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Prevalence of epilepsy in the 15 years and older in Benin: A door-to-door nationwide survey

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Prevalence

Summary
Purpose: Estimate the prevalence of epilepsy in the 15 years and older in Benin.
Methods: We used a random multistage sampling design to select a representative sample of the 15 years and older in Benin. From March to May 2010, people were screened door-to-door in the twelve regions of Benin. Screening and data collection were performed using a validated standardised questionnaire of epilepsy in tropical regions. A neurologist examined all people suspected of epilepsy.
Results: We identified 174 suspected epilepsy cases from 13,046 screened people; 105 were confirmed by the neurologist (54 men and 51 women). The mean age of PWE was 28.9 ± 14.3 years. The estimate of crude prevalence of epilepsy in the 15 years and older in Benin was 8.05/1000 (95% CI: 6.52—9.58/1000). The crude prevalence of epilepsy among men was 9.77/1000 (95% CI 7.35—12.73/1000) and 6.79/1000 (95% CI 5.06—8.91/1000) for women. The age-adjusted prevalence of epilepsy on sub-Saharan Africa population was 8.25/1000 and 7.33/1000 on world population. Substantial heterogeneity was noted, with differences from one region to another. The most common seizure types were generalised tonic—clonic (80.0%), partial secondary generalised seizures (14.3%) and partial seizures (5.7%).

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Significance: This nationwide study is the first in West Africa. It provides a low prevalence of epilepsy in Benin compared to previous studies performed in this country and in neighbouring countries. Restricted-area studies are often motivated by the presence of specific risk factors and could overestimate the prevalence, while large-scale studies could underestimate other subtle forms of epilepsy.

Introduction

Epilepsy is a major and mostly preventable neurological disorder with an estimate of 69 million people worldwide. Recent meta-analyses showed a high estimate in developing countries; the median prevalence of lifetime epilepsy (LTE) was 15.4/1000 (4.8—49.6/1000) and 10.3/1000 (2.8—37.7/1000) respectively in rural and urban studies settings (Ngugi et al., 2010).

In sub-Saharan Africa (SSA), numerous studies in restricted areas were performed on epilepsy; they provided a large variability of prevalence from 5.2/1000 in Ethiopia to 105/1000 in Cameroun (Tekle-Haimanot et al., 1990; Prischich et al., 2008). This variability was explained partially by the studies' characteristics, the differences in the sampling methods and aetiological factors (Sander, 2003; Preux and Druet-Cabanac, 2005; Yemadje et al., 2011). Higher prevalence estimates were associated with specific epilepsy risk factors and with small-scale studies (Mung'ala-Odera et al., 2008; Prischich et al., 2008). In Benin, a SSA country, three epidemiological studies on epilepsy were performed in rural settings; they provided high LTE prevalence of 15.2/1000 in Savalou, 24.5/1000 in Agbogbomé and 21.1/1000 in Zinvié (Gbenou, 1995; Avodé et al., 1996; Debrock et al., 2000).

Few nationwide investigations into epilepsy were done in SSA. To our knowledge, only one national survey was conducted in Rwanda. It provided an estimated prevalence of 7.0/1000 (95% CI 5.0—9.0/1000) lower than the median prevalence observed in small-scale studies in SSA (Simms et al., 2008). Nationwide surveys would probably be more accurate and valid for the allocation of the available prevention means. This study is part of the campaign against epilepsy in Benin.

Our purpose was to perform a nationwide survey to estimate the prevalence of epilepsy in Benin.

Methods

Study setting

We undertook a door-to-door national survey from March to May 2010 in Benin. It is a SSA country bounded by Togo in the West, Nigeria in the East, Burkina Faso and Niger in the North. Benin extends from the Niger River in the North to the Atlantic Ocean in the South with an area of 112,622 km^2. The estimated population in Benin was 8,791,832 inhabitants and the population density was 78 inhabitants/km^2 (2009 demographic projection of Benin population).

Study population

The population consisted of people aged of 15 years and older, residing in Benin in the 6 months preceding the study. The median prevalence of active epilepsy (AE) in rural areas in developing countries was 12.7/1000 (3.5—45.5/1000) (Ngugi et al., 2010). Considering a 5% level of significance, a precision of 2/1000 and an expected prevalence of 12/1000 it was necessary to include 11,368 people in the study. We added 10% for possible refusal, resulting in the inclusion of 13,046 people (Fig. 1).

