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Spatial and temporal distribution of *Taenia solium* and its risk factors in Uganda

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ABSTRACT

Objectives: The lack of subnational mapping of the zoonotic cestode *Taenia solium* in endemic countries presents a major challenge to achieving intensified *T. solium* control milestones, as outlined in the "World Health Organization neglected tropical disease roadmap by 2030". We conducted a mapping study in Uganda, considered to be endemic, to identify subnational high-risk areas.

Methods: *T. solium* prevalence data, adjusted for diagnostic sensitivity and specificity in a Bayesian framework, were identified through a systematic review. Spatial autocorrelation and interpolation techniques were used to transform demographic and health survey cluster-level sanitation and poverty indicators, overlaid onto a pig density map for Uganda into modelled porcine cysticercosis (PCC) risk maps.

Results: A total of 16 articles (n = 11 PCC and n = 5 human cysticercosis (HCC) and/or human taeniasis) were included in the final analysis. The observed HCC prevalence ranged from 0.01% to 6.0% (confidence interval range: 0.004-11.4%), whereas the adjusted PCC ranged from 0.3 to 93.9% (uncertainty interval range: 0-99.8%). There was substantial variation in the modelled PCC risk factors and prevalence across Uganda and over time.

Conclusion: The high PCC prevalence and moderate HCC exposure estimates indicate the need for urgent implementation of *T. solium* control efforts in Uganda.

Introduction

The endemic transmission of the zoonotic cestode *Taenia solium* continues to result in a substantial global human health burden and economic losses, particularly to communities and poor smallholder pig farmers across sub-Saharan Africa, South and Central America, and across Asia [1].

Humans are the definitive hosts harboring the adult worm (taeniasis) after consuming undercooked or raw pork infected with the larval stage of *T. solium*. Scavenging pigs are exposed to eggs dispersed in the environment through open defecation by taeniasis carriers. This results in the larval-stage cysts developing in the porcine intermediate host (porcine cysticercosis; PCC). Environmental contamination with *T. solium* eggs in areas with poor sanitation and hygiene provides a pathway for humans, as aberrant hosts, to accidentally ingest eggs, with the larval stages encysting in striated/heart muscles and subcutaneous tissues of the human host (human cysticercosis; HCC). There is also a potential for en-

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cystment in the central nervous system, including the brain, causing human neurocysticercosis (NCC).

NCC is a highly pleiomorphic disease in humans, largely due to variations in the location and number of cysts. However, the major burden is experienced due to seizures and other neurological sequelae due to the degeneration of viable cysts. In endemic settings, *T. solium* has been estimated to cause approximately 30% of all epilepsy cases [2], and in 2010, *T. solium* accounted for the greatest burden of any food-borne parasite, with around 28,000 deaths per year and 2.8 million disability-adjusted life-years [1].

Despite being declared eradicable nearly 3 decades ago [3], no existing national *T. solium* control programs are in operation in endemic countries. Under the 2012 World Health Organization (WHO) roadmap on neglected tropical diseases (NTDs), *T. solium* control was identified for scale-up by 2020 [4]. Although this goal was missed, *T. solium* was included in the new WHO NTD 2021-2030 roadmap, which calls for "intensified control" in hyperendemic areas of 17 countries by 2030. Endemicity at the country level has recently been updated [5]. However, there is little understanding of the distribution of *T. solium* at the subnational level, which hinders the ability to efficiently target the existing toolbox of interventions in hyperendemic areas. The intervention toolbox includes human mass drug administration with the taenicides (praziquantel, niclosamide, and albendazole). In addition, further interventions in the porcine host include pig treatment with oxfendazole, pig vaccination with TSOL18, and improved pig husbandry and hygienic practices through health education [6].

With endemic countries now able to request taenicides through the WHO to undertake pilot control efforts [7], countries are required first to conduct a rapid assessment of endemic/high-risk areas using the WHO toolkit, which guides the collection of simple, standardized indicators for the presence of infection to create a composite risk score at the subnational level [8]. These mapping efforts can be complemented by spatial statistical approaches developed within this study.

Uganda is the leading producer and consumer of pork, with the highest per capita pork consumption rate in East Africa at 3.4 kg per year, with demand continuing to rise locally and regionally [9–11], and is considered endemic for *T. solium* [5]. The national pig herd is predominately raised in smallholder systems, providing an important livelihood source to >1.1 million households in the country as of 2008 [12]. These systems are characterized by partial housing and outdoor rearing of pigs on pasture and poor sanitary conditions, which are known risk factors for *T. solium* [13]. At the country level, Dupont et al. [14] recently highlighted the large burden associated with *T. solium* in Uganda, estimating that in 2010, NCC resulted in more than 170,000 disability-adjusted life-years, with economic losses of more than $75 million. However, there has yet to be a systematic approach to understanding the variation in the level of risk for the presence or prevalence of *T. solium* across Uganda to support the targeting of interventions. Therefore, this study aimed to map all the available *T. solium* prevalence data and the PCC risk factors within Uganda, building a complete insight into the *T. solium* landscape and subnational variation of indicators.

Methods

Systematic literature review: T. solium *prevalence data*

The key elements of the review question are as follows: population (humans and pigs focusing on HCC and human taeniasis (HTT) in humans and PCC in pigs), interventions (baseline infection data measured or cross-sectional studies), context and study design (the review focused on any study conducted in any part of Uganda), and outcomes (prevalence and incidence infection markers). The time frame includes any relevant studies conducted in Uganda up to June 21, 2021, with no lower limit.

Search strategy: The search was conducted on June 21, 2021 and followed the Preferred Reporting Items for Systematic Reviews and Meta Analysis guidelines [15] on conducting systematic literature review (SLR), with a protocol developed before the implementation of the search. Full details on the search strategy, including information on the identification of additional studies, literature databases searched, search terms used for each database, inclusion/exclusion criteria, literature screening/reviewing, and data extraction (including variables extracted in Supplementary Table 1) are included in the Supplementary materials (pp. 12–13).

