PRIMER

Insights into the diagnosis, vaccines, and control of *Taenia solium*, a zoonotic, neglected parasite

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Abstract

Taenia solium taeniasis/cysticercosis (TSTC) is a foodborne, zoonotic neglected tropical disease affecting predominately low- and middle-income countries. Humans are definitive hosts for *T. solium*, whereas pigs act as intermediate hosts. Taeniasis, i.e. intestinal infection with adult *T. solium* in the human host, occurs through ingestion of undercooked pork infected with the larval stage (porcine cysticercosis, PCC). Human cysticercosis occurs after humans ingest *T. solium* eggs, acting as accidental intermediate hosts. Migration of cysticerci to the human brain results in neurocysticercosis (NCC), manifesting in a variety of clinical symptoms, most notably epilepsy. NCC is the leading cause of acquired epilepsy cases in endemic areas. PCC results in reduced pork value because of condemnation or the risk of condemnation of the meat. Available serological diagnostic tests for porcine and human cysticercosis are characterized by low sensitivity and are not cost-effective. An effective vaccine for *T. solium* cysticercosis in pigs has been developed, although it is not yet commercially available in all endemic countries, and still no vaccine is available for use in humans. This primer highlights the recent development in the field of diagnostic tests and vaccine production and explores possible strategies for future control and eradication of *T. solium*. In the absence of highly specific diagnostic tests and human vaccines, treatment of infected pigs and tapeworm carriers and prevention of disease transmission remain the principal means to interrupt the zoonotic cycle of *T. solium* in endemic countries.

Keywords *Taenia solium*, Neurocysticercosis, Porcine cysticercosis, Taeniasis, Pig, Human, Vaccine, Diagnosis

Life cycle of *Taenia solium*

The life cycle of *T. solium* involves humans as definitive hosts and pigs as intermediate hosts (Fig. 1) for a downloadable version of the poster see Additional File 1. Adult *T. solium* living in the human small intestine release eggs or egg-containing proglottids (50,000–100,000 eggs/proglottid) through stool into the environment. Several risk factors, like poor sanitation, open-air defecation, biofertilizer preparation from human stool and free-roaming pigs, help to transmit *T. solium* eggs in new areas and contaminate surface water as well as vegetation [1]. Pigs become infected by ingesting human stool or water/vegetation contaminated with *T. solium* eggs. Eggs hatch releasing the larval oncosphere in the pig intestine. Oncospheres penetrate the intestine wall, enter the bloodstream and develop into cysticerci. The larval cysticerci are mostly found in the striated muscles, subcutaneous tissues and central nervous system (CNS), resulting in porcine cysticercosis (PCC). Pigs with larval cysticerci in the brain suffer from neurocysticercosis (NCC) and

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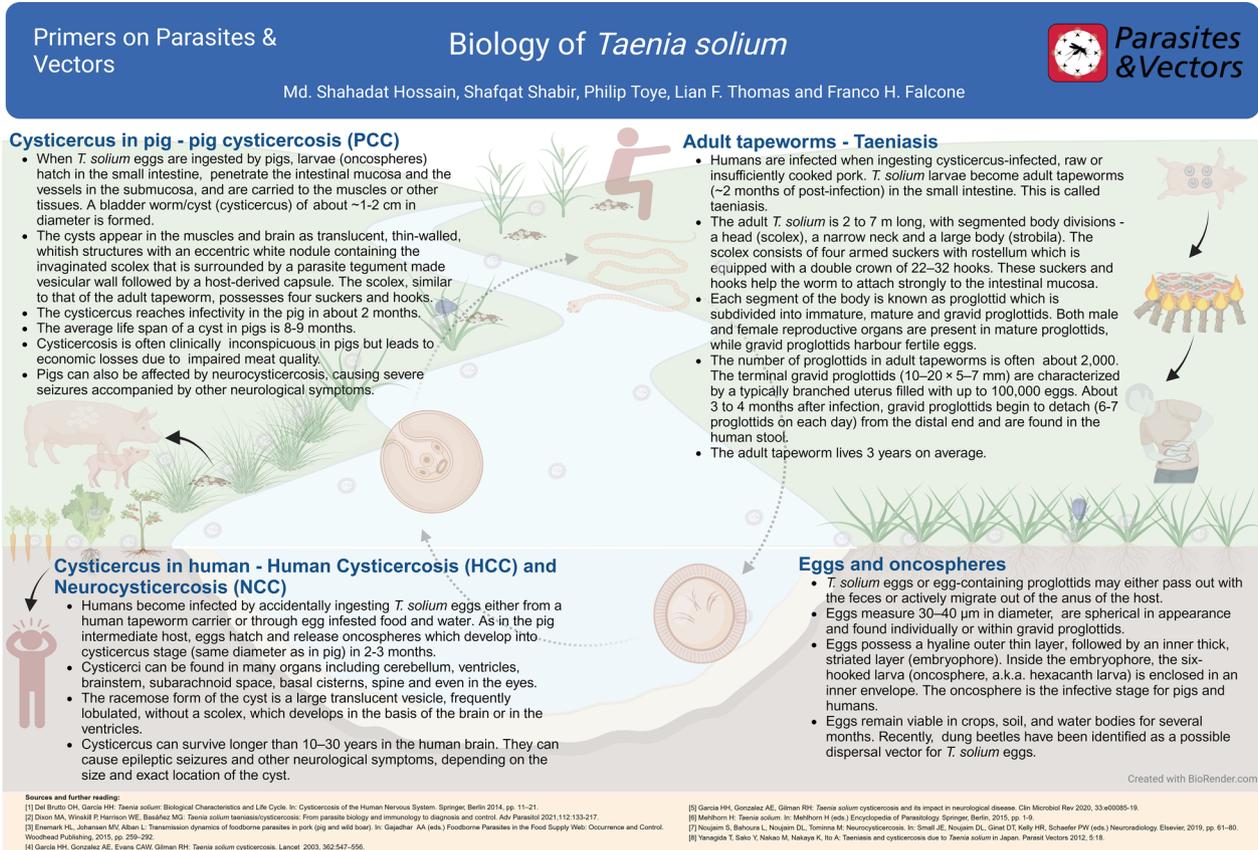[1] Department of Parasitology, Bangladesh Agricultural University, Mymensingh, Bangladesh
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Biology of *Taenia solium*

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Cysticercus in pig - pig cysticercosis (PCC)
- When *T. solium* eggs are ingested by pigs, larvae (oncospheres) hatch in the small intestine, penetrate the intestinal mucosa and the vessels in the submucosa, and are carried to the muscles or other tissues. A bladder worm/cyst (cysticercus) of about ~1-2 cm in diameter is formed.
- The cysts appear in the muscles and brain as translucent, thin-walled, whitish structures with an eccentric white nodule containing the invaginated scolex that is surrounded by a parasite tegument made vesicular wall followed by a host-derived capsule. The scolex, similar to that of the adult tapeworm, possesses four suckers and hooks.
- The cysticercus reaches infectivity in the pig in about 2 months.
- The average life span of a cyst in pigs is 8-9 months.
- Cysticercosis is often clinically inconspicuous in pigs but leads to economic losses due to impaired meat quality.
- Pigs can also be affected by neurocysticercosis, causing severe seizures accompanied by other neurological symptoms.

