Acta Tropica 165 (2017) 141–154

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

# The societal cost of *Taenia solium* cysticercosis in Tanzania

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ARTICLE INFO

*Article history:*
Received 13 May 2015
Received in revised form
11 December 2015
Accepted 29 December 2015
Available online 3 January 2016

*Keywords:*
*Taenia solium* taeniosis/cysticercosis
Epilepsy
Parasitic zoonoses
Societal cost
Disability-adjusted life years
Tanzania

ABSTRACT

*Taenia solium* is a zoonotic parasite prevalent in many low income countries throughout Latin America, Asia and sub-Saharan Africa, including Tanzania. The parasite is recognized as a public health threat; however the burden it poses on populations of Tanzania is unknown. The aim of this study was to estimate the societal cost of *T. solium* cysticercosis in Tanzania, by assessing both the health and economic burden. The societal cost of *T. solium* cysticercosis was assessed in humans and pigs based on data obtained by a systematic review. Experts' opinion was sought in cases where data were not retrievable. The health burden was assessed in terms of annual number of neurocysticercosis (NCC) associated epilepsy incident cases, deaths and disability-adjusted life years (DALYs), while the economic burden was assessed in terms of direct and indirect costs imposed by NCC-associated epilepsy and potential losses due to porcine cysticercosis. Based on data retrieved from the systematic review and burden assessments, *T. solium* cysticercosis contributed to a significant societal cost for the population. The annual number of NCC-associated epilepsy incident cases and deaths were 17,853 (95% Uncertainty Interval (UI), 5666–36,227) and 212 (95% UI, 37–612), respectively. More than 11% (95% UI, 6.3–17) of the pig population was infected with the parasite when using tongue examination as diagnostic method. For the year 2012 the number of DALYs per thousand person-years for NCC-associated epilepsy was 0.7 (95% UI, 0.2–1.6). Around 5 million USD (95% UI, 797,535–16,933,477) were spent due to NCC-associated epilepsy and nearly 3 million USD (95% UI, 1,095,960–5,366,038) were potentially lost due to porcine cysticercosis. Our results show that *T. solium* imposes a serious public health, agricultural and economic threat for Tanzania. We urge that a One Health approach, which involves the joint collaboration and effort of veterinarians, medical doctors, agricultural extension officers, researchers and relevant governmental agencies, is taken to find sustainable solutions for prevention, control and elimination of *T. solium*.



## 1. Introduction

*Taenia solium* taeniosis/cysticercosis is a parasitic zoonosis listed by the World Health Organization (WHO) in 2010 as one of the Neglected Tropical Diseases and ranked as the number one parasitic zoonosis by the Food and Agriculture Organization of the United Nations (FAO) in 2014 (FAO and WHO, 2014). Its lifecycle is maintained by the interaction of the human (main host) and the intermediate host (swine) with the environment (Johansen et al., 2014). The main host develops taeniosis (tapeworm infection) by eating raw or undercooked pork infected with cysticerci of *T. solium*. Due to lack of sanitation humans contaminate the environment (soil and water) with parasite eggs present in feces (Arriola et al., 2014; Johansen et al., 2014). Accidental ingestion of these eggs by both human and swine leads to cysticercosis/neurocysticercosis (NCC) when cysts lodge in the central nervous system. The latter causes a variety of symptoms, but most frequently epilepsy and headache (Carabin et al., 2011; Fabiani and Bruschi, 2013).

In Tanzania over the past years surveys on human and porcine cysticercosis have provided preliminary evidence that the parasite is widespread in almost all the regions of the country (Boa et al., 1995, 2006; Braae et al., 2014; Mwanjali et al., 2013; Ngowi et al., 2004; Winkler et al., 2009a). However, despite the availability of some epidemiological data on human and porcine cysticercosis, burden estimates are only available for human cysticercosis (IHME, 2014) while the broader picture is missing.

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http://dx.doi.org/10.1016/j.actatropica.2015.12.021
0001-706X/

Tanzania is one of the fastest growing countries in the world. To date agriculture accounts for over 25% of gross domestic product and employs approximately 85% of the workforce (The World Bank, 2015). As in other African countries, the human population in Tanzania is rising and the consumer demand for pork is increasing, especially in urban areas (United Nations, 2015). The pork consumed in these urban areas is produced mainly by rural small-scale farmers on free range production (Mkupasi et al., 2011; Phiri et al., 2003; Wilson, 2015).

In most regions of the country knowledge about the parasite and its zoonotic potential is lacking (Ngowi et al., 2008). Systems have inadequate sanitation and hygiene to prevent infection and treatment for human and porcine cysticercosis is not readily available (Mkupasi et al., 2013). In addition slaughter facilities in the country lack most basic requirements and meat inspection is often poor or non-existing (Kalage, 2008; Mkupasi et al., 2011; Mwanjali et al., 2013; Wilson, 2015), hence an increased risk in *T. solium* transmission is expected.

*T. solium* cysticercosis, endemic in some parts of the world and emerging/re-emerging in others, is believed to be controllable, as efficacious and effective intervention tools have been developed (Johansen et al., 2014; Lightowlers, 2013).

A prerequisite for assessing the cost-effectiveness of control programs is obtaining evidence of distribution and burden of disease. Being a zoonosis, the true burden of *T. solium* should include the health and economic burden (societal cost) for both the human and veterinary sectors rather than population health burden (e.g., expressed as disability-adjusted life years [DALYs]) alone.

The aim of this study was to assess the societal cost of *T. solium* cysticercosis by estimating the health and economic burden caused by the parasite including both human and porcine data in the analysis.

## 2. Materials and methods

To assess the societal cost of *T. solium* cysticercosis in humans and pigs a systematic review was conducted followed by the estimation of the societal burden.

### 2.1. Systematic review

A systematic search using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines was conducted through peer-reviewed literature and gray literature sources from government agencies, non-governmental organizations and university libraries (Moher et al., 2009). We sought expert opinion where it was not possible to retrieve data. Two Tanzanian experts, one on human cysticercosis and one on porcine cysticercosis were consulted.

The search phrase used for the systematic search is found in Appendix A. The search strategy was done according to the PRISMA guidelines and consisted of four phases: identification, screening, eligibility and inclusion (Fig. A1 in Appendix A describes the number of papers remaining at different phases) (Moher et al., 2009). In the identification phase the following databases were identified: PubMed, CAB Abstracts, Open Access library and 14 other search engines. Table A1 in Appendix A presents the list of databases screened and hits retrieved. Titles were searched up to February 27th 2015, date of the last online search. The search was done in English.

In the screening phase, the titles and abstracts were screened for eligibility by applying a set of criteria that were defined a priori. The exclusion criteria for this phase were: (a) wrong country (e.g., data from Zambia); (b) wrong agent (e.g., *Taenia saginata*); (c) not directly pertinent to the aim (e.g., vaccination against *T. solium*); (d) editorials or letters to the editors.

In the eligibility phase, all eligible papers were read and subjected to a second screening for qualitative assessment. One additional restriction on the full paper was added to the exclusion criteria, namely reviews or articles without original data were excluded. Further references were sought using a forward and backward reference search. In the forward reference search, the titles eligible for the qualitative assessment were entered in Google Scholar to obtain a list of articles citing the former. The articles obtained were then screened using the same criteria applied in the initial search. In the backward reference search the reference lists of the eligible articles were screened and if additional articles were found they underwent the same screening as the previously retrieved documents.

The inclusion phase consisted of data extraction and qualitative assessment of the information obtained from the papers included in the study. We initially aimed to collect data (incidence/prevalence) on porcine cysticercosis, human cysticercosis, taeniosis, NCC, and the major NCC-related symptoms, i.e., epilepsy, headache and hydrocephalus. To this end, an Excel spread sheet was prepared for the retrieved data (incidence/prevalence) on porcine cysticercosis, human cysticercosis, taeniosis, NCC and epilepsy. The sheet also included information on the study characteristics (geographic location, year of the study, study design), study population, cases definition and where applicable sex and age stratifications.