Prevalence confidence interval and adjustment method

All analyses were conducted using the R environment for statistical computing version 4.1.3 [16]. The binomial confidence intervals not provided by the authors were calculated using the in-built package 'stats'. Informed PCC district-level prevalence was estimated in a Bayesian framework [17] from the reported observed prevalence estimates extracted from the studies. To perform the adjustment, literature-based estimates for sensitivity and specificity of each diagnostic test were identified and used to specify uniform priors (Supplementary Table 2, adapted from Braae et al. [18]). The adjustment was performed using the 'prevalence' package in R [19]. Apparent prevalence was only adjusted for each study where information on the number sampled, and the number of positive individuals was available for each diagnostic used.

Porcine cysticercosis risk factor mapping

The information on risk factors and data sources are provided in Table 1, with PCC risk factor maps for Uganda produced in 2001, 2006, 2011, and 2016.

The variables for each year of the 2001-2016 Uganda Demographic and Health Surveys (DHS) were aggregated at the cluster level (approximately 20 households) to represent the proportion of households with each variable. First, the spatial autocorrelation for each clustered variable was assessed by computing a semivariogram and fitting variogram models (spherical or wave models to approximate the relationship between semivariance and distance; the parameters used for each model are found in Supplementary Table 3 and the model fits are provided in Supplementary Figure 1) with the gstat package (version 2.0.7) in R [20,21]. Spatial interpolation methods were then used to transform cluster-level point data into a smooth map of the proportion of households with the variable of interest across Uganda, using the ordinary kriging procedure (with the gstat package in R) and accounting for spatial autocorrelation assessed in the previous step. Pig population densities were already available as a smooth distribution map across Uganda, so the spatial analysis steps were not performed for this variable. For all three variables, the interpolated data points were categorized as high or low based on each variable's upper third (66th centile) distribution of the data (Table 1). Next, each variable (risk factor) was plotted as a binary variable, categorized as either high or low and overlayed into a single composite risk factor map for each year (2001-2016). In the composite maps, the risk factors are shown in yellow (poor sanitation coverage, risk factor A), purple (high pig density, risk factor B), and red (high levels of poverty C), with the highest risk zones indicated in brown (all three risk factors, ABC). The full reproducible code for this analysis can be found at: https://github.com/SCIFoundation/Uganda_porcine_cysticercosis_risk_mapping.

Table 1
Risk factor, data source and threshold values for modelled porcine cysticercosis risk mapping.

Year	Risk factors & data sources		Threshold values to define proportion of population between low/high[c]	
	Sanitation[a] & poverty index[b]	Pig population density	Poor sanitation	Poverty
2001	Uganda Demographic and Health Surveys (DHS) [47]	Modelled livestock densities from the Gridded Livestock of the World database for 2007 [48] and adjusted to 1 km spatial resolution in Robinson et al. [49]	0.384	0.338
2006	DHS [50]		0.441	0.728
2011	DHS [51]		0.408	0.666
2016	DHS [52]		0.885	0.675

[a] households with no latrine or open/uncovered latrine facilities;
[b] household-level poverty (based on the level of assets for each household, with those in the lowest/poorest 40% selected);
[c] Pig densities provided by Robinson et al. [49] with threshold set to ≥1 pig per km^2.

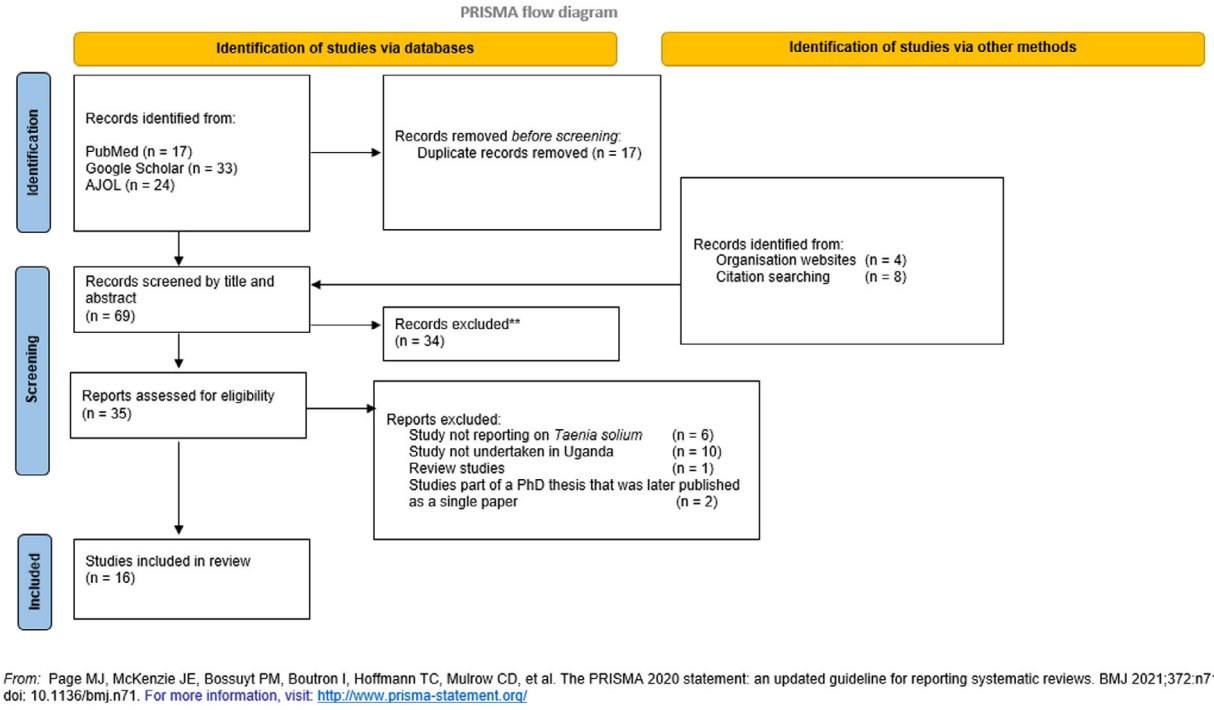

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta Analysis flow diagram detailing the number of studies identified, screened and assessed for eligibility, and included in the Uganda *Taenia solium* prevalence data review.

