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Standard of Care for People with Epilepsy in Sub-Saharan Africa: the Case of Nigeria

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Declaration of Authorship

"I, Musa Mamman WATILA hereby declare that I am aware of and understand the University's policy on plagiarism and I certify that this thesis is my own work, except where indicated by referencing. The work presented here has not been submitted for another degree or qualification. Any collaborative contributions have been duly acknowledged."

Signed: ……..

Dedication

To all those in the poor regions of the world who suffer and are neglected because of epilepsy

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Abstract

Epilepsy in low- and middle-income countries (LMICs) present unique challenges, as the burden is high and the majority of sufferers are not receiving even basic epilepsy care. This work aimed to determine the prevalence, incidence, treatment gap, determinants of access to care and potential risk factors for epilepsy in three Nigerian rural districts of Afikpo, Ijebu-Jesa and Gwandu. A population-based door-to-door screening was undertaken to identify people with epilepsy. This was preceded by a validation study of a screening questionnaire translated into three Nigerian languages. Of the 42,427 persons (six years and above) screened, 254 persons were confirmed to have active epilepsy. The overall age-standardised prevalence was 9.8/1,000 (95% CI: 8.6, 11.1). The prevalence varied between sites; 17.7 (95% CI: 14.2, 20.6) in Gwandu, 4.8 (95% CI: 3.4, 6.6) in Afikpo and 3.3 (95% CI: 2.0, 5.1) in Ijebu Jesa. The overall estimated 1-year age-standardized retrospective incidence was 101.3/100,000 (95% CI: 57.9, 167.6), higher in Gwandu compared to Afikpo and Ijebu-Jesa. The overall peak age-specific prevalence was 10–14 years, while the median age of seizure onset was 6 (IQR: 4–10) years. Epilepsy was of focal onset in 45.2% of the subjects. The treatment gap was 94.4% (95% CI: 90.9, 96.9). Cultural beliefs and stigma are the most important factors associated with the failure to seek medical care. Febrile seizures, poor perinatal care, family history, measles and meningitis are the main contributory factors associated with epilepsy in children and adults, while head injury and consanguinity were peculiar to adults. Physicians interviewed reported significant deficits in manpower, training, available facilities and antiseizure medications. In conclusion, this study hopes to contribute to the understanding and eradication of epilepsy in Nigeria. The varied estimates and potential risk factors observed require larger prospective cohort studies. Strengthening the primary health care and community education would improve the current treatment gap.

Impact Statement

Epilepsy is a major neurological condition that manifests with unpredictable seizures often associated with unpleasant psychosocial and economic experiences. The consequences are not limited to the sufferer, but it is rather a societal issue mostly misunderstood worldwide. This is despite current advances in epilepsy care. These difficulties with understanding and managing epilepsy are far worse in traditional African settings.

This piece of work focused on obtaining knowledge about epilepsy and the care standards in three rural areas of Nigeria. The data from this work constitutes a critical study in the understanding of epilepsy in Africa and has proved invaluable at this time. Part of the project translated and validated an epilepsy-screening questionnaire in three Nigerian languages. These screening instruments were used to conduct a community-based epidemiological study in three communities showing that with the appropriate motivation, it is possible to conduct research in a multicultural and multi-ethnic setting. The findings show that the incidence and prevalence of epilepsy vary considerably between regions, with Northwest Nigeria having the largest burden. Shared environmental, socioeconomic and possibly genetic factors appear to play a complex role in the aetiology. The findings show that more than 90% of people with epilepsy identified were not receiving appropriate treatment and this was influenced by negative cultural and belief systems. Apart from sociocultural issues, physicians involved in care reported that deficiencies in work force, training and facilities also limited the poor standard of care. They noted that traditional- and faith-based healers could negatively affect access to biomedical care. The evidence of poor epilepsy care and the attributing factors necessitated this work to propose modalities on how people with epilepsy can receive standard epilepsy care.

One important element from this project is the way it fostered communication between various disciplines including neurologist, linguists, social scientists, demographers,

statisticians, health workers and even lay people in the communities. It also engaged collaborations of researchers from several countries that contributed to the quality of the work. The training of health workers for the fieldwork served as a means of transferring skills on methodological and educational advances in epilepsy research. This research has generated a considerable number of questions that are potential research projects for other scientists. The improved information on epilepsy should help the government and stakeholders develop policies for better quality care. The dissemination of these findings could lead to a change in culture and practices and help towards evidence-based policy-making and influence legislation. This is relevant as the societal impact of a seizure-free life could mean that the sufferer, the family and the society are free from economic hardship that could contribute towards wealth creation and economic prosperity and better quality of life.

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List of Abbreviations

APN	Association of Psychiatrists in Nigeria
ASM	Antiseizure Medication
CI	Confidence Interval
CoD	Cause of Death
DALY	Disability Adjusted Life Years
EEG	Electroencephalogram
FETHA	Federal Teaching Hospital Abakaliki
GBD	Global Burden of Disease
HDSS	Health and Demographic Surveillance Site
HIC	High-income Countries
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
IBE	International Bureau for Epilepsy
ILAE	International League Against Epilepsy
KAWE	Kenya Association for the Welfare of People with Epilepsy
LGA	Local Government Area
LMIC	Low- and Middle-income Countries
mhGAP	Mental Health Gap Action Programme
MICE	Multiple Imputations by Chained Equation
NGO	Non-Governmental Organisation
NHIS	National Health Insurance Scheme
NHREC	National Health and Research Ethics Committee
NSNS	Nigerian Society of Neurological Sciences
OAUTHC	Obafemi Awolowo University Teaching Hospital Complex
OR	Odds Ratio
PAF	Population Attributable Fraction
PHC	Primary Health Care
QoL	Quality of Life
SE	Status Epilepticus
SES	Socioeconomic Status

SMR	Standardized Mortality Ratio
SSA	Sub-Saharan Africa
UDUTH	Usman Dan-Fodio University Teaching Hospital
WHO	World Health Organisation
YLD	Years Lost to Disability

List of publications and abstracts from this thesis

1. Watila MM, Keezer MR, Angwafor SA, Winkler AS & Sander JW. (2017) Health service provision for people with epilepsy in sub-Saharan Africa: A situational review. *Epilepsy Behav*; *7:* 24-32. https://doi.org/10.1016/j.yebeh.2017.03.014

2. Watila MM, Balarabe SA, Ojo O, Keezer MR, Sander JW. (2018) Overall and cause-specific premature mortality in epilepsy: A systematic review. *Epilepsy Behav;* 87: 213-25. https://doi.org/10.1016/j.yebeh.2018.07.017

3. Watila MM, Xiao F, Keezer MR, Miserocchi A, Winkler AS, McEvoy AW, Sander JW. (2019) Epilepsy surgery in low- and middle-income countries: A scoping review. *Epilepsy Behav;* 92: 311–26. https://doi.org/10.1016/j.yebeh.2018.07.017

4. Watila MM, Otte W, Van Diessen E, Joseph M, Balarabe S, Igwe S, Fawale M, Mshelia A, Komolafe M, Nyandaiti YW, Singh G, Sander JW. Prevalence and incidence of epilepsy in three regions of Nigeria: a cross-sectional door-to-door survey.
   Presented on a platform session at the 33rd International Epilepsy Congress, Bangkok, Thailand. Sunday 23rd June 2019

5. Watila MM, Joseph M, Otte W, Balarabe S, Igwe S, Fawale M, Singh G, Sander JW. Epilepsy treatment gap and determinants of access to care in Nigeria.
   A poster presentation at the 4th African Epilepsy Congress, Entebbe, Uganda. Thursday 22nd August 2019

Chapter 1: Introduction

1.1 Introduction

Epilepsy is a brain condition characterised by a tendency to produce recurrent unprovoked seizures, associated with psychosocial, cognitive, and economic consequences affecting all ages, races and social classes (Fisher et al., 2014). Due to its dramatic and unpredictable nature, it is still as yet a neglected, misunderstood and highly stigmatizing condition in the low- and middle-income countries (LMICs) (De Boer et al., 2008). Evidence from the Global Burden Disease (GBD) studies suggests that it contributes substantially to the global disability-adjusted life years (DALY) and the years lost to disability (YLD), with LMICs carrying the largest burden (Lozano et al., 2013, Vos et al., 2013). Epilepsy in Nigeria as in most parts of sub-Saharan Africa (SSA) has only been superficially researched. Many of the community-based studies on prevalence, risk factors, treatment gap are few and concentrated in the Southwest region of Nigeria. These studies limited by small sample size, have indicated that the prevalence of epilepsy varies between 4.3 and 37.0 per 1,000 (Osuntokun et al., 1982, Osuntokun et al., 1987a, Osuntokun et al., 1987b, Longe & Osuntokun, 1989, Mustapha et al., 2014, Osakwe et al., 2014, Mustapha & Preux, 2015, Nwani et al., 2015, Ezeala-Adikaibe et al., 2016). The treatment gap is also reported to be high and influenced mainly by sociocultural factors and belief systems (Osuntokun et al., 1987a, Nwani et al., 2013, Eseigbe et al., 2014). With very little information, more data is needed in Nigeria. My work aims to evaluate the standard of care for people with epilepsy. It determined the prevalence, treatment gap and determinants of access to care in three rural districts of Nigeria. In addition to the potential risk factors for epilepsy in these regions.

1.2 Motivation

In the last decades epilepsy in LMICs particularly SSA has drawn a lot of attention through the demonstration projects organized by the World Health Organisation (WHO), with the support of the International League Against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE) in a number of countries in different regions (Reynolds, 2001). These demonstration projects have offered models on how research can help identify needs, help diagnose and treat people with epilepsy and promote public education. Such programmes together with other studies have revealed the complex nature of epilepsy in LMICs, requiring concerted efforts to combat the enormity of this problem from all stakeholders. Relatively little is known however about the basic epidemiology and health care for people with epilepsy in some SSA countries such as Nigeria. The present work has therefore undertaken the objective of filling this knowledge gap in a resource-poor setting.

1.3 Problem statement

The research question this work seeks to answer is as follows:

"What is the standard of care for people with epilepsy in SSA and Nigeria in particular?"

To address this question, a community-based study is necessary to ascertain the burden of epilepsy with data on prevalence, incidence, risk factors, treatment gap and health service provision in Nigeria.

1.4 Aims

This project assessed the standard of care of people with epilepsy in Nigeria, by determining the prevalence, treatment gap and determinants of access to care in three rural districts of Nigeria.

1.5 Hypotheses

- The prevalence of epilepsy is higher in Nigeria than in the rest of the world.
- The epilepsy treatment gap in Nigeria will be above 70%.

- The differences in access to care can be explained by demographic and socio-cultural differences.

1.6 Research approach and Objectives

A community-based rural approach was undertaken. A framework was developed and implemented considering relevant steps of a rural door-to-door survey.

Primary Objective:

Determine the overall and age-specific epilepsy prevalence and incidence and the magnitude of the 'treatment gap' in these three rural communities in Nigeria.

Secondary objectives:

1. To assess the performance of a modified and translated epilepsy-screening questionnaire from English into the Hausa, Yoruba and Igbo speaking population in a validation study.
2. To identify factors associated with the epilepsy treatment gap in Nigeria.
3. To evaluate relevant factors determining access to care and adherence among rural populations.
4. To assess risk factors associated with epilepsy in the Nigerian population.
5. To investigate physicians and other health care professional perspectives on health care services.

1.7 Thesis Outline

An overview of the chapters constituting this thesis is presented below:

Chapter 2: Literature review

The main objective of this chapter is to introduce an understanding of the burden of epilepsy globally and regionally. This includes prevalence, incidence, risk factors and premature mortality. It highlights the health service provision for people with epilepsy in SSA and Nigeria. An additional review detailing epilepsy surgery in LMIC is described. To achieve this, careful reviews of the literature were undertaken.

Chapter 3: Methodology

This chapter introduces and justifies the proposed methodology. It explains the geographical regions where the study was conducted and briefly explains the methodological approach of the door-to-door survey. Ethical issues are also discussed. Further details of the methodology and analytical approaches are outlined in each chapter.

Chapter 4: The epilepsy-screening questionnaire and validation study

This section focuses on the development of a valid screening instrument used in the door-to-door survey. It explains in detail how the 9-item epilepsy-screening questionnaire was developed, translated and piloted. In order to produce a validated tool in the three Nigerian languages relevant to this study.

Chapter 5: Cross-sectional community-based surveys, prevalence and incidence of epilepsy

Complete detail of how a screening census was conducted is presented in this chapter. It describes in detail the stages of how people with epilepsy were screened to produce the primary data for each of the three rural sites. Step-by-step data acquisition and analysis to produce an age-standardised prevalence and a retrospective 1-year incidence are described.

Chapter 6: Socio-demographic and clinical characteristics of active epilepsy cases

This section describes in detail the characteristics of the subjects with active epilepsy that were screened and confirmed in the prior chapter.

Chapter 7: The epilepsy treatment gap and determinants of access to care in Nigeria

A determination of the epilepsy treatment gap and factors that determine access to care and adherence was undertaken in this section. It describes how the most

significant factors that produce and influence the treatment gap in Nigeria were detected, analysed and discussed.

Chapter 8: A case-control study for potential risk factors of epilepsy in Nigeria

This chapter examines and discusses potential risk factors for epilepsy using a case-control format. The statistical approaches for calculating odds ratios (ORs) and population attributable fractions (PAFs) are substantiated.

Chapter 9: Physician's perspective about epilepsy care in Nigeria

This chapter provides insight into what treatment options are available to the physicians and the challenges and suggestions for improving care are also discussed.

Chapter 10: Conclusions, Limitations and Future Work

This concluding section summarises the methodological steps and results to produce a general overview. It outlines the main contributions of the work and explores some of its limitations. The many questions generated, and the pertinence of this study to answer them are identified and future work can be based on this study.

Chapter 2: Literature Review

2.0 The epidemiology of epilepsy on a global scale

The recent global burden of disease (GBD) study reported that despite some improvement over the last three decades, epilepsy still accounted substantially to the global DALY and YLD, with the LMICs having a higher measure of the disease burden (Beghi et al., 2019). A worldwide meta-analysis of the prevalence and incidence of epilepsy reported an overall point prevalence for active epilepsy of 6.4/1,000, lifetime prevalence of 7.6/1,000, an annual cumulative incidence of 67.8/100,000 and an incidence rate of 61.4/100,000 person-years (Fiest et al., 2017). This report suggested considerable heterogeneity between its component studies, with higher figures coming from LMICs. The point prevalence of active epilepsy from the high-income countries (HIC) was 5.5/1,000 (95% CI: 4.2, 7.3) compared to 6.7/1,000 (95% CI: 5.5, 8.2) from LMIC, while the lifetime prevalence was 5.2/1,000 (95% CI: 3.8, 7.2) from HIC compared to 8.8/1,000 (95% CI: 7.2, 10.6) from LMIC (Fiest et al., 2017). These estimates for HICs have not changed much from a previous systematic review of epidemiological studies from Europe (Forsgren et al., 2005a), showing a prevalence ranging from 3.3 to 7.8/1,000 (median 5.2) and incidence ranging from 24 to 82/100,000. Recent evidence shows no significant changes in age-standardised incidence rates over the years. The incidence rate in 1990 was 35·8/100 000 person-years (95% CI: 30·1, 42·0), while in 2016 it was 38·0/100 000 person-years (95% CI: 31·7, 45·1) for people with idiopathic epilepsy (Beghi et al., 2019). The incidence and age-specific prevalence of epilepsy generally have two peaks, in the youngest and oldest age groups (Fiest et al., 2017).

The risk factors for epilepsy vary with age and geographical location. Genetic and environmental (including infections) factors appear to be important in children; while cerebrovascular disease and brain tumours have a bigger role in the elderly (Sander, 2003, Duncan et al., 2006). Cerebrovascular disease is now an important cause of

epilepsy in the HICs shifting the peak incidence towards the elderly (Everitt & Sander, 1998, Stephen & Brodie, 2000).

Epilepsy is significantly more prevalent in people with HIV/AIDS compared to the general population (Leading Edge, 2007). Opportunistic infections, treatment, metabolic abnormalities, and the direct effect of the virus all predispose to seizures (Satishchandra & Sinha, 2008, Hogan & Wilkins, 2011). A German study reported seizures in 6.1% of the 831 treated for HIV infection. Of which 67% developed epilepsy in the course of their infection, while only 0.36% had epilepsy before the onset of the HIV infection (Kellinghaus et al., 2008). In a South Korean study comprising 1,141 people with HIV, 3% had seizures or epilepsy, while only four persons had epilepsy before HIV infection (Kim et al., 2015). A Spanish study reported that 3% had a new-onset seizure during the study period (Pascual-Sedano et al., 1999). Better treatment even in LMICs has resulted in reduced opportunistic infections and may lead to decrease the risk of epilepsy (Gray et al., 2003).

The treatment gap of epilepsy, defined as “the percentage difference between the number of people with active epilepsy and the number whose seizures are being appropriately treated in a given population at a given point of time” (Meinardi et al., 2001), varies widely between countries. The treatment gap is less than 10% in HIC to more than 75% in poor regions of the world, significantly higher in rural areas (Meyer et al., 2010). The level of health care development and access to proper care remain the most important determinants of the epilepsy treatment gap (Meyer et al., 2012).

2.1 Epidemiology of epilepsy in sub-Saharan Africa

Since the pioneering work on epilepsy by Jilek and Al-Jilek among the Wapogoro tribe of the Mahenge people of Tanzania in the 1950s and 60s and other earlier observations through Christian missions, the burden of epilepsy from these observations is likely to be significantly higher among certain groups in Africa (Aall-Jilek, 1965, Jilek & Jilek-Aall, 1970). Over the years there have been several studies looking at the burden of epilepsy, albeit insufficient. These studies have suggested that

the incidence and prevalence of epilepsy in sub-Saharan Africa are higher and widely varied. The incidence is reported to be between 18.6 and 320/100.000 (Rwiza et al., 1992, Debouverie et al., 1993, Tekle-Haimanot et al., 1997, Kaiser et al., 1998a, Mung'ala-Odera et al., 2008, Winkler et al., 2009b, Ngugi et al., 2013b, Houinato et al., 2013, Wagner et al., 2015a, Kaddumukasa et al., 2016), and the lifetime prevalence between 4.5 and 49/1,000 (Fiest et al., 2017). The higher incidence and prevalence of epilepsy in sub-Saharan Africa is presumed to be due to poor socioeconomic status (SES), high prevalence of infections especially neurocysticercosis, cerebral malaria and meningitis (Dumas et al., 1989, Avode et al., 1998, Nsengiyumva et al., 2003, Carter et al., 2004, Veary & Manoto, 2008, Idro et al., 2008, Winkler et al., 2008, Winkler et al., 2009a, Snead et al., 2009, Ocana et al., 2009, Burton et al., 2012, Millogo et al., 2012, Mazigo et al., 2013, Mwape et al., 2015), febrile convulsions (Rwiza et al., 1992, Matuja et al., 2001, Dent et al., 2005), and poor obstetric practices (Senanayake & Roman, 1993, Newton & Garcia, 2012, Osakwe et al., 2014).

The extent to which an aetiology can be determined depends on the available diagnostic facilities, which vary across countries and healthcare facilities (Sander, 2003, Duncan et al., 2006). The majority of people with epilepsy in sub-Saharan Africa receive inadequate or no treatment. This treatment gap is worse and varies between 23% and 100% (Ndoye et al., 2005, Edwards et al., 2008, Simms et al., 2008, Koffi et al., 2009, Guinhouya et al., 2010, Amos & Wapling, 2011b, Ratsimbazafy et al., 2011, Mbuba et al., 2012b, Bora et al., 2015, Sebera et al., 2015, Hunter et al., 2016, Sokhi et al., 2016), with the diagnostic gap appearing to be worse (Meinardi et al., 2001). The most important factors for the high treatment gap are current cultural beliefs, poor health infrastructure, distance to health facilities, supply and cost of ASMs and lack of prioritization by the local administration and government (Meinardi et al., 2001).

Comparing these figures across Africa is challenging, however, data coming from Africa over the last two decades has greatly improved due to the positive intervention and collaborations with international organisations and institutions from Europe and

America, initiatives by ILAE/IBE and WHO global campaign against epilepsy and the efforts made by the Institute of Tropical Neurology Limoges (Reynolds, 2001, Preux, 2002, Ndoye et al., 2005, Preux & Druet-Cabanac, 2005, Ngugi et al., 2013a).

2.2 Epidemiology of epilepsy in Nigeria

2.2.1 Prevalence and Incidence

The number of people with epilepsy in Nigeria is unknown. The few community-based studies from rural and suburban communities of southern Nigeria (there are no community-based studies from northern Nigeria) are shown in Table 1. Using a conservative estimate of 5/1,000, and a population of 180 million (2015 estimate http://data.worldbank.org/indicator), Nigeria may have approximately a million people with epilepsy. The small sample size, differing methodologies, instruments, divergent definitions of epilepsy may be recognised as some of the reasons for the wide variation in prevalence (Thurman et al., 2011). The studies from Aiyete (Southwest Nigeria) (Osuntokun et al., 1982) and Ochiohu (Southeast Nigeria) (Osakwe et al., 2014) have a higher prevalence compared to other parts of Nigeria; the reasons are not fully understood. Temporal and spatial clustering due to hereditary forms of epilepsy or shared environmental and infectious aetiologies may be the reason (Goudsmit et al., 1983, Van der Waals et al., 1983). In Nigeria and other parts of Africa, it has been observed that people with similar diseases or disabilities appear to cluster more in one community, probably due to a form of socio-cultural exclusion or due to ease of access to forms of diagnosis and treatments (Komolafe et al., 2012).

Regrettably, there are no studies on the incidence of epilepsy in Nigeria. Incidence studies give more information on the rates of new cases irrespective of the prognosis or aetiology, but are logistically more difficult and resource intense, and require a longer period (Thurman et al., 2011).

Table 1: Prevalence studies of epilepsy in Nigeria

Community	Author-date	Number screened	Prevalence per 1,000 (95% CI)	By gender
Aiyete [a]	(Osuntokun et al., 1982)	903	37.0	M: 28 F: 44
Igbo-Ora[#]	(Osuntokun et al., 1987a, Osuntokun et al., 1987b)	18,954	5.3	M: 5.1 F: 5.6
Udo	(Longe & Osuntokun, 1989)	2925	6.2	-
Ochiohu	(Osakwe et al., 2014)	2500	20.8 (15.7, 27.4)	-
Ogobia[#]	(Osakwe et al., 2014)	6000	4.7 (3.2, 6.9)	-
Ilie	(Mustapha et al., 2014)	2212	4.5 (2.30, 8.04)	-
Ukpo[#]	(Nwani et al., 2015)	6800	4.3 (2.7, 5.9)	M: 4.9 (2.5-7.3) F: 3.7 (1.7-5.7)
Agu-Abor and Ugbodogwu[§]	(Ezeala-Adikaibe et al., 2016)	8228	6.0 (5.9, 6.0)	M: 4.4 (2.3–6.4) F:7.8 (4.9–10.4)

All studies were door-to-door involving all age groups, [a] Pilot study, [#]Sub-urban, [§]Urban

2.2.2 Risk factors for epilepsy

The only two case-control studies on risk factors of epilepsy in Nigeria (Ogunniyi et al., 1987, Ogunrin et al., 2014), reported that poor obstetric practices, febrile convulsions, infections, family history, and head injuries were most important. Neurocysticercosis may be an important aetiology for epilepsy in Nigeria, but it has not been well studied (Dozie et al., 2004, Kanu et al., 2005, Dozie et al., 2006, da Costa et al., 2013, Ogunrin et al., 2014, Osakwe et al., 2014). Malaria and filariasis are also reported to be associated with epilepsy (Adamolekun et al., 1993, Kanu et al., 2005).

2.2.3 Treatment Gap

Nigeria has a treatment gap ranging between 76 and 100% from three studies (Osuntokun et al., 1987a, Nwani et al., 2013, Eseigbe et al., 2014). The high treatment

gap is mainly due to a currently dysfunctional health care system, cultural perception and the high cost of treatment.

2.3 Overall and cause-specific premature mortality in epilepsy

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This section gives a summary of a systematic review conducted to ascertain the overall mortality and causes of premature mortality in epilepsy from HICs and LMICs.