### 2.2. Definition of epilepsy

Epilepsy was defined as an individual having two or more unprovoked seizures unrelated to any acute intracranial disease (e.g., cerebral malaria, meningitis), acute metabolic disorders or withdrawal of drugs or alcohol and occurring at least 24 h apart (Senanayake and Roman, 1993).

### 2.3. Estimation of the societal burden

The estimation of the societal cost for the year 2012 included a quantification of health burden in terms of the annual number of NCC-associated epilepsy cases, deaths and DALYs, a quantification of the economic burden in terms of total costs (direct and indirect) incurred due to NCC-associated epilepsy and a quantification of potential losses due to porcine cysticercosis.

DALY calculation was done according to established methods (Devleesschauwer et al., 2014b,c) and implemented in a fully stochastic framework in R (R Core Team, 2014) (Appendix B describes the formulas used to estimate the health burden, script available online at https://github.com/brechtdv/tsol-tanzania). Results were computed using two variants of DALYs[$K$;$r$] (with $K$ the age weighting constant and $r$ the discount rate) and using an incidence approach. The base case DALYs[0;0] were calculated without age weighting or time discounting, in line with current practice. In the scenario case DALYs[1;0.03], non-uniform age weighting and a 3% discount rate were applied. Informa-

**Table 1**
Age and sex specific human population size used in the assessment of the health and economic burden of *T. solium* cysticercosis in Tanzania (Census year 2012) (NBS, 2015).

| Age (years) | Male | Female | Total |
|---|---|---|---|
| 0–4 | 3,637,982 | 3,635,850 | 7,273,832 |
| 5–14 | 6,226,418 | 6,225,206 | 12,451,624 |
| 15–44 | 9,087,543 | 10,117,570 | 19,205,113 |
| 45–59 | 1,717,837 | 1,772,949 | 3,490,786 |
| 60+ | 1,200,210 | 1,307,358 | 2,507,568 |
| All ages | 21,869,990 | 23,058,933 | 44,928,923 |

**Table 2**
Epidemiological parameters used in the quantification of health burden.

| Parameter | Mean (95% UI*) | Distribution | Reference |
|---|---|---|---|
| Epilepsy prevalence | 0.007 (0.003–0.011) | Uniform (0.003, 0.012) | Uniform distribution based on lowest and highest observed value (Table B1 in Appendix B) |
| Proportion of NCC-associated epilepsy | 0.152 (0.081–0.223) | Uniform (0.077, 0.228) | Uniform distribution based on lowest and highest observed value (Table B2 in Appendix B) |
| Epilepsy case-fatality ratio | 0.012 (0.003–0.026) | Beta (4333) | Schaffert (2005) |
| Proportion of epilepsy patients receiving proper treatment | 0.434 (0.285–0.583) | Uniform (0.277, 0.590) | Dent et al. (2005) |

*UI—uncertainty interval.

**Table 3**
Mean disability durations (years) of epilepsy used in the quantification of health burden.

| Sex | Age range (years) | Value | Reference |
|---|---|---|---|
| Male | 0 and 4 | 1.4 | Murray and Lopez (1996) |
| | 5 and 14 | 2.0 | |
| | 15 and 44 | 3.6 | |
| | 45 and 59 | 2.8 | |
| | Older than 60 | 1.6 | |
| Female | 0 and 4 | 1.6 | Murray and Lopez (1996) |
| | 5 and 14 | 3.1 | |
| | 15 and 44 | 5.9 | |
| | 45 and 59 | 6.0 | |
| | Older than 60 | 2.8 | |

**Table 4**
Disability weights for epilepsy used in the quantification of health burden.

| Condition | Mean (95% UI*) | Distribution | Reference |
|---|---|---|---|
| Epilepsy (untreated) | 0.426 (0.286–0.565) | Uniform (0.279, 0.572) | GBD 2010 (Salomon et al., 2012) |
| Epilepsy (treated) | 0.328 (0.217–0.439) | Uniform (0.211, 0.445) | GBD 2010 (Salomon et al., 2012) |

*UI—uncertainty interval; GBD 2010—Global Burden of Disease Study 2010.

tion was collected on all possible NCC symptoms, but the burden was quantified where sufficient data were available. The NCC-associated epilepsy incidence was calculated by multiplying the proportion of epilepsy associated with NCC with the prevalence of epilepsy divided by its duration (Tables 2 and 3). To obtain the NCC-associated incident cases the NCC-associated epilepsy incidence was multiplied by the population of Tanzania, stratified by age and sex (Table 1). The number of deaths was calculated by multiplying the NCC-associated incidence cases by the case-fatality ratio of epilepsy (Table 2). Disability weights used in the quantification of the health burden are presented in Table 4.

The economic burden was estimated using a modified version of the stochastic cost analysis model built in R, proposed by Praet et al. (2009) (R Core Team, 2014). (Appendix B describes the equations used to estimate the economic burden, script available online at https://github.com/brechtdv/tsol-tanzania). The model included parameters related to direct medical costs (hospitalization, treatment and medical care of NCC-associated epilepsy patients), indirect costs (unemployment and inability to work due to NCC-associated epilepsy) and potential agricultural losses related to reduced economic value of pigs with porcine cysticercosis.

In Tanzania, the pork trade chain can follow various routes and include several stakeholders (farmers, traders, butchers or small retailers and consumers). Farmers sell the pigs to pig traders who at purchase, will inspect the pig's tongue and agree on the price. The price of a pig depends on presence or absence of infection and the animal's size; hence, all traders inspect the tongue before purchase. Once purchased, the trader transports the pig to the butcher or small-retailer. The latter will make sure the pig's tongue is free of cysts, and then compensate the trader. Pigs found infected at tongue examination are worth half the price of a healthy pig (Ngowi, personal communication).

Different distributions were used according to the type of information available for each of the parameters (Tables 2–7). Uniform distributions were parameterized based on the highest and lowest value of the retrieved studies (Table B1–3 in Appendix B). Beta distributions were parameterized by two positive shape parameters $\alpha$ and $\beta$. Gamma distributions were parameterized by a shape parameter $k$ and a scale parameter $\theta$. The parameters used for the estimation of the societal cost are presented in Tables 1–7.

**Table 5**
Parameters used to estimate the economic burden due to NCC-associated epilepsy.

| Parameter | Value (95% UI*) | Distribution | Reference |
|---|---|---|---|
| Population of the study zone | 44,928,923 | Fixed | NBS (2015) |
| Epilepsy prevalence | 0.007 (0.003–0.011) | Uniform (0.003, 0.012) | UD based on lowest and highest observed value (Table B1 in Appendix B) |
| Proportion of NCC-associated epilepsy | 0.152 (0.081–0.224) | Uniform (0.077, 0.228) | UD based on lowest and highest observed value (Table B2 in Appendix B) |
| People with epilepsy and with injury referred to the hospital | 0.05 (0.03–0.08) | Beta (17, 320) | Schaffert (2005) |
| People with epilepsy consulting a traditional healer | 0.357 | Multinomial | Dent et al. (2005) |
| People with epilepsy consulting a physician, nurse or neurologist | 0.024 | Multinomial | Dent et al. (2005) |
| People with epilepsy consulting both a doctor and a traditional healer | 0.048 | Multinomial | Dent et al. (2005) |
| People with epilepsy without treatment | 0.571 | Multinomial | Dent et al. (2005) |
| Number of visits to a doctor in case of epilepsy (per year) | 6.5 (1.3–12) | Uniform (1, 12) | Matuja, personal communication |
| Number of visits to a traditional healer in case of epilepsy (average per year) | 4 | Fixed | Matuja, personal communication |
| Length of stay in a hospital | 14 (1.7–26) | Uniform (1, 27) | Mosser et al. (2007) |
| Epilepsy patients on antiepileptic medication | 0.629 (0.577–0.680) | Beta (212, 125) | Schaffert (2005) |
| Loss of working time due to epilepsy (days per year) | 13 (1.6–23) | Uniform (1, 24) | Matuja, personal communication |
| Unemployed due to epilepsy | 0.30 | Fixed | Matuja, personal communication |
| Working days per year | 266 (222–310) | Uniform (220, 312) | Assumption |
| Population: | | | |
| Economically active | 0.491 | Fixed | NBS (2015) |
| Not economically active | 0.402 | Fixed | NBS (2015) |
| Unemployed | 0.107 | Fixed | NBS (2015) |

*UI—uncertainty interval.

