Incidence and prevalence of epilepsy and associated factors in a health district in North-West Cameroon: a population survey

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Abstract

This population-based cross-sectional survey with a follow-up case-control study assessed the prevalence, incidence and risk factors for epilepsy in a rural health district in the North-West Region of Cameroon. Community-based epilepsy screening targeted all inhabitants, six years and older, in all 16 health areas in the Batibo Health District. During door-to-door visits, trained fieldworkers used a validated questionnaire to interview consenting household heads to screen for epilepsy in eligible residents. Trained physicians subsequently assessed people with suspected seizures. After clinical assessment, they confirmed or refuted the diagnosis and estimated the date of epilepsy onset. A trained nurse interviewed people with epilepsy and randomly selected healthy individuals, obtaining relevant demographic details and information on exposure to risk factors for epilepsy. Out of 36,282 residents screened, 524 had active epilepsy. The age-standardized prevalence of active epilepsy was 33.9/1,000 (95% CI: 31.0-37.1/1,000). We estimated the one-year age-standardized epilepsy incidence at 171/100,000 (95%CI: 114.0-254.6). Active epilepsy prevalence varied widely between health areas, ranging between 12 and 75 per 1,000. The peak age-specific prevalence was in the 25-34 age group. In adults, multivariate analysis showed that having a relative with epilepsy was positively associated with epilepsy. Epilepsy characteristics in this population, geographical heterogeneity and the age-specific prevalence pattern suggest that endemic neurocysticercosis and onchocerciasis may be implicated. Further investigations are warranted to establish the full range of risk factors for epilepsy in this population.

Key words: seizures; epidemiology; parasitic diseases; risk factors; Batibo

Highlights

- The prevalence and incidence of epilepsy are high in the Batibo Health District
- There is a significant variation in epilepsy prevalence within the district
- The high epilepsy burden in the district could be attributable to parasitic infections
- Having a family history of epilepsy is a leading risk factor for epilepsy in adults

1. Introduction

Epilepsy is a significant cause of disease burden worldwide, especially in sub-Saharan Africa (SSA) [1]. In Cameroon, epilepsy is associated with a high level of stigma, discrimination and premature mortality [2-4]. Parts of Cameroon have an estimated epilepsy prevalence among the highest in SSA. Nevertheless, some of the values may be overestimated by surveys of relatively small populations, usually fewer than 2,000 people [5, 6]. A follow-up study in one of the previous survey sites in the Littoral Region [5] confirmed that the prevalence was probably previously overestimated [7]. Neurocysticercosis and, more recently, onchocerciasis have been reported as significant epilepsy risk factors in low and middle-income countries (LMICs). Both are endemic in many parts of Cameroon. For example, in the country's Western Region, there are an estimated 50,000 cases of neurocysticercosis [8]. There are also many endemic foci for onchocerciasis, mostly around fast-flowing rivers, suitable habitats for the Simulium fly, the onchocerciasis vector [9]. While recent studies in some onchocerciasis endemic areas in Cameroon show a high epilepsy prevalence [10-12], the true prevalence remains unknown in most communities where it is believed to be common. Epilepsy also coexists with endemic parasitic diseases with which it has been strongly linked. Due to the harmful effects of popular myths about epilepsy on health-seeking behavior, hospital data from such areas probably underestimate the epilepsy burden and are unreliable for public health planning. We investigated the prevalence, incidence, and risk factors for epilepsy in one such health district to generate evidence that may influence future research and public health policy on epilepsy prevention and management in Cameroon.

2. Methods

2.1. Study Setting

The Batibo Health District is located in a rural part of the North-West Region of Cameroon. It has a surface area of about 58 Km^2 covered by grasslands and a dense forest. It is divided into 16 health areas and has an estimated 82,000 inhabitants, most of whom speak either

Pidgin-English (lingua franca) or the Batibo language. Each area has at least one health center. There is a 75-bed capacity District Hospital, the only referral hospital in the district. Pig farming is widespread, driven by a high demand for pork in traditional ceremonies, and as a result, the district could be endemic for taeniasis and neurocysticercosis [13]. Onchocerciasis is also endemic, facilitated by the River Momo, which flows through most of the district and could favor breeding of the vector of *Onchocerca volvulus*. Malaria is the most common diagnosis at the district hospital. We chose this Health District based on community health workers' repeated claims that epilepsy is common in the area.

2.2. Procedure

We conducted a cross-sectional study to screen for epilepsy in the entire health district, followed by a case-control study to identify factors associated with epilepsy in this population. The investigation proceeded through the following stages (described in detail below and summarized in Figure 1): census of households and their occupants; epilepsy screening; and selection of people with epilepsy and controls for the case-control arm of the study.

2.2.1. Census of households and persons

The census covered all permanent residents of the Batibo Health District. Health areas were divided into zones. Teams, each with a community relay agent and a nurse, were assigned, to each zone for census and epilepsy screening. With the assistance of an interpreter with mastery of English, Pidgin English and the Batibo language, all received training on administering the questionnaires in Pidgin-English and in the Batibo language to ensure standardization of the interviews. Each team enumerated all dwellings within their zone and obtained demographic information on the occupants from the head or the household's most senior occupant. Unoccupied homes were revisited once.

2.2.2. Epilepsy screening

The population was screened for convulsive and non-convulsive epilepsy in a two-stage process. The screening targeted only permanent residents who were six years or older, to minimize the risk of misclassification of febrile seizures or other acute symptomatic seizures as epilepsy. Permanent residents were people living within the district for at least the preceding three months.

Stage 1: Immediately after enumerating people in a household, field workers interviewed heads of household, acting as proxies for the rest of the family, to identify people with suspected epilepsy in each house. The questionnaire included five symptom-based questions, previously used, which have high sensitivity in identifying people with seizures [14, 15] (See supplementary Table 1). A “yes” response to any of the five questions was recorded as a screen positive, and the person concerned was invited to the nearest designated health center for further assessment.

Stage 2: Within two to five days of the end of stage 1 screening in their community, people with suspected epilepsy were assessed by one of three trainee neurologists, who had training in epilepsy and had previously participated in community screening (SAA, LNN and LN). These physicians established the final diagnosis after a detailed event and medical history and a thorough general and neurological examination. For this study, we operationally defined active epilepsy as two or more unprovoked seizures with at least one in the 12-months preceding the survey, irrespective of antiseizure medication (ASM) treatment. We choose 12 months as the cut-off period for active epilepsy for two reasons. We were keen to determine the short-term seizure burden in this community and using this information to inform health providers on the real needs of antiseizure medication. Data on the epilepsy treatment gap and related factors are provided elsewhere (REF Angwarfor et al. Epilepsy in a health district in North-West Cameroon: clinical characteristics and treatment gap. Epilepsy & Behavior 2021 (in press)

2.2.3. Case-control study: selection of participants

All people identified with active epilepsy were invited to participate in the case-control study. Healthy individuals were randomly selected as controls from the database of people who screened negative during stage 1. People with epilepsy were interviewed by a nurse immediately after clinical assessment by the physician, using a structured questionnaire to identify exposure to known historical risk factors for epilepsy. Information from any who could not understand the questions was gathered with a caregiver's help. Controls were interviewed during a subsequent visit to their home by the survey teams. Controls who were absent from their homes during the initial visit were interviewed during subsequent visits.