Adult tapeworms - Taeniasis
- Humans are infected when ingesting cysticercus-infected, raw or insufficiently cooked pork. *T. solium* larvae become adult tapeworms (~2 months of post-infection) in the small intestine. This is called taeniasis.
- The adult *T. solium* is 2 to 7 m long, with segmented body divisions - a head (scolex), a narrow neck and a large body (strobila). The scolex consists of four armed suckers with rostellum which is equipped with a double crown of 22–32 hooks. These suckers and hooks help the worm to attach strongly to the intestinal mucosa.
- Each segment of the body is known as proglottid which is subdivided into immature, mature and gravid proglottids. Both male and female reproductive organs are present in mature proglottids, while gravid proglottids harbour fertile eggs.
- The number of proglottids in adult tapeworms is often about 2,000. The terminal gravid proglottids (10–20 × 5–7 mm) are characterized by a typically branched uterus filled with up to 100,000 eggs. About 3 to 4 months after infection, gravid proglottids begin to detach (6-7 proglottids on each day) from the distal end and are found in the human stool.
- The adult tapeworm lives 3 years on average.

Cysticercus in human - Human Cysticercosis (HCC) and Neurocysticercosis (NCC)
- Humans become infected by accidentally ingesting *T. solium* eggs either from a human tapeworm carrier or through egg infested food and water. As in the pig intermediate host, eggs hatch and release oncospheres which develop into cysticercus stage (same diameter as in pig) in 2-3 months.
- Cysticerci can be found in many organs including cerebellum, ventricles, brainstem, subarachnoid space, basal cisterns, spine and even in the eyes.
- The racemose form of the cyst is a large translucent vesicle, frequently lobulated, without a scolex, which develops in the basis of the brain or in the ventricles.
- Cysticercus can survive longer than 10–30 years in the human brain. They can cause epileptic seizures and other neurological symptoms, depending on the size and exact location of the cyst.

Eggs and oncospheres
- *T. solium* eggs or egg-containing proglottids may either pass out with the feces or actively migrate out of the anus of the host.
- Eggs measure 30–40 μm in diameter, are spherical in appearance and found individually or within gravid proglottids.
- Eggs possess a hyaline outer thin layer, followed by an inner thick, striated layer (embryophore). Inside the embryophore, the six-hooked larva (oncosphere, a.k.a. hexacanth larva) is enclosed in an inner envelope. The oncosphere is the infective stage for pigs and humans.
- Eggs remain viable in crops, soil, and water bodies for several months. Recently, dung beetles have been identified as a possible dispersal vector for *T. solium* eggs.

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Sources and further reading:
[1] Del Brutto OH, Garcia HH: *Taenia solium*: Biological Characteristics and Life Cycle. In: Cysticercosis of the Human Nervous System. Springer, Berlin 2014, pp. 11–21.
[2] Dixon MA, Winskill P, Harrison WE, Basáñez MG: *Taenia solium* taeniasis/cysticercosis: From parasite biology and immunology to diagnosis and control. Adv Parasitol 2021,112:133-217.
[3] Enemark HL, Johansen MV, Alban L: Transmission dynamics of foodborne parasites in pork (pig and wild boar). In: Gajadhar AA (eds.) Foodborne Parasites in the Food Supply Web: Occurrence and Control. Woodhead Publishing, 2015, pp. 259–292.
[4] Garcia HH, Gonzalez AE, Evans CAW, Gilman RH: *Taenia solium* cysticercosis. Lancet 2003, 362:547–556.

[5] Garcia HH, Gonzalez AE, Gilman RH: *Taenia solium* cysticercosis and its impact in neurological disease. Clin Microbiol Rev 2020, 33:e00085-19.
[6] Mehlhorn H: *Taenia solium*: In: Mehlhorn H (eds.) Encyclopedia of Parasitology. Springer, Berlin, 2015, pp. 1-9.
[7] Noujaim S, Bahoura L, Noujaim DL, Tomima M: Neurocysticercosis. In: Small JE, Noujaim DL, Ginat DT, Kelly HR, Schaefer PW (eds.) Neuroradiology. Elsevier, 2019, pp. 61–80.
[8] Yanagida T, Sako Y, Nakao M, Nakaya K, Ito A: Taeniasis and cysticercosis due to *Taenia solium* in Japan. Parasit Vectors 2012, 5:18.

Fig. 1 Biological characteristics and life cycle of *Taenia solium*. Humans harbor adult *T. solium* parasites in their small intestine. Adult parasites are hermaphrodites and release fertilised eggs or egg-containing mature proglottids, each containing up to 50,000–100,000 eggs, which are excreted with faecal material, contaminating the environment. Pigs are infected by oral ingestion of this faecal material or contaminated vegetation or feed. Upon ingestion, eggs hatch and oncospheres penetrate the gut wall, migrating to the musculature where they encyst, leading to pig cysticercosis (PCC). Human ingestion of undercooked or raw contaminated pork leads to the release of larval stages in the GI tract with subsequent development to an adult tapeworm (taeniasis). Accidental ingestion of mature eggs leads to human cysticercosis (HCC) and neurocysticercosis (NCC). Pigs do not harbor adult parasites; thus, infection is spread from humans to animals (anthropozoonosis). Created with BioRender.com.

can develop clinical signs and suffer from seizures, while some pigs may have some autonomic signs, like chewing motions with foamy salivation and ear stiffening [2]. Human taeniasis results from ingestion of raw or undercooked pork infected with viable *T. solium* cysticerci [3]. In the human intestine, adult tapeworms may produce some non-specific symptoms, such as abdominal pain, nausea, diarrhea, or constipation, approximately 8 weeks after infection [4, 5]. Tapeworm carriers shed *T. solium* eggs and proglottids through stool that can again contaminate the environment. Additionally, humans may be infected by ingestion of *T. solium* eggs with water, vegetables, or raw salad items contaminated with viable eggs from a tapeworm carrier stool. In this case, eggs develop into cysts and lodge within tissues such as the CNS, skeletal muscles, or subcutaneous tissues, resulting in human cysticercosis (HCC). When larval cysts develop within in the CNS, they cause human NCC [6]. NCC can result in a wide range of neurological and psychiatric manifestations including seizures/epilepsy, severe headaches, focal deficits and signs of increased intracranial pressure [7].