Results

The database search generated 86 records, 69 of which were retained after removing duplicates. After screening titles and abstracts, 35 full-text manuscripts were reviewed with 16 articles retained for data extraction (n = 11 pig studies and n = 5 human studies; see Supplementary appendix: Full data extraction tool). The search and screening strategy results are shown in Figure 1 and described in detail in the Supplementary material (p. 12–13).

There was an increased frequency of publications from 2015 onwards in comparison to previous years, with one study per year in 1996, 1997, 2002, 2008, 2009, 2013, 2015, 2018, and 2020 and two studies per year in 2017, 2019, and 2021 (Supplementary Figure 2).

The spatial distribution of the studies (Figure 2) shows a relative concentration of earlier studies in the central, mideastern, and western areas, followed by a larger concentration of later studies (*i.e.*, 2010 onwards) in northern regions of the country (HTT/HCC studies in Table 2 and PCC studies in Table 3). The areas in northeastern and southwestern Uganda are devoid of any *T. solium* studies.

The map was produced by finding the longitudinal average of the published informed occurrences. Districts with a zero prevalence for PCC included Kayunga, Kampala, Lwengo, Nakasongola, Wakiso, Mpigi, Bukedea, Kamuli, and Kumi. Owing to the higher number of PCC entries, the prevalence was divided into five class ranges. The other records represent the single-point estimates (circles with dots). The maps were produced in QGIS version 3.24 [22].

Human taeniasis and cysticercosis

Five human surveys (Table 2) were carried out between 1994 and 2013 [23–27]. The only study focusing on HTT sampled school-aged children [24], whereas the other studies focusing on HCC sampled all the age groups. The prevalence of HCC ranged between 0.01% and 6.0% based on indirect immunofluorescence test, immunoblot, and antibody enzyme-linked immunosorbent assay (ELISA) (assuming that Ngugi et al. [27] reported HCC only and not a combined HCC/HTT estimate, which was unclear from the study). Furthermore, in an onchocerciasis nodule prevalence survey conducted in Moyo and Kanungu, Katabarwa et al. [26] found that a proportion of 33.3% and 66.7% of the nodules, respectively, were *T. solium* cysts, indicating the presence of *T. solium* in this area, though without being able to determine prevalence.

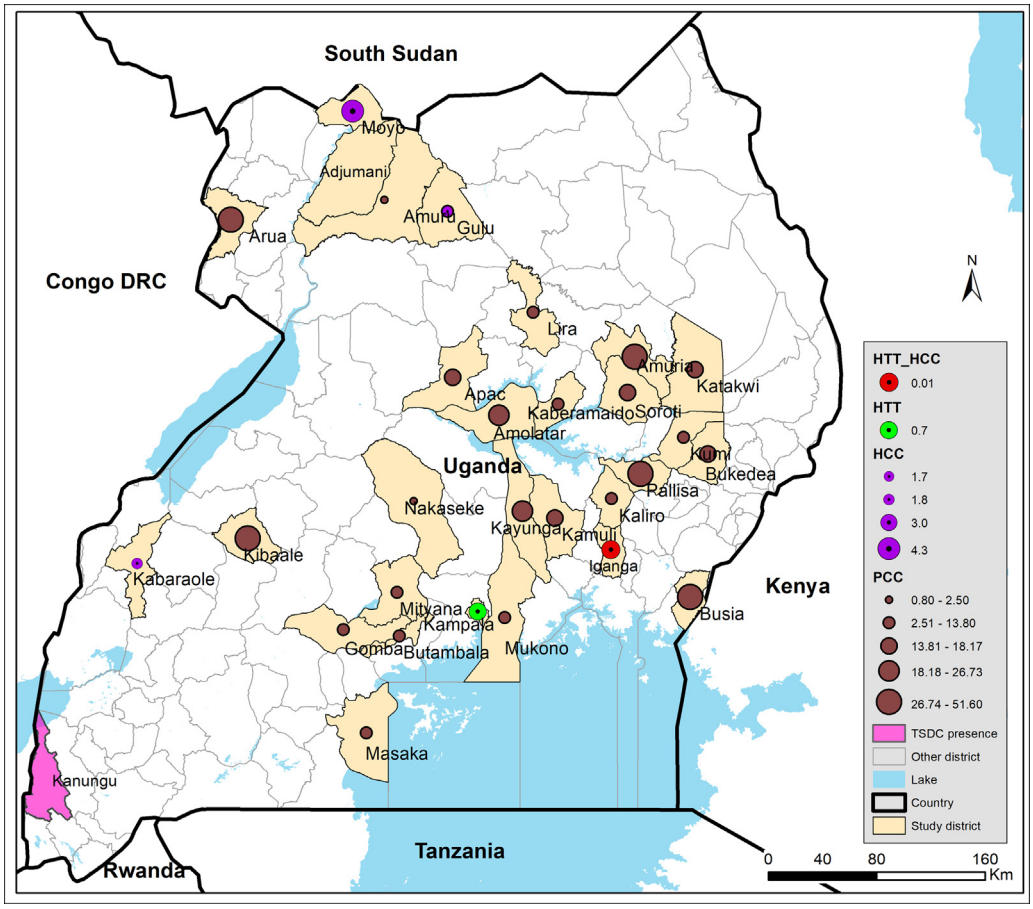

Figure 2. Spatial distribution of *Taenia solium* studies in Uganda.
HCC, human cysticercosis; HTT, human taeniasis; PCC, porcine cysticercosis.

