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RESEARCH ARTICLE

Community-based epilepsy care in an onchocerciasis-endemic area: A 3-year cohort study in Mahenge, Tanzania

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Abstract

Objective: In onchocerciasis-endemic areas, limited access to antiseizure medications (ASMs) contributes to a high epilepsy burden. This study evaluated the impact of a community-based epilepsy care program in Mahenge, Tanzania, an onchocerciasis-endemic area with high epilepsy prevalence.

Methods: A baseline survey (2017–2018) identified persons with epilepsy (PWE) in four rural villages. Subsequently, PWE were invited to enroll in the epilepsy treatment program (2019–2022), where trained community health workers (CHWs) screened for epilepsy, promoted ivermectin intake to treat onchocerciasis, distributed ASMs, and monitored seizure frequency and ASM adherence monthly under supervision from the project clinician trained in epilepsy diagnosis and treatment. A concluding survey (2022) collected sociodemographic data and participants' status as alive, deceased, or lost to follow-up. Mixed-effects negative binomial regression analyzed risk factors for weekly seizure incidence rate.

Results: Of 206 participants, 77.7% reported bilateral tonic–clonic seizures, and 32.0% reported focal seizures. More than one third (38.5%) were suspected of having nodding syndrome. Weekly seizure frequency decreased significantly from a mean of 1.9 seizures (interquartile range [IQR] =0–2) at enrollment to .4 seizures (IQR=0–0) at the last follow-up (Wilcoxon test $p<.0001$), with significantly improved ASM adherence (57.5%–94.7%, McNemar test $p<.0001$). Factors associated with lower weekly seizure incidence included longer program participation, ASM adherence, carbamazepine use compared to phenobarbital, and ivermectin intake in 2022. ASM adverse events were associated with increased seizure frequency. The mortality rate was 32.7 deaths per 1000 person-years, with most deceased not fully adhering to ASM (88%) and having epilepsy-related causes of death (60%).

Correction added on 15 January 2025, after first online publication: the third affiliation was added.

Dan Bhwana and Luís-Jorge Amaral contributed equally to this work.

Significance: The community-based program using CHWs was associated with a significant reduction in seizure frequency and improved ASM adherence. In onchocerciasis-endemic areas, it should be investigated whether carbamazepine should be a preferred ASM in PWE. Ivermectin's impact on seizure frequency merits further investigation in onchocerciasis-endemic areas. Community-based epilepsy care is a promising strategy for scaling up epilepsy care in rural areas in Africa.

KEYWORDS

antiseizure medication, community care, epilepsy, nodding syndrome, onchocerciasis, sub-Saharan Africa

1 | INTRODUCTION

Epilepsy affects more than 50 million individuals worldwide and disproportionately burdens low- and middle-income countries.[1] Epilepsy can be effectively treated with antiseizure medications (ASMs), leading to seizure freedom and terminal remission for more than two thirds of persons with epilepsy (PWE) when taken consistently and initiated early.[2] However, a considerable disparity persists between the number of PWE who require ASM and those who receive it, known as the epilepsy treatment gap. This gap is particularly pronounced in sub-Saharan Africa, reaching an estimated 68.5% (95% confidence interval [CI] = 59.5%–77.5%).[1]

In sub-Saharan Africa, a particularly high epilepsy prevalence has been reported in areas heavily affected by onchocerciasis, a parasitic disease caused by *Onchocerca volvulus* and transmitted by blackflies.[3–7] Although the potential causality of this connection remains under investigation,[8] this strong epidemiological association has led to the concept of onchocerciasis-associated epilepsy (OAE).[6] OAE usually occurs in previously healthy children and adolescents (3–18 years old) in regions highly endemic for onchocerciasis, where elimination strategies are suboptimal or absent.[7] OAE may present with a wide range of seizure types including head nodding (nodding syndrome).[8]

Over the past decade, a significant decrease in epilepsy incidence, including nodding syndrome, has been observed in areas with ongoing *O. volvulus* transmission, following the implementation and strengthening of onchocerciasis elimination interventions. This trend has been demonstrated in countries such as Tanzania,[4] South Sudan,[5,9] Uganda,[10] and Cameroon,[11] primarily through community-directed treatment with ivermectin (CDTI), which targets the progeny (microfilariae) of *O. volvulus* and temporarily sterilizes the adult worm. Additionally, vector control methods may have contributed to this decline in South Sudan and Uganda.

Key points

- A community-based epilepsy care program reduced seizure frequency in persons with epilepsy in an onchocerciasis-endemic area in Tanzania.
- Free ASM, improved adherence, and access to second- and third-line ASMs were key contributors for seizure control.
- Carbamazepine and ivermectin warrant further investigation for their effect on epilepsy outcomes in onchocerciasis-endemic regions.
- Most deaths among persons with epilepsy were related to epileptic seizures and poor ASM adherence.

However, despite the overall success of onchocerciasis elimination programs, certain onchocerciasis-endemic regions still exhibit a high *O. volvulus* prevalence.[12] By the end of 2015, an estimated 381 000 individuals (95% CI = 158 000–1 636 000) were believed to suffer from OAE across onchocerciasis-endemic settings in Central and East Africa.[13] Moreover, epilepsy prevalence in these areas can take years to decline after the suppression of onchocerciasis transmission and associated decrease of epilepsy incidence,[4,5,9,10] reflecting the lifespan of those already affected by the condition.[14]

In onchocerciasis-endemic areas, PWE experience numerous challenges, including burns, injuries, cognitive impairment, disability, behavioral disorders, and increased mortality.[14–17] These rural settings also present substantial barriers, such as epilepsy-related stigma,[18] high treatment costs,[19] and poor health-related quality of life.[20] Limited resources and health care access exacerbate these challenges,[5,10,21] contributing to a wide epilepsy treatment gap and subsequent poor seizure control.[14,22]

Studies conducted in sub-Saharan Africa suggest that community-based epilepsy care interventions offer a promising approach to addressing these challenges. These interventions have the potential to be cost-effective[23,24] and result in improvements in epilepsy awareness, diagnosis, and treatment,[25,26] even in remote onchocerciasis-endemic rural villages.[22,24] For instance, a community-based epilepsy treatment program in an onchocerciasis-endemic area of the Democratic Republic of Congo improved ASM adherence and lowered treatment expenses for affected families.[24] Another example, a randomized controlled trial in Kenya, observed increased ASM adherence, reduced stigma, and decreased epilepsy misconceptions following a 1-day epilepsy education program.[27]

Recent studies in onchocerciasis-endemic villages highlighted the need for comprehensive and effective epilepsy care strategies to improve health outcomes,[22] prevent disability,[16] enhance quality of life,[20] and decrease the observed high mortality rates.[14] In response to this need, a community-based epilepsy treatment program was established and delivered by trained community health workers (CHWs) in four rural villages in Mahenge, Tanzania, an onchocerciasis-endemic area where the epilepsy burden is three to four times higher than in other parts of the country.[4] This study investigated the impact of the community program on seizure frequency and ASM use and adherence.

