Abstract The cestode *Taenia solium* is responsible for a considerable cross-sectoral health and economic burden due to human neurocysticercosis and porcine cysticercosis. The 2012 World Health Organization (WHO) roadmap for neglected tropical diseases called for a development of a validated strategy for control of *T. solium*; however, such a strategy is not yet available. In 2019, WHO launched a global consultation aimed at refining the post-2020 targets for control of *T. solium* for a new roadmap for neglected tropical diseases. In response, two groups working on taeniasis and cysticercosis mathematical models (cystiSim and EPICYST models), together with a range of other stakeholders organized a workshop to provide technical input to the WHO consultation and develop a research plan to support efforts to achieve the post-2020 targets. The workshop led to the formation of a collaboration, CystiTeam, which aims to tackle the population biology, transmission dynamics, epidemiology and control of *T. solium* through mathematical modelling approaches. In this paper, we outline developments in *T. solium* control and in particular the use of modelling to help achieve post-2020 targets for control of *T. solium*. We discuss the steps involved in improving confidence in the predictive capacities of existing mathematical and computational models on *T. solium* transmission, including model comparison, refinement, calibration and validation. Expanding the CystiTeam partnership to other research groups and stakeholders, particularly those operating in different geographical and endemic areas, will enhance the prospects of improving the applicability of *T. solium* transmission models to inform taeniasis and cysticercosis control strategies.

Introduction

Infection by the cestode *Taenia solium*, a zoonotic tapeworm, exerts a considerable health and economic burden as the cause of cysticercosis in humans and pigs in endemic countries. The most acute human health burden results from neurocysticercosis-associated epilepsy, caused by cysticerci settled in the central nervous system. This disease was responsible for about 2.8 million disability-adjusted life years (DALYS) in 2010. In the United Republic of Tanzania, the economic burden for 2012 due to neurocysticercosis-associated epilepsy, has been estimated at 5.0 million United States dollars (US$) and the burden due to porcine cysticercosis, resulting from the reduced value of infected pork, at US$ 2.8 million. In Angónia district in Mozambique, with a human population of about 330,000, these estimations were about US$ 71,000 and US$ 22,000, respectively, in 2007. These data highlight the burden for 2012 due to neurocysticercosis-associated epilepsy, caused by cysticerci settled in the central nervous system. This disease was responsible for about 2.8 million disability-adjusted life years (DALYS) in 2010. In the United Republic of Tanzania, the economic burden for 2012 due to neurocysticercosis-associated epilepsy, has been estimated at 5.0 million United States dollars (US$) and the burden due to porcine cysticercosis, resulting from the reduced value of infected pork, at US$ 2.8 million. In Angónia district in Mozambique, with a human population of about 330,000, these estimations were about US$ 71,000 and US$ 22,000, respectively, in 2007. These data highlight the impact of *T. solium* across human and animal health sectors. *T. solium* infection disproportionately affects smallholder and subsistence farming communities in endemic settings, where the presence of common risk factors, such as free-roaming pigs and poor sanitation, allows high levels of direct and indirect (environmental) disease transmission. A collaborative One Health approach, which addresses *T. solium* control from the human health, animal health and environmental perspectives, is therefore essential to tackle this zoonotic neglected tropical disease.

Tackling *T. solium*

The 2012 World Health Organization (WHO) roadmap Accelerating work to overcome the global impact of neglected tropical diseases called for the development of a validated strategy for *T. solium* control and elimination by 2015, and for interventions to be scaled up in selected countries by 2020. Research in 2018 on the control of *T. solium* concluded that evidence on optimal interventions for control and elimination is still limited. A validated strategy has, therefore, not yet been identified and, hence, the 2015 target has not been met. Nevertheless, notable progress has been made, including an elimination trial with an intensive package over a 1-year period of interventions targeting both humans and pigs on a regional scale in northern Peru. This package included mass treatment of humans with niclosamide and pigs with oxendazole in combination with vaccination of pigs. In addition, a more targeted ring-screening intervention, in which people within a 100-m radius of pigs found positive for cysticercosis were screened and treated for taeniasis and cysticercosis control strategies. In this paper, we outline developments in *T. solium* control and in particular the use of modelling to help achieve post-2020 targets for control of *T. solium*. We discuss the steps involved in improving confidence in the predictive capacities of existing mathematical and computational models on *T. solium* transmission, including model comparison, refinement, calibration and validation. Expanding the CystiTeam partnership to other research groups and stakeholders, particularly those operating in different geographical and endemic areas, will enhance the prospects of improving the applicability of *T. solium* transmission models to inform taeniasis and cysticercosis control strategies.