We used a random multistage sampling design. People were screened door-to-door in the 12 regions of Benin. Three levels of simple random sampling were applied in order to reach the final sample.

1st stage: At the first stage we had the list of districts in each region and we randomly selected one district from the list of districts per region. We did that for each of the 12 regions in Benin.
2nd stage: Next, in each selected rural/urban district, we randomly selected 50% of villages/city districts. We had the list of villages/cities in each district and we selected 50% of villages/cities per district.
3rd stage: Starting from the centre of the village, we randomly selected the first block of residences to investigate. The blocks of residence generally follow the four cardinals. We considered the four cardinals and randomly selected one direction out of four. In each block, we selected one residence in two.

We investigated all people of 15 years or older in the selected residence. The number of people selected per region was proportional to the weight of region relative to the overall population.

Diagnostic criteria of epilepsy

Diagnosis of epilepsy was clinical, confirmed by a neurologist with expertise in epilepsy. No electroencephalogram (EEG) record was performed.

We followed the definition of epilepsy proposed by International League Against Epilepsy (ILAE, 1993). ''Epilepsy is a condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause. Multiple seizures occurring in a 24 h period are considered as a single event''. A case of AE was defined as a person with epilepsy who has had at least one epileptic seizure in the five years before the survey, regardless of anti-epileptic drug (AED) treatment.

Screening instrument

Screening and data collection were performed using a validated standardised questionnaire on epilepsy in tropical regions (Preux et al., 2000). The questionnaire was previously validated in Mauritania with a high sensitivity 95.1% (95% CI 87.3—98.4) and specificity 65.6% (95% CI 57.5—72.9) (Diagana et al., 2006). It was translated into local dialects and back-translated by the help of medical doctor native of each study region.

Data was collected by 16 investigators, who were trained medical doctors. The principal investigator trained all investigators in the application of the questionnaire, and he tested the good understanding of the questionnaire. Each investigator interviewed about 50 people every day. Through daily meetings, the principal investigator assured that working procedures remained standardised during the survey.

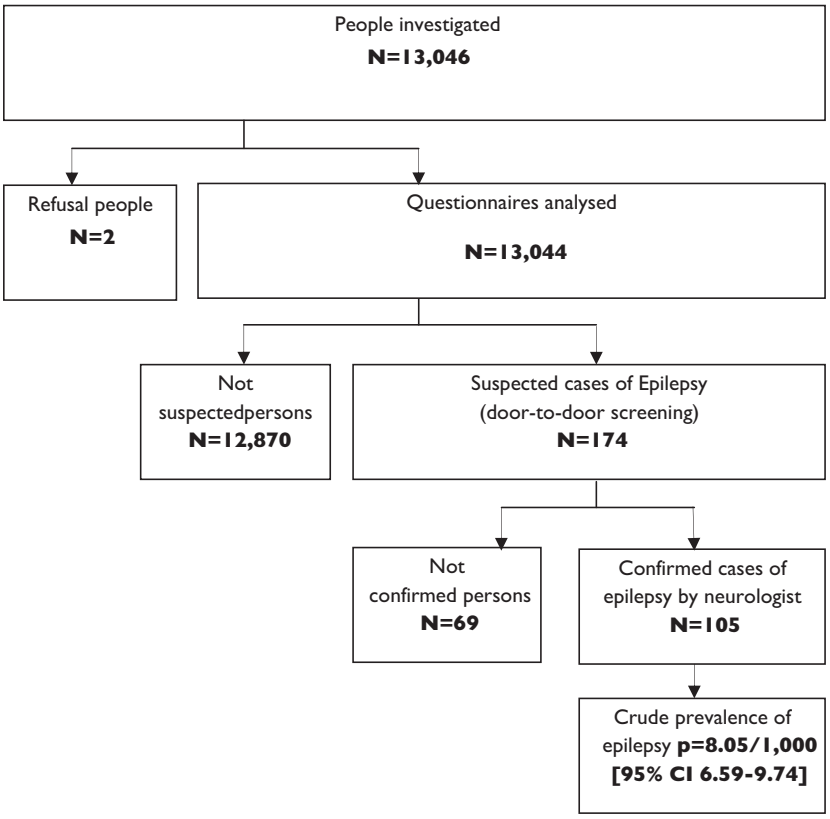

Figure 1 Flowchart of participants in the nationwide prevalence study of epilepsy in Benin 2010.

