Elsevier Editorial System(tm) for The Lancet Global Health

Manuscript Draft

Manuscript Number:

Title: Excess mortality in active convulsive epilepsy and associated risk factors in sub-Saharan Africa

Article Type: Article (Original Research)

Keywords: Epilepsy, excess mortality, SEEDS, SMR, risk factors

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Manuscript Region of Origin: TANZANIA, UNITED REPUBLIC OF

Abstract: Background
In sub-Saharan Africa, there is a paucity of evidence on the magnitude of excess mortality in epilepsy relative to the general population and risk factors associated to this excess. This study estimated excess mortality in people with active convulsive epilepsy (ACE) using data from the Studies of Epidemiology of Epilepsy in Demographic Surveillance Sites in three sub-Saharan African (SSA) countries.
Methods
We followed those with and without epilepsy and documented deaths in Agincourt (South Africa), Ifakara (Tanzania) and Kilifi (Kenya) for duration of seven, six and eight years, respectively.
Findings
A total of 199 deaths in ACE and 16,801 in general population were observed from the time of diagnosis to the most recent household survey. Mortality rates in ACE were estimated at 31.5 deaths per 1,000 person-years (95%CI: 19.4-43.6) in Agincourt, 23.9 (95%CI: 11.7-36.1) in Ifakara and 24.6 (95%CI: 19.5-29.6) in Kilifi. Pooled estimates of excess mortality (Standardized mortality ratio (SMR)), was 4.8 (95% CI: 4.2-5.6) times higher in PWE than those without epilepsy. Adjusting for age, SMRs were 3.20 (95%CI: 2.41-4.27) in Agincourt, 4.66 (95%CI: 3.46-6.29) in Ifakara and 6.22 (95%CI: 5.15-7.50) in Kilifi.
Interpretation
This study demonstrates evidence of excess mortality in PWE in SSA countries. Mortality burden may be reduced by managing seizures with improved access to antiepileptic drugs, preventive measures against accidents, reducing perinatal adverse events at birth, preventing parasite infections with proper management of domesticated animals and hygiene, empowering PWE with education and decent low-risk jobs and managing co-morbidities.
Funding
The Wellcome Trust, UK

Title: Excess mortality in active convulsive epilepsy and associated risk factors in sub-Saharan Africa.

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Abstract

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domesticated animals and hygiene, empowering PWE with education and decent low-risk jobs and managing co-morbidities.

Funding

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Research in context

Evidence before this study

In SSA, there is a paucity of evidence on the magnitude of excess mortality in people with epilepsy (PWE) relative to the general population and risk factors to this excess. Our recent systematic review highlighted the limited number of studies that estimated mortality in PWE relative to the general population. The review identified seven studies in LMIC over the period of 25 years. Estimated excess mortality measured by Standardized Mortality Ratio (SMR) range from 1.3-7.2 times higher in PWE than general population.

Meta-analysis of the review indicated that up to 80% of total variability's in the estimate of excess mortality was only due to differences between studies. These differences may be due to methodological variations between studies or other unknown factors. Pooled mortality rate in PWE could not be estimated due to large variability's between studies.

At the time the systematic review was concluded, there were no sufficient data to provide empirical evidence of excess mortality in PWE in LMIC. The review also revealed considerably large heterogeneity between studies, illustrating the high degree of uncertainty in the estimation of the true occurrence of deaths in PWE across Low and Middle-Income countries (LMICs).

Added value of this study

At the time the systematic review was completed, new data on mortality of PWE were emerging from Studies of Epidemiology of Epilepsy in Demographic Surveillance (SEEDS). SEEDS had already followed PWE for over eight years and documented deaths in people with and without epilepsy. SEEDS were designed to systematically collect comparable data on the prevalence and mortality in PWE and account for most methodological limitation identified by neurologist and epidemiologist in the past. Major methodological challenges addressed were on epilepsy screening and diagnosis, mortality follow-up, causes of death assessment, and population representativeness. SEEDS were nested within Health and Demographic Surveillance System in five sub-Saharan African countries (SSA) (Tanzania, South Africa, Uganda, Kenya and Ghana).

Analysis of SEEDS data reviled pooled excess mortality (SMR) of 4.8 times higher in PWE than general population (95% CI: 4.2-5.6). This study identified modifiable risk factors potential for mitigating the negative impact of epilepsy. The most influential risk factors for excess mortality were high frequency of seizures, past history of perinatal adverse events (obstructed labor, difficulties breathing and or crying), history of head injury, co-morbidities (sickle cell, hypertension, and motor, cognitive, and sleep disorders), and neurologic deficits.

Implications of all the available evidence

Mortality burden may be reduced by managing seizures with improved access to antiepileptic drugs, preventive measures against accidents, reducing perinatal adverse events at birth, empowering PWE with education and decent low-risk jobs and managing epilepsies' co-morbidities.

Introduction

Epilepsy is a neurological disorder that significantly impacts social and economic well-being and survival in people with epilepsy (PWE); this impact is often more pronounced in sub-Saharan African (SSA) countries when compared to high-income countries.[1] With poor access to antiepileptic drugs (AED) and health care services, mortality in PWE is higher than that of general population.[2] Untreated epilepsies are associated with increased seizure and mortality in status epilepticus, Sudden Death in Epilepsy (SUDEP) and accidents.[1,3] Uncontrolled convulsive seizures are the most important risk factor for excess mortality which is often linked to traffic accidents, burns, falls, or drowns. [4] Poor access to anti-epileptic drug (AED), seizures frequency, age onset of epilepsy, adverse perinatal events, and pre-existing health conditions such as cognitive and motor impairment are some of the risk factors for excess mortality in PWE.[5] Seizures are also associated with stigma, which often leads to exclusion from social and economic protective factors of premature mortality such as education, marriage, and employment.[6]

In sub-Saharan Africa, there is a paucity of evidence on the magnitude of excess mortality in PWE relative to the general population and risk factors to this excess.[7] The recent systematic review highlighted the limited number of studies that estimate mortality in PWE relative to the general population.[8] The review also revealed considerably large heterogeneity between studies, illustrating the high degree of uncertainty in the estimation of the true occurrence of deaths in PWE across Low and Middle-Income countries (LMICs).

Poor access to anti-epileptic drug (AED), seizures frequency, age onset of epilepsy, adverse perinatal events, and pre-existing health conditions such as cognitive and

motor impairment are some of the risk factors for excess mortality in PWE in SSA.[5] Uncontrolled convulsive seizures are the most important risk factor for excess mortality related to traffic accidents, burns, falls, or drowns in PWE SSA.[4] Certain risk factors can be modifiable, meaning; health interventions can significantly reduce excess mortality such as reducing seizures frequency through increased access to AED. Some risk factors are associated with both occurrences of epilepsy and excess mortality, including but not limited to, specific epilepsy etiology such as parasitic infections, adverse perinatal events, cerebrovascular diseases, and road traffic injuries. Identifying and preventing these risk factors is expected not only reduce excess mortality in PWE but prevent the development of epilepsy.

Studies of Epidemiology of Epilepsy in Demographic Surveillance (SEEDS) were designed to systematically collect comparable data on the prevalence and mortality in PWE in population-based and house-to-house surveys in five sub-Saharan African countries (Tanzania, South Africa, Uganda, Kenya and Ghana).[9] Epilepsy treatment gap is estimated at 70% across study sites. Majority of those on treatment are prescribed with phenobarbital.

Using data from SEEDS sites, we aims to estimate country-specific and overall excess mortality in PWE and assess associated risk factors.

Methods

Study settings and populations

SEEDS studies were nested within Health and Demographic Surveillance System (HDSS). The population characteristics, study designs, and core activities of the HDSS sites has been published elsewhere.[27-29] HDSS sites were established by enumerating the entire population in the selected sites. Following the establishment

these large population-based cohorts, continuous updates of residency status (in and out-migration and lost to follow-up) and vital events (birth and deaths and their causes) have been conducted on a regular basis ranging from 1 to 3 visits in every enumerated household per year. Total populations at the start of the SEEDS study in three HDSS were 83,121, 104,889 and 233,881 residents in Agincourt, Ifakara, and Kilifi, respectively.[9]

People with active convulsive epilepsy (ACE) were identified in a three stages screening process of the entire populations.[10] ACE was defined as the presence of at least "two or more unprovoked seizures occurred at least 24 hours apart" in the past 12 months.[11] Estimates of the prevalence of ACE in three sites have been published elsewhere.[9] After screening, cohorts of people with ACE were established and followed as part of standard HDSS population.