2 | MATERIALS AND METHODS

2.1 | Study setting

In February 2019, a community-based epilepsy treatment program was established in four rural villages in Mahenge, Tanzania: Mdindo, Msogezi, Mzelezi, and Sali (Figure 1). These villages were selected due to the documented high prevalence of both onchocerciasis and epilepsy, including nodding syndrome.[4] The primary occupations of the population are small-scale farming and livestock keeping (primarily chickens and goats), with a minority engaged in gemstone mining. Two of the study villages, Mdindo and Sali, participated in a community-based peer support program in 2019–2020 targeting PWE's quality of life.[29]

Baseline house-to-house surveys conducted in 2017–2018 revealed an epilepsy prevalence ranging from 2.9% (Mzelezi) to 3.7% (Sali), including an overall probable nodding syndrome prevalence of .6%, with 78% of PWE meeting the OAE criteria.[4] Onchocerciasis control was suboptimal, with CDTI coverage below the 80% threshold recommended for elimination and 42.6% of children aged 6–10 years testing positive for onchocercal antibodies.[21,28] In response, Tanzania's National Neglected Disease Control Program switched from annual to biannual CDTI in 2019.

2.2 | Community-based epilepsy treatment program

To implement the community-based epilepsy treatment initiative, local health care workers (HCWs) and CHWs who had previously received 1-year training in community health employed by the local government received training in epilepsy screening (using previously established evidence-based criteria[22]) and management. The latter included promoting participation in the biannual CDTI program, epilepsy awareness, and risk mitigation education (e.g., avoiding being near fires or rivers alone), distributing free ASM, and providing ongoing monitoring of PWE. In villages lacking health facilities (Mzelezi and Mdindo), epilepsy care was delivered by the CHWs with supervision from the project clinician (D.B.).[29] In villages with a health facility (Msogezi and Sali), both HCWs and CHWs were responsible for epilepsy care and supervised by a clinician (D.B.). The latter had been trained in epilepsy diagnosis and treatment, including a 1-month period at the neurology department of the Kilimanjaro Christian Medical Center in Moshi, Tanzania.

2.3 | Study design

This study employed a prospective open cohort design with baseline and concluding cross-sectional surveys to prospectively explore the impact of the community-based epilepsy treatment program on seizure frequency and determine the epilepsy-related mortality in four rural villages of Mahenge, Tanzania, from 2019 to 2022.

2.4 | Study procedures and participant follow-up

2.4.1 | Cross-sectional (baseline) survey

Between 2017 and 2018, two baseline surveys were carried out in six villages (two from urban and four from rural settings).[4] One hundred eighty-two PWE identified from the four rural villages, where the epilepsy prevalence was highest, were enrolled for the cohort follow-up study. During the baseline surveys, participants were asked whether they were taking ASM and, if so, if they fully adhered to their prescribed regimen without missing doses.

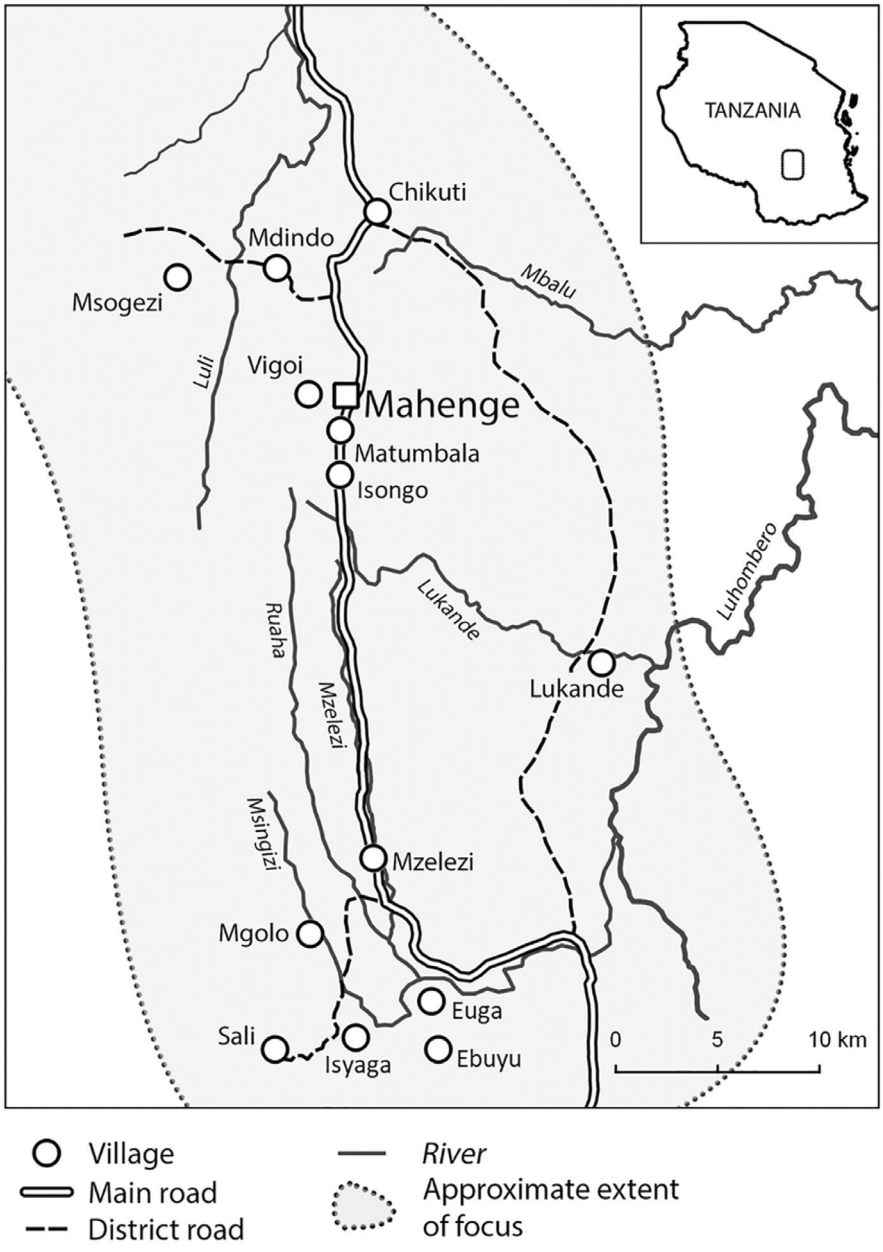

FIGURE 1 Map of the four study sites, Mdindo, Msogezi, Mzelezi, and Sali, in the Mahenge area.[28]

2.4.2 | Cohort study

From February 2019 to June 2022, PWE collected their medication on a monthly (28 days) basis at the health facility (Msogezi and Sali) or village office (Mzelezi and Mdindo). In villages without health facilities, CHWs collected ASM monthly from Mahenge Hospital to ensure an uninterrupted supply.

Missed collections prompted a CHW follow-up visit within 72 h to provide ASM. During ASM collection, information recorded included type and quantity of the past month's prescribed ASM, the remaining number of tablets from the previous prescription (to determine ASM adherence), seizure type and frequency in the week prior to the visit, seizure-related injuries, and observed ASM-related adverse effects. This information guided the monitoring of ASM effects and helped determine whether any treatment adjustments were needed. Subsequently, a new ASM prescription was issued and recorded along with the date for the next visit. Data were collected by CHWs and HCWs using Open Data Kit software on tablets. The data were transmitted daily to the central server at the National Institute for Medical Research (NIMR) in Tanga for assessment by study clinicians (D.B. and M.M.).