It is important to understand that an epilepsy diagnosis has the potential to impact negatively on survival with an increased risk of premature mortality compared to the general population (Forsgren et al., 2005b, Neligan et al., 2010, Nevalainen et al., 2014). Approximately 1,000 epilepsy-related deaths are reported in the UK each year (Hanna et al., 2002), with an estimated 180,000 dying annually worldwide (Lozano et al., 2013). The reasons for the increased risk of early death are not fully understood but may be accounted for by a complex inter-relationship between epilepsy aetiology, age, gender, geographical location and antiseizure medication (ASM) (Gaitatzis et al., 2004, Gaitatzis et al., 2012, Keezer et al., 2016). Uncontrolled seizures are suggested to initiate pathophysiological processes such as inflammation, glycation and oxidative stress, causing detrimental effects that lead to accelerated ageing and premature mortality (Yuen et al., 2007). This evidence is inconclusive, as those in remission continue to have a higher likelihood of dying than the general population, although the risk of early death is more likely among those with refractory epilepsy (Laxer et al., 2014).

A Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) standard for the search, extraction, synthesis and reporting was used (Moher et al., 2009). Pubmed and Embase were searched using Medline medical subject headings (MeSH) where appropriate and keyword terms to maximize the sensitivity of the search. The word "epilepsy" was combined with terms such as "mortality", "premature

mortality'', ''death'', “fatality”, “all-cause mortality”, “cause”, “cause-specific” and the various study types. Titles and abstracts were initially assessed from the search results to select potential articles. The articles were then read in full and screened for eligibility. Original prospective or retrospective (historic) cohort studies were included if they reported measures of overall or cause-specific mortality particularly standardized mortality ratio (SMR). A quality appraisal was done using the Newcastle-Ottawa Scale (Wells et al., 2014) and the ILAE’s standards for epidemiology research (Thurman et al., 2011). A test for publication bias was estimated using a funnel plot (Higgin et al., 2003).

Table 2, 3 and 4 illustrate studies reporting overall premature mortality for epilepsy. The results showed that the majority of studies are from HICs, with a skewed funnel diagram suggesting publication bias. The quality assessment showed that most of the older studies and those from LMICs were of poorer quality. These studies from LMICs were derived from community-based door-to-door surveys that recruited mainly active convulsive epilepsies and had a large loss to follow-ups. The overall SMR for population-based studies had a wide variability ranging between 0.76 (0.51, 1.01) to 22.40 (18.90, 26.20). Despite the wide variability, the overall SMR in the majority of the studies ranged between 2.0 to 4.0. The overall SMR for hospital-based studies ranged from 1.40 (1.10, 1.70) to 9.70 (5.70, 15.30). It showed an overall pooled SMR for LMIC as 3.71 (3.66, 3.76) which is higher than for HIC at 2.27 (2.24, 2.31).

Table 2: Overall SMR for population- or community-based studies

Country	Study	Cohort selection	Overall SMR (95% CI)	Male (95% CI)	Female (95% CI)
USA (Rochester) [a]	(Hauser et al., 1980)	Historic incident	2.30 (1.90, 2.60)	2.10 (1.50, 2.80)	1.60 (1.10, 2.20)
USA (Rochester)	(Annegers et al., 1984)	Historic incident	2.10 (1.90, 2.50)		
UK (NGPSE)[b]	(Cockerell et al., 1994)	Incident	3.00 (2.50, 3.70)		
Iceland (Epilepsy study)	(Olafsson et al., 1998)	Historic incident	1.60 (1.20, 2.20)		
France (Gironde)[c]	(Loiseau et al., 1999)	Incident	4.10 (2.50, 6.20)		
Sweden	(Lindsten et al., 2000)	Incident	2.50 (1.20, 3.20)	2.70 (1.80, 3.90)	2.30 (1.40, 3.70)
Iceland (Epilepsy study)	(Rafnsson et al., 2001)	Historic incident	1.60 (1.00, 2.30)	2.30 (1.60, 3.10)	0.80 (0.40, 1.50)
UK (NGPSE) [b]	(Lhatoo et al., 2001)	Incident	2.60 (2.10, 3.00)		
Canada (Nova Scotia)	(Camfield et al., 2002)	Incident	5.30 (2.29, 8.32)		
UK (Cardiff and Glamorgan)	(Morgan & Kerr, 2002)	Incident/ Prevalent	2.14 (1.70, 2.50)	2.26 (1.67, 2.85)	2.03 (1.48, 2.58)
USA (Connecticut Study)	(Berg et al., 2004)	Incident	7.54 (4.38, 12.99)		
India (Parsis) [d]	(Carpio et al., 2005)	Prevalent	0.76 (0.51, 1.01)	0.73 (0.52, 1.20)	0.81 (0.29, 1.10)
India (Vasai) [d]	(Carpio et al., 2005)	Prevalent	3.90		
Argentina, (Junin)	(Kochen & Melcon, 2005)	Prevalent	2.45		
USA (California)	(Day et al., 2005)	Historic incident	2.10 (1.90, 2.30)		
China (EMPHL) [e]	(Ding et al., 2006)	Incident/ Prevalent	3.90 (3.80, 3.90)	3.50 (3.40, 3.60)	4.10 (3.90, 4.40)
Uganda	(Kaiser et al., 2007)	Prevalent	7.20 (4.40, 11.60)	8.40 (4.20, 16.70)	6.30 (3.10, 12.10)
Bolivia	(Nicoletti et al., 2009)	Prevalent	1.34 (0.68, 2.39)		
USA (Northern Manhattan)	(Benn et al., 2009)	Incident	1.60 (1.10, 2.20)		
India (Kolkata)	(Banerjee et al., 2010)	Incident/ Prevalent	2.58 (1.50, 4.13)	3.67 (1.83, 6.57)	1.77 (0.65, 3.85)

Table 2: Overall SMR for population- or community-based studies

Country	Study	Cohort selection	Overall SMR (95% CI)	Male (95% CI)	Female (95% CI)
Finland (Turku)	(Sillanpaa & Shinnar, 2010)	Incident/ Prevalent	6.40 (5.90, 7.00)		
UK (GPRD) [f]	(Ackers et al., 2011)	Historic incident	22.40 (18.90, 26.20)	19.40 (15.50, 23.90)	27.10 (20.90, 34.50)
UK (NCDS) [g]	(Chin et al., 2011)	Historic incident	3.10 (1.10, 6.10)		
UK (NGPSE) [b]	(Neligan et al., 2011)	Incident	2.60 (2.20, 2.90)		
Estonia [h]	(Rakitin et al., 2011)	Incident	2.60 (1.80, 3.50)	2.30 (1.50, 3.30)	4.00 (1.90, 7.40)
		Prevalent	3.10 (2.50, 3.80)	3.30 (2.50, 4.20)	2.80 (2.00, 3.90)
China	(Mu et al., 2011)	Prevalent	4.90 (4.00, 6.10)		
USA (Rochester Epidemiology Project)	(Nickels et al., 2012)	Historic incident	9.04 (5.35, 14.37)		
China (EMPHL) [e]	(Ding et al., 2013)	Incident/ Prevalent	2.90 (2.60, 3.40)		
Kenya (KHDSS) [i]	(Ngugi et al., 2014)	Prevalent	6.50 (5.00, 8.30)		
USA (Ohio Medicaid)	(Kaiboriboon et al., 2014)	Open cohort analysis	1.80 (1.80, 1.90)		
South Africa (Agincourt) [j]	(Wagner et al., 2015a)	Prevalent	2.60 (1.70, 3.50)	2.60 (1.20, 5.40)	
UK (NGPSE) [b]	(Bell et al., 2016)	Incident	2.07 (1.83, 2.34)		

[a] Idiopathic epilepsy only; [b] NGPSE – National General Practice Study of Epilepsy UK, represents studies from same cohort with different follow-up periods; [c] Excludes those with provoked seizures (includes remote symptomatic + idiopathic + cryptogenic, [d] Retrieved four studies reporting SMR for mortality; [e] EMPHL – Epilepsy Management at Primary Health Level program China, represents the same cohort with different follow-up periods; [f] GPRD – General Practice Research Database this cohort consist of children with severe epilepsy, most had some underlying neurological disorder; [g] NCDS – National Child Development Study, a national birth cohort study; [h] Two cohorts of newly diagnosed (incident) and chronic (prevalent) epilepsy; [i] KHDSS – Kilifi Health and Demographic Surveillance System; [j] Agincourt Health and Socio-demographic Surveillance Site (HDSS)

Table 3: Overall SMR for hospital/institutional-based studies

Country	Study	Cohort selection	Overall SMR (95% CI)	Male (95% CI)	Female (95% CI)
Sweden	(Alstrom, 1949)	Clinical series	2.40 (2.00, 2.80)		
Denmark	(Henriksen et al., 1967)	Prevalent	2.70 (2.30, 3.20)		
Poland (Warsaw)	(Zielihski, 1974)	Prevalent	1.80	2.00	1.40
UK (Chalfont) [k]	(White et al., 1979)	Prevalent	3.00 (2.80, 3.30)	3.00	3.30
UK (Chalfont) [k]	(Klenerman et al., 1993)	Prevalent	1.90 (1.60, 2.30)		
UK (NHNN) [l]	(Nashef et al., 1995)	Historic incident	5.10 (3.30, 7.60)	4.40 (2.40, 7.50)	6.30 (3.20, 11.30)
UK (Chalfont) [k]	(O'Donoghue & Sander, 1997)	Incident	2.34 (2.12, 2.56)	2.37 (2.10, 2.65)	1.98 (1.66, 2.34)
Sweden	(Nilsson et al., 1997)	Incident/ Prevalent	3.60 (3.50, 3.70)	3.70 (3.60, 3.90)	3.40 (3.30, 3.60)
Netherlands (Heemstede)	(Shackleton et al., 1999)	Incident	3.20 (2.90, 3.50)	3.60 (3.10, 4.00)	2.60 (2.20, 3.00)
Netherlands (DSEC) [m]	(Callenbach et al., 2001)	Incident	7.00 (2.40, 11.50)	6.60 (2.20, 15.50)	7.40 (2.00, 19.00)
Chile	(Devilat Barros et al., 2004)	Incident	3.21 (1.48, 4.95)		
Ecuador [d]	(Carpio et al., 2005)	Incident	6.30 (2.00, 10.00)		
Martinique [d]	(Carpio et al., 2005)	Prevalent	4.25		
Taiwan	(Chen et al., 2005)	Incident	3.47 (2.46, 4.91)	5.07 (3.37, 7.63)	1.92 (1.00, 3.70)
UK (Glasgow) [h]	(Mohanraj et al., 2006)	Incident	1.42 (1.16, 1.72)		
		Prevalent	2.05 (1.84, 2.27)		
Netherlands (DSEC) [m]	(Geerts et al., 2010)	Incident	9.70 (5.70, 15.30)		
Taiwan	(Chang et al., 2012)	Prevalent	2.50 (2.20, 2.80)	2.60 (2.20, 3.00)	2.20 (1.70, 2.80)
Georgia	(Kobulashvili et al., 2013)	Prevalent	1.40 (1.10, 1.70		

Table 3: Overall SMR for hospital/institutional-based studies

Country	Study	Cohort selection	Overall SMR (95% CI)	Male (95% CI)	Female (95% CI)
Austria (Tyrol)	(Trinka et al., 2013)	Incident/ Prevalent	2.20 (2.00, 2.40)		
USA [n]	(Callaghan et al., 2014)	Prevalent	2.40 (1.70, 3.30)		
Austria (Tyrol)	(Granbichler et al., 2015)	Incident/ Prevalent	1.70 (1.60, 1.90)		
Hong Kong	(Chen et al., 2016)	Historic incident	5.09 (4.88, 5.31)		
Austria (Tyrol)	(Granbichler et al., 2017)	Incident/ Prevalent	2.20 (1.80, 2.60)	2.20 (1.70, 2.70)	2.30 (1.70, 3.00)
Spain	(Chamorro-Munoz et al., 2017)	Historic incident/ Prevalent	2.11 (1.79, 2.47)	2.13 (1.73, 2.59)	1.91 (1.45, 2.51)
NCP Study [o]	(Annegers et al., 1998)	Prevalent (VNS trial)	5.30 (3.00, 8.70)	4.20 (1.90, 8.00)	8.60 (3.20, 18.70)
NCP Study [o]	(Annegers et al., 1998)	Prevalent (VNS trial)	4.40 (0.90, 12.80)		
NCP Study [o]	(Annegers et al., 2000)	Prevalent (VNS trial)	3.60 (2.30, 5.40)	2.80 (1.50, 4.70)	5.80 (2.90, 10.40)

[d] Retrieved four studies reporting SMR for mortality; [h] Two cohorts of newly diagnosed (incident) and chronic (prevalent) epilepsy; [k] CCE- Chalfont Centre for Epilepsy; [l] NHNN – National Hospital for Neurology and Neurosurgery; [m] DSEC – Dutch Study of Epilepsy in Childhood; [n] A cohort of people with drug resistant epilepsy (DRE) from University of Pennsylvania Epilepsy Center and Columbia University Epilepsy Center; [o] A cohort of people with epilepsy receiving vagus nerve stimulation through the Neuro Cybernetic Prosthesis (NCP) System; VNS – Vagus nerve stimulation

Table 4: Overall mortality not reporting SMR

Country	Study	Cohort selection	Overall mortality [SMR (95% CI)]	Male (95% CI)	Female (95% CI)
Australia (Victoria)	(Harvey et al., 1993)[p]	Prevalent	13.20 (8.50, 20.70)		
Cameroon	(Kamgno et al., 2003)[q]	Prevalent	6.20 (2.70, 14.10)		
Finland	(Nevalainen et al., 2013)[r]	Incident	3.20 (3.10, 3.40)		
Sweden	(Fazel et al., 2013)[s]	Prevalent	11.10 (10.60, 11.60)		
Denmark	(Holst et al., 2013)[r]	Historic incident	11.90 (11.00, 12.90)		
Denmark	(Christensen et al., 2015)[p]	Historic incident	14.90 (13.90, 16.10)		
Denmark	(Olesen et al., 2011)[r]	Prevalent	1.92 (1.86, 1.97)		
Finland (Oulu)	(Nevalainen et al., 2012)[r]	Prevalent	2.66 (2.09, 3.39)	2.78 (2.05, 3.77)	2.48 (1.66, 3.70)

[p] Mortality rate ratio (MRR); [q] report relative risk; [r] reported hazard ratio (HR); [s] reported adjusted odds ratio (aOR);

Varieties of seizure-related and not seizure-related CoD were identified.The SMRs for malignant neoplasm excluding brain tumours were generally lower than for all malignant neoplasms. Cause-specific mortality for not seizure-related in hospital-based studies shows increased mortality for people with malignant neoplasms, but this is more pronounced for neoplasms of the brain with SMR more than 20 in the Swedish, Taiwanese and Austrian cohorts. Excess mortality was observed for most studies reporting SMRs for neoplasm of lungs, hepatobiliary neoplasms, ischaemic heart disease, cerebrovascular disease and pneumonia. The Swedish and Austrian cohorts reported high SMRs for congenital anomalies (17.0 (9.5, 28.1) and 7.1 (2.3, 16.6) respectively. Results for external causes or seizure-related mortalities showed excess

mortality reported for drowning especially higher in the Chinese reports (39.0 (26.4, 55.5) and 82.4 (46.4, 146.4)) and the Californian cohort (12.8 (7.0, 23.2)). SMRs for suicide, transport accidents and accidental falls were particularly high in Chinese rural areas. Excess mortality was also reported for drowning, suicide, injury and poisoning in the hospital-based studies, this was also high in the Taiwanese study. Studies reporting mortality according to aetiology, suggest excess mortality for idiopathic epilepsy, higher for remote symptomatic aetiology and much higher for those with a congenital deficit.

This review provides a comprehensive picture of the overall and cause-specific mortality in epilepsy. The overall SMR found supports the evidence that people with epilepsy are at an increased risk of premature mortality compared to the general population and in some studies were higher than previously reported (Gaitatzis et al., 2004, Forsgren et al., 2005b, Neligan et al., 2010, Nevalainen et al., 2014). Despite the heterogeneity, the results suggest an increased mortality risk that cannot be explained by chance alone. The observations from this review show that mortality may change in the same cohort over the years of follow-up and may even decrease, as observed in the NGPSE, Austrian and the Chinese cohorts. This notable finding of a decrease in SMRs throughout follow-up for a cohort may simply reflect the normal increased death rate in the aging population. It may also be due to the influence of treatment on a cohort, or the natural tendency for remission. The varying follow-up time used in different studies makes comparisons of mortality data challenging, as it tends to ignore the possible consequences of changing factors over the years. It has been suggested that predictors of mortality and health variables are more likely to be unstable during the first years of follow-up and this trend diminishes with longer follow-up periods (Meinow et al., 2004). These assumptions are inconclusive and require further studies. The wide variability and discrepancies in measures of mortality between primary studies may be due to differences in the age and sex composition, socioeconomic circumstances, access to treatment and ASM adherence. The heterogeneity of study

design employed, outcomes measured and the length of follow-up may also contribute (Gaitatzis et al., 2004, Forsgren et al., 2005b). These variations in SMRs have been shown to persist despite data from industrialized western countries with similar medical risks and cultures (Shackleton et al., 2002). The overall SMRs from LMIC appear to be higher than those from HIC, apart from the Indian (Parsi) cohort (SMR: 0.76). The reason for this isolated case is not known, but may be due to the small sample size with less severe epilepsy. It may also be related to the higher baseline mortality rate in India where epilepsy adds little compared to the huge impact of communicable diseases. Few studies reported measures of cause-specific mortality from LMIC but studies from China found higher SMRs for external causes of deaths such as drowning and suicide. These studies from LMIC had high attrition rates and shorter follow-up. They also included mainly people with convulsive epilepsy who are more likely to have severe uncontrolled epilepsy, are less likely to receive standard care, and therefore, have higher mortality rates. A possible confounder in epilepsy-related deaths is the role of psychiatric co-morbidity that is usually under-diagnosed and was not considered in the studies retrieved, except that reported by the Swedish study reporting hazard ratios. Whilst there is a concern about the possible role ASMs have in promoting suicidal tendencies; studies assessing suicidal risk with ASMs found that the risk of suicide was much higher in those not compliant with ASMs (Faught et al., 2008). There are no studies on premature mortality from Nigeria. One study reported a case fatality rate of 1.5% among children with epilepsy attending tertiary care over a follow-up period of 12 years (Sykes, 2002).

Several methodological issues are noted. The marked heterogeneity of mortality rates and different source populations precluded statistical pooling and meta-analysis. The difference in classifications used for the CoD in these studies may hamper the computation of aggregate SMR (Logroscino & Hesdorffer, 2005, Hitiris et al., 2007). Comparing data between studies may also be difficult due to differences in the methodology, follow-up period and varying sources of death records. Another limitation

recognised is that SMR can give information on how frequent a CoD is compared to the general population, but it cannot tell how frequently a CoD is in absolute terms. Therefore, a high SMR may not always be a confident indicator of high death rates when comparing two groups.

In conclusion, people with epilepsy from HIC and LMIC have a higher risk of dying from contributory causes compared to the general population. Those in LMIC have a particularly high ratio of death due to external causes such as drowning and suicide. A reduction over time of overall and cause-specific mortality in cohorts was observed. Further work is needed to elucidate the mechanisms, determine biomarkers for predicting those at risk, and to understand the implications of counselling and preventive strategies, especially in LMICs.

2.4 Health service provision for people with epilepsy in sub-Saharan Africa

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2.4.1 Introduction

In traditional African cultures, epilepsy is neither perceived nor understood as a solely bodily health issue. The traditional perception and resultant lack of awareness impede access to health care and contributes to the high epilepsy treatment gap (Dillip et al., 2012, Mbuba et al., 2012b). Inefficient health-care systems, high costs of treatment, long distances, geographic difficulties, and poor transportation negatively impact access to treatment (Meinardi et al., 2001). Even where functional health-care facilities exist, they are more likely to benefit the more affluent urban inhabitants than the rural poor. Structural issues and inequality increases the complexity of managing epilepsy in resource-poor countries (Radhakrishnan, 2009). The WHO mental health Gap Action Programme (mhGAP) in its attempt to scale-up services for mental, neurological, and substance-misuse disorders in LMICs, have observed that with proper care,

psychosocial assistance, and provision of ASMs the majority of currently underserved individuals could be treated (WHO, 2001). An understanding of the existing epilepsy care provision in SSA will provide background information for the development of appropriate health policies and interventions in Africa. The objective of this review was to identify and discuss information relating to epilepsy health care services in SSA, specifically focusing on the rationale and unique nature of services and available facilities.

2.4.2 Review Methods

The methodology employed followed the modified six-stage framework for conducting scoping reviews (Arksey & O'Malley, 2005, Levac et al., 2010) (Table 5). Relevant studies and information were identified from an online search of PUBMED, EMBASE, Web of Science, Scopus, Cumulative Index to Nursing and Allied Health Literature (CINAHL), African Index Medicus (AIM), Open Grey, the Cochrane database and Google Scholar. PubMed medical subject headings (MeSH) and Emtree for Embase were used to develop the most appropriate search strategy (Appendix 1 for search details). A backward search from the reference list of key publications and review articles was also done. A search of grey literature sources such as National Guidelines, the ILAE/IBE, and reports from non-governmental organisations (NGOs) was conducted using Google scholar. An initial study screening of the title and abstract was made by scanning each search result. The full texts of the selected articles were then read and screened for eligibility.

Table 5: Epilepsy healthcare provision in sub-Saharan Africa: methodological framework

Stages	Framework	Brief Description of Steps Taken
Stage 1	Identifying the research question	What is known about epilepsy health care provision in SSA? Types, nature of services, diagnostic facilities, funding sources and hindrances to optimal healthcare.
Stage 2	Identifying relevant studies	Searched databases, reference lists, and hand-searching journals by manual page-by-page examination of the entire content of journal references, and from websites and news reports of related organisations.
Stage 3	Study selection	All available articles reporting any form of epilepsy health service provision in SSA. Articles such as single cases, case series, and articles on special sub-populations, such as febrile seizures and cerebral malaria, were excluded.
Stage 4	Charting the data	Reviewed information of the selected literature, recorded the information on the type of care programme and interventions. Reviewed the uniqueness, successes and outcomes of each programme.
Stage 5	Collating, summarizing and reporting results	Summarised findings and reported results. Stratified results according to geographic regions and countries, stated care recipients, and population type (e.g. rural or urban). Commented on details of interests, the type and nature of epilepsy services, the diagnostic facilities available, and the sources of funding
Stage 6	Consultations with stakeholders	A stakeholders meeting was not conducted, but we communicated with contact persons who provided additional information about studies included in the review.

Based on the methodological framework by (Arksey & O'Malley, 2005)

2.4.3 Results

Thirty-nine services were identified from journal articles, newsletters and webpages. The resources available, funding sources and collaborators are summarised in Table 6. The distribution of care centres is shown on a map (Figure 1). Most of the programmes (75%) targeted rural or suburban populations. Even where care was based in tertiary

care centres, they also served rural and community outposts (Elafros et al., 2014, Nazziwa et al., 2014, Tsegabrhan et al., 2014). Some of the rural care programmes recruited individuals for treatment following epidemiological surveys, community engagements or after recognising particular needs, and some may no longer be in existence.

The majority of rural care facilities were led by non-physician health workers trained and supervised by physicians or foreign collaborators. The ASM readily available and used was phenobarbital, provided free or at a subsidized rate. The Nakuru project reported seizure freedom in 53%, with a further 26% having significant seizure reduction in the initial six months, with a compliance rate of 82% (Feksi et al., 1991b). The Tanzanian cohort showed that 52% were seizure-free and 36% had reduced seizures (Jilek-Aall & Rwiza, 1992). The Malian programme reported an 80% seizure-freedom and an additional 16% had significant seizure reduction (Nimaga et al., 2002). A similar follow-up programme in Mali observed that 60% of those followed-up for a year were seizure-free (Bruno et al., 2012). The Togolese programme reported over 90% being seizure-free for over 2 years (Balogou et al., 2007). A non-physician-led clinic at the rural Mbangassina area of Cameroon, using a management algorithm reported that 70% went into remission, while 16% had partial improvement (Dongmo et al., 2003). The programme at the Kabende parish in Uganda observed that about a third of subjects became seizure free (Kaiser et al., 1998b).

Some NGOs were identified; this includes the Kenya Association for the Welfare of People with Epilepsy (KAWE), Hope for Humans, the Epilepsy Support Foundations, Malawi Epilepsy Association, and the Federation of Disability Organisations in Malawi. They are involved in providing subsidized or free treatment, community engagement, counselling and educating people with epilepsy and their families. They also lobby for equal opportunities for schooling and income generation. These NGOs coordinate with urban healthcare facilities to form outreach programmes and train allied health workers to render services in rural areas using epilepsy protocols.

