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RESEARCH ARTICLE

Human health and economic impact of neurocysticercosis in Uganda

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Abstract

Objective: Neurocysticercosis (NCC), caused by the pork tapeworm *Taenia solium*, is a major cause of acquired epilepsy in endemic regions. The Republic of Uganda, one of the great-lakes nations in East Africa, has undergone major strives of political instability in the past century, impeding control of *T. solium* and other foodborne diseases. Building on data on the epidemiology of NCC, we aimed to assess the health and economic impact of NCC-associated epilepsy and headache in Uganda.

Methods: We used DisMod II to generate an internally consistent, complete and age-stratified set of epidemiological parameters for NCC epilepsy, and subsequently modelled the NCC headache incidence from the NCC epilepsy incidence. The health impact of both conditions was quantified in terms of Disability-Adjusted Life Years (DALYs), while the economic impact was quantified as the cost of illness associated with direct healthcare costs, patient costs and productivity losses. For both assessments, we adopted an incidence perspective and used 2010 as reference year. Uncertainty was propagated using 100,000 Monte Carlo simulations.

Results: In 2010, NCC was estimated to cause more than 9000 (CI: 7685–11,071) new cases of epilepsy and nearly 1500 new cases of headache, eventually leading to nearly 3000 deaths. Overall, it was estimated that NCC led to more than 170,000 DALYs (5.2 per 1000 person years; 16 per incident case) and an economic loss of more than USD 75 million (8000 per incident case). Non-fatal health outcomes were the largest contributors to the overall health impact, while productivity losses dominated the NCC cost of illness.

Conclusions: NCC imposes a substantial burden on public health and the economy in Uganda with poor attention given to this public health problem. Increased awareness among governments, international agencies, and general public, as well as targeted intervention studies using a One Health approach are needed to reduce the significant burden of NCC in Uganda.

KEYWORDS
disability adjusted life years, epilepsy, neurocysticercosis, socioeconomic impact, Uganda

Sustainable Development Goal: Good Health and Well-being, Reduced Inequality.

INTRODUCTION

Neurocysticercosis (NCC), caused by the pork tapeworm *Taenia solium*, is a major cause of acquired epilepsy in endemic regions. In addition to epilepsy, NCC may lead to various other neurological symptoms such as headache, raised intracranial pressure and focal deficits [1]. NCC is initiated by the ingestion of *T. solium* eggs, which are dispersed in the environment after expulsion of tapeworm segments by a human tapeworm carrier. The life cycle of *T. solium* is dependent on pigs and humans. When humans consume undercooked pork infected with viable cysticerci, the cysticerci develop into the adult tapeworm producing more than 50,000 eggs per day. The cycle is completed if pigs ingest *T. solium* eggs, which is facilitated by open defecation, improper sanitation and free range or semi-confined livestock farming [2].

WHO estimated that in 2010, more than 370,000 individuals developed NCC-associated epilepsy worldwide, leading to 28,000 deaths and nearly 3 million healthy life years lost (Disability-Adjusted Life Years, DALYs) [3]. This made *T. solium* the most important foodborne parasite worldwide and the fourth most important foodborne hazard overall. The burden was disproportionally high in sub-Saharan Africa, followed by the high mortality in low-income regions of Latin-America and South-East Asia [4], highlighting that NCC is disproportionally affecting the poor. Besides the human health implications, NCC may induce a significant economic burden to households and societies, due to cost of illness and losses for farmers [5–9]. This rather complex interplay of socio-economic burden and the lucrative business in piggery may make control efforts difficult if not impossible.

The Republic of Uganda (Uganda) is one of the great-lakes nations in East Africa, with an estimated population of over 40 million. The majority of the population (75%) is dependent on agriculture. Small-scale subsistence farming plays a major role in its overall agricultural production with 68% of the population in subsistence farming. Uganda has undergone major social and economic changes during the last century. In the last 100 years, Uganda has suffered from many social and economic drawbacks. Since Uganda gained independence from Britain in 1962, the country has been struggling with many economic and political difficulties, in parts through additional violent uprisings and phases of civil war. The dictatorship of Idi Amin was followed by the fight between the National Resistance Army (NRA) and remnants of Idi Amin's army in Northern Uganda. After Museveni seized power from the second government of President Apollo Milton Obote in 1986, this period was followed by another civil war in Northern Uganda between the Lord's Resistance Army (LRA) and the Government forces of Museveni. This period left especially the north devastated, without much social or health infrastructure. These strives of political instability caused many foodborne diseases to propagate freely, explaining the high prevalence of many tropical diseases related to socioeconomic prosperity and living standards. Since 2006, with the defeat of the LRA, a period of appeasement began, permitting research efforts in the area. International institutions, NGO's and the national government have tried to answer the repeated crises with initiatives trying to promote small-scale farming as a measure of securing self-sufficiency and social stability. As small-scale farming secures food security for families without relying on government services, it is an important step to prevent famines. Further food shortages and low protein intake were to be expected due to the armed uprisings. However, the increase in small-scale farming within the communities brought foodborne disease levels to rise to the prevalence we see today [10].

In this study, we aim to assess the socioeconomic impact caused by NCC in Uganda, by quantifying both the health and economic impact of NCC-associated epilepsy (NCC-epilepsy) and NCC-associated headache (NCC headache). These estimates may help evaluate efficacy of further intervention programs and may ensure that both health and financial interests are represented when pursuing new public health policies.