Individuals newly identified as suspected of having epilepsy within the study villages were referred to the study clinician for confirmation and seizure type determination. Confirmed PWE were treated with free ASM and invited to join the cohort.

2.4.3 | Cross-sectional (concluding) survey

An additional follow-up survey was conducted in June 2022, at the conclusion of the study (Questionnaire S1) in the four villages. The concluding survey aimed to ascertain the status of the cohort's participants and identify any PWE residing in the villages not enrolled in the cohort. The survey assessed their status as alive, relocated outside of the study village/lost to follow-up, or deceased. For deceased PWE, the time and cause of death were obtained from their relatives. Additionally, the survey captured ivermectin use in 2022 and baseline characteristics not directly influenced by the intervention received as part of the study (sex, age, and year of epilepsy onset).

2.5 | Epilepsy definition and classification

Epilepsy was defined as two or more unprovoked seizures at least 24 h apart.[30] The classification of seizure types followed the criteria set by the International League Against Epilepsy.[31]

Nodding seizures were defined as episodes of reduced consciousness during which the head dropped forward repeatedly. Suspected nodding syndrome was defined as a person with current or a history of nodding seizures.[7,32]

2.6 | Antiseizure medication

Phenobarbital was the primary ASM for all participants. Unsatisfactory responses to phenobarbital after adequate dose titration (e.g., no or suboptimal reduction in seizure frequency) prompted a switch to carbamazepine as a second-line treatment. If carbamazepine also proved ineffective, polytherapy combining both carbamazepine and phenobarbital was offered. Instances of persistent seizures despite these treatments led to a temporary shift in therapy to either phenytoin or lamotrigine (the latter for pregnant women), considering individual suitability, medication availability, and standard treatment guidelines.[33] Treatment adherence was defined as the consumption of all ASM tablets as prescribed.

2.7 | Statistical analysis plan

The sociodemographic and clinical features of PWE were described. Categorical variables were expressed as absolute (n) and relative (%) frequencies. Continuous variables were presented as the median and interquartile range (IQR) for nonnormally distributed data. Normality was assessed visually using histograms and verified with the Shapiro–Wilk test.

Because the data exhibited overdispersion, a mixed-effects negative binomial regression model was used to analyze the association between potential risk factors and the weekly number of seizures. Variables were retained in the final regression model controlled for age, sex, and village based on statistical significance and confounding relationships. The final negative binomial mixed-effects model was compared with an equivalent zero-inflated negative binomial model using both the Akaike information criterion (AIC) and Bayesian information criterion (BIC). The mixed-effects model was chosen due to its lower AIC/BIC and its ability to incorporate random effects by participant identifier to account for individual-level variability and nonindependence of reported seizures from the same participant over time. The model also retained an offset term reflecting the natural logarithm of the total number of follow-ups per participant.

The variable "months since the first visit" (enrollment duration) was logarithm-transformed and also included a squared term to capture the potential nonlinearity with seizure frequency. Similarly, a squared term for age was considered due to its link to epilepsy in onchocerciasis-endemic areas.[34]

A sensitivity analysis was performed by categorizing the village variable based on participation in the peer support program (Mdindo and Sali villages) or lack thereof (Msogezi and Mzelezi villages). Additionally, interaction terms were explored between (1) peer support and ASM adherence; (2) adherence to both ASM and ivermectin in 2022, to investigate a potential synergistic or antagonistic effect on seizure frequency[35]; (3) reported ASM side effects and ASM adherence; and (4) ASM use (sequential from phenobarbital to carbamazepine, and carbamazepine to polytherapy) and the logarithm-transformed "months since the first visit" variable to account for a potential time-dependent effect.

Regression assumptions (e.g., multicollinearity) were verified, and influential outliers were examined. Exponentiated results were reported as incidence rate ratios (IRRs), 95% CIs, and p-values (two-tailed, $p < .05$ significant).

The mortality rate of enrolled PWE was calculated as the number of deaths divided by the total number of person-years. All statistical analyses were performed using R software (version 2022.06.23, https://cran.r-project.org/bin/windows/base/old/4.2.1/).

2.8 | Ethical considerations

Ethical approval was obtained from the NIMR of Tanzania (reference: NIMR/HQ/R.8a/Vol. IX/3343)