Table 2
A table summarizing studies determining presence or prevalence of HTT and HCC. Ordered by year survey conducted (from earliest to most recent).

Reference	Year survey conducted	Disease	Diagnostic used	District	Prevalence	Confidence intervals
Kaiser et al. [25]	1994	HCC	Indirect immunofluorescence test	Kabarole	1.8	0.1-11.4[a]
Kabatereine et al. [24]	Not reported	HTT	Microscopy	Kampala	0.7	0.5-1.0[a]
Katabarwa et al. [26][b]	2005 2006	HCC	Excision, sectioning and staining of cysts	Moyo Kanungu	Not calculated[b]	
Ngugi et al. [27]	2009	HTT & HCC	[c]*Immunoblot*	Mayuge/ Iganga	0.01[c]	0.004-0.03
Alarakol et al. [23]	2012-2013	HCC	Ab-ELISA	Gulu Adjumani Moyo	5.7 6.0 3.3	4.2-7.2 4.5-7.5 1.8-4.8
			[c]Immunoblot	Gulu Adjumani Moyo	70.6 94.4 100.0	44.0-88.6 70.6-99.7 65.5-100.0

Ag, antigen; Ab, antibody; ELISA, enzyme-linked immunosorbent assay; HCC, human cysticercosis; HTT, human taeniasis.
[a] Confidence intervals calculated by systematic literature review authors.
[b] Report on nodule prevalence, not able to calculate population level prevalence from this data. Authors report results for *Taenia solium* based on exposure (Abs) to the larval-stage (cysticercosis) using western blot, and the adult tapeworm (taeniasis) using rES33 antigen [53], although not specified if immunoblot or ELISA-based-with *T. solium* positivity based on both tests used.
[c] Used as a confirmatory test for the Ab-ELISA.

Porcine cysticercosis

A total of 11 studies on PCC were conducted between 2002 and 2019 (Table 3). All studies reported the prevalence of PCC using different diagnostic techniques, including partial and full carcass dissection (used on n = 4 occasions), tongue/lingual palpation (n = 4), postmortem meat inspection conducted by meat inspectors/obtained from abattoir records (n = 1), antigen (Ag)-ELISA (n = 4), or a combination of these (n = 1). Only one study included a *T. solium* control intervention [28], with baseline prevalence estimates reported in Table 3.

Informed porcine cysticercosis prevalence variation across Uganda

Informed prevalence of PCC ranged from 0.3% to 93.9% (Table 4; grouped by district), with the districts with the lowest/highest informed prevalence (Figure 3) closely following the spatial distribu-

Table 3
A table summarizing studies estimating prevalence of porcine cysticercosis. Ordered by year survey conducted (from earliest to most recent).

Reference	Year survey conducted	Diagnostic used	District	Prevalence	Confidence intervals (if calculated)
Kisakye and Masaba [54]	2002	Partial CD	Lira	27.7	18.7-38.8[a]
Waiswa et al. [55]	2005	Ag-ELISA(B158/B60)	Kamuli	8.5	6-11
			Kaliro		
Nsadha [56]	2011	LP	Kaberamaido	6.9	5.6-8.4[a]
	Not reported	Ag-ELISA(HP10)	Kayunga	21.5	12.7-33.8[a]
			Kamuli	28.1	19-41.32[a]
			Kaliro	23.2	14.2-35.2[a]
			Kaberamaido	20.3	11.7-32.6[a]
			Apac	28.1	17.9-41.0[a]
			Amolator	33.9	22.6-47.1[a]
			Arua	73	60.1-83.1[a]
			Busia	89	77.8-95.0[a]
			Kibaale	86	72.6-93.7[a]
			Masaka	85	72.9-92.5[a]
		LP	Kayunga	0	
			Kamuli	12.9	
			Kaliro	4.1	
			Kaberamaido	6.9	
			Apac	7.7	
			Amolator	8.2	
			Arua	8.5	
			Busia	6	
			Kibaale	4	
			Masaka	7	
	2011	Ag-ELISA(HP10)	Kampala - Wambizzi Abattoir	38.0	
		Meat Inspection	Kampala - Wambizzi	0	
	2005	Retrospective review meat	[b]Kampala - Wambizzi Abattoir	0.005	
	2006	inspection records		0.007	
	2007			0.02	
	2008			0.02	
	2009			0.008	
	2010			0.009	
Kungu *et al.* [42]	2013	Ag-ELISA (HP10 and ApDia)	Kamuli	13.5	10.4-17.3[a]
			Masaka	11.7	8.7-15.5[a]
			Mukono	11.2	8.4-14.8[a]
Zirintunda and Ekou [40]	2014	Partial CD	Soroti	18.0	12.8-24.6
Kungu et al. [57]	2015	Ag-ELISA(B158C11A10/B60H8A4)	Lira	6.9	2.9-13.9
			Moyo	13.2	7.1-21.2
Nsadha *et al.* [28]	2016-2017	Full CD	Bukedea	17.2	9-29.9[a]
			Kumi	15.1	7.2-28.1[a]
			Kumi	8.1	3.3-20.4[a]
Kungu et al [58]	2017	Partial carcass dissection followed	Kayunga	0	
		by Ag-ELISA (HP10)	Lwengo	0	
			Nakasongola	0	
			Wakiso	0	
			Butambala	10.9	4.1-24.4[a]
			Gomba	9.7	5.2-17.1[a]
			Kampala	0	
			Masaka	1.2	0.2-4.7[a]
			Mityana	11.1	3.62-27[a]
			Mpigi	0	
			Mukono	10	1.8-33.1[a]
			Nakaseke	2.5	0.1-14.7[a]
			Bukedea	0	
			Kamuli	0	
			Kumi	0	
			Amuria	51.6	33.4-69.4[a]
			Pallisa	42.9	11.8-79.8[a]
			Katakwi	16.7	2.9-49.1[a]
			Soroti	15.9	8.3-27.7[a]
			Apac	16.7	6.3-34.5[a]
			Lira	20.7	8.7-40.3[a]
Agopiyo [59]	2018-2019	Partial carcass dissection	Arua	4.69	1.2-14.0[a]
Alarakol et al. [60]	2019	Lingual palpation	Amuru	0.8	0.04-5.0[a]
			Gulu	12.9	7.7-20.7[a]

Ag, Antigen; CD, carcass dissection; ELISA, enzyme-linked immunosorbent assay; LP, lingual palpation.
[a] Confidence Intervals calculated by systematic literature review authors (where numbers sampled, number positive data available).
[b] Prevalence calculated at abattoir and not district-level.