2.3. Statistical Analysis

Data analysis was conducted using R statistical software (version 3.2). The crude lifetime prevalence of epilepsy was determined by dividing the total number of people with a seizure in the past by the total population screened in stage 1. The crude prevalence of active epilepsy was estimated by dividing the total number of people with active epilepsy by the population screened in stage 1. The 1-year incidence of epilepsy was estimated by dividing those with 'new' epilepsy (those with active epilepsy with seizure onset in the preceding 12 months) by the sum of those with new epilepsy and the total population who screened negative for epilepsy in stage 1. Age-standardized prevalence and incidence were estimated with the epitools package, based on Cameroon's national demographic distribution across age bins for 2013 [16]. We excluded those with missing ages. The standardization and exact confidence intervals were determined by the direct method. The prevalence values were corrected for attrition by dividing the age-specific prevalence values by 0.48, the fraction of people who screened positive in stage 1 and who participated in the clinical assessment in stage 2. Analysis of the case-control study was performed separately for children (≤16 years) and adults (>16 years). For each group, the odds ratios, confidence intervals and p-values were generated, first from univariate analysis and then with multivariate analysis for the variables which were statistically significant in univariate analysis.

3. Ethical Considerations

The study obtained ethical clearance from Cameroon's National Ethics Committee (Ethical Clearance Reference: 2016/12/853/CE/CNERSH/SP). During the household survey, verbal consent was obtained from the household head before proceeding with the interview. Written informed consent was obtained from all participants who visited the health centre. All people with epilepsy were included in an epilepsy register shared with the District Medical Officer to facilitate follow-up of cases and public health planning. The District Medical Officer is duty-bound to respect participants' confidentiality. At the end of the study, a two-day epilepsy training program was provided for all the physicians and at least two nurses per health area.

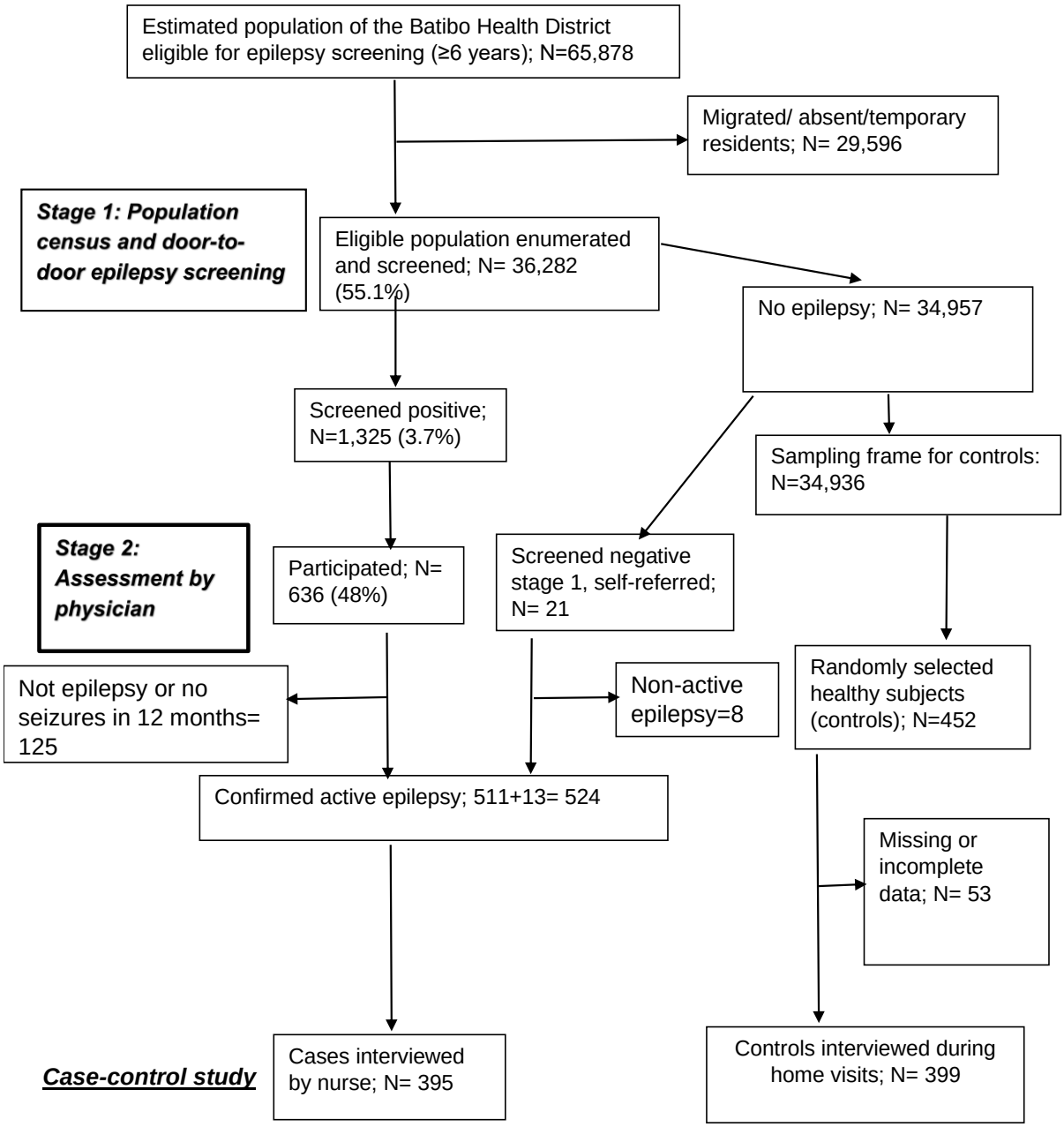

Figure 1. Flow chart of study design

4. Results

4.1. Census and epilepsy screening

Field workers visited 8,398 homes; basic demographic information was obtained for 36,282 permanent residents, who were all screened for epilepsy. Twelve per cent of households had a suspected case of epilepsy, and 2% had more than one. Of 1,325 residents identified in stage 1 with suspected epilepsy, 48% were assessed by the physician in stage 2 (Table 1). Twenty-one people who screened negative in stage 1 also chose to attend the health centre for clinical assessment. All of them had a history of epileptic events, and 13 were diagnosed with active epilepsy.