MATERIALS AND METHODS

Study population

We quantified the socioeconomic impact of NCC for Uganda, using 2005–2015 as reference period and 2010 as reference year. As the reign of the LRA in Northern Uganda finally shifted to the Democratic Republic of Congo, social and economic development started to slowly increase again since 2006. Assuming a constant development of the region, this time period was not disturbed by any further major setbacks comparable with the situation prior to 2005. Table 1 shows the composition of the 2010 population by age and sex, as estimated by the United Nations World Population Prospects 2015 Revision [11].

TABLE 1 Uganda population by age and sex for the year 2010 [11]

Age group	Male	Female	Total
0–4	3,252,000	3,191,000	6,443,000
5–14	4,922,000	4,867,000	9,789,000
15–44	6,877,000	6,793,000	13,670,000
45–59	925,000	1,038,000	1,963,000
60+	575,000	709,000	1,284,000
All ages	**16,551,000**	**16,598,000**	**33,149,000**

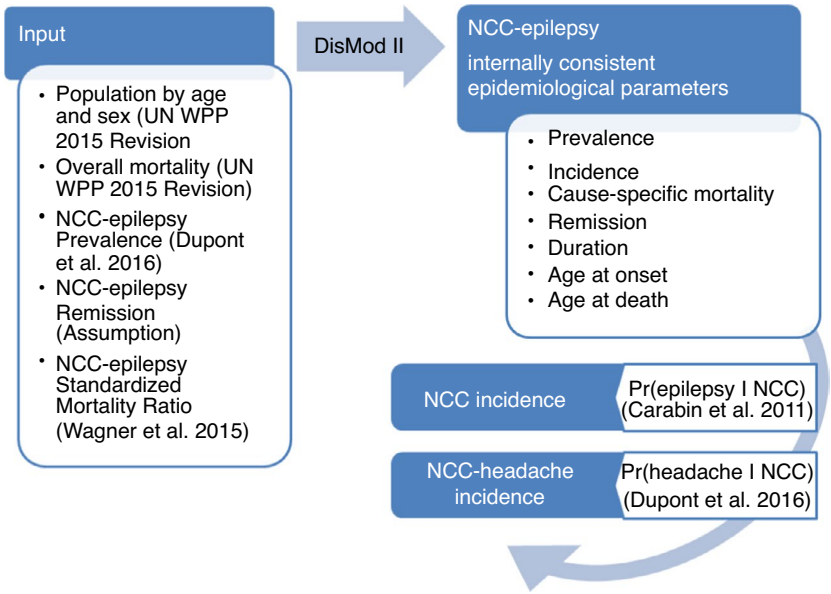

FIGURE 1 Strategy for modelling neurocysticercosis (NCC) epidemiology in Uganda

Epidemiological modelling

Figure 1 shows the process we followed for modelling the NCC epidemiology in Uganda. In brief, we used DisMod II to generate an internally consistent, complete and age-stratified set of epidemiological parameters for NCC epilepsy, and subsequently modelled the NCC headache incidence from the NCC epilepsy incidence.

DisMod II implements a Markov chain model that divides the population in four states, that is 'healthy', 'diseased', 'death caused by disease' and 'death through all other causes'. The transitions between these compartments are defined by four transition hazards, that is incidence, remission, case fatality and all other mortality rates. The model further allows estimating related epidemiological parameters, such as prevalence, duration, age at disease onset, age at death and standardised mortality rate. At least three disease input variables are needed to calculate the full disease epidemiology, allowing for the imputation of missing epidemiological data [12].

In our application, we used prevalence, remission rate and standardised mortality rate as input parameters. To estimate NCC epilepsy prevalence, we multiplied the epilepsy prevalence with the prevalence of NCC among people with epilepsy obtained by [13] (Table 2). We assumed the remission rate of NCC epilepsy to be zero, as in absence of neurosurgery NCC is unlikely to disappear completely. Even though the epileptogenic potential may change over time, there is no information available, as to whether there is a standardised decrease in expected seizure frequency. The NCC-epilepsy standardised mortality rate of 2.6 (95% Confidence Interval [CI]: 1.7–3.5) was adopted from Ref. [14]. In addition, we derived 2010 population sizes and all-cause mortality rates from the UN WPP 2015 [11].

TABLE 2 Prevalence of epilepsy and of neurocysticercosis (NCC) in people with epilepsy (PWE) in Uganda by sex and age ([13])), reference year 2010

Sex	Age group	Epilepsy prevalence (95%CI)	NCC prevalence in PWE (95%UI)
Male	0–12	N/A	*Assumed 0*
Male	12–18	0.051 (0.045–0.059)	0.065 (0.014–0.179)
Male	19–35	0.041 (0.035–0.047)	0.115 (0.044–0.234)
Male	36+	0.018 (0.014–0.023)	0.333 (0.118–0.616)
Female	0–12	N/A	*Assumed 0*
Female	12–18	0.085 (0.076–0.095)	0.081 (0.027–0.178)
Female	19–35	0.056 (0.048–0.064)	0.123 (0.051–0.237)
Female	36+	0.048 (0.040–0.057)	0.583 (0.366–0.779)

Abbreviations: CI, Confidence interval; UI, Uncertainty interval.