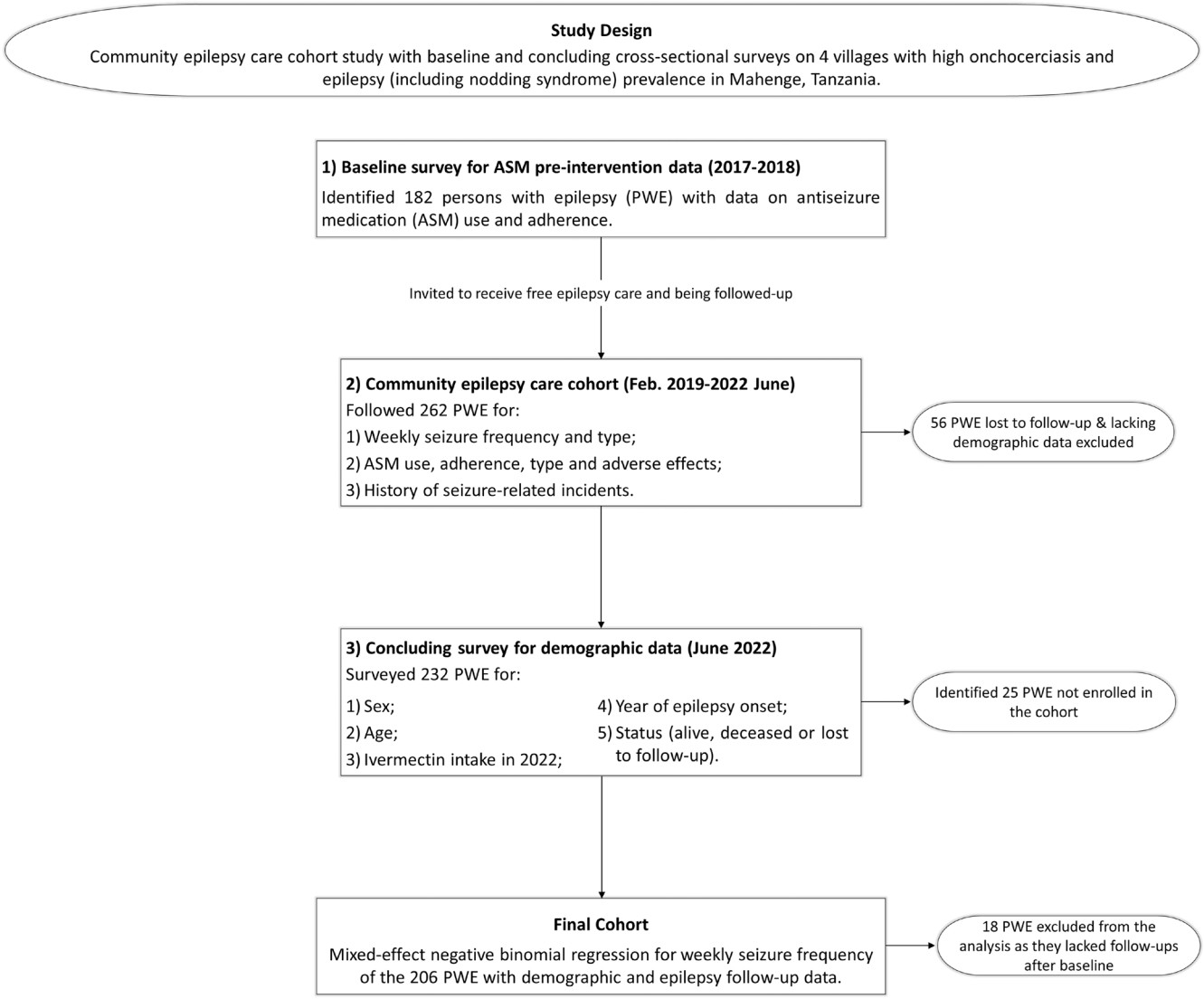

FIGURE 2 Flowchart of the community-based epilepsy care cohort study in Mahenge, Tanzania, which is endemic for onchocerciasis and epilepsy, including nodding syndrome.

and the University of Antwerp, Belgium (reference: B300201837863). All participants provided informed written consent before enrollment. For minors or non-competent participants, consent was obtained from a parent or guardian, with assent from those older than 12 years. Participants unable to read or write had the study explained orally and provided consent via fingerprint. All data were anonymized to ensure confidentially.

3 | RESULTS

A total of 262 PWE were enrolled in the cohort study (Figure 2). Data analysis included 206 PWE after excluding 56 (21.4%) lost to follow-up in the concluding survey, who lacked baseline demographic information (e.g., sex and age). The concluding survey identified 25 (8.7%) additional suspected PWE residing in the study villages but not enrolled in the cohort. An exploratory analysis investigated potential selection bias regarding the exclusion of PWE without baseline data (lost to follow-up) or those not enrolled in the cohort. No major differences were identified (Tables S1 and S2). However, those lost to follow-up had significantly lower seizure frequency and higher ASM adherence at baseline ($p = .019$), which became nonsignificant by the last follow-up ($p = .73$). Those not enrolled had a significantly higher proportion of deaths or emigrations ($p = .0012$) and epilepsy onset after the cohort began ($p = .015$).

3.1 | Sociodemographic characteristics

The median age of the 206 PWE was 26 years (range = 7–63 years; Table 1). In particular,

TABLE 1 Sociodemographic characteristics and ivermectin intake of the study participants in 2022.

Variable	Overall, $N = 206$
Age, years, median (IQR)	26 (20–37)
Sex, *n* (%, 95% CI)	
Female	103 (50.0, 43.2–56.8)
People with epilepsy available, *n* (%, 95% CI)	
Yes	176 (85.4, 79.7–89.8)
No, dead	16 (7.8, 4.7–12.5)
No, emigrated	14 (6.8, 3.9–11.4)
Ivermectin intake in 2022, *n*/T (%, 95% CI)[a]	151/166 (91.0, 85.3–94.7)

Note: The village-level analysis is available in Table S3.

Abbreviations: CI, confidence interval; IQR, interquartile range; T, total.

[a]Eleven participants did not know about their intake of ivermectin, 16 died, and 14 relocated outside of the study villages. Hence, these participants were excluded from this variable.

Mzelezi (25 years, IQR = 22–30) and Sali (19, IQR = 15–29 years) had younger demographics than Mdindo (32 years, IQR = 24–43) and Msogezi (30 years, IQR = 19–39; Table S3, $p = .003$). Half of the PWE were women (103, 50.0%). Ivermectin intake in 2022 was high overall (91.0%) and across all villages except Msogezi (73.7%).

3.2 | Epilepsy-related clinical characteristics in 2022

Only five (2.8%) of 176 PWE were diagnosed during the study period (2018–2022; two in Msogezi, two in Mzelezi, and one in Sali), with none diagnosed in the final year (2021–2022; Table 2). All these recent diagnoses were from individuals who had not received ivermectin for at least 1 year since 2018 (Table 3).

PWE were enrolled in the cohort for a median of 36 months (IQR = 26–38). Most participants (77.7%) reported experiencing bilateral tonic–clonic seizures. More than one--fourth (32.0%) reported focal seizures, of whom seven reported having seizures that progressed to bilateral tonic–clonic seizures. More than onethird of participants (38.5%) met the criteria for suspected nodding syndrome, with 13.8% reporting nodding seizures during follow-up.

Seventy participants (34.0%) reported ASM adverse events (e.g., dizziness or headache) during follow-up. Nearly half (43.2%) reported at least one seizure-related incident in the past, with the most prevalent events being abrasions (27.2%) and burn injuries (26.7%). Additional recorded events included lacerations (7.3%), head or dental injuries (6.8%), drowning incidents (6.3%), and instances of dislocation or fracture (3.4%).

TABLE 2 Epilepsy-related clinical characteristics of the study participants by 2022.

Variable	Overall, $N = 206$
Developed epilepsy in the past 4 years (2018–2022), *n*/T (%, 95% CI)	5/176 (2.8, 1.1–6.9)
Months enrolled in the study, median (IQR)	36 (26–38)
Type(s) of reported seizures during follow-up, *n*/T (%, 95% CI)	
Bilateral tonic–clonic	160/206 (77.7, 71.3–83.0)
Focal	66/206 (32.0, 25.8–38.9)
No seizures	26/206 (12.6, 8.6–18.1)
Nodding seizures[a]	24/174 (13.8, 9.2–20.0)
Suspected nodding syndrome, *n*/T (%, 95% CI)[b]	67/174 (38.5, 31.3–46.2)
Reported ASM adverse events during follow-up, *n*/T (%, 95% CI)	70/206 (34.0, 27.6–40.9)
Reported seizure-related incidents since epilepsy onset, *n*/T (%, 95% CI)	
Burn injury	55/206 (26.7, 20.9–33.4)
Submersion [drowning]	13/206 (6.3, 3.5–10.8)
Dislocation or fracture	7/206 (3.4, 1.5–7.2)
Laceration	15/206 (7.3, 4.3–12.0)
Abrasion	56/206 (27.2, 21.4–33.9)
Head or dental injury	14/206 (6.8, 3.9–11.4)
Overall	89/206 (43.2, 36.4–50.3)

Note: The village-level analysis is available in Table S4.

Abbreviations: ASM, antiseizure medication; CI, confidence interval; IQR, interquartile range; T, total.

[a]Only captured for seizures in 2022.

[b]In addition to individuals experiencing nodding seizures in 2022, "suspected nodding syndrome" accounts for those who had nodding seizures in the past.

3.3 | Baseline ASM use and adherence

Among the 182 individuals diagnosed with epilepsy in the baseline survey (2017–2018), 122 (67.0%) were receiving ASM treatment, with 89 (48.9%) reporting full adherence to an ASM treatment regimen.