Table 1. Epilepsy Screening

Health area	People screened	People with suspected epilepsy in Stage 1	People with suspected epilepsy in stage 1 seen in Stage 2	Total number of people screened in stage 2 *	People with confirmed epileptic event (s)	People with confirmed active epilepsy
Anjake	697	18 (2.6%)	12 (66.7%)	12	12 (100%)	11 (91.7%)
Ashong	3,170	83 (2.6%)	44 (53.0%)	44	40 (90.9%)	31 (77.5%)
Batibo	5,655	174 (3.1%)	85 (48.9%)	87	83 (95.4%)	66 (79.5%)
Bessi	1,948	56 (2.9%)	20 (35.7%)	21	14 (66.7%)	10 (71.4%)
Bifang	1,712	112 (6.5%)	48 (42.9%)	53	42 (79.2%)	38 (90.5%)
Eka	2,232	61 (2.7%)	39 (63.9%)	39	38 (97.4%)	33 (86.8%)
Ewai	2,950	107 (3.6%)	48 (44.9%)	48	42 (87.5%)	33 (78.6%)
Ewoh	1,312	77 (5.9%)	40 (51.9%)	41	39 (95.1%)	32 (82.1%)
Guzang	2,553	46 (1.8%)	25 (54.3%)	26	26 (100%)	20 (76.9%)
Gwofon	1974	66 (3.3%)	37 (56.1%)	37	36 (97.3%)	33 (91.7%)
Kugwe	2,168	69 (3.2%)	41 (59.4%)	43	40 (93.0%)	35 (87.5%)
Kulabei	2,565	121 (4.7%)	41 (33.9%)	46	46 (100%)	41 (89.1%)
Larinji	1,575	21 (1.3%)	11 (52.4%)	11	11 (100%)	11 (100%)
Olorunti	1,260	52 (4.1%)	30 (57.7%)	30	30 (100%)	24 (80.0%)
Tiben	1,469	101 (6.9%)	57 (56.4%)	58	57 (98.3%)	49 (86.0%)
Widikum	3,042	161 (5.3%)	58 (36.0%)	61	60 (98.4%)	57 (95.0%)

Overall	36,282	1,325 (3.7%)	636 (48.0%)	657	616 (93.8%)	524 (85.1%)

Data in bracket are percentages of the number in the preceding column
**Including 21 people who were negative in stage 1 but who turned up for stage 2 screening*

4.2. Epilepsy Prevalence

The crude lifetime epilepsy prevalence (at least one ever unprovoked seizure) was 17/1,000 (95% CI: 16-18/1,000). After age-standardization and adjusting for attrition, the lifetime prevalence was estimated at 41/1,000 (95% CI: 37-44/1,000). The crude prevalence of active epilepsy was 14.4/1,000 (95% CI: 13.3-15.7/1,000). After age-standardization and correction for attrition, the prevalence of active epilepsy was 33.9/1,000 (95% CI: 31.0-37.1/1,000).

4.2.1. Prevalence of active epilepsy by health area

The prevalence of active epilepsy was two to four times higher in Tiben, Ewoh, Bifang, Olorunti and Widikum relative to Ashong. In contrast, the prevalence in Bessi was about half that in Ashong (Table 2). We could not perform an analysis to compare the risk of epilepsy with geographical proximity to the Momo River. It seems, however, that many health areas with high prevalence (e.g Tiben, Bifang, Widikum, Gwofon, and Olorunti) are also closer to the Momo river than the other health areas (Figure 2)**.** Within health areas, zones with a crude prevalence of at least 2% were clustered around the Momo river.

Table 2. Prevalence of active epilepsy by health area

Health area	Population screened	People with confirmed active epilepsy	Crude prevalence/1,000	Age-standardised* prevalence/1,000	Age-standardised prevalence adjusted for attrition**/1,000	***Prevalence ratio
Anjake	697	11	15.8 (8.3-28.9)	17.1 (8.5-30.9)	35.6 (17.7-64.3)	1.6 (0.8-2.9)
Ashong	3,170	31	9.8 (6.8-14.0)	11.6 (7.7-16.9)	24.1 (16.0-35.2)	1
Batibo	5,655	66	11.7 (9.7-14.1)	12.7 (9.8-16.2)	26.4 (20.4-33.7)	1.2 (0.9-1.5)
Bessi	1,948	10	5.1 (2.6-9.8)	5.8 (2.7-11.2)	12.1 (5.6-23.3)	0.5 (0.2-1.0)
Bifang	1,712	38	22.2 (15.9-30.7)	23.8 (16.7-33.2)	49.6 (34.8-69.2)	2.3 (1.6-3.1)
Eka	2,232	33	14.8 (10.4-20.9)	16.4 (11.2-23.4)	34.2 (23.3-48.7)	1.5 (1.1-2.1)
Ewai	2,950	33	11.2 (7.8-15.9)	12.8 (8.7-18.2)	26.7 (18.1-37.9)	1.1 (0.8-1.6)
Ewoh	1,312	32	24.4 (17.0-34.7)	27.7 (18.9-39.4)	57.7 (39.4-82.0)	2.5 (1.7-3.5)
Guzang	2,553	20	7.8 (4.9-12.3)	10.2 (6.1-16.1)	21.2 (12.7-34.8)	0.8 (0.5-1.3)
Gwofon	1,974	33	16.7 (11.7-23.7)	21.4 (14.7-30.2)	44.6 (30.6-62.9)	1.7 (1.2-2.4)
Kugwe	2,168	35	16.1 (11.4-22.6)	19.7 (13.5-28.0)	41.0 (28.1-58.3)	1.7 (1.2-2.3)
Kulabei	2,565	41	16.0 (11.6-21.8)	18.3 (13.1-25.2)	38.1 (27.3-52.5)	1.6 (1.2-2.2)
Larinji	1,575	11	7.0 (3.7-12.9)	8.3 (4.0-15.5)	17.3 (8.3-32.3)	0.7 (0.4-1.3)
Olorunti	1,260	24	19.0 (12.5-28.7)	19.5 (12.5-30.6)	40.6 (26.0-63.7)	1.9 (1.3-2.9)
Tiben	1,469	49	33.4 (25.0-44.2)	36.0 (26.4-48.2)	75.0 (55.0-100.4)	3.4 (2.6-4.5)
Widikum	3,042	57	18.7 (14.3-24.4)	18.9 (14.3-24.7)	39.4 (29.8-51.4)	1.9 (1.5-2.5)
Overall	36,282	524	14.4 (13.3-15.7)	16.3 (14.9-17.8)	33.9 (31.0-37.1)	-

Values in parenthesis represent the 95% confidence interval

**Age standardization used the Cameroon census population of 2003*

*** 48% of people screened positive in stage 1 were assessed in stage 2. To correct for attrition, the age-adjusted prevalence was divided by 0.48.*

