Landscape analysis: control of *Taenia solium*

Commissioned by the
World Health Organization

Corresponding author:

Dr Lian Francesca Thomas
12 Hazeldene Road
Harare
Zimbabwe

Tel: +263778855050
Email: lianthomas1@gmail.com

Library Cataloguing-in-Publication Data

Landscape analysis: control of Taenia solium

I.World Health Organization.

ISBN 978 92 4 150864 3
Subject headings are available from WHO institutional repository

Contents

1 Summary

This landscape analysis has identified all the current evidence for *T. solium* control available in the literature published in English. We identify eight key intervention components, being: preventative chemotherapy (through mass drug administration, focus-orientated chemotherapy or identification and treatment of taeniasis cases), health education, improved pig husbandry, improved sanitation, anthelmintic treatment of pigs, vaccination of pigs, improved meat inspection and processing of meat products. Empirical data was available for preventative chemotherapy, health education, anthelmintic treatment of pigs and vaccination of pigs and some combinations thereof.

Valid comparison between control strategies is difficult due especially to short and variable durations of follow-up and differing methods of monitoring between studies. Over the short term, however, there is an indication that disruption of transmission has been achieved through mass drug administration to humans using niclosamide or praziquantel with and without the addition of health education or anthelmintic treatment of pigs. Some reduction in transmission has been reported through the use of health education although it has been difficult to attribute this directly to the interventions used. Oxfendazole administration and vaccination of pigs have both shown efficacy in the treatment and prevention of porcine cysticercosis, although the impact of these strategies on the prevalence of human taeniasis and cysticercosis infections has yet to be quantified.

Due to the paucity of data available it is difficult to make definitive recommendations on control strategies to be used for this parasite. Extrapolation from the evidence available along with modelled projections and the various recommendations of experts available in the literature, however indicates that a combined approach utilising the treatment of human taeniasis cases (through mass drug administration or selective chemotherapy) combined with the vaccination and treatment of the porcine host would be the 'best-bet' for rapid reduction of infection pressure. These core approaches should be supplemented where possible by longer-term sustainable measures such as health education, focusing on the need for improvements in sanitation, pig husbandry and meat inspection.

2 Objectives

This landscape analysis has been undertaken to identify the empirical data currently available for all suggested control strategies for *Taenia solium*. It is hoped that this document will guide discussion at an upcoming expert consultation to identify a control strategy to be undertaken in several identified pilot countries prior to the expected roll-out of control in 2020 according to the road-map for NTD control. This will supplement a landscape analysis on management of neurocysticercosis with an emphasis on low-and-middle-income countries.

3 Methods

This landscape analysis constituted a desk review of the currently available evidence for control of *Taenia solium.* Documentary evidence was collected as follows;

A literature search was conducted using the search engines; IngentaConnect, PubMed, Library of Congress, British Library, ScienceDirect, African Journals Online and Google Scholar using the search terms listed here; *Taenia solium,* Cysticercosis, Taeniasis, neurocysticercosis, neglected tropical diseases, Helminths, control, integrated, efficacy, praziquantel, niclosamide, albendazole, mass drug administration, TSOL18, vaccination, diagnos*, oxfendazole, education, latrines, sanitation, husbandry and combinations thereof. Duplicates were removed and English language citations were then screened firstly on title, then abstract and finally on full test and were excluded according to the following criteria;

1. studies not relating to humans or pigs
2. Studies not relating to Neglected Tropical Diseases (NTDs)
3. Studies on aspects of NTDs which DO NOT discuss issues relevant to *T. solium* control
4. studies on epilepsy NOT related to NCC
5. Papers relating to clinical symptoms, diagnoses and treatment of NCC including case studies
6. Purely epidemiological studies on *T. solium*
7. Papers on diagnoses of *T. solium* cysticercosis/taeniasis (including diagnostic imaging)
8. Papers on aspects of basic sciences (immunology/molecular biology/ physiology/bio chemistry/ basic pharmacology)

Additional resources were identified through solicitation from experts and accessing citations within selected papers which had not appeared in the original search. 12 such documents have so far been forthcoming. A flow diagram illustrating the search and exclusion process can be found in the appendices.

Of the 199 papers included in this analysis 36 are field trials relating to control, 28 studies contain experimental (non-field trials) data or data relating to aspects of other NTD control which were directly relevant to control. The remaining manuscripts comprised of reviews, opinion pieces, meeting reports and national/international guidelines and strategies.