Table 4
A table showing the informed PCC prevalence ranges by district. Ordered alphabetically by district.

District	Year range	PCC Informed prevalence range (95% uncertainty intervals)	References
Amolator	2011	22.7-27.6 (1.3-60.5)	[56]
Amuria	2017	46.2 (49.7-62.2)	[57]
Amuru	2019	5.30 (0.3-22)	[60]
Apac	2011-2017	7.4-25.7 (0.6-55.5)	[56,57]
Arua	2011-2019	4.5-80.1 (0.2-99.2)	[56,59]
Bukedea	2016-2017	14.8-18 (0.5-61.2)	[28,57]
Busia	2011	19.6-93.9 (1.1-99.8)	[56]
Butambala	2017	1.5 (0.1-8.4)	[57]
Gomba	2017	0.5 (0-3.0)	[57]
Gulu	2019	58.7 (9.9-96)	[60]
Kaberamaido	2011	5.3-23 (0.3-50.4)	[56]
Kaliro	2011	10.8-13.2 (0.5-32.9)	[56]
Kampala	2017	23.7 (1.0-81.8)	[57]
Kamuli	2011-2017	16.7-59.7 (0.9-92.7)	[56,57]
Katakwi	2017	7.8 (0.3-30.5)	[57]
Kayunga	2011-2017	5.1-9.6 (0.2-33.5)	[56,57]
Kibaale	2011	12.4-91.1 (0.7-99.8)	[56]
Kumi	2016-2017	9.9-23.7 (3.6-81.8)	[56,57]
Lira	2002-2015	1.8-34.1 (0.1-57.7)	[54,57]
Lwengo	2017	23.7 (1.0-81.8)	[57]
Masaka	2011-2017	0.3-91.1 (0-99.8)	[56,57]
Mityana	2017	5.1 (0.2-26.2)	[57]
Mpigi	2017	5.1 (0.2-26.2)	[57]
Moyo	2015	9.2 (3.8-15.4)	[57]
Mukono	2017	3.4 (0.1-16.2)	[57]
Nakaseke	2017	1.4 (0.1-6.5)	[57]
Nakasongola	2017	23.7 (1.0-81.8)	[57]
Pallisa	2017	39.1 (7-73.4)	[57]
Soroti	2014-2017	5.1-19.2 (0.5-34.3)	[40,57]
Wakiso	2017	11 (0.40-47.20)	[57]

PCC, porcine cysticercosis.
Note: The average (median) PCC value, where a range exists for a district (in Table 4), is calculated and then plotted in Figure 3, based on the appropriate median PCC prevalence band in the legend of Figure 3.

tion of apparent prevalence across districts (Figure 2). Large uncertainty ranges were observed around most estimates.

The average minimum and maximum prevalence values were calculated and plotted for districts with informed prevalence ranges. The maps were produced in QGIS version 3.24 [22].

Spatiotemporal variation in porcine cysticercosis risk factors between 2001 and 2016

The composite PCC risk maps for 2001, 2006, 2011, and 2016 show the varied risk factors geographically and over time (Figure 4; Supplementary Figures 3-6 show the individual risk factor maps for each year). In 2001, high levels of poor sanitation (A; yellow) and poor sanitation with high pig densities (AB; green) predominate in the northeast and northcentral regions, respectively, with pockets of high pig densities combined with high poverty levels (BC; pink) in the northwest, central, south, and southwest regions. Large parts of the northeast transitioned from high poor sanitation (yellow) to combined with high poverty (AC; orange), whereas the northcentral/east region transitioned to all three risk factors (ABC; brown). There were additional pockets in 2006 of high poor sanitation and poverty (orange), and all three (brown) emerged from the northwest. High poverty disappeared from combined high poverty pig densities (pink) in those pockets found from 2001. However, new pockets of high poor sanitation and high pig densities (green) emerged in central/southern parts of Uganda. In 2011, areas with all three risk factors (brown) spread into the northcentral regions. The areas of high poor sanitation with high poverty (orange) disappeared from the northeast tip and northwest/western regions. These re-emerged to some degree again in 2016 in these areas of Uganda, whereas areas with all three risk factors retreated largely from northcentral areas in 2016.

The distribution and confluence of risk factors (A = high poor sanitation, B = high pig density, C = high poverty) are indicated. The water bodies (lakes/rivers) are included in blue. Districts relevant for 2020.

Discussion

To the best of our knowledge, this is the first study to collate and assess national *T. solium* prevalence data in Uganda and explore the modelled spatiotemporal variation in PCC risk factors. This review has shown increasing interest in research on *T. solium* in Uganda in recent years. However, most studies focused on PCC and were cross-sectional in nature, aiming at establishing the prevalence and risk factors. Cross-sectional studies are often preferred in the study of disease prevalence because they are easier to conduct and require fewer resources and time than other the types of studies [29]. However, only one study reported the results of a control trial [28]. This is unlike the neighboring Tanzania, where many studies have been conducted for various reasons, including establishing prevalence, incidence, risk factors, and co-morbidity with other diseases, such as HIV and epilepsy, as summarized by Ngowi et al. [30]. The greater volume of research work conducted in Tanzania could be attributed to the existence of initiatives supporting research on *T. solium*, including the Cystinet Africa research consortium (https://www.cystinet-africa.net/), which has funded several research projects over the recent years.

