Disability assessment among persons with epilepsy in Mahenge, an onchocerciasis-endemic area in Tanzania : a cross-sectional study

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Dan Bhwana[1*], Joseph Nelson Siewe Fodjo[2*], Luís-Jorge Amaral[2], Lauren Vandevenne[2], Filbert Francis[1], Daniel P. Challe[1], Bruno P. Mmbando[1], Robert Colebunders[2]**

1. National Institute of Medical Research, Tanga, P. O Box 5004, Tanzania
2. Global Health Institute, University of Antwerp, 2610 Antwerp, Belgium

*Contributed equally

**Correspondence: robert.colebunders@uantwerpen.be
Doornstraat 331, 2610 Antwerp, Belgium

Author emails:

DB: danbhwana@yahoo.com

JNSF: josephnelson.siewefodjo@uantwerpen.be

L-JA: luis-jorge.telesdemenesesdoamaral@uantwerpen.be

LV: laurenvandevenne@hotmail.com

FF: ffrancis8@gmail.com

DPC: danielchalle77@yahoo.co.uk

BPM: b.mmbando@yahoo.com

RC: robert.colebunders@uantwerpen.be

ABSTRACT

Background: A high prevalence of epilepsy has been observed in the onchocerciasis-endemic focus of Mahenge, Tanzania. This study sought to assess the degree of disability experienced by persons with epilepsy (PWE) in Mahenge and identify associations with sociodemographic and clinical features.

Method: This cross-sectional study was conducted in Mahenge, Tanzania, between February and July 2020. PWE were recruited from the Mahenge epilepsy clinic and four neighbouring rural villages (Mdindo, Mzogezi, Mzelezi and Sali). Data was collected using the 36-item version of the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) questionnaire for adults. For children aged 5-17 years, we used the Module on Child Functioning developed by UNICEF and the Washington Group. Questionnaires were administered by trained research assistants. Descriptive statistics were performed, and multivariable analyses (gamma and logistic regressions) were conducted.

Results: A total of 321 adults (45.5% males) and 48 children (55.3% males) with epilepsy participated. The overall median WHODAS 2.0 score was 4.8% (IQR: 0.9 – 18.9). The most affected disability domain was “participating in the society” (median score: 12.5%, IQR: 0 – 29.2). Fifteen (31.3%) of the children with epilepsy had a disability in at least one domain of the child functioning module, with the “accepting change” domain harbouring the highest proportion of disabled children (12.5%). Higher seizure frequency and longer epilepsy duration were associated with more disability.

Conclusion: PWE in Mahenge experience variable degrees of disability. The affected domains indicate the need for societal rehabilitation of PWE in various community and/or social activities. Peer-support groups were instituted at the study sites to address these needs.

Keywords: Onchocerciasis, epilepsy, nodding syndrome, disability, WHODAS 2.0, anti-seizure medication.

1. INTRODUCTION AND BACKGROUND

Epilepsy is a chronic non-transmissible neurological condition characterised by repetitive unprovoked seizures [1]. Seizures are short episodes of involuntary movement, which involve a part (focal) or the whole body (generalised) and are often associated with loss of consciousness and control over the bowel or bladder function [1].

Epilepsy affects more than 50 million people, with a prevalence ranging between 4-10 per 1000 people in high-income countries and as high as 7-15 per 1000 people in low- and middle-income countries [2]. In a large proportion of persons with epilepsy (PWE), the cause of epilepsy is unknown [3]. Known causes of epilepsy in Africa include perinatal anoxia, head injury, parasitic diseases such as malaria, neurocysticercosis, and some genetic factors [4, 5]. A high prevalence of epilepsy is observed in onchocerciasis-endemic regions [6-16], and recent epidemiological studies strongly suggest that onchocerciasis can directly or indirectly induce epilepsy [17-20].

In Mahenge, an onchocerciasis-endemic area in Tanzania, the prevalence of epilepsy is high, attaining three times the national epilepsy prevalence in some rural villages such as Mdindo and Msogezi [21]. A majority of PWE in this area have epidemiological and clinical features consistent with onchocerciasis-associated epilepsy [22].

The Global Burden of Epilepsy Report estimated that 13 million disability-adjusted life years (DALYs) are due to epilepsy each year, which is 0.56% of total DALYs globally [23, 24]. According to the International Classification of Functioning, Disability and Health (ICF), disability is any condition of the body or mind that makes it more difficult for the person with the condition to do certain activities and interact with the world around them [25]. PWE are at high risk for developing disabilities or functional impairment due to frequent seizures, which can affect their cognitive function as well, causing trauma (e.g. burns [26] and fractures) or death [27]. This risk is further compounded by the physical and functional deficits caused by onchocerciasis in onchocerciasis-endemic communities.

Onchocerciasis-related physical or visual impairment comes with additional challenges, such as low education, decreased productivity, unemployment, higher healthcare

expenditures, poverty, and poor health [28]. Stigma from family and community members due to fear of contagion can worsen mental health and lead to low self-esteem, anxiety, depression, as well as reduced life expectancy [28, 29]. Besides, family members frequently bear the brunt of the burden, with some dropping out of school to care for the disabled person. In other cases, disability can also spark marital conflict [29].

Early detection of epilepsy-related disability is needed to minimise its negative impact on affected individuals, their families and society. Also, it is important for determining service needs, the required level of care, monitoring of disease prognosis, duration of hospitalisation, payment of disability benefits, work performance and social integration of the PWE. The characteristics of epilepsy-related disability in onchocerciasis endemic regions and its impact on individuals and their families are still largely unknown. This study was designed to assess the degree of disability among PWE in the Mahenge area, with the aim of responding to their needs and improving their quality of life. Moreover, we sought to investigate whether the degree of disability was related to the sociodemographic and clinical features of the PWE..

