



## Assessing the burden of Neurocysticercosis in Uganda: A Systematic Review of epidemiology, efforts, challenges, and recommendations.

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### Abstract

Neurocysticercosis (NCC) is caused by the helminth *Taenia solium*, which is of the same family as *Taenia saginata* and *Taenia asiatica*, with pigs as intermediate hosts. *Taenia solium* eggs are ingested through the fecal-oral route, where cysts form in the small intestines and cause human taeniasis. In the small intestines, the larvae of *Taenia solium* attach to the lumen of the small intestines with the help of scolex. When the cysts proliferate in the tissues, they cause human cysticercosis, and when they affect the central nervous system, they cause Neurocysticercosis. According to the WHO Guidelines on the Management of *T. solium* Neurocysticercosis published in 2021, there is an estimated total number of symptomatic and asymptomatic NCC cases of 2.56-8.30 million. In 2010, there were nearly 3000 deaths in Uganda due to NCC, leading to an estimated number of 9000 new cases of epilepsy that led to expenditures of accurately \$8,000 per new case. After about three months, the calcification of cysts is finalized, and mature cysts are formed, leading to brain granulomas responsible for seizures and other neurological complications. This article aims to assess the burden of NCC in Uganda and provide recommendations for mitigating and eradicating NCC in Uganda.

**Keywords:** Neurocysticercosis, Uganda, *Taenia solium*, Neglected tropical diseases, epidemiology

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## 1. INTRODUCTION

Neurocysticercosis (NCC) is caused by porcine helminth *Taenia solium*, of the same family as *Taenia saginata* and *Taenia asiatica*, characterized by cyst formation in the central nervous system (brain and spinal cord). Pigs are intermediate hosts of *T. solium*, and humans act as definitive helminth hosts. It is acquired by fecal-oral ingestion of eggs or larvae of *T. solium* from contaminated water or food, specifically raw and undercooked pork meat <sup>[1,2]</sup>.

It is accredited that NCC mainly targets the cortex and basal ganglia of the brain, even though evidence clearly states that it generally affects the supratentorial part of the brain more than the infratentorial <sup>[3]</sup>. Uniformly, NCC is clinically implicated with neurological symptoms such as

seizures, headaches, hydrocephalus, complications with maintaining a steady body balance, stroke, meningitis, hallucinations, and eventually, lack of thoughtfulness to people and surroundings<sup>[1,4,5]</sup>. Epilepsy is the most common clinical presentation of NCC, with an estimated prevalence of 70% in NCC patients in endemic areas. On a global scale, NCC accounts for 30% of epilepsy cases<sup>[1,4]</sup>, and epilepsy in adults is less prevalent than in children<sup>[6]</sup>. These statistics accounted for a total of 370,000 NCC-associated epilepsy cases and 28,000 deaths in the year 2010, 2.8 million disability-adjusted life-years (DALF) from *T. solium*, and 170,000 DALF from NCC in Uganda<sup>[7,8]</sup>.

Uganda, one of the low- and middle-income countries (LMICs), is the largest supplier of pork in neighboring East African countries and the biggest consumer of pork in Africa (second-largest after China on a global scale), with an estimated export value of 167 tons of pork in 2011 and consuming 3.5 kilograms per person per annum on average.<sup>[9,8]</sup> Accordingly, it makes Uganda a potential epicenter of taeniasis, cysticercosis, and neurocysticercosis. Recent statistics show an increase of 21.287% in the pig population in Uganda, which had an estimated population of 3.18 million in 2008 compared to 4.04 million in 2016<sup>[9]</sup>. These statistics clearly illustrate the economic significance of the pork industry to the Ugandan population. Accordingly, it is notable that NCC is more prevalent among farmers and non-Muslim people who eat pork.

Transmission of NCC in humans is interdependent with the hygiene and management of pork in pig sties and abattoirs. The lack of adequate inspection, access constraints to safe drinking water, inappropriate pork preparation, open defecation, and public awareness of proper hygiene and waste disposal have been critical factors for the spread and proliferation of NCC among communities in Uganda<sup>[6,7,10]</sup>. In abattoirs, butchers are expected to have no protective gloves or clothing and usually use one machete for several pigs in an unsanitary way<sup>[11]</sup>. These malpractices contribute to the eventual spread of *T. solium* in pigs, thus leading to NCC in humans<sup>[6,11,12]</sup>.