**** Ashong was arbitrarily used as the reference to compute the prevalence ratios and confidence intervals*

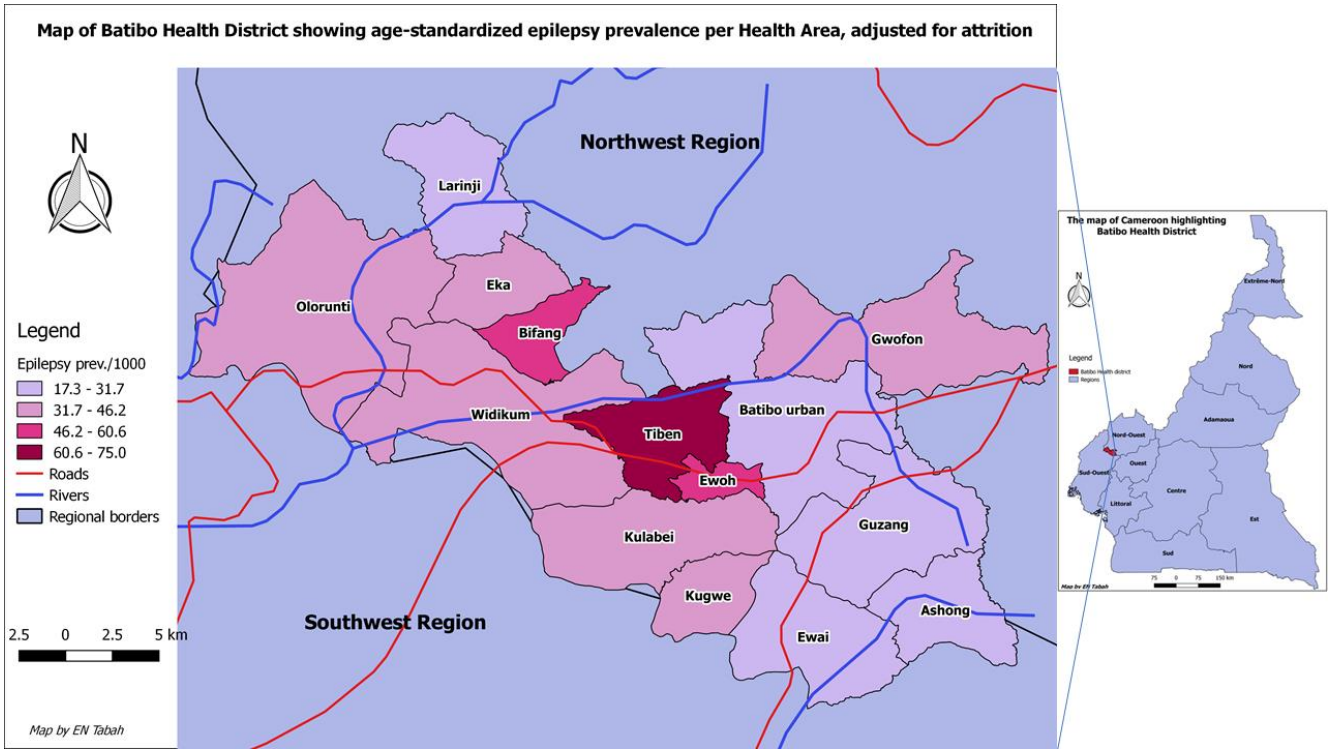

Figure 2. Map of Batibo Health District showing the prevalence of age-standardized epilepsy concerning the Momo River

4.2.2. Prevalence of active epilepsy by age and gender

Table 3 and Figure 3 show the gender- and age-specific prevalence of active epilepsy. The peak prevalence of active epilepsy was in the 25-34 age category, followed by people in the 20-24 and 15-19 age groups (Figure 3). Overall, there was no difference in the prevalence between genders except between 35 and 45 years, where prevalence seemed slightly higher in males than in females (Figure 3).

Table 3. Prevalence per 1,000 people of active epilepsy by age and gender

	Total Screened	Number of people with active epilepsy	Age/gender-specific prevalence adjusted for attrition (95% CI)	*Prevalence Ratio (95% CI)
Sex				
Female	19,322	275	29.6 (26.2-33.3)	1
Male	16,935	249	30.5 (27.0-33.8)	1.03
Age				
6-9	5,374	20	7.7 (4.8-12.1)	1
10-14	6,198	37	12.3 (8.8-17.3)	1.6 (1.2-2.2)
15-19	4,917	100	42.4 (34.6-51.6)	5.5 (4.5-6.7)
20-24	3,265	104	66.3 (54.5-80.5)	8.6 (7.0-10.4
25-29	2,761	112	84.4 (70.1-101.5)	10.9 (9.0-13.1)
30-34	2,236	85	79.2 (63.7-97.8)	10.3 (8.2-12.6)
35-39	2,181	30	28.5 (19.8-41.2)	3.7 (2.5-5.3)
40-44	1,946	9	9.6 (4.6-19.0)	1.2 (0.6-2.4)
45-49	1,704	1	1.2 (0.1-7.9)	0.2 (0.01-1.0)
50-54	1,509	8	10.9 (5.1-22.9)	1.4 (0.7-2.9)
55-59	937	5	11.8 (4.1-27.3)	1.4 (0.5-3.5)
60-64	1,086	4	7.6 (2.4-20.9)	1.0 (0.3-2.7
65-100	2,168	9	8.6 (0.5-17.1)	1.1 (0.5-2.2)

** 6-9 age group was used as reference to compute the prevalence ratio and confidence intervals*

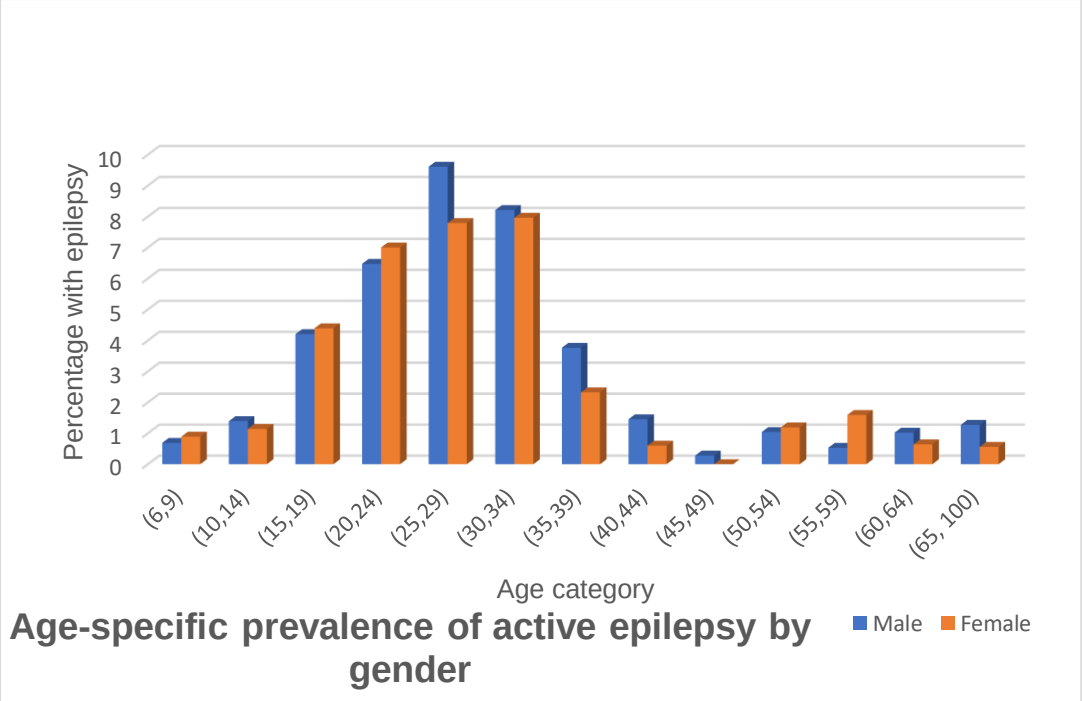

Figure 3. Gender-specific prevalence of active epilepsy by age category

4.3. Incidence of Epilepsy

The crude 1-year incidence of epilepsy was estimated as 66.7/1,000 (95%CI: 44.5-99.2/1,000). After age-standardization and correction for attrition, the incidence was 171.1/1,000 person-years (95%CI: 114.0-254.6/1,000). The median age of those with incident epilepsy was 13.5 years (IQR: 7-18 years).