2. METHODS

2.1 Study design and area

A health facility-based cross-sectional study was conducted between February and July 2020 involving PWE from Mahenge town and four rural villages (Mdindo, Msogezi, Mzelezi and Sali) in the Mahenge area in the Ulanga district, Morogoro Region (Tanzania). Details of the study area have been described previously [22, 30]. In brief, the study area is characterised by a high prevalence of epilepsy (ranging from 2.9% in Mzelezi to 3.5% in Mdindo and Sali) and high onchocerciasis transmission as suggested by a high seroprevalence of Ov16 antibodies (42%) among children aged 6-10 years [22, 30]. These study sites are also known hotspots for onchocerciasis-associated epilepsy, including nodding syndrome [22]. The main occupations of the inhabitants include subsistence farming, livestock keeping (chicken, goats, and pigs) and working in gemstone mining. Pogoro is the main ethnic group, while Christianity and Islam are the main religions in the area.

A community-based program was established in these villages to improve epilepsy care and decrease onchocerciasis transmission. Within this programme, healthcare workers (HCWs) and community health workers (CHWs) were trained to identify epilepsy in the community, treat PWE using anti-seizure medicines (ASM), and monitor treatment adherence. These activities were coordinated by an epilepsy clinic within each study site, which served as a focal point for the enrolment of newly diagnosed PWE, monthly follow-up of enrolled PWE, peer support groups for PWE and their families, and free provision of ASM.

2.2 Sampling and data collection

We consecutively recruited all consenting PWE aged five years and above who presented for a consultation or follow-up visit at the Mahenge epilepsy clinic of the Ulanga district Hospital or one of the community-based epilepsy clinics of the four rural villages. Data were collected using a structured questionnaire on paper forms administered to participants or their caregivers by trained research assistants.

The WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) was used to measure the degree of disability in adults (18 years and above) [31]. The WHODAS 2.0 consist of 36 items to describe the disability in six domains: cognition (communication, concentration, planning, problem-solving and learning; six items), mobility (indoor and outdoor travel; five items), self-care (dressing, washing, eating and independence; four items), getting along (friendship, relationships and conversations; five items), life activities (daily activities such as housekeeping or going to work; eight items), and participation (to what extent the community, laws, and religion makes it difficult to participate in society; eight items). Previous research has demonstrated that the WHODAS 2.0 instrument can be used satisfactorily among PWE [32].

For children 5-17 years, the Module on Child Functioning developed by UNICEF and the Washington Group was used [33]. This questionnaire is based on the “international classification of functioning, disability and health: children and youth version” (ICF-CY) and has already been used for research in sub-Saharan African settings [34]. It consists of 24 items grouped into 13 domains of functioning: seeing, hearing, walking, self-care,

communication, learning, remembering, concentrating, accepting change, controlling behaviour, making friends, anxiety, and depression.

For both children and adult participants, a questionnaire was also administered about the frequency and type of seizures, duration of epilepsy since the first seizures and epilepsy treatment.

The English data collection tools were translated into the local Kiswahili language and back-translated to English. The questionnaire was adapted by examining the cultural understanding of the questions by the respondents. Answers were illustrated on a 5-point Likert scale and summarised into percentages using the complex scoring approach recommended by the WHO, as this allows for comparisons with other studies) [30]. The results of this scale vary between 0% (no disabilities) and 100% (fully disabled).

2.3 Data analysis

The data collected on paper forms were verified and entered into a Microsoft Access database. The recoding and calculation of domain-specific and total disability scores for adults (WHODAS 2.0) were facilitated by the spreadsheet tool proposed by Castro *et al.* [35]. For children, data were recoded and summarised as directed by the Washington Group [33]. Data were analysed using the R software, version 4.2.2. Continuous variables were summarised using medians with interquartile range (IQR) and sometimes using the means, while categorical variables were summarised using frequencies and proportions. The outcome measure was the occurrence and/or extent of disability (expressed on a 0-100 scale for adults and dichotomous for children), calculated for each domain and overall. For descriptive bivariate analyses, we used the Chi-squared test (or Fisher exact test as appropriate) to compare proportions. Continuous variables were compared across groups using non-parametric tests (Mann-Whitney U or Kruskal Wallis). Correlation analysis between two continuous variables was done using the Spearman's non-parametric method. The internal consistency of the study tools was measured using Cronbach Alpha.

Two multivariable models were constructed: Firstly, a gamma regression model was used to investigate the determinants for increasing disability scores in adults with non-zero

WHODAS 2.0 scores. This model fitted best considering the right-skewed nature of the disability scores. Secondly, we merged adult and children's data to perform a multiple logistic regression to identify risk factors for disability among PWE. The dichotomous outcome variable was the occurrence of at least one disability in any domain and was coded as "1" for non-zero WHODAS scores and for children classified as disabled by the child functioning module. For all multivariable models, we included only data from participants under ASM to prevent spurious associations that could arise from the scanty group of untreated PWE. Purposefully selected independent variables were introduced into the model, including sociodemographic variables (questionnaire respondent, age, gender, urban/rural residence) and epilepsy-related variables (duration of epilepsy, monthly seizure frequency, history of nodding seizures, regular use of ASM, and type of ASM). We maintained age and gender in all the models to account for biological plausibility, while other covariates for the final model were selected by a backward step selection process. We verified the absence of multicollinearity in the models by ensuring that all variation inflation factors in the final models were below 2. The level of statistical significance for all analyses was set at 5%.

2.2 Ethical considerations

This study was approved by the ethical committees of the National Institute for Medical Research in Tanzania (NIMR/HQ/R.8a/Vol.IX/3342) and the University of Antwerp in Belgium (B300201942516). The study was carried out adhering to the principles of the Declaration of Helsinki. Meetings were held with the community leaders to explain the aims and procedures of the study. Information was provided to all study participants, and questions were discussed before obtaining consent. Individuals aged 18 years and above provided their own consent, while children and minors had their consent signed by their parents or guardians. Moreover, assent was obtained from those aged 12 years or above. For individuals who could read and/or write, consent was signed by fingerprint before an independent witness who also signed the form.