Baseline census and risk factors

Data on risk factors for ACE and mortality in PWE were collected by trained clinicians and field workers during baseline epilepsy surveys. General and adult-specific (such as alcohol consumption) data on social and demographic, historical and clinical factors were directly collected from individuals aged 18 years and older. For study participants younger than 18 years of age, or with cognitive impairment, the mother or caregiver was interviewed. Child and mother's specific data were collected including questions on antenatal (such as severe abdominal pain, vaginal bleeding, or infection during pregnancy) and perinatal events (difficulties breathing, feeding, or crying after birth, as recalled by the mother).

Clinical classification of seizures on the basis of electroencephalography (EEG) features of SEEDS cohorts have been published elsewhere.[12-14] In summary, EEGs

were performed on all participant diagnosed with ACE using 16 channel digital recording system (Grass Technologies, Warwick, RI, USA) according to the 10–20 international system with hyperventilation and photic stimulation. EEG activities were coded and classified into four categories of a normal, mild, moderate or severe excess of generalized slow of cerebral function. A binary classification was recorded as normal and abnormal (mild, moderate and severe). Identification of the location of epileptic seizures in the brain was done by analyzing waves, spikes, polyspike, and burst of interictal epileptiform discharges (IEDs). IEDs were classified as generalized (involving the entire brain), focal (involving a region of the brain) or multifocal (involving 3 or more discrete brain regions). An EEG summary indicator was categorized as abnormal if there was evidence of an abnormal background, focal changes, interictal epileptiform activity or an abnormal response to hyperventilation and photic stimulation.

Nutritional status was defined using body mass index (BMI; weight/height^2) and categorized using the standard World Health Organization (WHO) categories <18 (underweight), 18-24 (normal), 25-30 (over weight), and 30+ (obese). Detailed information on definitions and categories of risk factors have been published previously.[13]

Follow-up of ACE and the general population

Both people diagnosed with ACE and the general population (without epilepsy) continued to be part of routine population surveillance. Median follow-up durations were seven, six and eight years in Agincourt, Ifakara and Kilifi, respectively (Table 1). Data from Uganda and Ghana were not included in the final analysis because no robust long-term follow-up data were available at the time of data extraction. During

the follow-up, deaths in those diagnosed with ACE and the general population were documented in the longitudinal database and extracted for analysis.

Statistical analysis

Mortality rates in people with and without ACE were estimated using survival analysis models. Exposure time was estimated from individual's residence episodes started at the study's start date or birth or in-migration in each site and ended at out-migration, death or at the end of the analysis period. Mortality rate estimates were stratified by risk factors and rate ratio compared over different levels of risk factors. Mortality rate ratios were estimated using the Mantel-Haenszel method. Standardized Mortality Ratios (SMRs) were estimated to assess excess mortality in ACE compared to general population. The INDEPTH standard life table was used as standard population in comparing mortality between the three sites.[15] Stata software version 13 (StataCorp LP, College Station, Texas) was used for descriptive and statistical analysis.

The study protocol was approved by Ifakara Health Institution Internal Review Board (IHI/IRB/No. A 70-2009) and National Institute of Health Research and Commission of Science and Technology with reference NIMR/HQ/R.8a/Vol. IX/1256. All participants were enrolled through verbal consent.

Role of the funding source

Screening, diagnosis of PWE, and identification of risk factors for epilepsy in HDSS sites was supported by grants from The Wellcome Trust [Grant No. 083744] to C.R.N. Ifakara Health Institute and Basel Canton funded FL to lead this study. Routine mortality follow-ups in Agincourt, Ifakara and Kilifi HDSS sites were supported by multiple funders.

Funders had no role in the study design, data acquisition, data analysis, or writing of the paper. The corresponding author had full access to the data and had final decision of the content and submission of publication. SEEDS baseline data is available on request through INDEPTH Network. Site-specific mortality and residency status is available with prior permission from respective HDSS site Manager\Leaders.

Results

A total of 199 deaths were observed in the cohort of 1,268 individuals with ACE from the three sites. These deaths occurred between the time of diagnosis to the most recent HDSS visits for which data were available. In the general population, 16,801 deaths occurred in the total population of 506,813 residents (Table 1). Mortality rates in general population were 9.7 deaths per 1,000 person-years (95%CI: 9.6-10.1) in Agincourt, 7.7 (95%CI: 7.5-7.9) in Ifakara and 5.0 (95%CI: 4.9-5.1) in Kilifi. Estimated mortality rates in PWE were 31.5 deaths per 1,000 person-years (95%CI: 19.4-43.6) in Agincourt, 23.9 (95%CI: 11.7-36.1) in Ifakara and 24.6 (95%CI: 19.5-29.6) in Kilifi. Mortality rates in PWE were comparable across the sites when adjusted for INDEPTH standard population. Mortality rate stratified by site and risk factors are available in Supplement Table S1.

In analysis of risk factors for mortality in PWE, controlling for site, high mortality rates were observed for those who ate soil on regular bases (RR=1.70, 95% CI:1.27-2.26), snored more than 3 nights per week (RR=1.42, 95% CI: 1.04-1.93), adults who were previously married (divorced/separated/widowed) (RR=2.30, 95%CI: 1.46-3.63), adults who were illiterate (RR=1.69, 95%CI: 1.21-2.36), those with onset of epilepsy at adult ages of 29-49 years (RR=1.88, 95% CI: 1.01-3.50) or old ages of 50 years and above (RR=4.67, 95% CI: 2.71-8.05), those with daily seizures

(RR=1.54, 95%CI: 1.03-2.28), those with seizures occurs both day and night (RR=1.80,95%CI: 1.05-3.09), those with severe general EEG diagnosis (excessive slow of cerebral function) (RR=2.27, 95% CI: 1.34-3.83), those with burn marks (RR=1.46, 95%CI: 1.05-2.02), those with systolic blood pressure above 140mmHg (RR=2.58, 95%CI: 1.82-3.66) or a diastolic blood pressure above 90mmHG (RR=2.78, 95%CI: 1.90-4.06), those with pre-existing neurologic deficits (RR=1.78, 95%CI:1.31-2.43) or cognitive impairment (RR=2.11, 95%CI:1.57-2.84). The observed overall estimates were similar across sites based on the test of unequal RR controlling for a site (Table 2).

The site-specific analysis identified risk factors that were significantly associated with increased mortality in PWE but not observed in the overall analysis. In Agincourt, high mortality rates were observed in males (RR=2.12, 95% CI: 1.15-3.92), those with previous history of head injuries (RR=4.03, 95%CI: 2.09-7.79), adults who were married (RR=3.35, 95%CI: 1.50-7.52), and adults who consumed alcohol (RR=3.15, 95% CI: 1.57-6.31). In Ifakara, high mortality rates were observed in babies who had history of difficulties in breathing or crying soon after birth (RR=3.34, 95% CI: 1.09-10.25), and in those who had more than 12 seizures per year (RR=2.42, 95% CI: 1.12-5.21) and those with motor impairment (RR=4.07, 95% CI: 1.57-0.54). In Kilifi, high mortality rates were seen in those with sickle cell disease (RR=7.51, 95% CI: 1.86-30.44) and motor impairment (RR=2.75, 95% CI: 1.87-4.07) Table 2.

Overall estimates of excess mortality across the three sites as measured by SMR was 4.8 (95% CI: 4.2-5.6) times higher in PWE than the general population. Mortality estimates in PWE were higher than the general population in each HDSS sites. SMRs were 3.20 (95%CI: 2.41-4.27) in Agincourt, 4.66 (95%CI: 3.46-6.29) in Ifakara and 6.22 (95%CI: 5.15-7.50) in Kilifi. Analysis of excess mortality in PWE by site

identified several subpopulations with SMR greater than country-specific estimates. Supplement Table S2 provides estimates for SMR by subpopulation and site.