To estimate the incidence of NCC-headache, we first divided the age-specific NCC epilepsy incidence estimates by the proportion of symptomatic NCC patients that present with epilepsy as derived by [15], that is 79% (95%CI: 65%–90%). This estimate of the overall symptomatic NCC incidence was then multiplied with the NCC-attributable fraction of severe headaches as derived by [13], that is 15% (95%CI: 0.0%–34%). We further assumed zero remission and mortality for NCC headache.

Disability-adjusted life years

To quantify the health impact of NCC epilepsy and NCC headache, we calculated DALYs from an incidence perspective. To be in line with current practices, we applied

TABLE 3 Disability-Adjusted Life Year parameters for neurocysticercosis (NCC)-associated epilepsy and headache in Uganda, for the year 2010

Parameter	Distribution	Mean (95%UI)	Source
Proportion of NCC epilepsy patients receiving effective treatment	Beta($\alpha = 168, \beta = 126$)	0.571 (0.515–0.627)	[13]
Time between onset and effective treatment, age <35	Fixed	8.6	[13]
Time between onset and effective treatment, age ≥35	Fixed	4.4	[13]
Proportion of NCC headache patients presenting with migraine	Beta($\alpha = 8, \beta = 7$)	0.533 (0.289–0.770)	[13]
Proportion of NCC headache patients presenting with tension-type headache	Beta($\alpha = 7, \beta = 8$)	0.467 (0.230–0.711)	[13]
DW for epilepsy, severe (seizures once per month or more)	Beta($\alpha = 18, \beta = 14$)	0.552 (0.375–0.710)	[17]
DW for epilepsy, less severe (seizures less than once per month)	Beta($\alpha = 20, \beta = 57$)	0.263 (0.173–0.367)	[17]
DW for headache, migraine	Beta($\alpha = 19, \beta = 24$)	0.441 (0.294–0.588)	[17]
DW for headache, tension-type	Beta($\alpha = 16, \beta = 419$)	0.037 (0.022–0.057)	[17]
Time symptomatic for headache, migraine	Uniform(min = 0.066, max = 0.093)	0.079 (0.067–0.092)	
Time symptomatic for headache, tension-type	Uniform(min = 0.021, max = 0.029)	0.025 (0.021–0.029)	

Abbreviations: DW, Disability Weight; UI, Uncertainty interval.

standard formulas without age weighting or time discounting [16]. Years Lived with Disability (YLDs) were calculated for uncontrolled and controlled NCC epilepsy and for NCC headache. Disability weights to value these health states were adopted from the Global Burden of Disease (GBD) 2013 study [17] (Table 3). Uncontrolled epilepsy was defined as the GBD 2013 health state '*epilepsy*, *severe (seizures once per month or more)*'. Controlled epilepsy was defined as a transition from the health state '*epilepsy*, *severe (seizures once per month or more)*' to that of '*epilepsy*, *less severe (seizures less than once per month)*'. The time between disease onset and transition to less severe epilepsy was derived from Ref. [13]. NCC headache was defined as either '*headache*, *migraine*' or '*headache*, *tension-type*'. The proportion migraine versus tension-type headache among NCC patients was derived from Ref. [13](Table 3). The time symptomatic for migraine and tension-type headache was adopted from the GBD study (Vos et al., 2020).

Years of Life Lost (YLLs) were calculated for NCC epilepsy, using the standard life expectancy table proposed by the GBD 2010 study [16].

Cost of illness

To quantify the economic impact of NCC epilepsy and NCC headache for the year 2010, we calculated cost of illness from an incidence perspective, without time discounting as future predictions were not made and future costs not calculated. Cost estimates are presented in 2015 US Dollars, using an exchange rate of 3 300 Ugandan Shilling per US Dollar.

We applied a societal perspective and included direct healthcare costs (DHC), patient costs (also known as direct non-healthcare costs) and productivity losses (also known as indirect non-healthcare costs). For NCC epilepsy, we included direct and indirect costs due to hospitalisation, healthcare visits, treatment and productivity losses due to illness and death. For NCC headache, we only included treatment costs.

Tables 4–6 present the various input parameters used in estimating cost of illness. In general, use frequencies and travel data were derived from Ref. [13]. Unit costs were derived using an expert elicitation questionnaire. Three experts were chosen from local medical groups with at least 10 years of experience in local healthcare practices and costs. These provided a lower and upper cost estimate for the different items (Table S1). The hospitalisation costs took into account that in Uganda there is severe shortage of healthcare workers during hospitalisation periods, requiring patients to organise relatives who provide full board and basic healthcare interventions. Through that arrangement, healthcare is cheaper for the hospital but creates an additional financial burden for the affected family, in terms of additional patient costs and productivity losses.

Productivity losses were estimated using a human capital approach, using the 2010 gross national income per capita of 550 USD, as estimated by the World Bank (http://data.worldbank.org/indicator/NY.GNP.PCAP.CD?locations=UG). For fatal cases, we considered the potential years of life lost up to the age of 65 [18]. For productivity losses due to illness, we used data from Ref. [13] on the working time before and after epilepsy treatment, which suggested a 66% reduction in productivity for patients with severe epilepsy. For patients with less severe epilepsy (i.e. controlled epilepsy), we did not assume productivity losses because no reliable data were available.