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ongoing, including cost–effectiveness evaluations of both control and elimination objectives in Zambia. T. solium control could also be integrated into existing water, sanitation and hygiene projects. In addition, low-cost intervention strategies could include health education tools for human health and agricultural professionals, as well as for local communities. One such tool is the Vicious Worm. This tool has been used in the United Republic of Tanzania and Zambia to raise awareness of T. solium and reduce risk behaviours, such as not using latrines, improper hygiene, cooking and free-ranging pig management practices, and not seeking health care, among health-care and agricultural professionals, and schoolchildren. Computers were used in the United Republic of Tanzania, while in Zambia, the tool was projected on the wall in schools. The tool is also available as an app on smartphones with increasing numbers of people having access to such phones in sub-Saharan Africa. Studies have demonstrated a statistically significant increase in knowledge and attitudes scores in both the United Republic of Tanzania and Zambia. In Peru, mechanisms for transferring intervention strategies to local communities, such as community-based reporting of pig cysticercosis to inform ring strategies, have also been explored. While this study did not identify a significant change in the seroincidence of cysticercosis in the intervention group, efforts to develop locally sustainable interventions, for example, by transferring ownership of interventions, is important.

Modelling
Inclusion of dynamic transmission modelling in intervention trials and programmes can add considerable value by predicting the long-term effect of extending interventions beyond the immediate scope of the trial. Currently, several transmission models exist which capture, to different degrees of complexity, the transmission dynamics of T. solium and which can be used to assess the effect of interventions. Recent research has characterized and compared the structures of these models, and their parameters and capabilities to model particular interventions. Building on this research, formal comparisons of models are needed to understand the extent of the biological and epidemiological uncertainties associated with the life cycle of T. solium and its transmission properties in order to identify key unknown factors that would benefit from the collection of new data (further information available in the data repository) and ultimately to build consensus on the most suitable intervention options. Some ways to fill critical data gaps and hence improve our ability to capture baseline epidemiology in models in the absence of interventions include: better characterization of local transmission dynamics, such as force-of-infection estimates (individual rate of infection acquisition in susceptible hosts), which can be obtained from human and pig age-stratified prevalence data; risk factor analysis to improve the defining of

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**Fig. 1. Processes and outcomes for mathematical modelling priorities to tackle Taenia solium control and support progress in meeting control targets**

**Model comparison and refinement**

- List of key assumptions; identify structural and parametric similarities and differences
- Harmonize parameters where appropriate
- Compare the biological and setting-specific parameters on key model outcomes (e.g. stable infection prevalences)
- Identify pre-intervention (baseline) and longitudinal data (during intervention) for fitting and validation
- Identify residual structural and parametric differences that reflect biological, epidemiological and setting-specific uncertainties

**Supporting Taenia solium intervention assessments and policy questions**

- Define key outcome measures, intervention combinations (single, multiple, cross-sectional), and programmatic parameters (coverage, frequency, compliance) to test different scenarios
- Determine influence of characteristic diagnostic performance (serology, necropsy) on ability to measure key outcomes (e.g. control targets in low-prevalence settings)
- Compare and/or fit to available longitudinal intervention data to test predictive ability of models
- Link transmission and intervention modelling to burden of disease and cost–effective modelling
- Inform new feasible and achievable T. solium targets that align with the sustainable development goals, identifying challenges, uncertainties and risks. Specific goals should include:
  - consensus on control targets in areas with different pre-control endemities and standardized monitoring in context of limited diagnostics
  - design for further pilot and large-scale control programmes
  - identification of cost–effective validated control strategies