4.4. Factors associated with epilepsy

Of the 524 people with active epilepsy, data was obtained from 395 people (327 adults and 68 children). Of 452 randomly selected healthy community controls (286 adults and 166 children), data could be collected from 399 people (258 adults and 141 children), yielding a participation rate of 88.3%.

4.4.1. Factors associated with epilepsy in children

The results of the analysis of factors associated with epilepsy in children are summarised in Table 4. After multivariate analysis, a history of febrile seizures was the only factor significantly associated with epilepsy. Other perinatal factors such as a history of previous maternal stillbirth, pregnancy condition (normal vs abnormal), delivery condition (normal vs complicated), place of delivery (home vs health facility) and neonatal complications were not significantly associated with epilepsy (Table 4). More children with epilepsy than controls lived in the same house as someone with epilepsy or had a family history of a first or second degree relative with epilepsy. In each case, however, the association was not significant after multivariate analysis.

Table 4. Factors associated with epilepsy in children (≤16 years)

Risk Factor	Children with active epilepsy	Controls	Univariate Analysis		Multivariate Analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
Age (OR for 1-year increase)			**1.2 (1.1-1.3)**	**0.0004**	1.2 (0.9-1.4)	0.16
Gender (male)	36/68 (52.9%)	69/141(48.9%)	1.2 (0.6-2.2)	0.45		
Orphan	4/51 (7.8%)	5/112 (4.5%)	1.8 (0.3-8.8)	0.38		
History of maternal stillbirth	12/49 (24.5%)	10/109 (9.2%)	**3.2 (1.2-9.0)**	**0.001**	2.9 (0.5-16.3)	0.21
Normal term pregnancy	33/41 (80.5%)	100/104 (96.2%)	**0.2 (0.03-0.7)**	**0.002**	0.1 (0.01-26)	0.22
Normal delivery	44/48 (91.7%)	104/107 (97.2%)	0.3 (0.04-1.9)	0.12		
Delivery in hospital	37/52 (71.2%)	90/111 (81.1%)	0.6 (0.3-1.3)	0.15		
Birth/neonatal complication	15/49 (30.6%)	18/111 (16.2%)	**2.3 (1.0-5.3)**	**0.04**	1.1 (0.3-4.6)	0.86
Completed vaccines	38/49 (77.6%)	81/111 (73.0%)	1.3 (0.5-3.1)	0.54		
Febrile convulsion	23/50 (46.0%)	11/111 (9.9%)	**7.7 (3.1-19.7)**	**<0.001**	**5.7 (1.0-33.1)**	**0.02**
Febrile convulsion in sibling	8/51 (15.7%)	11/111 (9.9%)	1.7 (0.5-4.9)	0.29		
Poor toilet facilities	58/68 (85.3%)	123/140 (87.9%)	0.8 (0.3-2.1)	0.60		
Reliable water source	42/68 (61.8%)	90/140 (64.3%)	0.9 (0.4-1.7)	0.72		
Cats in household	16/67 (23.9%)	46/138 (33.3%)	0.6 (0.3-1.2)	0.17		
Dogs in household	6/68 (8.8%)	36/140 (25.7%)	**0.3 (0.1-0.7)**	**0.004**	0.2 (0.03-1.)	0.11
Pigs household	30/68 (44.1%)	70/140 (50.0%)	0.8 (0.4-1.5)	0.42		
Person with epilepsy in household	20/68 (29.4%)	23/140 (16.4%)	**2.1 (1.0-4.4)**	**0.03**	2.5 (0.6-11.6)	0.23
1st degree relative with epilepsy	14/68 (20.6%)	5/140 (3.6%)	**7.0 (2.2-25.7)**	**0.0001**	1.8 (0.2-18.0)	0.62
2nd degree relative with epilepsy	26/67 (38.8%)	27/136 (19.9%)	**2.6 (1.3-5.1)**	**0.004**	1.5 (0.4-5.5)	0.41
Parents related	3/59 (5.1%)	19/115 (16.5%)	**0.3 (0.05-1.0)**	**0.03**	0.1 (0.01-1.4)	0.098
History of meningitis	8/68 (11.8%)	1/136 (0.7%)	**18 (2.2-804.3)**	**0.0003**	2.4 (0.2-31.0)	0.49
Head injury	9/58 (15.5%)	4/119 (3.4%)	**5.3 (1.4-24.3)**	**0.004**	0.7 (0.08-7.2)	0.82
Received Ivermectin	57/68 (83.8%)	119/139 (85.6%)	0.9 (0.3-3.2)	0.73		
Had same meal in past 3 days	6/64 (9.4%)	12/133 (9.0%)	1.0 (0.3-3.2)	0.93		
Food taboos	35/68 (51.5%)	13/130 (10.0%)	**9.5 (4.3-21.8)**	**<0.001**	1.6 (0.4-7.0)	0.50
Attends school	31/55 (56.4%)	90/115 (78.3%)	**0.4 (0.2-0.8)**	**0.0032**	0.5 (0.1-1.9)	0.31

Values in bold indicate statistical significance

4.4.2. Factors associated with epilepsy in adults

The results of the analysis for factors associated with epilepsy in adults are presented in Table 5. After multivariate analysis, two factors were positively associated with epilepsy: family history of epilepsy and having food taboos. Factors that were negatively associated with epilepsy included: having pigs in the house, alcohol consumption, smoking, parents having a blood relationship, receiving ivermectin, attaining post-secondary education and being married. Increasing age was also negatively associated with epilepsy. Having dogs or cats in the household was less common among people with epilepsy than controls, but neither was statistically significant after multivariate analysis. A history of conditions predisposing to brain injury (such as coma, stroke, meningitis and head injury) were more common among adults with epilepsy than in healthy people. These differences were, however, non-significant after multivariate analysis.