Ethics

Ethical agreement was obtained from the Ethics Committee of School of Health Sciences in Benin and the government gave permission for this study. The week before the survey in each village, we talked to the village leader to obtain his agreement. The informed verbal consent of the head of family and all people investigated was collected, after an explanation of the study. The neurologist gave an appropriate treatment, provided free to people with epilepsy diagnosed in this study.

Study design

We performed a two-phase survey: door-to-door screening and confirmation.

Screening: We interviewed all inhabitants aged 15 years and older in one residence in two. We collected socio-demographic, medical data and we asked the five screening questions for epilepsy. Any person answering ''yes'' to at least one question of the screening section of the questionnaire was considered as ''suspected of epilepsy''.
Confirmation: After screening, a neurologist with expertise in epilepsy examined all ''suspected cases'' to confirm epilepsy using diagnostic criteria and a thorough neurological examination. The neurologist looked for the onset of seizure, checked if epilepsy was active, listed the AED used and classified seizure on the basis of the classification proposed by ILAE commission on classification and terminology (Berg et al., 2010).

Statistical analysis

Data was entered using EpiData 3.0. Sample-size calculation and statistical analyses were made with Epi-Info 3.5.1 (Centres for Disease Control and Prevention, Atlanta, GA). Quantitative variables were described by using mean and standard deviation. Frequencies were used to describe qualitative variables. We used Pearson chi-square test to perform frequency comparisons. Significance level was fixed to 5%. We performed sex and age-adjustment on world population and SSA population prospects from ''Department of Economic and Social Affairs of United Nations'' (http://esa.un.org/unpd/wpp/Excel-Data/population.htm). A multivariate analysis was made by using logistic regression. The initial model held relevant factors that were statistically associated with epilepsy with a preserving threshold ($p < 0.25$); the model was manually simplified in a descending way, according to Hosmer and Lemeshow's method, and Wald's test was used to evaluate nonsignificant variables (Hosmer and Lemeshow, 1989). First-degree interactions were evaluated concerning significant factors kept in the final model.

Results

During this study 13,046 people were interviewed. Two heads of household refused to participate but they were not opposed to the participation of their family. Analyses were performed on the remaining 13,044 people; 5527 (42.4%) men and 7517 (57.6%) women. The mean age was 34.2 ± 16.2 years (33.9 ± 16.4 for men and 34.5 ± 16.1 for women). The age range is from 15 to 102. Demographic and medical characteristics of 13,044 participants are summarized in Table 1.

Table 1 Characteristics of the 13,044 participants in prevalence study in Benin, 2010.

	Total		PWE		No Epilepsy		*p*-value
	N = 13,044	%	*N* = 105	%	*N* = 12,939	%	
Sex							
Men	5527	42.4	54	51.4	5473	42.3	
Women	7517	57.6	51	48.6	7466	57.7	0.03
Marital status							
Married	9086	69.6	33	31.5	9053	69.9	
Living with parents	2964	22.7	60	57.0	2904	22.4	
Living alone	990	7.0	12	11.5	9,78	7.6	<10—3
Occupation							
Active	9269	71.3	46	43.8	9223	71.3	
Not active	3775	28.7	59	56.2	3716	28.7	<10—3
Residence							
Urban	5151	39.5	41	39.0	5110	39.5	
Rural	7893	60.5	64	61.0	7829	60.5	0.47
Toilets							
Indoor toilets	667	5.1	4	3.8	667	5.1	
Outdoor toilets	5269	40.4	47	44.8	5222	40.4	
Nature	7108	54.5	54	51.4	7054	54.5	0.60
Religion							
Christians	6364	48.8	62	59.0	6302	48.7	
Muslim	3488	26.7	18	17.1	3470	26.8	
Animistes	2992	22.9	23	21.9	2969	22.9	0.05
Twins							
No	12,417	95.2	100	95.2	12,317	95.2	
Yes	604	4.6	5	4.8	599	4.6	0.45
Consanguinity							
No	11,562	88.6	90	85.7	11,472	88.7	
Yes	1423	10.9	14	13.3	1409	10.9	0.21
Family history epilepsy							
No	12,047	92.4	67	63.8	11,980	92.6	
Yes	862	6.6	33	31.4	829	6.4	<10—3
Birthplace							
hospital	6981	53.5	65	61.9	6916	53.5	
home	5942	45.5	39	37.1	5903	45.6	0.05
Caesarean							
No	12,743	97.7	100	95.2	12,643	97.7	
Yes	141	1.1	0	0.0	141	1.1	0.33
Measles							
No	10,168	78.0	72	68.6	10,096	78.0	
Yes	2244	17.2	21	20.0	2223	17.2	0.13
Meningitis							
No	12,234	93.8	81	77.1	12,153	93.9	
Yes	336	2.6	6	5.7	330	2.6	0.03
Head injuries							
No	12,712	97.5	99	94.3	12,613	97.5	
Yes	305	2.3	4	3.8	301	2.3	0.31