3. RESULTS

3.2 Participant characteristics

Overall, 321 adults (≥ 18 years) and 48 children (5-17 years) were recruited (Table 1). The majority of participants resided in Mahenge town (urban setting). Over 90% of PWE were treated with ASM. The most frequently used ASM was phenobarbital (84.4% of adult PWE and 81.2% of children), followed by carbamazepine (11.8% of adults and 16.7% of children).

Table 1. Sociodemographic and clinical characteristics of participants.

	Adults (Total = 321)		**Children (Total = 48)**	
Characteristics	**Findings**	**N***	**Findings**	**N***
Respondent: n (%)		321		47
PWE himself/herself	216 (67.3%)		6 (12.8%)	
Caregiver or relative	105 (32.7%)		41 (87.2%)	
Age of PWE in years: Median (IQR)	30.0 (25.0 – 39.0)	311	13.0 (10.0 – 14.8)	46
Gender: n (%)		321		47
Male	146 (45.5%)		26 (55.3%)	
Female	175 (54.5%)		21 (44.7%)	
Village: n (%)		321		48
Mahenge	188 (58.5%)		19 (39.5%)	
Mdindo	40 (12.5%)		7 (14.6%)	
Msogezi	36 (11.2%)		6 (12.5%)	
Mzelezi	32 (10.0%)		3 (6.3%)	
Sali	25 (7.8%)		13 (27.1%)	
Epilepsy duration in years: median (IQR)	18.0 (10.0 – 25.0)	280	4.0 (3.0 – 8.0)	45
History of nodding seizures: n (%)		308		45
Yes, ongoing	74 (24.0%)		15 (33.3%)	
Yes, in the past	27 (8.8%)		7 (15.6%)	
No	207 (67.2%)		23 (51.1%)	
Number of seizures last month: n (%)		316		48
No seizure	173 (54.7%)		19 (39.6%)	
Only one seizure	83 (26.3%)		16 (33.3%)	
More than one seizure	60 (19.0%)		13 (27.1%)	
Anti-seizure medication use: n (%)	310 (96.6%)	321	45 (95.7%)	47
Regular ASM intake: n (%)	293 (91.3%)	321	44 (95.7%)	46

ASM: Anti-seizure Medication; IQR: Interquartile Range; PWE: Person(s) With Epilepsy.
**The value of N for a given variable may differ from the total number of participants due to missing values.*

3.3 Disability among adults with epilepsy

The Cronbach Alpha value for the 36 items on the WHODAS 2.0 was 97.6% (95% CI: 96.5 – 98.2) in our adult PWE population, indicating very good internal consistency. The WHODAS 2.0 disability scores among adults ranged from 0% (79 PWE, 24.6% of adult participants) to 100% (2 PWE, 0.6% of adult participants). This implies that 242 (75.4%)

of adult PWE had some degree of disability in at least one of the assessed domains. Twenty-four (7.5%) adult PWE had disability scores ≥50%. The overall median WHODAS 2.0 score was 4.8% (IQR: 0.9 – 18.9), and the mean score was 13.7% (standard deviation: 19.9). Domain-specific scoring revealed that Domain 6 (participation in activities) had the highest mean WHODAS score, while the self-care and mobility domains had the lowest scores (see Table 2 and Fig. 1). During the past month, the mean number of days during which the PWE had to reduce his/her workload or not work at all because of his/health condition was two days (median=0, IQR: 0 – 2). All WHODAS 2.0 domains recorded lower scores when the respondent was the PWE him/herself. Consequently, the overall WHODAS 2.0 score was significantly higher when the questionnaire was administered to a relative/caregiver (median: 14.2%, IQR: 1.9 – 36.8) compared to when it was administered directly to the PWE (median: 3.8%, IQR: 0 – 12.5); $p<0.001$.

Table 2. WHODAS 2.0 findings among the adult population (n=321)

Domains of WHODAS 2.0 tool	**Median (IQR)**	**Mean**
Domain 1: Cognition (understanding and communicating)	0% (0 – 20.0)	14.6%
Domain 2: Mobility (getting around by oneself)	0% (0 – 0)	5.5%
Domain 3: Self-care (taking care of oneself)	0% (0 – 0)	5.2%
Domain 4: Getting along with people	0% (0 – 25.0)	15.7%
Domain 5: Life activities (household and work / school activities)	0% (0 – 20.8)	15.1%
Domain 6: Participation in society	12.5% (0 – 29.2)	19.7%
All domains (Overall WHODAS 2.0 score)	4.8% (0.9 – 18.9)	13.7%
Number of days impacted by the disability last 30 days		
Days with disability-related difficulties (H1*)	0 (0 – 1)	1.7
Days totally unable to carry out usual activities or work (H2*)	0 (0 – 2)	1.7
Days with reduced achievement of usual activities or work (H3*)	0 (0 – 2)	2