Discussion

Excess mortality

Understanding the magnitude of excess mortality in PWE as well as risk factors are important in developing epilepsy management programs aimed at reducing epilepsy-related causes of deaths and morbidities. Our previous systematic review identified only seven good quality population-based studies of excess mortality in PWE from LMIC in the study period of approximately 25 years (1990-2014).[8] The review also indicated substantial uncertainties in estimates of mortality in PWE in sub-Saharan Africa and other LMICs. Using standard definitions and methodology, this study provides evidence of excess mortality of a magnitude of five times greater in people diagnosed with active convulsive epilepsy, compared to the general population in large community/population-based surveys in SSA. The estimates are approximately twice of what has been previously reported in the literature. This study also identified sub-populations of PWE with greater excess mortality than the overall mortality in PWE and identified potentially modifiable risk factors for mortality in PWE.

In high-income countries (HICs), mortality in PWE is higher than the general population; however, the magnitude is lower than estimates observed in this study.[16] In studies conducted in HICs, excess mortality in PWE (SMR) was 1.3-3 times higher in population-based studies.[17] In clinical cohorts, mortality in PWE was much higher, especially in children where mortality was seven times higher than the general population.[17] Other studies in developed countries have observed no change over

time in both epilepsy mortality rate and excess mortality in PWE compared to general population.[18]

The estimates of excess mortality in PWE were comparable across the three SSA countries. These results were anticipated given the observed similarity in high epilepsy treatment gaps, population attributable risk and clinical features in the studied population.[3,13] Extended follow-up duration in Agincourt (from 4 to 7.4 years) and Kilifi (from 2.7 to 8 years) did not significantly change previous reported mortality estimates of excess mortality.[5,19] These findings indicate there is stable mortality in PWE compared to the general population in Agincourt and Kilifi HDSS sites.

Risks factors analysis

Risk factors for excess mortality in PWE identified behaviors, health conditions and characteristics or exposures that increase than usual the risk of death in PWE. Risk factors were only captured in those with epilepsy in order to identify subpopulation with excess mortality risk among those diagnosed with epilepsy.

This study identified overall and site-specific risk factors for excess mortality in PWE. We identified social and demographic factors, clinical, clinical historical conditions, as well as cerebral activities related to excess mortality in PWE. It is worth noting that a substantial number of factors were found to be associated with developing epilepsy and risk factors for excess mortality. These factors include; adverse perinatal events, history of head injuries, illiterate, poor hygienic practices (eating soil), and cerebrovascular diseases. Mitigating these factors with proposed public health interventions has the potential to reduce epileptogenic and excess mortality concurrently (Table 3).

Social and demographic factors

Males were observed to experience higher mortality than females in this study; however, the reasons behind these differences have not well researched. Some studies have linked the differences to the etiologies of epilepsy.[20] Epilepsies in females are more idiopathic and generalized while symptomatic and localized epilepsies are more prevalent in males. This may be explained by the fact that males are at higher risk of localized epilepsies caused by head injuries related to their occupations such as tree climbing, construction, driving, riding, and frequent travel. Individuals with regular alcohol consumption were observed to experience high mortality, possibly due to high exposure to accident-related injuries. PWE who are educated are more likely to be well informed about their condition hence avoid informal health seeking choices (such as consulting witchdoctors) that may increase their risks of premature mortality. Educating PWE may also lead to participation in less risky jobs such as teaching and customer care compared to high-risk jobs such as driving and physical labor. Higher mortality rates were observed among individuals who were previously married (divorced/separated/widowed). These individual are more likely to be suffering from psychosocial disabilities as a result of difficulties in social interaction.[21] High mortality in those in households with cats may be linked to severe brain complications caused animals and human interactions of pork parasites.[22] Eating soil or geophagia is an ancient practice in Africa and other parts of the world believed to be associated with psychiatric disorders, culture, poverty, famine, and mineral deficiency in pregnant women. Regardless of the reasons for the practice, eating soil has been linked to soil-transmitted parasites some of which are responsible for epilepsy.[22] Limited to access to comprehensive health care during delivery, such as resuscitation and caesarean, may result in epilepsy cases with severe brain damage and increased risk of mortality compared

to normal deliveries. Antenatal and perinatal events such as obstructed labor, difficulties breathing and crying have been well described in the literature as risk factors of a severe form of childhood epilepsies in LMIC[23] and have been found to be a risk factor for death in this study.

Clinical history

High mortality in people with onset of epilepsy at older ages indicates that the etiology of epilepsy may be linked to cerebrovascular diseases, parasitic infections, and accidents/cerebral trauma.[7,24] In study areas where the epilepsy treatment gap is high, a positive association between seizure frequency and mortality was expected especially in those with daily seizure, seizure occurring both day and night, and in PWE having more than 12 seizures per year. Reducing seizure frequency and severity by expanding treatment with AED may be an effective approach in reducing both epilepsy and accident-related causes of death in PWE.[4,21]

Clinical examination

Co-morbidities with neurological disorders such as cardiovascular and cerebrovascular diseases have been observed to increase mortality in PWE in many developed countries as observed in this study.[16] Co-morbidities with motor and cognitive impairment were also found to be associated with an increased mortality in PWE in this study as well as sickle cell disease. Addressing these co-morbidities could be effective in reducing premature mortality in epilepsy. [25] Premature mortality in PWE could be prevented by streamlining interventions targeting management of severe cases of neurological disorders and infections as well as severe cases of status epilepticus. Preventive measures against accidents (head injuries) which were also associated with higher mortality in PWE could reduce the incidence of epilepsy associated with cerebrovascular accidents. Excessive snoring is among risk

factor found to be more common in people with epilepsy than healthy individuals.[26] Snoring is thought to be strongly associated with sleep apnea, a dangerous condition that, when untreated, can lead to death. We observed high mortality in PWE who were snoring more than three nights per week. Several studies suggest that up to 70% of SUDEP occurred during sleep.[27] There is limited information on causes of sleep disorders in PWE but the contribution of certain AED, seizures, and various epilepsy syndromes are likely.[28]

EEG

Generalized slowing of brain functions is often observed in PWE and is indicative of diffuse brain dysfunction. Severe abnormal EEG has been liked to increased seizures frequency. In this study, PWE with severe abnormal EEG features were observed to experience a higher mortality compared to those with normal EEG features. These results are consistent with other studies that linked abnormal EEG features in PWE with higher seizure recurrence.[29] These findings demonstrate the need for health system's investments imaging equipment's that will be essential in early identification of the individual at risk of premature mortality not only in PWE but also in people with other neurological disorders. Other forms of diagnosis such as prolonged implantable electrocardiography monitoring may be potential in reducing a high rate of misdiagnosis of epilepsy.

Limitations

Based on our current knowledge, the SEEDS project is the largest, standardized population-based study of prevalence and mortality in PWE in sub-Saharan Africa. This study accounted for common and major methodological limitations such as epilepsy definition, cases identification, and mortality ascertainment previously identified in the epidemiological literature on epilepsy in sub-Saharan Africa.[3,30] The

focus on ACE in this study limits the ability to fully determine the excess mortality in PWE with non-convulsive seizures in SSA. There was also no enough data to classify excess mortality by type epilepsy within those with ACE. However, the choice to focus on ACE was due to the difficulty in ascertaining non-active cases of epilepsy.

Conclusion

This study provides evidence of excess mortality, with a pooled magnitude of mortality five times greater in PWE compared to those without epilepsy in sub-Saharan Africa. These findings indicate that PWE in sub-Saharan Africa are at substantially greater risk of death than people without epilepsy. In this study, we identified sub-populations and risk factors of excess mortality in PWE that could potentially mitigate the development of epilepsy and the increased mortality. These findings suggest that the mortality in PWE may be reduced by implementing interventions that strengthen clinical management of epilepsy, including better access to AED, reducing adverse perinatal events with improved care at birth, implementing community preventive measures against accidents, introducing hygienic behavior changes (discourage eating soil), properly managing parasitic infections in both human and domestic animals, increasing access to education to PWE, empowering PWE with less risk jobs and adequately managing co-morbidities such as cerebrovascular, cardiovascular, and motor and cognitive impairment.