**Table 6**
Parameters used to estimate the potential losses due to porcine cysticercosis.

| Parameter | Value or mean (95% UI*) | Distribution | Reference |
|---|---|---|---|
| Pigs reared under free range conditions | 1,573,080 | Fixed | The United Republic of Tanzania (2012) |
| Prevalence of porcine cysticercosis obtained by tongue examination | 0.117 (0.063–0.171) | Uniform (0.060, 0.174) | UD based on lowest and highest observed value (Table B3 in Appendix B) |
| Proportion of pigs sold per year | 0.333 | Fixed | Assumption based on pork sold/year (t) and average hanging weight (kg) (Wilson, 2015) |

*UI—uncertainty interval.

**Table 7**
Cost parameters used to estimate the economic burden due to NCC-associated epilepsy and the potential losses due to porcine cysticercosis.

| Parameter | Value or range of values | Distribution | Reference |
|---|---|---|---|
| Average monthly salary (TSH) | 94,081 (10,259–268,620) | Gamma (1.87, 1.99e-05) | The World Bank (2015) |
| Cost of a visit to a physician (public hospital) (TSH) | 5000 | Fixed | Matuja, personal communication |
| Cost of one day at the hospital (TSH) | 20,000 | Fixed | Matuja, personal communication |
| Average cost of a traditional healer (TSH) | 28,453 (1010–100,002) | Gamma (1.12, 3.94e-05) | Mayer (2005) |
| Antiepileptic drugs (1 month treatment) (TSH) | 30,000 | Fixed | Matuja, personal communication |
| Average value of an adult pig (TSH) | 153,234 (79,977–249,910) | Gamma (12.32, 8.04e-05) | Ngowi, personal communication |
| Value reduction of infected pork (%) | 50 | Fixed | Ngowi, personal communication |

~Based on 2012 exchange rate: 1USD = 1695 TSH.

**Table 8**
Estimated annual number of NCC-associated epilepsy incident cases, deaths and DALYs (base scenario: no age weighting or time discounting).

| Estimate | Mean | 95% UI* |
|---|---|---|
| Cases | 17,853 | 5666–36,227 |
| Deaths | 212 | 37–612 |
| YLD* | 18,788 | 5672–40,300 |
| YLL* | 13,076 | 2250–37,713 |
| DALYs* | 31,863 | 9136–72,078 |
| DALYs per 1000 person-years | 0.7 | 0.2–1.6 |

*UI—uncertainty interval; NCC—neurocysticercosis; DALY—disability-adjusted life year; YLD—year lived with disability; YLL—year of life lost.

The prevalence of epilepsy, NCC among people with epilepsy and porcine cysticercosis were obtained based on data of studies carried out around the country. Homogeneity had to be assumed, as it was not possible to make assumptions on the epidemiology of the parasite across the country. To account for this source of uncertainty these parameters were modeled as uniform distributions ranging between the lowest and highest retrieved value (Table B1–3, in Appendix B). The uncertainty of the parameters was modeled using 100,000 Monte Carlo simulations. This allowed the calculation of the 95% uncertainty intervals (UI) for each result. Sensitivity analyses were conducted to show the contribution of each uncertain variable to the overall uncertainty of the end result (script available online at https://github.com/brechtdv/tsol-tanzania). The partial correlation coefficients presented in the results section indicate the impact of the uncertainty in the different parameters on the overall uncertainty in total DALYs, costs and potential losses.

## 3. Results

### 3.1. Systematic review

In total 32 original research articles, 3 unique dissertations and one report were identified during the systematic review. A detailed flowchart with the number of papers retrieved in each phase and reasons for exclusion is presented in Fig. A1 in Appendix A. Studies on *T. solium* cysticercosis were carried out in 10 regions of the country. Fig. 1 presents a detailed map where studies on porcine cysticercosis, human cysticercosis, taeniosis and epilepsy were conducted. The details of the map are found in Table A2 in Appendix A.

### 3.2. Health burden

For the year 2012 the estimated number of NCC-associated epilepsy incident cases and deaths were 17,853 (95% UI, 5666–36,227) and 212 (95% UI, 37–612), respectively. The estimated number of DALYs due to NCC-associated epilepsy was 31,863 (95% UI, 9136–72,078) and the estimated number of DALYs per thousand person-years was 0.7 (95% UI, 0.2–1.6). Sixty-one percent (95% UI, 38–84) of DALYs due to NCC-associated epilepsy were attributed to the morbidity component, years lived with disability (YLD) and the remaining 39% (95% UI, 16–62) was attributed to the mortality component, years of life lost (YLL) (Table 8).

When using non-uniform age weighting and a 3% discount rate, the estimated number of DALYs[1;0.03] was 27,225 (95% UI, 8129–58,921) and the estimated number of DALYs[1;0.03] per thousand person-years was 0.6 (95% UI, 0.2–1.3). Of the total DALYs[1;0.03], 76% (95% UI, 57–92) were attributed to YLD and 24% (95% UI, 8–43) to YLL, respectively.

For the year 2012 the estimated number of pigs with porcine cysticercosis detected by tongue examination was 183,927 (95% UI, 98,938–269,036), corresponding to an estimated 11.7% (95% UI, 6.3–17) of the total pig population of Tanzania.

### 3.3. Economic burden

For the year 2012 the economic burden estimated for human and porcine cysticercosis in Tanzania was 7.9 million USD (95% UI, 2.8–19.8). Of the total costs 5.9 million USD (95% UI, 0.7–20.6) were related to direct and indirect costs linked to NCC-associated epilepsy and 2.8 million USD (95% UI, 1.1–5.4) were related to potential pig production losses. The costs per NCC-associated epilepsy case amounted to 106 USD (95% UI, 23–281). In total 49.2% (95% UI, 10–84) of the total costs were due to reduced working capacity of people with NCC-associated epilepsy, while 9.4% (95% UI, 3.4–21.4) of the total costs were spent for direct costs, such as hospitalization, medical doctor, traditional healer and antiepileptic medication (Table 9).

### 3.4. Sensitivity analyses

Figs. 2 and 3 present the partial correlations coefficients, showing the impact of the different uncertain parameters on the uncertainty of the overall estimates. For both, the health and economic burden estimates, the epilepsy prevalence and the proportion of NCC associated epilepsy had a great impact on the end results. For the health burden, also the case-fatality ratio had a high influence on the end result. While for the economic impact,

**Table 9**
Estimated direct and indirect costs due to NCC-associated epilepsy and potential losses due to porcine cysticercosis in Tanzania.

| Type of cost | Mean (USD)* | 95% UI* | % of total costs | 95% UI |
|---|---|---|---|---|
| Hospital | 409,015 | 114,896–935,488 | 5.9 | 1.8–15 |
| Medical doctor | 69,032 | 13,460–124,502 | 1.1 | 0.1–3.1 |
| Traditional healer | 85,104 | 3017–300,782 | 1.4 | 0.0–5.6 |
| Antiepileptic medication | 67,601 | 47,084–103,486 | 1.0 | 0.4–2.2 |
| Inactivity¤ | 4,534,186 | 349,763–16,029,628 | 49.2 | 10–84 |
| Potential pig losses | 2,768,155 | 1,095,960–5,366,038 | 41.4 | 11–80 |
| Total | 7,933,094 | 2,784,398–19,806,224 | 100 | |
| Cost per NCC-associated epilepsy case | 106 | 23–281 | | |

~Based on 2012 exchange rate: 1USD = 1695 TSH.
¤ Indirect costs.
*USD—United States Dollar; UI—uncertainty interval.