Table 6: Summary of health service provision and resources available for people with epilepsy in sub-Saharan Africa

Country	Project name/Location	Author(s)/Date	Population	Type of epilepsy care		Resources available				Funding/support
				Nurse/ health-worker-led	Physician supervised	ASM available	EEG	Neuro-imaging	Psycho-social supports	
Kenya	Nakuru ICBERG project, Nakuru district	(Feksi et al., 1991a, Feksi et al., 1991b, Feksi, 1993)	Rural & Semi-urban	✓	✓	PB, CBZ	×	×	✓	Ciba Foundation, UK National Society for Epilepsy,
	Kilifi Health and Demographic Surveillance System	(Scott et al., 2012)	Rural	✓	✓	PB, CBZ, PHT, VPA	✓	✓	✓	Wellcome Trust, KEMRI, University of Oxford
	Kenya Association for the Welfare of People with Epilepsy	(Dekker, 1993, Dekker-de Kiefte, 1994, ILAE, 2012.) http://www.kawe-kenya.org	Rural & Urban	✓	✓	PB	×	×	✓	Netherlands Epilepsy Fund, personal donations and run by volunteers
Tanzania	The Mahenge Epilepsy Clinic/ Muhimbili epilepsy project	(Aall-Jilek, 1965, Jilek-Aall & Rwiza, 1992, Rwiza, 1994, Jilek-Aall et al., 1997)	Rural	✓	✓	PB, PHT, PRIM	×	×	✓	IDRC, University of British Columbia, EPICADEC, Private donations
	Epilepsy clinic Hai district demographic surveillance system	(Burton et al., 2012, Hunter et al., 2012)	Rural	✓	✓	✓	✓	✓	✓	Wellcome Trust, DfID
	Haydom Lutheran Epilepsy Clinic	(Winkler et al., 2008, Winkler et al., 2009b, Winkler et al., 2009c, Blocher et al., 2011)	Rural	✓	✓	✓	✓	✓	✓	Savoy Epilepsy Foundation Canada, Centre for International Migration Germany
	Tanzanian Epilepsy Association	(Rwiza, 1994, Kok, 1998)	Rural & Urban	✓		✓			✓	British Columbia Epilepsy Society
Malawi	Embangweni Hospital + rural care, Malawi Epilepsy Association, Federation of Disability Organisations in Malawi (FEDOMA)	(Watts, 1989, Watts, 1990, Watts, 1992, Wada et al., 2004, Amos & Wapling, 2011a, IBE, 2014) (Amos A, Personal communication)	Rural	✓	✓	PB, PHT	×	×	✓	Sue Ryder Foundation, non-governmental organisations
Ethiopia	Gondar NCD project, nurse-led epilepsy clinics	(Berhanu et al., 2002, Berhanu et al., 2009)	Rural	✓		PB	×	×	×	Tropical health education trust,

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				Nurse/ health-worker-led	Physician supervised	ASM available	EEG	Neuro-imaging	Psycho-social supports	
										Government funded NCD project.
	Amanuel Mental Specialized Hospital, Addis Ababa	(Tegegne et al., 2015)	Urban	✓	✓	PB, PHT, CBZ, VPA	✓	×	✓	Financial support from Gondar University and AMSH
	Jimma University Specialized Hospital	(Kiflie et al., 2011, Tsegabrhan et al., 2014)	Urban	✓	✓	✓	✓	×	✓	JUSH
Uganda	Rural epilepsy treatment at Kabende Parish	(Kaiser et al., 1998a, Kaiser et al., 1998b)	Rural	✓	✓	PB	×	×	×	Local community
	Mulago National referral and teaching hospital in Kampala	(Kaddumukasa et al., 2013, Nabukenya et al., 2014, Nazziwa et al., 2014, Settumba et al., 2015) (Kakooza A, Personal communication)	Urban	✓	✓	PB, PHT, CBZ	✓	✓	✓	Ugandan Goverment, Belgium Technical Cooperation, other international organisations
	Hope for Human (Nodding syndrome)	http://hopeforhumans.org (Gazda, Suzanne, personal communication)	Rural	✓	✓	✓	×	×	✓	Donations from individuals, Geneva global
Zimbabwe	Epilepsy Support Foundation (ESF) and Murambinda Mission Hospital	(Mugumbate & Mushonga, 2013), (Kadziti, Taurai, personal communication),www.epilepsyzimbabwe.co.zw	Rural	✓	✓	PB	✓	×	✓	ESF, ILAE
	Management of PWE by nurses at Chitungwiza and ESF	(Adamolekun et al., 1997, Adamolekun et al., 2000)	Rural	✓	✓	PB	✓	×	✓	W.K. Kellog Foundation.
	Zvimba health district and ESF	(Adamolekun et al., 1999)	Rural	✓	✓	PB	✓	×	✓	ESF of Zimbabwe, ILAE educational grant.
	Hwedza demonstration project	(Global Campaign Against Epilepsy, 2012)	Rural	✓	✓	PB	✓	×	✓	Zimbabwe Committee of the Global Campaign Against Epilepsy, WHO, ILAE, and IBE

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				Nurse/ health-worker-led	Physician supervised	ASM available	EEG	Neuro-imaging	Psycho-social supports	
Zambia	University of Zambia's Teaching Hospital and Chikankata mission + affiliated area clinics	(Birbeck, 2000, Atadzhanov et al., 2010, Elafros et al., 2013, Elafros et al., 2014)	Urban & Rural	✓	✓	PB CBZ, PHT	✓	✓	✓	NIH USA
Rwanda	Gikonko Health Center, Kabutare District Hospital, and Butare University Teaching Hospital	(Rottbeck et al., 2013)	Rural & Urban	✓	✓	PB, CBZ, VPA, PHT	×	×	×	German Federal Ministry for Economic Cooperation and Development via the ESTHER programme
South Africa	Agincourt Health and Demographic Surveillance Site	(Ngugi et al., 2013a, Wagner et al., 2014, Wagner et al., 2015b)	Rural & Suburban	✓	✓	✓	✓	✓	✓	Wellcome Trust, Flora Hewlett Foundation USA, NIH, INDEPTH Network, CSIR SA, Rockefeller Foundation
	Mamre Community Health Project	(McQueen & Swartz, 1995)	Rural & Urban	✓	✓	PB, CBZ, PHT, VPA	×	×	✓	Centre for Science Development, University of Cape Town
	The NCD service Hlabisa Hospital	(Coleman et al., 1998)	Rural	✓	×	PHT, CBZ, PB	×	×	×	Government health services
	Red Cross War Memorial Children's Hospital	(Williams et al., 2015)	Urban	×	✓	✓	✓	✓	✓	RCWMCH, Epilepsy South Africa Western Cape Branch (ESA-WCB)
Nigeria	Epilepsy clinic at University College Hospital Ibadan 1950s to 1970s.	(Dada et al., 1969, Osuntokun & Odeku, 1970, Osuntokun, 1972, Osuntokun, 1979, O'callaghan et al., 2004, Lagunju et al., 2009) (Ogunniyi AO, Personal communication)	Rural & urban	×	✓	PB, PHT, CBZ, VPA	✓	×	×	Government hospital.
Mali	RARE (Re´seau Action-	(Farnarier et al., 2002,	Rural	✓	✓	PB	×	×	×	Sanofi-Aventis, Sante´-

Table 6: Summary of health service provision and resources available for people with epilepsy in sub-Saharan Africa

Country	Project name/Location	Author(s)/Date	Population	Type of epilepsy care		Resources available				Funding/support
				Nurse/ health-worker-led	Physician supervised	ASM available	EEG	Neuro-imaging	Psycho-social supports	
	Recherche sur l'Epilepsie) program	Nimaga et al., 2002, Genton et al., 2003, Bruno et al., 2012)								Sud, Institut Rhone-Poulenc Rorer.
Senegal	Demonstration project at Pikine Health District	(Reynolds, 2001, Sow & Gueye, 2003, Ndoye et al., 2005, Fall et al., 2015)	Rural & Suburban	✓	✓	PB	×	×	✓	ILAE, IBE. WHO
	Mobile epilepsy clinics	(Boissy, 2005, Boissy, 2008)	Suburban & rural	✓	×	✓	✓	×	✓	
Gambia	Demographic surveillance Medical Research Council	(Coleman et al., 2002)	Rural	✓	✓	PB	×	×	×	Gambian government and General medical council of Gambia
	Royal Victoria Hospital (RVH)	(Burton & Allen, 2003)	Urban	×	✓	CBZ, PB, PHT	×	×	×	Gambian Government
Togo	Batamariba project at the Nadoba health centre	(Balogou et al., 2007)	Rural	✓	×	PB, CBZ	✓	×	×	WHO
	Community-based care for epilepsy at six pilot districts	(Guinhouya et al., 2010)	Rural	✓	✓	✓	×	×	✓	WHO/AFRO, NPMH supply of ASMs
Guinea-Bissau	Community-based rehabilitation at Buba	(Otte et al., 2013)	Rural & Urban	✓	✓	✓	×	×	✓	CBR programme
Cameroon	Essential NCD health intervention project	(Unwin et al., 1999, Kengne et al., 2008, Kengne et al., 2009)	Rural	✓	×	PB, PHT, CBZ	×	×	✓	UK Government's DfID Health in the Next Millennium' programme.
	Epilepsy clinics Mbangassina area	(Dongmo et al., 2003)	Rural	✓	×	PB, CBZ, PHT	×	×	×	Efforts of medical personnel

✓available, × not available or not sure, ASM – antiseizure medicationPB – Phenobarbitone, PHT – Phenytoin, CBZ – Carbamazepine, VPA – Valproate, PRIM – Primidone, ICBERG – International Community-based Epilepsy Research Group, KEMRI – Kenyan Medical Research Institute, IDRC – International Development Research Centre, EPICADEC – The Foundation Epilepsy Care Developing Countries, DfID – Department for International Development, NCD – Non-Communicable Disease, ESF – Epilepsy Support Foundation, NIH – National Institutes of Health, ESTHER – Ensemble pour une Solidarite Therapeutique Hospitaliere en Reseau, CSIR – Council for Scientific and Industrial Research, NPMH – National Program for Mental Health, ENHIP – Essential NCD health intervention project

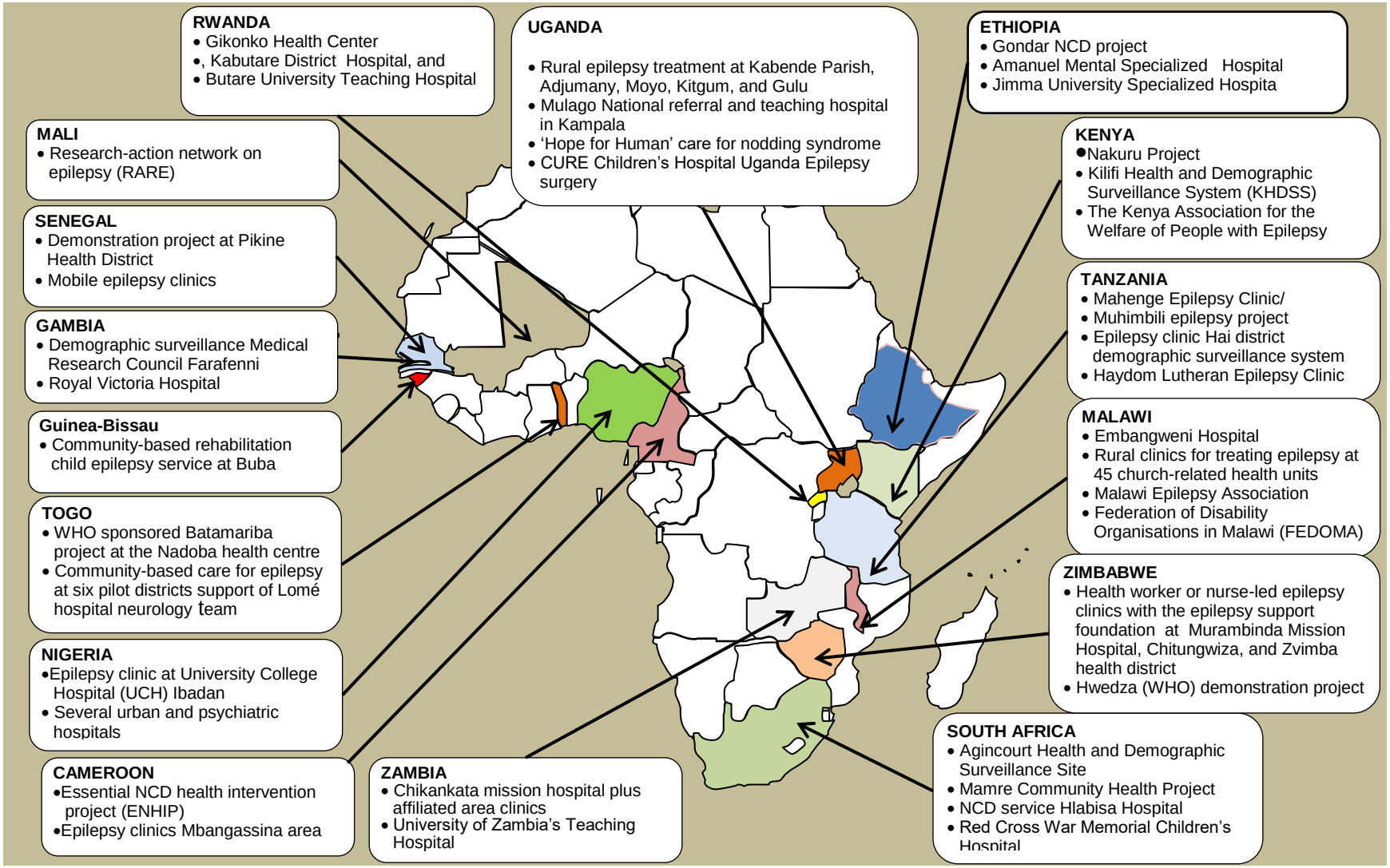


Figure 1: Map showing health care centres for people with epilepsy in sub-Saharan Africa

2.4.4 Discussion

This review explored the range of epilepsy services and programmes available in SSA. This is an important first step towards developing a better understanding of the nature and scope of the literature related to epilepsy care provision in SSA. A scoping approach was preferred over a systematic review as an initial method for reviewing existing health research evidence to understand the range of services available rather than the quality of individual studies (Colquhoun et al., 2014). The most notable finding was that the overwhelming majority of African epilepsy care services are provided through centres based in rural areas. Three reasons can explain why rural programmes are popular and could represent the best model to reduce the treatment gap in Africa. Firstly, people in rural areas particularly need assistance due to economic disadvantage. These populations can hardly afford most ASMs and the specialised epilepsy services often concentrated in major urban conurbations. Secondly, programmes that are run in rural centres are usually integrated within existing primary health care systems and are thus more sustainable. Thirdly, most programmes in rural areas do not need sophisticated diagnostic technology, and non-physician health workers can easily be trained to diagnose and provide some level of quality care. It has recently been shown that a community-based approach to providing care for chronic medical conditions is cost-effective and more sustainable (Vaughan et al., 2015). With adequate training, people in allied medical professions can provide quality care in areas where access to physicians is limited and, as a result, significantly reduce the treatment gap (Wagner et al., 2016a). The efficiency of such community-based rural programmes can sometimes be reinforced by the existence of a strong referral and counter-referral system with a specialist centre. The specialist centres will evaluate and establish a treatment plan, after which they return to community care based on a formulated treatment plan. In Zambia (Birbeck et al., 2012a) and Ethiopia (Kiflie et al., 2011) for example, rural clinics were linked with tertiary hospitals for the referral of those needing specialist assessment and further investigations. A care model is

proposed for a national epilepsy programme where 60% of individuals can be successfully managed in the rural community, while 30% may be referred to a secondary facility, with only 10% ever reaching tertiary care (Birbeck et al., 2012a). Apart from reducing the treatment gap, it is possible that establishing a well-coordinated rural health programme would reduce the total cost of epilepsy care provision in SSA, although this requires further research.

Community engagement and education seem critical in improving access to care and drug adherence. The Zimbabwean study reported that educating community health workers in epilepsy care improved recruitment and drug adherence (Adamolekun et al., 1999). Educating community leaders improved health-seeking behaviour amongst people of the community (Ball et al., 2000). While the myths and stigmas surrounding epilepsy appear to be changing for the better in many of these rural care facilities after the community intervention projects, providing epilepsy care to people in rural settings in Africa remains challenging due to a considerable knowledge gap (Winkler et al., 2010, Mugumbate & Mushonga, 2013). Support groups are useful in dispelling social stigma, improving treatment compliance, and enhancing social acceptance and integration (Jilek-Aall et al., 1997, Adamolekun et al., 2000, Williams et al., 2015). Support groups have also been shown to improve psychosocial indicators such as positive self-management, social outlook, better coping strategies and quality of life (QOL) (DiIorio et al., 1996, Chung et al., 2012). The work by KAWE in rural Kenya illustrates how community-based NGOs can coordinate with the nurse-led system to cover more of the population especially concerning aspects of education and social support (http://www.kawe-kenya.org). More studies are needed on the role of support groups and the influence of community education in improving public perception, social integration and the quality of life for people with epilepsy.

An important observation is the role of mobile epilepsy care including home visits to provide drugs and support. This helped improve compliance in rural communities of Malawi (Watts, 1989), Senegal (Boissy, 2005), Mali (Nimaga et al., 2002), Togo

(Balogou et al., 2007), and by KAWE (Dekker, 1993, Dekker-de Kiefte, 1994). The long-term sustainability and value of mobile or home-based care need to be examined in larger longitudinal studies. It has been suggested that healthcare centres located within a convenient walking distance would substantially reduce out-of-pocket expenses and may be of better long-term usefulness (Coleman et al., 2002, Mbuba et al., 2012b, Wagner et al., 2016a, Wagner et al., 2016b).

Phenobarbital was found to be the cheapest and most readily available ASM used in the majority of rural areas. In the Nakuru project, phenobarbital had similar efficacy and tolerability to carbamazepine (Feksi et al., 1991b). Based on the success of trials and the cost advantage of phenobarbital in India (Mani et al., 2001), Brazil (Li & Sander, 2003), and China (Wang et al., 2006), WHO has suggested the use of phenobarbital as a drug of choice for treating epilepsy in resource-poor settings (Kwan & Brodie, 2004, Chisholm, 2005). The cost-effectiveness of managing epilepsy has been observed in the Malian (Nimaga et al., 2002) and Zambian studies (Chomba et al., 2010, Birbeck et al., 2012a), where the overall cost of epilepsy management is between US$15 and US$25/person/year, which is substantially less than the expenses incurred in treating other chronic health conditions. A study assessing the expected resource needs for scaling up mental health care plans, also reported that the cost of epilepsy care packages is significantly lower than the cost of treating psychosis (Chisholm et al., 2016). The renewed interest in the use of barbiturates as a cost-effective option for epilepsy treatment in Africa calls for further research to verify the availability and the quality of these drugs available in African health facilities.

One important determinant of the success of epilepsy treatment in SSA is medication adherence. A Ugandan study found that almost 80% of the people who reported being adherent to ASM, only about a quarter were adherent when serum drug levels were employed to verify adherence (Nazziwa et al., 2014). Good adherence to ASM is associated with better seizure control, improved job prospects, increased productivity, reduced road traffic accidents and a better overall QOL (Hovinga et al., 2008). Studies

on how to improve medication adherence is an important area for future research. Even though serum drug monitoring is rarely available in Africa due to cost, its use may help reduce the adherence gap, but this is not established and needs to be further investigated (Mbuba et al., 2012b, Winkler, 2012). This review suggests the use of non-physician health workers in rural areas, but the diagnostic gap in SSA requires improvement by providing access to trained diagnosticians, EEG and neuroimaging to better characterise cases. The diagnostic gap, the cost and possibly the lack of skilled manpower have limited the use of epilepsy surgery (Wieser & Silfvenius, 2000). A few centres reported performing surgery on a small subset of children with hippocampal sclerosis (Ruperti, 1997, Butler, 2005, Boling et al., 2009).

Collaborations between epilepsy care facilities in African countries and European and North American countries, concerning funding, provision of drugs, diagnostic facilities, and transfer of technical and intellectual skills are common. They help reduce the treatment gap but are vulnerable to economic and political changes. African governments must take the responsibility of setting up proper primary health care services (Lu et al., 2010). Epilepsy care provision is more concentrated in East and South Africa compared to West and Central Africa. This difference could be due to several factors: publication bias; under-reporting of epilepsy care programmes; disproportionate exposure to research partnerships and funding from international donor agencies; and differences in the commitment of the local Ministries of Health.

In many countries in SSA, health insurance is poorly developed and payment for health services is out-of-pocket, making long-term management of people with chronic conditions challenging. In Nigeria, the National Health Insurance Scheme (NHIS) covers only 3% of the population mainly living in urban areas (Dutta & Hongoro, 2013). A robust health insurance scheme to cover the basic needs of the rural populace of Africa will probably improve access to epilepsy care and should be a priority. The WHO has recommended the policy of Universal Health Coverage where citizens can access health care without incurring financial hardship; this could alleviate the burden of

epilepsy and contribute to greater equality in access to care, by reducing the out-of-pocket expenses that exacerbate poverty (Megiddo et al., 2016).

This review has limitations. Firstly, there is a bias for reporting rural epilepsy care compared to urban care, which may reflect the rapidly growing weight of literature reporting model rural care. Rural epilepsy care programmes are more likely to be publicly or internationally funded, and therefore more likely to be published. Secondly, this review may have excluded information as only scientific articles and few grey kinds of literatures were retrieved. The potential for researchers to be unwilling to publish unfavourable results and the inequalities of SSA studies to be published in indexed journals should be recognised. Thirdly, epilepsy services are often provided as an adjunct to mental health services (Gureje & Alem, 2000, Ofori-Atta et al., 2010), and may not have been reported. Fourthly, a stakeholders' meeting, as recommended for most scoping reviews (Arksey & O'Malley, 2005), was not performed, due to limited resources. Such a meeting would have provided an avenue where information on the true situation at these sites may have been further elucidated, as these sites may be no more functional. This is a challenging process in SSA and could be a possible area for future research. Lastly, the description of epilepsy services presented here may not reflect all care available in all of SSA as much of it is unlikely to be recorded in the literature.

2.4.5 Conclusion

This review has provided a broad overview of epilepsy care provision in SSA to inform health policy. The main finding highlights the usefulness of rural epilepsy care in meeting health care needs. This success was attributed to using the existing primary health care system and employing community nurses and health workers in epilepsy care. This practice of using allied health workers in providing primary healthcare needs, despite the lack of modern diagnostic facilities, is noteworthy and could be replicated. Epilepsy care should be integrated into established health systems if possible and modelled after successful interventional programmes (Chin, 2013). Phenobarbital is

effective in over 60% of people and remains the cheapest most readily available ASM. We recognise the usefulness of community engagement and education in improving access to epilepsy care and compliance. The long-term sustainability of epilepsy care will ultimately lie in the hands of the government of these countries.

2.5 Health services provision for people with epilepsy in Nigeria

In contrast to the situational report of epilepsy care in most parts of sub-Saharan Africa reported above, there have been little or no research partnerships or funding from international donor agencies on epilepsy care in Nigeria. Tertiary institutions (part of a general adult or paediatric neurology clinics and general medicine clinics) mainly render epilepsy care services in Nigeria. Little is known about the treatment of epilepsy care in rural areas due to the scarcity of official information or evidence. If it exists, it is most likely rudimentary. Psychiatric hospitals provide healthcare service for a large number of people with epilepsy, suggesting that epilepsy is considered a psychiatric illness by the populace (Adewuya, 2006, Igwe et al., 2014, Ipingbemi, 2015). Most of these tertiary care centres do not have specialised epilepsy clinics or units and even when they do, they are usually underfunded and ill-equipped. A few of the tertiary hospitals have rural outposts that may deliver epilepsy care in villages. An example of such tertiary epilepsy care is the Ibadan epilepsy cohort (the 1950s to 70s) from University College Hospital (UCH) Ibadan. It was the earliest recorded epilepsy care initiative in Nigeria initiated by the neurologist, Professor Osuntokun. Between 1957 and 1971 up to 802 individuals were attending the clinic, with outreach to rural areas (Dada et al., 1969, Osuntokun & Odeku, 1970, Osuntokun, 1972, Osuntokun, 1979, Pacheco et al., 1996). Over the years they were incorporated into the general neurology clinic of the hospital. There is no documentation of long-term morbidity and mortality of this UCH cohort, but the majority, if not all, were lost to follow-up or presumed to have died (Personal communication with Professor Ogunniyi, UCH Ibadan). A cohort of 540 children was assessed at UCH, looking at the pattern, predisposing factors and outcomes (Lagunju et al., 2009). Most of the children were on

monotherapy with phenobarbital, carbamazepine, phenytoin or valproate. At the end of the first year, three quarters were lost to follow up, and of those regular with medication, half were seizure-free. The loss to follow-up and non-adherence to medication are common occurrences in sub-Saharan (Chin, 2012). The issue of fake or sub-standard ASMs is also a major concern in Nigeria (Otte et al., 2015).