Table 5. Factors associated with epilepsy in adults (>16 years)

Risk Factor	**People with active epilepsy**	**Controls**	**Univariate analysis****		**Multivariate analysis****	
			OR (95% CI)	P value	OR (95% CI)	P value
Age (OR for 1-year increase)			**0.94 (0.93-0.96)**	**<0.0001**	**0.95 (0.94-0.98)**	**0.001**
Gender (male)	155/327 (47.4%)	119/258 (46.1%)	1.05 (0.8-1.6)	0.84		
Married	76/324 (23.5%)	160/247 (64.8%)	**0.2 (0.1-0.2)**	**<0.0001**	**0.3 (0.2-0.6)**	**<0.0001**
Consumes alcohol	140/325 (43.1%)	181/243 (74.5%)	**0.3 (0.2-0.4)**	**<0.0001**	**0.5 (0.3-0.9)**	**0.03**
Smokes Cigarettes	4/325 (1.2%)	27/243 (11.1%)	**0.1 (0.02-0.3)**	**<0.001**	**0.1 (0.02-0.8)**	**0.02**
Uses recreational drugs	4/326 (1.2%)	12/243 (4.9%)	**0.2 (0.05-0.8)**	**0.008**	0.3 (0.03-3.2)	0.32
History of stroke	7/326 (2.1%)	3/244 (1.2%)	1.8 (0.4-10.7)	0.41		
History of Coma	47/325 (14.5%)	16/242 (6.6%)	**2.4 (1.2-4.6)**	**0.003**	2.4 (0.8-7.3)	0.102
Poor toilet facilities	271/327 (82.9%)	220/257 (85.6%)	0.8 (0.5-1.3)	0.37		
Clean water source	180/327 (55.0%)	170/257 (66.1%)	**0.6 (0.4-0.9)**	**0.006**	0.6 (0.3-1.1)	0.102
Have cats in household	91/326 (27.9%)	84/256 (32.8%)	0.8 (0.5-1.2)	0.20		
Have dogs in household	51/327 (15.6%)	59/255 (23.1%)	**0.6 (0.4-0.9)**	**0.02**	0.9 (0.4-2.0)	0.78
Have pigs in household	107/327 (32.7%)	140/257 (54.5%)	**0.4 (0.3-0.6)**	**<0.0001**	**0.4 (0.2-0.7)**	**0.003**
Have a person with epilepsy in household	115/327 (35.2%)	48/257 (18.7%)	**2.4 (1.6-3.6)**	**<0.0001**	0.4 (0.2-1.1)	0.07
1st degree relative with epilepsy	133/327 (40.7%)	16/257 (6.2%)	**10.3 (5.9-19.2)**	**<0.0001**	**12.4 (4.5-34.5)**	**<0.0001**

2nd degree relative with epilepsy	131/315 (41.6%)	34/250 (13.6%)	**4.5 (2.9-7.1)**	**<0.0001**	**9.9 (4.1-24.1)**	**<0.0001**
Parents are related	4/307 (1.3%)	29/195 (14.9%)	**0.1 (0.01-0.2)**	**<0.0001**	**0.04 (0.01-0.2)**	**0.008**
History of meningitis	16/324 (4.9%)	3/244 (1.2%)	**4.2 (1.2-22.6)**	**0. 015**	2.3 (0.3-20.4)	0.45
History of head injury	41/322 (12.7%)	6/239 (2.5%)	**5.7 (2.3-16.6)**	**<0.0001**	3.7 (0.99-13.6)	0.051
Received Ivermectin	201/326 (61.7%)	223/250 (89.2%)	**0.2 (0.1-0.3)**	**<0.0001**	**0.2 (0.1-0.5)**	**0.001**
Same meal past 3 days	34/297 (11.4%)	16/248 (6.5%)	**1.9 (1.0-3.7)**	**0.04**	1.5 (0.5-4.2)	0.44
Food taboos	148/319 (46.4%)	32/246 (13.0%)	**5.8 (3.7-9.2)**	**<0.0001**	**5.2 (2.4-11.1)**	**0.0001**
Post-secondary education	6/325 (1.8%)	16/247 (6.5%)	**0.3 (0.1-0.7)**	**<0.0001**	**0.05 (0.01-0.3)**	**0.002**

Values in bold indicate statistical significance

5. Discussion

We estimated epilepsy prevalence and incidence and associated risk factors in a rural health district in Cameroon's North-West Region. The low participation rate in stage 2 of the screening may be due to limited accessibility to the centers by people from remotely located villages. Non-participation could also result from temporary migration in between the screening stages and concealment due to fear of disclosing epilepsy to other community members where stigma towards epilepsy is high [3]. Concealment may also explain why some people who screened negative in stage 1 opted to be assessed by the clinician in stage 2. All had a history of epileptic seizures, and more than half had active epilepsy. The screening questionnaire is unlikely to be responsible for these missed cases, as it has good sensitivity to detect epilepsy in diverse communities. The missed cases probably reflect the low sensitivity of community screening of epilepsy in SSA [17,18], driven by misconceptions and high levels of stigma regarding epilepsy, which is well documented in this community (Njamnshi et al. 2008,2009, 2010). This limitation notwithstanding, the use of well-trained community members involved in other health programs to screen for epilepsy in

communities may be the most cost-effective approach to map the burden of epilepsy in Cameroon [18].

5.1. Lifetime prevalence of epilepsy

The age-standardized lifetime epilepsy prevalence we found (41/1,000) is significantly higher than the median lifetime prevalence of epilepsy for developed countries (6 per 1,000) [19]. It is similar to the value reported in a rural population in the Centre Region of Cameroon (49/1,000) [20] and close to the 95th percentile of values of epilepsy lifetime prevalence in rural communities in LMICs [19].

5.2. Prevalence of active epilepsy

The prevalence of active epilepsy in this area is above the 75th percentile of estimates from SSA studies [21]. It can be misleading to compare estimates of the prevalence between individual studies in SSA given differences in study designs. In a survey in five SSA countries, using a similar multi-stage method to screen for epilepsy in the community, the prevalence ranged between 7.4 and 15.5 per 1,000 [14]. We included non-convulsive seizures in our study, while the multi-country African survey was restricted to convulsive epilepsy, which may partially explain the difference. The sensitivity of the multi-stage epilepsy screening method used in the study in SSA was estimated at 48.6% [17]. Assuming the same sensitivity in this study, the prevalence of active epilepsy in our study population is likely to be significantly underestimated. Table 5 shows how epilepsy prevalence in this study compares with previous studies in Cameroon. While actual differences may exist between communities because of differences in exposure to risk factors for epilepsy, it seems clear that the size of the study populations contributed significantly, as small study populations yielded the highest values. Differences in the study designs, study population size and definitions of epilepsy can easily account for the variations in the prevalence between the study populations.