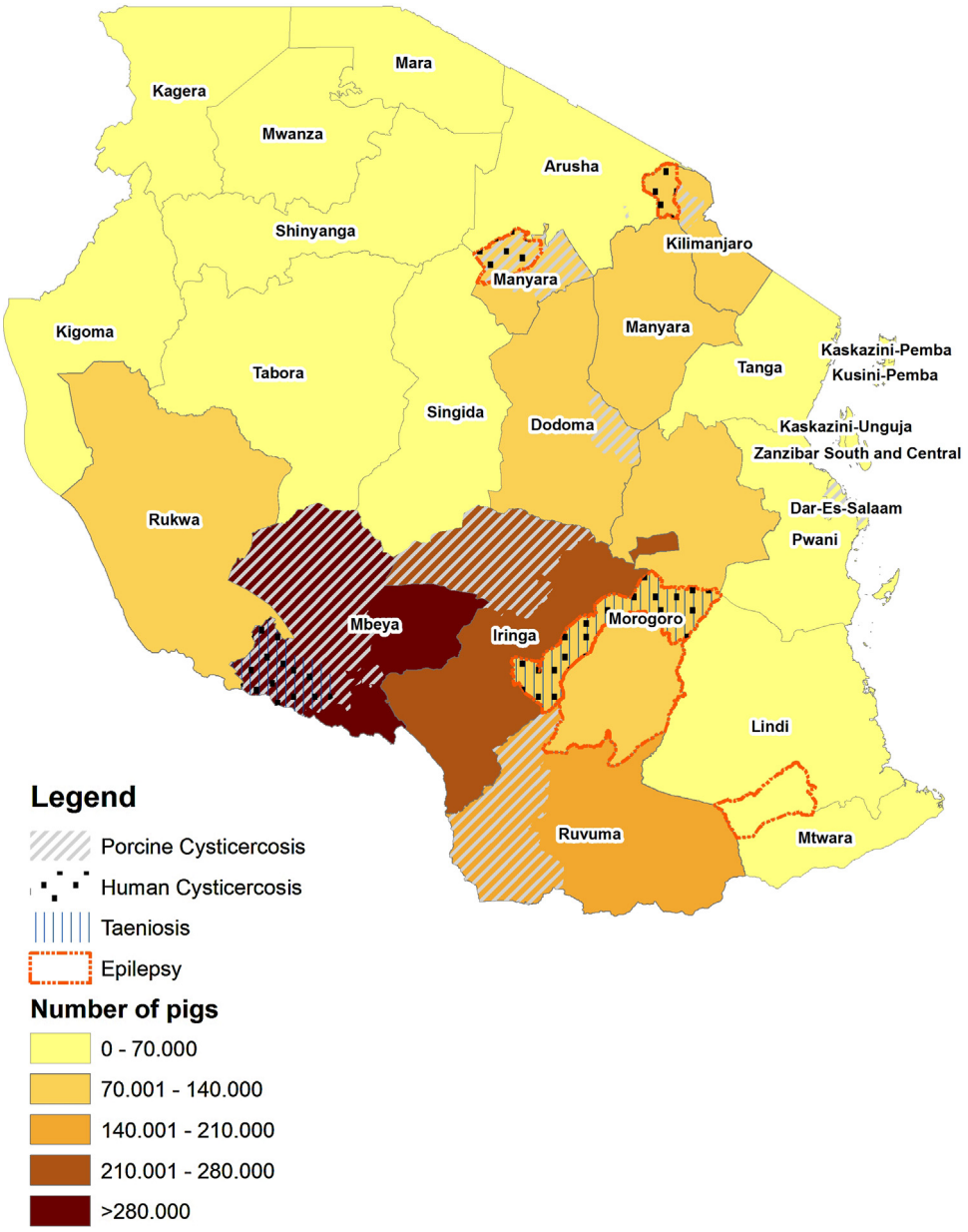


**Fig. 1.** Map of Tanzania with number of pigs present per region, and where studies on porcine cysticercosis, human cysticercosis, taeniosis and epilepsy were retrieved in the systematic review.

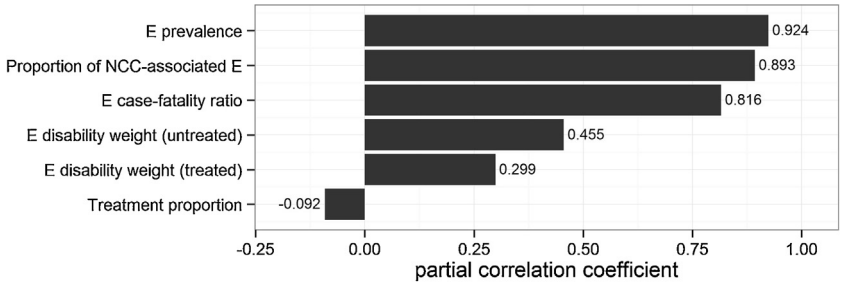


**Fig. 2.** Results of the sensitivity analysis indicating which parameter influences the estimated DALYs due to NCC-associated epilepsy for the year 2012 in Tanzania. E—epilepsy; NCC—neurocysticercosis.

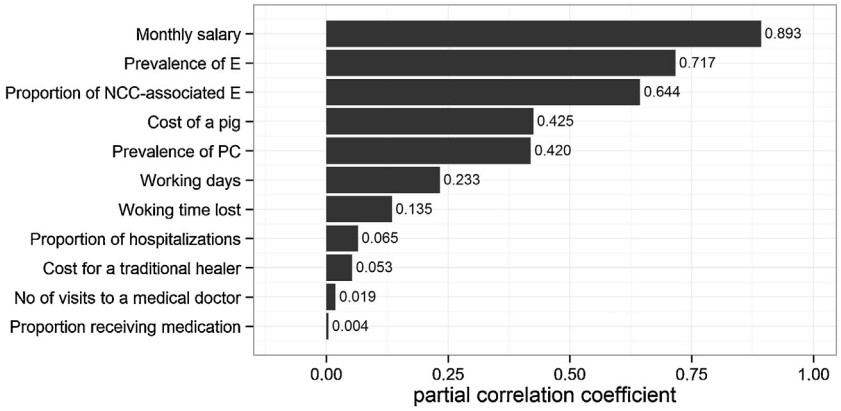


**Fig. 3.** Results of the sensitivity analysis indicating which parameter influences the estimated economic burden due to NCC-associated epilepsy and porcine cysticercosis for the year 2012 in Tanzania. E—epilepsy; NCC—neurocysticercosis; PC—porcine cysticercosis.

the variable impacting the end result the most was the monthly salary.

## 4. Discussion

The present study is the first to estimate the societal cost of *T. solium* cysticercosis in Tanzania.

The estimated DALYs per thousand person-years for NCC-associated epilepsy in Tanzania were higher than DALYs recently estimated for other countries (Bhattarai et al., 2012; Devleesschauwer et al., 2014a). For NCC-associated epilepsy in Nepal, Devleesschauwer et al. (2014a,b,c) estimated 0.42 DALYs [1;0.03] per thousand person-years, while in Mexico, Bhattarai et al. (2012) estimated 0.25 DALYs [1;0.03] per thousand person-years. Although when compared to the results for Cameroon (9 DALYs [1;0.03] per thousand person-years for NCC-associated epilepsy) the burden presented in this study was more than twelve times lower (Praet et al., 2009). An analysis carried out by Bhattarai et al. (2012) suggested a fourfold overestimation of the results by Praet et al. (2009), when comparing to results of the Global Burden of Disease (GBD) study 2004. Assuming that overestimation, the results of this study were much more in line with the results of Cameroon.

Similarly, the annual number of deaths due to NCC-associated epilepsy in this study (1.2% of the total annual incident cases) was estimated to be lower than reported in Cameroon (6.9% of the total annual incident cases) but in line with the results of the study in carried out in Nepal (1.5% of the total annual incident cases). Annual numbers of deaths were significantly lower in Mexico (0.5% of the total annual incident cases). This difference may be due to Mexican patients being five times more likely to receive treatment.

