# Evaluation of a point-of-care test for the diagnosis of *Taenia solium* neurocysticercosis in rural southern Tanzania: a diagnostic accuracy study

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## Summary

**Background** **Neurocysticercosis is a common cause of epilepsy in *Taenia solium*-endemic areas in sub-Saharan Africa but is often undiagnosed because of an absence of affordable diagnostic tools. This study evaluated the diagnostic accuracy of a *T solium* cysticercosis antibody-detecting lateral-flow point-of-care assay (TS POC test) for the neuroimaging-based diagnosis of neurocysticercosis.**

**Methods** **Patients with epileptic seizures or severe progressive headache were recruited consecutively from three hospitals in southern Tanzania. All patients were tested with the TS POC test. All patients positive for cysticercosis on the TS POC test and every tenth patient who was negative for cysticercosis received a brain CT examination and underwent reference testing for *T solium* cysticercosis (ie, rT24H-EITB, LLGP-EITB, and antigen ELISA). The primary outcome of the study was the sensitivity of the TS POC test for the diagnosis of neurocysticercosis.**

**Findings** **Of the 601 recruited participants, 102 (17%) tested positive for cysticercosis with the TS POC test. Overall, 48 (62%) of the 77 patients positive for cysticercosis and five (17%) of the 29 patients negative for cysticercosis on the TS POC test had CT-confirmed neurocysticercosis. The TS POC test yielded a sensitivity of 49% (uncertainty interval [UI] 41–58) for neurocysticercosis. Sensitivity was similar to that of the rT24H-EITB (44%, UI 37–51) and the antigen ELISA (50%, 43–56). For the subset of neurocysticercosis cases with at least one active (ie, vesicular) lesion, sensitivity was above 98% for the TS POC test, the rT24H-ETIB, and the antigen ELISA.**

**Interpretation** **The TS POC test showed promising results for the diagnosis of neurocysticercosis in patients with vesicular lesions, which need to be confirmed in a larger study. This test could be considered to support policies on screening patients with suspected neurocysticercosis in clinical settings, which would allow appropriate referral for neuroimaging and early treatment.**

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For the Swahili translation of the abstract see **Online** for appendix 1

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## Introduction

Neurocysticercosis is a neglected tropical disease caused by the zoonotic tapeworm *Taenia solium*. The Food and Agriculture Organization (FAO) and WHO have ranked *T solium* first on the global scale of zoonotic foodborne parasites, and the World Health Assembly has recognised the need for its control and elimination.[1] Humans and pigs are likewise affected and can develop cysticercosis by ingesting *T solium* eggs from a contaminated environment associated with poor sanitation and hygiene.[2,3] After ingestion, *T solium* eggs hatch and oncospheres enter the blood circulation through the intestinal mucosa and spread to different organs, where they encyst and become cysticerci. The disease is called neurocysticercosis if the oncospheres encyst in the CNS. In humans, cysticerci can persist for several years without becoming symptomatic. When symptomatic, the most common neurological signs and symptoms are epileptic seizures, severe progressive headache, or other focal neurological deficits, including hemiparesis and cranial nerve deficits.[4,5]

For the diagnosis of neurocysticercosis, two similar sets of criteria have been suggested: one by Del Brutto and colleagues[6] and another by Carpio and colleagues.[7] Both sets rely on neuroimaging, serological tests, and clinical and epidemiological characteristics. For neuroimaging, the tool of choice is a combination of MRI and CT. For serology, the LLGP-EITB, rT24H-EITB, and antigen ELISA tests are recommended.[8–10] Serological testing for neuroimaging selection is problematic because tests are costly, in formats that are either not easily applicable or not available, and their diagnostic accuracy is not ideal.[11–13] For these reasons, patients in resource-poor areas are rarely diagnosed with neurocysticercosis. An inexpensive, easy-to-use, field-adapted, sensitive, and specific diagnostic tool for the

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## Research in context

### Evidence before this study

Neurocysticercosis, caused by the larvae of the pork tapeworm *Taenia solium,* is common in low-income and middle-income countries. The disease presents with different neurological signs and symptoms, but most commonly with epileptic seizures. Most patients are never diagnosed because of a paucity of serological testing and neuroimaging.

In this context, WHO recognised the need for a cheap and easy-to-use point-of-care (POC) test for the disease and experts specified minimum and optimal target product profile requirements. We searched PubMed from database inception on May 13, 2023, without language restrictions, using the following terms: ("neurocysticercosis" OR "cysticercosis") AND ("point-of-care" OR "diagnostic test"). The search yielded 47 results; among those were a proof-of-concept study for a urine *T solium* antigen POC test in patients with subarachnoid neurocysticercosis using a dipstick assay, a feasibility study of a POC test based on quantum dots with a mobile phone reader for detection of *T solium* antibodies, a study on an alternating current electrokinetics biosensor for screening of *T solium* antibodies, and a review on loop-mediated isothermal amplification for the diagnosis of *Taenia* species.