IQR: Interquartile Range

**H1, H2, and H3 refer to the additional questions on the WHODAS 2.0 tool, not included in any domain.*

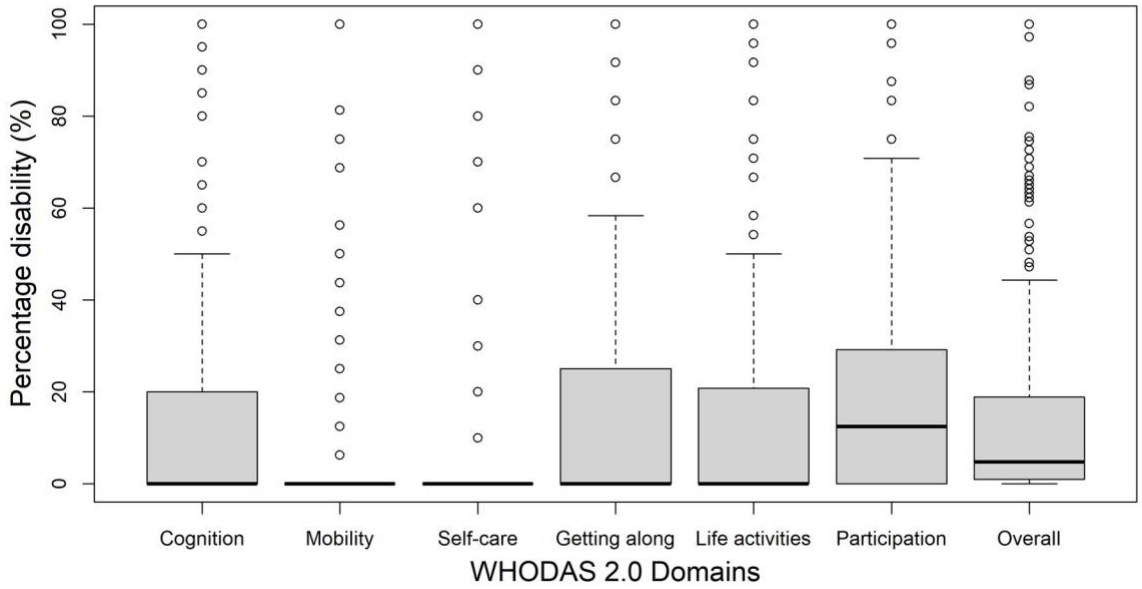

Fig 1. Boxplot of WHODAS 2.0 scores of participants by domain and overall.

Of the 242 adult PWE with non-zero WHODAS 2.0 scores (implying some degree of disability), 173 (71.5%) were affected in more than one domain. When comparing the adult PWE with disability in only one domain versus those with disability in several domains, all sociodemographic characteristics were similar. However, PWE with disability in multiple domains had significantly higher seizure frequencies ($p<0.001$).

While age was not significantly associated with WHODAS scores ($p=0.694$), the duration of epilepsy was found to be positively correlated with disability scores (Spearman-rho: 0.16, $p=0.006$). Having a history of nodding seizures (in the past or ongoing) was not associated with higher disability scores ($p=0.600$) in descriptive analyses. Concerning the degree of disability by gender, our findings show that WHODAS scores were not significantly different among males (median: 4.8%) and females (median: 5.7%; $p=0.935$). Additionally, adult PWE residing in rural settings had higher median WHODAS scores than those in urban settings (8.5 versus 3.8, $p=0.018$) and also had more days of reduced activity during the past 30 days because of their health condition (0 days with IQR: 0 – 2 versus 0 days with IQR: 0 – 1.5; p-0.015).

A significant association was found between seizure frequency and disability score among adult PWE, with those having one or more seizures per month experiencing greater disability (Kruskal-Wallis test, $p<0.001$). Post-hoc analysis using Dunn's test with Bonferroni adjustment found that the significant differences in WHODAS 2.0 scores occurred between PWE with no seizures (median score: 1.9%) and those with either one seizure during the last 30 days (median score: 13.2%) or those with more than one seizure per month (median score: 17.5%); $p<0.001$. The WHODAS 2.0 scores among PWE with one seizure versus those with more than one seizure per month were not significantly different ($p=0.883$).

Participants who reported taking phenobarbital (n=268) had similar seizure frequencies with those under carbamazepine (n=38); $p=0.447$. However, PWE on phenobarbital had significantly lower WHODAS 2.0 median scores (5.2%) compared to their counterparts treated with carbamazepine (8.5%) ($p=0.034$).

Concerning the determinants of the extent of disability among adult PWE, self-response to the WHODAS 2.0 by the PWE him/herself was significantly associated with lower disability scores. For epilepsy related covariates, having experienced at least one seizure in the past month were each associated with increased disability scores (Table 3).

Table 3. Gamma regression model investigating risk factors for increased disability among adults with non-zero WHODAS 2.0 scores

Model* covariates	**Regression estimate (95% CI)**	**P-value**
Age in years	0.171 (-0.003 – 0.345)	0.056
Gender		
Female	Reference	
Male	-1.515 (-4.975 – 1.945)	0.392
Respondent to WHODAS 2.0		
Informant / relative	Reference	
Person with epilepsy	-14.410 (-20.432 – -8.388)	**< 0.001**
Number of seizures in the past month		
No seizure	Reference	
At least one seizure	6.001 (2.174 – 9.828)	**0.002**
Anti-seizure medicine		
Phenobarbita	Reference	
Carbamazepine	1.425 (-4.312 – 7.163)	0.627

Regular ASM use		
No	Reference	
Yes	-5.011 (-15.227 – 5.206)	0.338

ASM: Anti-seizure Medication; CI: Confidence interval.
**N = 223 (after removal of observations with missing values).*
**Pseudo-R^2 (Cragg-Uhler): 20.6%; AIC: 1701.3*

3.3 Disability among children with epilepsy

The Cronbach Alpha value for the 13 domain-specific scores on the child functioning module used to assess PWE aged 5-17 years was 82.5% (95% CI: 40.2 – 91.2), indicating good internal consistency. Of the 48 children with epilepsy, 15 (31.3%) were classified as having some degree of disability, 32 (66.7%) as not disabled, and one (2.1%) as missing disability data. None of the children had a disability in the domains of seeing (domain 1) or hearing (domain 2). The domain with the greatest number of disabled children was that which pertained to "accepting change", with a total of six (12.5%) children (Table 4).

Table 4. Child functioning findings among the children population (n=48)

Domains of Child Functioning Module	**Disabled** n (%)	**Not disabled** n (%)	**Missing** n (%)
Domain 1: Seeing	0 (0%)	48 (100%)	0 (0%)
Domain 2: Hearing	0 (0%)	48 (100%)	0 (0%)
Domain 3: Walking	3 (6.2%)	44 (91.7%)	1 (2.1%)
Domain 4: Self-care	2 (4.2%)	46 (95.8%)	0 (0%)
Domain 5: Communication (being properly understood inside or outside the household)	3 (6.2%)	45 (93.8%)	0 (0%)
Domain 6: Learning	4 (8.3%)	43 (89.6%)	1 (2.1%)
Domain 7: Remembering	4 (8.3%)	44 (91.7%)	0 (0%)
Domain 8: Concentrating	5 (10.4%)	43 (89.6%)	0 (0%)
Domain 9: Accepting Change	6 (12.5%)	42 (87.5%)	0 (0%)
Domain 10: Controlling Behavior	2 (4.2%)	44 (91.7%)	2 (4.2%)
Domain 11: Making Friends	4 (8.3%)	44 (91.7%)	0 (0%)
Domain 12: Anxiety	5 (10.4%)	43 (89.6%)	0 (0%)
Domain 13: Depression	3 (6.2%)	45 (93.8%)	0 (0%)
Overall Child functioning classification	15 (31.3%)	32 (66.7%)	1 (2.1%)

Considering the 47 children with non-missing child functioning classification, there were no significant differences in the sociodemographic and clinical characteristics of children in the disabled vs non-disabled groups (Table 5).