PWE, people with epilepsy.

Prevalence

Among the 13,044 people, 174 were suspected of epilepsy in the screening procedure. After a clinical examination by a neurologist, 105 people were confirmed as PWE (Fig. 1). The diagnosis of the 69 suspected persons, not confirmed as PWE were seizures induced by alcohol abuse or loss of consciousness or syncope in patients with low blood pressure.

Epilepsy was active for the 105 PWE. The overall prevalence of epilepsy in Benin was 8.05/1000 (95% CI 6.59—9.74/1000). The crude prevalence of epilepsy among men was 9.77/1000 (95% CI 7.35—12.73/1000) and 6.79/1000 (95% CI 5.06—8.91/1000) for women. The age-specific prevalence was high in age groups 15—24 years (12.4/1000) and then declined in the oldest age groups (Table 2). A substantial variation of epilepsy prevalence was

Table 2 Age specific prevalence of epilepsy, Benin, 2010.

Age	Number of people	PWE	Prevalence (‰)	95% CI
[15—19]	2371	34	14.34	9.95—19.98
[20—24]	1826	18	9.86	5.85—15.54
[25—29]	1950	14	7.18	3.93—12.02
[30—34]	1555	11	7.07	3.54—12.62
[35—39]	1338	5	3.74	1.21—8.70
[40—44]	948	6	6.33	2.33—13.73
[45—49]	685	5	7.30	2.37—16.95
[50—54]	575	3	5.22	1.08—15.17
[55—59]	437	2	4.58	0.56—16.43
[60—64]	438	4	9.13	2.49—23.22
[65—70]	921	3	3.26	0.67—9.49
Total	13,044	105	8.05	6.59—9.74

PWE, people with epilepsy; CI, confidence interval.