Only one study reported the prevalence of taeniasis in school-aged children from 98 primary schools using microscopy [24]; however, no attempt was made to identify the parasite at the

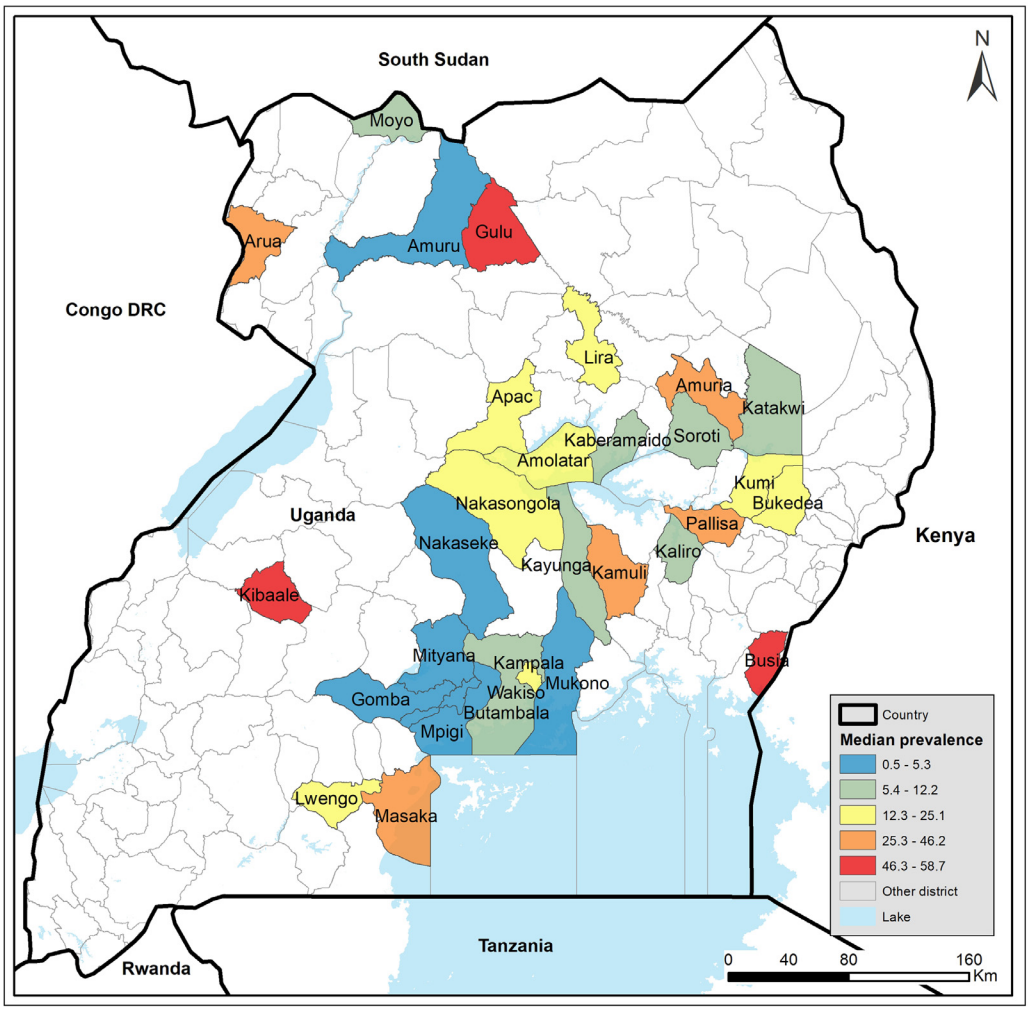

Figure 3. A map of Uganda illustrating the informed prevalence of porcine cysticercosis.

species level, and the infection could have been due to *Taenia saginata* (beef tapeworm). The study also reported co-infection with other intestinal parasites, including *Trichuris trichiura, Ascaris lumbricoides*, and hookworm. Unlike taeniasis, these intestinal parasites have received more attention from researchers in Uganda, especially in school-aged children [24,31]. This reaffirms that *T. solium* research has been neglected due to limited stakeholder awareness and possibly competing public health priorities in many endemic countries, particularly in relation to taeniasis. Three studies reported HCC, two in northern Uganda, and one in the mideastern region. The possibility of NTD co-infections in some regions in Uganda was highlighted in an onchocerciasis survey [26], where a proportion of excised nodules were incidental HCC cysts. Ngugi et al. [27] also identified a low level of exposure to *T. solium* antibodies (0.01% seroprevalence) in the Iganga and Mayuge districts. However, whether these estimates referred to HCC or HTT antibodies was not evident.

Most studies in Uganda were clustered in the mideastern and central regions, where there is a confluence of risk factors, including high pig densities, poverty, and poor sanitation [32]. Study site selection is generally guided by several factors, including the probable presence of infection risk factors and the contextual factors, to support the research in a specific study area [33]. From 2001 to 2016, a highly dynamic picture emerged of changing *T. solium* PCC risk as captured through the risk mapping analysis. The most significant changes are observed in the northern regions, particularly in northcentral and northeastern Uganda. In the northeast, from 2001 to 2006, there was a transition from poor sanitation in isolation to poor sanitation combined with high poverty. In addition, in 2006, all three risk factors in combination emerged in large parts of northcentral Uganda. The appearance of poverty across the northern regions in 2006 may be related to the large population movement of internally displaced persons, attributed to the civil conflict experienced in this region [34]. The earliest study in the central region was published in 1997 [24], in contrast to the earliest PCC study in northern Uganda published in 2017 [23]. Lack of research in northern Uganda until recently is likely driven by previous insecurity in the region and by assumed low pig densities due to the traditional predominance of pastoral systems, with pig populations in the northern region estimated at 340,460 compared with 1,307,460 and 699,680 in central and eastern regions respectively [34]. In addition, geographic targeting of earlier studies in regions close to major universities in Kampala may have driven research priorities particularly before 2010.

