Chapter 3

The Burden of Cysticercosis

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1. Introduction

Taenia solium cysticercosis is a major public health and agricultural problem in many developing countries. It is predominantly found and considered endemic in Latin American, Asian, and African countries where pigs are raised using traditional methods, veterinary meat inspection is insufficient, and sanitation is poor [1-3]. However, it is now increasingly being diagnosed in other regions such as the United States, Western Europe, and Canada due to an increasing flow of immigrants from endemic areas who may have taeniasis or cysticercosis [4-7]. The parasite not only impacts human health, but also pig farmers and their communities. In humans, the larvae of the parasite (metacestodes) may migrate to the brain resulting in neurocysticercosis (NCC). The natural history of NCC infection remains poorly understood, and the proportion of cases with lesions in their brains that will manifest at some point during the course of the infection remains unknown. According to a recent systematic review of the literature, among diagnosed NCC patients who sought care in clinics where imaging was available, epileptic seizures were by far the most common presenting symptom, followed by headaches, focal deficits, and cranial hypertension/hydrocephalus [8]. Depression has been reported to be very common among NCC patients, but it has not been determined if this is due to the presence of epilepsy or NCC itself [9]. Other manifestations of NCC include stroke and dementia, but those aspects have been very poorly described [10, 11]. The social consequences of NCC possibly include stigmatization, incapacitation, and decreased work productivity. Epilepsy has been shown, in several countries, to lead to social discrimination, and NCC-associated epilepsy is no different. In many endemic countries, the stigma associated with epilepsy may have a greater impact on patients' lives and families than the disease itself [12]. In addition, due to the reduction in quality of life and the psychological effects of the condition, work productivity might be further decreased.

In pigs, infection with the larval stages of the parasite results in the development of cysts primarily in the muscles, and less commonly in the tongue muscles, heart, diaphragm,

brain, and other organ systems. The presence of these cysts can lead to partial or full condemnation of the carcass and economic losses in areas where meat is inspected. In some areas, pig traders look for the presence of cysts under the tongue before buying them, and will offer a lower price for animals affected. This parasite, therefore, can reduce the household income of farmers and whole communities that share the same environment. Porcine cysticercosis is most commonly associated with small holder farming practices and is often under-reported due to the absence of clinical signs in affected pigs and lack of meat inspection facilities and expertise in endemic countries.

Because cysticercosis impacts human and pig heath and results in economic losses, there is a need to evaluate the socioeconomic impact, or burden, of this condition on endemic communities. Both non-monetary and monetary methods can be employed. These estimates may then be compared among diseases to better target which diseases to control. Disease burden estimates can subsequently be used to compare alternative control strategies for cysticercosis, as well as other diseases affecting the population, through cost-utility and cost-benefit analyses. These analyses can guide stakeholders as to which diseases and control strategies should be prioritized to reduce the burden of diseases in the population.

2. Methods for evaluation of the burden of zoonotic infections

Taenia solium cysticercosis results in mortality, morbidity, and economic losses in affected human and animal populations. To evaluate the burden of cysticercosis, the monetary and non-monetary impacts of the disease on human health, agriculture, and society must be considered comprehensively. Measuring burden is challenging because it requires various types of data from valid studies conducted in humans and pig populations. Because of those challenges, it is recommended to focus the evaluation on a certain period and to one geographical area where high quality epidemiological and clinical studies have been conducted, preferably in both pigs and humans. The disadvantage of such an approach is that the data cannot be generalized to other areas. Some data are required for the estimation of both the non-monetary and the monetary burden of cysticercosis. In humans, these data include: the death rate of NCC (the number of deaths, if available, can also be used); the proportion of patients with NCC who seek care in clinics (and hospitals); the number (or incidence rate) of cases of NCC diagnosed after care has been sought; and the frequency and duration of each NCC manifestation. In pigs, the data required include the proportion of pigs that are inspected pre or post-mortem and the proportion of infected pigs diagnosed pre or post-mortem. Such data may be found in the published/unpublished literature and national or regional databases. When some aspects of the data are unavailable, opinion of local experts may be sought and uncertainty analyses can be run. In estimating the burden of NCC, there is the additional challenge that the internationally recognized definition of NCC requires the use of diagnostic imaging (computed tomography (CT) scan or magnetic resonance imaging (MRI)), autopsy or biopsy of skin nodules [13]. The absence of advanced diagnostic imaging facilities limits the evaluation of the burden of NCC in many areas of the world, and especially in the poorest regions where the disease is likely to be most prevalent.