Author contributions

Francis Levira: Conducted statistical analysis, interpretation of data and drafting/revising the manuscript. Honorati Masanja, Ryan G Wagner, Stephen Tollman, Peter Odermatt: Revised the manuscript of its scientific content and

contribution. Charles Newton: Conceived and designed the study, collected data, interpreted results, revised the manuscript, and supervised the study.

Acknowledgments

This work was supported by grants from The Wellcome Trust [Grant No. 083744] to C.R.N.; Ifakara Health Institute under Training Unit and Basel Canton. The Agincourt HDSS is funded by the Wellcome Trust, UK (grants 058893/Z/99/A; 069683/Z/02/Z; 085477/Z/08/Z), with important contributions from the University of the Witwatersrand, the South African Medical Research Council, and the William and Flora Hewlett Foundation, National Institute on Aging (NIA) of the NIH, and Andrew W Mellon Foundation, USA.

The authors wish to acknowledge Ms. Rachael Odhiambo for developing and overseeing the study's database as well as the fieldworkers of the Ifakara HDSS, Kilifi and MRC/Wits Agincourt Research Unit involved in the Studies of Epidemiology of Epilepsy in Demographic Surveillance Systems (SEEDS) study and the sub-district population who took part in the study.

Declaration of interest

Authors declare no conflict of Interest.

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Table 1: Key summary findings by population

	Argincourt				Ifakara				Kilifi				Total			
	GP	**%**	**PWE**	**%**	**GP**	**%**	**PWE**	**%**	**GP**	**%**	**PWE**	**%**	**GP**	**%**	**PWE**	**%**
Overall																
Initial cohort size	83,121		245		104,889		366		233,881		697		421,891		1,308	
Lost to follow-up			9	3.7			4	1.1			27	3.9			40	3.1
Final cohort																
Sex																
Males	38,983	48	124	53	103,980	49	171	47	98,889	46	340	51	241,852	48	635	50.1
Females	41,987	52	112	47	108,443	51	191	53	113,697	53	327	49	264,127	52	630	49.7
Age						0										
0-5	7,029	9	5	2.1	55,150	26	20	5.5	12,668	6	22	3	74,847	15	47	3.7
6-18	18,897	23	39	17	55,416	26	113	31	85,393	40	233	35	159,706	32	385	30.4
19-49	41,714	52	137	58	80,691	38	190	52	83,910	39	344	51	206,315	41	671	52.9
50+	13,330	16	55	23	21,166	10	39	11	31,449	15	71	11	65,945	13	165	13.0
Residency status																
Alive	52,776	65	136	58	126,676	60	222	61	115,853	54	369	55	295,305	58	727	57.3
Out-migration	23,453	29	53	22	80,096	38	97	27	91,159	43	192	29	194,708	38	342	27.0
Deaths	4,741	6	47	20	5,651	3	43	12	6,409	3	109	16	16,801	3	199	15.7
Total	**80,970**	**100**	**236**	**100**	**212,423**	**100**	**362**	**100**	**213,420**	**100**	**670**	100	**506,813**	100	**1,268**	**100.0**
Median follow-up(years)	7.4		7.4		3.3		6.3		7.4		8.1		5.6		6.5	
Mortality rate																
Crude	9.7		35.2		7.7		23.8		5.0		26.0		6.7		27.1	
Adjusted	8.0		31.5		7.9		23.9		4.7		24.6					
95% CI Lower	7.7		19.4		7.7		1.7		4.6		19.5					
95% CI Upper	8.3		43.6		8.1		6.1		4.8		29.6					

GP: General Population; PWE: People with Epilepsy; CI: Confidence interval

Table 2: Relative risks and 95% CI of mortality in epilepsy by site and risk factors

Risk/condition	Agincourt	Ifakara	Kilifi	Overall		
		RR (95%CI)		RR (95%CI)	chi	p-value
Males	2.12 (1.15-3.92)†	1.22 (0.67-2.22)	1.09 (0.75-1.58)	1.29 (0.98-1.71)	3.42	0.181
Head injury	4.03 (2.09-7.79)†	2.48 (0.89-6.96)	1.23 (0.72-2.09)	1.84 (1.26-2.69)†	8.29	0.016
Eat soil	1.23 (0.68-2.23)	1.74 (0.95-3.19)	1.93 (1.31-2.85)†	1.70 (1.27-2.26)†	1.57	0.455
Snore > 3 nights a week	1.00 (0.54-1.86)	1.38 (0.76-2.52)	1.70 (1.09-2.66)†	1.42 (1.04-1.93)†	1.88	0.391
Marital status-Single	Ref	1	1	1		
Marital status-Married	3.35 (1.50-7.52)†	0.42 (0.16-1.08)	1.04 (0.61-1.78)	1.16 (0.79-1.70)	2.3	0.002
Marital status-Previous married	3.58 (1.55-8.26)†	1.28 (0.42-3.84)	2.16 (1.14-4.07)†	2.30 (1.46-3.63)†	2.26	0.324
Illiterate adult	2.88 (1.54-5.41)†	2.15 (0.98-4.71)	1.22 (0.76-1.95)	1.69 (1.21-2.36)†	5.07	0.079
Adult consuming alcohol	3.15 (1.57-6.31)†	0.73 (0.25-2.16)	1.09 (0.54-2.20)	1.42 (0.92-2.21)	7.35	0.025
Difficulties crying after birth	1.84 (0.22-5.77)	3.34 (1.09-0.25)†	1.16 (0.36-3.77)	1.84 (0.87-3.89)	1.72	0.424
Age onset 6-12	Ref	1	1	1		
Age onset 29-49	3.47 (1.22-9.85)†	1.21 (0.24-5.98)	1.25 (0.49-3.19)	1.88 (1.01-3.50)†	2.42	0.299
Sickle cell disease			7.51 (1.86-0.44)†	3.54 (0.88-4.26)	2.22	0.33
> 12 seizure per year	0.73 (0.36-1.49)	2.42 (1.12-5.21)†	1.08 (0.64-1.82)	1.16 (0.81-1.66)	5.39	0.068
Seizure frequency-Monthly	Ref	1	1	1		
Seizure frequency-Daily	0.71 (0.22-2.36)	1.55 (0.77-3.11)	1.87 (1.10-3.17)†	1.54 (1.03-2.28)†	2.18	0.336
Seizure time-Night						
Seizure time-Day & Night	1.67 (0.65-4.33)	1.41 (0.59-3.35)	2.47 (0.91-6.74)	1.80 (1.05-3.09)†	0.71	0.7
EEG GB-Normal	Ref	1	1	1		
EEG GB-Severe	3.12 (1.17-8.32)†	1.45 (0.19-1.26)	2.12 (1.10-4.08)†	2.27 (1.34-3.83)†	0.63	0.728
No BCG vaccine scar	0.81 (0.39-1.68)	0.69 (0.21-2.22)	1.69 (1.13-2.54)†	1.28 (0.91-1.79)	4.45	0.108
Burn marks	1.88 (0.97-3.63)	1.26 (0.56-2.83)	1.39 (0.91-2.12)	1.46 (1.05-2.02)†	0.75	0.686
Systolic blood pressure: > 140	2.32 (1.23-4.36)†	3.17 (1.25-8.08)	2.65 (1.66-4.23)†	2.58 (1.82-3.66)†	0.31	0.857
Diastolic blood pressure: > 90	2.29 (1.21-4.35)†	2.51 (0.90-7.04)	3.39 (2.01-5.72)†	2.78 (1.90-4.06)†	0.95	0.623
Pre-existing neurological	1.19 (0.66-2.17)	2.74 (1.33-5.66)	1.98 (1.30-3.00)†	1.78 (1.31-2.43)†	3.36	0.186
Cognitive impairment	1.53 (0.84-2.78)	2.25 (1.04-4.86)	2.41 (1.64-3.54)†	2.11 (1.57-2.84)†	1.61	0.448
Motor impairment	0.75 (0.32-1.77)	4.07 (1.57-0.54)	2.75 (1.87-4.07)†	2.16 (1.56-2.99)†	9.63	0.008