Moreover, the smaller dispersed pockets of high PCC risk in northern areas also require further work to determine whether these pockets are of sufficient geographic scale to maintain the *T. solium* transmission cycle. For example, the local migration patterns and extensive pig trade networks are essential for maintaining endemic equilibria in other settings [35]. Within Uganda, pig trading occurs at varying geographic scales. Pigs are moved locally during trading through brokers located in the villages and

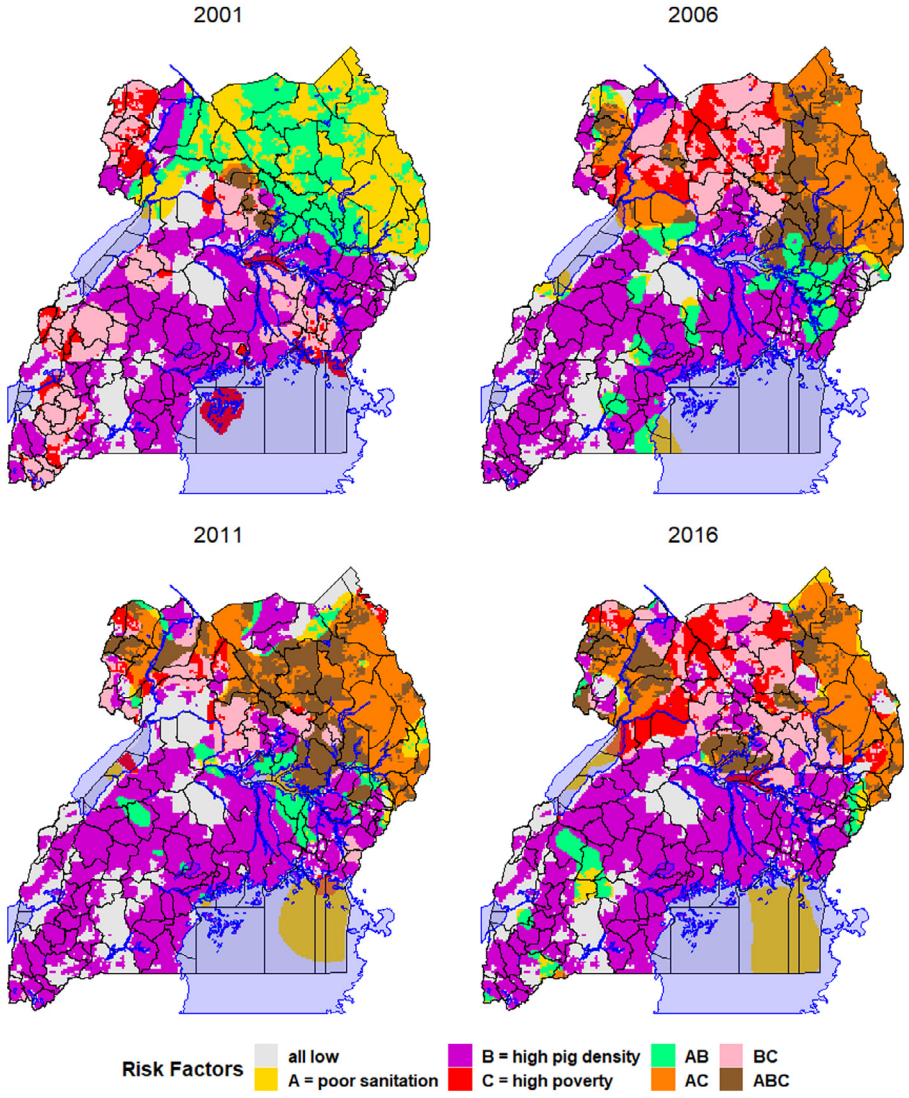

Figure 4. A map showing the distribution of porcine cysticercosis risk factors over time in Uganda.

then often moved from farm to farm or from village to village, before being shipped to urban centers for slaughter [11]. Reducing the distance pigs travel for processing is both an animal welfare and a disease-mitigating practice [36]. Although, a high prevalence of PCC in a particular village may not strongly correlate with high HCC prevalence in that village, the correlation may be high within surrounding villages and districts. Infected pigs transported to slaughter in larger cities, such as Lira in the north and Kampala, may be detected because meat inspection is relatively better enforced in these slaughter places than the rural districts. In addition, PCC cases have been shown to cluster around a tapeworm carrier [37]. This scenario may also present a risk for HCC infections within the villages due to the potential contamination of the environment with eggs from the taeniasis carrier.

One major limitation associated with the risk mapping analysis was the lack of pig density distribution maps for each of the four DHS years, with pig density mapping underpinned by data from 2007 in the Gridded Livestock of the World database. The temporal changes in pig densities may have therefore been missed, such as changing husbandry systems in northern areas, reflecting the settlement of internally displaced populations or refugees from South Sudan or fluctuating pig densities in southern areas, depending on the changes in localized pig production systems. The risk mapping, however, highlights potential gaps in epidemiological knowledge where there are varying yet high levels of risk factors for PCC, such as those identified in northern areas (*e.g.*, Abim and Agago districts). There are additional interesting spatiotemporal patterns, such as the transition from the overlap of the three risk factors from 2006 to 2011 in the western region and northeastern tip, leaving only high pig densities or areas of no risk only for these zones. The multiple risks re-emerged again in 2016. These patterns may be a true reflection of changing risk or underpinned by changes in the coding of the DHS, such as the presence of the latrine type (*e.g.*, uncovered with slab or without a slab) between 2011 and 2016.