TABLE 4 Cost-of-illness parameters—hospitalisation due to neurocysticercosis-associated epilepsy in Uganda, for the year 2010

Parameter	Distribution	Mean (95%UI)	Source
Cost per km, bus	*See S1 Table*	0.03 (0.01–0.06)	*Expert elicitation*
Cost per km, boda	*See S1 Table*	0.59 (0.31–1.12)	*Expert elicitation*
Cost per km, taxi	*See S1 Table*	1.83 (0.69–2.94)	*Expert elicitation*
Probability hospitalisation	Beta($\alpha = 57, \beta = 243$)	0.191 (0.148–0.237)	[13]
Hospitalisation events per year	Gamma($\mu = 0.407, \sigma = 0.036$)	0.406 (0.341–0.481)	[13]
Hospitalisation days per event	Gamma($\mu = 5.63, \sigma = 0.524$)	5.63 (4.76–6.70)	[13]
Hospitalisation cost per day, patient	*See S1 Table*	67 (6–322)	*Expert elicitation*
Hospitalisation cost per day, relative	*See S1 Table*	4.4 (3.1–5.7)	*Expert elicitation*
Probability of undergoing EEG	PERT(min = 0.02, mode = 0.10, max = 0.13)	0.09 (0.05–0.12)	*Expert elicitation*
Cost per EEG	*See S1 Table*	49 (19–129)	*Expert elicitation*
Distance to hospital	2 * Gamma($\mu = 10.7, \sigma = 2.04$)	21.39 (14.52–30.46)	[13]
Probability travelling by boda	Beta($\alpha = 15, \beta = 45$)	0.252 (0.150–0.373)	[13]
Probability travelling by taxi	Beta($\alpha = 9, \beta = 51$)	0.152 (0.0752–0.252)	[13]

Abbreviations: EEG, Electroencephalogram; UI, Uncertainty interval.

TABLE 5 Cost-of-illness parameters—healthcare seeking due to neurocysticercosis-associated epilepsy in Uganda, for the year 2010

Parameter	Distribution	Mean (95%UI)	Source
Probability healthcare seeking	Beta($\alpha = 290, \beta = 10$)	0.967 (0.945–0.985)	[13]
Probability of visiting a physician	Beta($\alpha = 8, \beta = 282$)	0.027 (0.012–0.048)	[13]
Probability of visiting a nurse	Beta($\alpha = 143, \beta = 147$)	0.492 (0.435–0.552)	[13]
Probability of visiting a health officer	Beta($\alpha = 135, \beta = 155$)	0.467 (0.409–0.525)	[13]
Probability of visiting a traditional healer	Beta($\alpha = 22, \beta = 268$)	0.080 (0.049–0.111)	[13]
Number of visits per year to a physician	Gamma($\mu = 0.375, \sigma = 0.070$)	0.376 (0.242–0.530)	[13]
Number of visits per year to a nurse	Gamma($\mu = 0.607, \sigma = 0.079$)	0.603 (0.462–0.753)	[13]
Number of visits per year to a health officer	Gamma($\mu = 0.409, \sigma = 0.049$)	0.408 (0.318–0.502)	[13]
Number of visits per year to a traditional healer	Gamma($\mu = 0.489, \sigma = 0.133$)	0.484 (0.261–0.755)	[13]
Cost per visit, physician	*See S1 Table*	11 (0.7–2)	*Expert elicitation*
Cost per visit, nurse	*See S1 Table*	1.4 (0.1–2.9)	*Expert elicitation*
Cost per visit, health officer	*See S1 Table*	5.1 (1.6–14)	*Expert elicitation*
Cost per visit, traditional healer	*See S1 Table*	10 (1.7–37)	*Expert elicitation*
Distance to physician	2 * Gamma($\mu = 10.7, \sigma = 2.04$)	21.64 (14.69–29.86)	[13]
Distance to nurse	2 * Gamma($\mu = 10.9, \sigma = 0.63$)	21.83 (19.59–24.27)	[13]
Distance to health officer	2 * Gamma($\mu = 9.9, \sigma = 0.59$)	19.87 (17.70–22.20)	[13]
Distance to traditional healer	2 * Gamma($\mu = 10.9, \sigma = 1.47$)	22.01 (16.84–27.77)	[13]
Probability of using boda to visit a physician	Beta($\alpha = 2, \beta = 7$)	0.222 (0.032–0.527)	[13]
Probability of using taxi to visit a physician	Beta($\alpha = 3, \beta = 6$)	0.336 (0.080–0.660)	[13]
Probability of using boda to visit a nurse	Beta($\alpha = 25, \beta = 115$)	0.180 (0.122–0.246)	[13]
Probability of using taxi to visit a nurse	Beta($\alpha = 7, \beta = 133$)	0.050 (0.021–0.092)	[13]
Probability of using boda to visit a health officer	Beta($\alpha = 27, \beta = 106$)	0.204 (0.141–0.279)	[13]
Probability of using taxi to visit a health officer	Beta($\alpha = 3, \beta = 130$)	0.0231 (0.005–0.058)	[13]
Probability of using bus to visit a traditional healer	Beta($\alpha = 1, \beta$=17)	0.057 (0.002–0.202)	[13]

Abbreviation: UI, Uncertainty interval.