Ref: Reference category, EEG: Electroencephalogram, BCG: Bacillus Calmette–Guérin, RR: Risk ratio, CI: Confidence interval, GB: General background, †: Statistically significant (P-value < 5%)

Table 3: Proposed action for modifiable risk factors for excess mortality in PWE

Risk factor	Sector	Action
Perinatal adverse events (obstructed labor, difficulties breathing and or crying)	Health	1. Improve care at birth, 2. Provide training to midwifes, 3. Improve emergency obstetric care, 4. Promote safe facility delivery.
1. Parasite infection 2. Poor hygiene (eating soil)	Health and agriculture	1. Educate the public on animal human disease transition, 2. Assist community on deworming domesticated animal, 3. Educate the community on soil transmitted infections.
Illiterate	Education and health	1. Improve access to education, 2. Health in primary education curriculum 3. Develop advocacy strategies that target illiterate individuals such as radio programs, 4. Educate the public on causes of epilepsy and associated misconception such as those linking epilepsy with curse and demonic possession
High seizures frequency	Health	1. Increase government support in procurement and supply of AED 2. Improve access to AED especially in remote area
Co-morbidities (sickle cell, hypertension, and motor, cognitive, and sleep disorders)	Health Researchers	1. Incorporate screening of co-morbidities on treatment guidelines 2. Train health care providers in managing co-morbidities. 3. Conduct research on incidence of co-morbidities and associated risk factors in PWE.
Head injuries	Health	1. Develop community interventions on road safety 2. Improve access imaging diagnosis (CT scan, MRI)
Neurologic deficits	Health	1. Train workers on diagnosing neurologic deficits 2. Improve access imaging diagnosis (EEG)

PWE: People with epilepsy, EEG: Electroencephalography, AED: Antiepileptic drugs, MRI: Magnetic resonance imaging, CT: computed tomography

Table

Supplement Table S1: Estimates of mortality rate (MR) in people with epilepsy per 1000 person years by site and characteristics

Characteristic/risk factor for all people with epilepsy	Agincourt			Ifakara			Kilifi		
	D	PYS*	MR (95%CI)	D	PYS*	MR (95%CI)	D	PYS*	MR (95%CI)
Females	15	0.666	22.52 (13.58-37.36)	20	0.935	21.38 (13.80-33.14)	51	2.044	24.96 (18.97-32.84)
Males	32	0.669	47.82 (33.82-67.63)	23	0.881	26.12 (17.36-39.31)	58	2.139	27.11 (20.96-35.07)
Facility deliveries	5	0.242	20.65 (8.60-49.62)	12	0.537	22.33 (12.68-39.33)	5	0.318	15.73 (6.55-37.79)
Home deliveries	1	0.074	13.58 (1.91-96.42)	6	0.372	16.13 (7.25-35.91)	34	2.052	16.57 (11.84-23.19)
Seizure history in family	1	0.026	39.19 (5.52-278.21)	1	0.021	46.92 (6.61-333.07)	15	0.531	28.24 (17.02-46.84)
Seizure in family	4	0.176	22.76 (8.54-60.65)	8	0.398	20.10 (10.05-40.18)	23	0.688	33.43 (22.21-50.30)
Head injury	12	0.107	111.82 (63.51-196.90)	4	0.073	55.05 (20.66-146.68)	16	0.540	29.65 (18.16-48.39)
Recent hospital admission	14	0.341	41.06 (24.32-69.33)	26	0.859	30.27 (20.61-44.46)	72	2.643	27.24 (21.62-34.32)
Eat cassava	32	0.892	35.89 (25.38-50.75)	26	1.120	23.22 (15.81-34.10)	83	3.416	24.29 (19.59-30.13)
Eat soil	30	0.778	38.55 (26.95-55.13)	21	0.655	32.08 (20.92-49.20)	69	1.959	35.22 (27.82-44.59)
Dog in the household	17	0.322	52.80 (32.82-84.93)	37	1.479	25.02 (18.13-34.53)	34	1.315	25.86 (18.47-36.19)
Cat in the household	4	0.046	86.52 (32.47-230.53)	39	1.639	23.80 (17.39-32.58)	61	2.214	27.56 (21.44-35.42)
Eat pork	14	0.262	53.52 (31.70-90.37)	23	1.212	18.98 (12.61-28.56)	28	0.930	30.12 (20.79-43.62)
Snore > 3 nights a week	27	0.814	33.18 (22.75-48.38)	24	0.851	28.20 (18.90-42.07)	73	2.475	29.49 (23.45-37.10)
BMI <18	1	0.058	17.16 (2.42-121.80)	4	0.247	16.17 (6.07-43.09)	14	1.029	13.60 (8.05-22.96)
BMI 18-24	2	0.080	24.90 (6.23-99.57)	4	0.334	11.97 (4.49-31.89)	14	0.645	21.72 (12.87-36.68)
BMI 25-30	9	0.163	55.38 (28.82-106.44)	11	0.388	28.39 (15.72-51.26)	28	0.964	29.05 (20.06-42.08)
BMI 30+	27	0.714	37.81 (25.93-55.14)	17	0.776	21.90 (13.62-35.24)	38	1.388	27.38 (19.92-37.62)
Adult specific risk factors									
Adult marital status									
Single	9	0.507	17.74 (9.23-34.09)	15	0.413	36.34 (21.91-60.28)	35	1.032	33.92 (24.36-47.25)
Married	17	0.286	59.48 (36.98-95.68)	6	0.396	15.17 (6.82-33.77)	22	0.621	35.41 (23.31-53.77)
Divorced/separated/widow	14	0.221	63.43 (37.56-107.09)	4	0.086	46.34 (17.39-123.46)	13	0.178	73.14 (42.47-125.96)
Illiterate adult	18	0.231	77.97 (49.12-123.75)	12	0.267	44.94 (25.52-79.13)	39	0.928	42.05 (30.72-57.55)
Adult consuming alcohol	11	0.109	101.39 (56.15-183.08)	4	0.194	20.62 (7.74-54.93)	9	0.216	41.72 (21.71-80.18)
Child specific risk factors									
Maternal marital status									