Table 5. Characteristics of children with and without disability (N=47).

Characteristics	Children with disability (n=15)	Children without disability (n=32)	p-value	N*
Respondent: n (%)			0.647	46
PWE himself/herself	1 (6.7%)	5 (16.1%)		
Caregiver or relative	14 (93.3%)	26 (83.9%)		
Age: median (IQR)	13.0 (12.0 – 13.0)	13.5 (10.0 – 15.0)	0.762	45
Gender: n (%)			0.305	46
Male	10 (71.4%)	16 (50.0%)		
Female	4 (28.6%)	16 (50.0%)		
Epilepsy duration: median (IQR)	5.0 (3.0 – 8.0)	5.0 (3.0 – 8.0)	0.866	44
History of nodding seizures: n (%)	5 (33.3%)	17 (58.6%)	0.203	44
Number of seizures per month: n (%)			0.216	47
No seizure	3 (20.0%)	15 (46.9%)		
Only one seizure	7 (46.7%)	9 (28.1%)		
More than one seizure	5 (33.3%)	8 (25.0%)		
Anti-seizure medication use: n (%)	12 (92.3%)	31 (96.9%)	0.499	45
Phenobarbital use: n (%)	13 (86.7%)	25 (78.1%)	0.697	47
Carbamazepine use: n (%)	1 (6.7%)	7 (21.9%)	0.406	47
Residence: n (%)			0.120	47
Rural	6 (40.0%)	22 (68.8%)		
Urban	9 (60.0%)	10 (31.2%)		

IQR: Interquartile Range; PWE: Person With Epilepsy
**The value of N for a given variable may differ from the total number of participants due to missing values*

3.4 Risk factors for having at least one disability among both children and adult persons with epilepsy in Mahenge

In the adjusted logistic regression model, the epilepsy-related variables which were significantly associated with having a disability included: longer duration of epilepsy and

having at least one seizure in the past month. A history of nodding seizures was associated with reduced odds of disability (Table 6).

Table 6. Multiple logistic regression model investigating risk factors for having at least one disability among persons with epilepsy in Mahenge.

Model* covariates	Odds Ratio (95% CI)	P-value
Age in years	0.998 (0.970 – 1.026)	0.871
Gender		
Female	Reference	
Male	1.374 (0.790 – 2.388)	0.260
Residence		
Rural	Reference	
Urban	0.594 (0.336 – 1.049)	0.072
Duration of epilepsy in years	1.045 (1.009 – 1.082)	**0.014**
Number of seizures in the past month		
No seizure	Reference	
At least one seizure	2.462 (1.391 – 4.356)	**0.002**
History of nodding seizures		
No	Reference	
Yes (in the past/ongoing)	0.459 (0.262 – 0.805)	**0.007**
Regular anti-seizure medicine use		
No	Reference	
Yes	0.157 (0.019 – 1.305)	0.087

CI: Confidence interval

**N = 287 (after removal of observations with missing values)*

**Pseudo-R^2 (Cragg-Uhler): 17.6%; AIC: 326.9*

4. DISCUSSION

Our study evaluated the occurrence and extent of disability among PWE in Mahenge, Tanzania, using validated instruments. We found that 75.4% of the adult PWE and 31.3% of the children with epilepsy had at least some degree of disability in one or more of the assessed domains. The 13.7% mean WHODAS 2.0 score obtained in our study was close to 12.9% reported by Kesselmayer *et al.* among persons with childhood-onset epilepsy in the USA [32] but still higher than what was observed among the controls recruited in that same study. Our data, therefore, support the long-known fact that epilepsy is indeed a disabling condition, more so in onchocerciasis-endemic areas where onchocerciasis-

associated epilepsy (OAE) is prevalent [36]. We surmise that the degree of disability would have been much higher than what we observed if most of the PWE were not on regular ASM treatment provided for free by the epilepsy clinics at the study sites. Our data suggest that first-line ASMs dispensed via local clinics can effectively control the seizures of PWE in Mahenge (including nodding seizures), thereby improving their well-being and hampering the degree of disability.

A negative association was found between a history of nodding seizures and disability in Mahenge, contrasting with previous findings from South Sudan, where persons with nodding syndrome were often more disabled [36]. Given that the Mahenge disability study was not a clinical survey and there was no nodding syndrome confirmation by neurologists, we suspect that nodding seizures were misdiagnosed by the respondents. Indeed, a similar situation occurred in a Ugandan study whereby any head movements during the seizures (which may occur even in generalised epilepsy) were considered as nodding seizures [37]. This caveat in the identification of nodding syndrome cases has been discussed at length in a recent review focusing on case definitions for OAE [38]. In summary, more caution should be exercised when classifying an OAE case as nodding syndrome, especially when the solely available information is from the patient and/or caregivers who are not healthcare workers.

The WHODAS 2.0 domains which recorded high numbers of disabilities were those pertaining to: participating in society, conducting life activities related to household/work/school, and getting along with people (see Table 2). All these domains relate to social inclusion and self-fulfilment of the PWE in the community and might have been adversely impacted by the prevailing epilepsy-related stigma, which is frequently encountered in onchocerciasis-endemic areas [39]. Due to misconceptions about epilepsy, affected individuals are often rejected from school or places of work and find it difficult to mingle with the rest of the community. This situation warrants a comprehensive community-based approach that would not only provide care for the PWE but also sensitise the communities to ensure the societal rehabilitation of PWE [40]. Implementing peer support groups as a means to bring PWE into a larger community shows promising prospects and has already been implemented in some of the Mahenge study sites [41].