According to the World Health Organization (WHO), the last map on *T. solium* was published in 2015, with the updated version published in April 2022 significantly elaborating on the necessity of thorough control over Neglected Tropical Diseases (NTDs) by the year 2030 in endemic territories (including Uganda)<sup>[10]</sup>. According to the published WHO roadmap on NTDs, it is critical to note that there must be more data on specifically NCC in endemic regions (including Uganda). More data on NCC in Uganda (especially in the southern part) needs to be made available, and this systematic review serves as a call for further research on NCC in Uganda and tropical regions at large. This review will investigate the distribution of NCC in Uganda (in the Northern and Eastern parts of Uganda), its epidemiology, efforts to mitigate NCC in Uganda, challenges faced throughout the process, and recommendations for implications.

## 2. EPIDEMIOLOGY

Usually, the treatment of NCC cysts requires precautions since the destruction of the cyst can lead to severe inflammations. The proper treatment of NCC involves high doses of praziquantel

accompanied with albendazole (if necessary), along with supporting therapy of corticosteroids and/or anti-epileptic drugs, and arguably surgery [1]. In most cases, complications can occur due to improper dosage, drug administration, or ignoring the severity of the disease, thus causing the degeneration of the cyst into a granuloma that can drastically result in a calcified lesion that is believed to be a significant cause of seizures (the calcified lesion proliferates in the parenchyma of the brain) [3,13,14,15]. These findings are incredibly vital because 10% to 20% of people in endemic populations display calcified cysts on computer tomography (CT) scans of the head [16], even though 5% to 22% of these patients are asymptomatic [9].

Recent data published in 2021 by WHO highlight an estimated total number of both symptomatic and asymptomatic NCC cases of 2.56-8.30 million [14]. According to the undermentioned Table 1 that was illustrated in 2010, there were nearly 3,000 deaths in Uganda due to NCC, leading to an estimated number of 9000 new cases of epilepsy that led to expenditures of accurately \$8,000 per new case [7,17].

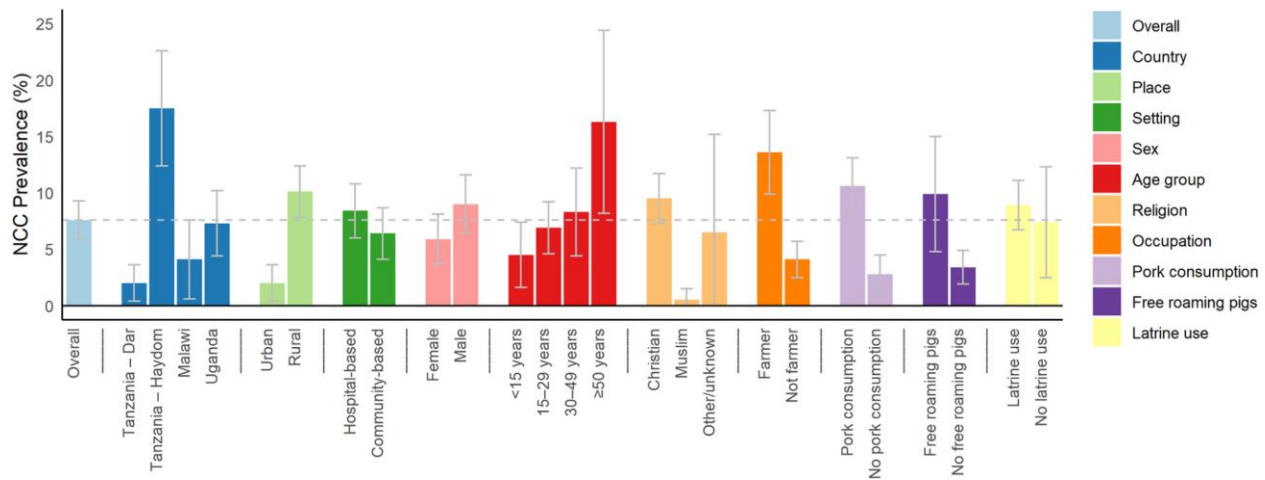
**TABLE 1: Prevalence of epilepsy and neurocysticercosis (NCC) in people with epilepsy (PWE) in Uganda by sex and age, the reference year 2010**