2.6 Alternative treatment options for people with epilepsy in low- and middle-income countries: A focus on epilepsy surgery.

This section is an abridged version of a scoping review published in: *Watila et al. Epilepsy Behav 92 (2019) 311–326 https://doi.org/10.1016/j.yebeh.2019.01.001*

2.6.1 Introduction

The extent of epilepsy surgery utilisation, cost and outcome measures are not well known in LMICs. Between 1980 and 1990 a global survey reported few published literature on epilepsy surgery from LMIC and none from Africa (Silfvenius, 1997). By the end of 1999, epilepsy surgery was present in only 26 (18.3%) of 142 LMICs (Wieser & Silfvenius, 2000). Whether this high 'surgical treatment gap' is due to mere exclusions from international surveys or underreporting of surgical practices, it is certain that underutilization is a more serious problem in LMIC than HIC, with majority of health centres lacking the capacity to perform neurosurgery and most health personnel referring patients elsewhere for epilepsy surgery (Wilmshurst et al., 2015). Reasons for the high surgical treatment gap in LMIC include the absence of organised structured care, lack of infrastructure, shortage of specialists and the cost of surgery (Wieser & Silfvenius, 2000, Diop et al., 2003, Chin, 2012). A recent review observed that barriers to epilepsy surgery are perpetuated by the uncertainty portrayed by medical practitioners towards surgical treatments, reflecting the knowledge gap, which may be more pervasive in LMIC (Jetté et al., 2016). This scoping review aimed to i)

identify the availability of epilepsy surgery in LMIC; ii) determine the minimum standard requirements at these centres; iii) determine the outcome and cost of surgical procedures; and iv) discuss the challenges and possible potentially areas of closing the gap.

2.6.2 Methodology

A scoping review was preferred over a systematic review or meta-analysis as it allows a range of study with varying designs to be incorporated. It examined the extent, range, and nature of a study, and identified research gaps without necessarily assessing the quality of included studies (Arksey & O'Malley, 2005, Levac et al., 2010). A scoping review was found to be ideal to help clarify surgical alternatives for people with medically intractable epilepsy in resource-poor settings. The 6-stage methodological framework for scoping review was adopted (Arksey & O'Malley, 2005). This framework includes: (i) identify the research question, (ii) identify relevant studies; (iii) study selection; (iv) data charting; (v) collate, summarise, and report the results; and (vi) stakeholders consultation. The primary interest was to map and widely examine the literature on epilepsy surgery in LMIC using the following research questions:

a. What are the available epilepsy surgical options in LMIC?
b. What are the types of surgeries and outcomes and cost?
c. The importance of collaboration and skill transfer between HIC and LMIC?
d. The barriers and possible areas of research?

The following databases were searched: PubMed, Embase, Global health archives. Index Medicus for South-East Asia Region (IMSEAR), Index Medicus for Eastern Mediterranean Region (IMEMR), Latin American & Caribbean Health Sciences Literature (LILACS), Western Pacific Region Index Medicus (WPRIM) and African Index Medicus (AIM) via the WHO Global Index Medicus, and the African Journal Online (AJOL). The key words combined were ‘‘epilepsy’’ and ‘‘surgery’’ or ‘’surgical’’ or ‘’surgical procedures’’ or ‘’resecti*’’ or ‘’disconnecti*’’, or ‘’neurostimulati*’ and LMICs using the World Bank classification (www.worldbank.org) (Appendix 2 for search

detail). Observational studies, clinical trials, case series and relevant publications reporting epilepsy surgeries, outcomes (based on Engel classification or equivalent), mortality, complication, QoL or costs were included. Epilepsy surgery was defined as procedures undertaken to control drug-resistant epilepsy as opposed to removing an acquired structural brain lesion. These surgical procedures include resective, disconnective, or neurostimulative surgical modality irrespective of year of publication or language. Neurosurgeries offered exclusively for brain tumours, infections and other conditions not associated with epilepsy were excluded. A data-charting form (Table 7) was developed from the revised version of quality guidelines for presurgical epilepsy evaluation and surgical epilepsy treatment by the Austrian, German, and Swiss working group to extract data (Rosenow et al., 2016). The guideline aims to instruct on the minimum standard requirement for running an epilepsy surgery facility and served as a guide to understand what is available from LMIC, as what is a minimum requirement in Europe may not be the same elsewhere in LMIC (Nayel, 2000).

Table 7: The data-charting form for epilepsy surgery

Data of Interest* [To be reported as Present (✓); Absent (×); Not mentioned (NA)]		
1.	Bibliometric	Author, year of publication, country, period (year) of recruitment, type of surgery, number operated, follow-up duration, outcome measure, mortality, complications, QOL and cost
2.	Sufficient staffing of qualified personnel	Epileptologist, neurosurgeon, neuropsychologist, and neuroradiologist, psychiatrist, nursing and technical staff
3.	Technical equipment (minimum)	Video-EEG monitoring (VEM) unit (≥64-channel EEG, 1.5-Tesla MRI, at least two of any epilepsy-specific imaging (single-photon emission computed tomography [SPECT], positron emission tomography [PET], functional MRI [fMRI], MRI post-processing, magnetoencephalography [MEG], and 64-256-channel EEG with source imaging [ESI]).
4.	Training of staff	A certain period of training at an epilepsy centre is required.
5.	Intensive monitoring /VEM evaluation	24-h continuous supervision during VEM is required in case of ASM reduction and for immediate recognition of emergencies.
6.	Follow-up, quality assurance, and data acquisition	Appropriate minimum data capture. Recording of relevant pre- and post-operative data at regular intervals to ensure patient's course is documented
7.	Cooperation/Collaboration	Close and collegial contact with leading epilepsy centres

*To instruct on the minimum standard requirement for running an epilepsy surgery facility and help chart the area of interest, we developed the charting form from the revised version of quality guidelines for presurgical epilepsy evaluation and surgical epilepsy treatment by the Austrian, German, and Swiss working group (Rosenow et al. 2016). Serial number 2 to 7 is based on the recommendation. QOL – Quality of Life, MRI – Magnetic Resonance Imaging, ASM – antiseizure medication, EEG – Electroencephalography.

2.6.3 Results

A total of 148 articles on epilepsy surgery from 31 countries representing 22% of the 143 LMIC were retrieved. The publications were mainly longitudinal studies, case series, case-control studies, and one randomized controlled study. They include nine publications from six African countries, 52 originating from 12 Latin American and the Caribbean countries, 85 from 13 Asian countries, and three publications from two

Eastern European countries. The bulk of the published items are from India, China, and Brazil. The papers retrieved spanned over 60 years, but only seven were published before the year 2000. A closer look at some of these papers especially from India, Brazil, and China reveal multiple publications from the same cohort. These publications show that a more recent paper incorporates subjects or is a subset of a cohort reported from older papers.

The results on the minimum standard requirements showed that most centres had the minimum technical equipment, however, information on whether they had sufficient qualified personnel or adequate training was mainly not mentioned or difficult to extract. Some papers reported on collaborative work between HIC and LMIC in Uganda (Boling et al., 2009, Fletcher et al., 2015, Mandell et al., 2015), Tunisia (Khiari et al., 2010), Thailand, India and Argentina (Zaknun et al., 2008, Barbaro et al., 2018), Pakistan (Tahir et al., 2012), and Iran (Asadi-Pooya et al., 2014). The collaborative epilepsy surgery program between North America and the CURE Children's Hospital of Uganda (CCHU) assessed the feasibility of an epilepsy surgery program in a resource-poor setting using just video-EEG and CT volumetric analysis (Mandell et al., 2015). The Tunisian epilepsy surgery program at the Charles Nicolle Hospital Tunis and the French hospital at Rouen via the EUMEDCONNECT was an internet network project in which clinical, EEG and radiological information are transferred from Tunis to France for discussion and evaluation (Khiari et al., 2010). Epilepsy surgery appears established in some of these centres in Asia and Latin America, while some are in their embryonic stage reporting procedures in a small cohort performed mostly by motivated neurosurgeons. The commonest surgical procedure reported was temporal lobectomies. The reported outcome measures ranged mostly between 40% to 80% (for Engel Class I) and 50% to 90% (for Engel Class I and II) in carefully selected subjects. Complications are transient or minor; while major complications or mortality is rare. These results appear better for temporal lobe surgeries. Some articles reported neurostimulative techniques like VNS (Wang et al., 2009, Alonso-Vanegas et al., 2010,

Arhan et al., 2010, Jayalakshmi et al., 2011, Meneses et al., 2013, Aburahma et al., 2015, He et al., 2015, Meng et al., 2015, Pakdaman et al., 2016, Terra et al., 2016) and DBS of posteromedial hypothalamus (pHyp) in DRE associated with aggressive behaviour (Benedetti-Isaac et al., 2015). They reported more than 50% seizure reduction with follow-ups ranging one to four years. QoL of epilepsy surgery candidates showed improved indicators of the QoL after surgery. The cost of epilepsy surgery ranges from about US$500 in Saudi Arabia to approximately US$8,000 in China.

2.6.4 Discussion

The status of published evidence reports epilepsy surgery in about a fifth of LMICs. The findings suggest that the utilisation of epilepsy surgery has evolved considerably in some centres in Asia and Latin America with an increasing trend in countries such as India, China and Brazil (Qiu, 2009), but appears embryonic in other countries, and particular sub-Saharan Africa. A large proportion of the retrieved papers are case series or experiences using a small sample size of carefully selected candidates performed by some motivated neurosurgeons and may not necessarily portray that epilepsy surgery is an established current practice in these countries. Epilepsy centres were not evenly distributed, but located in bigger cities that are more affluent. This geographical disparity has also been recognised in a previous review (Wieser & Silfvenius, 2000). A review of epilepsy surgery in India showed that geographical disparity is a common problem, and only 2 centres contributed to more than 50% of 420 surgeries performed annually, which is still far from adequate (Menon & Radhakrishnan, 2015).

It is noteworthy that the seizure outcome after surgery was good in the majority of patients and comparable to other centres in developed countries. Similarly, complications and mortalities from surgery were not significantly different from those reported (Hader et al., 2013, Sperling et al., 2016). Those who had surgery also had an improved QOL, employability and lower perceived stigma compared to those who did not, especially for those who are seizure-free (Locharernkul et al., 2005, Zanni et al.,

2009, Fletcher et al., 2015). The long-term outcome of some of the individuals is unknown, but these studies had a high loss to follow-up which is a common problem in LMICs (Perucca, 2007).

Some of the established centres had adequate infrastructure, workforce and training, but this is not universal. The Ugandan experience, however, shows that the lack of sophisticated modern equipment should not be a limitation to surgery (Boling et al., 2009, Mandell et al., 2015). Their model utilized technology and expertise that was reasonably available and could function sustainably in an African setting. Training was possible through the establishment of collaborations with neurosurgeons in developed countries. This form of collaboration where expert skill and knowledge were exchanged with centres in HICs was also noted at the Charles Nicolle Hospital in Tunisia (Khiari et al., 2010), Aga Khan University Hospital in Pakistan (Ahmed et al., 2009), and Shiraz University of Medical Sciences in Iran (Asadi-Pooya et al., 2014). The successes of these models were achieved through the tri-facetted approach of technological transfer, twinning, and manpower training (Nayel, 2000). It also showed the role information and communications technology (ICT) can play in intellectual and skills transfer, showing that the model used could be replicated elsewhere using the minimum available requirements more likely to be available in LMIC in comparison to the myriad of equipment used in more affluent societies.

Studies evaluating the costs of surgical versus medical treatment observed that although surgical treatment requires a large initial expenditure it was superior because of the greater seizure-free rate. The long-term cost-analysis favours surgery as the cost-time curves intersect in a few years (Wiebe et al., 1995, Malmgren et al., 1996, Schiltz et al., 2016). Cost-effectiveness of epilepsy surgery in LMIC should be an area for further studies, as analysis from HICs may not simply reflect what obtains in LMICs due to the weak economic capacity of families and health care bills paid out-of-pocket. The benefit of epilepsy surgery to a substantial number of persons in Africa with medically intractable epilepsy may far outweigh the cost, with regards to a transforming

power of a seizure-free life, the capacity to empower a sufferer and the community, restoration of livelihood and the contribution to the local economy. This is because it frees the sufferer, caregiver and family from the economic and social burden (Platt & Sperling, 2002). An important research priority will be to investigate the burden of lesion-related epilepsy and the number of potential surgical candidates within a geographical context, this will provide a means to appropriate and prioritise solutions in locally sustainable ways.

2.6.5 Conclusion

Surgical treatment for epilepsy is available in some LMIC, with an increasing provision in a limited few. Some experiences have shown that epilepsy surgery can be performed within the resource-poor settings through collaboration with international partners. ICT can be an important tool for skill transfer. These collaborations with international partners can provide an opportunity to bring high-quality academic training and technological transfer directly to surgeons and should be encouraged. The high cost of implementing surgery may not be a limitation for some LMIC but rather a problem of deciding how to prioritize and allocate resources (Klein, 1993). The cost of surgery is still a fraction of what is available in HIC. This review acknowledges the current limitation of data acquisition in LMIC and the full information regarding epilepsy surgery may not have been retrieved. The small number operated and varying reporting methods make any reasonable conclusions regarding its definite continued existence difficult. An extended stakeholders meeting was unfortunately not conducted due to lack of funds. This is an iterative work in progress, providing a descriptive and visual presentation of epilepsy surgery in LMICs. These findings will enable stakeholders to identify action areas and to determine where in-depth analysis is required.

Chapter 3: Methodology

The fieldwork was a rural cross-sectional (door-to-door) survey design in three rural communities of Nigeria. An initial pilot study to validate an epilepsy-screening questionnaire translated into the local languages of the three study sites was conducted at the tertiary hospitals in the network of the sites.

3.1 Study Setting

3.1.1 Nigeria

Located in West Africa (latitudes 4 – 14^{O} N and longitudes 2 – 15 ^{O} E); Nigeria is the most highly populated nation in Africa and has a total area of 925,796 km^2. It has varying climatic conditions from dry Sahel weather in the north to rain/mangrove forest in the south (Oguntunde et al., 2011). With over 400 ethnic groups, Nigeria is one of the most culturally diverse country in the world. The three largest ethnic groups are the Hausa, Igbo and Yoruba (Agheyisi, 2015). Most of the population live in rural areas and engage in primary activities such as farming and animal husbandry. There is increasing rural-urban migration due to poverty, poor standards of living and the absence of even primary education and basic amenities (Bah et al., 2003).

This study was conducted in three local government areas (LGAs) of Gwandu, Afikpo, and Oriade (Figure 2). These sites have varying demographic and cultural characteristics. The climate, vegetation, source of water, food and eating habits are different. The rural communities are within the networks of three tertiary hospitals that render neurological and epilepsy services, namely: Usman Dan-Fodio University Teaching Hospital (UDUTH) Sokoto, Northwest region; Federal Teaching Hospital Abakaliki (FETHA), Southeast region; and Obafemi Awolowo University Teaching Hospital Complex (OAUTHC), Ile-Ife, Southwest region. Designated primary healthcare centres (PHCs) within these villages acted as local coordinating centres where subjects were attended to.

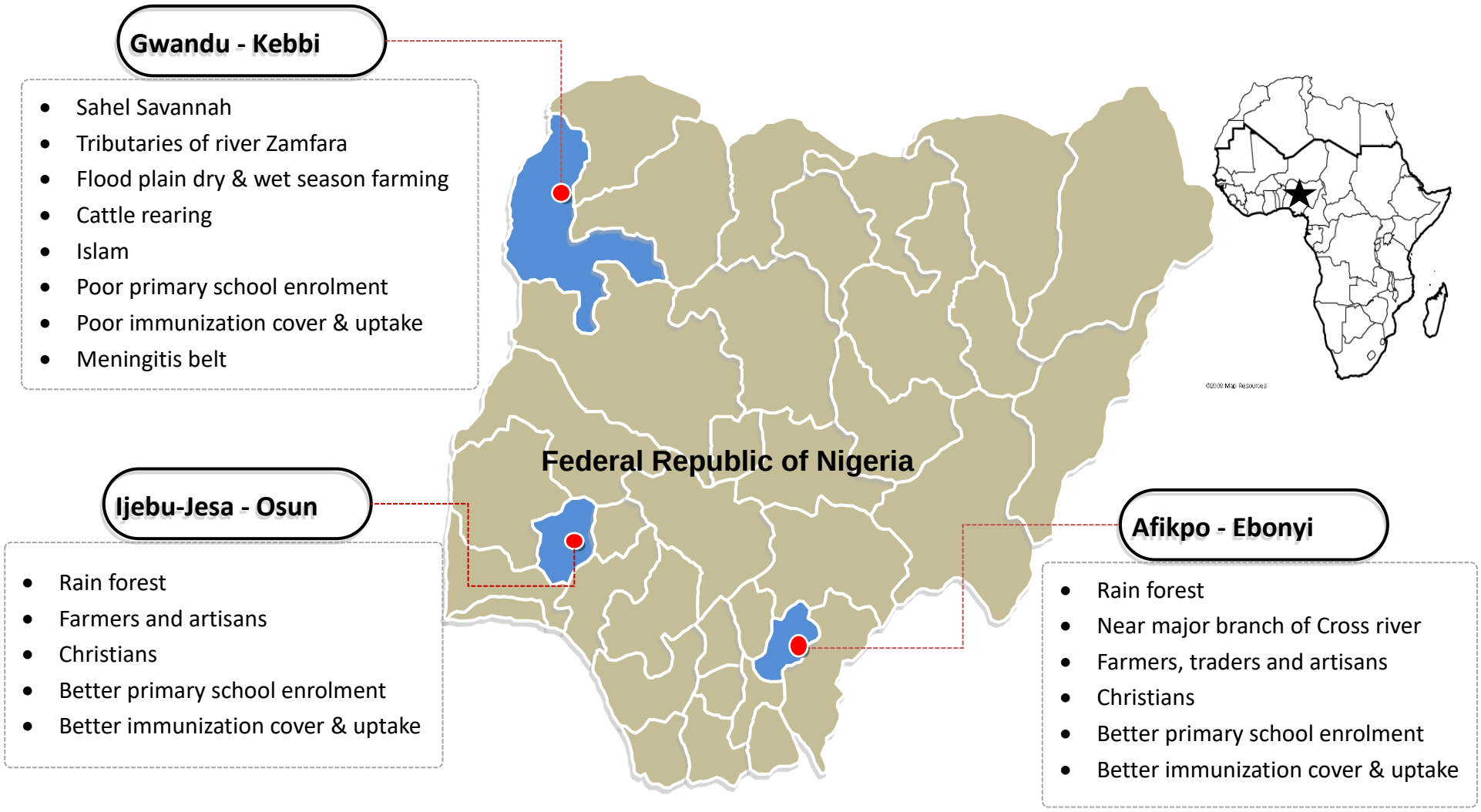


Figure 2: Map of Nigeria showing the sites and summary of their characteristics

These three communities were selected as there is a good collaboration between the team, the local health authorities and the tertiary hospitals. The safety of the environment was considered, avoiding areas with insurgency or civil unrest. The prevalence of epilepsy is unknown in these communities and no information is available regarding epilepsy care.

3.1.2 Gwandu – Kebbi State

Gwandu LGA in Kebbi State Northeast Nigeria covers an area of 1,018 km²; it has 10 wards (Cheberu, Dalijan, Dodoru, Gulmare, Gwandu Marafa, Gwandu Dangidan Galadima, Kambaza, Malissa, Maruda and Masama). It had been designated as a rural outpost of the Usman Danfodio University Sokoto (UDUS) for consanguinity studies (Obembe et al., 2016) and was earmarked to be used as a Health and Demographic Surveillance Site (HDSS). It is located near a branch of the Zamfara River, a tributary of River Sokoto in the Sahel Savannah climatic zone with an average annual temperature of 28.3^{0}C. The rainy season lasts an average of 3 months, usually from June to September (Abdullahi et al., 2013). Kebbi state has a population of about 3.6 million. Gwandu LGA has a population of 151,077 (74,610 males and 76,467 females) according to the 2006 census (http://www.population.gov.ng/). Hausa and Fulani are the main ethnic groups. The main local occupations are cattle rearing and subsistence farming, although recently rice is cultivated in commercial quantity in the State. Sources of water are wells, ponds, seasonal fast flowing rivers, and occasionally boreholes. Health care is provided by PHCs. The Federal Medical Centre Birnin-Kebbi and UDUTH Sokoto serve as major referral centres.

3.1.3 Afikpo – Ebonyi State

Afikpo (also called *Ehugbo*) in Ebonyi state southeast Nigeria is located in a transitional area between open grassland and tropical rain forest zone and temperatures hardly exceed 30^0 C. It has a mean annual rainfall of about 2 meters. It is a rural community inhabited primarily by Igbo speaking people. Ebonyi state has a population of 2.17

million and Afikpo North has an area covering 240km² with a population of 156,611 people (http://www.population.gov.ng/), (Moses & Chinemerem, 2017). The source of water is mainly from the streams, shallow wells and boreholes. Their main occupation is subsistence farming, but also many are artisans and traders. Oha-Isu ward A (with 5 contiguous communities – Amangbala, Amachi, Amachara, Ngodo and Ukpa) and Nkpoghoro ward (with 7 contiguous communities – Ndibe, Amankwo, Amaobolobo, Amauzu, Amaoku, Amangwu and Amaekwu) were randomly selected from a total of 4 wards in Afikpo North LGA. These communities are located next to the major branch of the Cross river. Nkpoghoro has a population of about 12,947 from 3,684 households, while Ohaisu ward A has a population of 12,955 from 2,681 households. Health care is provided by PHCs. The FETHA and other general hospitals serve as referral centres.

3.1.4 Ijebu-Jesa – Osun State

The Yoruba predominantly populate Ijebu-Jesa in Oriade local Government Area (LGA). With a population of 3.42 million, it is situated in the tropical rain forest zone of Osun state Southwest Nigeria. It is mainly an agrarian society. Source of water is either from wells, boreholes or streams. The population of the local government is about 148,379, with an average coverage area of 465 km² (Kayode, 2010). Ijebu-Jesa community is located within the Oriade HDSS as one of the International Network for the Demographic Evaluation of Populations and Their Health (INDEPTH) and overseen by the Obafemi Awolowo University (OAU) Ile-Ife, with the aim of providing data on trends and causes of under-5 mortality (Sankoh & Byass, 2012, Utazi et al., 2018). The demographic health survey conducted about six years ago by the Public Health Department of OAU reported a total population of 7,398 (3,460 males and 3,938 females) enumerated from 2,198 households in Ijebu Jesa. The Oriade HDSS is, however, poorly represented and less active and censuses have not been recently updated (Utazi et al., 2018). Health care for these areas is provided by nearby primary health care facilities and general hospitals, while tertiary care is provided by OAUTH in Ile-Ife town and the Wesley Guild Hospital in Ilesa.

3.1.5 Health care delivery in Nigeria

Health care is shared among the three tiers of government. The Federal Government handles tertiary healthcare (Teaching Hospitals and Federal Medical Centres), State Governments the secondary healthcare (General and District Hospitals), and the PHC by the Local Governments. Many factors contribute to the poor health indices in Nigeria (Table 8), these include poor health structure, very low health budget, lack of human resources, unequal economic relations, corruption, illiteracy, high out-of-pocket costs, poor access to health care, and shortage of essential drugs (Timothy et al., 2014).