The rural-urban disparity in the disability landscape was evident in the descriptive analysis of the adult PWE data. Those residing in Mahenge town scored lower on the WHODAS 2.0 compared to their counterparts in the rural villages who had higher scores. This concurs with previous findings in South Africa, which also employed the WHODAS 2.0 tool to report that functional disability (i.e., higher disability scores) was more frequent in rural settings than urban settings [42]. While there are currently conflicting results in the literature regarding the possible role of urban versus rural residence on disabilities [43, 44], it is plausible that reduced access to healthcare could predispose rural residents to experience poorer health. However, considering the community-based epilepsy treatment programs that were established in the four rural villages, the epilepsy care/ASM offered at the Mahenge urban hospital and the four rural epilepsy clinics were comparable. Slight differences may be in the practicalities of attending the epilepsy clinic at the Mahenge hospital compared to the four rural villages. Some of PWE enrolled at the Mahenge hospital clinic come from nearby rural villages where ASM are not available. In this case, only the less disabled PWE will be apt to cover the distance from their village to the Mahenge hospital. More research is needed to identify the specific factors in urban/rural settings that could influence PWE disability scores.

In the descriptive analysis, PWE who reported one or more seizures during the past month had significantly higher scores compared to seizure-free PWE. Furthermore, the multivariable models confirmed that having seizures during the past month predisposed the PWE to worse disability outcomes. This underscores the urgency to close the epilepsy treatment gap, which is still over 50% in developing countries [2]. Making ASM more available and accessible to PWE would not only decrease the seizure frequency but potentially decrease epilepsy-related disability and increase their quality of life. Future research with larger sample sizes may be required to further determine the ASM regimen which would yield optimal disability outcomes among PWE.

The fact that self-reported disability scores were lower than informant-reported scores has been previously documented in other conditions that impacted cognition and were explained by the fact that persons with reduced cognitive capacities tend to overestimate their well-being [45, 46]. This could also hold true for our study, in which informant-provided WHODAS 2.0 information yielded significantly higher disability scores. It is also

likely that only very disabled PWE would be unable to answer by themselves, requiring the caregiver to respond to the questionnaire. The source of information (self-reported versus informant) did not significantly influence the classification of the enrolled children into disabled or not disabled, probably because very few children responded by themselves, and most of the information was obtained from their caregivers (parents). Obtaining the correct information regarding the subjective well-being of persons with impaired cognition and/or very young individuals remains an important research gap that deserves to be addressed.

A main limitation of the study is the self-reporting nature of the study instrument, which could be subject to social desirability bias and reduced objectivity. Complementing our study with qualitative research could help to obtain a more in-depth understanding of the individuals' disabilities and the needs of PWE in Mahenge. Also, the sample size was small, particularly for the children, making it difficult to draw firm conclusions from our findings.

5. CONCLUSION

PWE in Mahenge, both children and adults alike, experience disabilities to different extents. The most affected domains point towards their limited involvement in societal activities as a major contributing factor. Comprehensive management schemes should be deployed to narrow the epilepsy treatment gap and promote acceptance and support of PWE in the Mahenge communities, particularly in rural areas. In addition, the implementation of peer support groups for PWE and their families could improve their psychosocial well-being, potentially resulting in lower disability scores.

DECLARATIONS

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Availability of data

After de-identification, all individual participant data underlying the results reported in this article will be made available immediately and indefinitely via the Zenodo repository following publication for anyone who wishes to access the data for any purpose.

Author contributions

The study was conceptualised by Dan Bhwana (DB), Bruno P. Mmbando (BPM) and Robert Colebunders (RC). The data collection was coordinated and implemented by DB, Lauren Vandevenne (LV), Filbert Francis (FF) and Bruno P. Mmbando (BPM). Data management was done by Daniel P. Chale (DPC), FF and BPM. Analysis and interpretation of data were done by Joseph Nelson Siewe Fodjo (JNSF) and BPM. The original draft was written by: JNSF, DB, BPM, and RC. Reviewing and editing was done by JNSF, DB, FF, Luís-Jorge Amaral (L-JA), DC, BM, and RC. All authors read and approved the final draft before submission.

Ethics approval and consent to participate

This study was approved by the ethical committees of the National Institute for Medical Research in Tanzania (NIMR/HQ/R.8a/Vol.IX/3342) and the University of Antwerp in

Belgium (B300201942516). The study was carried out adhering to the principles of the Declaration of Helsinki. Meetings were held with the community leaders to explain the aims and procedures of the study. Information was provided to all study participants and questions discussed before obtaining the consent. Individuals aged 18 years and above provided their own consent, while children and minors had their consent signed by their parents or guardians. Moreover, assent was obtained from those aged 12 years or above. For individuals who could read and/or write, consent was signed by fingerprint before an independent witness who also signed the form.

Consent for publication

Written informed consent was obtained from all participants described in this paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Beghi E, Giussani G, Sander JW: **The natural history and prognosis of epilepsy**. *Epileptic Disord* 2015, **17**(3):243-253.

2. **World Health Organisation, Epilepsy https://www.who.int/news-room/fact-sheets/detail/epilepsy**.

3. Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, Pringsheim T, Lorenzetti DL, Jette N: **Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies**. *Neurology* 2017, **88**(3):296-303.

4. Ba-Diop A, Marin B, Druet-Cabanac M, Ngoungou EB, Newton CR, Preux PM: **Epidemiology, causes, and treatment of epilepsy in sub-Saharan Africa**. *Lancet Neurol* 2014, **13**(10):1029-1044.

5. Angwafor SA, Bell GS, Njamnshi AK, Singh G, Sander JW: **Parasites and epilepsy: Understanding the determinants of epileptogenesis**. *Epilepsy Behav* 2019, **92**:235-244.