Data analysis

All analyses were performed in R 3.3.1 [19]. We used 100,000 Monte Carlo simulations to propagate uncertainty from the input parameters to the DALY and cost-of-illness outputs. The resulting uncertainty distributions are summarised by the mean and 95% uncertainty interval (UI) defined as the 2.5th and 97.5th percentile of the uncertainty distribution.

TABLE 6 Cost-of-illness parameters—treatment of neurocysticercosis-associated epilepsy and headache in Uganda, for the year 2010

Parameter	Distribution	Mean (95%UI)	Source
Compliance of anti-epileptic drug treatment	Beta($\alpha = 225, \beta = 74$)	0.753 (0.702–0.800)	[13]
Probability of carbamazepine treatment for epilepsy	Dirichlet($\alpha_1 = 30, \alpha_2 = 141, \alpha_3 = 53$)	0.134 (0.093–0.181)	[13]
Probability of phenytoin treatment for epilepsy	Dirichlet($\alpha_1 = 30, \alpha_2 = 141, \alpha_3 = 53$)	0.629 (0.656–0.691)	[13]
Probability of phenobarbital treatment for epilepsy	Dirichlet($\alpha_1 = 30, \alpha_2 = 141, \alpha_3 = 53$)	0.237 (0.183–0.294)	[13]
Probability of scarification treatment for epilepsy	Beta($\alpha = 12, \beta = 288$)	0.040 (0.021–0.063)	[13]
Cost carbamazepine per month	*See S1 Table*	4.4 (1.3–10)	*Expert elicitation*
Cost phenytoin per month	*See S1 Table*	1.2 (0.3–2.8)	*Expert elicitation*
Cost phenobarbital per month	*See S1 Table*	2.9 (0.4–7.4)	*Expert elicitation*
Cost scarification per event	*See S1 Table*	9.5 (0.6–37)	*Expert elicitation*
Cost paracetamol per month for headache treatment	*See S1 Table*	1.2 (0.4–2.4)	*Expert elicitation*

Abbreviation:UI, Uncertainty interval.

Tables 3–6 present the uncertainty distributions used for the input parameters. For the input parameters that were elicited through expert opinion, we simulated the individual expert opinions as individual Gamma distributions (with 2.5^{th} and 97.5^{th} quantile corresponding to the lower and upper bound provided by the expert) and combined the different expert distributions using equal weights. As DisMod II only allows a limited number of uncertainty distributions, we implemented three independent scenarios to capture the uncertainty in the epidemiological input parameters. Specifically, we implemented a most likely-, best-, and worst-case scenario based on the mean, the lower and upper confidence level of both the NCC epilepsy prevalence and standardised mortality rate, respectively. We then used PERT distributions to simulate the uncertainty across these three scenarios.

To assess the influence of the individual input parameters' uncertainty on the output uncertainty, we performed sensitivity analyses by calculating the partial correlation coefficients between the input and output distributions.

RESULTS

NCC epidemiology

Table 7 presents the estimated NCC epilepsy and NCC headache prevalence, by age and sex. In general, females were estimated to be more affected, due to higher overall epilepsy prevalence. Table 8 presents the estimated NCC-epilepsy incidence and mortality, based on the DisMod II output and the ensuing NCC headache incidence. Overall, we estimated more than 9000 new cases of NCC-epilepsy and nearly 1500 new cases of NCC headache, eventually leading to nearly 3000 deaths.

Socioeconomic impact

Overall, it was estimated that NCC led to more than 170,000 healthy life years lost (Table 9) and an economic loss of more than 75 million USD (Table 10). Non-fatal health outcomes were found to be the largest contributors to the overall health impact (66%; 95%UI: 57%–74%). YLDs associated with NCC-headache contributed to 0.3% (95%UI: 0%–0.9%) of the total DALY estimate. The NCC cost of illness was found to be dominated by productivity losses, in particular the productivity losses due to severe epilepsy. DHC, primarily due to hospitalisation, were the next major contributor to the cost of illness.

Sensitivity analyses

Figures 2 and 3 show tornado graphs of the results of the sensitivity analyses for the DALY and cost-of-illness estimates. The uncertainty in the DALY estimates was mainly influenced by the uncertainty in the incidence of NCC epilepsy and in the disability weight for severe epilepsy. The uncertainty in the cost-of-illness estimate was mainly influenced by the uncertainty in the hospital cost per patient per day and in the incidence of NCC epilepsy.

DISCUSSION

NCC is a leading cause of epilepsy and other neurological disorders in developing regions where pork is consumed. This study provides the first comprehensive assessment of the human health and economic impact of NCC in Uganda and may become an essential evidence base for creating awareness among governments, international agencies, and the general public, as well as a baseline for assessing the efficacy of future intervention programmes.

Unlike other studies that assessed the socioeconomic burden of *T. solium* on country level [6–9], we applied the DisMod II model to generate internally consistent epidemiological data for the study population in question. DisMod II further allowed us to calculate missing epidemiological parameters, that is incidence, duration, age at onset and age at death. Furthermore, our estimates provide the first comprehensive assessment of the health and economic impact of both NCC epilepsy and NCC headache.