Taenia solium tapeworm, a poverty-related neglected tropical disease (NTD)

Taenia solium cysticercosis is one of the 20 major neglected tropical diseases and a member of the neglected zoonotic disease (NZD) subset listed as a potentially eradicable disease by the World Health Organization (WHO), while the World Organization for Animal Health (WOAH) identifies PCC as a notifiable disease. *Taenia solium* infection in both human and pig is endemic in low- and middle-income countries (LMIC) of Latin America, sub-Saharan Africa, South and Southeast Asia [8]. Imported cases of human cysticercosis have

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been reported in most Western European countries[9], though recent studies have reported autochthonous cases of NCC in Europe, with eastern European countries most at risk [10–13]. A meta-analysis of sero-epidemiological data from endemic areas reported 7.30% (95% CI [4.23–12.31]), 4.08% (95% CI [2.77–5.95]) and 3.98% (95% CI [2.81–5.61]) prevalence of circulating *T. solium* antigens, for Africa, Latin America and Asia, respectively. Sero-prevalence estimates of *T. solium* antibodies were 17.37% (95% CI [3.33–56.20]), 13.03% (95% CI [9.95–16.88]) and 15.68% (95% CI [10.25–23.24]), respectively [14]. NCCs affects between 2.5 and 8.3 million people annually with a disability-adjusted life year (DALY) burden of 2.8 million (95% CI) [7]. The most common clinical manifestations associated with NCC are seizures/epilepsy, followed by headaches, focal deficits and signs of increased intracranial pressure [15]. It is one of the leading cause of acquired epilepsy (30% of epilepsy cases) in endemic countries [16]. The reported prevalence of NCC in people with epilepsy in endemic areas of sub-Saharan Africa was 22% (95% CI, 17.0–27.0) [17]. The estimated number of individuals with epilepsy due to NCC are 0.45–1.35 million in Latin America, 1 million in India and 0.31–4.6 million in Africa [18]. Infection of pigs with the larval stage of *T. solium* results in PCC. It is widely prevalent in sub-Saharan Africa with a meta-analysis reporting a high-pooled prevalence using available diagnostic tests (17%, 95% CI: 14–20%) across the continent [19] but hyper-endemic (i.e. persistent, high levels of disease occurrence) in Central Africa [8, 20]. In this hyper-endemic region, the recent reported prevalence of PCC was 45.6% (95% CI, 40.2–51.0) by antigen-ELISA, 24.8% (95% CI, 20.1–30.5) by antibody-ELISA, 15.5% (95% CI, 12.3–18.7) and 9.2% (95% CI, 7.9–10.7) by tongue palpation in the Democratic Republic of the Congo (DRC), Cameroon, Burundi and Rwanda, respectively [21–24]. Taeniasis has been poorly studied and is underreported in many endemic countries. The reported prevalence of taeniasis varies between 0% (95% CI [0.00–1.62]) and 17.25% (95% CI [14.55–20.23]) using different diagnostic techniques in Africa, Latin America and Asia [14]. Even low prevalence of taeniasis can sustain high prevalence of PCC and NCC because of the high number of eggs shed and the ability of a single taeniasis case to infect many pigs and humans.

While taeniasis itself has little impact on human health despite rare sequelae, cysticercosis not only has direct effects on human and animal health but also on the socioeconomic status of the former. NCC-associated epilepsy has direct effects on human health-related expenses like diagnosis, treatment and medicine cost for patients during hospitalization. Besides, indirect effects of NCC are linked to people who either become unemployed or are unable to work because of epilepsy [25]. PCC results in carcass condemnation and decreased value of pigs, which is estimated to cause 20–60% production losses in pig-raising countries or pig-based industries [25–28]. A regional study in western and central African countries estimated annual losses of about 25 million euros [20]. In many countries pig farming is an important source of emergency cash flow for marginalized households. In Uganda, for example, pig farming solely supports the livelihoods of > 1.1 million households [29].

TSTC is a focal disease, affecting the poorest communities of developing countries. In many of these communities pigs are raised in free-roaming systems (Fig. 2), and low latrine coverage results in open defecation, exposing roaming pigs to stool of tapeworm carriers [14, 29]. Home slaughter of those pigs, without appropriate veterinary inspection, is another practice among smallholder farmers, which increases the zoonotic risk in the community [30]. In this way, *T. solium* transmission persists, ultimately increasing the global burden of this NTD and affecting the livelihood of the pig-raising community in endemic regions.

Taenia solium: three recent advances
Rapid diagnosis of *T. solium* infection
As cysticercosis is mainly a problem in LMICs, diagnostic technologies not requiring specialized equipment or highly trained personnel would be advantageous. This has prompted the development of rapid detection technologies for *T. solium* infection, which has shown promising capability in recent times using recombinant antigens [31].

A lateral flow assay-based diagnostic tool was developed using up-converting phosphor (UCP) nanoparticles to detect binding of UCP to TSOL18 (oncosphere-stage protein) and GP50 (cystic larval-stage protein) antigen of *T. solium*, whose signal is then transferred to a biosensor for analysis. This technology has higher sensitivity and specificity compared with ELISA, with a sensitivity of 93.59% and 97.44% for TSOL18 and GP50, respectively, and a specificity of 100% for both antigens [32]. However, it needs to be stressed that UCP technology is not equipment-independent, as the technology is based on conversion of infrared to visible light.

Another study developed a point-of-care (POC) assay using quantum dot nanoparticles in a lateral flow assay format and detected rT24h antigen of *T. solium* in NCC patients with a mobile phone reader. The assay specificity was 99% (95–100%) while sensitivity was 89% (79–95%) in patients with two or more viable cysts [33].