6. Colebunders R, J YC, Olore PC, Puok K, Bhattacharyya S, Menon S, Abd-Elfarag G, Ojok M, Ensoy-Musoro C, Lako R *et al*: **High prevalence of onchocerciasis-associated epilepsy in villages in Maridi County, Republic of South Sudan: A community-based survey**. *Seizure* 2018, **63**:93-101.

7. Boussinesq M, Pion SD, Demanga N, Kamgno J: **Relationship between onchocerciasis and epilepsy: a matched case-control study in the Mbam Valley, Republic of Cameroon**. *Trans R Soc Trop Med Hyg* 2002, **96**(5):537-541.

8. Mukendi D, Tepage F, Akonda I, Siewe JNF, Rotsaert A, Ndibmun CN, Laudisoit A, Couvreur S, Kabutako B, Menon S *et al*: **High prevalence of epilepsy in an onchocerciasis endemic health zone in the Democratic Republic of the Congo, despite 14 years of community-directed treatment with ivermectin: A mixed-method assessment**. *Int J Infect Dis* 2019, **79**:187-194.

9. Jada SR, Dusabimana A, Abd-Elfarag G, Okaro S, Brusselaers N, Carter JY, Logora MY, Rovarini JM, Newton CR, Colebunders R: **The Prevalence of Onchocerciasis-Associated Epilepsy in Mundri West and East Counties, South Sudan: A Door-to-Door Survey**. *Pathogens* 2022, **11**(4).

10. Levick B, Laudisoit A, Tepage F, Ensoy-Musoro C, Mandro M, Bonareri Osoro C, Suykerbuyk P, Kashama JM, Komba M, Tagoto A *et al*: **High prevalence of epilepsy in onchocerciasis endemic regions in the Democratic Republic of the Congo**. *PLoS Negl Trop Dis* 2017, **11**(7):e0005732.

11. Lenaerts E, Mandro M, Mukendi D, Suykerbuyk P, Dolo H, Wonya'Rossi D, Ngave F, Ensoy-Musoro C, Laudisoit A, Hotterbeekx A *et al*: **High prevalence of epilepsy in onchocerciasis endemic health areas in Democratic Republic of the Congo**. *Infect Dis Poverty* 2018, **7**(1):68.

12. Pion SD, Kaiser C, Boutros-Toni F, Cournil A, Taylor MM, Meredith SE, Stufe A, Bertocchi I, Kipp W, Preux PM *et al*: **Epilepsy in onchocerciasis endemic areas: systematic review and meta-analysis of population-based surveys**. *PLoS Negl Trop Dis* 2009, **3**(6):e461.

13. Raimon S, Dusabimana A, Abd-Elfarag G, Okaro S, Carter JY, Newton CR, Logora MY, Colebunders R: **High Prevalence of Epilepsy in an Onchocerciasis-Endemic Area in Mvolo County, South Sudan: A Door-To-Door Survey**. *Pathogens* 2021, **10**(5).

14. Siewe Fodjo JN, Tepage F, Colebunders R: **Epidemiological evidence concerning the association between onchocerciasis and epilepsy**. *Int J Infect Dis* 2019, **82**:77-78.

15. Siewe Fodjo JN, Remme JHF, Preux PM, Colebunders R: **Meta-analysis of epilepsy prevalence in West Africa and its relationship with onchocerciasis endemicity and control**. *Int Health* 2020, **12**(3):192-202.

16. Tumwine JK, Vandemaele K, Chungong S, Richer M, Anker M, Ayana Y, Opoka ML, Klaucke DN, Quarello A, Spencer PS: **Clinical and epidemiologic characteristics of nodding syndrome in Mundri County, southern Sudan**. *Afr Health Sci* 2012, **12**(3):242-248.

17. Chesnais CB, Boussinesq M: **Onchocerciasis-associated epilepsy - Authors' reply**. *Lancet Infect Dis* 2019, **19**(1):22.

18. Chesnais CB, Bizet C, Campillo JT, Njamnshi WY, Bopda J, Nwane P, Pion SD, Njamnshi AK, Boussinesq M: **A Second Population-Based Cohort Study in Cameroon Confirms the Temporal Relationship Between Onchocerciasis and Epilepsy**. *Open Forum Infect Dis* 2020, **7**(6):ofaa206.

19. Colebunders R, Njamnshi AK, Menon S, Newton CR, Hotterbeekx A, Preux PM, Hopkins A, Vaillant M, Siewe Fodjo JN: **Onchocerca volvulus and epilepsy: A comprehensive review using the Bradford Hill criteria for causation**. *PLoS Negl Trop Dis* 2021, **15**(1):e0008965.

20. Hadermann A, Amaral LJ, Van Cutsem G, Siewe Fodjo JN, Colebunders R: **Onchocerciasis-associated epilepsy: an update and future perspectives**. *Trends Parasitol* 2022.

21. Mbando B MM, Makunde M, Kakorozya A, Matuja W, Greter H, Suykerbuyk P, Colebunders R. : **High prevalence of epilepsy and onchocerciasis after 20 years of ivermectin use in four villages of the Mahenge are in Tanzania** In: *10th European Conference on Tropical Medicine and International Health , Antwerp, Belgium, 16-20 October 2017 Abstract 3OS54.* 2017.

22. Bhwana D, Mmbando BP, Dekker MC, Mnacho M, Kakorozya A, Matuja W, Makunde WH, Weckhuysen S, Colebunders R: **Clinical presentation of epilepsy in six villages in an onchocerciasis endemic area in Mahenge, Tanzania**. *Epileptic Disord* 2019, **21**(5):425-435.

23. Singh G, Sander JW: **The global burden of epilepsy report: Implications for low- and middle-income countries**. *Epilepsy Behav* 2020, **105**:106949.

24. Collaborators GBDE: **Global, regional, and national burden of epilepsy, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016**. *Lancet Neurol* 2019, **18**(4):357-375.

25. Leonardi M, Lee H, Kostanjsek N, Fornari A, Raggi A, Martinuzzi A, Yanez M, Almborg AH, Fresk M, Besstrashnova Y *et al*: **20 Years of ICF-International Classification of Functioning, Disability and Health: Uses and Applications around the World**. *Int J Environ Res Public Health* 2022, **19**(18).