TABLE 3 Cohort characteristics during the first and last appointments.

Variable	First follow-up	Last follow-up[a]	p[b]
Current ASM, n/T (%)			
Phenobarbital	162/188 (86.2)	139/188 (73.9)	<.0001
Carbamazepine	26/188 (13.8)	42/188 (22.4)	
Polytherapy [phenobarbital and carbamazepine]	0/188 (.0)	7/188 (3.7)	
ASM adherence, n/T (%)[c]	108/188 (57.5)	178/188 (94.7)	<.0001
Reported ASM-related adverse events n/T (%)	8/170 (4.7)	1/188 (.5)	.015
Seizures reported in the past week, n, mean (median, IQR)	1.9 (0, 0–2)	.42 (0, 0–0)[d]	<.0001

Abbreviations: ASM, antiseizure medication; IQR, interquartile range; T, total.

[a]Data from January 2022 and June 2022 were excluded from the analysis due to a temporary shortage of ASM during these months, which was not representative of the overall cohort's ASM adherence and related seizure frequency (Figure S1).

[b]Wilcoxon signed rank test with continuity correction for continuous variables and McNemar test for categorical variables (Fisher exact test if expected values < 5).

[c]There was no significant correlation between ASM adherence and the type of ASM.

[d]At the concluding survey, participants who were not lost to follow-up or deceased reported a mean number of weekly seizures of .25 (median = .0, IQR = 0–0).

3.4 | Cohort follow-up

Of 206 participants, 18 (8.7%) were excluded from the cohort analysis because they did not have a recorded follow-up after baseline (Figure 2). These individuals had significantly fewer seizures at baseline (Table S1, $p = .044$); however, this difference was no longer present when compared to those not excluded at the last follow-up ($p = .68$). The remaining 188 participants, who had at least one follow-up, had a median of 31 recorded monthly follow-ups (IQR = 21–36).

At enrollment, 162 of 188 participants (86.2%) were on phenobarbital and 26 (13.8%) were on carbamazepine (Table 3). At the last follow-up, there was a significant increase ($p < .0001$) of PWE on carbamazepine (22.4%) and polytherapy of carbamazepine and phenobarbital (3.7%) and a consequent decrease in those using phenobarbital (73.9%). Eight participants (4.3%) received treatment with lamotrigine or phenytoin either because of poor seizure control response to phenobarbital and carbamazepine or pregnancy.

Adherence to ASM improved significantly ($p < .001$) from 57.5% at enrollment to 94.7% at the last follow-up. Reported ASM-related adverse events significantly decreased from 4.7% to .5% ($p = .015$). These events were not significantly different between phenobarbital (2.4%) and carbamazepine (2.3%; $p = .99$). Participants reported a significant decrease ($p < .0001$) in weekly seizure frequency from a mean of 1.9 seizures (range = 0–74) at enrollment to .4 seizures (range = 0–28) at the last follow-up. This trend was captured by a significant negative linear association between seizure frequency and the time enrolled in the cohort (Figure S2).

Several predictors were significantly associated with reduced weekly seizure frequency, including older age ($p = .0002$), adherence to ASM ($p < .0001$), ivermectin use in 2022 ($p = .034$), and taking carbamazepine compared to phenobarbital ($p = .0092$; Table 4). Over time enrolled and compared to phenobarbital, carbamazepine use was also associated with a significant reduction in seizure incidence rate ($p = .014$), whereas polytherapy use was linked to a marginally significant reduction ($p = .063$). Conversely, factors significantly associated with a higher weekly seizure incidence rate included residing in Mzelezi village compared to Mdindo ($p = .0040$) and Msogezi ($p = .0016$) villages and experiencing ASM adverse events ($p < .0001$).

The frequency of seizures significantly decreased as the natural logarithm (ln) of the months since the first visit (time enrolled) increased, suggesting that participants experienced a lower weekly seizure incidence rate with longer enrollment. However, the association was not constant. Both the ln-transformed and the squared term of the ln-transformed months since the first visit were significant, indicating that the initial decline in seizure frequency slows over time, with the reduction rate decelerating at later stages of the program (Figure S3).

Due to missing data from 23 participants (12.2%), the final model excluded the variable for suspected nodding syndrome. However, an exploratory analysis incorporating this variable revealed no statistically significant association with weekly seizure frequency

TABLE 4 Predictors of seizure frequency using a negative binomial mixed model.

Variable	Incidence rate ratio (95% CI)	*p*
Age per year	.97 (.95–.98)	.0002
Sex, Ref: male		
Female	1.16 (.74–1.83)	.52
Village, Ref: Mzelezi		
Mdindo	.40 (.22–.75)	.0040
Msogezi	.34 (.18–.67)	.0016
Sali	.91 (.49–1.69)	.77
ln(months since first visit + .01)	.91 (.88–.94)	<.0001
(ln[months since first visit + .01])^2	.98 (.97–.99)	.0019
Ivermectin intake in 2022, Ref: No		
Yes	.39 (.17–.93)	.034
Other: died/relocated outside of the study village/ unknown	.62 (.23–1.71)	.36
ASM provided at each follow-up, Ref: phenobarbital		
Carbamazepine	.69 (.52–.91)	.0092
Polytherapy [phenobarbital and carbamazepine]	5.60 (.69–45.43)	.11
Other phenytoin/lamotrigine[a]	.09 (.00–2.94)	.17
ASM adherence at each follow-up, Ref: No		
Yes	.33 (.28–.40)	<.0001
Reported ASM adverse events during the study, Ref: No		
Yes	2.39 (1.82–3.13)	<.0001
Interaction term between ASM provided at each follow-up and ln(months since first visit + .01), Ref: phenobarbital[b]		
Carbamazepine	.90 (.83–.98)	.014
Polytherapy phenobarbital and carbamazepine	.53 (.27–1.04)	.063
Other phenytoin/lamotrigine[a]	1.28 (.43–3.81)	.66

Abbreviations: ASM, antiseizure medication; CI, confidence interval; ln, natural logarithm; Ref, reference category.

[a]Lamotrigine and phenytoin were grouped as "other," as they shared a similar association with the outcome variable and to improve model performance and stability.

[b]Exploration of potential interaction effects between variables revealed no statistically significant interactions or substantial model improvement except between ASM provided at each clinic visit and the follow-up variable "ln (months since first visit + .01)." The sensitivity analysis included interactions between ASM adherence and ivermectin adherence ($p = 1.00$), ASM adherence and ASM reported adverse events ($p = .67$), and village participation in the peer support program and ivermectin adherence ($p = .23$) as well as the age-squared term ($p = .21$). While including a dummy variable for each village significantly accounted for clustering effects, grouping villages by peer support intervention did not improve model fit and was not a significant term ($p = .32$). The correlation between age and ASM adherence was also not significant ($p = .22$). Lastly, there was a significant interaction between village and age, with Mdindo × age having fewer seizures than Mzelezi × age. However, this interaction increased the model's risk of overfitting (higher Bayesian information criterion and wider 95% CIs) and did not affect the coefficients of other variables (Table S5).