Table 6. Prevalence of epilepsy in various communities in Cameroon

Study Location	Study Population	Identification of people with epilepsy	Definition of epilepsy	Prevalence /1,000 (95% CI)
Batibo, North-West Region, 2017 (Present study*)	36,282	2-stage screening: House-to-house screening with a follow-up assessment of people with suspected epilepsy by physicians with epilepsy training	Two or more unprovoked seizures with at least one in the preceding 12 months	33.9 (31.0-37.1)
Billomo, Centre Region, 2007 [20]	1, 898	House-to-house: confirmation of cases by physician	NA	49·0 (39·6–60·0) **
Bilomo, Centre Region, 2000 [6]	1,900	House-to-house: confirmation of cases by physician	NA	58·4 (48·1–70·4) **
Kelleng, Littoral Region, 2008 [5]*	181	Cross-sectional: 2-stage house-to-house screening in stage 1 followed by confirmation of cases by a physician at health centre	Two or more seizures, with at least one in the past 12 months	134·5 (90.0–178.0)
Kelleng, Littoral Region, 2018 [7]	204	Cross-sectional: 2-stage house-to-house screening in stage 1 followed by confirmation of cases by a physician at health centre	The occurrence of at least 2 unprovoked seizures occurring at least 24 hours apart	78 (49.0-124.0)
Billomo, Centre Region, 2018 [7]	1321	Cross-sectional: 2-stage house-to-house screening in stage 1 followed by confirmation of cases by a physician at health centre	The occurrence of at least 2 unprovoked seizures occurring at least 24 hours apart	46.0 (36.0-59.0)
Monatélé (Centre Region), Ndikiniméki & Pouma (Littoral Region) [18]	53,044	Community screening for epilepsy by trained community drug distributors	The occurrence of at least 2 unprovoked seizures occurring at least 24 hours apart	14/1000

**Studies limited to active epilepsy (at least 1 seizure in the past 12 months)*

***values not age-standardized*

NA: Not available

5.2.1. Variation in the prevalence of active epilepsy between health areas

The prevalence found varied significantly between and within health areas. This may be attributable to differences in exposure to environmental and genetic risk factors**.** It is not clear to what extent any potential discrepancies in the concealment of cases due to stigma

or other unknown factors contribute to the difference in prevalence between health areas. It is also possible that, because of the solid reputation of traditional medicine in epilepsy management in this district [22], people may migrate to be closer to the traditional healers, contributing to case clustering with time.

5.2.2. Age-specific differences in the prevalence of epilepsy

We found peak prevalence between ages 25 and 34 when people are also likely to be the most productive, reflecting epilepsy's substantial social and economic burden on the individuals and the community. Our findings contrast with most African studies showing a peak prevalence before age 20 years [23-26]. The age-specific epilepsy prevalence in this population is similar to that in other African studies where epilepsy has been linked to infectious aetiologies such as neurocysticercosis and onchocerciasis [28-30]. A study in an onchocerciasis-endemic area in the Centre region of Cameroon found that the age-specific prevalence was highest in the 20-29 age group [7], similar to ours. Differences in incidence, seizure remission rates and premature mortality between countries could also be responsible for discrepancies in age-specific prevalence of epilepsy in SSA.

5.3. Incidence of epilepsy

The one-year incidence of epilepsy in this population (171.1/100,000 people) is lower than that reported in a study from the Centre Region of Cameroon (350/100,000 person-years) [10]. It is higher than the median incidence for LMICs (81.7 /100,000) [31]. Comparisons between incidence reports in Africa are, however, challenging mainly due to methodological differences. Compared with cross-sectional studies, longitudinal studies generally provide a more reliable estimate of the incidence of epilepsy, but unfortunately, few such studies are available from SSA [28, 31]. Cross-sectional studies of epilepsy incidence [29, 30, 33]], such as ours, may underestimate the epilepsy risk. There is an apparent mismatch between the incidence and the prevalence in our population. In Cameroon's Centre Region, the incidence of 350/100,000 person-years was reported in an area where the lifetime epilepsy prevalence

was 49/1,000 [10], which is similar to ours. Extrapolating from this example, we would expect a higher epilepsy incidence in our study to match with the prevalence in the same population. Recall bias may have contributed to this underestimation of the incidence. Epilepsy stigma is common in this district [3]. This may also have contributed to underreporting recent onset seizures. People with new-onset seizures and their families may be more hesitant than those with established epilepsy to disclose their condition. Other plausible explanations include differences in etiological factors, seizure remission rates, and premature mortality associated with epilepsy between populations.

5.4. Risk factors for epilepsy

5.4.1. Taenia solium cysticercosis

In the context of the high epilepsy burden in this pig-breeding population with overall poor hygiene and sanitation, neurocysticercosis is an important etiological factor to consider. Many studies in LMICs show a correlation between the level of pig-husbandry and epilepsy prevalence in a community [34, 35]. In one case-control study in a neighbouring district with a similar socio-demographic structure, epilepsy was not associated with cysticercosis [36]. For logistic reasons, we were unable to assess for neurocysticercosis. We speculate, however, that neurocysticercosis is a significant epilepsy risk factor in Batibo. This is based on the age pattern of people with epilepsy. In many LMICs where epilepsy was strongly linked with neurocysticercosis, seizures typically start around the mid-teens, and the prevalence consistently peaks in the 20-40 age group [37-42]. The reasons for this relationship between neurocysticercosis-associated epilepsy and age are not clear but may reflect age-dependent differences in parasite exposure and susceptibility to epilepsy after neurocysticercosis. The attributable population fraction of epilepsy due to neurocysticercosis needs to be investigated in future studies in this area.

5.4.2. Onchocerciasis and mass treatment with ivermectin

The high prevalence and incidence observed in this hyperendemic focus corroborate with findings in other SSA communities reporting the co-existence of a high epilepsy prevalence

and onchocerciasis hyperendemicity [26, 43-47], including in Cameroon's Centre Region [10, 45, 48]. Epilepsy prevalence was 49/1000 in this area which is the highest reported in Cameroon [20]. It was recently reported that over 90% of epilepsy in this region could be attributed to onchocerciasis [10]. Differential exposure to the Onchocerca volvulus and its vector may be responsible for the differences in epilepsy prevalence between areas within the Batibo District. Epilepsy prevalence was generally higher in communities close to the Momo river than those located further away (Figure 3). Similar observations have been made elsewhere in Cameroon, and the Democratic Republic of Congo [24, 45], where bathing in rivers seems to be associated with an increased epilepsy risk [24].

Ivermectin is the main anti-parasitic drug used for many decades for mass treatment to eradicate onchocerciasis in endemic areas in SSA. Interestingly, adults with epilepsy in this study were less likely to have received ivermectin than controls. It has been suggested that ivermectin treatment could reduce epilepsy risk (by preventing onchocerciasis) [49]. Lower ivermectin therapeutic coverage among people with epilepsy could, however, have resulted from the misconception that ivermectin prophylaxis was contraindicated in people with epilepsy (Personal communication, District Medical Officer). Sustained community treatment with ivermectin has been ongoing for almost 15 years, and the therapeutic coverage has been good, with little variation between health areas (Personal communication, District Medical Officer).

In light of evidence showing that ivermectin treatment is associated with a reduction in epilepsy burden in other parts of Cameroon where onchocerciasis is endemic [7, 10, 11], it would be interesting to observe how long-term ivermectin treatment affects the incidence in this population. A study in an onchocerciasis-endemic area in another Cameroonian region found that the age-specific prevalence was highest in the 20-29 age group, similar to the current study. It was also observed that there had been a shift of peak prevalence from the 10-19 years age group 20 years earlier; this was attributed to the effectiveness of ivermectin control in preventing onchocerciasis in this population [7].