Table 8: Nigeria key health indicators	Value
Population (million)[a]	182
Those below the poverty level ($1.25/day) (2011)	54.4%
Total expenditure on health as a percentage of GDP (2014)	3.67%
Physicians density (per 1,000 population) (2009)	0.38
Nursing and midwifery personnel density (per 1,000 population) (2008)	1.49
Neonatal mortality rate (per 1,000 live births) (2015)	34.3
Under-five mortality rate (per 1,000 live births) (2015)	108.8
Maternal mortality ratio (per 100,000 live births) (2015)	814
Population using improved drinking-water sources (2015)	68.5%
Diphteria, Pertussis and Tetanus immunisation coverage (1-year-olds) (2017)	42.0%
Population using improved sanitation facilities (2015)	29.0%
Life expectancy at birth (2015)	54.5 years
Births attended by skilled health personnel (2013)	35.2%
Literacy rate among adults aged ≥ 15 years (2007-2012)	61%
National Health Insurance Scheme (NHIS) coverage [b]	3%

[a]http://www.population.gov.ng/, all data from WHO country key indicators: [b](Dutta & Hongoro, 2013)

Over the decades, there has not been any remarkable improvement in the health indicators. The health budget is still poor. The total expenditure on health as a percentage of GDP was 2.64% in 2000, in 2015 it was 3.56%, which is below the

average for sub-Saharan Africa of 5.34% (Oni, 2014). The shortage of doctors and health care personnel are recognised as a major problem facing the Nigerian health care system. 'Brain-drain' has resulted in half of its doctors practising in Europe and North America. The doctors remaining in Nigeria are poorly remunerated and unequally distributed, with most concentrating in cities where healthcare facilities and basic amenities are more likely to be available. This inequity is largely a result of the government's level of involvement and investment in health care programmes and education (Audu et al., 2013). The actual number of qualified neurologists is not known, but they may be about one hundred, including neurology registrars. There is practically no government policy on epilepsy. The social stigma associated with epilepsy and the failures of the government to appreciate the burden of epilepsy are some of the reasons contributing to the lack of epilepsy services. Besides the availability and cost of ASMs have hindered people with epilepsy being on treatment.

3.2 The Rural Survey

Most epilepsy surveys to determine the prevalence and other epidemiological characteristics follow a two-stage process of initial screening followed by a detailed review to exclude false positives (Placencia et al., 1992). The survey was, therefore, a rural prospective cross-sectional (door-to-door) design in three rural communities. The success of the initial process depends on the accuracy of the measuring instrument (screening questionnaire). This is determined by the proper translation and validation in culturally relevant terms. Development, translation and validation of screening questionnaires were developed before the survey commenced.

3.2.1 Pre-study consultations, Key personnel and Training of enumerators

Before commencing the rural survey, traditional and religious leaders were consulted and approval for the smooth running of the project was sought. This is important in an African setting where people will not participate in any project without the prior permission of their local leaders. Community health workers working in the same

communities were employed to conduct the door-to-door census, particularly those who have participated in previous community-based studies or immunisation programmes as they had more experience with community-based health programmes. They understand the common terminologies, cultural practices, and behaviours to help in approaching the communities. Before the commencement of the rural survey, a two-day training workshop was undertaken for the study personnel using a training manual (For further details of what the training sessions entails, see training manual in Appendix 3). Due to the logistic difficulty of conducting one training session for the three sites, individual sessions were held at each site. The principal investigator had to travel between sites and was present at all the training sessions and commencement of the censuses to ensure uniformity between sites.

3.2.2 Estimated sample size calculation to be screened

Using the EpiTools epidemiological calculator the sample size was found to be 4,364 (see Table 9). For convenience the sample size was doubled to screen at least 10,000 from each site, that is approximately 2,000 households from each site using an average Nigerian household size of six persons (Pfitzner et al., 1998).

Table 9: Estimated sample size output using EpiTools calculator

Inputs	
Assumed true prevalence	**0.01**
Sensitivity	**0.8**
Specificity	**0.8**
Desired precision	**0.02**
Confidence interval	**0.95**
Sample size	**4364**

http://epitools.ausvet.com.au/content.php?page=PrevalenceSS&HTP=0.01&HSENS=0.8&HSPEC=0.8&Precision=0.02&Conf=0.95

3.2.3 Census

The current projected population figures may not be reliable as the last census was conducted in 2006. A household census was therefore conducted to get a reliable denominator. The census was done alongside the door-to-door epilepsy screening to save cost; using a simple census form (Appendix 4) to collect information on the number of persons in each household, their age and gender. The household unique identification numbering system of the National Population Commission (NPC) or the polio eradication immunization/immunization plus days (PEI/IPDs) census was used to identify them.

3.2.4 Recruitment of study participants from the rural door-to-door survey

The list of households and starting point of the respective wards and settlements used for the survey was obtained from the enumeration area (EA) maps. The screening began by asking the household head or the next senior member of each household if any member has had a history suggestive of a seizure using the epilepsy-screening questionnaire. This methodology of asking the household head has been used in a previous study (Ngugi et al., 2012). This is important for cultural and religious reasons in Nigeria. Any member screening positive in the first stage was given a referral slip (Appendix 5) to attend a health facility where they underwent a second stage consultation and diagnostic interview by the physicians. Subjects to be recruited are those six years and above with "*active epilepsy*". Those below six years of age were excluded to reliably exclude those with febrile seizures (Burton et al., 2012). "*Epilepsy*" was defined based on the International League Against Epilepsy (ILAE) (Thurman et al., 2011). Those with single cluster or solitary episode of epileptic seizure(s), less than six years of age, febrile seizures only, seizures associated with an acute systemic, metabolic, vascular or toxic injury were excluded. To promote consistency in definitions, classification and methods, and to facilitate comparison with other population-based studies, definitions were based on the ILAE commission report on the standards for epidemiologic studies and surveillance of epilepsy (Thurman et al., 2011)

(See Table 10 for the definition of terms). Classification of seizure and epilepsy types was based on the revised version of the ILAE's Commission for Classification and Terminology (Fisher et al., 2017).

Table 10: Definition of terminologies used in this work

Epilepsy	A brain disorder characterised by two or more unprovoked (or reflex) seizures occurring >24 h apart (Fisher et al., 2014).
Seizure	Transient signs and/or symptoms from an abnormal excessive or hypersynchronous neuronal activity in the brain.
Active epilepsy	Unprovoked seizures occurring in the last one year or currently on antiseizure medication (Thurman et al., 2011).
Focal epilepsy	Seizure with a focal onset, manifesting as seizure ab-initio starting from a body part.
Generalised epilepsy	Seizures involving the entire body ab-initio. Originating within and rapidly engage bilateral distributed networks. Although focal onset may rapidly engage bilateral networks.
Febrile seizures	Defined as seizures associated with a high fever between the ages of 6 months and 5 years (Capovilla et al., 2009).
Status epilepticus	Seizures lasting more than 30 min or a succession of seizures without full recovery of consciousness (Trinka et al., 2015).
Prevalence	The proportion of the population with a condition of interest at a particular point in time (Thurman et al., 2011).
Incidence	The number of new cases of a particular condition occurring in a population over a specified period (Thurman et al., 2011).
Treatment gap	Defined as the number of people with active epilepsy not on treatment or not appropriately treated divided by the total number of those with active epilepsy. This includes therapeutic and diagnostic gap (Meinardi et al., 2001).
Therapeutic gap	Those not on treatment or adherent based on the prescribed regimen (Mbuba et al., 2012b).
Diagnostic gap	The percentage of those not diagnosed by a physician or a trained health worker divided by the total number of those with active epilepsy (Mbuba et al., 2012b).
Adherence	Defined as the extent to which a person follows the recommendations given by a health care provider (Kenreigh & Wagner, 2005).

A structured epilepsy questionnaire was administered to those screening positive and confirmed to have epilepsy (Appendix 6). The questionnaire was modified from 'Questionnaire for Investigation of Epilepsy in Tropical Countries' developed by the Institute of Neurological Epidemiology and Tropical Neurology of Limoges France, the Pan-African Association of Neurological Sciences and the ILAE for standardizing epilepsy study in tropical countries (Preux, 2002). If the individual was a child or a cognitively impaired adult, a next of kin or caregiver was interviewed. All answers to questions were recorded on the copies of the questionnaire along with study identification numbers. The main survey was conducted during the dry season and after harvest, a time when rural dwellers were less busy. Details of the methodology of the screening exercise, prevalence study, treatment gap, and risk factors are described in their respective chapters.

Figure 3 shows the timescales and dates of the major activities of the study.

3.2.5 Statistical Analysis

All the census data were entered into Microsoft Excel 2010. The prevalence and incidence data were calculated using the *R epitools* epidemiological calculators (R Core Team, 2013). All other analyses were done using STATA (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). The detail of each statistical method used is described in each chapter.

3.3 Physician's perspective about epilepsy care in Nigeria

This was a questionnaire-based descriptive study to acquire information from physicians (mainly psychiatrists and neurologists) attending their professional annual meetings. The questionnaire (Appendix 7) was developed to get general background information on epilepsy care in Nigeria. Statistical analyses were mainly descriptive.

3.4 Ethical issues

The UCL ethics committee and the Nigerian National Health and Research Ethics Committee (NHREC) approved the study protocol, consent forms, and questionnaires (copies of the ethical approvals in Appendix 8). An information sheet (Appendix 9) that sets out what the research entails was provided for the participants. Written informed consent for adults or a modified assent form for children (Appendix 10) was obtained from the subjects or next of kin. All aspects of the study were conducted according to the declaration of Helsinki (Carlson et al., 2004).

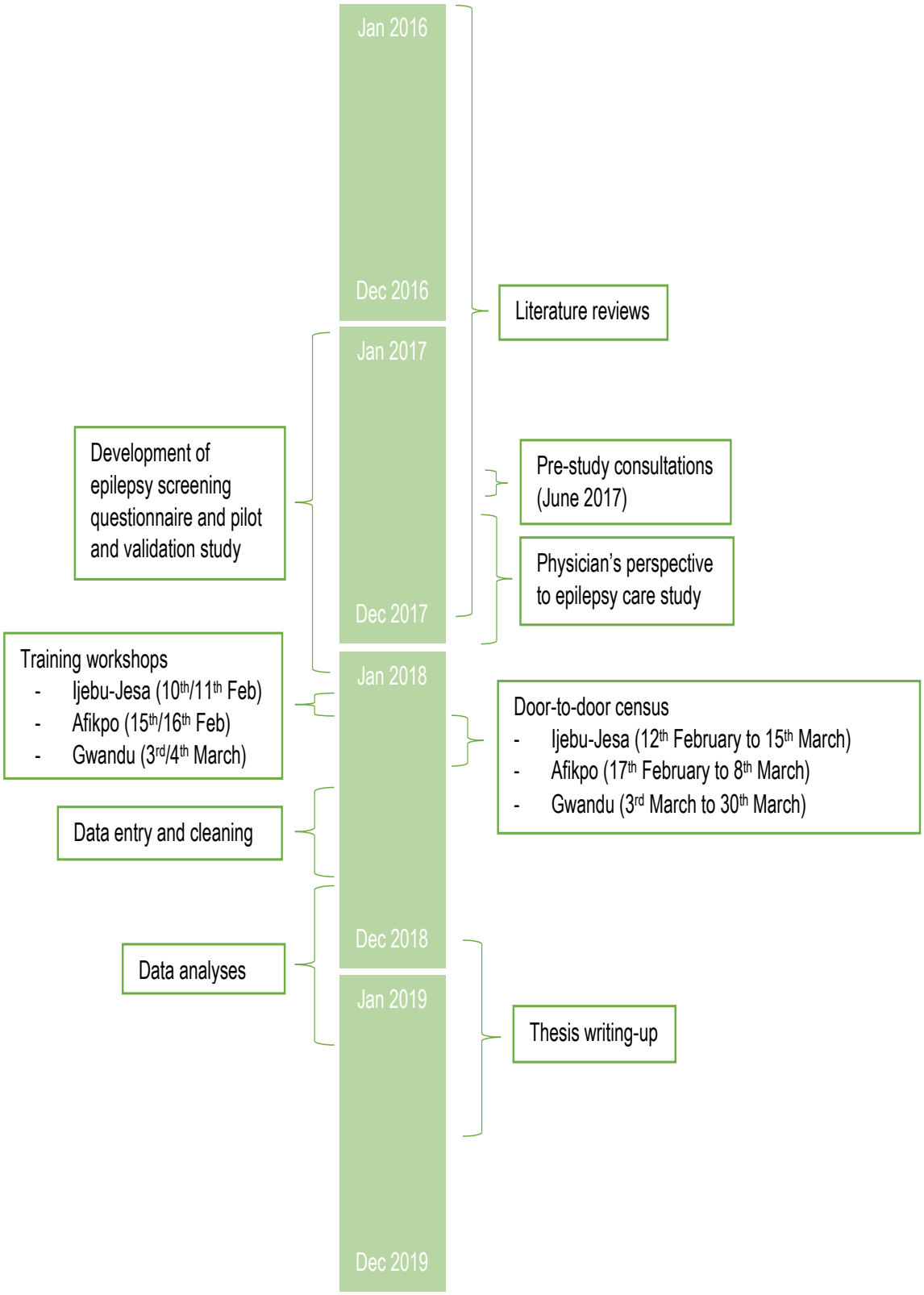


Figure 3: Timescales and dates of the project

Chapter 4: The epilepsy screening questionnaire and validation study

4.1 Abstract

Background: The success of an epilepsy screening survey critically depends on a well-translated and validated tool in the local language. This study describes the development, translation and validation of an epilepsy-screening questionnaire in three Nigerian languages, Hausa, Igbo and Yoruba. **Methods:** A 9-item epilepsy-screening questionnaire was developed with modifications from previously validated questionnaires. Multilingual experts translated the nine questions into the three languages using the forwards- and backwards-translation method. The translations were further discussed with fieldworkers and lay members of the community for ethnolinguistic acceptability and comprehension. An unmatched affected-case versus unaffected-control design for the pilot study was used. Cases recruited were people confirmed to have epilepsy by a neurologist attending the outpatient's departments of tertiary hospitals from three regions of Nigeria where these languages are spoken, while controls were subjects attending clinics for other medical conditions and patient's relatives who did not have epilepsy. **Results:** From the three regions, 153 (75 cases and 78 controls), 106 (45 cases and 61 controls) and 153 (66 cases and 87 controls) subjects were recruited for the Hausa, Igbo and Yoruba questionnaires respectively. Based on the affirmative response to any of the nine questions having a positive diagnosis of epilepsy; the Hausa questionnaire had a sensitivity of 97.3%, a specificity of 88.5%, positive predictive value (PPV) of 85.9% and negative predictive value (NPV) of 97.1%. The Igbo version had a sensitivity of 91.1%, a specificity of 88.5%, PPV of 85.4% and NPV of 93.1%, while the Yoruba version had a sensitivity of 93.9%, a specificity of 86.7%, PPV of 87.3% and NPV of 95.1%. **Conclusion:** A translated and validated epilepsy screening questionnaires in three Nigerian languages to be used for

community-based epilepsy survey is presented here. They will be a useful tool for epilepsy surveys in Nigeria and can further be developed for other Nigerian languages.

Keyword: Epilepsy, Screening, Questionnaire, Validation, Sensitivity, Specificity, Survey.

4.2 Introduction

The ability to acquire quality epidemiological data depends on a well planned and designed study; which is influenced by the population of interest, methodological design, the screening tool, collaborative partnerships, and involvement of the community and resources available (Israel et al., 1998). In HICs methods like electronic healthcare and insurance databases, postal mails, internet, telephones, apps and social media are increasingly being used for health surveys (O'Mahony et al., 1995, Sheehan, 2001, Edwards et al., 2002, Curtin et al., 2005). In LMICs however, door-to-door surveys are still relied on as a valuable tool for collecting health-related data due to lack of infrastructures and poor literacy among the population (Hillier et al., 2014). Despite the drawbacks like cost, their intrusive nature, the dangers posed to interviewers and the issue of negotiating doorstep access (Hazel & Clark, 2013); the WHO recognises door-to-door survey as an important method for recruiting participants for health surveys particularly in rural communities (WHO, 2002). It also has the advantage of offering an ethnographic complement to interviews. The preparation for and the subsequent face-to-face interviews in a door-to-door survey offers the opportunity to spend time with residents, understand their cultures, customs and mutual habits, and discussing their concerns and suggestions gives them a sense of responsibility of being integral to the research. This ethnographic complement which is often overlooked contributes to the quality of the data (Hillier et al., 2014).

The door-to-door method usually utilises a two-stage approach for epilepsy screening. The first stage commonly uses a simple screening tool to identify people suspected to have epilepsy in the community, administered by purpose-trained lay field staff and

followed by a second stage requiring a more detailed diagnosis by qualified personnel (Placencia et al., 1992). The entire exercise is purely clinical and does not require any specific investigation. The success of this approach depends on a sensitive screening questionnaire, a concise diagnostic criterion and an appropriate reference population (Sander & Shorvon, 1987, Placencia et al., 1992).

The degree to which a questionnaire produces quality data is determined by its design, accuracy and how well it is administered (Boynton & Greenhalgh, 2004). As with all diagnostic tests, there should be a balance between sensitivity and specificity, in addition to their predictive values. This will help ensure its ability to detect those with the condition of interest in sufficient numbers and at an acceptable cost (Boynton, 2004). A systematic review estimating the sensitivity and specificity of non-physician administered epilepsy questionnaires, found that validity depends on multiple factors in time and space and noted that the included studies had wide variation in the application of reference standards, definitions of epilepsy and high risk of bias in patient selection (Keezer et al., 2014). An important characteristic of a good questionnaire is that it must be in the native language of the respondents or at least a language that the majority of responders fully understand. It should be easy to comprehend and concise (Boynton & Greenhalgh, 2004), as too many questions put off a responder (Placencia et al., 1992). A proper translation of the screening tool uses the forward- and back-translations following set guidelines (Cramer et al., 1998, Nieuwenhuijsen, 2005). Since stigma and perception are of concern in studies involving epilepsy in SSA, questionnaires must take into account psychosocial influences. Ethnolinguistic issues must be considered important as meaning, perceptions and clinical manifestations of epilepsy vary within communities (Sander & Shorvon, 1987, Cramer et al., 1998). To develop a reliable and uniform screening tool for epilepsy in Nigeria; a screening questionnaire must be translated into the local languages. Nigeria has about 400 diverse ethnic groups and languages (Agheyisi, 2015) but 70% of the population people speak at least one of the three most popular

languages of Hausa, Igbo, or Yoruba. Hausa is widely spoken in the North, Igbo in the Southeast and Yoruba in the Southwest regions. A multi-lingual tool will be useful in reaching the majority of our target population in a multi-site study.

Apart from designing and translating a questionnaire, a pilot study among a representative sample of the target population will help determine its accuracy. The piloting process establishes the degree of accuracy by essentially identifying potential problems with the design or comprehension of the questionnaire. It determines if questions are ambiguous and need to be rephrased into a culturally acceptable format (Placencia et al., 1992, Tsang et al., 2017). At present, there are no standardised questionnaires for epilepsy in any of the major Nigerian languages. The few epilepsy surveys conducted in Nigeria reported using previously validated questionnaires (Osuntokun et al., 1982, Osuntokun et al., 1987a, Osakwe et al., 2014, Mustapha et al., 2014, Ezeala-Adikaibe et al., 2016). The southeast Nigerian study reported validating an Igbo epilepsy-screening questionnaire limited by small sample size (Ezeala-Adikaibe et al., 2016). It is, however, unclear if other studies translated and validated the questionnaires in the local languages. This chapter describes the development, translation and validation of an epilepsy screening questionnaire in three of the major Nigerian languages using set guidelines (Tsang et al., 2017), with the aim of having a standard screening tool for community-based prevalence study in Nigeria.

4.3 Methodology

4.3.1 Development of the epilepsy screening questionnaire

A screening questionnaire was developed using evidence from a systematic review of the diagnostic accuracy of epilepsy screening questionnaires as a guide (Keezer et al., 2014). Of the questionnaires pooled from this systematic review, the Ecuadorian epilepsy survey (Placencia et al., 1992) and the Rochester study (Ottman et al., 2010) were considered to be the most adaptable to our community. The questions were discussed and rated by collaborators from the three regions of Nigeria. A 9-item questionnaire (Table 11) was developed from the modification of these two versions.

The Ecuadorian questionnaire or a modified version has questions that deal with convulsive and non-convulsive epilepsy and has been widely used in SSA (Birbeck & Kalichi, 2004, Winkler et al., 2009b, Ngugi et al., 2013a). The order of the questions was rearranged, to begin with questions relating to clinical manifestations rather than direct inquiry of having been diagnosed with epilepsy, primarily for sociocultural reasons. If the diagnosis of epilepsy is mentioned first, many respondents may not want to proceed for stigma reasons. The questions were compiled to capture and detect other seizure types and not just generalised convulsive seizures.

Table : The 9-item epilepsy screening questions

	Questions	Yes	No
Q1	Have you or anyone in this household ever had attacks of twitching, jerking or shaking of the arms or legs which you/they could not control?		
Q2	Have you or anyone in this household ever lost consciousness; or fallen and become pale?		
Q3	Have you or anyone in this household ever had attacks in which you/they fall and bite your tongue?		
Q4	Have you or anyone in this household ever had attacks in which you/they fall and lose control of your/their bladder?		
Q5	Have you or anyone in this household ever had brief attacks of shaking or trembling in one arm or leg, or face?		
Q6	Have you or anyone in this household ever had attacks in which you/they lose contact with your/their surroundings and experience abnormal smells?		
Q7	Did you or anyone in this household when you/they were a small child, daydream or stare into space more than other children?		
Q8	Shortly after waking up, either in the morning or after a nap have you or anyone in this household ever noticed uncontrolled jerking or clumsiness, such as dropping things or things suddenly “flying” from your/their hands?		
Q9	Have you or anyone in this household ever been told that you/they have or have had epilepsy or epileptic fits, or have taken medication for seizures/epilepsy?		
The questions will be answered as ‘No’ or ‘Yes’ with a tick (✓).			

4.3.2 Translation of the screening questionnaire to the local languages

The screening questionnaire was translated into Igbo, Hausa and Yoruba. It was forward- and back-translated, following the published guidance on the translation of questionnaires to ensure that the meaning remains the same (Nieuwenhuijsen, 2005). For the translations and to better reflect the nuances of the target languages we involved bilingual individuals, fluent native speakers, have spent a considerable number of years in those regions where these languages are widely spoken and have an idea of sociocultural characteristics of the target population. This is to ensure that each translation would be culturally acceptable for each of those regions.

4.3.2.1 The Igbo questionnaire

The initial forward-translation was done independently by Dr Henry Chima Emeanwu (a medical officer who reads and writes Igbo) and back-translated by Dr Obiora Eneanya (a Public Health PhD student at Imperial College London who has been involved in community-based research and translations). Concurrently, the questionnaire was forwards- and backwards-translated by a team who have experience in medical translations and community-based research at FETHA, Ebonyi State. Dr Stanley Igwe together with another consultant psychiatrist at FETHA discussed on the two versions to get an initial translation. The initial draft was also discussed with a language and linguistics lecturer at the Ebonyi State University to deal with discrepancies and to develop a final draft that is generally understood.

4.3.2.2 The Yoruba version

Dr Sunday Jagun a medical officer in Ibadan who had been involved with researching Yoruba speaking people did the initial forward-translation and Janet Olufomilayo an anatomy graduate did backward translation. Dr Olaitan Okunoye an MSc clinical neurology student and a native Yoruba speaker independently reviewed the initial translation. Concurrently, the questionnaire was sent to the Department of Public Health OAUTHC Ile-Ife, Osun State where an independent forward- and backwards-

translation was conducted. The department has a professional team with experience in translation of questionnaires. The two versions were further analysed by two consultant Neurologists – Professor Morenikeji Komolafe and Dr Fawale Michael to produce a final draft. Both are collaborators in this study and have several years of experience in neurology and epilepsy research among the Yoruba people.

4.3.2.3 The Hausa version

The first forward- and back-translation was done by the Department of Community Medicine UDUTH in collaboration with the Department of Language and Linguistics. The departments have a vast experience in translation of medically related questionnaires. Dr Salisu Balarabe did another independent translation, while Dr Ibrahim Gezawa (a consultant physician from Aminu Kano Teaching Hospital, Kano) and Ms Amina Wakili (a library science graduate) did the back-translations. The author and Dr Balarabe to get a final draft discussed the two versions.

Before the variously translated questionnaires were piloted, all the individual questions were compared with the original English version. A form of a cognitive interview for the questionnaire was done, where the research team and community health workers for linguistic anomalies and sociocultural issues discussed the individual questions in detail. Discussions were also made with elderly members of the communities for ethnographic considerations.