Married	1	0.132	7.58 (1.07-53.83)	15	0.778	19.28 (11.63-31.99)	28	1.960	14.28 (9.86-20.69)
Single	4	0.133	30.01 (11.27-79.97)	1	0.080	12.48 (1.76-88.57)	2	0.044	45.79 (11.45-183.10)
Divorced/separated/widow	1	0.055	18.13 (2.55-128.72)	2	0.063	31.58 (7.90-126.28)	8	0.293	27.35 (13.68-54.69)
Unemployed mother	5	0.231	21.62 (9.00-51.94)	0	0.024		17	1.024	16.61 (10.32-26.72)
Illiterate mother	1	0.017	58.37 (8.22-414.34)	3	0.182	16.52 (5.33-51.24)	23	1.297	17.73 (11.78-26.69)
Mother's history of seizure	0	0.007		0	0.023		2	0.036	56.34 (14.09-225.27)
Delivery problem-Mothers	2	0.029	68.06 (17.02-272.14)	2	0.085	23.64 (5.91-94.51)	6	0.331	18.11 (8.14-40.32)
Difficulties crying after birth	1	0.030	33.87 (4.77-240.47)	4	0.078	51.55 (19.35-137.34)	3	0.158	18.98 (6.12-58.86)
Difficulties breathing after birth	0	0.022		3	0.061	49.41 (15.94-153.20)	2	0.087	23.01 (5.75-92.00)
Incomplete immunization	1	0.026	38.11 (5.37-270.55)				2	0.099	20.26 (5.07-80.99)
Clinical history									
Age onset 0-5	10	0.408	24.52 (13.19-45.57)	20	0.760	26.32 (16.98-40.79)	53	2.646	20.03 (15.30-26.22)
Age onset 6-12	5	0.276	18.15 (7.55-43.60)	6	0.382	15.72 (7.06-34.98)	16	0.600	26.68 (16.35-43.56)
Age onset 13-18	3	0.156	19.26 (6.21-59.70)	4	0.271	14.74 (5.53-39.28)	9	0.354	25.40 (13.22-48.82)
Age onset 19-28	8	0.154	52.04 (26.03-104.07)	4	0.171	23.37 (8.77-62.27)	8	0.240	33.29 (16.65-66.57)
Age onset 29+	17	0.249	68.33 (42.48-109.91)	7	0.146	48.08 (22.92-100.86)	21	0.319	65.78 (42.89-100.88)
Sickle cell disease	0	0.004		0	0.006		2	0.010	191.68 (47.94-766.43)
< 12 seizure per year	32	0.838	38.18 (27.00-53.98)	11	0.797	13.79 (7.64-24.91)	49	2.408	20.35 (15.38-26.92)
> 12 seizure per year	10	0.357	27.98 (15.05-52.00)	16	0.479	33.38 (20.45-54.48)	20	0.908	22.02 (14.21-34.14)
Seizure type-Generalized	26	0.684	37.99 (25.87-55.79)	19	0.882	21.55 (13.74-33.78)	27	1.047	25.80 (17.69-37.62)
Seizure type-Focal	20	0.554	36.11 (23.30-55.97)	14	0.527	26.55 (15.72-44.82)	76	2.800	27.14 (21.68-33.98)
Seizure type-Others	0	0.014		0	0.048		6	0.190	31.61 (14.20-70.36)
Untreated with AED	12	0.459	26.17 (14.86-46.08)	19	0.946	20.09 (12.82-31.50)	57	2.412	23.63 (18.23-30.63)
No of different type of seizure-1	38	1.033	36.80 (26.78-50.58)	35	1.455	24.05 (17.27-33.50)	88	3.408	25.82 (20.95-31.82)
No of different type of seizure-2	5	0.230	21.75 (9.05-52.25)	8	0.304	26.29 (13.15-52.58)	20	0.744	26.90 (17.35-41.70)
No of different type of seizure-3	0	0.007		0	0.017		1	0.010	101.46 (14.29-720.26)
Seizure frequency-Daily	3	0.097	31.06 (10.02-96.31)	11	0.265	41.48 (22.97-74.90)	23	0.518	44.37 (29.49-66.78)
Seizure frequency-Monthly	27	0.621	43.45 (29.80-63.36)	28	1.046	26.76 (18.48-38.76)	34	1.430	23.77 (16.99-33.27)
Seizure frequency-Weekly	2	0.065	31.02 (7.76-124.04)	1	0.139	7.19 (1.01-51.05)	19	0.471	40.36 (25.75-63.28)
Seizure time-Day & Night	29	0.704	41.22 (28.64-59.31)	35	1.310	26.71 (19.18-37.20)	82	2.605	31.48 (25.36-39.09)
Seizure time-Day	12	0.396	30.33 (17.22-53.41)	1	0.154	6.52 (0.92-46.26)	23	1.261	18.24 (12.12-27.45)
Seizure time-Night	5	0.203	24.61 (10.24-59.13)	6	0.317	18.95 (8.51-42.18)	4	0.314	12.75 (4.78-33.97)

Imaging									
EEG general background									
Mild	11	0.252	43.62 (24.16-78.77)	6	0.211	28.50 (12.81-63.44)	16	0.726	22.03 (13.49-35.95)
Moderate	1	0.033	30.54 (4.30-216.78)	3	0.124	24.20 (7.81-75.05)	2	0.182	11.00 (2.75-43.97)
Normal	20	0.647	30.90 (19.94-47.90)	11	0.560	19.64 (10.88-35.46)	36	1.730	20.81 (15.01-28.85)
Severe	5	0.052	96.44 (40.14-231.71)	1	0.035	28.55 (4.02-202.67)	12	0.272	44.16 (25.08-77.76)
EEG Asymmetry	3	0.085	35.20 (11.35-109.14)	1	0.031	31.83 (4.48-225.96)	1	0.046	21.59 (3.04-153.29)
EEG Focal feature	23	0.578	39.79 (26.44-59.87)	6	0.355	16.92 (7.60-37.65)	19	0.683	27.81 (17.74-43.60)
EEG epileptiform activity	13	0.244	53.28 (30.94-91.76)	4	0.368	10.88 (4.08-28.99)	19	1.043	18.21 (11.62-28.55)
EEG Focal temporal	11	0.219	50.14 (27.77-90.55)	4	0.291	13.73 (5.15-36.58)	19	0.744	25.55 (16.30-40.06)
EEG Focal extra temporal	9	0.183	49.24 (25.62-94.64)	3	0.285	10.54 (3.40-32.68)	12	0.733	16.38 (9.30-28.85)
EEG involve Temporal lobe	5	0.079	62.95 (26.20-151.25)	2	0.164	12.23 (3.06-48.90)	11	0.366	30.03 (16.63-54.23)
EEG Generalized	1	0.009	114.68 (16.15-814.11)	0	0.091		5	0.241	20.73 (8.63-49.81)
EEG photosensitivity: abnormal	1	0.033	29.90 (4.21-212.26)	4	0.067	59.64 (22.38-158.91)	2	0.116	17.20 (4.30-68.76)
EEG hyperventilation: abnormal	3	0.112	26.77 (8.63-83.00)	1	0.098	10.16 (1.43-72.16)	0	0.206	
EEG Summary-Abnormal	21	0.488	43.05 (28.07-66.03)	12	0.547	21.95 (12.47-38.65)	41	1.712	23.95 (17.63-32.53)
EEG Summary-Normal	8	0.297	26.94 (13.47-53.87)	8	0.379	21.11 (10.56-42.21)	26	1.182	22.00 (14.98-32.32)
EEG Summary-Undetermined	7	0.202	34.60 (16.49-72.57)						
Clinical features and examination									
Falls to the ground during seizure	41	0.963	42.58 (31.36-57.83)	34	1.424	23.88 (17.07-33.43)	91	3.521	25.85 (21.05-31.74)
Seizure duration-10 min+	2	0.083	24.16 (6.04-96.62)	8	0.316	25.33 (12.67-50.66)	47	1.446	32.50 (24.42-43.26)
Seizure duration-5-9 minutes	4	0.134	29.84 (11.20-79.50)	18	0.756	23.81 (15.00-37.79)	27	1.296	20.83 (14.28-30.37)
Seizure duration-< 5 minutes	40	0.953	41.98 (30.79-57.23)	12	0.499	24.04 (13.65-42.33)	30	1.306	22.98 (16.06-32.86)
No BCG vaccine scar	9	0.294	30.67 (15.96-58.94)	3	0.180	16.67 (5.38-51.68)	34	0.895	38.01 (27.16-53.20)
Burn marks	12	0.199	60.32 (34.26-106.21)	7	0.246	28.45 (13.56-59.67)	29	0.869	33.36 (23.18-48.00)
Systolic blood pressure: > 140	15	0.204	73.59 (44.37-122.07)	5	0.066	75.72 (31.52-181.92)	23	0.360	63.92 (42.48-96.19)
Diastolic blood pressure: > 90	14	0.196	71.62 (42.42-120.93)	4	0.065	61.83 (23.21-164.74)	17	0.221	76.83 (47.76-123.58)
Pre-existing neurological	17	0.410	41.49 (25.79-66.74)	11	0.225	48.95 (27.11-88.38)	31	0.685	45.26 (31.83-64.36)
Cognitive impairment	17	0.345	49.31 (30.65-79.31)	9	0.215	41.88 (21.79-80.50)	44	0.895	49.16 (36.58-66.06)
Motor impairment	6	0.212	28.35 (12.74-63.10)	5	0.062	81.17 (33.79-195.01)	40	0.706	56.67 (41.57-77.25)
Previous status epilepticus				3	0.064	47.03 (15.17-145.81)	34	1.439	23.63 (16.88-33.07)

Febrile seizure				0	0.013		24	1.139	21.08 (14.13-31.44)
History of encephalopathy	0	0.019		1	0.017	58.66 (8.26-416.40)	22	0.989	22.25 (14.65-33.79)
History of febrile seizure	4	0.084	47.58 (17.86-126.78)	8	0.472	16.95 (8.47-33.88)	26	1.359	19.13 (13.03-28.10)