According to estimates provided by the GBD 2010 study in Tanzania the number of DALYs due to cysticercosis was 14,230 (95% UI, 9637–20,047) (IHME, 2014). However, estimates provided by GBD 2010 are predominantly based on regional extrapolations and the methodology and data sources used for the estimations are not always made available, hence the comparisons and conclusions drawn from those results need to be made carefully.

Putting the DALY burden in the context of other neglected tropical diseases such as rabies and trypanosomiasis, Coleman et al. (2004) provided an extrapolated country-level rabies estimate of 42,669 DALYs in 2000. In our study we estimated 31,863 DALYs (95% UI, 9136–72,078). Results show that both neglected zoonoses have a high impact of human health, however the estimates by Coleman et al. (2004), were estimated for the year 2000 (Coleman et al., 2004), while our results are estimated for the year 2012. Depending on how effective control intervention programs have been for rabies in Tanzania, in 12 years the number of DALYs for rabies might have changed significantly. Furthermore the authors did not specify if age weighting and 3% discount rate were applied. Both factors might have further skewed the results and need to be considered when comparisons are made. In 2004 DALYs were also estimated for human African trypanosomiasis in Urambo district, Tanzania (Matemba et al., 2010). The authors estimated a total of 215.7 DALYs (95% CI, 155.3–287.5) for the single district. To compare those results with the ones of our study which is based on the whole country, we multiplied the number of DALYs estimated in Urambo district with 169, the number of districts in Tanzania (The United Republic of Tanzania, 2013). Doing this rough calculation, 36,453 DALYs (95% CI, 26,246–48,588) were estimated for human African trypanosomiasis in Tanzania. The mean of the latter would be slightly higher than 27,225 DALYs (95% UI, 8129–58,921) estimated for *T. solium* cysticercosis in 2012 using non-uniform age weighting and a 3% discount rate, but be within the 95% UI.

The total cost for NCC-associated epilepsy case in this study was lower when compared to total costs recently estimated in other countries (Carabin et al., 2006; Praet et al., 2009). In Eastern Cape Province South Africa (ECP) the average price per NCC-associated epilepsy case per year was 738 USD, while in Cameroon the average was estimated to be 240 USD, nearly seven and two and a half times the average cost of an NCC-associated epilepsy case in Tanzania (106 USD). The large difference in costs per NCC-associated epilepsy case may be due to the fact that in Tanzania the proportion of untreated cases is two and three times higher than compared to ECP and Cameroon, respectively.

Compared to other countries, the costs of a visit to the hospital, doctor or traditional healer were much lower in Tanzania. In this study, a large proportion of the total costs were related to indirect costs. Around half the total costs were due to unemployment and/or inactivity of patients with NCC-associated epilepsy. This result was in line with the conclusions of Praet et al. (2009) and Carabin et al. (2006) who observed a very high contribution of inability to work to the total costs. The potential losses in revenue from pig production contributed to nearly one third of the total costs. With an estimated prevalence of porcine cysticercosis of 11.7% (95% UI, 6.3–17), detected using tongue examination and a price reduction of 50% for an infected pig, 2.8 million USD (95% UI, 1.1–5.4) were potentially lost in the agricultural sector alone. The losses related to porcine cysticercosis were also estimated for other countries. Compared to Tanzania, in ECP and Cameroon the agricultural losses contributed less to the total costs (20 and 4.7%, respectively). The potential losses due to porcine cysticercosis were estimated taking into account: the pig population, the proportion of infected pigs, the price reduction/infected pig and the price/pig. Compared to Tanzania (1,573,080 pigs reared in small-scale productions), the pig population was four and a half and five and a half times lower in ECP (339,083 pigs) and Cameroon (285,606 pigs),

respectively. Furthermore, in the aforementioned studies, the proportion of tongue inspection infected pigs (half and one third lower, respectively) and the price reduction (30 and 20% lower, respectively) were lower compared to our study, explaining the lower contribution of the potential losses due to porcine cysticercosis to the total costs (Carabin et al., 2006; Praet et al., 2009). Praet et al. (2009) and Carabin et al. (2006) assumed that the number of pigs slaughtered per year was the same as the total pig population. If the latter was assumed the potential losses due to porcine cysticercosis for Tanzania would be much higher, underlying the importance of choice of data, assumptions and models.

In Tanzania, infected pork rarely reaches official slaughterhouses where meat inspection is present (Boa et al., 2006; The Cysticercosis Working Group in Peru, 1993). On the contrary, pigs with high levels of infection are slaughtered at home, and meat is sold for 50% of the price on the market (Ngowi et al., 2004, 2008). Where home slaughtering is not practiced, pig traders buy infected pigs for 50% of the price and sell them to owners of brew bars/shops or use them to pay their own workers. In these brew bars/shops cheap pork is fried and sold in small portions (from one to several pieces of meat). The pork chops are either eaten on the spot, or taken home for family members (Maridadi et al., 2011).

Results of the sensitivity analysis have shown the prevalence of epilepsy and the proportion of NCC associated epilepsy, together with epilepsy case-fatality ratio and monthly salary to be some of the most influential parameters. A limited number of studies could be retrieved through the systematic review; hence homogeneity had to be assumed suggesting that more research should be conducted to obtain more extensive data across the country. Results of the sensitivity analyses carried out by Carabin et al. (2006) showed similar results, concluding that more research was needed to obtain more precise estimates for the parameters that had a biggest impact on the uncertainty of the final results.

There were a number of limitations to this study. The total estimated number of DALYs was most likely underestimated as only NCC-associated epilepsy could be included in the assessment, underlining the lack of disease specific information for NCC.

The number of migraine and tension-type headache incident cases and the corresponding DALYs in this study could not be estimated for NCC, as to date the proportions of NCC-associated migraine and tension-type headache are not available for any African country. To estimate the burden of NCC-associated headache in Mexico, Bhattarai et al. (2012) used the proportion of NCC-associated headache found in the systematic review by Carabin et al. (2011). As the review did not mention what type of headache was taken into consideration, we preferred not to use such extrapolation and hence not include migraine and tension-type headache in the overall health burden estimates.

Furthermore to what extent NCC contributes to the burden associated with other neurological/psychiatric signs/symptoms urgently requires assessment.

As sound epidemiological data are among the first requirements for more accurate burden assessments (Essink-Bot et al., 2002; Haagsma et al., 2013; Polinder et al., 2012) especially for the case of headache and other NCC related conditions, prevalence studies with well-defined epidemiological methods should be further carried out (Winkler et al., 2010a).

Prevalence of epilepsy and porcine cysticercosis, as well as the proportion of NCC-associated epilepsy were obtained based on data of studies carried out around the country. However homogeneity had to be assumed, as it was not possible to make assumptions on the epidemiology of the parasite across the country. To account for this source of uncertainty, we modeled these parameters as uniform distributions ranging from the lowest to the highest observed value, essentially implying that we assume the true value to be anywhere in between these extremes. Furthermore data were not stratified by age and gender, as currently the NCC burden in Tanzanian children is not known.

To estimate the potential losses due to porcine cysticercosis we had to strongly rely on expert opinion regarding the 50% reduction in price of an infected pig at slaughter. The uncertainty around the parameters and results based on the UI, suggest that more research should be conducted to improve the precision of the parameters and of disease burden estimates.

Epilepsy is believed to be contagious and caused by witchcraft or evil spirits in many rural areas of Africa, (Carod and Vazquez-Cabrera, 1998; Winkler et al., 2010b). This belief is associated with significant stigma and social exclusion and as such imposes a large but completely undocumented further burden of disease. Based on estimates of this study, more than 14,000 people with NCC-associated epilepsy never received treatment in Tanzania. Lack of financial resources, extreme distances from health care centers and fear of stigmatization were among the causes cited for a high treatment gap in Tanzania (Mushi et al., 2012). Epilepsy is a debilitating condition with damaging personal, familial and social consequences (Matuja et al., 1995; Winkler et al., 2010b), hence integrated control programs across sectors should include community education to reduce stigma, promote early care-seeking behavior, avoid misleading thoughts and hereby improve the quality of people that suffer from this disease (Mushi et al., 2012).