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 (0.118-0.0616)
Female	0-12	N/A	Assumed 0
Female	12-18	0.085 (0.076-0.0095)	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)	0.0583 (0.366-0.779)

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

According to the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH), there are five forms of NCC notably, viable parenchyma (VPN), single enhancing lesions (SEL), calcified parenchymal NCC (CPN), ventricular NCC (IVN), and subarachnoid NCC (SAN) [16]. Notably, the statistics show a higher prevalence of extraparenchymal NCC (another form of NCC) in females than in males; arguably, some scientists attribute some clinical NCC forms to the higher values of CSF Pleocytosis in

females than in males<sup>[18]</sup>. Gender differences in the presentation and management of neurocysticercosis may exist, but they are not typically a primary focus of research in the scientific field; thus, we cannot precisely attribute the variations in NCC symptoms to gender differences.



**Fig 1. Neurocysticercosis prevalence disaggregated by study-specific and socio-demographic factors.**

According to Figure 1, NCC commonly affects people who live in rural settings more than those living in urban settings. This finding is elucidated by the fact that there is more prevalence in poor hygiene locations and communities associated with contact with free-roaming pigs<sup>[19]</sup>. It is commonly seen in rural settings where hygiene is trivial to the communities that lack knowledge on promoting hygiene to fight communicable diseases. Additionally, communities dominated by Muslim individuals are generally unaffected or minimally affected by *T. solium* and its related forms, including NCC. Theoretically, it is because Muslim communities are typically prohibited from consuming pork, thus causing the disease to be barely prevalent<sup>[19]</sup>. With over 1.1 million pig farmers and several other shareholders in the pork value chain whose sustenance depends on pork<sup>[9]</sup>, it is fundamental to note the necessity of quality control and mandatory inspection of pigsties and abattoirs to mitigate NCC, particularly in Uganda.

### 3. EFFORTS TO MITIGATE NCC IN UGANDA

It is fundamental to highlight the significance and the value of pig sties for the population. In the development projects instilled by the government, the pig industry is a vital pillar towards agricultural sustainability in Uganda<sup>[20]</sup>.

The mitigation of NCC in Uganda is not an impossible and insurmountable objective. Some regions are adequately tackling this problem and have been using different approaches and medical drugs to mitigate *T. solium* and NCC. Medical drugs, namely praziquantel, and niclosamide, are to help to eliminate such foci steadfastly<sup>[10]</sup>.

A study in Peru showed that a nation could completely eradicate *T. solium* transmission, where they successfully eliminated cysticercosis in 105 of 107 villages. Health education or sanitation control must be followed to have a long-lasting effect. Studies showed that six intervention types were collectively summarized, and these can effectively eradicate NCC in Uganda; these interventions were community sanitation improvement, mass drug administration, national policy, health education, pig vaccination and treatment, and combined human and pig treatment [21,22,23].

Another study showed that in most endemic regions, NCC could be mitigated by mass drug administration, pig vaccination and treatment, and combined human and pig treatment because they decrease *T. solium* prevalence rapidly and don't require country administrative infrastructures [22].

Another effort that can be put in place is establishing a committee or a single person responsible for implementing preventive and control measures at various organizational levels (regional, national, district, or community). Promote and justify the control program at the district, national, and international levels using valid estimates of the health and economic burden of human taeniasis/cysticercosis [24].

Also, creating a reporting system - as simple as possible - at all levels of existing medical (taeniasis, cysticercosis) and veterinary (cysticercosis) services will help eradicate NCC. Also, creating and supporting groups of people at the national or local levels involved in developing and implementing prevention and control programs in highly endemic areas will promote the effective mitigation of NCC in Uganda [24].

#### **4. CHALLENGES TO MITIGATE NCC IN UGANDA**

Even though the prevention of NCC is required, some challenges hinder its mitigation. Some households had latrines that some family members could not use. This was associated with a significant increase in cysticercosis seroprevalence. Also, children under the age of 5 years and weak, less mobile people (the old and sick) tend to defecate carelessly, thereby increasing the risk of environmental contamination with the *T. solium* eggs [24].