Most of the data inputs we used were derived from Ref. [13]. Although these data were collected in 2010/11, they represent the most up-to-date source of epidemiological information on NCC in Uganda. These authors conducted a field survey among 38,303 individuals in Northern Uganda using the Cysticercosis Working Group in Eastern and Southern Africa (CWGESA) questionnaire and identified 1245 people with epilepsy. Three hundred epilepsy patients were examined in more detail, resulting in the identification of 40 NCC patients (13%). We extrapolated the data presented by [13] to Uganda as a whole, as other studies on human or porcine *T. solium* cysticercosis in Uganda have indicated that the entire country may be considered endemic [20], and that there is no effective control of porcine cysticercosis in different regions in Uganda [10,21]. The only exception to this assumption may be the highly developed regions of Kampala or Entebbe. Affluent neighbourhoods in that region may show a slightly lower prevalence. However, as this affects only a small percentage of the population (even within those regions), we assumed this portion of deviation to be negligible.

Neurocysticercosis health impact

We estimated that in 2010, NCC epilepsy and NCC headache resulted in more than 170,000 healthy life years lost, or 5.2 per 1 000 person years. This estimate is somewhat higher than most other country-level estimates (Table 11). In addition to true differences in NCC epidemiology, these discrepancies may to some extent also be explained by methodological differences.

TABLE 7 Estimated prevalence of neurocysticercosis (NCC)-associated epilepsy and headache in Uganda, for the year 2010

Sex	Age group	NCC-epilepsy prevalence per 1000 (95%UI)	NCC-headache prevalence per 1000 (95%UI)
Male	0–12	0	0
Male	12–18	3.00 (0.64–7.09)	0.46 (0.00–1.50)
Male	19–35	4.07 (1.54–7.73)	0.62 (0.00–1.74)
Male	36+	4.37 (1.54–8.31)	0.67 (0.00–1.88)
Female	0–12	0	0
Female	12–18	5.86 (1.96–11.7)	0.89 (0.00–2.59)
Female	19–35	5.80 (2.40–10.5)	0.88 (0.00–2.42)
Female	36+	16.7 (9.86–24.7)	2.55 (0.00–6.28)

Abbreviation:UI, Uncertainty interval.

TABLE 8 Estimated annual number of neurocysticercosis (NCC)-associated incident cases and deaths in Uganda, for the year 2010

Indicator	Absolute number (95%UI)	Rate per 100 000 (95%UI)
Incident cases, NCC epilepsy	9 344 (7 685–11 071)	28 (23–33)
Incidence cases, NCC headache	1 426 (0–3 254)	4.3 (0.0–9.8)
Deaths, NCC epilepsy	2 749 (2 346–3 167)	8.3 (7.1–9.6)

Abbreviation: UI, uncertainty interval.

A main difference between our assessment and previously published studies is our assumption of a zero-remission rate, leading to a longer duration of NCC epilepsy than in previous studies—that assumed the duration of NCC-epilepsy to equal that of primary epilepsy. Indeed, the pathophysiology of primary and secondary epilepsy is not comparable, final remission of secondary epilepsy is only expected if the causative agent stops disturbing neuronal network functioning. In the absence of neurosurgery, the cysticercus is expected to remain in the patient's brain, possibly in a calcified stage, but nonetheless making spontaneous remission of NCC epilepsy less likely than for primary epilepsy. With the help of future NCC

TABLE 9 Estimated incident Years Lived with Disability (YLDs), Years of Life Lost (YLLs) and Disability-Adjusted Life Years (DALYs) of neurocysticercosis (NCC), in Uganda, for the year 2010

Indicator	Absolute number (95%UI)	Rate per 1000 (95%UI)	Rate per incident case (95%UI)
YLDs, NCC epilepsy, receiving proper treatment	51,462 (35,244–71,076)	1.6 (1.1–2.1)	5.5 (4.1–7.1)
YLDs, NCC epilepsy, not receiving proper treatment	62,415 (39,264–89,707)	1.9 (1.2–2.7)	6.7 (4.5–9)
YLDs, NCC headache	563 (0–1,588)	0.02 (0–0.05)	0.4 (0.2–0.7)
YLLs, NCC epilepsy	58,569 (49,043–68,579)	1.8 (1.5–2.1)	6.3 (4.9–8.1)
DALYs	**173,010 (135,955–214,828)**	**5.2 (4.1–6.5)**	**16 (13–20)**

Abbreviation: UI, Uncertainty interval.

TABLE 10 Estimated incident cost of illness of neurocysticercosis (USD), in Uganda for the year 2010