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Note: This pathway is underpinned by One Health collaboration between modelling groups, field epidemiologists, programme stakeholders and policy-makers from human health, animal health and environment sectors.
parameters, for example, of contact rates with stages infective to humans and pigs; biological factors of adult tapeworm, for example, life span and reproductive output; and environmental factors, which will likely be highly dependent on setting, for example, egg viability studies and dispersal mechanisms to better understand the distribution of environmental contamination. Research has been conducted in Peru to understand location-specific spatial dynamics, such as clustering of cysticercosis infection in pigs around human cases of taeniasis (tapeworm infection), and seasonal drivers of transmission, which could be used to inform clear spatial and seasonal transmission models. A further data are required to support model validation of intervention strategies, particularly longitudinal data before, during, and after the intervention. To effectively incorporate field data into models, serological markers for true infection need to be identified because existing serological diagnostic methods for both human and pig infection have many limitations.

Collaboration to improve modelling

Existing *T. solium* models can be improved through collaboration between modelling groups, field epidemiologists, programme stakeholders and policymakers, and used jointly to support the design, implementation and assessment of interventions in endemic countries. To this end, a recent workshop brought together the modelling groups for the cystiSim and EPICYST models and other stakeholders to work on *T. solium* modelling (further information available in the data repository). As a result of the workshop, the CystiTeam was formed, which is a coalition of epidemiologists and programme stakeholders within the *T. solium* taeniasis and cysticercosis field. The team aims to tackle collaboratively questions on the population biology, transmission dynamics, epidemiology and control of *T. solium* through mathematical modelling approaches. Fig. 1 shows a pathway identifying *T. solium* modelling research priorities aimed at supporting progress towards *T. solium* control targets. Formal model comparison research will require initial identification of similarities and differences in key structural and parametric assumptions, which has begun to be addressed by researchers. After this step, the parameters shared between the models need to be harmonized, such as the ratio of human-to-pig population sizes, to test their influence on model outcomes, for example, stable, viable *T. solium* endemic prevalences. Through this process, the residual differences between the models will point to important epidemiological, biological and setting-specific uncertainties that will inform the research agenda.

With the time fast approaching for the fulfilment of the goals set in the 2012 WHO roadmap on neglected tropical diseases, attention is refocusing on defining post-2020 targets, aligned with the Sustainable Development Goals that are relevant to neglected tropical diseases. The expanding evidence base on interventions to control *T. solium* infection will provide new opportunities to define optimal, feasible and sustainable strategies that can use existing delivery platforms. At the same time, refinement of existing *T. solium* transmission models in a collaborative framework (Fig. 1) will help to re-evaluate control goals and set realistic and attainable ones. The WHO post-2020 targets for *T. solium* are based on impact indicators for the countries with intensified control in hyperendemic areas. However, technical definitions of both intensified control and hyperendemicity need clarification for progress towards these goals over the next decade to be effectively evaluated. A key modelling activity should involve predicting, in a variety of epidemiological settings, the effect of various interventions in the currently available set

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**Box 1. Tackling *Taenia solium* taeniasis and cysticercosis**

**WHO goals**
- validated strategy for control of *T. solium* taeniasis and cysticercosis available by 2015
- interventions scaled up in selected countries for *T. solium* taeniasis and cysticercosis control by 2020

**2030 target**
- endemic countries (*n* = 17) with intensified control in hyperendemic areas

**Is the 2030 target technically feasible with the current intervention options and tools?**
- yes, if realistic control targets are proposed
- modelling can inform the design and evaluation of pilot and large-scale control programmes with current and complementary intervention strategies
- cystiSim and EPICYST, computational transmission models, are applicable
- cystiSim is already in use in Zambia and Latin America, and an additional transmission model has also been developed for Latin America

**What is required to achieve the target?**
- standardized definition of control put forward by WHO expert group
- standardized monitoring to evaluate progress of intervention strategies
- long-term intervention approaches to assess long-term epidemiological impact

**Are current tools able to reliably measure the target?**
- many limitations exist with current (serological and other) diagnostic methods
- necropsy in pigs is the most reliable measure of infection, but limitations remain in assessment of long-term effectiveness of interventions (models can assist)

**What are the biggest unknowns?**
- true prevalence of *T. solium* infection in humans and pigs because of poor diagnostic methods
- adult tapeworm life span
- effect of pig-to-people population ratio on transmission
- processes regulating parasite acquisition in humans and pigs
- health and economic burden and cost-effectiveness of interventions (DALYs likely to underestimate disease burden); possible use of the zoonotic zDALY metric
- linking infection to disease models, particularly to human neurocysticercosis and epilepsy