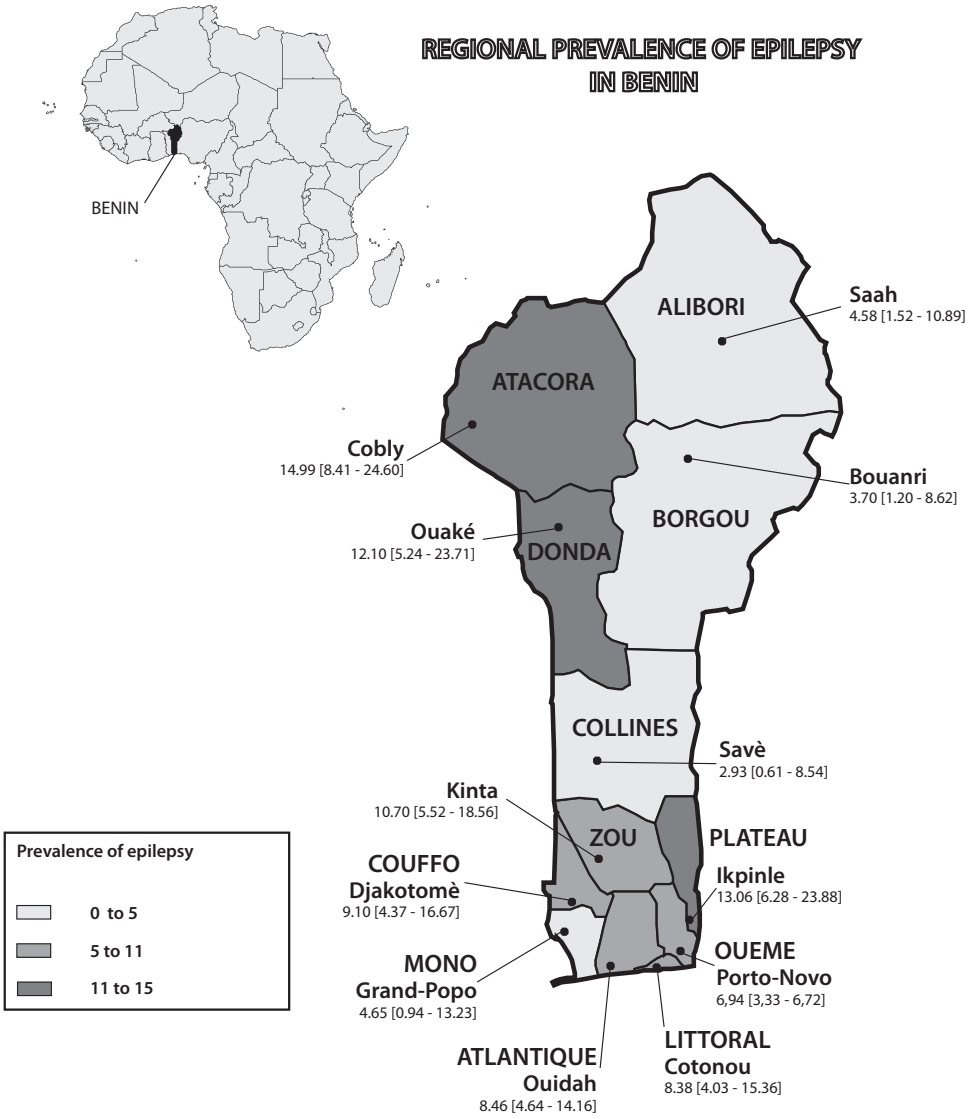

Figure 2 Regional prevalence of epilepsy in Benin.

Table 3 Age-adjusted prevalence of epilepsy, Benin, 2010.

	Global [95%CI]	Men [95% CI]	Women [95% CI]
Crude prevalence	8.05 [6.59—9.74]	9.77 [7.35—12.73]	6.79 [5.06—8.91]
Age-adjusted on SSA	8.23 [8.23—8.24]	9.67 [9.66—9.68]	7.17 [7.16—7.18]
Age-adjusted on world	7.32 [7.32—7.33]	8.61 [8.60—8.61]	6.40 [6.39—6.40]

CI, confidence interval; SSA, sub-Saharan Africa.

observed in regions of Benin, ranging from 2.93/1000 in one region (Savè) to 14.99/1000 in another (Cobly) (Fig. 2).

Prevalence was adjusted to the SSA population and to the world population. The overall age-adjusted prevalence of epilepsy on SSA population was 8.23/1000. The age-adjusted prevalence of epilepsy on world population was 7.32/1000. Crude and age-adjusted prevalence of epilepsy are summarized in Table 3.

Characteristics of PWE

Among the 105 PWE; 54 (51.4%) were men and 51 (48.6%) were women. The mean age of PWE was 28.9 ± 14.3 years (28.3 ± 14.1 for men and 29.4 ± 14.7 for women). The age of onset of the first seizure was before 20 for most PWE ($n = 73$, 69.0%); few PWE ($n = 8$, 7.6%) experienced their first seizure after the age of 40 years.

In the study, we identified 84 (80.0%) patients with generalised seizures, 15 (14.3%) with partial seizures secondary generalised and 6 (5.7%) with partial seizures.

About treatment, few PWE ($n = 14$, 13.3%) had received or were currently receiving medical treatment; the treatment gap was 86.7%. Phenobarbital, Keppra and Valproic acid are the most often AED used. The usual reason given for not having treatment was inability to pay. Some PWE ($n = 31$, 29.5%) received traditional treatment or a mix of traditional and medical treatment. Among traditional treatments, vegetal treatment was commonly used and prescribed by traditional healers.

Of the 105 PWE, 31.4%, and 6.4% of the people without epilepsy had family history of epilepsy ($p < 0.001$). We considered here ''family history'' as epilepsy in first or second-degree relatives. Multivariate analysis revealed that family history of epilepsy, bacterial meningitis and occupation, are significantly associated with the development of epilepsy. Results of the final model are displayed in Table 4.