Indicator	Mean (95%UI)	Relative contribution (95%UI)
Hospitalisation	11,871,872 (3,810,642–41,892 447)	0.15 (0.06–0.40)
Direct healthcare costs	*7,791,415 (741,697–37,589,660)*	*0.09 (0.01–0.36)*
Patient costs	*3,734,121 (1,737,844–7,053,030)*	*0.05 (0.02–0.09)*
Productivity losses	*346,336 (221,504–507,754)*	*0.00 (0.00–0.01)*
Healthcare seeking	1,217,845 (691,774–1,984,607)	0.02 (0.01–0.03)
Direct healthcare costs	*485,576 (172,080–1,037,388)*	*0.01 (0.00–0.01)*
Patient costs	*525,683 (243,398–976,048)*	*0.01 (0.00–0.01)*
Productivity losses	*206,586 (150,159–273,484)*	*0.00 (0.00–0.00)*
Drugs, epilepsy	4,861,675 (2,173,501–8,932,231)	0.06 (0.03–0.11)
Drugs, headache	555,318 (0–1,701,736)	0.01 (0.00–0.02)
Productivity losses due to severe epilepsy	51,587,633 (39,590,561–64,613,736)	0.69 (0.49–0.78)
Productivity losses due to premature death	5,375,711 (3,921,188–6,979,108)	0.07 (0.05–0.10)
TOTAL	**75,470,055 (56,386,713–108,895,694)**	**1.00 (1.00–1.00)**
Direct healthcare costs	***13,693,984 (5,124,107–43,593,850)***	***0.17 (0.08–0.41)***
Patient costs	***4,259,804 (2,050,394–7,851,802)***	***0.06 (0.03–0.10)***
Productivity losses	***57,516,267 (45,341,603–70,751,565)***	***0.77 (0.54–0.87)***
TOTAL, PER CASE	**8,068 (6,825–11,323)**	**1.00 (1.00–1.00)**
Direct healthcare costs	***1,463 (572–4,660)***	***0.17 (0.08–0.41)***
Patient costs	***455 (230–811)***	***0.06 (0.03–0.10)***
Productivity losses	***6,150 (5,567–6,761)***	***0.77 (0.54–0.87)***

Abbreviation: *UI, uncertainty interval.*

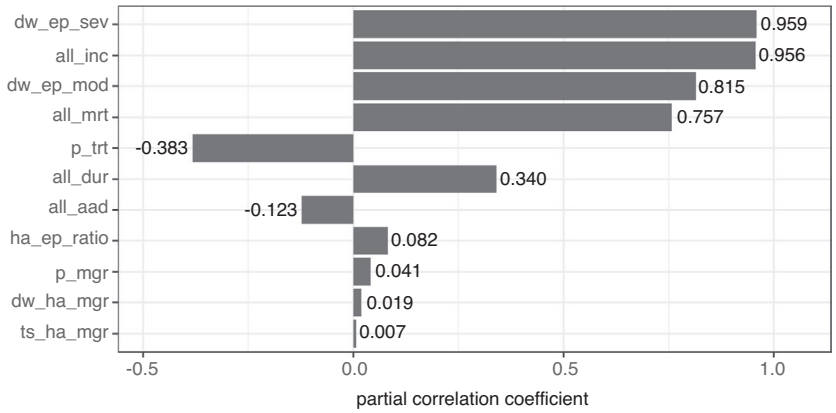

FIGURE 2 Tornado graph of sensitivity analysis of Disability-Adjusted Life Years (DALY) (only coefficients with $p < 0.05$ are shown). dw_ep_sev: disability weight for severe epilepsy; all_inc: NCC epilepsy incidence both sexes; dw_ep_mod: disability weight for moderate epilepsy; all_mrt: NCC epilepsy mortality both sexes; p_trt: proportion treated; all_dur: NCC epilepsy duration both sexes; all_aad: average age at death NCC epilepsy both sexes; ha_ep_ratio: NCC headache to epilepsy ratio; p_mgr: proportion migraine-type headache; dw_ha_mgr: disability weight for migraine; ts_ha_mgr: time symptomatic for migraine

epilepsy and headache remission studies, this approximation can be amended. This will provide a more precise image of the NCC socioeconomic burden.

On the other hand, we had assumed the prevalence of NCC epilepsy in children below the age of 10 to be zero, potentially underestimating the burden. This was motivated by the generally assumed long period between infection and onset of seizures [22] and empirically supported by Dupont [13] who found the prevalence of NCC in Ugandan adolescents and adults with epilepsy to increase with age. Furthermore, we obtained a high compliance level (75%). As this estimate was based on self-reported data, compliance might have been overreported by patients. If this was assumed, disease burden might be overall slightly underestimated. In order to evaluate this phenomenon, compliance would need to either be cross checked by blood samples of treating physician estimation.