A further limitation surrounds the lack of quantitative thresholds linking a level (proportion) of a risk factor that equates to a high risk for *T. solium* exposure. Therefore, we assumed values equal to or above the third quartile of values from distributions of DHS cluster-level values for each variable that represented a high risk for *T. solium* transmission. This cut-off was therefore used to select high-risk values from the modelled risk factor maps. Determining a quantitative relationship between pig density levels/proportion of high poverty, poor sanitation, and sustained *T. solium* transmission constitutes an important area for future research. Equally, poor sanitation, poverty, and high pig densities

are currently equally weighted. Therefore, more information is required to elucidate each risk factor's relative contributions and therefore weighting toward *T. solium* transmission. The validation of the spatial mapping method, which remains a challenge due to the paucity of prevalence data, also forms a critical future step. For example, our group will focus on validating the method against the current epidemiological situation in Uganda. This will involve updating the risk mapping for the next available DHS and identifying or conducting prevalence surveys in different modelled risk zones to validate these different risk areas.

As with many other regions of the world, most studies (11/16) focused on PCC, perhaps because it is easier to measure the study outcomes in pigs due to their short life cycle and less stringent ethical considerations. The 11 studies reported varying prevalence across different regions of Uganda using different diagnostic techniques with different sensitivities and specificities. Only one study [28] used full carcass dissection, which is considered the "gold standard" test for PCC detection because of its high sensitivity and specificity [38]. Most studies used serological tests, which are inherently imperfect [38], so the prevalence was adjusted within a Bayesian framework. Notably, there was substantial spatial heterogeneity in the informed prevalence, with a number of districts recording relatively high informed prevalence, reaffirming the high endemicity in the country as illustrated by WHO [5]. The recent systematic review of PCC in eastern/southern Africa [39] identified moderate PCC prevalence (10-20%) in Uganda. However, these were only based on four studies and reported the apparent prevalence estimates. Second, there were large uncertainty intervals associated with the informed prevalence estimates, for example, in Zirintunda and Ekou [40], where the uncertainty ranges reflected wide confidence intervals for the sensitivity/specificity values and small district-level sample sizes in 10 districts, where less than 10 pigs were sampled [41]. A few studies also lacked the full data requirements to adjust to informed prevalence. For example, Kungu et al. [42] used two Ag-ELISA tests in parallel; however, a breakdown in the numbers positive and sampled for each test was only available for the value chain type and rural/urban settings and not by district. In those studies where adjustment was not possible, findings of low (sero)prevalence may have instead reflected the presence of false positives arising from low specificity of the diagnostic test. More generally, the need to include all the studies reporting any *T. solium* infections in Uganda may have led to the inclusion of studies with potential risk for bias and studies of low quality, which is acknowledged as a limitation of the systematic literature reviews (SLR) component of the analysis.

Although, there was no extensive search of gray literature, which could be a limitation, the review highlights the dearth of data regarding the effectiveness of *T. solium* interventions in Uganda. Among all the papers, only one study by Nsadha et al. [28] explored an intervention focused on control of the parasite in the porcine host. This control trial study demonstrated a statistically significant PCC prevalence decrease in vaccinated pigs with TSOL18 and treated with oxfendazole compared with controls. Although the tools for control are available, no nationally supported control program has been implemented in Uganda thus far, with high maintained *T. solium* prevalence likely due to the absence of control efforts to date. The effective control of this parasite requires understanding the context in which the control interventions are carried out and exploring effective combinations of these control tools [33,43,44]. Therefore, this finding calls for a focus of efforts toward *T. solium* control while engaging and involving the national government. In addition, to fully benefit from the approach proposed in this study, there is a need to bring together the coordinators of the national NTD programs from both the national and regional government, veterinary departments, and academics or researchers to tap into the added value of the One Health approach, as described by Rüegg et al. [45].

Subnational *T. solium* mapping has been highlighted in the recent global *T. solium* endemicity map as a key research gap [5]. One previous study conducted for Central America and the Caribbean basin region mapped first-level administrative subdivision PCC data (obtained from a systematic literature review and assessment of gray literature sources) with pig density distributions [44]. Our study uses multiple risk factors to identify PCC risk zones, in combination with the identification and mapping of *T. solium* prevalence data, to provide a comprehensive approach to developing situational awareness for the landscape of *T. solium* in Uganda. This comprehensive risk mapping approach can help to target (i) further or new research efforts to determine the presence/prevalence of *T. solium*, (ii) the implementation of control activities, and (iii) the potential to characterize at-risk human populations for serious adverse events associated with praziquantel treatment in schistosomiasis mass drug administrations, where latent NCC may also be present [46].

The WHO mapping tool provides an important step in supporting countries to rapidly assess the epidemiological context by collating in-country knowledge and expertise to conduct desk reviews and risk assessments, with the aim of identifying high-risk geographic units. Our approach is complementary to this by providing a protocol to conduct a more systematic and technical approach using spatial statistics. This approach can build on the rapid assessment collated through the WHO mapping toolkit, providing a more structured yet timely approach to mapping the *T. solium* epidemiological landscape in a country.

The approach presented in this paper uses a spatial statistics approach within a flexible framework to complement and extend existing rapid mapping efforts, such as those based on the WHO mapping tool, or scoping studies, such as that carried out by Ngowi et al. [30]. This will not only help countries prioritize where these initial pilot control efforts are concentrated but also identify other areas for expanding control efforts or undertaking further research to understand the endemicity landscape better.

Conclusion

An accurate mapping of *T. solium* is becoming increasingly urgent, given the WHO goal to see intensified control in hyperendemic areas by 2030. Our analysis reveals marked variation in *T. solium* prevalence across Uganda and, in combination with the PCC risk maps, highlights geographic areas of potential risk, especially in northern areas, where limited research has been undertaken to date. In addition, informed PCC prevalence estimates suggest high levels of PCC infection, particularly in central areas; although, these estimates are subject to substantial uncertainty due to limited study sample sizes and suboptimal diagnostic performance. Taken together, there is clear evidence for need of further research and the urgent implementation of *T. solium* control efforts in Uganda.

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Ethical approval

Approval not required.

Declaration of Competing Interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2023.02.001.

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