D: Deaths, PYS: Person years per 1000, MR: Mortality rate, EEG: Electroencephalogram, BCG: Bacillus Calmette–Guérin, CI: Confidence interval

Table

Supplement Table S2: Standardized mortality ratio of death in people with epilepsy by risk factors and site

Characteristic/risk factor for all people with epilepsy	Agincourt		Ifakara		Kilifi	
	Obs (exp)	SMR (95%CI)	Obs (exp)	SMR (95%CI)	Obs (exp)	SMR (95%CI)
Overall	47 (14.64)	3.21 (2.41-4.27)	43 (9.22)	4.66 (3.46-6.29)	109 (17.53)	6.22 (5.15-7.50)
Females	15 (8.33)	1.80 (1.09-2.99)	20 (4.74)	4.22 (2.72-6.54)	51 (8.56)	5.96 (4.53-7.84)
Males	32 (6.31)	5.07 (3.59-7.17)†	23 (4.48)	5.14 (3.41-7.73)	58 (8.93)	6.49 (5.02-8.40)
Facility deliveries	5 (0.38)	13.10 (5.45-31.48) †	12 (1.04)	11.56 (6.57-20.36) †	5 (0.32)	15.86 (6.60-38.11) †
Home deliveries	1 (0.09)	10.59 (1.49-75.16)	6 (0.77)	7.76 (3.48-17.26) †	34 (1.95)	17.39 (12.43-24.3)†
Seizure history in family	1 (0.24)	4.24 (0.60-30.12)	1 (0.05)	19.36 (2.73-137.46)	15 (3.12)	4.81 (2.90-7.97)
Seizure in family	4 (2.15)	1.86 (0.70-4.97)	8 (2.22)	3.60 (1.80-7.20)	23 (2.78)	8.27 (5.49-12.44) †
Head injury	12 (1.39)	8.63 (4.90-15.20) †	4 (0.78)	5.10 (1.92-13.60)	16 (3.42)	4.68 (2.87-7.64) †
Recent hospital admission	14 (4.17)	3.35 (1.99-5.66)	26 (4.66)	5.58 (3.80-8.20) †	72 (9.60)	7.50 (5.95-9.45) †
Eat cassava	32 (11.22)	2.85 (2.02-4.03)	26 (5.78)	4.50 (3.06-6.61)	83 (13.92)	5.96 (4.81-7.39)
Eat soil	30 (11.04)	2.72 (1.90-3.89)	21 (4.87)	4.31 (2.81-6.61)	69 (12.57)	5.49 (4.34-6.95)
Dog in the household	17 (4.17)	4.08 (2.53-6.56) †	37 (7.57)	4.89 (3.54-6.74) †	34 (5.62)	6.05 (4.32-8.46)
Cat in the household	4 (0.55)	7.30 (2.74-19.46) †	39 (8.17)	4.77 (3.49-6.53) †	61 (9.79)	6.23 (4.85-8.00)
Eat pork	14 (3.15)	4.44 (2.63-7.50) †	23 (6.35)	3.62 (2.41-5.45)	28 (6.18)	4.53 (3.13-6.56)
Snore > 3 nights a week	27 (9.99)	2.70 (1.85-3.94)	24 (4.50)	5.33 (3.57-7.95) †	73 (10.83)	6.74 (5.36-8.48) †
BMI <18	1 (0.09)	10.53 (1.48-74.74)	4 (0.72)	5.53 (2.07-14.73)	14 (0.98)	14.25 (8.44-24.06) †
BMI 18-24	2 (0.15)	13.48 (3.37-53.91) †	4 (1.04)	3.86 (1.45-10.29)	14 (1.00)	13.99 (8.28-23.62) †
BMI 25-30	9 (1.74)	5.18 (2.69-9.95) †	11 (1.94)	5.68 (3.14-10.25)	28 (5.67)	4.94 (3.41-7.15)
BMI 30+	27 (8.62)	3.13 (2.15-4.57)	17 (4.83)	3.52 (2.19-5.66) †	38 (8.95)	4.25 (3.09-5.84)
Adult specific risk factors						
Adult marital status						
Single	9 (4.71)	1.91 (0.99-3.67)	15 (2.08)	7.22 (4.35-11.98) †	35 (2.81)	12.44 (8.93-17.32) †
Married	17 (4.40)	3.86 (2.40-6.21)	6 (3.48)	1.72 (0.77-3.84)	22 (9.03)	2.43 (1.60-3.70)
Divorced/separated/widow	14 (5.05)	2.77 (1.64-4.68)	4 (1.82)	2.20 (0.83-5.86)	13 (3.41)	3.82 (2.22-6.57)
Illiterate adult	18 (4.28)	4.20 (2.65-6.67) †	12 (2.85)	4.21 (2.39-7.41)	39 (10.38)	3.76 (2.75-5.14)
Adult consuming alcohol	11 (2.27)	4.86 (2.69-8.77) †	4 (1.93)	2.07 (0.78-5.51)	9 (3.66)	2.46 (1.28-4.73)
Child specific risk factors						

Maternal marital status						
Married	1 (0.19)	5.34 (0.75-37.89)	15 (1.55)	9.69 (5.84-16.07) †	28 (1.88)	14.89 (10.28-21.5) †
Single	4 (0.22)	18.51 (6.95-49.31) †	1 (0.13)	7.91 (1.11-56.13)	2 (0.04)	45.87 (11.4-183.4) †
Divorced/separated/widow	1 (0.08)	12.69 (1.79-90.08)	2 (0.17)	11.97 (2.99-47.88)	8 (0.27)	29.11 (14.56-58.2) †
Unemployed mother	5 (0.32)	15.74 (6.55-37.82) †			17 (0.99)	17.20 (10.69-27.6) †
Illiterate mother	1 (0.03)	39.45 (5.56-280) †	3 (0.31)	9.62 (3.10-29.82)	23 (1.22)	18.87 (12.54-28.3) †
Mother's history of seizure			0 (0.06)		2 (0.03)	61.25 (15.3-244.9) †
Delivery problem-Mothers	2 (0.07)	28.61 (7.15-114.3) †	2 (0.20)	9.94 (2.49-39.74)	6 (0.32)	18.60 (8.36-41.41) †
Difficulties crying after birth	1 (0.08)	12.99 (1.83-92.24)	4 (0.20)	20.10 (7.54-53.56) †	3 (0.15)	20.14 (6.49-62.43) †
Difficulties breathing after birth			3 (0.17)	17.55 (5.66-54.42) †	2 (0.08)	25.02 (6.26-100.0) †
Incomplete immunization	1 (0.05)	21.25 (2.99-150.8) †			2 (0.09)	21.59 (5.40-86.32) †
Clinical history						
Age onset 0-5	10 (2.24)	4.46 (2.40-8.28)	20 (2.12)	9.45 (6.10-14.65) †	53 (4.19)	12.65 (9.66-16.55) †
Age onset 6-12	5 (2.12)	2.36 (0.98-5.67)	6 (0.94)	6.37 (2.86-14.18)	16 (1.56)	10.25 (6.28-16.73) †
Age onset 13-18	3 (1.50)	2.00 (0.64-6.19)	4 (1.26)	3.19 (1.20-8.49)	9 (1.38)	6.51 (3.39-12.52) †
Age onset 19-28	8 (2.28)	3.51 (1.75-7.01)	4 (1.11)	3.59 (1.35-9.57)	8 (1.55)	5.16 (2.58-10.31) †
Age onset 29+	17 (5.48)	3.10 (1.93-4.99)	7 (3.12)	2.25 (1.07-4.71)	21 (8.51)	2.47 (1.61-3.78)
Sickle cell disease					2 (0.01)	200.0 (50.0-799.9) †
< 12 seizure per year	32 (8.31)	3.85 (2.72-5.45) †	11 (4.48)	2.45 (1.36-4.43)	49 (12.07)	4.06 (3.07-5.37)
> 12 seizure per year	10 (4.84)	2.06 (1.11-3.84)	16 (2.94)	5.45 (3.34-8.89)	20 (3.34)	5.99 (3.87-9.29)
Seizure type-Generalized	26 (7.57)	3.43 (2.34-5.04)	19 (4.62)	4.11 (2.62-6.44)	27 (6.21)	4.35 (2.98-6.34)
Seizure type-Focal	20 (6.38)	3.14 (2.02-4.86)	14 (2.42)	5.78 (3.42-9.75)	76 (10.50)	7.24 (5.78-9.06) †
Seizure type-Others					6 (0.56)	10.63 (4.78-23.66)
Untreated with AED	12 (4.28)	2.81 (1.59-4.94)	19 (5.65)	3.36 (2.15-5.27)	57 (9.07)	6.29 (4.85-8.15)
No of different type of seizure-1	38 (11.76)	3.23 (2.35-4.44)	35 (8.01)	4.37 (3.14-6.09)	88 (14.99)	5.87 (4.76-7.23)
No of different type of seizure-2					1 (0.05)	19.53 (2.75-138.65)
No of different type of seizure-3	5 (2.16)	2.31 (0.96-5.56)	8 (0.93)	8.58 (4.29-17.15) †	20 (2.39)	8.38 (5.41-12.99) †
Seizure frequency-Daily	3 (1.06)	2.84 (0.92-8.81)	11 (0.87)	12.61 (6.98-22.77) †	23 (1.09)	21.05 (13.9-31.67) †
Seizure frequency-Monthly	27 (7.44)	3.63 (2.49-5.29) †	28 (6.23)	4.49 (3.10-6.51)	34 (6.14)	5.54 (3.96-7.75)
Seizure frequency-Weekly	2 (0.87)	2.31 (0.58-9.23)	1 (0.48)	2.08 (0.29-14.73)	19 (1.21)	15.69 (10.0-24.5) †
Seizure time-Day & Night	29 (8.38)	3.46 (2.41-4.98)	35 (6.66)	5.25 (3.77-7.32)	82 (10.50)	7.81 (6.29-9.70) †
Seizure time-Day	12 (3.68)	3.26 (1.85-5.74)	1 (0.48)	2.09 (0.29-14.82)	23 (5.16)	4.46 (2.96-6.71)