### Added value of this study

We assessed the accuracy of a novel *T solium* (TS) blood-based lateral-flow POC test for the diagnosis of neurocysticercosis based on neuroimaging and compared the results with the accuracy of current serological reference tests. We found that the TS POC test performed well for neurocysticercosis at any stage and was very sensitive in patients with neurocysticercosis and vesicular lesions (considered as reflecting active infection). This subgroup often benefits from treatment with anthelmintic medication. Also, the TS POC test did not perform worse than current serological reference tests (ie, rT24H-EITB, LLGP-EITB, and antigen ELISA).

### Implications of all the available evidence

The TS POC test has potential for diagnosing people with neurocysticercosis in low-resource settings. The test fulfils most of the minimum and many of the optimal target product profile characteristics defined in the context of a WHO expert consultation. The patient access and commercialisation attributes have not been assessed yet. The test could be used to screen patients with neurological signs and symptoms consistent with neurocysticercosis to select them for neuroimaging, which treatment decisions will then be based on.

detection of cysticercosis and neurocysticercosis could overcome this laboratory challenge. Such a test does not exist yet.[14]

A WHO expert consultation identified the urgent need for diagnostic tests applicable to low-resource settings.[15,16] Therefore, research teams at the Technical University of Munich and the US Centers for Disease Control and Prevention collaborated to develop an antibody-detecting lateral-flow point-of-care test to diagnose *T solium* taeniasis, cysticercosis, and neurocysticercosis (*T solium* point-of-care [TS POC] test).

The primary aim of this study was to evaluate the diagnostic accuracy of this novel TS POC test for referral to the neuroimaging-based diagnosis of neurocysticercosis in patients with disease-typical signs and symptoms. The secondary aim of the study was to compare the accuracy of this TS POC test with current serological reference tests for the diagnosis of neurocysticercosis.

See Online for appendix 2

## Methods

### Study design

This two-stage, hospital-based, multicentre, diagnostic accuracy study was part of the SOLID project in Tanzania. The project protocol has been published elsewhere.[17,18] The study was done in the Mbeya and Songwe regions in southern Tanzania, where pigs tend to roam freely, sanitation is poor, and *T solium* is highly endemic. Patients were recruited consecutively from the mental health clinics and outpatient departments of three district hospitals (ie, Ifisi, Tukuyu, and Vwawa). Recruitment was between Jan 17, 2018, and Jan 29, 2020.

All study partners obtained ethical clearance for the SOLID project: Technical University of Munich, Klinikum rechts der Isar, Ethical Committee (299/18S); the National Ethics Health Research Committee of the National Institute for Medical research (NIMR) of Tanzania (NIMR/HQ/R.8a/Vol.IX/2597); Institute of Tropical Medicine, Belgium (IRB/AB/ac/112 Ref 1177/17); and the University of Antwerp, Belgium (EC UZA 17/31/352). The SOLID study was registered in the Pan African Trials Registry (PACTR201712002788898).

The reporting of this study followed the STARD checklist (appendix 2 pp 4–5).

### Participants

Individuals were required to have epileptic seizures and severe progressive headache for inclusion. The criteria for epileptic seizures and severe progressive headache are available in appendix 2 (p 2). All patients were informed about all parts of the study before inclusion and all patients signed a written informed consent form. For illiterate patients and patients younger than 18 years a guardian signed the informed consent form after assent was given.

### Study procedures

At inclusion, every patient was tested with the TS POC test (stage 1) and every patient who was positive for cysticercosis was selected for further laboratory and clinical testing, including neuroimaging (stage 2).[17]

Additionally, every tenth patient who had a negative TS POC test result was also selected for clinical work-up.

Patients selected for stage 2 gave a venous blood sample that was analysed with a range of serological reference tests for cysticercosis (LLGP-EITB, rT24H-EITB, and serum B158/B60 antigen ELISA).[8–10] Patients underwent a neurological examination and an in-depth questionnaire on epileptic seizures, headache, and other past medical and neurological history. Patients also underwent a brain CT scan with and without contrast medium. In some cases, there was a time lag of more than 2 months between point-of-care testing and neuroimaging. In these cases, we did another TS POC test on the day of the CT scanning without additional reference testing. Separate analyses were done for those who received a repeat TS POC test.

CT scanning was done at the Mbeya Referral Hospital Radiology Center with a Revolution ACT (GE HealthCare, Chicago, IL, USA; slice thickness 1·25 mm). CT scans were evaluated by two independent reviewers (CR [neuroradiologist] and AF [neurocysticercosis specialist and neurologist]) who were masked to the TS POC test results. In case of disagreement, a third reviewer (ASW [neurologist]) adjudicated the case. The number and the stage (active: vesicular, degenerative: colloidal-vesicular or granular-nodular, or inactive: calcified) of neurocysticercosis lesions were recorded.[19] The stage of neurocysticercosis was categorised as active (at least one lesion in thevesicular stage) or inactive (only calcified lesions). Details on the criteria for neurocysticercosis diagnosis can be found in appendix 2 (p 3).