**What are the biggest risks?**
- long-term sustainability of interventions

DALY: disability-adjusted life year; WHO: World Health Organization.
| Priority issue identified in discussion with WHO | How can modelling address this issue? | What data are required and are they currently available? | Next steps and likely timeline |
|---|---|---|---|
| Identify risk areas where data and surveillance are lacking | • geospatial mapping and modelling for environmental suitability analysis of likely endemic areas and populations at risk | • proxy variables available | • geospatial model expected to be completed by 2021 by CystiTeam members and other collaborators (funding application submitted) |
| Identify the needs to start looking for potential interventions | • models to predict the effect of various interventions available (e.g. cystiSim and EPICYST) | • control pilot data (e.g. Madagascar) | • control pilot data expected to be available in 2020; longitudinal intervention data expected to be available in 2020; further data to follow work planned by CystiTeam in 2019–2021 |
| Set thresholds for control and risk areas | • inform control targets and different thresholds; need for standardized monitoring | • current models can be used with available data on diagnostic sensitivity and specificity | • model comparison planned by CystiTeam for 2020 |
| Correlate with impact of schistosomiasis MDA | • geospatial models | • epidemiological and programmatic data from co-endemic areas before and after MDA | • adaptation of agent-based model (CystiSim) assessed with data from Zambia (2020) |
| Cost–effectiveness analysis of different interventions | • adaptation of current models to simulate the added value of schistosomiasis MDA | • cost–effectiveness data on various interventions and settings | • linking T. solium transmission models to burden of disease frameworks being explored by CystiTeam (2019–2021) |
| Best way to monitor and evaluate the impact of interventions | • prevalence of cysticercosis in pigs | • reliable necropsy data: full carcass dissection best option for pig cysticercosis, but not always possible as requires removing animals from study areas | • work planned by CystiTeam in 2019–2021 |

WHO: World Health Organization, MDA: mass drug administration, FERG: Foodborne disease burden Epidemiology Reference Group, DALY: disability-adjusted life year. Note: The CystiTeam is a coalition of field and quantitative epidemiologists and programme stakeholders working on T. solium taeniasis and cysticercosis, which was recently formed to tackle collaboratively questions on population biology, transmission dynamics, epidemiology and control of T. solium through mathematical modelling approaches (list of contributors available in data repository).
of tools through the different phases of a control to elimination programme. Engagement of researchers with ongoing control programmes, e.g. pilot control programme in the Antananarivo district of Madagascar, will help evaluate the effect of interventions, both in communities that have specific taeniasis and cysticercosis interventions and in communities where anthelmintic drugs that are effective against *T. solium* are used to target other neglected tropical diseases, for example, mass administration of praziquantel for schistosomiasis. Intervention trials and control programmes will provide setting-specific data on programme parameters, such as coverage, frequency and compliance, and diagnostic performance uncertainties (Fig. 1), which will help refine modelling simulations. Integrating dynamic transmission models with burden of zoonotic disease and economic framework will help quantify the human health and agricultural sector gains and the cost-effectiveness of achieving newly defined global targets for zoonotic neglected tropical diseases. In northern Lao People’s Democratic Republic, the cost-effectiveness of different intervention options was assessed. The interventions assessed included *T. solium* taeniasis and cysticercosis control alone and in integrated programmes that incorporated classical swine fever and soil-transmitted helminth control. Such efforts could help define model parameter values for a dynamic economic analysis in an Asian context.

Model comparison, refinement, calibration and validation lies at the heart of the CystiTeam collaboration, which aims to improve confidence in the predictive capacities of mathematical and computational transmission models and raise awareness of their usefulness. The collaboration recently provided technical input to the WHO consultation on refinement of the post-2020 neglected tropical disease goal (Box 1 and Table 1; data repository). The collaboration will bring about better engagement and dialogue between a broad spectrum of actors and stakeholders and will facilitate progress in tackling the persistent global public health and economic problems caused by *T. solium* beyond 2020. To this end, expanding this partnership to include other research groups, particularly based in Asia and Latin America, will be crucial to broaden the applicability of efforts to model *T. solium* transmission.