Seizure time-Night	5 (2.12)	2.36 (0.98-5.66)	6 (1.94)	3.09 (1.39-6.87)	4 (1.82)	2.20 (0.82-5.85)
Imaging						
EEG general background						
Mild	11 (4.13)	2.66 (1.47-4.81)	6 (0.99)	6.06 (2.72-13.49)	16 (1.81)	8.82 (5.40-14.40) †
Moderate	1 (0.23)	4.33 (0.61-30.70)	3 (0.36)	8.26 (2.66-25.62)	2 (0.53)	3.77 (0.94-15.09)
Normal	20 (7.33)	2.73 (1.76-4.23)	11 (3.31)	3.33 (1.84-6.01)	36 (9.52)	3.78 (2.73-5.24)
Severe	5 (0.30)	16.76 (6.97-40.26) †	1 (0.07)	14.37 (2.02-102.04)	12 (0.57)	21.21 (12.0-37.3) †
EEG Asymmetry	3 (0.76)	3.94 (1.27-12.21)	1 (0.05)	19.37 (2.73-137.53)	1 (0.07)	13.80 (1.94-97.98)
EEG Focal feature	23 (6.88)	3.35 (2.22-5.03)	6 (1.74)	3.44 (1.55-7.66)	19 (2.70)	7.04 (4.49-11.04)
EEG epileptiform activity	13 (2.40)	5.41 (3.14-9.32) †	4 (1.23)	3.26 (1.22-8.68)	19 (2.90)	6.55 (4.18-10.26)
EEG Focal temporal	11 (2.20)	5.00 (2.77-9.03) †	4 (0.93)	4.31 (1.62-11.47)	19 (2.37)	8.03 (5.12-12.58) †
EEG Focal extra temporal	9 (1.71)	5.26 (2.74-10.11) †	3 (0.94)	3.21 (1.03-9.94)	12 (2.13)	5.63 (3.20-9.91)
EEG involve Temporal lobe	5 (0.60)	8.39 (3.49-20.15) †	2 (0.48)	4.17 (1.04-16.66)	11 (1.02)	10.79 (5.98-19.49) †
EEG Generalized	1 (0.03)	38.84 (5.47-275.7) †	0 (0.20)		5 (0.51)	9.89 (4.11-23.75)
EEG photosensitivity: abnormal	1 (0.48)	2.10 (0.30-14.93)	4 (0.13)	31.67 (11.88-84.37)	2 (0.15)	13.08 (3.27-52.28)
EEG hyperventilation: abnormal	3 (1.09)	2.74 (0.88-8.50)	1 (0.29)	3.48 (0.49-24.68)		
EEG Summary-Abnormal	21 (5.13)	4.10 (2.67-6.28) †	12 (2.70)	4.45 (2.52-7.83)	41 (5.92)	6.93 (5.10-9.40)
EEG Summary-Normal	8 (3.73)	2.14 (1.07-4.28)	8 (2.00)	4.00 (2.00-7.99)	26 (6.48)	4.01 (2.73-5.89)
EEG Summary-Undetermined	7 (3.17)	2.21 (1.05-4.63)				
Clinical features and examination						
Falls to ground during seizure	41 (11.55)	3.55 (2.61-4.82) †	34 (7.44)	4.57 (3.26-6.39)	91 (15.37)	5.92 (4.82-7.27)
Seizure duration-10 min+	2 (0.73)	2.74 (0.69-10.98)	8 (1.20)	6.68 (3.34-13.36)	47 (6.31)	7.45 (5.60-9.91) †
Seizure duration-5-9 minutes	4 (1.35)	2.97 (1.11-7.91)	18 (4.47)	4.03 (2.54-6.39)	27 (6.48)	4.17 (2.86-6.08)
Seizure duration-< 5 minutes	40 (11.21)	3.57 (2.62-4.87) †	12 (1.75)	6.87 (3.90-12.09) †	30 (4.21)	7.13 (4.99-10.20)
No BCG vaccine scar	9 (2.20)	4.10 (2.13-7.87)	3 (1.14)	2.63 (0.85-8.15)	34 (10.37)	3.28 (2.34-4.59)
Burn marks	12 (3.06)	3.93 (2.23-6.91)	7 (1.33)	5.25 (2.50-11.01)	29 (3.53)	8.21 (5.71-11.82) †
Systolic blood pressure: > 140	15 (4.17)	3.60 (2.17-5.97)	5 (1.30)	3.86 (1.61-9.28)	23 (5.53)	4.16 (2.76-6.26)
Diastolic blood pressure: > 90	14 (4.31)	3.25 (1.92-5.48)	4 (1.27)	3.15 (1.18-8.39)	17 (2.05)	8.29 (5.16-13.34) †
Pre-existing neurological	17 (4.80)	3.54 (2.20-5.70)	11 (1.01)	10.94 (6.06-19.75) †	31 (2.02)	15.35 (10.80-21.8) †
Cognitive impairment	17 (3.93)	4.32 (2.69-6.96) †	9 (0.92)	9.80 (5.10-18.84) †	44 (1.80)	24.38 (18.14-32.7) †
Motor impairment	6 (2.30)	2.61 (1.17-5.81)	5 (0.20)	24.76 (10.31-59.4) †	40 (2.13)	18.77 (13.77-25.5) †

Previous status epilepticus			3 (0.21)	14.48 (4.67-44.90) †	34 (2.97)	11.44 (8.17-16.0) †
Febrile seizure					24 (1.88)	12.78 (8.56-19.0) †
History of encephalopathy			1 (0.05)	20.02 (2.82-142.09)	22 (1.69)	13.05 (8.59-19.8) †
History of febrile seizure	4 (0.27)	14.95 (5.61-39.83) †	8 (1.33)	6.00 (3.00-11.99)	26 (2.22)	11.73 (7.99-17.23) †

† Statistically significant different from the overall site estimate (Based on non-overlapping confidence intervals)

Obs: Observed, exp: expected, SMR: Standardized mortality ratio, AED: Antiepileptic drugs, CI: Confidence Interval