4 Background

As early as 1976 a joint FAO/UNEP/WHO consultation Nairobi, Kenya aimed to formulate practical recommendations which would lead towards planning of successful control of *T. solium* (FAO/UNEP/WHO, 1977). In the intervening 38 years there has been much progress in terms of tool development (diagnostics, treatment) and in the international communities' recognition of this important issue. In 1993 International Task Force on Disease Eradication (ITFDE) declared that *T. solium* was one of six potentially eradicable diseases, due to; 1) the life cycle requires humans as its definitive host, 2) tapeworm infection in humans is the only source of infection for pigs, the natural intermediate hosts, 3) domestic pigs, the intermediate hosts, can be managed, 4) no significant wildlife reservoir exists, and 5) practical intervention is available in the form of chemotherapy for human taeniosis and porcine cysticercosis with safe and effective drugs (CDC, 1992). In 2003 the ITFDE agreed that *T. solium* was indeed eradicable but that there was need for

a national scale pilot as 'proof of principle' (ITFDE, 2003). This need for evidence was re-iterated in 2013 when the ITFDE also noted the challenges still remaining for eradication, specifically the paucity of routine surveillance and reporting, the need to convince farmers that there is a financial incentive in better husbandry, a fact which in itself need evidence, the on-going need for rapid diagnostic tests and the need for data of how preventative chemotherapy (PC) effects prevalence (Center, 2013).

The World Health Organisation (WHO) has been instrumental in engaging and maintaining international interest in this parasite, with *T. solium* being highlighted as both a 'Neglected Zoonotic Disease' (NZD) (World Health Organization, 2006, World Health Organization, 2007b, World Health Organization, 2010). More recently *T. solium* was included in the road map to tackle the 'Neglected Tropical Diseases' (NTDs), which requires a **validated** strategy for control to be available by 2015, with interventions scaled up in selected countries by 2020 (World Health Organization, 2012a). The international community pledged their commitment to this goal in the London Declaration (World Health Organization, 2013a) and World Health Assembly Resolution WHA66.12 also requested member states, international partners and the Director General WHO to provide support for the activities outlined in this road map.

WHA66.12 specifically requested that the leadership of the WHO be sustained, with emphasis on the development and updating of evidence-based norms, standard and policies. It is hoped that the current report and expert consultation will assist the achievement of this goal for *T. solium* (World Health Organization, 2013b).

Despite the agreement that the control of *T. solium* has been considered 'tool ready' for several years, and various strategies have been proposed, no evidence is yet available of wide-scale reduction. As we discuss the evidence regarding the control of this parasite, it is important that we are consistent in our uses of the terms control, eradication and elimination and that agreement is made on what we wish to achieve in both the short and long terms. The ITFDE agreed upon definitions of the following terms (Molyneux et al., 2004);

- Control; Reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate efforts. Continued intervention measures are required to maintain the reduction
- Elimination; Reduction to zero the incidence of a specified disease in a **defined geographical area** as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission are required
- Eradication; Permanent reduction to zero of the **worldwide** incidence of infection caused by a specific agent as a result of deliberate efforts. Intervention measures are no-longer needed
- Extinction; The specific infectious agent no longer exists in nature or the laboratory

The WHO Strategic and Technical Advisory Group for NTDs then agreed in 2012 on the above use of the terms Control, Elimination and Eradication and that the term "elimination as a public-health problem" should be used only for political rather than scientific reasons (World Health Organization, 2012b). For the purposes of this review the term 'control' will be used at all times as no evidence is available for elimination or eradication of the parasite.

5 Suggested Interventions with current evidence

Suggested measures for control of *T. solium* have consistently focused on 8 key interventions and combinations thereof. These interventions and current evidence for their use are reviewed here:

5.1 Preventative chemotherapy

Preventative chemotherapy (PC) involves the distribution of anthelmintic drugs to populations at risk at regular intervals and is a cornerstone intervention in the control of several NTDs including lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminths (STH) (Gabrielli et al., 2011). Gabrielli e*t al* in 2011 suggested criteria by which a helminth infection could be judged eligible for PC, these being: slow or unclear onset of clinical symptoms, slow increase in the likelihood of morbidity or disease transmission, high efficacy, safety, and ease of treatment and low cost of PC intervention (Gabrielli et al., 2011). *T. solium* is eligible for PC on these criteria as Taeniasis is characterised by mild or no symptoms, gravid proglottids are not released until approximately 2 months after infection (García et al., 2003), Praziquantel and Niclosamide are effective and safe drugs available for the treatment of taeniasis (Pearson and Guerrant, 1983, Pearson and Hewlett, 1985) at a cost of $5/person (niclosamide) (Alexander et al., 2011) and $0.05-0.1/person (praziquantel) (Engels et al., 2003).