**Acknowledgements**

MW is member of the London Centre for Neglected Tropical Disease Research.

**Funding:** UBS Optimus Foundation funded the workshop. MAD is funded by the Medical Research Council Doctoral Training Partnership research studentship. MAD, PW and MGB acknowledge joint centre funding by the Medical Research Council (MRC) and the Department for International Development (DFID) of the United Kingdom of Great Britain and Northern Ireland under the MRC and DFID concordat agreement, which is also part of the European & Developing Countries Clinical Trials Partnership programme (EDCTP2) supported by the European Union.

**Competing interests:** None declared.
2020 年后猪带绦虫控制策略的建模

猪带绦虫对人类脑囊虫病和猪囊虫病造成相当大的经济和卫生负担。2012年世界卫生组织（世卫组织）关于被忽视的热带病蓝图要求制定一项有效控制猪带绦虫的策略；然而，这一策略尚未出台。2019年，世卫组织发起了一场全球磋商，旨在对被忽视的热带病制定新的蓝图，完善2020年后控制猪带绦虫的目标。对此，两个研究绦虫病和囊虫病数学模型的小组（cystiSim和EPICYST）与一系列其他利益相关者一起组织了一场研讨会，为世卫组织的磋商提供技术意见，并支持实现2020年后目标制定一项研究计划。该研讨会上成立了CystiTeam合作小组，其目的是通过数学建模方法解决种群生物学、传播动力学、流行病学和猪带绦虫的控制。本文概述了猪带绦虫控制的发展，特别是利用建模帮助实现2020年后猪带绦虫控制目标。我们讨论了提高现有数学和计算模型对猪带绦虫预测能力的可信度所涉及的步骤，包括模型比较、优化、校准和验证。将CystiTeam合作关系扩大到其他研究小组和利益相关者，特别是那些在不同地理区域和病区开展工作的研究小组和利益相关者，将进一步改善猪带绦虫传播模型的应用前景，为绦虫病和囊虫病的控制策略提供参考。

Résumé

Modélisation des stratégies de contrôle de *Taenia solium* après 2020

*Taenia solium* est un cestode qui entraîne une charge intersectorielle économique et sanitaire considérable en provoquant une neurocysticercose humaine et une cysticercose porcine. La feuille de route sur les maladies tropicales négligées, publiée en 2012 par l’Organisation mondiale de la Santé (OMS), appelait à développer une stratégie de contrôle validée pour *T. solium* ; cependant, cette stratégie n’est pas encore disponible à l’heure actuelle. En 2019, l’OMS a lancé une procédure de consultation mondiale visant à préciser les objectifs de contrôle de *T. solium* après 2020, afin de rédiger une nouvelle feuille de route sur les maladies tropicales négligées. Deux groupes qui travaillent sur des modèles mathématiques de taeniasis et cysticercose (modèles cystiSim et EPICYST) ainsi qu’une série d’autres intervenants ont donc organisé un atelier pour fournir une contribution technique à cette consultation et développer un programme de recherche destiné à soutenir les efforts de réalisation des objectifs ultérieurs à 2020. L’atelier a donné naissance à une collaboration, CystiTeam, qui s’intéresse à la biologie des populations, à la dynamique de transmission, à l’épidémiologie et au contrôle de *T. solium* en employant des méthodes de modélisation mathématique. Le présent document retrace l’évolution du contrôle de *T. solium*, en particulier l’usage de la modélisation pour contribuer à atteindre les objectifs d’après 2020 en la matière. Nous abordons les diverses étapes de renforcement de la confiance accordée aux capacités prédictives des modèles mathématiques et informatiques existants sur la transmission de *T. solium*, notamment la comparaison, l’optimisation, le calibrage et la validation des modèles. Élargir le partenariat CystiTeam en intégrant d’autres groupes de recherche et intervenants, surtout ceux opérant dans différentes zones géographiques et endémiques, accroîtra les chances d’amélioration de l’applicabilité pour les modèles de transmission de *T. solium*, et permettra ainsi d’établir des stratégies de lutte contre la taeniasis et la cysticercose.