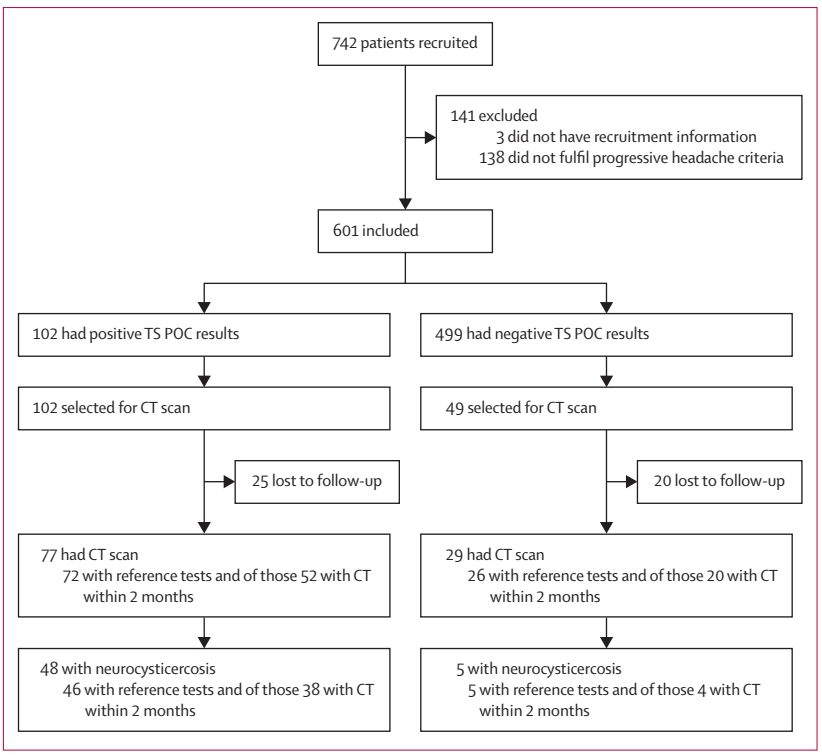


***Figure 1:*** **Trial profile**
TS POC=*Taenia solium* point-of-care test.

## Statistical analyses

The required sample size was 600 patients based on an assumed neurocysticercosis prevalence of 20% and TS POC test sensitivity of 93% and specificity of 99%. Details on the TS POC test and the calculation can be found in the published protocol.[17]

We report descriptive results using all available data of the TS POC test. The primary outcomes of this study were the sensitivity, specificity, and predictive values of the TS POC test against the neurocysticercosis diagnosis as established by the presence of at least one absolute or major neuroimaging criterion according to Del Brutto and colleagues[6] (appendix 2 p 3). We assessed the performance of the TS POC test for all patients in relation to the primary endpoints irrespective of the timepoint of the CT examination. To evaluate a potential disease progression bias, we also evaluated the TS POC test performance only in those patients with a CT examination within 2 months of POC testing (ie, sensitivity analysis). We also assessed the performance for active stage neurocysticercosis (ie, at least one lesion in the vesicular stage) and for neurocysticercosis with more than two lesions (irrespective of lesion stage). Predictive values were disaggregated by recruitment reason (ie, epileptic seizures, severe progressive headache, or both) and by study site (ie, Ifisi, Tukuyu, and Vwawa). Subgroup analyses included only patients with epileptic seizures. The 95% CIs for the predictive values were determined using the binom.test function in R (version 4.1.1).

For the assessment of sensitivity and specificity, data were imputed using the mice package in R to account for the study design (ie, partial verification bias).[20] Data were assumed to be missing at random and were imputed by means of logistic regression models. Missing reference test results were imputed by models adjusted for the TS POC test result and study site. Neuroimaging results were imputed for each test (ie, TS POC test and reference tests) by models adjusted for study site and age. The imputation was done using the parlmice function. The number of cores was set to 5 and for each core, 20 imputations were done, totalling in 100 imputations per analysis. The uncertainty intervals (UIs) around the mean of the diagnostic values (ie, sensitivity and specificity) were derived from 95% CIs of β distributions using the mean and SE from the imputed datasets.

## Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

| | Overall | Ifisi | Tukuyu | Vwawa |
|---|---|---|---|---|
| **Recruitment** | | | | |
| Epileptic seizures and headache | 307/601 (51%) | 52/169 (31%) | 54/193 (28%) | 201/239 (84%) |
| Epileptic seizures only | 169/601 (28%) | 34/169 (20%) | 97/193 (50%) | 38/239 (16%) |
| Headache only | 125/601 (21%) | 83/169 (49%) | 42/193 (22%) | 0/239 |
| **Sex** | | | | |
| Female | 313/601 (52%) | 98/169 (58%) | 105/193 (54%) | 110/239 (46%) |
| Male | 288/601 (48%) | 71/169 (42%) | 88/193 (46%) | 129/239 (54%) |
| **Age** | | | | |
| ≤20 years | 97/601 (16%) | 33/169 (20%) | 34/193 (18%) | 30/239 (13%) |
| 21–40 years | 291/601 (48%) | 69/169 (41%) | 94/193 (49%) | 128/239 (54%) |
| 41–60 years | 158/601 (26%) | 40/169 (24%) | 47/193 (24%) | 71/239 (30%) |
| 61–80 years | 54/601 (9%) | 27/169 (16%) | 17/193 (9%) | 10/239 (4%) |
| >80 years | 1/601 (<1%) | 0/169 | 1/193 (1%) | 0/239 |
| Median (IQR, years) | 33 (24–47) | 34 (23–50) | 31 (23–47) | 34 (25–46) |
| **Positive TS POC result*** | | | | |
| Total | 102/601 (17%) | 43/169 (25%) | 16/193 (8%) | 43/239 (18%) |
| Epileptic seizures and headache | 49/307 (16%) | 29/52 (17%) | 5/54 (9%) | 35/201 (17%) |
| Epileptic seizures | 26/169 (15%) | 9/34 (27%) | 9/97 (9%) | 8/38 (21%) |
| Headache | 27/125 (22%) | 25/83 (30%) | 2/42 (5%) | 0/0 |

Data are n/N (%), unless otherwise specified. TS POC=*Taenia solium* point-of-care test. *Denominators are number of individuals recruited, by study sites.

***Table 1:*** **Baseline characteristics**

## Results

Between Jan 17, 2018, and Jan 29, 2020, 742 patients were recruited, of whom 601 patients were ultimately enrolled in the study (figure 1). 307 (51%) patients were recruited with epileptic seizures and severe progressive headache, 169 (28%) with epileptic seizures only, and 125 (21%) with severe progressive headache only. Reasons for recruitment differed between study sites. 83 (49%) of 169 patients recruited from Ifisi were recruited with severe progressive headache only while none (0/239) from Vwawa were recruited for this reason (table 1).

Of all 601 patients, 102 (17%) tested positive for cysticercosis with the TS POC test. All of these patients were selected for CT examination, with an additional 49 (10%) of the 499 patients who tested negative for cysticercosis on the TS POC test, according to the protocol (figure 1). 25 (25%) of 102 patients positive for cysticercosis on the TS POC test were lost to follow-up, of whom 16 had reference test results available (appendix 2 p 6). Of the 77 patients with a positive TS POC test result who had a CT, 48 (62%) had neurocysticercosis. 72 (94%) of 77 patients had CT-confirmed reference test results available and of those 46 (64%) had neurocysticercosis (28 in active stage and 18 in the calcified stage; table 2, figure 2). 20 (41%) of the 49 patients negative for cysticercosis on the TS POC test were lost to follow-up, of whom 18 had reference test results available; 17 were negative in all reference tests and one was positive in all reference tests (appendix 2 p 6). Five (19%) of the remaining 29 patients who had CT examination had neurocysticercosis, all in calcified stage (figure 1, figure 2, table 2). In total, 98 patients had reference tests results available; 47 (48%) of these had at least one positive reference test result, of which 42 (43%) had neurocysticercosis (28 in active stage and 14 in calcified stage). 51 (52%) patients had all reference tests negative and nine (9%) of those had neurocysticercosis (all in calcified stage). 13 (22%) of the 58 patients with negative rT24H-EITB results had neurocysticercosis (all in calcified stage); 27 (37%) of the 73 patients with negative LLGP-EITB results had neurocysticercosis (nine in active and 18 in calcified stage); and 12 (21%) of the 57 patients with negative antigen ELISA results had neurocysticercosis (all in calcified stage; figure 2, table 2).

The positive predictive values and negative predictive values of the TS POC test differed by recruitment cause and site (figure 3). The positive predictive value for all patients together was 62% (95% CI 51–73) for neurocysticercosis at any stage; this value differed by site and was lower in Ifisi (31%, 95% CI 15–51) than in Tukuyu (85%, 55–98) and Vwawa (80%, 63–92). For patients recruited for headache only, none of the 13 who were positive or the four who were negative on TS POC test had neurocysticercosis. Among all patients with epileptic seizures, the positive predictive value was similar between those recruited with epileptic seizures only (82%, 60–95) and those recruited with epileptic seizures and headache (73%, 57–86; figure 3, appendix 2 p 7).

The TS POC test had a sensitivity of 49% (UI 41–58) and specificity of 91% (89–94) for any type of neurocysticercosis. The sensitivity of the TS POC test was comparable to that of the antigen ELISA (50%, UI 43–56) and the rT24H-EITB (44%, 37–51) and higher than that of the LLGP-EITB (23%, 18–28). For all tests, sensitivity and specificity were higher for neurocysticercosis with more than two lesions, compared with only one or two lesions. For neurocysticercosis with at least one vesicular lesion, sensitivity was above 98% for the TS POC test, the rT24H-ETIB, and the antigen ELISA; the sensitivity of the LLGP-EITB was 40% (31–48; figure 4). Restricting the analyses to people with a CT examination within 2 months of the original TS POC and reference tests resulted in a lower sensitivity for all tests: 43% (UI 36–50) for TS POC test, 38% (32–44) for rT24H-EITB, 21% (16–26) for LLGP-EITB, and 43% (36–49) for antigen ELISA (appendix 2 p 8). Restricting the analyses to people with epileptic seizures did not considerably affect the sensitivity of any test (appendix 2 p 8). Results of repeat TS POC tests for those who had a lag between tests can be found in appendix 2 (pp 9–10). The TS POC test met almost all minimum and many optimal characteristics specified in the target product profile for a point-of-care test for the diagnosis of neurocysticercosis, with the exception of