Serological tests are designed to measure the exposure to, or current infection with, cysticercosis [14], but can show low specificity and sensitivity in the diagnosis of NCC, depending on the number and stages of lesions present in the brain [15].

3. Measuring the non-monetary burden of cysticercosis

Specific measures have been designed to estimate the non-monetary burden of human diseases [16, 17]. We will not discuss here measures of mortality and morbidity that can also be used in animals. The most informative measure of non-monetary burden is believed to be "utility", an economical concept which has been adapted to health economics, and measures the preference that people have for certain health status along a continuum [18].The greater the preference for a particular health state, the greater the "utility" associated with it. Several Health Adjusted Life Years (HALYs) metrics have been developed as indicators of "utility". HALYs are summary measures of population health that enable measures of mortality to be combined with measures of disability associated with each sequela (manifestation) of the disease of interest into one metric.

There are two types of HALYs that have been commonly used in estimating human burden of disease: Quality Adjusted Life Years (QALYs) and Disability Adjusted Life Years (DALYs). Even though QALYs and DALYs may be used to estimate utilities, they were developed to serve different purposes. Where DALYs are meant as an objective, population-based measure, QALYs are meant to be used as a subjective, individual-based measure of utility and health. In addition, these measures use opposite scales. The DALY is a negative concept, with one DALY being the equivalent of one year lived completely disabled (analogous to death) whereas the QALY is a positive concept, with one QALY being the equivalent of one year of healthy life [18]. Therefore, control strategies would aim to minimize DALYs and maximize QALYs.

3.1. Quality Adjusted Life Years (QALYs)

The ideal way of measuring quality of life is to attribute a utility, or a weighted preference for a certain health status, to each disease and its associated manifestations. In theory, the utility of health status is best measured with choice-based methods which include uncertainty, such as the standard gamble method. Other choice-based methods, without uncertainty, include paired person-trade-off and time-trade-off techniques [19]. Utility measures are based on the fact that Paretian welfare economics requires that each individual be the judge of his or her own welfare. However, in practice, these methods are difficult to implement because different people have different reactions when faced with uncertainty and choices, especially when these are theoretical. For example, in the standard gamble method, the patients are asked to find the probability "p" at which they would be unable to choose between remaining in their current state of health or dying immediately with a probability of p (and living healthy with a probability of 1-p). Given the difficulty in implementing such measures, several groups of researchers have developed multi-attribute classification systems implemented in the form of scale-based

questionnaires. Each answer to the scaled questions contributes a certain weight towards calculating utility. The utility weights are determined during studies where both the questionnaire and one of the choice-based methods are used, and then assumed to be generalizable to other contexts. Multi-attribute questionnaires are more commonly used than choice-based measures in QALYs studies. One advantage of multi-attribute questionnaires is that they may not only be used to estimate utility, but also to assess the perceptions of patients regarding different aspects of their health (i.e., mental, physical, social functioning, etc.).

When used at a population level, QALYs combine quantitative estimates of death, frequency and duration of disease with a qualitative assessment of how well (or not) patients can live with the disease. In other words, rather than just counting the number of people with the disease, QALYs try to "adjust" for how well people can live with the disease. Therefore, QALYs are a product of life expectancy and a measure of the quality of remaining life years, with weights placed on time spent in different health states. Most preferable state receives more weight. A year of perfect health is worth 1 and a year of less than perfect health is worth less than 1. Death is considered to be equivalent to 0. However, some health states may be considered worse than death and have negative values [19].

The multi-attribute measurement scales most commonly used in developing countries, where NCC is endemic, are the Euro-Qol (EQ-5D) and the Short Form-12 (SF-12) [20, 21]. These tools provide patient-based determination of quality of life and can be used to compare perceptions of physical, mental, and social health among patients with different diseases (or lack of disease), different stages of the same disease, or before and after treatment of the disease. The latter approach is often used in clinical trials where a drug, while very effective in treating the disease, may be linked to numerous side effects which could lead to worse quality of life than the disease itself.

The EQ-5D is a standardized measure of health status developed by the EuroQol Group. The EQ-5D questionnaire has 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each domain, there are three levels of response: individuals are asked whether they have no problems, some problems, or severe problems. The answers to each domain are combined to generate a summary score, for a total of 125 possible combinations of answers, which indicates the overall utility. Table 1 provides an example of utility scores that can be allocated to different combinations of answers to the five EQ-5D questions [22].

