neglected interests and involvement <p>2. <i>Political agency (power over other stakeholders):</i></p> <ul style="list-style-type: none"> (i) Internal stakeholders (e.g., public health sector) possessed highest power, but considered the CE program low priority. Only the National Office for Food Safety (ONSSA) considered CE program a high priority (ii) External political stakeholders: high power, but considered the program low priority (iii) External stakeholders: abattoir workers, the WHO, and Municipal Hygiene Offices considered the program a high priority, but had minimal power (iv) Intermediate stakeholders (e.g., the Ministry of Education) considered the program low priority and possessed little power <p>3. <i>Sociotechnical agency (influence and importance to stakeholder work or income):</i></p> <ul style="list-style-type: none"> (i) Internal stakeholders: high influence and importance. However, the Municipal Hygiene Offices, local authorities and Ministry of the Interior (responsible for program infrastructures and local enforcement) had limited agency, due to low priority ascribed (ii) Intermediate stakeholders: low importance, low influence, as primary role was to improve the work quality of internal stakeholders (iii) External stakeholders: some considered programs high importance, but little influence (e.g., slaughterers and breeders' associations). External funders (OIE and WHO) had medium influence and medium importance (iv) External stakeholders who competed with program resources (e.g., politicians) or provided human resources (e.g., researchers, private physicians, and veterinarians) were categorized as low influence and low importance (v) Internal actors relied upon external factors, such as the WHO, for funding support and program promotion (vi) The current control program failed to represent the interests of external actors: OIE, abattoir workers, breeder associations, local politicians, researchers, private-sector physicians, and veterinarians <p><i>Recommendations:</i></p> <ul style="list-style-type: none"> (i) Create a central office: representative for each stakeholder interest, with high power and involvement, who places high priority on program (ii) To address high number of stakeholders/complexities: assign stakeholders subgroups based upon similar interests and focus on one or more program aspects (iii) Create a working group that represents multi-stakeholder interests (iv) Address neglected control areas (e.g., dog population control, de-worming, and health education)
Main findings:	
Limitations:	<ul style="list-style-type: none"> (i) <i>Confounding bias:</i> seven study areas had different climate, human habits, and geography (ii) Results from individuals within the same institution were semi-quantified and mean average calculated. While this captures common trends, it may not account for assessment of individual skill, knowledge, and world views (iii) <i>Research Bias:</i> no conflict of interest statement and unclear if "anonymity" meant interviewees were blinded to respondents' institutional affiliation (iv) Central office recommendation suggests a representative with high power, but internal stakeholders who possessed high power considered the CE program a low priority. Thus, central office may simply continue current power dynamics

vaccinations may account for the few livestock specific studies identified.

4.6. *Improve Human and Animal Health Data Collection to Monitor Program Efficacy.* As discussed, cohort studies are advantageous when it comes to consistent follow-up and the production of data on disease incidence rate. However, within rural transient populations, and low socioeconomic contexts, such studies may not be practical. Nevertheless, prevalence could be monitored over time by training community members to conduct simple data collection. This

could encompass recording dates, the number of cases and clinical signs, on supplied template forms. Specifically, local human and veterinary medical clinic, and abattoir workers, could be trained to recognize key CE clinical signs (e.g., hepatic or pulmonary cysts identified during postmortems or meat inspections, respectively).

4.7. *Multi-stakeholder Analysis: Interdisciplinary Research, Resource Sharing, and Formal Organization.* The OIE advises that "feedback from the local community" and "relevant professionals (e.g., veterinarians, medical doctors, law

enforcement agencies, educators)” [59] is essential to producing program indicators that reflect multi-stakeholder interests. Saadi et al. [50] and Qian et al. [15] conducted multi-stakeholder analyses, using qualitative field research in Morocco, China, and Mongolia. Qian et al. [15] conducted in depth interviews with representatives from the WHO Mongolia Office, Mongolian government sectors, local hospitals, veterinary institutes, and laboratories. Participants identified the benefit of bilateral China-Mongolia cooperation, in terms of joint research and training. To optimize this benefit, Qian et al. [15] suggested interdisciplinary collaboration between the fields of medicine, veterinary science, parasitology, epidemiology, and government departments. Indeed, a key WHO recommendation is adopting a “One Health” approach that entails medical and veterinary collaboration [16]. Saadi et al.’s [50] study also concluded that stakeholder relationships promote the sharing and development of knowledge, resources, and new technologies (e.g., diagnostics or treatment methods) (p.6). Thus, sustained stakeholder collaboration proves an important means to ensuring program sustainability.