Multiplex Bead Assay is one of the recombinant antigen-based diagnostic tools, which can estimate the intensity of the antibody response and allow direct comparison
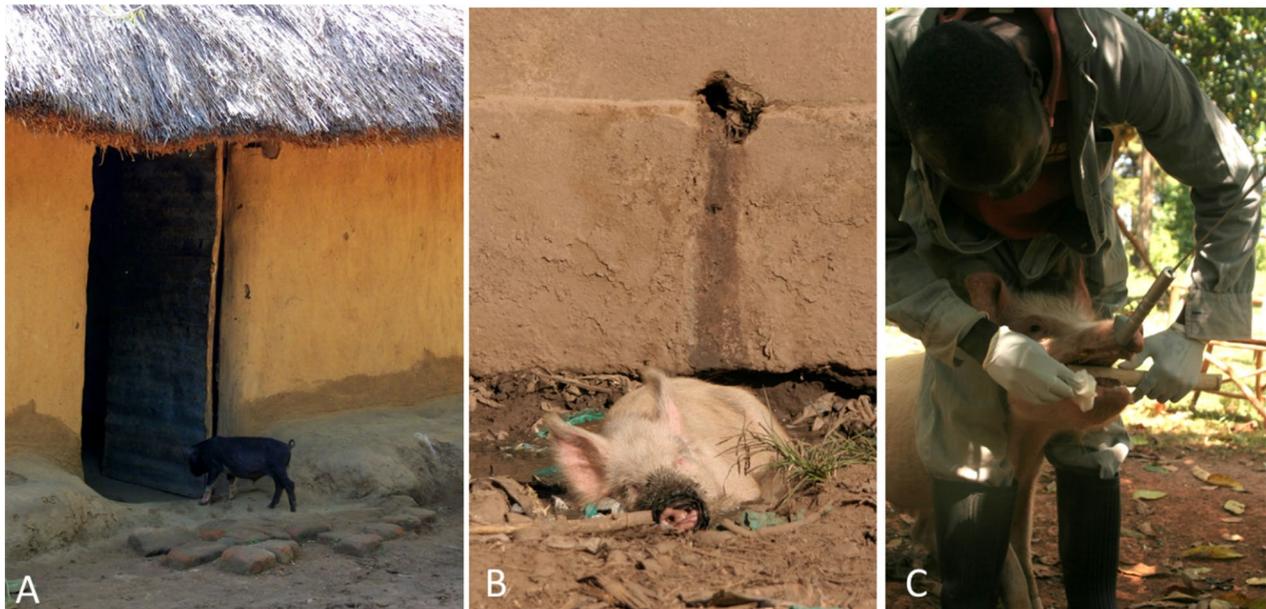
Fig. 2 A Lack of separation between pig and human habitats, as illustrated in (**A**); where pigs are allowed to roam freely, the potential for pigs to come into contact with human faecal material containing infective eggs is increased. **B** Pig wallowing in a pit containing human excrement from a draining latrine. **C** Assessment of pig cysticercosis by tongue palpation. All photographs courtesy of Lian F. Thomas

of antibody levels between samples. In one study, this assay was used for evaluating two recombinant antigens, rT24H (*T. solium*-specific) and r2B2t (*Echinococcus granulosus*-specific) for simultaneous and differential diagnosis of NCC and cystic echinococcosis. For the diagnosis of NCC, the sensitivity and specificity of this assay ranged from 57.94 to 63.49% and 90.87–91.30%, respectively [34].

Molecular identification of *T. solium*

DNA-based diagnostic methods have been developed to identify *T. solium* DNA specifically, either from human stool or directly from tapeworm-derived segments. LAMP (loop-mediated isothermal amplification) is a DNA-based isothermal PCR technique, which has emerged as a good diagnostic tool in the last decade for the detection of different taeniids at species level. A multiplex LAMP (mLAMP) assay uses mitochondrial cytochrome oxidase subunit 1 (COX1) marker in combination with dot enzyme-linked immunosorbent assay (dot-ELISA). This assay was successfully used to identify *Taenia* species from genomic and copro-DNA samples with 100% specificity, making it the first field-based test for sensitive and specific identification of human *Taenia* species [26]. Lyophilized LAMP has been developed with long shelf life and does not require any type of cold chain support, which can therefore facilitate its use for diagnosing *T. solium* in endemic countries [35, 36]. Recently, quantitative molecular approaches

like quantitative polymerase chain reaction (qPCR) have become an attractive platform for biomarker and diagnostic test development for identifying specific *T. solium* sequences. In the *T. solium* genome, TsolR13 sequence has shown high sensitivity (97.3%) and specificity (100%) for diagnosis of NCC [37]. Another study used qPCR for the differentiation among *Taenia solium*, *T. saginata* and *T. asiatica* in human stool. This study targeted the internal transcribed spacer I (ITS-1) gene of *Taenia solium* and COX1 gene of *T. saginata* and *T. asiatica*. For the diagnosis of taeniasis, this study showed 94% sensitivity and 98% specificity [38].

Recombinant vaccine development for pig immunization

Vaccination of pigs is an efficient method to reduce human exposure to infected pork, which ultimately reduces both taeniasis and cysticercosis. For pig vaccine development, different *T. solium* antigens have been explored for their suitability, for instance, *T. solium* scolex protein antigen [39]; TSOL16, TSOL18, TSOL45-1A, TSOL45-1B (oncosphere protein) [40, 41]; *T. solium* paramyosin, a muscle and tegument protein [42]. Among those antigens, TSOL18 has been identified as the most promising candidate for recombinant vaccine development against PCC. This vaccine can provide 99.5% protection against PCC [43]. TSOL18 vaccine was first commercialised by GALVmed, Indian Immunologics (IIL) and University of Melbourne [44]. The vaccine was then licensed in 2016 in India. Field trials in Cameroon

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[45] and Nepal [46] evaluated a combination of TSOL18 vaccine (Cysvax™) and Oxfendazole (Paranthic 10%™) drug against PCC. Oxfendazole removes existing cyst infection in pig while TSOL18 checks subsequent infection with *T. solium*. This combined therapy increases the protection level up to 99.7% of all animals exposed to subsequent infection and results in significant reduction in prevalence of PCC in endemic countries [47–50]. Another two synthetic vaccine candidates against *T. solium* SP3VAC (KETc7, KETc1 and KETc12) and a modified parenterally administered SP3Vac-phage version have undergone trials in Mexico [43]. Whilst TSOL18 vaccine (Cysvax™) is now commercially available at a relatively low cost (US$ 2.31) in many of the endemic countries, there is evidence from Uganda that pig farmers are not yet willing to pay for the vaccine without a market premium for vaccinated pigs and in the absence of intrinsic health benefits for the vaccinated animals [28].