The SF-12 is another tool developed by Quality Metric Inc. to assess the quality of life of an individual at a given time. It uses 12 questions to measure eight domains of functional health and well-being namely physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health (Table 2) [21]. Physical and mental component summary scores can be calculated by aggregating the eight domains [23].

Description	Utility score
No problems	1.000
No problems walking; no problems with self-care; some problems with performing usual activities; some pain or discomfort; not anxious or depressed	0.760
Some problems walking; some problems washing or dressing self; some problems with performing usual activities; moderate pain or discomfort; moderately anxious or depressed	0.5616
No problems walking; some problems washing or dressing self; unable to perform usual activities; some pain or discomfort; not anxious or depressed	0.329
Some problems walking; no problems with self-care; no problems with performing usual activities; moderate pain or discomfort; extremely anxious or depressed	0.222
Some problems walking; unable to wash or dress self; unable to perform usual activities; moderate pain or discomfort; moderately anxious or depressed	0.079
Confined to bed; unable to wash or dress self; unable to perform usual activities, extreme pain or discomfort; moderately anxious or depressed	-0.429

Table 1. Example of utility scores for the EQ-5D

Domain	Description
Physical functioning	Degree to which health limits everyday physical activities
Role physical	Degree to which physical problems interfere with usual daily activities such as work or school
Bodily pain	Degree of pain to the body
General health	Ratings of current health in general
Vitality	Ratings of energy level
Social functioning	Degree to which health interferes with social activities
Role emotional	Degree to which emotional problems interfere with usual daily activities such as school or work
Mental health	Degree to which health limits emotional well- being, including depression, anxiety and well being

Table 2. Description of the health domains used in the SF-12 v2 quality of life survey

Although QALYs are commonly used metrics in health economics, they also present some limitations. For example, adaptation of patients to certain symptoms may mask the impact of chronic disability. In addition, it is difficult to assign a single utility score to those diseases which cause a variety of clinical manifestations, such as NCC [24]. Another limitation is that scale-based measures can sometimes lead to "ceiling" or "flooring" effects where a majority of people consistently choose the "best" scenario or "worst" scenario. One important criticism of QALYs (which some view as an advantage), is that QALYs measures are subjective and not meant to be generalized to the society as a whole. QALYs associated with a disease in one country (or region) could not be used to estimate the burden in another

region (or country). For example, having epilepsy in the United States would have very different social and role functioning values than in Sub-Saharan Africa. This difficulty in using QALYs for international comparison led a group of researchers to develop a completely different type of metric for measuring burden: the DALY.

3.2. Disability Adjusted Life Years (DALYs)

DALYs were first constructed for the Global Burden of Disease (GBD) Study in order to provide a comparable measure of output for interventions, program and sector evaluations, and planning [25]. The GBD Study was conducted to evaluate the non-monetary burden of a variety of infectious and non-infectious conditions, as well as risk factors, on pre-defined regions of the world. The latest comprehensive assessment of the burden of diseases is for the year 2004. However, DALY estimates from the 2010 GBD Study are expected to be released in late 2012 [26]. The DALY is a summary measure of population health that assesses the disability and early mortality associated with the condition of interest. DALYs measure the gap in years between age at death and gender-specific average life expectancy in Japan and combines it with time lived in states other than excellent health (disabled). They are obtained by summing years of life lost (YLL) from premature death and healthy years lost due to disability (YLD). The formulas used for the calculation of YLL and YLD are described below:

$$YLL = N * L \quad (1)$$

where N = number of deaths per age-sex group, L = remaining life expectancy at age of death

$$YLD = I * DW * D \quad (2)$$

where I = age and sex specific estimates of incidence, DW = disability weight, D = average duration of disability.

Disability weights are allocated according to the opinion of experts on how disabling a certain health status is perceived to be. Disability is placed on a uni-dimensional scale between 0 (perfect health) and 1 (death). In theory, utility is equal to 1-disability weight. Disability weights of clinical manifestations (referred to as indicator states) were determined for the original GBD Study by the person trade-off (PTO) method [27]. The PTO method is a way of estimating social preferences for different health states by asking people how many people affected by the health state of interest they would be willing to trade for extending the lives of 100 healthy people. This question is asked using two different formats. For the 2010 GBD Study, community assessment of selected sequelae using discrete choice methods, assessment by health professionals of all sequelae using ranking and visual analog scale methods, and multi-method studies among highly educated respondents were utilized rather than the PTO method [28]. Results from the new disability weights have not yet been published. Examples of disability weights used to calculate DALYs for the original GBD Study are provided in table 3.