## 5. Conclusion

The present study is the first to estimate the societal cost of *T. solium* cysticercosis in Tanzania. Nearly one DALY per thousand person-years for NCC-associated epilepsy, a cost of around 5 million USD per year due to NCC-associated epilepsy and a loss of nearly 3 million USD due to porcine cysticercosis, makes *T. solium* a serious public health, agricultural and economic threat. Further research is urgently needed to unravel the contribution of NCC to headache and other neurological conditions. This study provides evidence that *T. solium* contributes to a reduced societal and economic wellbeing of the population of Tanzania. We urge that a One Health approach, which involves the joint collaboration and effort of veterinarians, medical doctors, agricultural extension officers, researchers and relevant governmental agencies, is taken to find sustainable solutions for prevention, control and elimination of *T. solium*.

## Acknowledgements

The study was conducted under the ICTC-project (Integrated Control of Taeniosis/Cysticercosis in sub-Saharan Africa) funded by Bill and Melinda Gates foundation and further supported by the Danish International Development Agency (DANIDA) with its project: SLIPP-project (Securing rural Livelihoods through Improved smallholder Pig Production in Mozambique and Tanzania), file no. 09-007LIFE. The study was done in collaboration within the framework of CYSTINET, the European Network on taeniosis/cysticercosis, COST ACTION TD1302. The authors would like to acknowledge Professor W. Matuja and Dr. H. Ngowi for providing their expert opinion and Dr. F. Gianoli for assisting the authors with the creation of Fig. 1.

## Appendix A.

*Systematic review*

*Search strategy*

The search phrase consisted of the key work “Tanzania” and any element of a list containing the name of the parasite, possible synonyms and the causative symptoms. For example in Pub Med the search phrase was as follows: “Tanzania” AND (“taeni*ÖR

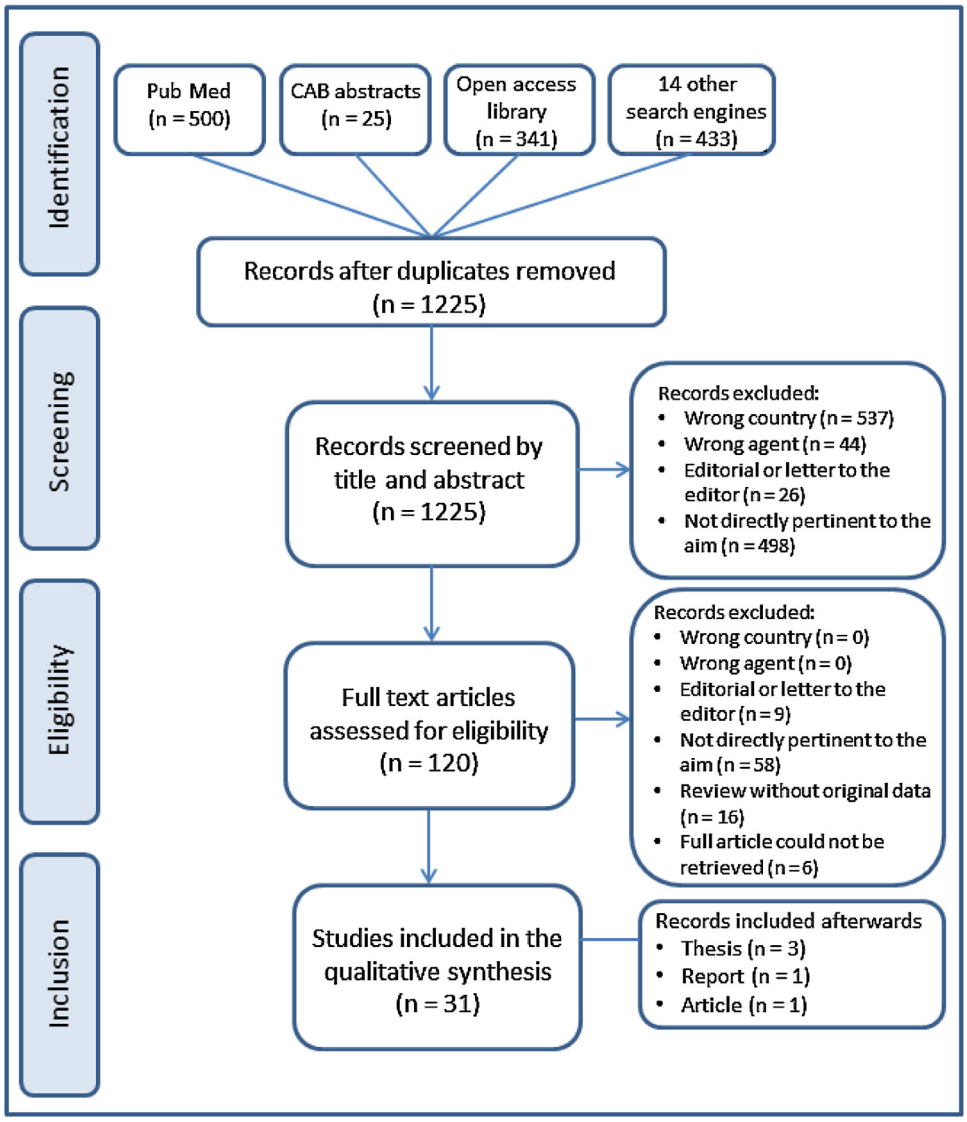


**Fig. A1.** Flowchart adapted from Moher et al., the PRISMA group, 2009 describing the number of papers remaining at different phases (Moher et al., 2009).

**Table A1**
List of databases screened and hits retrieved.

| Database | Link | Hits |
|---|---|---|
| African Journal Online | http://ajol.info | 326 |
| African Journal of Medicine and Medical Sciences | http://ajol.info/index.php/jmms | 0 |
| African Journal of Neurological Sciences | http://ajns.paans.org/ | 25 |
| African Neurology Database | http://unilim.fr/ient | 0 |
| Annals of Medical and Health Sciences Research | http://amhsr.org/ | 0 |
| CAB Abstracts | http://cabdirect.org | 25 |
| Dar es Salaam Medical Students' Journal | http://ajol.info/index.php/dmsj | 0 |
| East African Journal of Public Health | http://eajph.org/ | 0 |
| IMTU Medical Journal | http://imtu.ac.tz/ | 0 |
| Open Access Library | http://oalib.com | 341 |
| Open Grey | http://opengrey.eu | 11 |
| PubMed | http://pubmed.org | 500 |
| Tanzania Medical Journal | http://ajol.info/index.php/index/search/search | 0 |
| Tanzania Veterinary Journal | http://ajol.info/index.php/tvj | 0 |
| Web of Science | http://webofknowledge.com | 71 |
| WHO Africa | http://indexmedicus.afro.who.int | 0 |
| Total | | 1299 |

**Table A2**
List of regions and districts where studies on porcine cysticercosis, human cysticercosis, taeniosis, epilepsy and headache were carried out.

| Region | District | PC* | HC* | T* | E* | H* | Source |
|---|---|---|---|---|---|---|---|
| Ruvuma | Songea and Mbinga | √ | | | | | Boa et al. (2006) |
| Mbeya | Mbozi | √ | √ | √ | | | Mwanjali et al. (2013); Komba et al. (2013); Braae et al. (2014) |
| Mbeya | Mbeya | √ | | | | | Komba et al. (2013); Braae et al. (2014) |
| Mbeya | Chunya | √ | | | | | Boa et al. (2006) |
| Iringa | Iringa rural | √ | | | | | Boa et al. (2006); Yohana et al. (2013); Chacha et al. (2014) |
| Iringa | Kilolo | √ | | | | | Maridadi et al. (2011) |
| Dar es Salaam | NA | √ | | | | √ | Matuja et al. (1995); Mkupasi et al. (2011) |
| Morogoro | Kilombero | | √ | √ | √ | | Kamuyu et al. (2014); Ngugi et al. (2013) |
| Morogoro | Ulanga | | | | √ | | Rwiza et al. (1992) |
| Dodoma | Kongwa | √ | | | | | Mkupasi et al. (2014) |
| Manyara | Mbulu | √ | √ | | √ | √ | Mwang'onde et al. (2012); Blocher et al. (2011); Ngowi et al. (2004); (Nsengwa (1995); Winkler et al. (2009b, 2010a) |
| Manyara | Babati | √ | | | | | Kavishe (2009) |
| Lindi | Nachingwea | | | | √ | √ | Dent et al. (2004, 2005) |
| Kilimanjaro | Hai | | √ | | √ | √ | Hunter et al. (2012); Dewhurst et al. (2013) |
| Kilimanjaro | Moshi rural | √ | | | | | Boa et al. (1995) |
| Arusha | Arusha rural | √ | | | | | Boa et al. (1995); Mellau et al. (2011) |

*PC—porcine cysticercosis; HC—human cysticercosis; T—taeniosis; E—epilepsy and H—headache.