PC can be implemented in three ways: as Mass drug administration (MDA) when the entire population of a pre-defined area is treated at regular intervals, irrespective of clinical status, targeted chemotherapy where specific risk groups are treated, again irrespective of clinical status and selective chemotherapy, where following screening infected or suspected infected individuals are then treated (Gabrielli et al., 2011). Both MDA and selective chemotherapy have been recommended at different times for the control of *T. solium* and some evidence is available on their relative efficacy and cost-effectiveness.

MDA has been used as a stand-alone strategy for control in Ecuador (Cruz et al., 1989), Guatemala (Allan et al., 1997), Mexico (Diaz et al., 1991, Sarti et al., 2000) and China (Wu et al., 2012) and its effect on transmission modelled (Kyvsgaard et al., 2007).

The use of a single round of praziquantel at 5mg/kg was studied in Ecuador where a population of over 13,000 people was targeted and coverage of over 75% was achieved (all but <6yrs, those with history of epilepsy, currently pregnant or ill were invited to participate). Efficacy of the intervention was monitored through the lingual palpation of pigs, which found a reduction from 11.4% to 2.6% prevalence one year later. The prevalence of taeniasis in the population was 1.6% upon treatment (based upon reported expulsion of tapeworms) and was found to be 0% among a sub-population of 539 people who underwent re-treatment and examination one year later suggesting a low re-infection rate in this population. Two taenia carriers were however detected on microscopy (n=420) during the follow-up period, both of whom had not been treated in the first round, highlighting the potential for untreated individuals or new arrivals to an area to re-establish transmission (Cruz et al., 1989).

A single dose of praziquantel at 5mg/kg was also used in Mexico in 1991 where treatment was offered to all consenting individuals in a community of over 3000 excluding those <4yrs, pregnant or with history of hepatic disease. Treatment coverage of 87% was reported and the prevalence taeniasis, human and porcine cysticercosis was monitored at 6 and 42 months post treatment to evaluate efficacy. The sero-prevalence of human cysticercosis (as evaluated by antibody ELISA) was 5.7% at treatment, rising to 10.1% at 6mths following treatment before falling to 2.2% at 42 months post treatment (a reduction of 60%). Sero-prevalence of porcine cysticercosis (Ab-ELISA) was found to be 4.8% at initiation of the program, there was a significant reduction in 6 months to 2.2%, but at 42 months post-treatment 3.4% of pigs were positive on Ab-ELISA, which was not significant reduction from initiation. Prevalence of porcine cysticercosis identified by lingual palpation was reduced at 42mths from 1.2% to 0.6%. The prevalence of taeniasis by copro-Ag ELISA in the 304 people who provided 3 stool samples, decreased during the program from 2% to 1% at 6mths and 0.7% at 42mths, a reduction of 67% overall. Late onset epilepsy as identified by a questionnaire also showed a significant reduction in 42mths from 1.5% to 0.4% indicating a possible reduction in NCC cases (Sarti et al., 2000).

A higher dose of praziquantel (10mg/kg) was utilised in another Mexican study in a village of 559 individuals in which all community members over 5yrs and without history suggestive of NCC were invited to participate (8 suspected NCC cases were treated with 2g niclosamide as were all those with *Taenia spp* identified on initial microscopy). Coverage of 71% was achieved, with 339 people receiving one round of treatment. Seroprevalence measured by Ab-ELISA was found to be 11% at the start of the study and 7.1% 12mths post treatment, including 9 individuals who had been exposed after the drug administration. The reduction in prevalence was only significant in the 30-39yr age group (27% to 7%). Prevalence of porcine cysticercosis ascertained by lingual palpation and taeniasis cases as identified by microscopy were not found to be significantly reduced (Diaz et al., 1991).

In 1994 niclosamide was used for MDA in Guatemala, with all consenting individuals within a population of approximately 2000 offered treatment. The program achieved treatment coverage of 74.9%. Individuals over 6yrs of age were offered a single dose of 2g niclosamide, with those under 6yrs receiving 1g. A magnesium sulphate purgative was given to those who were positive for *Taenia spp*. on microscopy. Ten months post treatment the prevalence of human and porcine cysticercosis was monitored by EITB and taeniasis by microscopy. This study found a significant reduction in taeniasis (3.5% to 1%, $p<0.0001$) and porcine cysticercosis (55% to 7%, $p<0.0001$).

In the 1970's a 6yr MDA program in Henan Province, China using Agrimophol, a herb extract from Hairyvein Agrimonia, found a reduction in taeniasis of 90.8% and human cysticercosis of 96.8% (diagnostic techniques were not disclosed in review) (Wu et al., 2012).