Degree of morbidity	Disability weight
Healthy	0
Limited ability to perform at least one activity in one of the following areas: recreation, education, procreation or occupation	0.096
Limited ability to perform most activities in one of the following areas: recreation, education, procreation or occupation	0.220
Limited ability to perform most activities in two or more of the following areas: recreation, education, procreation or occupation	0.400
Limited ability to perform most activities in all of the following areas: recreation, education, procreation or occupation	0.600
Requires assistance with instrumental activities of daily living such as meal preparation, shopping or housework	0.810
Requires assistance with activities of daily living such as eating, personal hygiene or toilet use	0.920
Dead	1

Table 3. Examples of disability weights used to calculate DALYs [25]

Disability weights for NCC were not included in the original GBD study. However, in the 2010 GDB estimates, NCC will be included as causing an average of 29% of all epilepsy cases in endemic countries. This estimate is based on a meta-analysis of the percentage of NCC lesions present in the brain of people with epilepsy [29]. Disability weights of epilepsy will be used as there is no clinical difference between NCC-associated and other types of epilepsy. As better estimates of the distribution of manifestations among NCC patients become available, more sequelae will be added to DALYs estimates associated with NCC. The only two available estimates of DALYs associated with NCC used the disability weights associated with epilepsy (both studies) and migraine (1 study) [30, 31].

The original GBD Study calculations considered two additional parameters: 1) discounting future time and 2) age weighting [25]. Discounting future time is a common concept in economic and social policy. In burden of disease estimations, a discount rate is applied so that future healthy life has less value than the net value of life today [27]. In the context of DALYs, a disability occurring today is worth more than the same disability occurring in the future. The subject of discounting is complex and several papers have been published in favor and against its use in the context of DALYs and health outcomes [27, 32]. By including age weighting, the original GBD Study incorporated social preferences for the value of life lived during adulthood over life lived during childhood or later years. However, the newest version of the GBD Study (the GBD 2010 Study) will not include age weighting in the DALYs calculations. Therefore, the influence of age weighting will be eliminated.

The use of DALYs remains controversial, especially in measuring utilities. According to Anand (1997), DALYs understate the burden of disease of females relative to males since the standard expectation of life at birth in Japan is very similar in men and women [32]. DALYs

also measure the burden of disease without considering cultural or socioeconomic differentiation of tested populations so that it underestimates the disease burden in developing countries [33]. DALYs also go against Paretian welfare economics where each individual is the best judge of his or her own welfare. By using utility weights measured by people that are unaffected by the disease of interest, this concept is not respected. Even with these controversies, the DALY remains a widely used summary measure of population health.

4. Measuring monetary burden

Estimates of the monetary burden of zoonotic diseases that impact both human and livestock health should include assessment of both animal health costs and human health costs. The overall estimated cost can be calculated using the following equation: [34]

$$\sum_{s=1}^{S}\sum_{a=1}^{A}\left[N_{a,s}\beta_{a,s}\left(\sum_{x=1}^{X}\pi_{x,a,s}C_{x,a,s}\right)\right] \tag{3}$$

This equation corresponds to the additive societal costs for all affected species (S) across all age groups (A). For the age-species-specific population of size ($N_{a,s}$), with the age-species-specific annual incidence ($\beta_{a,s}$), there is an age-species proportion ($\pi_{x,a,s,}$) of infected individuals with symptoms X. The treatment and consequences of each of these symptoms have a monetary burden of $C_{x,a,s}$. Ideally, the whole spectrum of symptoms and losses in humans and animals is included in the estimate [34].

4.1. Human health costs

Human health costs are classified into direct (health provider) and indirect (out-of-pocket) costs. Direct costs are costs associated with the diagnosis and treatment of patients. Commonly used diagnostic tests incorporated into direct costs include diagnostic imaging, sero-immunological and blood tests, and tests on cerebral spinal fluid (CSF). Diagnostic costs, for a neurological condition such as NCC, can be high since CT scans and MRI confirmatory tests are not readily available in developing countries and, if available, are often distantly located and expensive. Cost of treatment typically includes the cost of medicines, medical consultations, surgical charges, and hospital charges. In contrast to direct costs, indirect costs include costs of working days lost due to clinical manifestations or visits to hospitals, losses in productivity, buying over-the-counter drugs to relieve symptoms, costs of traditional treatment, and costs associated with transportation to and from medical treatment. Costs associated with the family members taking care of the patients would also need to be included.