'tapeworm' OR "cysticerc*ÖR 'neurocysticercosis' OR "epilepsy" OR "headache" OR "migraine" OR "hydrocephalus" OR "seizure" OR "neurological disorders" OR "cysticercosis/mortality" OR "neurocysticercosis/mortality").

## Appendix B.

*Estimation of the societal burden*

The estimation of the societal burden included a quantification of health burden in terms of the annual number of NCC-associated epilepsy incident cases, deaths and disability-adjusted life years (DALYs) and a quantification of economic burden in terms of total costs (direct and indirect) imposed by human cysticercosis and potential losses due to porcine cysticercosis. The assessment was based on an agent related disease model (Fig. B1).

*Health burden*

The number of DALYs lost per year was estimated by summing the years lived with disability (YLD) and the years of life lost (YLL) (Devleesschauwer et al., 2014c). The formulas used for the DALY calculation are described in Eqs. (1) and (2).

$$\text{YLD} = I \times \text{DW} \times L \quad (1)$$

where '*I*' represents the number of incident cases per year, 'DW' is the disability weight and '*L*' the average duration of the disease until remission.

$$\text{YLL} = N \times L \quad (2)$$

where '*N*' is the number of deaths per year and '*L*' is the standard life expectancy at the age of death in years.


**Fig. B1.** Agent related disease model. Green shapes contribute to YLDs and red shapes contribute to YLLs.

As the annual incidence rates of NCC-associated epilepsy were not known in the area, these parameters were derived from the prevalence and disease duration estimates as described in Eq. (3).

$$I = \frac{P}{D} \quad (3)$$

where '*I*' is the incidence of NCC-associated epilepsy, '*P*' is the prevalence of NCC-associated epilepsy and '*D*' is the duration of epilepsy.

Epilepsy incidence rates and disease durations were assumed to be constant over time.

To account for this source of uncertainty these parameters were modeled as uniform distributions ranging between the lowest and highest retrieved value. The uncertainty of the parameters was modeled using 100,000 Monte Carlo simulations. This allowed the calculation of the 95% uncertainty intervals (UI) for each result.

*Economic burden*

*Costs due to NCC-associated epilepsy.* A decision tree (Fig. B2) was constructed in order to identify the proportion of the population with epilepsy due to NCC, with or without injury, with or without treatment and hospitalized. The patients without injury were divided into those who sought medical care and those who did not. The patients with NCC-associated epilepsy that sought medical care were divided in: patients consulting a traditional healer, patients consulting a medical doctor, and patients consulting both a medical doctor and a traditional healer.

It was assumed that all the patients with injury would be hospitalized and the ones without injury, that sought medical care, would be treated.

The uncertainty of the parameters was modeled using 100,000 Monte Carlo simulations.

The formulas used to estimate the costs due to NCC-associated epilepsy are described in the Eqs. (4)–(13).

$$\text{N\_EP} = \text{PrevE} \times \text{POP} \quad (4)$$

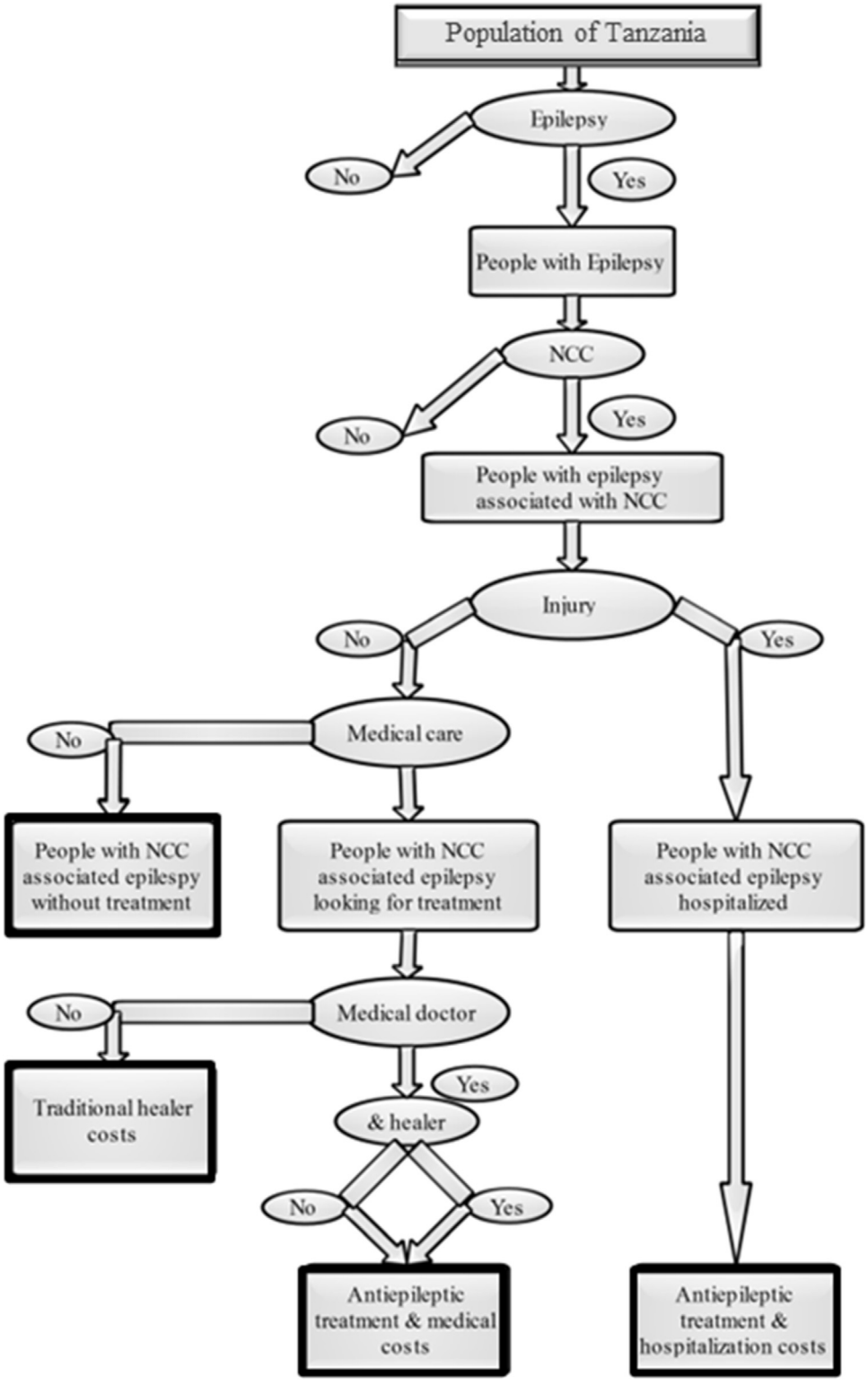


**Fig. B2.** Decision tree used to estimate the economic burden (4 terminal nodes are indicated by rectangles with bold lines).

where 'N_EP' represents the estimated number of people with epilepsy, 'PrevE' is the prevalence of epilepsy and 'POP' is the human population of Tanzania.

$$\text{N\_NCC} = \text{N\_EP} \times \text{PropNCC} \quad (5)$$

where 'N_NCC' represents the estimated number of people with NCC-associated epilepsy, 'N_EP' is the estimated number of people with epilepsy and 'PropNCC' is the proportion of NCC-associated epilepsy.