5.4.3. Family history of epilepsy

We found that family history is associated with epilepsy in this Cameroonian population, and this is similar to findings in other SSA countries [41, 50-52]. Having a relative with epilepsy was associated with epilepsy in adults but not children. This may suggest inherited genetic factors predisposing to epilepsy which depend on some environmental triggers later in life. A family history of epilepsy may also be attributed to the likelihood of exposure to the same environmental risk factors in people sharing the same household. This may not apply in this study because living in the same house as another person with epilepsy was not significantly associated with epilepsy.

5.4.4. Adverse perinatal and childhood events

The lack of a significant association between epilepsy and many adverse perinatal events contrasts with most case-control studies in SSA [27, 50-53]. While this may be surprising given that basic obstetric and neonatal care remain inaccessible for most people in rural areas, high premature mortality in children with perinatal complications may explain this discrepancy. A history of febrile seizures was significantly associated with epilepsy. This association between febrile seizures and epilepsy does not necessarily imply causation since febrile seizures could be the first manifestation of some epilepsy disorders beginning in childhood. EEG and imaging studies in this cohort may reveal focal epileptiform discharges and structural abnormalities from birth-related brain injuries due to low perinatal and neonatal care standards.

5.4.5. Head Injury

Head injury was not significantly associated with epilepsy after multivariate analysis in this study, and this corroborates with most studies in SSA [41, 52, 53]. A few studies in Africa have found a significant association between head injury and epilepsy [27, 50]. Batibo is mainly rural, and most movement is either by foot or motorbike through narrow bush roads. People living here are less likely to suffer from head injuries due to road traffic accidents

than those living in urban centers and are less predisposed to head injury and epilepsy afterwards.

5.4.6. Nutritional habits

The high proportion of people with epilepsy having food taboos in this study supports a study from Benin [54]. Certain foods are avoided, reflecting cultural beliefs about epilepsy which are deeply rooted. Pork is avoided because of knowledge that the pork tapeworm is associated with epilepsy. In this case, there is a misconception that it is eating pork that predisposes to seizures. Soup made with okra is avoided because of misconceptions that its slimy texture increases the risk of falls. Chickens and other birds are avoided because of a belief that epilepsy is caused by evil spirits found in certain birds [3]. These readily available staple foods have high caloric and protein value in this community; avoiding them increases malnutrition risk, further increasing vulnerability to seizures.

5.4.7. Contact with animals

Sustained contact with dogs and cats may increase exposure to toxocariasis and toxoplasmosis [55, 56]. In this study, contact with animals (pigs, dogs and cats) was not significantly associated with an increased epilepsy risk. This does not necessarily imply that the zoonoses related to them (Cysticercosis, Toxoplasmosis and Toxocariasis) are not involved in epilepsy in this community. The risk of infection with these zoonoses depends more on poor personal and food hygiene than on contact with these animals. For example, in neurocysticercosis, proximity to a *Taenia solium* carrier and poor personal hygiene are essential for the transmission of cysticercosis [57]. These parasitic diseases need to be investigated in future studies of the risk factors for epilepsy in this population.

5.4.8. Alcohol, smoking and use of recreational drugs

People with epilepsy in this study were significantly less likely to be smokers or to drink alcohol than controls. They were also less likely to have taken recreational drugs, although the difference was not statistically significant in multivariate analysis. These results may

suggest that people with epilepsy avoid alcohol and similar products for fear of triggering seizures.

6. Limitations

Some limitations need to be considered when interpreting our findings. The study questionnaires were prepared in English but administered mainly in Pidgin-English and the Batibo language. There may have been variability between field workers in the interpretation and administration of the questionnaires. This was limited by involving interpreters with good knowledge of these languages to train the field workers at each site. Translation of the questionnaires was not feasible because most people cannot read or write these languages.

Towards the end of the study, serious political unrest began in the North-West and South-West Regions of the country. This unrest has since morphed into armed conflict, with Batibo as one of the most affected districts. It is difficult to ascertain the extent to which this conflict and the resulting migration of some people out of the district affected prevalence and incidence estimation.

In estimating epilepsy prevalence, correction for attrition between the screening stages assumed that the prevalence would be identical for those assessed in stage 2 and those who screened positive in stage 1 but were not considered in stage 2 (52%). This may have led to over- or under-estimation of the prevalence depending on the reasons for their non-participation.

For certain factors such as family history, perinatal/childhood history, and head injury, epilepsy risk may have been overestimated because of recall bias. Conversely, epilepsy risk associated with factors such as alcohol consumption, smoking and recreational drug use may have been underestimated as participants may be inclined to provide socially acceptable responses to avoid embarrassment. As ours was a cross-sectional assessment, we could not estimate a Population Attributable Risk (PAR) which would have been of more

value. This emphasizes the importance of prospective cohort studies to ascertain fully these potential risk factors for epilepsy in SSA.

7. Conclusion

We found a high incidence and prevalence of active epilepsy in the Batibo Health District in Cameroon's North-West Region. Infectious etiologies such as onchocerciasis and cysticercosis could be implicated, based on prevailing ecological factors favoring transmission of the parasites. Significant differences in epilepsy prevalence between areas and case clustering in some communities are probably the combined effect of differential exposure to these parasites and underlying inherited genetic factors predisposing to epilepsy. Case-control and longitudinal studies are needed to ascertain the significant etiologies of epilepsy in this part of Cameroon.

Acknowledgements

This work as carried out at NIHR University College London Hospitals Biomedical Research Centre, which receives a proportion of funding from the UK Department of Health's Research Centres funding scheme. JWS receives research support from the Dr Marvin Weil Epilepsy Research Fund, the UK Epilepsy Society and the Christelijke Vereniging voor de Verpleging van Lijdersaan Epilepsie, The Netherlands. SAA was a Commonwealth scholar funded by the UK Department of International Development.

Special appreciation goes to the District Medical Officer of the Batibo, Dr Ajabmoh Henry and the Chief of Bureau for Health for Batibo, Flora Avera Fonyuy, for their collaboration in the recruitment and training of field workers. We would like to acknowledge all the chiefs of health areas and the community volunteers for sacrificing their time to participate in this study.

Supplementary Table 1. Epilepsy Screening Questions

Questions	Answers		
	Yes	**No**	**Don't know**
Q1) Do you/this member of the household have fits or has someone ever told you that you/they have fits?			
Q2) Do you/this member of the household experience episodes in which you/they fall to the ground and lose consciousness or wet yourself or bite your tongue?			
Q3) Have you/this member of the household ever fallen to the ground without a reason and experienced jerking movements of the legs/arms?			
Q4) Have you/this member of the household experienced an unexplained change in mental state or level of awareness that you/they could not control?			
Q5) Did anyone ever tell you/this member of the household that when you/they were a small child, you/they would daydream or stare into space more than other children?			

If the response to any of the questions "Yes" then the person concerned should be invited to the hospital for assessment by the clinicians

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