Taenia solium: three areas ripe for research
Developing human vaccines
Most vaccine research work on *T. solium* to date has primarily focused on identifying candidate vaccines for pig to control PCC in endemic countries. Animal vaccines are comparatively easier and cheaper to develop than human vaccines. Therefore, until now human vaccination has not been considered an effective control strategy for TSTC in humans [47]. *Taenia solium* calreticulin, a tegument protein of the parasite, is essential for embryogenesis, oogenesis and spermiogenesis. This protein has been explored as a candidate vaccine target, and several studies showed reduced worm burden in an experimental hamster model of taeniasis [51–53]. In another study, fatty acid-binding proteins of *T. solium* showed only 45% reduction of parasite load against an intraperitoneal challenge with *T. crassiceps* cysts in a murine model of cysticercosis [54]. More candidate antigens of *T. solium* still need to be explored to identify a reliable and affordable vaccine for human use. While there is currently little willingness to pay by farmers for the highly effective TSOL18 vaccine for pig, the development and incorporation of a human vaccine into childhood vaccination schedules may be an option to significantly reduce infection in exposed populations.

Further improving available diagnostic tests
The available diagnostic tests are still not fully suitable for sensitive and specific field level diagnosis of TSTC. To help overcome this gap, WHO defined four new target product profiles (TPPs) for researchers, diagnostic developers and manufacturers to develop effective and useful diagnostic tests for *T. solium*. Among four TPPs, two were classified for taeniasis-specific test and POC

test development, one for NCC POC test development and one for porcine cysticercosis-specific diagnostic test development [31]. TPPs mandate that for a specific test of taeniasis, the sensitivity and specificity should be ≥ 95% and 99%, respectively. Furthermore, the cost of the test should be between 0.5 and 2 USD per test and the developed test kit should be stable for 24–36 months at 2–40 °C. For the POC test of taeniasis, sensitivity should range between 95 and 99% and specificity between 80 and 99% with same cost and storage conditions as mentioned above. For POC test for NCC the sensitivity should be between 98–99% with 90–95% specificity and the cost of the test should be between 2–3 USD along with 24–36-month stability at 2–30 °C. However, TPPs for PCC diagnostic test need 50–70% sensitivity for around 50 cysts and 80–90% for > 50 cysts, and the test should at least detect one single viable cyst in pig, while the specificity should range between 95 and 98%. The test should not show cross-reaction with either *Taenia* species or other parasites and not show any positive response in the absence of viable cysts. In addition, the cost of this test should be 0.5–2 USD per test with 24–36 month stability at 2–40 °C temperature [31].

The current reference methods for PCC and NCC are the full carcass muscle/brain dissection and imaging techniques, which are not feasible economically in developing countries. There is no dry LAMP format for the detection of *T. solium* infections in both humans and animals. Moreover, specific methods and diagnostic tools are still unavailable for inspecting vegetables or other possible transmission vehicles (soil, water) for *T. solium* eggs [55].

Supporting intervention design and evaluation: transmission modelling, economic evaluation and risk mapping
To tackle *T. solium* taeniasis and cysticercosis in endemic countries, the WHO aims to scale up the intervention methods used to control *T. solium*. WHO projected that 27% of endemic countries will achieve intensified *T. solium* control in hyperendemic areas by 2030 [56]. This target is achievable by revealing unknown transmission dynamics of *T. solium*, including risk factor identification in both host and environment. In endemic countries, spatial distribution and risk factor analysis for human and porcine cysticercosis is one of the best options to unravel the transmission patterns of *T. solium*. A new agent-based model, CystiAgent, has created a model for analysing spatial and behavioural features of *T. solium* transmission in northern Peru. This model has the ability to represent key spatial and environmental features of transmission and simulate spatially targeted interventions, such as ring strategy [57]. Another model,

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CystiHuman, based on CystiAgent, was also developed to simulate human NCC and associated pathologies in the endemic community setting of Peru [58]. A deterministic, compartmental transmission model for pig and human transmission of *T. solium* (EPICYST) has also been developed [59]. These models can support the design and *ex ante* assessment of control options for *T. solium* but maximising the utility of these models will require continued collaborative efforts between modelling teams to improve and harmonise models and model parameters [59, 60]. As well as determining the efficacy of control programmes in reducing infection pressure, it is important to quantify the impact on burden of disease. Whilst human health burden can be measured in DALYs, for the evaluation of zoonotic disease control strategies such as for *T. solium*, a novel metric, zoonotic disability-adjusted life years (zDALY), may be more appropriate [61]. zDALYs estimate the actual impact of a zoonotic disease across both animal and human health and may be used to better assess the cost-effectiveness of a control programme across multiple sectors [62]. Appropriate geographical targeting of control programmes requires accurate endemicity mapping. Recently, WHO updated a new endemicity map at country level in 2022, but lack of subnational mapping is still a major challenge to achieving intensified *T. solium* control milestones [13]. A recent study in Uganda mapped all the available *T. solium* prevalence data and the PCC risk factors to obtain a complete insight into the *T. solium* landscape and subnational variation of indicators [63]. Better understanding of adult *T. solium* biology with identification of environmental dynamics of eggs and risk factors analysis of pig-to-people and environment-to-pig transmission will be paramount to achieving WHO 2030 targets.

Conclusions

Taken together, although eradication of TSTC appears possible in principle, it is still far from being achieved. Some very effective components, such as combined treatment/vaccination with oxfendazole and TSOL18, are available, but there are still economic and sociocultural factors hindering their implementation in many endemic countries, and affordable, effective diagnostic technologies still lag behind. In the meantime, an achievable, immediate objective will be to implement highly targeted, small-scale control programmes in the most impacted areas by taking advantage of the improved new mapping tools combined with better transmission models.

Abbreviations

CNS	Central nervous system
DALY	Disability-adjusted life years
HCC	Human cysticercosis
LAMP	Loop-mediated isothermal amplification
LMIC	Low and middle income country
NTD	Neglected tropical disease
NCC	Neurocysticercosis
NZD	Neglected zoonotic disease
PCC	Porcine cysticercosis
POC	Point of care
PWE	People with epilepsy
TPPs	Target product profiles
TSTC	*Taenia solium* taeniasis/cysticercosis
WHO	World Health Organization
WOAH	World Organization for Animal Health
zDALY	Zoonotic disability-adjusted life years

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13071-023-05989-6.