($p = .099$), although there was a trend suggesting individuals with suspected nodding syndrome might have a higher incidence rate of seizures (Table S6). The remaining coefficients and trends were consistent with those observed in the final model.

The analysis showed a significant association between ASM adherence and seizure frequency. Notably, temporary ASM shortages in December 2021 and May 2022 reduced adherence in the following month and were followed by increased seizures (Figure S3). The regression analysis included these months to reflect the real-world impact. A sensitivity analysis found no major difference when these months were removed, as the variability was explained by ASM adherence.

3.5 | Mortality and loss to follow-up

At the end of the follow-up, 176 of the 206 PWE (85.4%) were alive and residing in the study villages. Fourteen (6.8%) PWE relocated and were lost to follow-up, and 16 (7.8%) died during the follow-up period (out of 6029 person-months at risk). Fourteen (88%) of the deceased did not fully adhere to ASM, and more than one half (6/10) of the known causes of death were epilepsy-related (Text S1). Excluding those who relocated, the mortality rate among PWE was 32.7 (95% CI = 19.5–53.7) deaths per 1000 person-years.

4 | DISCUSSION

In Tanzania, where the epilepsy treatment gap remains significant (40%–85%),[1] the need for effective, scalable solutions is critical. This study investigated the effectiveness of a community-based epilepsy treatment program in Mahenge, an area coendemic for onchocerciasis and epilepsy, where epilepsy prevalence is significantly higher than in other parts of the country.[4] The program had a positive impact on seizure control, likely due to several key factors, which are discussed below.

Improved ASM adherence was likely a critical factor in better seizure control. The program provided consistent access to ASM, leading to a substantial rise in adherence rates. At baseline and the first clinic appointment, adherence fluctuated at approximately one half of the population (48.9% and 58.6%, respectively). By the final follow-up, adherence had significantly increased to more than nine out of 10 (94.7%). ASM adherence was significantly associated with a reduced seizure incidence rate, highlighting its importance in epilepsy management. Temporary ASM shortages in December 2021 and May 2022, followed by increased seizure frequency, underscored the importance of uninterrupted ASM supply, especially as seizure frequency promptly returned to lower levels once adherence was restored (Figure S1).

Although the free ASM provision was followed by a decrease in seizure frequency over time, ASMs are not universally effective. Studies suggest that up to 30% of PWE may not achieve complete seizure control with medication.[2] This might be reflected in the regression model, which includes the significant ln-transformed months enrolled variable and its squared term, suggesting that the initial decline in seizure frequency slows down at later stages of the program. This deceleration could be due to drug-resistant epilepsy in some participants or temporary ASM shortages. Additionally, approximately one third (34%) of participants reported ASM-related adverse events during follow-up.

The program facilitated a shift in ASM use when phenobarbital, the first-line therapy, failed to control seizures, transitioning PWE to carbamazepine or polytherapy (second- and third-line therapies, respectively). Carbamazepine use was associated with lower seizure frequency compared to phenobarbital, potentially due to broader efficacy and fewer side effects.[36] However, carbamazepine was introduced as a second-line therapy in this cohort, which warrants cautious interpretations. To address the difference in the timing of drug introduction, an interaction term between ASM type and time enrolled in the cohort was included in the model. Carbamazepine remained significantly associated with fewer seizures, both independently and in the interaction term, reinforcing its potential as a valuable ASM option in these settings.

In contrast, polytherapy was linked to a nonsignificant increase in seizure incidence compared to phenobarbital, possibly reflecting more severe, drug-resistant epilepsy. These participants had already shown poor response to both monotherapies, so direct comparisons may not be appropriate. Nevertheless, the model indicated a marginally significant decrease in seizure frequency over time for those on polytherapy (IRR = .53), suggesting that the program contributed to improved seizure management even for these more challenging cases.

A systematic review comparing carbamazepine and phenobarbital found limited evidence suggesting carbamazepine may have greater efficacy and fewer adverse events for generalized seizures.[36] However, in the current study, adverse event rates were similar between carbamazepine and phenobarbital, at 2%–3%, suggesting no major differences in tolerability. Recent studies highlight the benefits of carbamazepine in onchocerciasis-endemic areas. In Mahenge, carbamazepine, sodium valproate, and phenytoin were significantly associated with better quality of life for PWE compared to phenobarbital.[20] In Maridi, South Sudan, where 80% of PWE meet the criteria for OAE, health care workers preferred carbamazepine.[5,37] Additionally, a study in an onchocerciasis-endemic region of Cameroon reported lower cognitive scores in PWE treated with phenobarbital compared to those using carbamazepine, albeit not statistically significant.[38] These findings, along with results from the current study, suggest carbamazepine may warrant consideration as a preferred ASM in onchocerciasis-endemic settings with high epilepsy prevalence.

The intriguing association between ivermectin intake and reduced seizure frequency observed in this study aligns with previous research indicating a potential antiseizure effect of ivermectin in mice[39] and humans in onchocerciasis-endemic areas.[40] However, the mechanism by which ivermectin might exert this effect remains unclear. A possibility is a direct effect on the brain.

Nonetheless, given ivermectin's limited penetration of the mammalian brain, the therapeutic doses used for onchocerciasis control are unlikely to reach concentrations necessary for direct pharmacological action.[35] A more likely explanation is an indirect effect through the reduction of *O. volvulus* microfilarial load, as high microfilarial density has been associated with an increased risk of developing epilepsy.[17,35] Further research is necessary to explore the link between ivermectin use and reduced seizure frequency in these areas.

Although the epilepsy care program improved seizure control, mortality outcomes require further investigation. This study observed a mortality rate of 32.7 deaths per 1000 person-years, consistent with previous studies in Mahenge, which reported mortality rates of 10–76 deaths per 1000 person-years among PWE.[41–43] A recent systematic review of sub-Saharan Africa found that PWE have nearly five times higher mortality than the general population, with even higher rates in onchocerciasis-endemic areas.[14,44] Notably, 88% of the deceased in this cohort had not fully adhered to ASM, and six out of 10 deaths with known causes were epilepsy-related, closely mirroring another study in Mahenge where 52% of PWE deaths were epilepsy-related.[45] These findings underscore the importance of consistent ASM adherence in reducing the epilepsy burden.

Nearly half of the participants (43.0%) reported at least one seizure-related incident, such as drowning or burns, which significantly contribute to the elevated mortality risk among PWE.[44,46,47] In this cohort, seizure-related incidents accounted for 30% of deaths (Text S1), a proportion similar to that found in a previous study in Mahenge (26.7%).[45] This emphasizes the need for comprehensive and effective seizure management strategies that not only reduce seizure frequency but also incorporate preventive measures to minimize injury risk. Such strategies could include supervision near water or fire sources and avoiding high-risk activities like biking and tree/rock climbing.[47]

4.1 | Limitations

The study faced several limitations, such as the reliance on self-reported data susceptible to recall bias. This bias was mitigated by limiting the seizure frequency reports to the previous week, reducing the likelihood of inaccurate reporting over longer periods. Additionally, the observational design introduces the possibility of unobserved confounding factors, such as *O. volvulus* microfilarial load in the association between ivermectin and seizure frequency. There was also a lack of neurologist-supervised epilepsy classification, including to confirm the probable diagnosis of nodding syndrome. Another limitation was the absence of a systematic follow-up schedule for participants at the clinic, which was addressed in the regression model by incorporating an offset term for the varying follow-up frequencies among participants.