Discussion

This first nationwide study in West Africa showed that it is possible to get a national estimate by simple and reproducible sampling technique. We used door-to-door method, the gold standard for epidemiological studies in developing countries, promoted by ILAE. Our study benefited from good population compliance; the response rate was 99.98% with 13046 people screened. A nationally representative sample of the 15 years and older of Benin was selected. About 60% of people lived in rural areas as in Benin population. Women represent about half of Benin population; they were 57% of our sample. Several religions are practiced in Benin. Animism is widespread (50%); Muslims account for 20% of the population and Christians for 30%. In our sample, about 50% declared they are Christians although they also practice animist traditions through the ''voodoo''. The difference in religion distribution in the study was partially due to the high number of Christians compared to the other religions. In Benin, people who practice other religions are stigmatized. So most people preferred revealing they are Christians even they practice also other religions.

Screening and data collection were performed using a standardised questionnaire of epilepsy in tropical regions, validated and used in many African studies (Preux et al., 2000). A limitation of this study is the use of the questionnaire in local languages. This would cause an underestimate of prevalence, if epilepsy was translated using stigmatizing words.

Table 4 Multivariate logistic regression, final model, Benin, 2010.

	No Epilepsy *n* (%)	PWE *n* (%)	OR	95%CI	*p*-value
Family history of epilepsy (reference = yes)	829 (6.4)	33 (31.4)	5.89	3.56—9.41	<10—3
Occupation (reference = not active)	3716 (28.7)	59 (56.2)	3.81	2.47—5.88	<10—3
Meningitis (reference = yes)	330 (2.6)	6 (5.7)	2.39	1.02—5.64	0.046

PWE, people with epilepsy; OR, odds ratios; CI, confidence interval.

We selected a nationally representative sample of people aged 15 years and older. There is no neuro-pediatrician in Benin to confirm juvenile epilepsy. To avoid errors in recognition of juvenile epilepsy cases, we did not included children under 15 years. We used a random multistage sampling design more accurate than cluster sampling to select our sampling population. A neurologist with expertise in epilepsy examined all people suspected to confirm epilepsy. No EEG was performed because of the lack of specialized technician and the absence of EEG equipment. The identification of seizures was clinical by neurologist. The use of EEG in epidemiological studies could help to reclassify only a few seizures (Diagana et al., 2005). In this study 60% of suspected cases were confirmed as PWE; close to that found in a previous study in Zinvié, Benin. Those who were not confirmed as PWE have seizures induced by alcohol abuse or low blood pressure.

This nationwide representative survey shows a crude prevalence of epilepsy of 8.05/1000 in the 15 years and older in Benin; in accordance with observations in other large-scale studies, nationwide or not, in Rwanda, Tanzania and Kenya (Rwiza et al., 1992; Dent et al., 2005; Edwards et al., 2008; Simms et al., 2008). By contrast, it is less than those found in restricted-areas studies in Benin (Gbenou, 1995; Debrock et al., 2000) and in other SSA countries (Prischich et al., 2008; Ngugi et al., 2010). Small-scales studies are often motivated by the presence of specific risk factors and could overestimate the prevalence while the estimates from nationwide surveys would probably be more accurate and valid. Prevalence of epilepsy differs between regions in Benin. In district of Savè, prevalence of epilepsy is lower than in other regions in Benin. Seizures may have been unreported probably due to stigma surrounding the condition in this region. Alternatively, the high prevalence of epilepsy reported in district of Cobly may be explained by the good medical facilities in the region; PWE speak more easily about their illness.

The need for age-adjustment is well demonstrated by studies of epilepsy prevalence conducted in Africa, where the age distribution of the population differs substantially from that in developed countries. The age-adjusted prevalence of epilepsy on SSA was not different from the crude prevalence. By contrast, the age-adjusted prevalence on world population was lower than crude prevalence. Age-specific prevalence was highest for people aged 15—24 years and thereafter a decline was observed in the oldest age groups. Prevalence was low for people aged 45—64 years (6.7/1000) as reported in a study in Zambia (Birbeck and Kalichi, 2004). The low prevalence of epilepsy in >65 years could partially be explained by the mortality risks.