$$H = \text{N\_NCC} \times \text{PropH} \times S \times \text{CH} \quad (6)$$

where '$H$' represent the estimated costs for hospitalisation, 'N_NCC' the number of people with NCC-associated epilepsy, 'PropH' is the

**Table B1**
Retrieved epilepsy prevalence.

| Reference | Geographic location | Study period | Study population | No of people with epilepsy | Prevalence ‰ (95% CI*) | Study subjects age range |
|---|---|---|---|---|---|---|
| Ngugi et al. (2013) | Kilombero district | 2009 | 93,645 | 366 | 3.9 (3.5–4.3) | All ages |
| Dewhurst et al. (2013) | Hai district | 2009–2010 | 2232 | 10 | 4.5 (2.2–8.2) | Adults (≥70 years) |
| Hunter et al. (2012) | Hai district | 2009 | 103,026 | 291 | 2.8 (2.5–3.2) | Adults (≥15 years) |
| Burton et al. (2012) | Hai district | 2009 | 38,523 | 112 | 2.9 (2.4–3.5) | Children (6–14 years) |
| Winkler et al. (2009b) | Mbulu district | 2003–2004 | 7399 | 83 | 11 (8.9–14) | All ages |
| Dent et al. (2005) | Nachingwea district | 1999 | 4905 | 42 | 8.6 (6.2–12) | All ages |
| Rwiza et al. (1992) | Ulanga District | 1989 | 18,000 | 207 | 12 (10–13) | All ages |

*CI—confidence interval.

**Table B2**
Retrieved proportions of epilepsy cases associated with NCC*.

| Reference | Geographic location | Study period | Study population | Definitive NCC | Probable NCC | Proportion of NCC-associated epilepsy (95% CI*) | Diagnostic method |
|---|---|---|---|---|---|---|---|
| Mwanjali et al. (2013) | Mbozi district | 2009 | 123 | NA | 28 | 23 (16–31) | CT-scan, Ag-ELISA |
| Hunter et al. (2012) | Hai district | 2009 | 51 | NA | 8 | 16 (7.0–29) | CT-scan |
| Burton et al. (2012) | Hai district | 2009 | 26 | NA | 2 | 7.7 (1.0–25) | CT-scan |
| Winkler et al. (2009a) | Mbulu district | 2006 | 212 | 7 | 22 | 14 (9.4–19) | CT-scan, Western blot |
| Blocher et al. (2011) | Mbulu district | 2006 | 212 | 7 | 22 | 14 (9.4–19.1) | CT-scan, Western blot |
| Blocher et al. (2011) | Mbulu district | 2006 | 212 | 17 | 18 | 17 (12–22) | CT-scan, CDC EITB |

* NCC—neurocysticercosis; CI—confidence interval; CT-scan—computed tomography scan; Ag-ELISA—antigen enzyme linked immunosorbent assay; CDC EITB—Centers for Disease Control and prevention Enzyme Linked Immunoelectrotransfer Blot.

**Table B3**
Retrieved porcine cysticercosis studies using tongue examination as a diagnostic method.

| Reference | Study period | Region | No of pigs examined | No of pigs infected | Prevalence (%) (95% CI) |
|---|---|---|---|---|---|
| Yohana et al. (2013) | 2012 | Iringa | 308 | 23 | 7.5 (4.8–11) |
| Komba et al. (2013) | 2007–2008 | Mbeya | 300 | 18 | 6.0 (3.6–9.3) |
| Komba et al. (2013) | 2007–2008 | Mbeya | 300 | 35 | 12 (8.3–16) |
| Boa et al. (2006) | 1999–2000 | Mbeya | 772 | 55 | 7.1 (5.4–9.2) |
| Boa et al. (2006) | 1999–2000 | Iringa | 808 | 68 | 8.4 (6.6–11) |
| Boa et al. (2006) | 1999–2000 | Ruvuma | 302 | 51 | 17 (13–22) |
| Ngowi et al. (2004) | 1998 | Manyara | 770 | 134 | 17 (15–20) |

proportion of epilepsy patients going to the hospital, 'S' stay (days) in the hospital and 'CH' the cost of a day at the hospital.

$$T = (\text{N\_H} + \text{N\_MD} + \text{N\_MDH}) \times \text{PropC} \times \text{CC} \quad (7)$$

where '*T*' represent the estimated costs for treatment, 'N_H' are the number of people hospitalized, 'N_MD' are the number of people visiting a medical doctor, 'N_MDH' are the number of people visiting both, a traditional healer and a medical doctor, 'PropC' is the proportion of people receiving treatment and 'CC' are the cost of treatment.

$$\text{MC} = (\text{N\_VM} \times (\text{N\_MD} + \text{N\_MDH}) \times \text{CMD}) + (\text{N\_VH} \times \text{N\_TH} \times \text{CTH}) \quad (8)$$

where 'MC' represent the costs for medical care, 'N_VM' the number of visits to the medical doctor, 'N_MD' is the proportion of people visiting a medical doctor, 'N_MDH' is the proportion of people visiting both, a traditional healer and a medical doctor, 'CMD' the costs for a medical doctor, 'NVH' the number of visits at the tradi-

tional healer, 'N_TH' is the proportion of people visiting a traditional healer and 'CTH' are the costs for a traditional healer.

$$DC = H + T + MC \quad (9)$$

where 'DC' represent the direct costs, '*H*' the hospitalisation costs, '*T*' the treatment costs and 'MC' the costs for medical care.

$$U = N\_NCC \times Prop\_PA \times Prop\_LJ \times WD \quad (10)$$

where '*U*' represents work time lost because of unemployment, N_NCC' the number of people with NCC-associated epilepsy, 'Porp_PA' is the proportion of active people, 'Prop_LJ' is the proportion of people that have lost their job because of epilepsy and 'WD' are the working days in one year.

$$WLI = N\_NCC \times Prop\_PA \times (1 - Prop\_LJ) \times WTL \quad (11)$$

where 'WLI' is work lost because of inability to work, N_NCC' the number of people with NCC-associated epilepsy, 'Prop_PA' is the proportion of active people, 'Prop_LJ' is the proportion of people that have lost their job and 'WTL' is the working time lost in one year.

$$IC = (U + WLI) \times MS \quad (12)$$

where 'IC' represent the indirect costs, '*U*' is work time lost because of unemployment, 'WLI' is the work lost because of inability to work and 'MS' is the monthly salary.

$$TC\_NCC = DC + IC \quad (13)$$

where 'TC_NCC' are the total cost due to NCC-associated epilepsy, 'DC' are the direct costs and 'IC' are the indirect costs.

*Potential pig losses due to porcine cysticercosis.* The formulas used to estimate the potential losses due to porcine cysticercosis are described in the Eqs. (14) and (15).

$$N\_PP = PrevE \times POP \quad (14)$$

where 'N_PP' represents the estimated number of pigs with porcine cysticercosis diagnosed by tongue examination, 'PP' is the prevalence of porcine cysticercosis detected by tongue examination and 'PSP' is the population of smallholder pigs in Tanzania.

$$L\_PP = N\_PP \times PS \times PLP \times PVP \quad (15)$$

where 'L_PP' represent the estimated potential losses due to porcine cysticercosis, 'N_PP' is the estimated number of pigs with porcine cysticercosis diagnosed by tongue examination, 'PS' is the proportion of pigs sold per year, 'PLP' is the price loss per infected pig and 'PLP' is the price value of a pig.

In 2012 15,000 tons of pork were sold (Wilson, 2015). By assuming a carcass weight of 30 kg we estimated that around 1/3 of all the animals were sold in one year.

As most slaughterhouses do not have proper meat inspection, we assumed that all infected pigs not detected by tongue examination would be sold for the full price. Furthermore potential losses due to taxed income were not taken into account because apparently these are not paid by the pig traders when the meat is sold.

The uncertainty of the parameters was modeled using 100,000 Monte Carlo simulations. This allowed the calculation of the 95% UI for each result.

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