Additional file 1: Biological characteristics and life cycle of *Taenia solium*. Humans harbor adult *T. solium* parasites in their small intestine. Adult parasites are hermaphrodites and release fertilised eggs or egg-containing mature proglottids, each containing up to 50,000–100,000 eggs, which are excreted with faecal material, contaminating the environment. Pigs are infected by oral ingestion of this faecal material or contaminated vegetation or feed. Upon ingestion, eggs hatch and oncospheres penetrate the gut wall, migrating to the musculature where they encyst, leading to pig cysticercosis (PCC). Human ingestion of undercooked or raw contaminated pork leads to the release of larval stages in the GI tract with subsequent development to an adult tapeworm (taeniasis). Accidental ingestion of mature eggs leads to human cysticercosis (HCC) and neurocysticercosis (NCC). Pigs do not harbor adult parasites; thus, infection is spread from humans to animals (anthropozoonosis). Created with BioRender.com.

Author contributions

FHF, PT, LFT, SS and MSH were involved in the conception of the primary article. MSH wrote the original draft of the manuscript. All authors critically reviewed and commented on the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

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References

1. Chávez-Ruvalcaba F, Chávez-Ruvalcaba MI, Moran Santibañez K, Muñoz-Carrillo JL, León Coria A, Reyna MR. Foodborne parasitic diseases in the neotropics—a review. Helminthologia. 2021;58:119–33. https://doi.org/10.2478/helm-2021-0022.
2. Trevisan C, Mkupasi EM, Ngowi HA, Forkman B, Johansen MV. Severe seizures in pigs naturally infected with *Taenia solium* in Tanzania. Vet Parasitol. 2016;220:67–71. https://doi.org/10.1016/j.vetpar.2016.02.025.
3. Garcia HH, Gonzalez AE, Gilman RH. *Taenia solium* cysticercosis and its impact in neurological disease. Clin Microbiol Rev. 2020. https://doi.org/10.1128/cmr.00085-19.
4. WHO. Taeniasis/cysticercosis. 2021. https://www.who.int/news-room/fact-sheets/detail/taeniasis-cysticercosis.
5. Symeonidou I, Arsenopoulos K, Tzilves D, Soba B, Gabriël S, Papadopoulos E. Human taeniasis/cysticercosis: a potentially emerging parasitic disease in Europe. Ann Gastroenterol. 2018;31:406–12.
6. Noujaim S, Bahoura L, Noujaim DL, Tominna M. Neurocysticercosis. Neuroradiology. 2019. https://doi.org/10.1016/B978-0-323-44549-8.00009-2.
7. Li M, Havelaar AH, Hoffmann S, Hald T, Kirk MD, Torgerson PR, et al. Global disease burden of pathogens in animal source foods, 2010. PLoS ONE. 2019;14:e0216545. https://doi.org/10.1371/journal.pone.0216545.
8. Acosta Soto L, Parker LA, Irisarri-Gutiérrez MJ, Bustos JA, Castillo Y, Perez E, et al. Evidence for transmission of *Taenia solium* taeniasis/cysticercosis in a rural area of Northern Rwanda. Front Vet Sci. 2021. https://doi.org/10.3389/fvets.2021.645076.
9. Del Brutto OH. Neurocysticercosis in Western Europe: a re-emerging disease? Acta Neurol Belg. 2012;112:335–43. https://doi.org/10.1007/s13760-012-0068-3.
10. Fabiani S, Bruschi F. Neurocysticercosis in Europe: Still a public health concern not only for imported cases. Acta Trop. 2013;128:18–26. https://doi.org/10.1016/j.actatropica.2013.06.020.
11. Zammarchi L, Strohmeyer M, Bartalesi F, Bruno E, Muñoz J, Buonfrate D, et al. Epidemiology and management of cysticercosis and *Taenia solium* taeniasis in Europe, systematic review 1990–2011. PLoS ONE. 2013. https://doi.org/10.1371/journal.pone.0069537.
12. Devleesschauwer B, Allepuz A, Dermauw V, Johansen MV, Laranjo-González M, Smit GSA, et al. *Taenia solium* in Europe: still endemic? Acta Trop. 2017;165:96–9. https://doi.org/10.1016/j.actatropica.2015.08.006.
13. Donadeu M, Bote K, Gasimov E, Kim S, Lin Z, Lucianez A, et al. WHO *Taenia solium* endemicity map—2022 update. Wkly Epidemiol Rec. 2022;97:169–72.
14. Coral-Almeida M, Gabriël S, Abatih EN, Praet N, Benitez W, Dorny P. *Taenia solium* human cysticercosis: a systematic review of sero-epidemiological data from endemic zones around the world. PLoS Negl Trop Dis. 2015. https://doi.org/10.1371/journal.pntd.0003919.
15. Carabin H, Ndimubanzi PC, Budke CM, Nguyen H, Qian Y, Cowan LD, et al. Clinical manifestations associated with neurocysticercosis: a systematic review. PLoS Negl Trop Dis. 2011;5:e1152. https://doi.org/10.1371/journal.pntd.0001152.
16. Ndimubanzi PC, Carabin H, Budke CM, Nguyen H, Qian YJ, Rainwater E, et al. A systematic review of the frequency of neurocyticercosis with a focus on people with epilepsy. PLoS Negl Trop Dis. 2010;4:e870. https://doi.org/10.1371/journal.pntd.0000870.
17. Owolabi LF, Adamu B, Jibo AM, Owolabi SD, Imam AI, Alhaji ID. Neurocysticercosis in people with epilepsy in Sub-Saharan Africa: a systematic review and meta-analysis of the prevalence and strength of association. Seizure. 2020;76:1–11. https://doi.org/10.1016/j.seizure.2020.01.005.
18. Coyle CM, Mahanty S, Zunt JR, Wallin MT, Cantey PT, White AC, et al. Neurocysticercosis: neglected but not forgotten. PLoS Negl Trop Dis. 2012;6:e1500. https://doi.org/10.1371/journal.pntd.0001500.
19. Gulelat Y, Eguale T, Kebede N, Aleme H, Fèvre EM, Cook EAJ. Epidemiology of porcine cysticercosis in Eastern and Southern Africa: systematic review and meta-analysis. Front Public Heal. 2022;10:836177. https://doi.org/10.3389/fpubh.2022.836177.
20. Zoli A, Shey-Njila O, Assana E, Nguekam JP, Dorny P, Brandt J, et al. Regional status, epidemiology and impact of *Taenia solium* cysticercosis in Western and Central Africa. Acta Trop. 2003;87:35–42. https://doi.org/10.1016/s0001-706x(03)00053-6.
21. Madinga J, Kanobana K, Lukanu P, Abatih E, Baloji S, Linsuke S, et al. Geospatial and age-related patterns of *Taenia solium* taeniasis in the rural health zone of Kimpese, Democratic Republic of Congo. Acta Trop. 2017;165:100–9.
22. Assana E, Awah-Ndukum J, Djonmaïla JD, Zoli AP. Prevalence of porcine *Taenia solium* and *Taenia hydatigena* cysticercosis in Cameroon. Prev Vet Med. 2019;169:104690. https://doi.org/10.1016/j.prevetmed.2019.104690.
23. Minani S, Dorny P, Trevisan C. Prevalence and risk assessment of porcine cysticercosis in Ngozi province, Burundi. Vet Parasitol Reg Stud Reports. 2021;23:100514. https://doi.org/10.1016/j.vprsr.2020.100514.
24. Mushonga B, Habarugira G, Birori A, Kandiwa E, Samkange A, Bhebhe E. An epidemiological survey of the magnitude and local perceptions of porcine cysticercosis by two methods in Nyaruguru district, Rwanda. Vet Parasitol Reg Stud Reports. 2018;14:18–24. https://doi.org/10.1016/j.vprsr.2018.07.010.
25. Trevisan C, Devleesschauwer B, Praet N, Pondja A, Assane YA, Dorny P, et al. Assessment of the societal cost of *Taenia solium* in Angónia district, Mozambique. BMC Infect Dis. 2018;18:127. https://doi.org/10.1186/s12879-018-3030-z.
26. Nkouawa A, Sako Y, Okamoto M, Ito A. Simple identification of human *Taenia* species by multiplex loop-mediated isothermal amplification in combination with dot enzyme-linked immunosorbent assay. Am J Trop Med Hyg. 2016;94:1318–23. https://doi.org/10.4269/ajtmh.15-0829.
27. Praet N, Speybroeck N, Manzanedo R, Berkvens D, Nsame Nforninwe D, Zoli A, et al. The disease burden of *Taenia solium* cysticercosis in Cameroon. PLoS Negl Trop Dis. 2009;3:e406. https://doi.org/10.1371/journal.pntd.0000406.
28. Ouma E, Dione M, Mtimet N, Lule P, Colston A, Adediran S, et al. Demand for *Taenia solium* cysticercosis vaccine: lessons and insights from the pig production and trading nodes of the Uganda pig value chain. Front Vet Sci. 2021. https://doi.org/10.3389/fvets.2021.611166.
29. Ngwili N, Thomas L, Githigia S, Muloi D, Marshall K, Wahome R, et al. Co-infection of pigs with *Taenia solium* cysticercosis and gastrointestinal parasites in Eastern and Western Uganda. Parasitol Res. 2022;121:177–89. https://doi.org/10.1007/s00436-021-07380-9.
30. Assana E, Lightowlers MW, Zoli AP, Geerts S. *Taenia solium* taeniosis/cysticercosis in Africa: risk factors, epidemiology and prospects for control using vaccination. Vet Parasitol. 2013;195:14–23. https://doi.org/10.1016/j.vetpar.2012.12.022.
31. Donadeu M, Fahrion AS, Olliaro PL, Abela-Ridder B. Target product profiles for the diagnosis of *Taenia solium* taeniasis, neurocysticercosis and porcine cysticercosis. PLoS Negl Trop Dis. 2017;11:e0005875. https://doi.org/10.1371/journal.pntd.0005875.
32. Zhang D, Qi Y, Cui Y, Song W, Wang X, Liu M, et al. Rapid detection of *Cysticercus cellulosae* by an up-converting phosphor technology-based lateral-flow assay. Front Cell Infect Microbiol. 2021;11:762472. https://doi.org/10.3389/fcimb.2021.762472.
33. Lee C, Noh J, O'Neal SE, Gonzalez AE, Garcia HH, Handali S. Feasibility of a point-of-care test based on quantum dots with a mobile phone reader for detection of antibody responses. Periago MV, editor. PLoS Negl Trop Dis. 2019;13:e0007746. https://doi.org/10.1371/journal.pntd.0007746.
34. Hernández-González A, González-Bertolín B, Urrea L, Fleury A, Ferrer E, Siles-Lucas M, et al. Multiple-bead assay for the differential serodiagnosis of neglected human cestodiases: Neurocysticercosis and cystic echinococcosis, Goletti D, editor. PLoS Negl Trop Dis. 2022;16:e0010109. https://doi.org/10.1371/journal.pntd.0010109.
35. Chander Y, Koelbl J, Puckett J, Moser MJ, Klingele AJ, Liles MR, et al. A novel thermostable polymerase for RNA and DNA loop-mediated isothermal amplification (LAMP). Front Microbiol. 2014. https://doi.org/10.3389/fmicb.2014.00395.