4.2. Animal health costs

Animal health costs can be associated with partial or full condemnation of the carcass at slaughter or reduction in price of an infected carcass. The value of live animals can also be

reduced when, in the case of *T. solium* cysticercosis, reduction in the price of pigs due to the presences of cysts can lower a farmer's household income. In addition, presence of *T. solium* in a country's pig population results in restrictions on the export of pork products.

4.3. Decision tree analysis

Decision trees are very helpful in organizing the information gathered on the distribution of manifestations and treatment seeking pattern in the study population. They can also be used to incorporate the probability of receiving different types of diagnoses and treatments. The tree usually starts with a "trunk" which is the disease of interest (in the case of NCC, this can be epilepsy). From this trunk, a probability (chance node) corresponding to the frequency of the disease is used to create the first two "branches" of the tree: the presence or absence of the disease in the study population. Additional branches are added each time a new probability is added. Each probability (node) may lead to more than two branches. The end of each branch corresponds to the probability that a patient has of following a certain treatment/diagnosis path, including the path of not seeking any medical care. The probability of each branch of a path can be multiplied by the costs corresponding to the options in this branch. An example, the use of decision tree analysis to estimate losses due cysticercosis in South Africa is shown in Figure 1 [35]. In this example, for the branch of people with epilepsy who have NCC but do not seek medical attention, we would multiply 1.33% by 36.7% by 70% to obtain the frequency of having NCC but not being treated (0.34%, as shown in Figure 1) [15, 36-41]. This percentage would be multiplied by the salary lost due to a reduction in productivity among people with epilepsy. Such trees can be developed for very complex treatment paths and for the impact of animal disease as well.

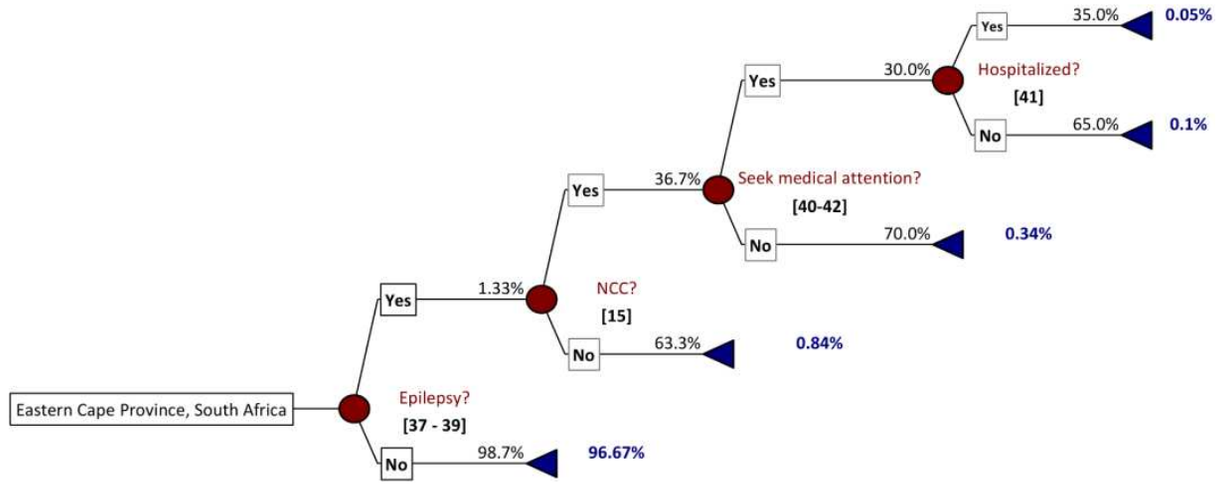

Figure 1. Decision tree analysis tree for estimating the monetary burden of NCC in Eastern Cape Province, South Africa. Circle is a chance node and triangle is an end node [35].