The significant association between older age and reduced seizure frequency may be influenced by survivor bias, as individuals with more severe epilepsy may have experienced higher mortality before the free ASM provision,[48] possibly leading to their underrepresentation in older age groups and the observed lower seizure frequency among older participants. A previous study in Mahenge reported higher mortality rates among PWE compared to the general Tanzanian rural population, especially among younger PWE and those unable to achieve seizure control.[45] This may also explain why Mdindo and Msogezi villages were associated with fewer seizures compared to Mzelezi, as the former had significantly older PWE populations ($p = .003$), as also observed in the baseline study.[49] Although survivor bias could affect age-related seizure outcomes, it is unlikely to compromise the cohort results. The regression model accounted for age as a confounding factor, and seizure frequency findings were adjusted accordingly. Additionally, sensitivity analyses, including a squared term for age and interaction terms with village, did not alter the significance or coefficients of other variables (Table S5).

Lastly, there is potential for selection bias due to the exclusion of participants lost to follow-up, as they lacked essential demographic information. Given that these individuals and their households could not be located during the concluding survey, many likely moved out of the study area. An exploratory analysis showed no major differences between those included in the study and those lost to follow-up, except that the latter group had lower baseline seizure frequency and higher ASM adherence at baseline. This may partially explain their loss to follow-up, as participants fully adherent to ASM prior to the study may have been less reliant on the program for seizure management. At the last follow-up, both groups had similar seizure frequency and ASM adherence (Table S1), reducing the likelihood of significant selection bias. The 21% loss to follow-up falls within acceptable limits for a cohort study, especially given the study's multiyear duration and rural, resource-limited settings.[50] Nevertheless, some underestimation of the mortality rate remains possible.

5 | CONCLUSIONS

This study demonstrates the effectiveness of a community-based epilepsy treatment program in Tanzania, resulting in a significant decrease in seizure frequency. Key factors contributing to this reduction include increased ASM

adherence, a shift toward second- and third-line ASMs when necessary, and the possible influence of ivermectin intake.

The program highlights the value of such community-based interventions in resource-limited settings, particularly for improving treatment access and adherence, and exploring alternative ASMs. Such interventions have the potential to decrease the epilepsy burden. Although the current study demonstrated the benefits of free treatment and close monitoring by CHWs, sustaining these efforts will require continuous financial and logistical support. Future research should focus on the cost-effectiveness and long-term sustainability of these programs. Additionally, the potential for carbamazepine to be a preferred ASM in onchocerciasis-endemic areas should be explored.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests. The study sponsor was involved in neither performing the research nor in the writing of the paper. The authors confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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REFERENCES

1. Owolabi LF, Owolabi SD, Adamu B, Jibo AM, Alhaji ID. Epilepsy treatment gap in sub-Saharan Africa: meta-analysis of community-based studies. Acta Neurol Scand. 2020;142:3–13.
2. Sillanpää M, Schmidt D. Long-term outcome of medically treated epilepsy. Seizure. 2017;44:211–6.
3. Pion SD, Kaiser C, Boutros-Toni F, Cournil A, Taylor MM, Meredith SE, et al. Epilepsy in onchocerciasis endemic areas: systematic review and meta-analysis of population-based surveys. PLoS Negl Trop Dis. 2009;16(3):e461.
4. Bhwana D, Amaral LJ, Mhina A, Hayuma PM, Francis F, Siewe Fodjo JN, et al. Impact of a bi-annual community-directed treatment with ivermectin programme on the incidence of epilepsy in an onchocerciasis-endemic area of Mahenge, Tanzania: A Population-Based Prospective Study. PLoS Negl Trop Dis. 2023;17:e0011178.
5. Jada SR, Amaral LJ, Lakwo T, Carter JY, Rovarini J, Bol YY, et al. Effect of onchocerciasis elimination measures on the incidence of epilepsy in Maridi, South Sudan: a 3-year longitudinal, prospective, population-based study. Lancet Glob Health. 2023;11:e1260–e1268.
6. Colebunders R, Njamnshi AK, Menon S, Newton CR, Hotterbeekx A, Preux PM, et al. *Onchocerca volvulus* and epilepsy: a comprehensive review using the Bradford Hill criteria for causation. PLoS Negl Trop Dis. 2021;15:e0008965.