More specifically, acknowledging the interest of multiple state and non-state stakeholders has been viewed as important in addressing a “democratic deficit” ([61], p.353, [62], p. 778-9) within self-regulatory governance models. This “deficit” is linked to actors governing themselves without equally representing the interests of public, private, and civil society actors. Indeed, in Morocco, Saadi et al. [50] highlighted different levels of power and interest. Internal government stakeholders wielded the most power but considered CE programs a lower priority when compared to external actors (e.g., WHO, OIE, physicians or veterinarians) who possessed less political agency. This web of stakeholders transcends animal and human health spheres and highlights the difficulty in representing multiple interests.

A reported neglect of stakeholder interests ([50], p.5) represents why measuring social outcomes is essential to program analysis. A primary social outcome indirectly identified by three studies ([39], p.146; [42, 43]) was cultural competency. Local cultural and religious beliefs may not always align with program measures. For example, Yang et al. [43] explained that within ethnic communities in North-Western China, Buddhist religion forbids the killing of any animals (p.358), which complicates dog population control measures. Indeed, Yu et al.’s [39] study, in China, Tibet, and Mongolia, also concluded that cultural acceptance of roaming stray dogs, over population control, is common ([39], p.146).

Participatory versus top-down programs, which enable open communication, are essential to fostering mutual respect between medical and veterinary practitioners with communities. Achieving this entails avoiding an over-reliance on divisional dichotomies (e.g., developed/developing, core/periphery, and modern/traditional) [63] to explain the world through one dominant western lens [64, 65]. This simply reproduces a hegemonic form of medical knowledge that may disregard local knowledge. Local cultural beliefs and practices regarding dogs’ roles in communities will continue to shape how people respond to prevention measures.

Indeed, for people of Turkana, Kenya, dogs played multiple roles, which included acting as cattle rustlers, protectors against wildlife, as pets, and family members [42]. Thus, achieving mutual understanding ultimately increases the chance of positive behavioral change, which can reduce CE transmission.

To formally represent multiple stakeholders, Saadi et al. [50] recommended creating a national central office, which contains representative stakeholders who prioritize CE programs. However, most internal stakeholders who wielded relatively higher power considered CE programs a low priority. Thus, including both external and internal state actors is recommended to overcome these power dynamics. For example, a veterinarian could represent animal health interests; a human medical physician for public health interests; a government official for state interests; a representative for breeders, production animal, and slaughterhouse worker interests; and a community member for cultural interests.

5. Conclusion

To conclude, ten studies situated across three major CE endemic regions (Central Asia, Africa, and South America) were selected using pre-defined inclusion/exclusion criteria from the four databases. Common research limitations included no sample size calculation and numerous confounding variables, which limited result validity. One major confounder was the absence of standardized PZQ administration methods for stray and domestic dogs. Nevertheless, the studies produced useful comparisons, in terms of program barriers faced in remote, low to middle income countries. Generally, more research and/or programs are recommended within African and South American regions.

More broadly, future research and program development are essential, in terms of focusing more on prevention versus diagnostics and treatment. Future research recommendations included the following: measuring the effects of program outputs, in terms of multiple program outcomes, especially the social outcome of behavioral change. Going further, to test these outcomes for significant correlation to CE prevalence is essential. Additionally, research on live-stock prevention measures to clearly establish the practicality and benefit of program outputs, distinguish between stray versus owned dogs to calculate population sizes and clearly target program outputs, and identify the transmission role of waterways and sanitation, is essential.

Finally, the key program recommendations include the following: regular local community training to deliver sustainable program outputs (e.g., PZQ), and conduct data collection to monitor CE prevalence; organized representation of multi-stakeholder interests; clearer or standardized guidelines around PZQ and livestock vaccination administration frequency; programs that encompass multiple prevention methods (e.g., dog de-worming, public health education, and sheep vaccination) and integrated canine disease management; and enhanced veterinary-human medical training and resource sharing to improve program sustainability.

Data Availability

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Conflicts of Interest

No conflict of interest to declare.

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Supplementary Materials

Appendix A (Table A1): exclusion/inclusion criteria applied to 34 Journals within the ScienceDirect database (2015–2021), across two relevant animal and human health subject areas: “Veterinary Science and Veterinary Medicine” and “Medicine and Dentistry.” (*Supplementary Materials*)

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