4.4. Uncertainty and sensitivity analysis

Common sources of epidemiological and economic data used in the assessment of disease burden include government and agency reports and values reported in the scientific

literature. Values for neglected zoonotic diseases, such as *T. solium* cysticercosis, are often underreported or else the method of collection might be biased. In short, exact estimates of these parameters are difficult to identify. Therefore, in order to account for uncertainties, the distribution of these parameters should be selected carefully. So, instead of using an exact value for each probability and cost value, a distribution of values is used to reflect uncertainty. To include these distributions into the final estimate, sampling methods such as the Monte Carlo or Latin Hypercube are often applied. The final estimate will itself be a distribution reflecting the uncertainty of all included parameters. Uniform distribution can be applied to parameters for which we have very limited knowledge. For example, instead of assuming that 1.33% of the population has epilepsy in the Eastern Cape Province of South Africa, we could assume that the prevalence lies anywhere between 0.5% and 2.8%, with an average at 1.33% [35]. The sampling method would start by sampling one value (for example, 1%) from this distribution, provide and save the estimate of the cost of NCC using this value. Next, another value would be sampled from the distribution and lead to another estimated cost, which will also be saved. This process is usually repeated up to 10,000 times until a distribution of the overall costs is obtained. The Latin Hypercube and Monte Carlo sampling methods are simply efficient tools of sampling several uncertain parameters iteratively.

The sampling method described above will generate a database of 10,000 observations each associated with a different value for the uncertain parameters. We can then use linear regression using the estimated costs as the outcome and all of the uncertain parameters as "independent" variables to assess which parameters have the largest impacts on the estimated costs. The uncertain parameters with the largest impacts should be those that need to be better studied in the future because they have a strong influence on how much a disease costs a society. Sensitivity must be conducted with care to limit the values to those that are most likely and realistic. Including impossible values would lead to biased estimates and a false impression that they have an important impact on the overall cost estimate.

5. Review of morbidity and mortality associated with neurocysticercosis

There are only a few studies in the literature which report the distribution of manifestations among definitive or probable cases of NCC as defined by the Garcia and Del Brutto criteria (2005) [42]. The challenge in studying the natural history of NCC is that it is impossible to diagnose the presence of brain cysts without the use of imaging, and using radiation among a population without symptoms is unethical. Hence, the only information available is the distribution of manifestations among NCC patients that are already under care in facilities where imaging is available. This introduces a major selection bias which leads to likely overestimation of the frequency of more severe (and less stigmatizing) manifestations, or manifestations which are more likely to lead to a medical visit (and a referral to a clinic with imaging). In countries where epilepsy is stigmatized, people may be afraid to seek care which would lead to an underestimate of the distribution of epilepsy among people with

NCC. Similarly, people with cranial hypertension suffering from headaches may never seek medical attention. In contrast, people with hydrocephalus or stroke will most likely seek care.

In a systematic review of studies conducted in clinics or hospitals with imaging facilities, the distribution of presenting symptoms among diagnosed NCC patients was as follows: seizures/epilepsy were the most common (78.8%, 95% CI: 65.1% - 89.7%) followed by headaches (37.9%, 95% CI: 23.3% - 53.7%), focal deficits (16.0%, 95% CI: 9.7% - 23.6%), and signs of increased intracranial pressure (11.7%, 95%CI: 6.0% - 18.9%) [8]. These results, though consistent with what is usually believed for NCC, may be biased by what presenting symptoms the clinicians assessed at admission. This systematic review of the literature also revealed that NCC may contribute to an important percentage of stroke cases in endemic areas. Unfortunately, to our knowledge, there is only one case-control study which has been conducted on this topic [10]. If NCC is truly linked to strokes, this could lead to a very important burden in endemic regions.

The studies included in the systematic review described above were all clinical-based. There have also been several studies conducted in communities and small rural hospitals where, instead of sampling NCC cases, people with epilepsy received imaging for the diagnosis of NCC. When those studies were analyzed systematically, the percentage of people with epilepsy with lesions of NCC at imaging was 29% (95% CI: 23% - 36%) [29]. This finding is important as it suggests that nearly one third of all epilepsy cases living in endemic areas could possibly be prevented with appropriate control strategies. The measure of burden described above could help guide stakeholders as to which control strategy may lead to the best cost-utility or cost-benefit for their area.