7. 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;107:132–5.
8. Hadermann A, Amaral LJ, Van Cutsem G, Siewe Fodjo JN, Colebunders R. Onchocerciasis-associated epilepsy: an update and future perspectives. Trends Parasitol. 2023;39:126–38.
9. Amaral LJ, Jada SR, Ndjanfa AK, Carter JY, Abd-Elfarag G, Okaro S, et al. Impact of annual community-directed treatment with ivermectin on the incidence of epilepsy in Mvolo, a two-year prospective study. PLoS Negl Trop Dis. 2024;18:e0012059.
10. Gumisiriza N, Mubiru F, Siewe Fodjo JN, Mbonye Kayitale M, Hotterbeekx A, Idro R, 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;2(9):12.
11. Siewe Fodjo JN, Tatah G, Tabah EN, Ngarka L, Nfor LN, Chokote SE, et al. Epidemiology of onchocerciasis-associated epilepsy in the Mbam and Sanaga river valleys of Cameroon: impact of more than 13 years of ivermectin. Infect Dis Poverty. 2018;3(7):114.
12. Schmidt CA, Cromwell EA, Hill E, Donkers KM, Schipp MF, Johnson KB, et al. The prevalence of onchocerciasis in Africa and Yemen, 2000-2018: a geospatial analysis. BMC Med. 2022;7(20):293.
13. Vinkeles Melchers NVS, Mollenkopf S, Colebunders R, Edlinger M, Coffeng LE, Irani J, et al. Burden of onchocerciasis-associated epilepsy: first estimates and research priorities. Infect Dis Poverty. 2018;19(7):101.
14. Siewe Fodjo JN, Van Cutsem G, Amaral LJ, Colebunders R. Mortality among persons with epilepsy in onchocerciasis-endemic and non-endemic areas of sub-Saharan Africa: a systematic review and meta-analysis. Seizure. 2023;110:253–61.
15. Abd-Elfarag G, Carter JY, Raimon S, Sebit W, Suliman A, Fodjo JNS, 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;1(22):301–8.
16. Bhwana D, Siewe Fodjo JN, Amaral LJ, Vandevenne L, Francis F, Challe DP, et al. Disability assessment among persons with epilepsy in Mahenge, an onchocerciasis-endemic area in Tanzania: a cross-sectional study. Epilepsy Behav. 2023;146:109367.
17. Siewe Fodjo JN, Mandro M, Mukendi D, Tepage F, Menon S, Nakato S, et al. Onchocerciasis-associated epilepsy in the Democratic Republic of Congo: clinical description and relationship with microfilarial density. PLoS Negl Trop Dis. 2019;13:e0007300.
18. O'Neill S, Irani J, Siewe Fodjo JN, Nono D, Abbo C, Sato Y, 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;20(8):34.
19. Colebunders R, Siewe Fodjo JN, Kamoen O, Amaral LJ, Hadermann A, Trevisan C, et al. Treatment and prevenetion of epilepsy in onchocerciasis-endemic areas is urgently needed. Infect Dis Poverty. 2024;12(13):5.
20. Amaral LJ, Bhwana D, Fomo MF, Mmbando BP, Chigoho CN, Colebunders R. Quality of life of persons with epilepsy in Mahenge, an onchocerciasis-endemic area in Tanzania: a cross-sectional study. Epilepsy Behav. 2023;145:109302.
21. Mmbando BP, Suykerbuyk P, Mnacho M, Kakorozya A, Matuja W, Hendy A, et al. 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;20(7):64.
22. Siewe Fodjo JN, Dekker MCJ, Idro R, Mandro MN, Preux PM, Njamnshi AK, et al. Comprehensive management of epilepsy in onchocerciasis-endemic areas: lessons learnt from community-based surveys. Infect Dis Poverty. 2019;10(8):11.
23. van Diessen E, van der Maas F, Cabral V, Otte WM. Community-based rehabilitation offers cost-effective epilepsy treatment in rural Guinea-Bissau. Epilepsy Behav. 2018;79:23–5.
24. Dusabimana A, Mandro MN, Siewe Fodjo JN, Dolo H, Coenen S, Colebunders R. Coemmunity perceptions and attitudes regarding epilepsy and disease cost after implementation of a community-based epilepsy treatment program in onchocerciasis-endemic communities in the Democratic Republic of Congo. Epilepsy Behav. 2021;116:107773.
25. Idro R, Namusoke H, Abbo C, Mutamba BB, Kakooza-Mwesige A, Opoka RO, et al. Patients with nodding syndrome in Uganda improve with symptomatic treatment: a cross-sectional study. BMJ Open. 2014;14(4):e006476.
26. Ball DE, Mielke J, Adamolekun B, Mundanda T, McLean J. Community leader education to increase epilepsy attendance at clinics in Epworth. Zimbabwe Epilepsia. 2000;41:1044–5.
27. Ibinda F, Mbuba CK, Kariuki SM, Chengo E, Ngugi AK, Odhiambo R, et al. Evaluation of Kilifi epilepsy education programme: a randomized controlled trial. Epilepsia. 2014;55:344–52.
28. Hendy A, Krüger A, Pfarr K, De Witte J, Kibweja A, Mwingira U, et al. The blackfly vectors and transmission of *Onchocerca volvulus* in Mahenge, south eastern Tanzania. Acta Trop. 2018;181:50–9.
29. Bhwana D, Das L, Siewe Fodjo JN, Francis F, Challe DP, Makunde HW, et al. A peer support group intervention to decrease epilepsy-related stigma in an onchocerciasis-endemic area in Mahenge, Tanzania: a pilot study. Epilepsy Behav. 2021;28(124):108372.
30. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55:475–82.
31. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the international league against epilepsy: position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58:522–30.
32. Iyengar PJ, Wamala J, Ratto J, Blanton C, Malimbo M, Lukwago L, et al. Prevalence of nodding syndrome–Uganda, 2012–2013 MMWR. Morb Mortal Wkly Rep. 2014;18(63):603–6.
33. World Health Organization. Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders. https://www.who.int/publications/i/item/9789240084278
34. Raimon S, Dusabimana A, Abd-Elfarag G, Okaro S, Carter JY, Newton CR, et al. High prevalence of epilepsy in an onchocerciasis-endemic area in Mvolo County, South Sudan: A door-to-door survey. Pathogens. 2021;14:10.

35. Löscher W. Is the antiparasitic drug ivermectin a suitable candidate for the treatment of epilepsy? Epilepsia. 2023;64:553–66.
36. Nevitt SJ, Marson AG, Tudur Smith C. Carbamazepine versus phenobarbitone monotherapy for epilepsy: an individual participant data review. Cochrane Database Syst Rev. 2018;10:Cd001904.
37. Kamoen O, Jada SR, Rovarini JM, Abd-Elfarag G, Amaral LJ, Bol Y, et al. Evaluating epilepsy management in an onchocerciasis-endemic area: case of Maridi, South Sudan. Seizure. 2024;S1059-1311:00133-X.
38. Morin A, Guillaume M, Ngarka L, Tatah GY, Siewe Fodjo JN, Wyart G, et al. Epilepsy in the Sanaga-Mbam valley, an onchocerciasis-endemic region in Cameroon: electroclinical and neuropsychological findings. Epilepsia Open. 2021;6:513–27.
39. Manavi MA, Mohammad Jafari R, Shafaroodi H, Ejtemaei-Mehr S, Sharifzadeh M, Dehpour AR. Anticonvulsant effects of ivermectin on pentylenetetrazole- and maximal electroshock-induced seizures in mice: the role of GABAergic system and K(ATP) channels. Heliyon. 2022;8:e11375.
40. Dusabimana A, Tsebeni Wafula S, Raimon SJ, Fodjo JNS, Bhwana D, Tepage F, et al. Effect of Ivermectin treatment on the frequency of seizures in persons with epilepsy infected with *Onchocerca volvulus*. Pathogens. 2020;31:10.
41. Kaiser C, Kipp W, Gumisiriza N, Asaba G. Long-term observation and mortality of children with nodding syndrome in western Uganda, 1994–2018. Seizure. 2024.S1059-1311(24) :00185-7.
42. Levira F, Thurman DJ, Sander JW, Hauser WA, Hesdorffer DC, Masanja H, et al. Premature mortality of epilepsy in low- and middle-income countries: a systematic review from the mortality task force of the international league against epilepsy. Epilepsia. 2017;58:6–16.
43. Kegele J, Wagner T, Kowenski T, Wiesmayr M, Gatterer C, Alber M, et al. Long-term clinical course and treatment outcomes of individuals with nodding syndrome. J Neurol Sci. 2024;15(457):122893.
44. 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.
45. Jilek-Aall L, Rwiza HT. Prognosis of epilepsy in a rural African community: a 30-year follow-up of 164 patients in an outpatient clinic in rural Tanzania. Epilepsia. 1992;33:645–50.
46. Wirrell EC. Epilepsy-related injuries. Epilepsia. 2006;47(Suppl 1):79–86.
47. Nguyen R, Téllez Zenteno JF. Injuries in epilepsy: a review of its prevalence, risk factors, type of injuries and prevention. Neurol Int. 2009;16(1):e20.
48. Sperling MR, Feldman H, Kinman J, Liporace JD, O'Connor MJ. Seizure control and mortality in epilepsy. Ann Neurol. 1999;46:45–50.
49. Bhwana D, Mmbando BP, Dekker MC, Mnacho M, Kakorozya A, Matuja W, et al. Clinical presentation of epilepsy in six villages in an onchocerciasis endemic area in Mahenge. Tanzania Epileptic Disord. 2019;1(21):425–35.
50. Kristman V, Manno M, Côté P. Loss to follow-up in cohort studies: how much is too much? Eur J Epidemiol. 2004;19:751–60.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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