Резюме

Моделирование для разработки стратегий по борьбе с тениозом (Taenia solium) в период с 2020 года

Цестода *Taenia solium* наносит значительный урон экономике и межотраслевому сотрудничеству в области здравоохранения, поскольку она является возбудителем нейроцистицеркоза у людей и цистицеркоза у свиней. Принятая в 2012 году дорожная карта Всемирной организации здравоохранения (ВОЗ) в отношении остающихся без внимания тропических болезней призывает к разработке проверенной стратегии по борьбе с тениозом (*T. solium*), однако данная стратегия до сих пор не разработана. В 2019 году ВОЗ объявила о проведении глобальных консультаций с целью уточнения целей по борьбе с тениозом (*T. solium*), однако данная стратегия до сих пор не разработана. В 2019 году ВОЗ объявила о проведении глобальных консультаций с целью уточнения целей по борьбе с тениозом (*T. solium*) на период с 2020 года. В рамках данных консультаций две группы, работающие над математическими моделями тениоза и цистицеркоза (модели cystiSim и EPICYST), совместно с рядом других партнеров организовали семинар с целью оценки технической поддержки для консультаций ВОЗ и разработки плана исследований для обеспечения эффективности усилий, предпринимаемых для достижения целей в период с 2020 года. В результате семинара была создана совместная научно-исследовательская группа CystiTeam, задача которой состоит в исследовании вопросов популяционной биологии, динамики распространения, эпидемиологии и борьбы с тениозом (*T. solium*) на основе математического моделирования. В этой статье авторы рассказывают о разработках в сфере борьбы с тениозом (*T. solium*) и, в частности, о применении моделирования для достижения намеченных целей по борьбе с *T. solium* на период с 2020 года. Авторы обсуждают шаги, необходимые для повышения надежности возможностей прогнозирования имеющихся математических моделей и вычислительных методов передачи тениоза (*T. solium*), включая сравнение, уточнение, калибровку и валидацию моделей. Включение в группу CystiTeam других исследовательских групп и партнеров из различных географических и эндемических областей позволит совершенствовать применимость моделей распространения тениоза (*T. solium*) и предоставит необходимую информацию для разработки стратегий по борьбе с тениозом и цистицеркозом.
Resumen

Modelos para las estrategias de control de *Taenia solium* a partir de 2020

El cestodo *Taenia solium* es responsable de una importante carga sanitaria y económica transversal debido a la neurocisticercosis humana y la cisticercosis porcina. En la hoja de ruta de la Organización Mundial de la Salud (OMS) de 2012 sobre las enfermedades tropicales desatendidas se solicitaba la elaboración de una estrategia válida para el control de *T. solium*; sin embargo, dicha estrategia aún no está disponible. En 2019, la OMS inició una consulta mundial destinada a perfeccionar los objetivos de control de *T. solium* aplicables a partir de 2020 con miras a elaborar una hoja de ruta nueva sobre las enfermedades tropicales desatendidas. Consiguientemente, dos grupos que trabajan en modelos matemáticos de teniasis y cisticercosis (modelos cystiSim y EPICYST), junto con un grupo de otros interesados, organizaron un seminario para contribuir técnicamente a la consulta de la OMS y elaborar un plan de investigación a fin de apoyar los esfuerzos para lograr los objetivos a partir de 2020. El seminario impulsó la formación de un equipo de colaboración, CystiTeam, para abordar la biología de la población, la dinámica de la transmisión, la epidemiología y el control de *T. solium* mediante enfoques de modelos matemáticos. En el presente documento se describen las novedades en el control de *T. solium* y, en particular, la aplicación de modelos para ayudar a lograr los objetivos a partir de 2020 sobre el control de *T. solium*. Se analizan las etapas necesarias para mejorar la confianza en las capacidades de predicción de los modelos matemáticos y computacionales existentes sobre la transmisión de *T. solium*, incluyendo la comparación, el perfeccionamiento, el ajuste y la validación de los modelos. La ampliación de la asociación CystiTeam a otros grupos de investigación e interesados, en particular los que operan en diferentes zonas geográficas y endémicas, reforzará las perspectivas de mejorar la aplicabilidad de los modelos sobre la transmisión de *T. solium* para fundamentar las estrategias de control de la teniasis y la cisticercosis.

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