26. Boschini LP, Tyson AF, Samuel JC, Kendig CE, Mjuweni S, Varela C, Cairns BA, Charles AG: **The role of seizure disorders in burn injury and outcome in Sub-Saharan Africa**. *J Burn Care Res* 2014, **35**(6):e406-412.

27. Mbizvo GK, Bennett K, Simpson CR, Duncan SE, Chin RFM: **Epilepsy-related and other causes of mortality in people with epilepsy: A systematic review of systematic reviews**. *Epilepsy Res* 2019, **157**:106192.

28. Kuper H: **Disability, mental health, stigma and discrimination and neglected tropical diseases**. *Trans R Soc Trop Med Hyg* 2021, **115**(2):145-146.

29. Kuper H: **Neglected tropical diseases and disability-what is the link?** *Trans R Soc Trop Med Hyg* 2019, **113**(12):839-844.

30. Mmbando BP, Suykerbuyk P, Mnacho M, Kakorozya A, Matuja W, Hendy A, Greter H, Makunde WH, Colebunders R: **High prevalence of epilepsy in two rural onchocerciasis endemic villages in the Mahenge area, Tanzania, after 20 years of community directed treatment with ivermectin**. *Infect Dis Poverty* 2018, **7**(1):64.

31. **Measuring Health and Disability, Manual for WHO Disability Assessment Schedule, WHODAS 2.0** [https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health/who-disability-assessment-schedule]

32. Friefeld Kesselmayer R, McMillan T, Lee B, Almane D, Hermann BP, Jones JE: **Psychosocial and functional outcomes in young adults with childhood-onset epilepsy: a 10-year follow-up**. *Dev Med Child Neurol* 2020, **62**(5):587-592.

33. **WG/UNICEF Child Functioning Module (CFM). Published 2020** [https://www.washingtongroup-disability.com/question-sets/wg-unicef-child-functioning-module-cfm/]

34. Zia N, Loeb M, Kajungu D, Galiwango E, Diener-West M, Wegener S, Pariyo G, Hyder AA, Bachani AM: **Adaptation and validation of UNICEF/Washington group child functioning module at the Iganga-Mayuge health and demographic surveillance site in Uganda**. *BMC Public Health* 2020, **20**(1):1334.

35. Castro S, Leite CF, Coenen M, Buchalla CM: **The World Health Organization Disability Assessment Schedule 2 (WHODAS 2.0): remarks on the need to revise the WHODAS**. *Cad Saude Publica* 2019, **35**(7):e00000519.

36. Abd-Elfarag G, Carter JY, Raimon S, Sebit W, Suliman A, Fodjo JNS, Olore PC, Biel KP, Ojok M, Logora MY *et al*: **Persons with onchocerciasis-associated epilepsy and nodding seizures have a more severe form of epilepsy with more cognitive impairment and higher levels of Onchocerca volvulus infection**. *Epileptic Disord* 2020, **22**(3):301-308.

37. Gumisiriza N, Mubiru F, Siewe Fodjo JN, Mbonye Kayitale M, Hotterbeekx A, Idro R, Makumbi I, Lakwo T, Opar B, Kaducu J *et al*: **Prevalence and incidence of nodding syndrome and other forms of epilepsy in onchocerciasis-endemic areas in northern Uganda after the implementation of onchocerciasis control measures**. *Infect Dis Poverty* 2020, **9**(1):12.

38. Van Cutsem G, Siewe Fodjo JN, Dekker MCJ, Amaral LJ, Njamnshi AK, Colebunders R: **Case definitions for onchocerciasis-associated epilepsy and nodding syndrome: A focused review**. *Seizure* 2023, **107**:132-135.

39. O'Neill S, Irani J, Siewe Fodjo JN, Nono D, Abbo C, Sato Y, Mugarura A, Dolo H, Ronse M, Njamnshi AK *et al*: **Stigma and epilepsy in onchocerciasis-endemic regions in Africa: a review and recommendations from the onchocerciasis-associated epilepsy working group**. *Infect Dis Poverty* 2019, **8**(1):34.

40. Siewe Fodjo JN, Dekker MCJ, Idro R, Mandro MN, Preux PM, Njamnshi AK, Colebunders R: **Comprehensive management of epilepsy in onchocerciasis-endemic areas: lessons learnt from community-based surveys**. *Infect Dis Poverty* 2019, **8**(1):11.

41. Bhwana D, Das L, Siewe Fodjo JN, Francis F, Challe DP, Makunde HW, Mmbando BP, Colebunders R: **A peer support group intervention to decrease epilepsy-related stigma in an onchocerciasis-endemic area in Mahenge, Tanzania: A pilot study**. *Epilepsy Behav* 2021, **124**:108372.

42. Peltzer K, Phaswana-Mafuya N, Pengpid S: **Rural-urban health disparities among older adults in South Africa**. *Afr J Prim Health Care Fam Med* 2019, **11**(1):e1-e6.

43. Zimmer Z, Wen M, Kaneda T: **A multi-level analysis of urban/rural and socioeconomic differences in functional health status transition among older Chinese**. *Soc Sci Med* 2010, **71**(3):559-567.

44. Kabir ZN, Tishelman C, Aguero-Torres H, Chowdhury AM, Winblad B, Hojer B: **Gender and rural-urban differences in reported health status by older people in Bangladesh**. *Arch Gerontol Geriatr* 2003, **37**(1):77-91.

45. Ermel J, Carter CS, Gold JM, MacDonald AW, 3rd, Daniel Ragland J, Silverstein SM, Strauss ME, Barch DM: **Self versus informant reports on the specific levels of functioning scale: Relationships to depression and cognition in schizophrenia and schizoaffective disorder**. *Schizophr Res Cogn* 2017, **9**:1-7.

46. Siu CO, Harvey PD, Agid O, Waye M, Brambilla C, Choi WK, Remington G: **Insight and subjective measures of quality of life in chronic schizophrenia**. *Schizophr Res Cogn* 2015, **2**(3):127-132.