Compared to other helminthic infections, the socioeconomic burden of cysticercosis tends to be higher because the condition not only causes severe clinical manifestations, but can also result in mortality. Although limited data exist on NCC-related mortality, a study conducted in the United States and a study conducted in Brazil reported age-adjusted annual mortality rates of 0.06 (95% CI: 0.05 - 0.07) and 1.68 (95% CI: 1.58 - 1.78) deaths per million population, respectively [4, 43]. Additional studies from the U.S. states of California and Oregon reported crude mortality rates of 0.33 (95% CI: 0.27 - 0.38) and 0.29 (95% CI: 0.11 - 0.64) deaths per million population, respectively [44, 45].

6. The monetary and non-monetary burden of neurocysticercosis

Very few studies have been conducted to evaluate the burden of NCC. At present, two studies have been carried out in Africa evaluating the burden of cysticercosis/NCC. A study in West Cameroon revealed that 1.0% of the total population had NCC-associated epilepsy (based on serological results) and 5.6% of the pig population had cysticercosis [31]. Average number of DALYs lost due to NCC was 9.0 per 1,000 person-years and the monetary burden per case of NCC-associated epilepsy was 194 Euro in 2009. The total annual costs due to *T. solium* cysticercosis in West Cameroon were estimated at 10,255,202 Euro (95% CR

6,889,048–14,754,044), of which 4.7% were due to losses in pig husbandry and 95.3% to direct and indirect losses caused by human cysticercosis. This estimate only accounted for the disease burden due to NCC-associated epilepsy and used serology for the diagnosis of NCC.

Similarly, another study conducted in the Eastern Cape Province of South Africa estimated that the monetary burden of NCC-associated epilepsy in 2004 varied from US$632 to US$844 per case, indicating high financial losses associated with this condition [35]. The total number of estimated NCC-associated epilepsy cases was 34,662 (95% CI: 17,167 – 50,068) and among them, expert opinion and a review of the literature suggested that 70% of cases of epilepsy did not seek medical attention. Annual losses to the agricultural sector were estimated at US$5.0 million (95% CI: 2.4 – 8.1), with the overall monetary burden estimated at US$34.2 million (95% CI: 12.8 – 70.0) using the mean wage approach, US$20.1 million (95% CI: 9.6 – 35.3) using generalist replacement costs, and US$18.6 million (95% CI: 9.0 – 32.3) using the traditional opportunity costs approach.

A study conducted in Mexico showed that 0.25 DALY was lost per 1,000 person-years due to NCC-associated epilepsy and severe headaches, with NCC associated epilepsy responsible for 90% of this value [30]. According to 2004 GBD estimates, 1.7 DALYs per 1,000 person-years were estimated to be lost due to epilepsy in Mexico, with approximately the same number of DALYs lost due to migraine. This indicates that almost 15% of DALYs lost due to epilepsy were associated with NCC. This study used only epilepsy and severe chronic headaches as clinical manifestations due to lack of frequency data and disability weights for other known clinical manifestations associated with NCC. Therefore, like the African studies, the total estimated number of DALYs lost was most likely underestimated.

Three studies have been conducted to evaluate the quality of life of NCC patients. A study conducted at two tertiary neurology referral hospitals in Mexico City, Mexico indicated that NCC outpatients had significantly lower scores for each of the SF-12's eight domains of health compared to an age-sex-hospital-day matched control group [46]. Similarly, a study conducted in Peru showed that patients with parenchymal NCC had decreased quality of life compared with healthy neighborhood controls and controls with epilepsy as measured by the short-form 36 (SF-36) quality of life survey [47]. In addition, a study conducted in Brazil showed the presence of depression had a significant impact on the quality of life of patients with NCC as measured by a direct subjective quantification scale and the Functional Assessment of Cancer Therapy Quality of Life Measurement System (FACT-HN version IV) [48].

7. Suggested methods to improve the burden assessment of neurocysticercosis

While there are currently numerous ways in which to evaluate disease burden, each method has its pros and cons. Table 4 provides an overview of the established measures of disease burden currently available with which to evaluate the non-monetary or monetary burden of

T. solium cysticercosis. While non-monetary burden metrics, such as the DALY, are most often used by international agencies, these metrics are not capable of capturing the burden of disease associated with animal infection. Therefore, in order to fairly compare the burden of cysticercosis with that of non-zoonotic diseases, studies need to be conducted to evaluate how cysticercosis in pigs affects individuals in endemic regions in terms of income/livelihood losses and social impact. This information can then be used to develop questions to incorporate into a QALY scale or else be added to DALYs to capture this burden.