4.3.3 Pilot study to validate the screening questionnaire

The validation was an unmatched affected-case versus unaffected control study design, with the diagnosis by a neurologist as the gold standard. The sample size for the pilot study was calculated to demonstrate a sensitivity of 80% and a precision of 10%; which gave a sample size of 61 cases and 61 controls. The cases were recruited consecutively from the neurology clinics or attending EEG test at the Federal Neuropsychiatric Hospital Kware and UDUTH Sokoto for the Hausa version; FETHA Abakiliki for the Igbo version and OAUTHC and the Wesley Guild Hospital for the

Yoruba version. The cases were people confirmed by a neurologist to have epilepsy, defined as those who had two or more unprovoked epileptic seizures separated by >24 hours (Fisher et al., 2014). The controls were consecutively recruited as unmatched non-affected healthy volunteers attending hospitals for other purposes or healthy relatives who had never had a seizure in their lifetime. The cases and controls were from the same geographic location and ethnicity. Questionnaires were administered in-person by trained nurses and research assistants, after obtaining informed consent. The nurses and research assistants were not blinded to the diagnosis.

The entire study (translation and validation) was conducted between January 2017 and January 2018.

Statistical analysis: Data were entered into Microsoft Excel 2010and statistical analysis was performed using Stata version 15 (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). A chi-squared test was used to compare categorical variables and Mann-Whitney U test for continuous variables between the cases and the controls, after using a Sharipo-Wilk test to check for normality. Using a two-by-two table, the "*diagti*" command in Stata was used to calculate the diagnostic tests (Seed, 2010). These include the sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) and their 95% confidence intervals for the individual questions and the entire questionnaire (see Table 12 for the definition of terms and Table 13 for the formulae for calculating the measures of accuracy). A highly sensitive test helps "rule out" a diagnosis, while a highly specific test helps "rule in" a diagnosis. PPV is particularly relevant in evaluating the ability of a screening test to identify disease in healthy populations (Akobeng, 2007, Altman & Bland, 1994). The kappa statistic (κ) was calculated to examine the level of agreement between different combinations of screening questions and a clinical diagnosis of epilepsy (Table 14). The strength of agreement was interpreted using Altman's Kappa Benchmark Scale (Altman, 1991).

Table 12: Definition of terms for measures of accuracy

Sensitivity	The proportion of people with the disease who are positive on the test.
Specificity	The proportion of subjects without the disease who are negative on the test.
PPV	The probability that a person with a positive result actually has the disease.
NPV	The probability that a person with a negative result does not have the disease.
Validity	The degree to which an instrument measures what is intended to be measured and reflects the instrument's generalisability.
Reliability	The extent to which instrument's results are stable and consistent, concerned mainly with repeatability.
Precision	The ability of an instrument to have repeated measurements close to each other.
Accuracy	The degree to which the result of an instrument conforms to the correct value or a standard. It is also how close repeated measurement is to the 'true' value.
Validation	It is the process of collecting and analysing data to assess the accuracy of an instrument.

PPV – Positive predictive value, NPV – Negative predictive value. Definitions from (Altman & Bland, 1994, Akobeng, 2007, Taherdoost, 2016)

Table 13: Formulae for calculating the accuracy of a screening tool

		Epilepsy Present		**Total**
		Cases	Controls	
Screening result	Positive	TP	FP	TP + FP
	Negative	FN	TN	FN + TN
Total		TP + FN	FP + TN	

$$\boldsymbol{Sensitivity} = \frac{TP}{TP+FN},$$

$$\boldsymbol{Specificity} = \frac{TN}{TN+FP},$$

$$\boldsymbol{Positive\ predictive\ value} = \frac{TP}{TP+FP},$$

$$\boldsymbol{Negative\ predictive\ value} = \frac{TN}{TN+FN}$$

TP = True positive, FP = False positive, FN = False negative, TN = True negative

Table 14: Interpretation of kappa statistics

Value of κ	**Strength of agreement**
<0.20	Poor
0.21 – 0.40	Fair
0.41 – 0.60	Moderate
0.61 – 0.80	Good
0.81 – 1.00	Very good

4.4 Results

4.4.1 Translations

4.4.1.1 The Hausa version of the questionnaire

The general Hausa was adopted for the translation; the majority of people in Northern Nigeria understands this version and the Sokoto/Kebbi States dialect was also considered in the translation. Some difficulties were encountered translating Q2 “Have you or anyone in this household ever lost consciousness, or fallen and become pale?” The word ‘loss of unconsciousness’ is not a very clear term in Hausa, as it usually means “*fitan hankali*” – which can also mean loss of cognition. Most people use “*suma*” to mean a loss in consciousness, but it could also mean syncope or any brief loss of awareness. It was decided that “*dogon suma*” (“*dogon*” means “longer”) which is commonly used as a longer unconsciousness (usually a few minutes) will be more appropriate to closely reflect unconsciousness associated with epilepsy. The word “pale” appeared ambiguous and difficult to understand and thought that it may not be useful to add it, as paleness in people with darker skins is more difficult to observe. It is possible, however, for some to understand paleness as “*fari fat*”. After some debate it was decided that it should read “*Ka/Kin taba fadi ko ka/kin yi dogon suma kuma sai jiki yayi fari fat?*” Translating Q6 “Have you or anyone in this household ever had attacks in which you/they lose contact with your/their surroundings and experience abnormal smells?” was a bit problematic as in Hausa an “abnormal smell” could either be unpleasant (“*wari*”) or pleasant (“*kamshi*”) and both mean different things so we decided that both types of smells should be used. In Q9 the word “seizures” can be translated as “*bugun tsunsu*” meaning the “shaking of the bird” for example, the seizure-like activity a dying chicken/bird manifest after slaughtering. The other word “*farfadiya*” is a more common term for epilepsy or seizure disorder. The Hausa language does not use ‘neuter gender’; for example, “*ka*” means “you” for a male, “*kin*” means “you” for a female, these differences were used in various questions.

4.4.1.2 The Igbo version of the questionnaire

The Igbo version was developed using the 'general Igbo' that is understood by the majority. Even though the Afikpo version of the Igbo language has some dialectical differences from the general Igbo, Afikpo people understand the central Igbo language and hence no modification was required. In the translation process; some English words could not be translated with a single word and therefore were described with a phrase. For example in Q2, *"…has anyone lost consciousness…"*? The word 'loss of consciousness' was translated descriptively with the phrase "*amatazigi gburugburu ebe ino*", since no single Igbo word completely describes it. There were no separate words for terms like seizures, convulsions and epilepsy. The Igbo term for convulsion irrespective of any aetiology is generally referred to as "*ihe odido*", while epilepsy specifically is referred to as "*oria ihe odido*" or "*akwukwu"*. The word "*akwukwu"* was preferred and used for Q9. To portray the meaning of "abnormal smells"; the word "*isi ojoo*'' was used, which means "bad odour", the "bad" signify "abnormal". In Q7 "staring into space" was difficult to translate, to imply similar meaning in Igbo, the phrase "*ile anya puru iche*" was used. In Q5 the "shaking of the arm, leg or face" was translated "*aka ima jijiji*", this may describe any tremulous medical condition such as essential tremor and Parkinson disease. In Igbo writing, accents and diacritical signs are often used, these glyphs were difficult to type using a Word document, so we added them manually after typing. The research assistant and enumerators were trained on how to recognise the glyphs.

4.4.1.3 The Yoruba version of the questionnaire

The translation was made using generally spoken Yoruba which the people of Ijebu-Jesa understand and speak, so no modifications of words or expressions were needed to reflect meaning. In Q1, the three terms "twitching, jerking or shaking" are closely related and no separate Yoruba translations could be found for each. A single Yoruba word, *"ngbon-riri"* was used for the 3 words which means "shaking". The word "attacks" in Q1 was difficult to translate and may have several negative connotations. This was

translated as "*ikolu*", which means "illness" or "bodily problem". This seems to help carry the meaning, although it may give an impression of a long-standing medical disorder, but not necessarily a paroxysmal event. The words "loss of consciousness" in Q2 were not easily translated in Yoruba but explained. The Yoruba word "*daku*" was used which means "lost consciousness". A sentence that has "loss of consciousness" will need to be rephrased such that "*daku*" can be used to reflect the meaning, as the word also means a "faint" or "syncope" or any form of unconsciousness. In Q6 "abnormal smell" was translated "*oorun* (smell) *abami* (strange or abnormal)" which means strange smell. The word "*abami*" corresponds to "strange" rather than to "abnormal". An alternative word "*ajeji*" also means strange or abnormal but "*abami*" was used as it was thought to be more appropriate in the context of a seizure. The phrase "stare into space" in Q7 was difficult to translate; if the literal translation is used, it will just mean "looking into the sky". The words *"wo bọọn*", which means more like to gawk or stare without purpose was used. In Q8, a Yoruba word that translates the word "clumsiness" was not found. A closer explanatory phrase *"wa ni airorun"* which means "not at ease" or "uneasiness" was used instead. This did not change significantly the overall meaning of the sentence. "Shortly after waking up, either in the morning or after a nap" in Q8 was translated *"nigbati o ji lati oju orun, yala ni aaro ni abi ni osan"* which literally means "after waking up from sleep, either in the morning or afternoon". We used "afternoon sleep" since no term for "nap" exists. In Q9, epilepsy was translated *"aisan giri"* which means "convulsive disorder". Another term *"warapa",* which refers to recurrent generalized convulsive seizures in the Yoruba language, was avoided due to the stigma associated with it. People with recurrent generalized convulsive seizures and their families avoid being associated with this term and can deny having epilepsy if used in the survey. The Yoruba language often uses accents and diacritical signs; this alters pronunciation and changes the meaning of words. Some of these diacritical marks on top of vowels (e.g. e, é and è) which determine how they sound were absent. Once someone reads and understands Yoruba well, they can understand how the

words sound even without the glyphs. These omissions were taken into cognisance when the research assistant and enumerators were trained.

Final versions of the questionnaires in the three languages are provided in Appendix 11.

4.4.2 Pilot Study

The Shapiro-Wilk test for normality shows that the age of those recruited was skewed.

Table 15 provides the demographic features of subjects recruited for the validation study. A total of 153 subjects (75 cases and 78 controls) were recruited from FNPH Kware and UDUTH for the Hausa questionnaire (42 cases and 45 controls recruited from FNPH Kware, and 33 cases and 33 controls from UDUTH). The cases were significantly older than controls (Mann Whitney U test: $z = 3.175$, $P = 0.0015$), but no significant gender difference ($\chi2$ (1) = 2.3248, $P = 0.127$). For the Igbo questionnaire 106 subjects (45 cases and 61 controls) were recruited from FETHA, with no significant age (Mann Whitney U test: $z = 1.184$, $P = 0.2363$) or gender differences ($\chi2$ (1) = 0.8536, $P = 0.356$). While 153 subjects (66 cases and 87 controls) were recruited from OAUTHC Ile-Ife and the Wesley Guild Hospital Ilesha for the Yoruba questionnaire, with no significant age (Mann Whitney U test: $z = 0.740$, $P = 0.4596$) or gender ($\chi2$ (1) = 0.6950, $P = 0.404$) differences between the cases and controls. All the cases recruited in this study were follow-up cases known to have epilepsy. The majority of the controls (81%) were patient relatives, while 19% of the controls were attending the medical clinics for hypertension, headaches, and respiratory complaints. Two subjects with essential tremor and one with Parkinson's disease were observed in our control arm.

Table 15: Summary of subjects recruited for the validation study

	Epilepsy Status	Gender (female)	Mean ± SD (years)	Median (years)	IQR (years)	Range (years)
Sokoto (Hausa)	Total (N=153)	81 (52.9%)	28.1 ± 8.9	26.0	21 – 32	15 – 60
	Cases (n=75)	35 (46.7%)	30.6 ± 9.9	29.0	22 – 39	15 – 59
	Control (n=78)	46 (59.0%)	25.6 ± 7.1	24.0	20 – 28	18 – 60
Ebonyi (Igbo)	Total (N=106)	51 (48.1%)	28.7 ± 10.5	26.0	23 – 29	11 – 76
	Cases (n=45)	24 (53.3%)	32.1 ± 14.7	28.0	21 – 43	11 – 76
	Control (n=61)	27 (44.3%)	26.1 ± 4.7	25.0	24 – 27	19 – 47
Osun (Yoruba)	Total (N=153)	87 (56.9%)	27.5 ± 9.4	25.0	21 – 30	15 – 61
	Cases (n=66)	35 (53.0%)	30.0 ± 13.0	26.0	19 – 35	15 – 61
	Control (n=87)	52 (59.8%)	25.6 ± 4.6	25.0	22 – 29	18 – 35

Recruitment sites are Usmanu Danfodio University Teaching hospital and Federal Neuropsychiatric Kware Sokoto for the Hausa version; Federal Teaching Hospital Abakiliki Ebonyi for the Igbo version; and Obafemi Awolowo University Teaching Hospital Complex and Wesley Guild Hospital Ilesha Osun for the Yoruba version. SD – Standard deviation

The accuracy measures are reported in Table 16. According to the original design, a person who has an affirmative response to any of the questions Q1 to Q9 is said to have a positive diagnosis. For the Hausa questionnaire, only 2 (2.7%) had a negative screen despite having a diagnosis of epilepsy (Q1 to Q9), compared to 11 (14.1%) who were not persons with epilepsy but had a positive screen, resulting in a sensitivity of 97.3%, a specificity of 88.5%, PPV of 85.9% and NPV of 97.1%. For the Igbo version, those who truly had epilepsy but had a negative screen were only 4 (8.9%), compared to 54 (88.5%) who were not persons with epilepsy, with a sensitivity of 91.1%, a specificity of 88.5%, PPV of 85.4% and NPV of 93.1%. For the Yoruba version, only 4 (6.1%) had a negative screen despite having a diagnosis of epilepsy, compared to 9 (10.3%) who were not persons with epilepsy but had a positive screen, resulting in a sensitivity of 93.9%, a specificity of 86.7%, PPV of 87.3% and NPV of 95.1%.

Table 16: Validation results of the epilepsy screening questionnaire in three languages

		Hausa [% (CI)]	**Igbo [% (CI)]**	**Yoruba [% (CI)]**
Question 1	Sensitivity	78.7 (67.7, 87.3)	60.0 (44.3, 74.3)	50.0 (37.4, 62.6)
	Specificity	94.9 (87.4, 98.6)	96.7 (88.7, 99.6)	98.9 (93.8, 100.0)
	PPV	93.7 (84.5, 98.2)	93.1 (77.2,99.2)	97.1 (84.7, 99.9)
	NPV	82.2 (72.7, 89.5)	76.6 (65.6, 85.5)	72.3 (63.3, 80.1)
Question 2	Sensitivity	78.7 (67.7, 87.3)	64.4 (48.8, 78.1)	50.0 (37.4, 62.6)
	Specificity	97.4 (91.0, 99.7)	93.4 (84.1, 98.2)	97.7 (91.9, 99.7)
	PPV	96.7 (88.7, 99.6)	87.9 (71.8, 96.6)	94.3 (80.8, 99.3)
	NPV	82.6 (73.3, 89.7)	78.1 (66.9, 86.9)	72.0 (63.0, 79.9)
Question 3	Sensitivity	54.7 (42.8, 66.2)	46.7 (31.7, 62.1)	43.9 (31.7, 56.7)
	Specificity	98.7 (93.1, 99.9)	98.4 (91.2, 99.9)	97.7 (91.9, 99.7)
	PPV	97.6 (87.4, 99.9)	95.5 (77.2, 99.9)	93.6 (78.6, 99.2)
	NPV	69.6 (59.9, 77.8)	71.4 (60.5, 80.8)	69.7 (60.7, 77.7)
Question 4	Sensitivity	38.7(27.6, 50.6)	42.2 (27.7, 57.9)	50.0 (37.4, 62.6)
	Specificity	96.2 (89.2, 99.2)	95.1 (86.3, 98.9)	98.9 (93.8, 100.0)
	PPV	90.3 (75.0, 98.0)	86.4 (65.1, 97.1)	97.1 (84.7, 99.9)
	NPV	62.0 (52.7, 70.7)	69.1 (58.0, 78.7)	72.3 (63.3, 80.1)
Question 5	Sensitivity	76.0 (64.8, 85.1)	57.8 (42.2, 72.3)	50.0 (37.4, 62.6)
	Specificity	97.4 (91.0, 99.7)	95.1 (86.3, 99.0)	98.9 (93.8, 100.0)
	PPV	96.6 (88.3, 99.6)	89.7 (72.7, 97.8)	97.1 (84.7, 99.9)
	NPV	80.9 (71.4, 88.2)	75.3 (64.2, 84.4)	72.3 (63.3, 80.1)
Question 6	Sensitivity	29.3 (19.4, 41.0)	57.8 (42.2, 72.3)	51.5 (38.9, 64.0)
	Specificity	96.2 (89.2, 99.2)	95.1 (86.3, 99.0)	96.6 (90.3, 99.3)
	PPV	88.0 (68.8, 97.5)	89.7 (72.7, 97.8)	91.9 (78.1, 98.3)
	NPV	59.6 (49.6, 67.2)	75.3 (64.2, 84.4)	72.4 (63.3, 80.3)
Question 7	Sensitivity	60.0 (48.0, 71.2)	51.1 (35.8, 66.3)	24.2 (14.5, 36.4)
	Specificity	97.4 (91.0, 99.7)	95.1 (86.3, 99.0)	95.4 (88.6, 98.7)
	PPV	95.7 (85.5, 99.5)	88.5 (69.9, 97.6)	80.0 (56.3, 94.3)
	NPV	71.7 (62.1, 80.0)	72.5 (61.4, 81.90)	62.4 (53.6, 70.7)
Question 8	Sensitivity	42.7 (31.3, 54.6)	53.3 (37.9, 68.3)	37.9 (26.2, 50.7)
	Specificity	94.9 (87.4, 98.6)	98.4 (91.3, 100.0)	97.7 (91.9, 99.7)
	PPV	88.9 (73.9, 96.9)	96.0 (79.7, 99.9)	92.6 (75.7, 99.1)
	NPV	63.3 (53.8, 72.0)	74.1 (63.6, 83.4)	67.5 (58.5, 75.5)
Question 9	Sensitivity	73.3 (61.9, 82.9)	60.0 (44.3, 74.3)	66.7 (54.0, 77.8)
	Specificity	97.4 (91.0, 99.7)	98.4 (91.2, 99.9)	98.9 (93.8, 100.0)

Table 16: Validation results of the epilepsy screening questionnaire in three languages

		Hausa [% (CI)]	**Igbo [% (CI)]**	**Yoruba [% (CI)]**
	PPV	96.5 (87.9, 99.6)	96.4 (81.7, 99.9)	97.8 (88.2, 99.9)
	NPV	79.2 (69.7, 86.8)	76.9 (66.0, 85.7)	79.6 (70.8, 86.8)
Combination	Sensitivity	97.3 (90.7, 99.7)	91.1 (78.8, 97.5)	93.9 (85.2, 98.3)
1: Positive to	Specificity	85.9 (76.2, 92.7)	88.5 (77.8, 95.3)	89.7 (81.3, 95.2)
any Q1 to Q9	PPV	86.9 (77.8, 93.3)	85.4 (72.2, 93.9)	87.3 (77.3, 94.0)
	NPV	97.1 (89.9, 99.7)	93.1 (83.3, 98.1)	95.1 (88.0, 98.7)
Combination	Sensitivity	97.3 (90.7, 99.7)	84.4 (70.5, 93.51	86.4 (75.7, 93.6)
2 : Q1,Q2,	Specificity	87.2 (77.7, 93.7)	88.5 (77.8, 95.3)	92.0 (84.1, 96.7)
Q5,Q7,Q9	PPV	88.0 (79.0, 94.1)	84.4 (70.5, 93.5)	89.1 (78.8, 95.5)
	NPV	97.1 (90.1, 99.7)	88.5 (77.8, 95.3)	89.9 (81.7, 95.3)
Combination	Sensitivity	94.7 (86.9, 98.5)	80.0 (65.4, 90.4)	84.9 (73.9, 92.5)
3: Q1,Q2,	Specificity	88.2 (79.2, 94.6)	90.2 (79.8, 96.3)	97.7 (91.9, 99.7)
Q5,Q9	PPV	88.8 (79.7, 94.7)	85.7 (71.5, 94.6)	96.6 (88.1, 99.6)
	NPV	94.4 (86.6, 98.5)	85.9 (75.0, 93.4)	89.5 (81.5, 94.8)
Combination	Sensitivity	96.0 (88.8, 99.2)	80.0 (65.4, 90.4)	80.3 (68.7, 89.1)
4: Q1,Q2,	Specificity	88.5 (79.2, 94.6)	86.9 (75.8, 94.2)	93.1 (85.6, 97.4)
Q5,Q7	PPV	88.9 (80.0, 94.8)	81.8 (67.3, 91.8)	89.8 (79.2, 96.2)
	NPV	95.8 (88.3, 99.1)	85.5 (74.2, 93.1)	86.2 (77.5, 92.4)
Combination	Sensitivity	70.7 (59.0, 80.6)	73.3 (58.1, 85.4)	84.9 (73.9, 92.5)
5: Q3,Q4,	Specificity	89.7 (80.8, 95.5)	91.8 (81.9, 97.3)	93.1 (85.6, 97.4)
Q6,Q8	PPV	86.9 (75.8, 94.2)	86.8 (71.9, 95.6)	90.3 (80.1, 96.4)
	NPV	76.1 (66.1, 84.4)	82.4 (71.2, 90.5)	89.0 (80.7, 94.6)

CI – confidence interval; PPV – positive predictive value; NPV – negative predictive value; Q – Question.

The details of the sensitivity, specificity, PPV and NPV of individual questions and combinations are shown in Table 16. For the Hausa version, each of questions Q1, Q2, Q7 and Q9 had a good sensitivity; while the combination of Q1 to Q9, Q1Q2Q5Q7Q9, Q1Q2Q5Q9 and Q1Q2Q5Q7 had the best sensitivity. The specificity was between 95% and 100% for all individual questions but dropped to less than 90% when the questions were combined. For the Igbo version the Q1, Q2 and Q9 had good sensitivity, while the

best sensitivity was for Q1 to Q9 and Q3Q4Q6Q8. The sensitivity for the individual questions was lower in the Yoruba version, with most questions having a sensitivity of 50% and below, apart from Q9 with 67%. The sensitivity, however, improved to above 90% when the questions where combined.

Table 17 illustrates the predictive ability of various questions and combinations compared to the combination with the best accuracy (combination of Q1 to Q9). It shows that the best combinations with very good predictive ability are combinations Q1Q2Q5Q7Q9, Q1Q2Q5Q9 and Q1Q2Q5Q7 for all the three languages. The individual questions do not have very good predictive ability.

Table 17: Predictive ability of various questions and combinations

	HAUSA		**IGBO**		**YORUBA**	
	Kappa (κ)	**Predictive ability**	**Kappa (κ)**	**Predictive ability**	**Kappa (κ)**	**Predictive ability**
Q1Q2Q5Q7Q9	0.93	Very good	0.90	Very good	0.91	Very good
Q1Q2Q5Q7	0.91	Very good	0.88	Very good	0.84	Very good
Q1Q2Q5Q9	0.90	Very good	0.85	Very good	0.83	Very good
Q3Q4Q6Q8	0.68	Good	0.77	Good	0.88	Very good
Q1	0.68	Good	0.59	Moderate	0.50	Moderate
Q2	0.68	Good	0.67	Good	0.51	Moderate
Q3	0.45	Moderate	0.48	Moderate	0.45	Moderate
Q4	0.36	Fair	0.44	Moderate	0.50	Moderate
Q5	0.68	Good	0.63	Good	0.50	Moderate
Q6	0.28	Fair	0.59	Moderate	0.54	Moderate
Q7	0.53	Moderate	0.56	Moderate	0.30	Fair
Q8	0.40	Fair	0.54	Moderate	0.40	Fair
Q9	0.66	Good	0.57	Moderate	0.65	Good

Combination of all questions Q1 to Q9 possibly has the best sensitivity and predictive value and was considered as the gold standard

4.5 Discussions

The success of community-based surveys in epilepsy depends on the availability of a valid screening tool. In Nigeria, the few epilepsy surveys conducted have no clear uniformity in the use of screening tools (Longe & Osuntokun, 1989, Mustapha & Preux, 2015, Nwani et al., 2015); only a few reported using validated questionnaires for surveys (Osuntokun et al., 1982, Osuntokun et al., 1987a, Osakwe et al., 2014). The lack of a validated tool usually hampers the conduct of surveys and these studies may have relied on verbal translations. This study in trying to remedy this deficiency developed and piloted a 9-item epilepsy questionnaire in three Nigerian languages that are simple, highly sensitive and specific and that can easily be used by health workers to screen people for epilepsy in the community. This instrument showed a good level of sensitivity, specificity, PPV and NPV for all the languages, especially when the nine questions were combined. Most of the results show a much higher specificity compared to the high sensitivity. A higher specificity compared to sensitivity means that the screening tool is unlikely to include people without epilepsy, but more likely to miss people who have epilepsy in the community. On the other hand, a screening instrument with a higher sensitivity means that those who truly have the disease will be seen, with the least likely chance of losing false negatives. Irrespective of the results, an advantage of conducting a validation study is that the prevalence can be adjusted using the known sensitivity and specificity of the screening test.