| | Positive TS POC result | | | | Negative TS POC result | | | |
|---|---|---|---|---|---|---|---|---|
| | Neurocysticercosis | Active stage neurocysticercosis | Inactive neurocysticercosis | >2 lesions (any stage) | Neurocysticercosis | Active stage neurocysticercosis | Inactive neurocysticercosis | >2 lesions (any stage) |
| **POC test results** | | | | | | | | |
| All patients | 48/77 (62%) | 29/48 (60%) | 19/48 (40%) | 42/77 (55%) | 5/29 (17%) | 0/5 | 5/5 (100%) | 2/29 (7%) |
| Those with both POC and reference test results | 46/72 (64%) | 28/46 (61%) | 18/46 (39%) | 41/72 (57%) | 5/26 (19%) | 0/5 | 5/5 (100%) | 2/26 (8%) |
| **Reference tests** | | | | | | | | |
| All negative | 5/26 (19%) | 0/5 | 5/5 (100%) | 2/26 (8%) | 4/25 (16%) | 0/4 | 4/4 (100%) | 2/25 (8%) |
| At least one positive | 41/46 (89%) | 28/41 (68%) | 13/41 (32%) | 39/46 (85%) | 1/1 (100%) | 0/1 | 1/1 (100%) | 0/1 |
| rT24H-EITB | | | | | | | | |
| Negative | 8/32 (25%) | 0/8 | 8/8 (100%) | 5/32 (16%) | 5/26 (19%) | 0/5 | 5/5 (100%) | 2/26 (8%) |
| Positive | 38/40 (95%) | 28/38 (74%) | 10/38 (26%) | 36/40 (90%) | 0/0 | 0/0 | 0/0 | 0/0 |
| LLGP-EITB | | | | | | | | |
| Negative | 22/47 (47%) | 9/22 (41%) | 13/22 (59%) | 17/47 (36%) | 5/26 (19%) | 0/5 | 5/5 (100%) | 2/26 (8%) |
| Positive | 24/25 (96%) | 19/24 (79%) | 5/24 (21%) | 24/25 (96%) | 0/0 | 0/0 | 0/0 | 0/0 |
| Antigen ELISA | | | | | | | | |
| Negative | 8/32 (25%) | 0/8 | 8/8 (100%) | 4/32 (13%) | 4/25 (16%) | 0/4 | 4/4 (100%) | 2/25 (8%) |
| Positive | 38/40 (95%) | 28/38 (74%) | 10/38 (26%) | 37/40 (93%) | 1/1 (100%) | 0/1 | 1/1 (100%) | 0/1 |

Data are n/N (%). TS POC=*Taenia solium* point-of-care test.