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36. Carter C, Akrami K, Hall D, Smith D, Aronoff-Spencer E. Lyophilized visually readable loop-mediated isothermal reverse transcriptase nucleic acid amplification test for detection Ebola Zaire RNA. J Virol Methods. 2017;244:32–8. https://doi.org/10.1016/j.jviromet.2017.02.013.

37. O'Connell EM, Harrison S, Dahlstrom E, Nash T, Nutman TB. A novel, highly sensitive quantitative polymerase chain reaction assay for the diagnosis of subarachnoid and ventricular neurocysticercosis and for assessing responses to treatment. Clin Infect Dis. 2020;70:1875–81. https://doi.org/10.1093/cid/ciz541.

38. Ng-Nguyen D, Stevenson MA, Dorny P, Gabriël S, Van VT, Nguyen VAT, et al. Comparison of a new multiplex real-time PCR with the Kato Katz thick smear and copro-antigen ELISA for the detection and differentiation of *Taenia* spp. in human stools. PLoS Negl Trop Dis. 2017;11:e0005743. https://doi.org/10.1371/journal.pntd.0005743.

39. Nascimento E, Costa JO, Guimarães MP, Tavares CAP. Effective immune protection of pigs against cysticercosis. Vet Immunol Immunopathol. 1995;45:127–37. https://doi.org/10.1016/0165-2427(94)05327-o.

40. Gauci CG, Jayashi CM, Gonzalez AE, Lackenby J, Lightowlers MW. Protection of pigs against *Taenia solium* cysticercosis by immunization with novel recombinant antigens. Vaccine. 2012;30–540:3824.

41. Jayashi CM, Kyngdon CT, Gauci CG, Gonzalez AE, Lightowlers MW. Successful immunization of naturally reared pigs against porcine cysticercosis with a recombinant oncosphere antigen vaccine. Vet Parasitol. 2012;188:261.

42. Vázquez-Talavera J, Solís CF, Terrazas LI, Laclette JP. Characterization and protective potential of the immune response to *Taenia solium* paramyosin in a murine model of cysticercosis. Petri WA, editor. Infect Immun 2001;69:5412–6. https://doi.org/10.1128/iai.69.9.5412-5416.2001.