In this study, the combination of the nine questions had the best sensitivity. The combination of about 4 to 5 questions could be used with acceptable indices of accuracy as the questions had a good predictive ability. This shows that it is possible to reduce the number of screening questions and thus reduce the time and logistics for the study. These 4 to 5 questions are mainly for convulsive epilepsy and therefore just using them means we risk losing people with non-convulsive epilepsy. It could be argued that people with only non-convulsive seizures are probably few and may have a coexistent generalized convulsive seizure, which would inevitably be detected by those

four or five questions. From a public health perspective, a short concise questionnaire would be better for evaluation of a large population in the shortest possible time but would risk losing subjects who have non-convulsive epilepsy. Even though the questionnaire includes questions to screen for non-convulsive seizures, it has a bias to recruit more people with convulsive seizures when used in the community (Sander et al., 1990). An instrument that screens for non-convulsive should be more accurate than those looking at convulsive seizures only (Anand et al., 2005, Giuliano et al., 2017). It was agreed that the nine questions should be used as it would not significantly prolong the interview. Differences in the measures of accuracy were observed between various languages, these may be due to differences in the source population, the dynamics of the translation process, the dialectical differences and how the questionnaires were delivered between centres.

One of the limitations of this study is that it is clinic-based rather than community-based. The clinic-based setting has the potential for selection bias as questions are administered to people with a formal diagnosis and are more likely to be severe cases. The generalization of the results is limited by the selection criteria and by the fact that it is carried out in an artificial setting. A community-based study would have been better as data is obtained in a less biased setting. It, however, has logistic difficulties like cost and the relatively rare occurrence of epilepsy in the community (Placencia et al., 1992). Another potential problem with clinic-based studies is the 'spectrum effect', which is a phenomenon in which the performance of a diagnostic test may vary in different clinical settings because each setting has varied patients. Therefore the predictive ability of a tool when used in a general population may differ from the study sample in which it was first developed (Usher-Smith et al., 2016). This is one reason why study samples should as much as possible be similar to the population in which the test is intended to be used. Other limitations were the inability to acquire information on clinical data and the severity of epilepsy during recruitment. This is important as any test that is applied only to the severest of epilepsy cases is more likely to have a high sensitivity, whereas

any test applied to a perfectly healthy group of controls is more likely to have a high specificity (Delgado-Rodriguez & Llorca, 2004). Bias in recruitment is also possible as randomisation of the subjects was not done and no attempt was made to match the cases with the controls. The inability to study the inter- and intra-observer errors and the lack of blinding for the health workers administering the questionnaires is another limitation. These steps would have been important to reduce bias and to observe the individual differences in administration of the questionnaires. The use of patient's proxies or care-giver questionnaire was an option considered in this study. It would have been useful since it is difficult to get affirmative answers to some questions as subjects may not be aware of other seizure symptoms. This part of the study was abandoned because of the time available and in many cases; the informant interviewed was not helpful as they were not necessarily the main carers. This could be a future study to see the inter-observer reliability and the utility of using proxy questionnaires.

Conclusion: For the first time in Nigeria using set guidelines a translated and validated epilepsy screening questionnaire in the three most popular Nigerian languages is described. The screening tool represents a valid instrument with an acceptable level of sensitivity and specificity that can easily be used by trained health workers in community-based surveys to screen for people with epilepsy. Although there may be some shortcomings with translation, it can be adopted or modified for research purpose, as the questionnaires can further be improved.

Chapter 5: Cross-sectional community-based surveys, prevalence and incidence of epilepsy

5.1 Abstract

Purpose: This chapter describes the work that determined the prevalence and retrospective incidence of epilepsy from three diverse regions of Nigeria. **Methods:** A two-stage door-to-door survey was undertaken from February to April 2018 in Oha-isu and Nkpoghoro in Ebonyi, Ijebu-Jesa in Osun and Gwandu in Kebbi States; located in the Southeast, Southwest and Northwest regions, respectively. Validated 9-item epilepsy screening questionnaire was administered to household heads by trained fieldworkers to identify suspected cases, followed by confirmatory screening by neurologists using set criteria. The age-standardised prevalence adjusted for non-response and sensitivity and 1-year incidence for active epilepsy were calculated. **Results:** Overall, 42,427 people (21,293 females and 21,134 males) aged ≥ 6 years from 10,449 households were screened from the three sites (Afikpo – 15,738, Ijebu-Jesa – 10,316, and Gwandu – 16,373). A total of 254 persons (Afikpo - 42, Ijebu-Jesa – 24 and Gwandu – 188) were confirmed to have active epilepsy. The adjusted prevalence of active epilepsy (per 1,000) was 17.7 (95% CI: 14.2, 20.6), 4.8 (95% CI: 3.4, 6.6) and 3.3 (95% CI: 2.0, 5.1) in Gwandu, Afikpo and Ijebu Jesa, respectively. The adjusted prevalence of active epilepsy combining data from the three sites was 9.8 (95% CI: 8.6, 11.1). The prevalence was marginally higher in males [10.2 (95% CI: 8.4, 12.4)] compared to females [9.3 (95% CI: 7.7, 11.2)]. The estimated 1-year age-standardized retrospective incidence (per 100,000) in Afikpo was 27.6 (95% CI: 3.3, 128.0) and 23.9 (95% CI: 3.2, 157.0) in Ijebu-Jesa. Gwandu had a much higher incidence of 201.2 (95% CI: 105.0, 358.9). Combining data for the three sites gave a pooled incidence of 101.3 (95% CI: 57.9, 167.6) [Female: 95.1 (95% CI: 41.5, 191.0); Male: 110.4 (95% CI: 46.5, 230.7)]. **Conclusion:** This study reported the varying prevalence and incidence estimates between sites, the Northwest having higher

estimates than the Southeast and Southwest. The differences may be explained by the varied population structure, genetic and environmental factors. Stigma and sociocultural issues may have influenced the measurement of disease frequency.

Keywords: Epilepsy, Census, Screening, Prevalence, Incidence, Survey

5.2 Introduction

Epilepsy has received more attention in recent years, and despite the increasing number of epidemiological studies (Reynolds, 2001), existing information proves that significant variations in the measures of disease frequency exist between countries and they are inadequate to ascertain the true burden of epilepsy (Mac et al., 2007, Ba-Diop et al., 2014). Precise information on the burden of epilepsy in Nigeria is uncertain at the national level, because over the last four decades, only seven community-based prevalence studies have been conducted (Osuntokun et al., 1982, Osuntokun et al., 1987b, Osuntokun et al., 1987a, Longe & Osuntokun, 1989, Osakwe et al., 2014, Mustapha et al., 2014, Mustapha & Preux, 2015, Nwani et al., 2015, Ezeala-Adikaibe et al., 2016). The studies screened small populations, representing a combined population strength of approximately 49,000 persons. These studies were undertaken in the southern parts of Nigeria. In these studies, the reported prevalence varied between 4.3 and 37 per thousand. The largest community-based study in Nigeria using standard WHO protocols in a sub-urban community 80 km north of Lagos more than three decades ago yielded a prevalence of 5.3 per thousand (Osuntokun et al., 1987a, Osuntokun et al., 1987b). This study was preceded by a pilot study in a neighbouring community which screened only 903 people yielding a widely differing prevalence of 37 per thousand (Osuntokun et al., 1982). These studies indicate a wide variation in the burden of epilepsy; therefore, it is inadvisable to extrapolate the prevalence of epilepsy from these studies within or from other countries to reflect the true size of the problem in Nigeria. The lack of understanding of the magnitude of the problem often hinders health-planning, provision of resources and services required to care for people. To

facilitate health policy formulation at global and regional levels regular updates on the burden of diseases is required (Murray & Lopez, 1996).

There is increasing evidence that a community-based approach has unique strengths and is valuable in acquiring health-related knowledge particularly in rural communities (Thurman et al., 2011). Additionally, people with health needs can be encouraged through education to seek medical care and to start or monitor treatment (Leung et al., 2004). The success of population research depends on methodological robustness, taking into cognisance sociocultural dynamics of communities, differences in cultural perceptions and values, and even the use of language which can hamper data acquisition (Israel et al., 1998). As epidemiological studies are useful to understand disease burden and the derived information useful for planning health care interventions (Kapiriri et al., 2003), a community-based survey was conducted to ascertain the prevalence and retrospective incidence of epilepsy from three culturally and geographically diverse regions of Nigeria and the prevalence was compared with other national and African figures. We hypothesize that the prevalence would be around 1% across the sites.

5.3 Methods

5.3.1 Study Design and Population

This was a cross-sectional door-to-door survey conducted at Oha-isu and Nkpoghoro wards in Afikpo North local government areas (LGA) Ebonyi State, Ijebu-Jesa ward in Oriade LGA Osun State and 10 wards in Gwandu LGA Kebbi State; they are located in the Southeast, Southwest and Northwest regions of Nigeria respectively (see Appendix 12 for the maps of this wards). These sites were chosen, as there was an availability of research facilitators in the form of willing collaborators and with stable population.

5.3.2 Pre-study consultations and training of field workers

An official pre-study consultation was conducted seven months before (June 2017) the proposed date for the rural survey. The administrative, traditional and spiritual heads of

these communities were visited seeking their cooperation and explaining how the study would be conducted. Cooperation from the PHCs and the tertiary hospitals in the network of these centres was also sought. The tertiary hospitals were: OAUTHC Ile-Ife, Osun State; FETHA Ebonyi State; and UDUTH Sokoto State. The tertiary hospitals and the primary health care and immunisation coordinators helped with providing logistics and experienced field workers. The National Population Commission (NPC) in the states provided enumeration area maps to assist with the surveys. Most of the enumerators were part of the PHC and already had some training in health surveys, particular door-to-door immunisation programmes. In each site, two health workers with more experience were nominated to serve as supervisors with the function to oversee the enumeration and to ensure the quality of the data acquired.

A training workshop for fieldworkers was held at each field site the week prior to the commencement of the survey to accomplish a high level of uniformity. The training provided the team with basic information on seizures and epilepsy and the use of the census forms, questionnaires and referral forms. The training was interactive with focus group discussions, practical (mock) sessions and video sessions. The individual components of the validated screening questionnaires were discussed for any potential refinements to optimise its use in the field. A feedback session and further re-training for enumerators were conducted a day after the fieldwork began (Figure 3). These training provided an informal opportunity for health workers to get some training in providing epilepsy services. The reference diagnosticians were three consultant neurologists (Prof Morenikeji Komolafe and Dr Michael Fawale from OAUTHC, and Dr Salisu Balarabe from UDUTH) who have a background in epilepsy research and a neuropsychiatrist (Dr Stanley Igwe from FETHA) who has a UK training in epileptology and has publications in epilepsy. The physicians had discussions on terminologies, definitions and new diagnostic concepts to ensure uniformity in the diagnosis of epilepsy across centres (Thurman et al., 2011).

Training of enumerators at the primary health secretariat Afikpo (with permission)

Dr Fawale (arrow) having a feedback session with enumerators after a day's census outing in Ijebu-Jesa (with permission).

Figure 4: Photos of training sessions

5.3.3 Procedures for the census and screening

A complete census was conducted in Ohaisu and Nkpoghoro wards of Afikpo North LGA with five and seven enumeration areas respectively and Ijebu-Jesa is mainly considered as one large ward with 166 small subdivisions, and therefore we considered Ijebu-Jesa as a single entity for the ease of analysis. Villages from the 10

wards of Gwandu were randomly selected. A population census of these communities was conducted alongside the epilepsy screening to reduce cost. The periods for the censuses were 12th February to 15th March 2018, 17th February to 8th March 2018 and 3rd March to 30th March 2018 in Ijebu-Jesa, Afikpo and Gwandu, respectively. The last dates were selected as the prevalence dates. The screening process at all the three sites was a two-phase survey; the targeted population were people living in these communities aged 6 years and above.

Stage 1: Each household underwent an interview using the validated 9-item screening questionnaire to identify people suspected to have epilepsy. The questionnaires (which capture convulsive and non-convulsive seizures) were administered to head of households or the next senior member if not available in accordance with a previous study (Ngugi et al., 2013a). Locked houses were visited a second time in the evenings. A positive response to at least one of the nine screening questions was considered a positive screen. Those screened positive were given an identification number and a referral slip and asked to visit designated PHCs.

Stage 2: Subjects who screened positive in stage one underwent a confirmatory evaluation by physicians. During the case ascertainment, all diagnoses were reviewed and confirmed by the neurologist. *Epilepsy* was defined as two or more unprovoked seizures occurring at least 24 hours apart according to the ILAE recommendation (Fisher et al., 2014). The *Lifetime prevalence* of epilepsy was considered as those persons who manifested the condition at any point in their life up to the time of the survey (MacDonald et al., 2000). People with *active epilepsy* were evaluated as those currently on treatment or whose seizures have occurred within the last one-year period. The one year period rather than the 2- to 5-year period was chosen due to problems in recalling dates (Thurman et al., 2011). The 1-year incidence was taken as the number of persons whose onset of seizures was in the last one year per 100,000 of the population at risk.

People with either convulsive or non-convulsive epilepsies were recruited. With the information available from an eyewitness (usually a relative or an acquaintance) and as practical as possible, the research team discussed and confirmed the seizure and epilepsy types based on the ILAE's Commission for Classification and Terminology (Fisher et al., 2017). A pro-forma modified from the questionnaire developed by the Institute of Neurological Epidemiology and Tropical Neurology, Limoges, France, and the Pan African Association of Neurological Sciences was used to acquire information during the structured interview for those confirmed to have epilepsy (Preux, 2002). Information on sociodemographic, clinical and seizure characteristics, risk factors and treatment patterns were collected. Parent or caregivers were interviewed if the participant was a child or cognitively impaired.

Case ascertainment commenced the same week as the census and an extra one-month was given after concluding the census to give time for those invited for stage 2 screening to respond. In each of these sites, the enumerators made efforts to trace all the individuals by visiting them at home or by phone calls to ensure that they were aware of what the study entailed.

The UCL Ethics Committee and the National Health and Research Ethics Committee (NHREC) in Nigeria approved the study protocol, consent forms, and questionnaires. All subjects or their next of kin gave informed consent.

Statistical analysis: All the census data were entered into Microsoft Excel 2010. The crude prevalence per 1,000 and the 1-year retrospective incidence per 100,000 were calculated using the *R epitools* epidemiological calculators (R Core Team, 2013). Crude prevalence for each site was calculated and the total population combined to get overall prevalence in Nigeria from the three sites. To look for evidence of clustering of cases within the sites, prevalence estimates were calculated to the smallest enumeration area where possible.

To allow for rates to be compared across populations with different age profiles, age-standardisation to the Nigerian standard population (National Population Commission,

2014) was carried out using the direct method. Age- and sex-specific prevalence rates were calculated in five-year age-bands. Prevalence estimates were also adjusted for non-response and the sensitivity of the screening questionnaire for each centre. The 95% confidence intervals (CIs) were calculated using the 'Wilson score interval assumption', which provides a more reliable coverage (Brown et al., 2001). The denominator population for the lifetime prevalence was taken from the household population census.

5.4 Results

5.4.1 Census: Population

A total of 50,438 (25,864 females and 24,574 males) persons from 10,449 households were screened from the three sites (average ≈ five persons per household), of whom 42,427 (84.1%) were aged six years and above (21,293 females and 21,134 males). The total population screened at each site is shown in Table 18.

Table 18: Census results and population screened by site

Sites	Household screened	Total population (%)*	Persons per household	Females	Population ≥ 6 years (% of total)	Females
Afikpo	3,378	18,066 (8.7%)	5.4	9,299	15,738 (87.1%)	8,019 (50.95%)
Ijebu-Jesa	3,996	12,390 (6.1%)	3.1	6,503	10,316 (83.3%)	5,398 (52.3%)
Gwandu	3,075	19,982 (9.7%)	6.5	10,062	16,373 (81.9%)	7,876 (48.1%)
Total	10,449	50,438 (8.2%)	4.8	25,864	42,427 (84.1%)	21,293 (50.2%)

*Percentage population of the entire Local Government Area using the current projected population [Afikpo North - 207,300, Oriade - 204,300, Gwandu - 206,000 (https://www.citypopulation.de/php/nigeria-admin.php)].

5.4.1.1 First stage screening

Of those screened using the 9-item epilepsy questionnaire, 104 (0.7%), 121 (1.2%) and 384 (2.3%) were positive in Afikpo, Ijebu-Jesa and Gwandu respectively. The positive rate at stage one was lowest for Afikpo and highest for Gwandu. For a better understanding of the performance of the questionnaires at this stage, the response rates of the individual questions are shown in Appendix 13. Question (Q) 1, Q2, Q3, and Q9 have the most positive responses, screening mainly convulsive epilepsies apart from Q9.

5.4.1.2 Second stage screening and case ascertainment

Of those suspected to have epilepsy invited for second stage screening, 61 (58.7%), 104 (86.5%) and 278 (72.4%) effectively made it for assessment. The highest non-response rate of 41.3% was in Afikpo, followed by 27.6% in Gwandu and the least was 13.5% in Ijebu-Jesa. There was a wide variation in the response rate between wards and communities (Appendix 14). Potential reasons why some of those screened in the second stage were not confirmed to have epilepsy are shown in Appendix 15. Those screened in the second stage but not confirmed to have epilepsy were more likely to be females (P= 0.008) and older (61.3 $\pm$ 15.8 years vs 31.5 $\pm$ 16.3, P <0.0001) in Afikpo while in Gwandu there was no significant age (21.5 $\pm$ 10.5 years vs 20.2 $\pm$ 11.6, P < 0.4008) or gender (P= 0.870) differences. In Ijebu-Jesa sociodemographic details of most of these persons could not be obtained as the collaborator situated there failed to capture this information. By the end of the screening process 280 (43 in Afikpo, 26 in Ijebu-Jesa and 211 in Gwandu) were diagnosed to have or had past diagnosis (lifetime) of epilepsy, out of which 254 (42 in Afikpo, 24 in Ijebu-Jesa and 188 in Gwandu) persons were diagnosed to have active epilepsy (Table 19).

5.4.2 Prevalence of epilepsy

The highest crude lifetime prevalence of epilepsy and prevalence of active epilepsy was found in Gwandu and lowest in Ijebu-Jesa (Table 19). After age-standardization

and adjustment for attrition and sensitivity; the prevalence of active epilepsy increased by 78% in Afikpo, 43% in Ijebu-Jesa, and 54% in Gwandu. The adjusted prevalence of active epilepsy in Gwandu was 3.7 and 5.4 times higher than in Afikpo and Ijebu-Jesa, respectively. The adjusted prevalence was 9.8 (8.6, 11.1) when the data from the three sites were combined. The values for the age-standardized lifetime prevalence by site and gender are shown in Table 20. The estimates had appreciably narrow confidence intervals within which the true prevalence lies.

Table 19: Prevalence of epilepsy from the three sites

Sites	Population (≥ 6 years)	Number positive stage 1	Responded and screened in stage 2	Gender response (females)	Diagnosed after stage 2	Crude Lifetime prevalence (per 1,000)	Crude prevalence active epilepsy (per 1,000)	Age standardised Prevalence active epilepsy	Prevalence adjusted for attrition and sensitivity (per 1,000)	Prevalence ratios
Afikpo	15,738	104 (0.7%)	61 (58.7%)	57.4%	43 (70.5%)	2.7 (2.0, 3.7)	2.7 (2.0, 3.6)	2.5 (1.8, 3.5)	4.8 (3.4, 6.6)	1.0
Ijebu-Jesa	10,316	121 (1.2%)	104 (86.5%)	51.0%	26 (25.0%)	2.5 (1.7, 3.7)	2.3 (1.6, 3.5)	2.6 (1.6, 4.0)	3.3 (2.0, 5.1)	0.7 (0.4, 1.1)
Gwandu	16,373	384 (2.3%)	278 (72.4%)	41.7%	211 (75.9%)	12.9 (11.3, 14.7)	11.5 (10.0, 13.2)	11.5 (9.8, 13.5)	17.7 (14.2, 20.6)	3.7 (3.0, 4.3)
Total	42,427	609 (1.4%)	443 (72.7%)	50.0%	280 (63.2%)	6.6 (5.9, 7.4)	6.0 (5.3, 6.8)	6.2 (5.5, 7.1)	9.8 (8.6, 11.1)	-

The Nigerian census figure of 2006 was used for the age standardisation. Attrition was corrected by dividing with a factor of 0.587, 0.865 and 0.724 for Afikpo, Ijebu-Jesa and Gwandu respectively. For the total (combined) dataset, attrition was corrected by calculating a weighted attrition factor based on the number of subjects per regions [Attrition_factor = (#N_regionX * 0.587 + #N_regionY * 0.865 + #N_regionZ * 0.724) / #N_total = 0.7075]. The values were also adjusted for the sensitivity of the screening questionnaire, dividing by a factor of 0.9. Percentages are those of the previous column. Figures in parenthesis are the 95% confidence intervals.

Table 20: Prevalence of lifetime epilepsy by site and gender

Gender	Total Screened	Number of people with active epilepsy	Age-standardized lifetime prevalence adjusted for attrition and sensitivity (95% CI)
Afikpo	15738	42	4.8 (3.5, 6.7)
Female	8019	20	4.5 (2.7, 7.3)
Male	7719	23	4.9 (3.1, 8.2)
Ijebu-jesa	10316	26	3.6 (2.3, 5.4)
Female	5398	12	3.2 (1.6, 6.0)
Male	4918	14	3.9 (2.1, 7.1)
Gwandu	16373	211	19.8 (17.1, 22.9)
Female	7876	119	17.1 (13.7, 21.4)
Male	8497	92	22.6 (18.4, 27.7)
Combined	42427	280	10.8 (9.6, 12.3)
Female	21,293	124	9.4 (7.8, 11.3)
Male	21134	156	12.6 (10.6, 15.0)

Attrition was corrected by dividing with a factor of 0.587, 0.865 and 0.724 for Afikpo, Ijebu-Jesa and Gwandu respectively. A weighted attrition factor based on the number of subjects per regions [Attrition_factor = (#N_regionX * 0.587 + #N_regionY * 0.865 + #N_regionZ * 0.724) / #N_total = 0.7075] was used for adjustment of the combined values. The values were also adjusted for the sensitivity of the screening questionnaire of approximately 90% (divided by a factor of 0.9). Figures in parenthesis are the 95% confidence intervals.

5.4.2.1 Prevalence of epilepsy by enumeration area

Tables 21 and 22 show a varied crude prevalence of active epilepsy between enumeration areas. The crude prevalence in Ohaisu ward was 40% higher than in Nkpoghoro ward. A further breakdown of the prevalence by community shows a more varied result, with Ngodo, Amauzu and Amangbala having the highest crude prevalence. Varied prevalence of epilepsy was observed between the 10 wards in Gwandu, with the highest crude prevalence reported in Dodoru, Gwandu Dangidan Galadima and Maruda wards, which is about thrice that in Gulmare ward.

Table 21: Crude prevalence by wards and enumeration area in Afikpo

Ward and enumeration area	**Population**	**Crude prevalence active Epilepsy**	**Prevalence ratio**
Ohaisu (All)	9,459	3.3 (2.3, 4.6)	1.0
Amangbala	2,444	4.1 (2.2, 7.5)	1.2 (0.7, 2.3)
Amachi	1,755	3.4 (1.6, 7.4)	1.0 (0.5, 2.2)
Amachara	1,267	1.6 (0.4, 5.7)	0.5 (0.1, 1.7)
Ngodo	1,247	8.8 (4.9, 15.7)	2.7 (1.5, 4.8)
Ukpa	2,746	0.7 (0.2, 2.7)	0.2 (0.06, 0.8)
Nkpoghoro (All)	6,279	1.9 (1.1, 3.3)	0.6 (0.3, 1.0)
Ndibe	1,421	2.8 (1.1, 7.2)	0.8 (0.3, 2.2)
Amankwo	1,118	NA	-
Amaobolobo	451	NA	-
Amauzu	889	7.9 (3.8, 16.2)	2.4 (1.2, 4.9)
Amaoku	603	1.7 (0.3, 9.3)	0.5 (0.1, 2.8)
Amangwu	708	NA	-
Amaekwu	1,089	NA	-

Figures in parenthesis are the 95% confidence intervals.