In most of Sub-Saharan Africa, insufficient awareness regarding these latter conditions may impede endeavors aimed at managing the most preventable trigger of epilepsy within the sub-Saharan African locale, which is NCC [25]. Despite possessing adequate knowledge and awareness among pig farmers regarding the significance of pig confinement for disease control, the practice of free-range pig keeping persisted. Additionally, there existed misconceptions and beliefs surrounding pig confinement, including the notion that confined pigs exhibit inferior growth compared to their free-range counterparts. This may be true if the latter are poorly fed, which can cause more severe complications [26]. Another challenge in Uganda is irregular and ineffective meat inspection of pigs slaughtered by the butchers due to the lack of a centralized slaughter place, adequate transport for the meat inspectors, and political interference [27].

In most LMICs, including Uganda, diagnosis of NCC is complex and most accurately diagnosed using clinical neuroimaging, which is unavailable in most hyper-endemic regions and many areas endemic to NCC; this technology is either unavailable or prohibitively expensive [28]. Also, Within LMICs, limited economic capacity makes it difficult to allocate resources given other national priorities, such as HIV/AIDS, tuberculosis, malaria, and so on [21].

Finally, the active participation of village residents can be strenuous, even though the involvement of these essential stakeholders is vital. Disregarding and neglecting the disease is considered a significant barrier to mitigating NCC in the community [28].

## 5. RECOMMENDATION

NCC is one of the NTDs that requires immediate national, regional, and international attention from policymakers. The appropriate measures for controlling NCC have to be conducted from the perspectives of various factors. Regarding the causative agent, there must be expeditious control of the pork industry that acts as a catalyst for spreading *T. solium* in the community. Controlling the pork industry implies vaccinating pigs to prevent them from acquiring *T. solium* eggs. According to a study that was conducted in various districts of Uganda, including Bukedea, Kumi, Lira, and Kampala, it was concluded that vaccinating pigs with the TSOL18 vaccine and treating infected pigs with oxfendazole led to a significant reduction in the prevalence of porcine cysticercosis in the intervention area, with the prevalence dropping from 17.2% at baseline to 0% at the end of the study thus making TSOL18 and oxfendazole efficacious approaches for reducing the transmission on *T. solium* in pigs [19].

The utilization of vaccines and anti-helminthic drugs acts as the foundation for the mitigation and eradication of NCC in Uganda and on a global scale. In light of these approaches, there are some actions that policymakers should take to control NCC and other manifestations of *T. solium*. Respectively, people should be educated on proper food hygiene and eradicating open defecation. Additionally, policymakers should monitor pigsties, conduct regular meat inspections, and ensure no free-roaming pigs to reduce the spread of *T. solium* and its manifestations in humans (including NCC) [1].

Finally, there is a necessity for profound and updated studies on the prevalence of NCC in Uganda. Many available data are from 2010, and many changes have occurred throughout the past fourteen years. The essential requirements for diagnosing NCC include neuroimaging tools, which include computerized tomography (CT) for calcified lesions and magnetic resonance imaging (MRI) for seizures or hydrocephalus, with the support of serology [16]. These facilities are not available or scarce, especially in rural areas of Low-income countries like Uganda, making it challenging to identify and treat patients. Availing of these facilities would firmly and steadfastly support the mitigation and eradication of NCC in Uganda and on a global scale.

## 6. CONCLUSION

NCC is considered an NTD, and it requires the attention of both the local and international forces. Its spread is not only associated with hygiene but also the management in the clinics, as well as a necessary erudition of the severity of the disease from experts in neuroscience, academic institutions, and the general healthcare system. It is imperative to properly manage the cysts in the brain as they can calcify and cause severe consequences. The scarcity of diagnosis equipment should discard the responsibilities of local forces, but this should be an acquaintance that ignoring NCC and not treating it at an early age contributes to severe symptoms that can, unfortunately, lead to death.

## AUTHOR CONTRIBUTIONS

**Divin Jonathan IGIRANEZA:** Conceptualization; methodology; project administration; writing-original draft. **Darius BENIMANA:** Conceptualization; methodology; project administration; writing-original draft. **Dr Taofeek Tope Adegboyega, PhD:** Supervisor-editing.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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