43. Butala C, Brook TM, Majekodunmi AO, Welburn SC. Neurocysticercosis: current perspectives on diagnosis and management. Frontiers. 2021;8:256. https://doi.org/10.3389/fvets.2021.615703.

44. Thomas LF. Landscape analysis: Control of *Taenia solium*. Geneva: World Health Organization; 2015. https://apps.who.int/iris/handle/10665/164359.

45. Assana E, Kyngdon CT, Gauci CG, Geerts S, Dorny P, De Deken R, et al. Elimination of *Taenia solium* transmission to pigs in a field trial of the TSOL18 vaccine in Cameroon. Int J Parasitol. 2010;40:515–9. https://doi.org/10.1016/j.ijpara.2010.01.006.

46. Poudel I, Sah K, Subedi S, Singh DK, Kushwaha P, Colston A, et al. Implementation of a practical and effective pilot intervention against transmission of *Taenia solium* by pigs in the Banke district of Nepal. PLoS Negl Trop Dis. 2019;13:e0006838.

47. Dailey Garnes NJM, White AC, Serpa JA. *Taenia solium*, *Taenia asiatica*, and *Taenia saginata*. Principles and practice of pediatric infectious diseases. Elsevier; 2018. pp. 1397–1404.e4. https://doi.org/10.1016/B978-0-323-40181-4.00280-2.

48. Kato H. Mucosal vaccine for parasitic infections. Mucosal Vaccines. 2020. https://doi.org/10.1016/B978-0-12-811924-2.00050-X.

49. CystiTeam Group for Epidemiology and Modelling of *Taenia solium* Taeniasis/Cysticercosis. The World Health Organization 2030 goals for *Taenia solium*: insights and perspectives from transmission dynamics modelling. Gates Open Res. 2019;3:1546. https://doi.org/10.12688/gatesopenres.13068.2.

50. Kabululu ML, Ngowi HA, Mlangwa JED, Mkupasi EM, Braae UC, Colston A, et al. TSOL18 vaccine and oxfendazole for control of *Taenia solium* cysticercosis in pigs: a field trial in endemic areas of Tanzania. PLoS Negl Trop Dis. 2020;14:e0008785. https://doi.org/10.1371/journal.pntd.0008785.

51. Mendlovic F, Cruz-Rivera M, Diaz-Gandarilla JA, Flores-Torres MA, Avila G, Perfiliev M, et al. Orally administered *Taenia solium* Calreticulin prevents experimental intestinal inflammation and is associated with a type 2 immune response, Cominelli F, editor. PLoS ONE. 2017;12:e0186510. https://doi.org/10.1371/journal.pone.0186510.

52. Salazar AM, Mendlovic F, Cruz-Rivera M, Chávez-Talavera O, Sordo M, Avila G, et al. Genotoxicity induced by *Taenia solium* and its reduction by immunization with calreticulin in a hamster model of taeniosis. Environ Mol Mutagen. 2013;54:347–53. https://doi.org/10.1002/em.21782.

53. Leon-Cabrera S, Cruz-Rivera M, Mendlovic F, Romero-Valdovinos M, Vaughan G, Salazar AM, et al. Immunological mechanisms involved in the protection against intestinal taeniosis elicited by oral immunization with *Taenia solium* calreticulin. Exp Parasitol Academic Press. 2012;132:334–40. https://doi.org/10.1016/j.exppara.2012.08.006.

54. Illescas O, Carrero JC, Bobes RJ, Flisser A, Rosas G, Laclette JP. Molecular characterization, functional expression, tissue localization and protective potential of a *Taenia solium* fatty acid-binding protein. Mol Biochem Parasitol. 2012;186:117–25. https://doi.org/10.1016/j.molbiopara.2012.10.002.

55. Saelens G, Robertson L, Gabriël S. Diagnostic tools for the detection of taeniid eggs in different environmental matrices: a systematic review. Food Waterborne Parasitol. 2022;26:e00145. https://doi.org/10.1016/j.fawpar.2022.e00145.

56. World Health Organization. Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030. Geneva PP, Geneva: World Health Organization; 2020. https://apps.who.int/iris/handle/10665/338565.

57. Pray IW, Wakeland W, Pan W, Lambert WE, Garcia HH, Gonzalez AE, et al. Understanding transmission and control of the pork tapeworm with CystiAgent: a spatially explicit agent-based model. Parasit Vectors. 2020;13:1–13. https://doi.org/10.1186/s13071-020-04226-8.

58. Bonnet G, Pizzitutti F, Gonzales-Gustavson EA, Gabriël S, Pan WK, Garcia HH, et al. CystiHuman: a model of human neurocysticercosis. PLOS Comput Biol. 2022;18:e1010118. https://doi.org/10.1371/journal.pcbi.1010118.

59. Winskill P, Harrison WE, French MD, Dixon MA, Abela-Ridder B, Basáñez MG. Assessing the impact of intervention strategies against *Taenia solium* cysticercosis using the EPICYST transmission model. Parasit Vectors. 2017;10:1–14. https://doi.org/10.1186/s13071-017-1988-9.

60. Dixon MA, Braae UC, Winskill P, Devleesschauwer B, Trevisan C, Van Damme I, et al. Modelling for *Taenia solium* control strategies beyond 2020. Bull World Health Organ. 2020;98:198–205. https://doi.org/10.2471/blt.19.238485.

61. Torgerson PR, Rüegg S, Devleesschauwer B, Abela-Ridder B, Havelaar AH, Shaw APM, et al. zDALY: an adjusted indicator to estimate the burden of zoonotic diseases. One Heal. 2018;5:40–5. https://doi.org/10.1016/j.onehlt.2017.11.003.

62. Okello WO, Okello AL, Inthavong P, Tiemann T, Phengsivalouk A, Devleesschauwer B, et al. Improved methods to capture the total societal benefits of zoonotic disease control: demonstrating the cost-effectiveness of an integrated control programme for *Taenia solium*, soil transmitted helminths and classical swine fever in northern Lao PDR. PLoS Negl Trop Dis. 2018. https://doi.org/10.1371/journal.pntd.0006782.

63. Ngwili N, Sentamu DN, Korir M, Adriko M, Beinamaryo P, Dione MM, et al. Spatial and temporal distribution of *Taenia solium* and its risk factors in Uganda. Int J Infect Dis. 2023;129:274–84. https://doi.org/10.1016/j.ijid.2023.02.001.

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