***Table 2:*** **CT scan results of patients, by TS POC test results**

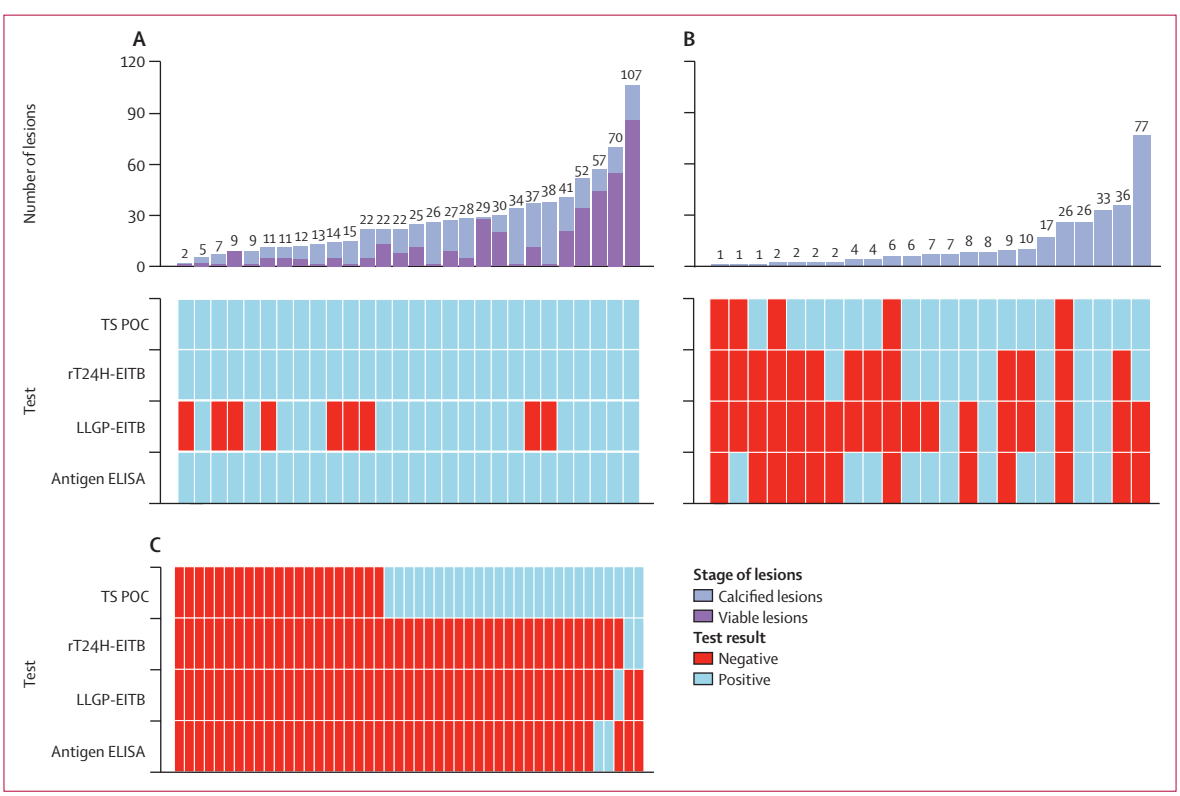


***Figure 2:*** **Relationship between results of the TS POC test, the reference tests, and number and stage of neurocysticercosis lesions**
(A) Patients with active stage neurocysticercosis. (B) Patients with calcified neurocysticercosis. (C) Patients with CT examination but no neurocysticercosis-typical finding. TS POC=*Taenia solium* point-of-care test.

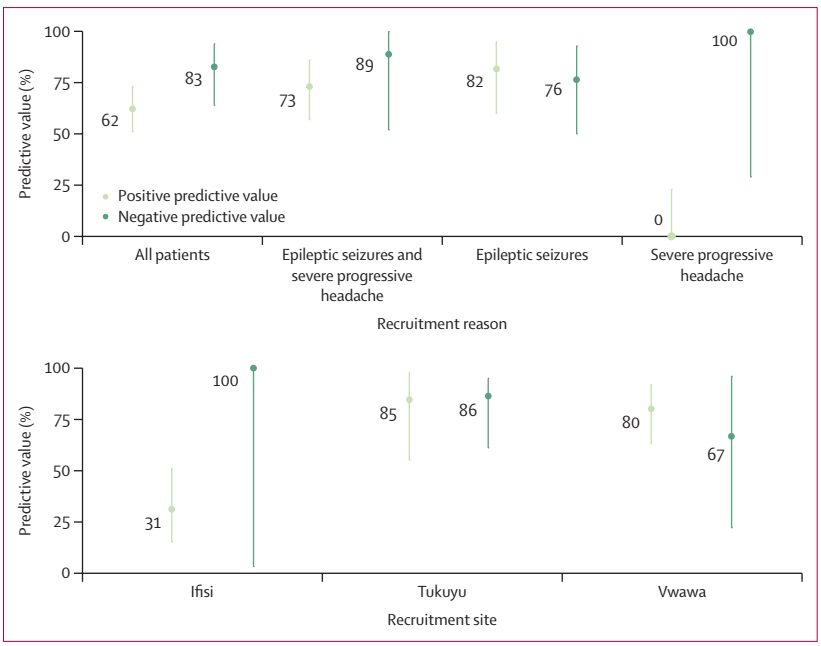


***Figure 3:*** **Predictive values of the TS POC for neurocysticercosis by recruitment site and recruitment reason**
Error bars show 95% CIs. TS POC=*Taenia solium* point-of-care test.

those relating to access and commercialisation (appendix 2 pp 11–12).

## Discussion

We assessed the diagnostic accuracy of a novel lateral-flow point-of-care test for referral to imaging-based diagnosis of neurocysticercosis and specifically for neurocysticercosis with active stage lesions, which are treatable with anthelmintic medication. We found that in people with epileptic seizures, sensitivity and specificity of the TS POC test were similar to those of reference tests for neurocysticercosis. For neurocysticercosis with at least one lesion in vesicular stage, the sensitivity of the TS POC test was very high. The diagnostic accuracy of the TS POC test was similar to rT24H-EITB and the antigen ELISA, while LLGP-EITB did not perform well in our study.

Predictive values of the diagnostic tests depended on the recruitment reason and study site. Of those patients recruited with severe progressive headache only, none had neurocysticercosis, which could be due to difficulties with the non-specificity of the screening questionnaire. This finding is not surprising as, to date, there are no good and specific descriptions of the headache associated with neurocysticercosis. At the district hospital in Ifisi, the positive predictive value was considerably lower than at the other study sites; the many people with false positive tests could be due to a difference in interpretation of a positive test, and possibly only slightly visible lines were considered as positive. This hypothesis is likely as many of these patients were negative on their second TS POC test. Retraining in reading the POC test might have improved the results of the evaluation.