Most PWE identified suffer from generalised seizures (80%) as in earlier report from Senegal (Ndoye et al., 2005). Despite the use of a validated questionnaire, this large survey seems to have higher sensitivity for convulsive epilepsies and underestimated other subtle forms of epilepsy (Racoosin, 2003). Prevalence of epilepsy in women was significantly different than in males as in other studies, where prevalence of males was significantly higher than females (Dent et al., 2005; Edwards et al., 2008). As in a study conducted in Zambia, PWE in Benin were found to have substantially poorer social status than those without epilepsy (Birbeck et al., 2007). In Benin, the occupation seems to be a consequence of epilepsy. People with epilepsy do not reveal their disease because of stigmatization and they can therefore have an occupation. A study in workers in Benin reported that 54% of PWE had experienced epileptic seizure before their employment but no case was reported to the employer (Houinato et al., 2007). In the same study and in line with other surveys from SSA, more than half (69%) PWE reported that they developed epilepsy before the age of 20 (Houinato et al., 2007). This pattern is not seen in high-income countries (Forsgren et al., 2005). This may be because young people make up a large proportion of the population in Africa; people aged 0—14 years account for 43% of the population in Benin. All PWE had active epilepsy (at least one epileptic seizure in the last 5 years). Many of them are getting insufficient or no AED treatment because they were afraid to reveal their epilepsy. In Benin, especially in the North regions, epilepsy is still considered to be related to witchcraft or to spirits and PWE prefer the traditional healer treatment. We identified an East-West gradient in the North regions. The prevalence in the North-East was lower (3.7/1000 in Borgou and 4.7/1000 in Alibori) than in the North-West (15.0/1000 in Atacora and 12.1/1000 in Donga). The low prevalence in the North-East could arise from an underestimate of this indicator probably due to stigmatization of epilepsy. Studies are needed to assess the impact of this factor. All PWE identified in the study were treated by the neurologist. A nurse, in each region, will visit PWE every four months for monitoring and further treatment.

We used multivariate analysis to test the statistical relationships that may exist between epilepsy and several other variables. But the coefficients were not interpreted as risks because causality cannot be tested in such a study. Head trauma is not associated with epilepsy. We defined head trauma as cranial injuries after road accident or war, with or without coma. This large definition could explain why it was not associated with epilepsy in our study. We noted a family history of seizures in 31.4% of cases; in SSA, it was noted in 25% to 60% of cases (Preux and Druet-Cabanac, 2005). Family history of seizures was associated with epilepsy same as in Tanzania (Matuja et al., 2001) and Ethiopia (Tekle-Haimanot et al., 1990). This may be related to environmental factors and genetic factors, which predispose individuals in a family to epilepsy. Epilepsy was also associated with bacterial meningitis. Benin is part of the classic ''meningitis belt'' of Lapeyssonnie (Lapeyssonnie, 1963). Large-scale epidemics are confined to the semi-arid area of SSA from Senegal in the West, to Ethiopia in the East. Bacterial meningitis frequently occurred in North of Benin (75% of meningitis cases) and the population is exposed to an inappropriate self-medication of antibiotic. Of the six cases of bacterial meningitis in PWE, four were located in the North of Benin.

Conclusion

This study identified a high burden of epilepsy in Benin, but lower than the median prevalence of epilepsy in SSA. Interventions are needed to increase awareness of epilepsy as a treatable disorder and reduce the treatment gap. Family history of epilepsy and bacterial meningitis were associated with epilepsy, but further studies are required to assess their contribution as risk factors. This study is part of the

national fight against epilepsy in Benin that echoes the program ''epilepsy out of the shadows'' of the ILAE, 1997. It provided a methodology for a reliable estimate of the overall prevalence of epilepsy for policy-makers in Benin.

Ethical considerations

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this paper is consistent with those guidelines.

Conflict of interest

None of the authors has any conflict of interest to disclose.

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Table 4 Screening questionnaire (based on Preux et al., 2000).

Does the subject have a history of:		Yes = 1	No = 2	Unknown = 9
1	Loss of consciousness and/or loss of bladder control and/or foam at the mouth?	☐	☐	☐
2	Absence(s) or sudden lapse(s) of consciousness during a short time?	☐	☐	☐
3	Involuntary clonic movements or muscular jerks of arm(s) and/or leg(s) (convulsions) that start suddenly and stop within minutes?	☐	☐	☐
4	Does the subject sometimes experience sudden and brief bodily sensations, see or hear things that are not there, or smell strange odors?	☐	☐	☐
5	Did someone tell the subject that he/she had epilepsy or that he/she already had epileptic fits?	☐	☐	☐

Appendix A.

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