Measure of burden	**Items**	**Availability / quality of data**	
		Humans	***Animals***
QALYs	Cause specific death rates	Quality highly variable between countries	Not applicable
	Life expectancy	Largely available	
	Disease-specific incidence rates	Notifiable / registry disease data Quality / completeness highly variable	
	Time evolution of disease states	Knowledge of natural history of disease needed	
	Quality of life measure at various disease states	Special studies Place / time specific	
DALYs	Cause specific death rates	Quality highly variable between countries	Not applicable
	Disease-specific incidence rates	Notifiable / registry disease data Quality / completeness highly variable	
	Distribution of sequelae associated with disease in treatment free individuals	Knowledge of natural history of disease needed	
	Duration of each sequelae in treatment free individuals	Knowledge of natural history of each sequelae needed	
	Distribution of sequelae associated with disease among people under treatment	Special studies required	
	Duration of each sequelae under treatment	Special studies required	

Measure of burden	**Items**	**Availability / quality of data**	
		Humans	***Animals***
	Disability weights for each sequela (treated / non treated)	Available from GBD initiative Not all sequelae have been attributed disability weights	
Monetary burden	Cause-specific death rates	Quality highly variable between countries	Rarely available except for notifiable diseases
	Disease-specific prevalence	National / special survey data Special survey data often overestimate the truth	Abattoir data where home slaughtering is rare Special survey data often overestimate the truth
	Distribution of sequelae associated with disease	Knowledge of natural history of disease needed	Knowledge of natural history of disease needed
	Frequency of care / treatments / diagnoses and productivity losses for each sequel	Special studies Expert opinion	Special studies Expert opinion
	Costs associated with care / treatments / productivity losses of each sequel	Country-level health / labor statistics Special surveys	Agricultural statistics Special surveys

Table 4. Comparison of using QALYs, DALYs and monetary estimates to evaluate the disease burden of cysticercosis/NCC and other neglected zoonotic diseases with a livestock component [17]

8. Conclusions

T. solium cysticercosis is believed to contribute to high levels of human morbidity and some mortality, as well as pig production losses. This parasitic disease tends to disproportionately affect areas of low socio-economic status and should be prioritized for preventive measures because the disease is, in essence, 100% preventable. However, in order to make *T. solium* cysticercosis/NCC a priority condition, efforts to obtain more accurate estimates of disease burden must be made. In particular, a better understanding of the distribution of manifestations among all NCC cases would be very helpful. In addition, studies on the impact of NCC on productivity are needed. Such estimates could be used to show policy makers the true socioeconomic impact of this disease in various regions of the world. One of

the biggest limitations, for most of the measures of disease burden currently used for NCC/cysticercosis, is the lack of available high quality epidemiologic and/or financial data. Adherence to recommended guidelines for the diagnosis of cysticercosis in humans and pigs and declaring NCC a reportable disease would contribute greatly towards better burden estimates for this condition.

9. Nomenclature

Cysticercosis: Infection or disease of humans or animals caused by the larvae of *Taenia* spp. In this chapter, the term refers to infection of humans or pigs with *Taenia solium*.
Decision tree analysis: A method of organizing epidemiological data into infections and the frequency of their consequences.
Direct costs: Costs associated with the diagnosis and treatment of a medical condition, in addition to, costs associated with condemnation of all or part of an infected carcass.
Disability Adjusted Life Year (DALY): A measure of overall disease burden, expressed as the number of years lost due to ill-health, disability, or early death.
Disability weight: A score between 0 and 1 that is assigned to a condition depending on the degree of debilitation.
Euro-Qol (EQ-5D): A standardized instrument for use as a measure of health outcome.
Health Adjusted Life Year (HALY): An umbrella term for a family of measures of population health that includes, for example, Disability Adjusted Life Years (DALYs) and Quality Adjusted Life Year (QALYs).
Indirect costs: Costs associated with lost wages or decreased productivity arising indirectly from infection.
Neurocysticercosis (NCC): A neurological disease caused by invasion of the CNS by larvae of *Taenia solium*.
Quality Adjusted Life Year (QALY): A measure of disease burden, including both the quality and the quantity of life lived. It is used in assessing the value for money of a medical intervention. A year of full health is equivalent to 1 QALY, whereas, death corresponds to 0 QALYs.
Short-Form 12 (SF-12): A generic dual (i.e., mental and physical health) scale measure of quality of life.

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