We report several diagnostic values, however the focus of this analysis was the sensitivity. The TS POC test and the reference tests are cysticercosis-specific tests, but we assessed them regarding accuracy for the subgroup of patients finally diagnosed with neurocysticercosis (ie, lesions in the CNS). This circumstance is also why the TS POC test could be a starting point for a diagnostic algorithm that begins with the screening of patients. As with all screening tests, high sensitivity is key, if it is followed by a test with good specificity, such as brain CT scanning.

In our study, we found 13 people with positive antigen ELISA but no vesicular neurocysticercosis lesions or no neurocysticercosis at all; 12 of those were also positive on the TS POC test. There are different explanations for this finding: these patients could have cysticercosis but not neurocysticercosis; there could be cross-reactivity of the antigen ELISA and the TS POC test; or the CT results could be inaccurate. One study[21] showed that the likelihood of finding vesicular lesions on MRI increased when only calcified lesions were seen on CT but the antigen ELISA was positive. In 12 of these 13 cases, the TS POC test was also positive, which means that if these patients did have vesicular lesions, the TS POC test would have detected most of them.

In our study, the TS POC test had very good performance for patients with vesicular lesions, as did the antigen ELISA and the rT24H-EITB. For the two reference tests, this has been shown before.[8,9,22,23] By comparing the results of the TS POC test with the current reference tests, we were able to show the reliability of our findings, and that our study was representative for patients with neurocysticercosis. This finding is important because patients with vesicular lesions might benefit from anthelmintic medication, which can cure their neurocysticercosis and associated neurological signs and symptoms, such as epileptic seizures. However, treatment with antihelmintic medication together with corticosteroids can only be initiated after neuroimaging. Treatment before neuroimaging must be discouraged as number and location of lesions and cerebral inflammation can only be assessed with neuroimaging, and this information is crucial for treatment decisions and patient safety.

In our study, the LLGP-EITB performed worse than has been reported previously.[2,8,21] Reasons for poorer performance are still being investigated and could include differences in the cysticerci material on which the tests were developed and in the reagents that were used for the test.

Our results highlight the potential of TS POC tests. In low-resource settings, shipping samples to reference laboratories for daily testing is often not feasible and, even if possible, the reference tests easily fail to perform the way they should. We showed that even in highly standardised laboratories in high-income countries, some tests might not perform as intended. For TS POC

tests, a more standardised quality of production and test implementation can be ensured, whereby accuracy would drop only slightly when used in low-resource settings, even if the personnel administering the test only receive minimal training.[22] In a previous review,[23] POC testing was highlighted as easy to use and not difficult to read. Also, most local clinicians and other health-care personnel are used to lateral-flow tests (eg, for malaria, HIV, or syphilis).[24,25]

We believe the TS POC test can have a positive effect in local hospitals and communities. The burden of neurocysticercosis varies considerably between countries and regions, in some regions more than 10% of the general population are affected, as are up to 50% of all people with epilepsy.[2,3,26,27] In our study, none of the patients with negative TS POC test results had active stage neurocysticercosis, which means that the test might have potential to be used as a rule-out test for active neurocysticercosis. In this context, the TS POC test should also be further studied as a screening tool before mass drug administration programmes (such as those with albendazole or praziquantel) for control and elimination of neglected tropical diseases.[28] During these mass drug administration programmes, side-effects in individuals with previously undiagnosed symptomatic or asymptomatic neurocysticercosis might occur, but are rarely reported and might in fact be under-reported. Although seemingly infrequent, these side-effects can be lethal, which is why the Pan American Health Organization recognises the risk of asymptomatic neurocysticercosis in their guidelines for mass drug administration for the control of *T solium* taeniasis and recommends active surveillance for 3 days after administration.[29] Identification of individuals at risk of neurocysticercosis before mass drug administration would be a major advancement for these programmes. The TS POC test showed reliable results in this study in people with epileptic seizures, but TS POC test results for people with asymptomatic neurocysticercosis in a community-based study in Zambia are still pending.

Our study had several strengths. First, to our knowledge, this is the first study to evaluate a point-of-care lateral-flow assay against neuroimaging confirmed neurocysticercosis in sub-Saharan Africa. Second, the study was rigorously conducted and included more than 600 participants with neurological signs and symptoms associated with neurocysticercosis, and among those, nearly 500 patients with epileptic seizures. Third, we assessed the test by lesion stage and number.

However, our study also had some limitations. First, different people at the three different sites assessed neurological signs and symptoms of the patients and did the TS POC test. This method could have led to selection bias, especially for patients recruited with headache only, and to some variability in TS POC test results. Another limitation was that there were few enrolled patients with neurocysticercosis with a low number of vesicular lesions. Patients with few lesions are the group of patients who are often serologically negative, and therefore could have been missed by the study design. Due to the small number of such patients, we could not confidently assess the accuracy in patients with few active stage lesions. Finally, due to the long distance between the study sites and the CT centre, we had an important loss to follow-up of 31% and the CT examinations were often (36%) delayed by more than 2 months after initial testing. We accounted for the effect of the loss to follow-up via imputation. Also, the demographic factors of these patients did not differ from those with CT examination. Regarding the delay of the CT examination, our sensitivity analyses yielded similar results, so we do not consider that this factor significantly influenced our results. Patient loss to follow-up and delay in CT examination also reflect the difficulties faced by medical staff in Tanzania, where CT scanners are not widely available and often require days of travel.