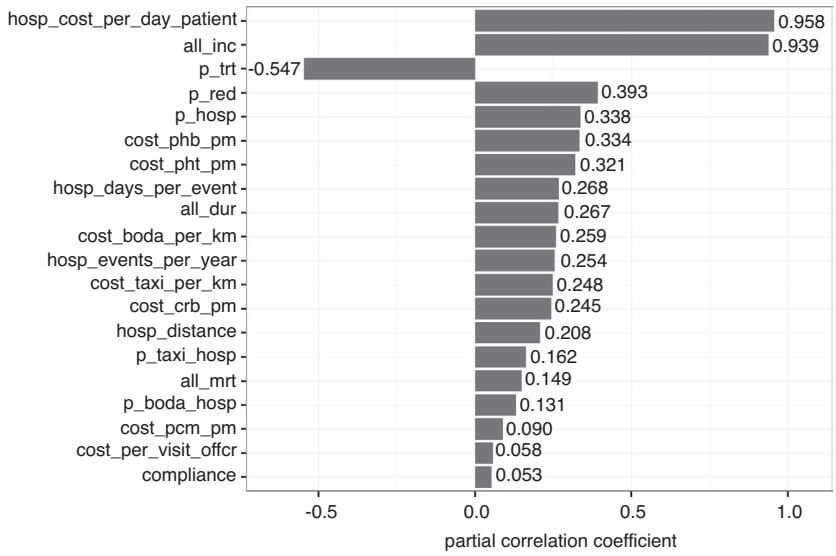

FIGURE 3 Tornado graph of sensitivity analysis of cost of illness (only 20 highest values with $p < 0.05$ are shown). hosp_cost_per_day_patient: hospital cost per day per patient; all_inc: NCC epilepsy incidence both sexes; p_trt: proportion treated; p_red: proportion reduced productivity; p_hosp: proportion hospitalised; cost_phb_pm: cost phenobarbitol per month; cost_pht_pm: cost phenytoin per month; hosp_days_per_event: number of days in hospital per hospitalisation event; all_dur: NCC epilepsy duration both sexes; cost_boda_per_km: cost boda per km; cost_crb_pm: cost carbamazepine per month; hosp_distance: distance to hospital; p_taxi_hosp: probability of going to hospital by taxi; all_mrt: mortality NCC epilepsy both sexes; p_boda_hosp: probability of going to hospital by boda; cost_pcm_pm: cost paracetamol per month; cost_per_visit_offcr: cost per health officer visit; compliance: compliance of anti-epileptic drug treatment

Our study is only the second to include NCC headache to the health burden assessment. In Uganda, YLDs associated with NCC headache contributed to merely 5 percent of the total DALY estimate, but had the highest patient-level morbidity impact (7.1 DALYs per incident case). The latter result is significantly higher than the one obtained by [9] for Mexico, that is 2 321 DALYs for 25 253 incident cases of NCC-headache, or 0.09 DALYs per incident case.

Bhattaraiet al. [9] included severe chronic headaches, defined as severe headaches that last for more than three continuous days, and applied disability weights of 0.007 and 0.028 for treated and untreated severe headaches, respectively. To be in line with the GBD 2013 disability weights, in our study we based the NCC headache evaluation on two sub-groups, that is tension-type headache and migraine, with disability weights of 0.037 and 0.441, respectively [17]. As no secure clinical data were available, we based our distinction on clear signs for migraine, that is patients presenting with visual aura. Further discrepancy is due to our aforementioned assumption of a zero-remission rate, whereas Bhattaraiet al. [9] adopted an NCC headache duration of 2.9–4.8 years.

Neurocysticercosis economic impact

Overall, we estimated that NCC led to an economic loss of more than 75 million USD, or 8000 USD per NCC case. In line with other NCC cost-of-illness studies, productivity losses dominated the estimates; however, our estimates were larger than previous studies where the losses for NCC were ranged around 5 million USD in Tanzania, 10.3 million Euro in West Cameroon and 34.2 million USD in Eastern Cape Province, South Africa [6,7,23]. On the other hand, in India, 185.14 million USD were spent for NCC [8]. In Uganda, healthcare staff during hospitalisation periods is scarce, requiring relatives who will provide basic healthcare interventions to hospitalised family members; and thus, increasing productivity losses. Furthermore, we included productivity losses due to both inactivity and death, whereas previous studies only considered inactivity.

The cost-of-illness estimates were based on several simplifying assumptions. For NCC epilepsy, we assumed hospitalised patients to undergo only an electroencephalogram (EEG) and assumed more expensive computed tomography or magnetic resonance imaging not to be available. Even though recommended in certain clinical scenarios, neuroimaging is not accessible for the majority of the population. As EEG is largely unavailable on short notice, we estimated it was only done in 10% of hospitalised patients. For NCC headache, average, one-off doses of paracetamol were considered as main treatment option available. Patient costs or productivity losses were not assumed for headache.

By only focusing on the economic impact of NCC, we did not give fair attention to the fact that *T. solium* taeniosis/cysticercosis is in fact a one health issue. New data on porcine cysticercosis prevalence in Uganda became available early 2017 [24]. This could be the foundation for a more exhaustive economic burden assessment, also evaluating the economic losses due to infected pigs especially as porcine cysticercosis and NCC can only be combated together.

TABLE 11 Country-level Disability-Adjusted Life Year (DALY) calculations for *Taenia solium* neurocysticercosis

Reference	Setting	Included symptoms	Social weighting	Estimated DALY per 1000 person-years (95%UI)
Praet et al. (2009)	West Cameroon	Epilepsy	Age weighting, 3%-time discounting	9.0 (2.8–20.4)
Bhattarai et al. (2012)	Mexico	Epilepsy, severe chronic headaches	No age weighting, no time discounting	0.25 (0.12–0.46)
Devleesschauwer et al. (2014)	Nepal	Epilepsy	No age weighting, no time discounting	0.54 (0.21–1.05)
Singh et al. (2017)	India	Epilepsy	No age weighting, no time discounting	1.73 (0.82–3.39)
Trevisan et al. (2017)	Tanzania	Epilepsy	No age weighting, no time discounting	0.7 (0.2–1.6)

Abbreviation: UI, Uncertainty interval.

CONCLUSION

Compared to other studies, we used a disease model to generate internally consistent epidemiological estimates and assessed the health and economic burden of both NCC-related epilepsy and NCC-related headache. We have demonstrated that the public health and economic burden of NCC in Uganda are substantial and have provided evidence to policy makers of the urgent need to address this public health problem. To reduce the significant burden of NCC in Uganda, there is an urgent need for greater awareness raising among governments, international organisations, and the general public, as well as targeted intervention studies using a One Health approach.

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