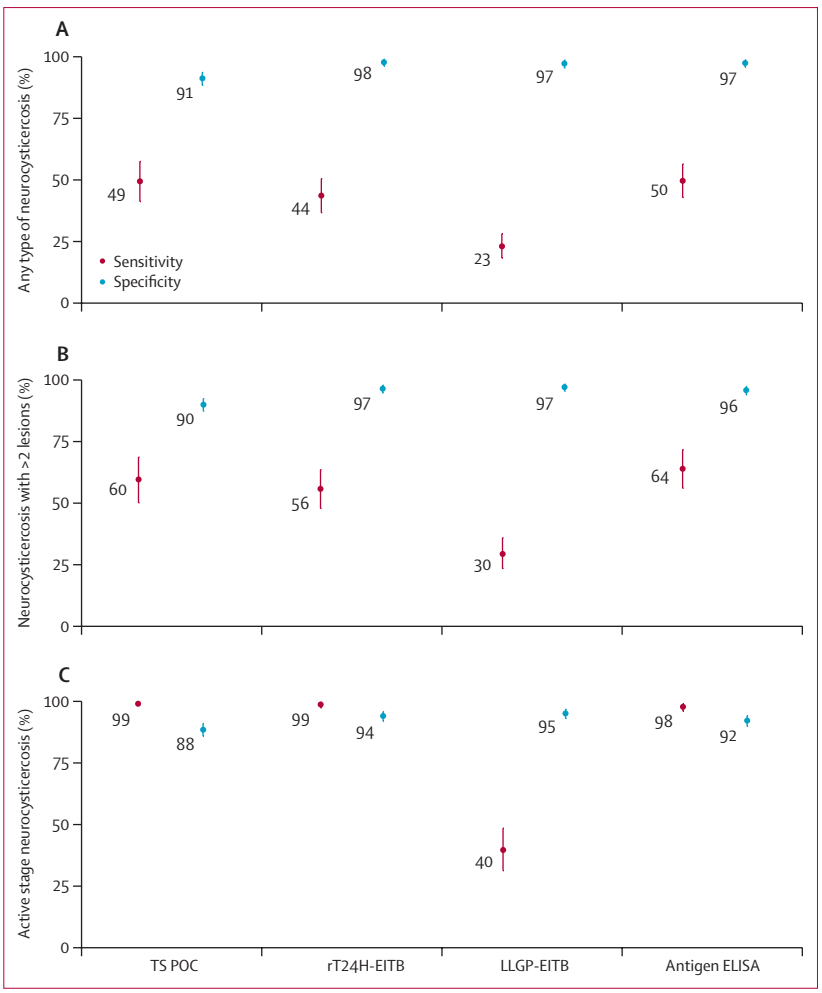


***Figure 4:*** **Diagnostic accuracy of the TS POC and the reference tests for neurocysticercosis**
Error bars show uncertainty intervals. TS POC=*Taenia solium* point-of-care test.

The TS POC lateral-flow assay showed promising results for the diagnosis of neurocysticercosis and was very sensitive for the subgroup of patients with neurocysticercosis with vesicular lesions. These results are encouraging but need to be confirmed in larger populations, especially in patients with few active stage lesions. This test could be the first step towards the development of a diagnostic algorithm that will allow faster and cost-saving neurocysticercosis diagnosis in clinical settings, or even in communities, pending the results of ongoing studies. In addition, the TS POC test should be further explored for community-based mass drug administration programmes to identify people with undiagnosed symptomatic and asymptomatic neurocysticercosis. The TS POC test could represent a major step towards reducing the burden of neurocysticercosis and improving the health of people living in *T solium* endemic regions worldwide.

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**Contributors**
DS, VS, IVD, CT, PD, PM, SG, BJN, and ASW conceptualised the paper. DS, CEM, CT, SG, BJN, and ASW curated the data. DS and IVD did the formal analysis. VS, PD, SG, BJN, and ASW acquired funding. DS, VS, IVD, CT, SG, and ASW designed the methodology. VS, SG, BJN, and ASW did the project administration. SG, BJN, and ASW supervised the study. DS, VS, IVD, SG, and ASW validated the analyses. DS visualised the results and wrote the original draft. All authors did the investigation and reviewed and edited the paper. DS, CEM, and ASW accessed and verified all data. All authors decided to submit the manuscript.
All authors who are members of the SOLID consortium had full access to all the data in the study and had final responsibility for the decision to submit for publication.

**Declaration of interests**
We declare no competing interests.

**Data sharing**
De-identified participant data will be made available upon request to both corresponding authors after approval of a proposal by the SOLID consortium.

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