Table 22: Crude prevalence by wards in Gwandu

Ward and Enumeration Area	Population	Crude prevalence of active epilepsy	Prevalence ratio
Cheberu	1,752	11.4 (7.4, 17.6)	1.0
Dalijan	1,890	11.6 (7.7, 17.6)	1.02 (0.7, 1.5)
Dodoru	1,832	15.8 (11.0, 22.6)	1.4 (1.0, 2.0)
Gulmare	1,261	5.6 (2.7, 11.4)	0.5 (0.2, 1.0)
Gwandu D/Galadima	1,401	15.7 (10.4, 23.7)	1.4 (0.9, 2.1)
Gwandu Marafa	1,434	12.6 (8.0, 19.8)	1.1 (0.7, 1.7)
Kambaza	1,880	6.4 (3.7, 11.1)	0.6 (0.3. 1.0)
Malisa	1,986	7.6 (4.6, 12.4)	0.7 (0.4, 1.1)
Maruda	1,505	16.6 (11.3, 24.4)	1.5 (1.0, 2.1)
Masama	1,432	12.6 (8.0, 19.8)	1.1 (0.7, 1.7)

Figures in parenthesis are the 95% confidence intervals.

5.4.2.2 Prevalence of epilepsy by age

The age-specific prevalence for active epilepsy for each site is illustrated in histograms (Figures 4, 5 and 6). The peak prevalence mostly in children varied between sites. The peak prevalence in Afikpo was found in those 50 – 54 years, followed by those in theage bracket 40 – 44 years. This peak prevalence in the middle age was 70% higher than the two peak prevalence in childhood 15 – 19 years and 20 – 24 years (Figures 4). In Ijebu-Jesa the peak was found in the age group 25 – 29 years, followed by 6 – 9 years (Figures 5). While in Gwandu the peaks were the age groups 6 – 9 years and 10 – 14 years (Figures 6). In Ijebu-Jesa and Gwandu another smaller peak was noted at the age group 55 – 59 years. When the data from the three sites were combined the chart smoothened out showing a clear bimodal distribution (Figure 7), with the highest peak in the age group 6 – 9 years and 10 – 15 years and a second but smaller peak at the age group 55 – 59 years.

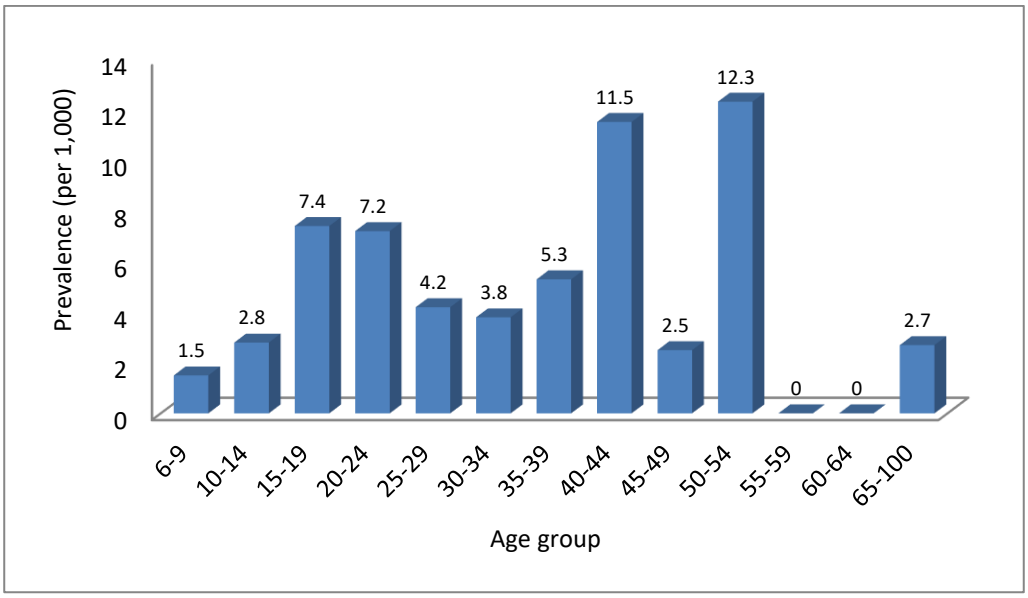


Figure 5: Prevalence of active epilepsy by age group in Afikpo

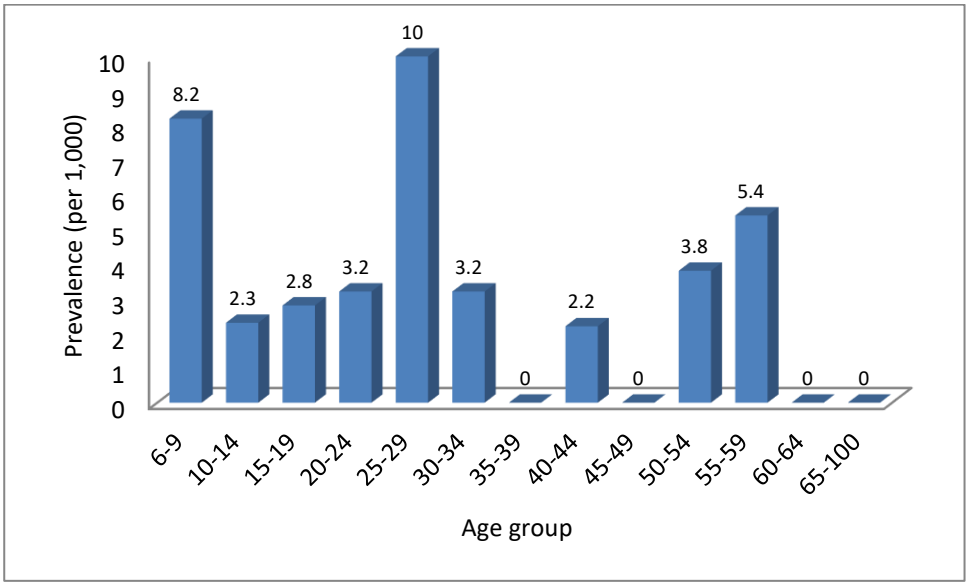


Figure 6: Prevalence of active epilepsy by age group in Ijebu-Jesa

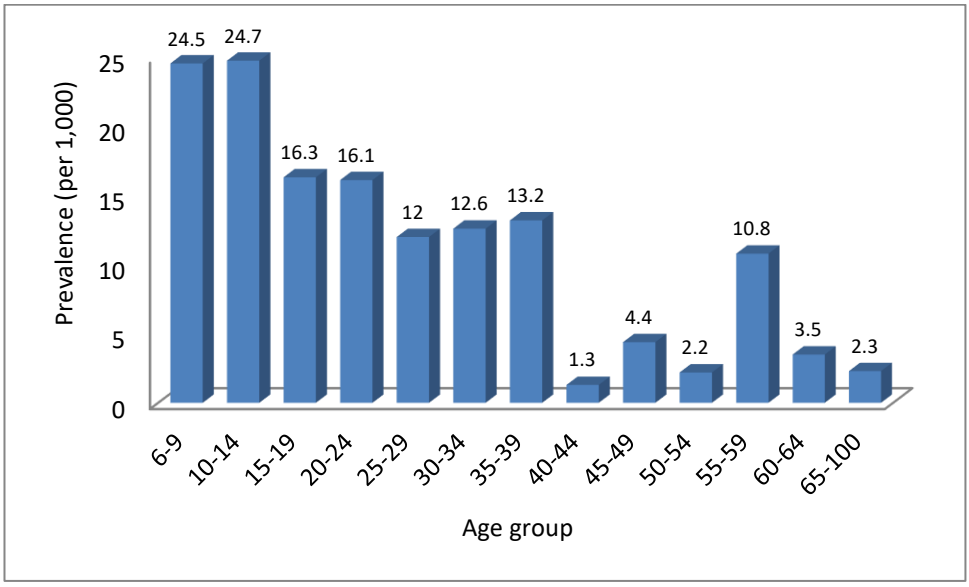


Figure 7: Prevalence of active epilepsy by age group in Gwandu

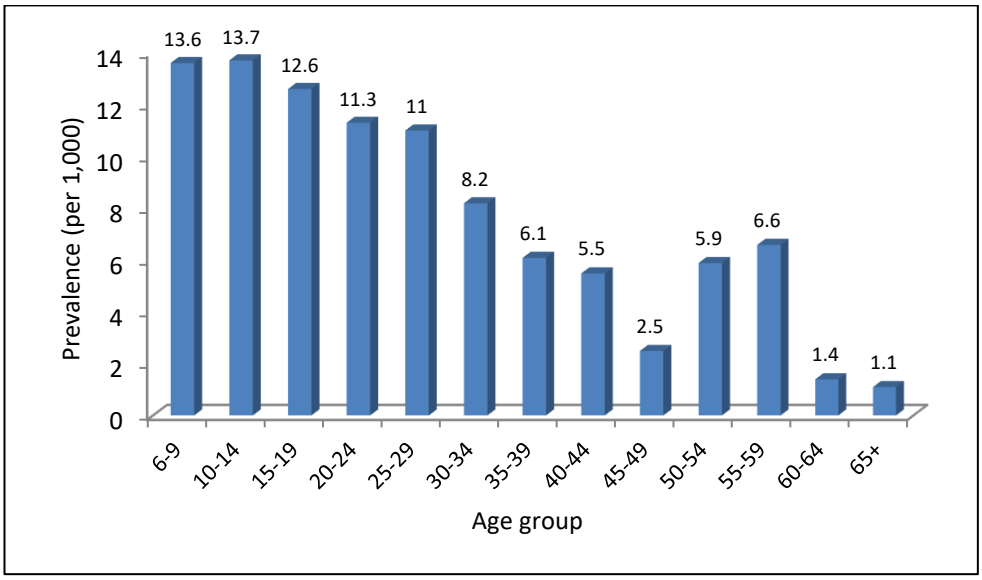


Figure 8: Prevalence of active epilepsy by age group combining three centres

5.4.2.3 Prevalence of epilepsy by gender

Table 20 shows the adjusted lifetime prevalence of epilepsy by gender. Table 23 reports the adjusted prevalence of active epilepsy by gender, the prevalence was marginally higher in males compared to females in Ijebu-Jesa and Gwandu, while in Afikpo the prevalence was approximately 40% higher in males compared to females.

Table 23: Prevalence of active epilepsy by gender

Gender	Total Screened	Number of people with active epilepsy	Age-standardized prevalence (95% CI)	Age-standardized prevalence adjusted for attrition and sensitivity (95% CI)	Prevalence Ratio (95% CI)
Afikpo					
Female	8019	19	2.3 (1.4, 3.7)	4.3 (2.6, 7.1)	1.0
Male	7719	23	3.1 (2.0, 4.7)	5.9 (3.7, 9.0)	1.4 (0.9, 2.1)
Ijebu-Jesa					
Female	5398	12	2.5 (1.2, 4.7)	3.2 (1.6, 6.0)	1.0
Male	4918	12	2.6 (1.3, 4.9)	3.3 (1.6, 6.3)	1.03 (0.5, 2.0)
Gwandu					
Female	7876	91	10.9 (8.6, 13.6)	16.7 (13.3, 20.9)	1.0
Male	8497	95	11.6 (9.3, 14.7)	17.9 (14.2, 22.5)	1.07 (0.9, 1.3)
Combined					
Female	21,293	122	5.9 (4.8, 7.1)	9.3 (7.7, 11.2)	1.0
Male	21,134	130	6.5 (5.3, 7.9)	10.2 (8.4, 12.4)	1.1 (0.9, 1.3)

Attrition was corrected by dividing with a factor of 0.587, 0.865 and 0.724 for Afikpo, Ijebu-Jesa and Gwandu respectively. For the total dataset attrition was corrected by calculating a weighted attrition factor based on the number of subjects per regions [Attrition_factor = (#N_regionX * 0.587 + #N_regionY * 0.865 + #N_regionZ * 0.724) / #N_total = 0.7075].The values were also adjusted for the sensitivity of the screening questionnaire of approximately 90% (divided by a factor of 0.9). Figures in parenthesis are the 95% confidence intervals.

5.4.3 Incidence of epilepsy

Table 24 reports the crude and age-standardized 1-year incidence (per 100,000) by site and gender. The estimated 1-year crude incidence was highest in Gwandu and lowest in Afikpo. With age-standardization, the incidence more than doubled in Afikpo and Gwandu, but increased by only 23% in Ijebu-Jesa, making it the site with the lowest age-standardised incidence. The age-adjusted incidence in Gwandu was seven and almost 8.5 times higher than in Afikpo and Ijebu-Jesa respectively. Females had higher 1-year crude incidence in Afikpo and Ijebu-Jesa and this difference widened with standardization. In Gwandu, the crude incidence was 12% higher in males, after standardization the incidence became 40% higher compared to females.

Table 24: One-year incidence of epilepsy by centre and gender

	Total Screened	**Number of new cases**	**Crude 1- year incidence (95% CI)**	**Age-standardized incidence (95% CI)**
Afikpo	15,738	2	12.7 (3.5, 46.3)	27.6 (3.3, 128.0)
Female	7,719	1	13.0 (2.3, 73.4)	33.0 (0.8, 199.6)
Male	8,019	1	12.5 (2.2, 70.6)	25.6 (0.6, 263.2)
Ijebu-Jesa	10,316	2	19.4 (5.3, 70.7)	23.9 (3.2, 157.0)
Female	5,398	2	37.1 (10.2, 135.0)	76.5 (5.7, 348.8)
Male	4,918	0	0.0	0.0
Gwandu	16,373	14	85.5 (50.9, 143.5)	201.2 (105.0, 358.9)
Female	8,497	6	76.2 (34.9, 166.1)	168.3 (56.9, 397.2)
Male	7,876	8	94.2 (47.7, 185.7)	236.7 (92.3, 518.8)
Total (combined)	42,427	18	42.4 (26.8, 67.1)	101.3 (57.9, 167.6)
Female	21,293	9	42.3 (22.2, 80.3)	95.1 (41.5, 191.0)
Male	21,134	9	42.6 (22.4, 80.9)	110.4 (46.5, 230.7)

Figures in parenthesis are the 95% confidence intervals.

Figure 8 illustrates a bimodal pattern of the age distribution of 1-year incidence combining data from the three sites, with most incident cases occurring in the younger age groups. The highest peak incidence in Gwandu was in the age group 6 – 9 years with a decrement over the next two decades. In Afikpo the highest peak was in the age groups 6 – 9 years and 15 – 19 years, while in Ijebu-Jesa the two peaks were 10 – 14 years and 55 – 59 years.

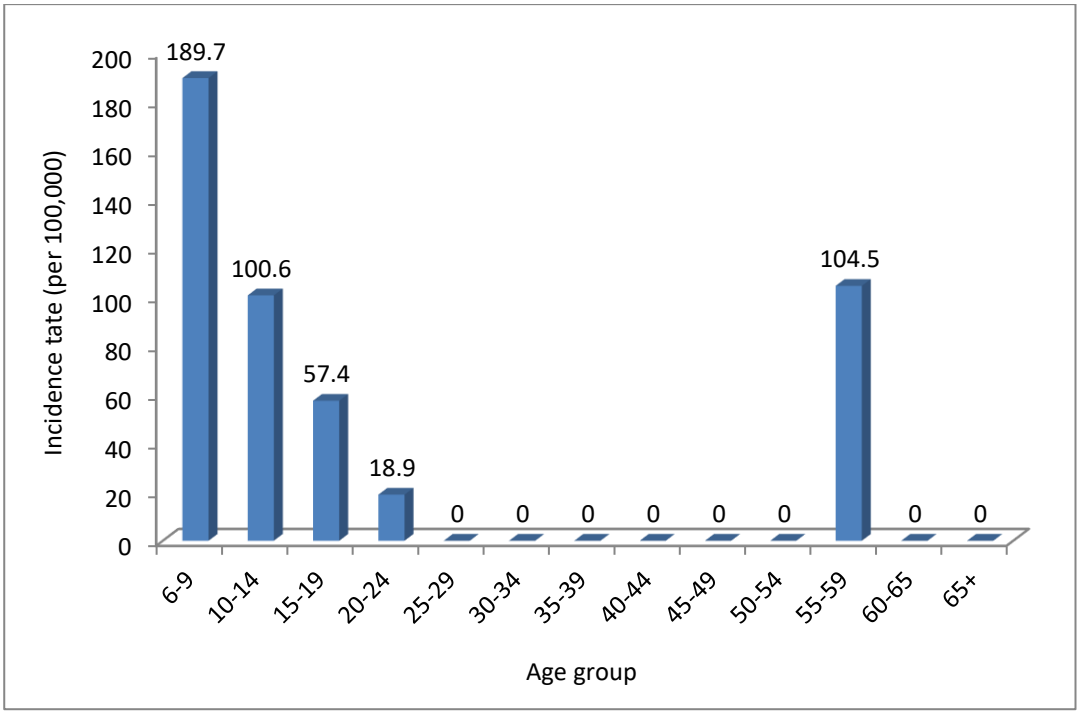


Figure 9: Incidence of active epilepsy by age group combining three sites

5.5 Discussion

In this quasi-nationally representative cross-sectional population-based study from three regions of Nigeria, the prevalence and incidence of epilepsy vary between sites, even between communities in the same local government area. The estimates are much higher in Gwandu Northwest Nigeria than in Afikpo and Ijebu-Jesa Southeast and Southwest Nigeria. Higher in childhood than in adults, apart from the finding in Afikpo where the highest peak prevalence was in adults. The estimates were

substantially lower in Southern Nigerian and higher in Northern Nigerian than the 1% hypothesized. The prevalence reported in our study from each site and the combined data falls within the range of estimates reported from Africa and elsewhere in the world (Fiest et al., 2017). The prevalence estimates had appreciably narrow confidence intervals and therefore we are more certain that the true prevalence lies within the intervals. It also suggests an adequate sample size. The finding in Ijebu-Jesa is among some of the lowest in Africa. A list of prevalence studies from Africa and where our estimates are placed is shown in Appendix 16. The prevalence from Gwandu and Afikpo is similar to the Nigerian study from two sites of Ochiohu Ebonyi state and Ogobia Benue state respectively (Osakwe et al., 2014). The adjusted gender-specific prevalence for active epilepsy in this study was marginally higher in males. Higher prevalence rates for males have been reported in some Nigerian and African studies (Edwards et al., 2008, Birbeck & Kalichi, 2004, Hunter et al., 2012, Nwani et al., 2013), while female preponderance was reported in other studies from Nigeria and Africa (Osuntokun et al., 1982, Osuntokun et al., 1987a, Tekle-Haimanot et al., 1990, Rwiza et al., 1992, Winkler et al., 2009b). A study in a riverine community in Southwest Nigeria reported an equal prevalence (Mustapha et al., 2014). Our finding of a higher prevalence in childhood and early adulthood is consistent with previous Nigerian studies (Osuntokun et al., 1982, Osuntokun et al., 1987a, Osakwe et al., 2014, Nwani et al., 2015) and African studies (Tekle-Haimanot et al., 1991, Preux & Druet-Cabanac, 2005, Winkler et al., 2009b, Ngugi et al., 2013a). In Afikpo we observed different highest peak prevalence in late adulthood followed by a smaller peak in children. There are no previous community-based studies in Afikpo to compare, however, this different peak prevalence may suggest the possible increase in the occurrence of head trauma and strokes which contributes enormously to the burden of epilepsy in these age groups (Bell & Sander, 2001), or a true decline in the occurrence of epilepsy from reasons not fully known. This change in temporal trend in age-specific peak occurrence of epilepsy has been reported in India and may be linked to demographic transition,

improved living conditions and healthcare services, and better health-seeking behaviours (Amudhan et al., 2015). Conversely, a small number of people screened could have skewed the results.

Our reported incidence rates also vary, with estimates in Afikpo and Ijebu-Jesa being much lower than in Gwandu. The higher incidence in Gwandu is similar to reports from rural Uganda, Kenya and the Andean region of Ecuador (Placencia et al., 1992, Kaiser et al., 1998a, Mung'ala-Odera et al., 2008, Kaddumukasa et al., 2016). The incidence in Ijebu-Jesa and Afikpo are much lower than previously reported (Ngugi et al., 2013b, Fiest et al., 2017), but higher than in a South African study (Wagner et al., 2015a). The incidence rate combining data from the three sites was higher than the median incidence and pooled incidence rates for Africa and the HIC from previous meta-analyses (Ngugi et al., 2011, Kotsopoulos et al., 2002, Fiest et al., 2017). The bimodal peak incidence rates observed in the first and second decade of life, with very few incident cases in the older subjects is consistent with previous reports in Africa (Tekle-Haimanot et al., 1997, Kotsopoulos et al., 2002, Winkler et al., 2009b). The few incident cases and a smaller denominator in older subjects must be taken into account. The temporal trend is changing in HIC with the incidence of epilepsy is higher in the elderly compared to children, because of improved perinatal care and enhanced immunisation (Everitt & Sander, 1998, Sander, 2003). This change has also been reported in a recent systematic review from India (Amudhan et al., 2015). The variation in the incidence rate between sites observed in this study and others done elsewhere are largely due to differences in study design, aetiology and socioeconomic characteristics, in addition to unexplained heterogeneity between studies (Fiest et al., 2017). Our incidence data should be interpreted with caution because of the short period (one year) and the retrospective nature. A higher incidence, particularly in Gwandu, suggests that on-going risk factors are at play leading to brain insult, in our case among children. A higher incidence is observed in people with a poorer socioeconomic background (Heaney et al., 2002) and those areas with poor obstetric practices

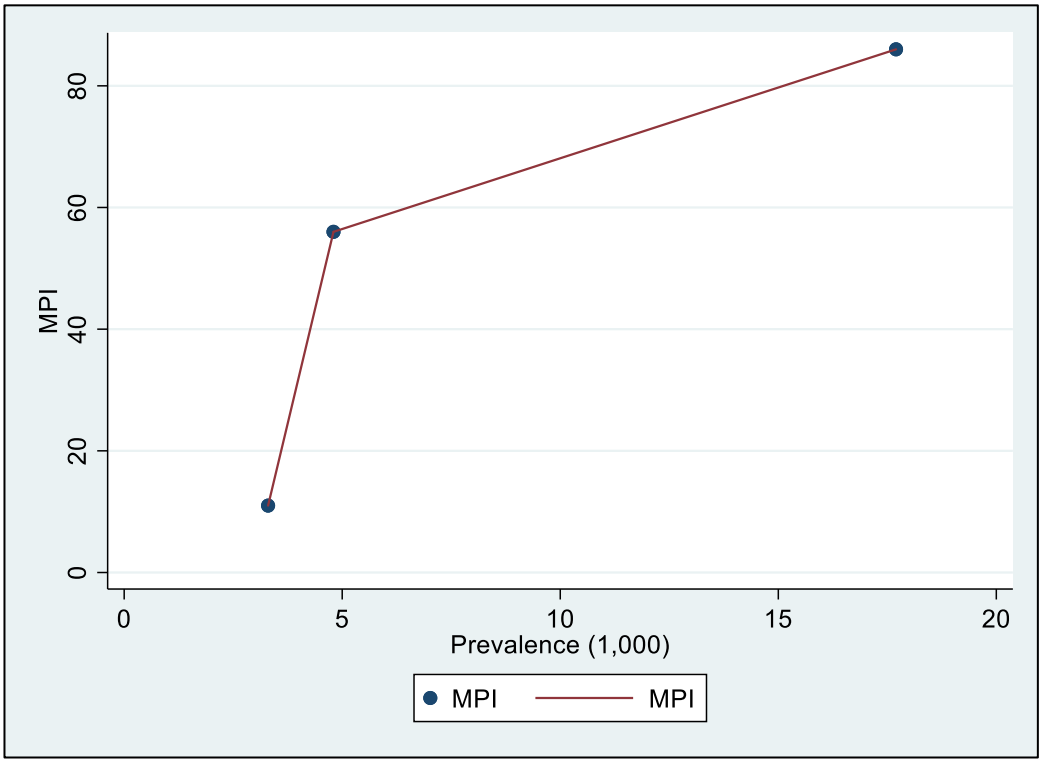
(Yemadje et al., 2011). The UK General Practice Research Database (GPRD) reported a prevalence of 5.2/1,000 and an incidence of 80.8/100.000; however, the prevalence and incidence were lower in children and higher in older people, which is different from our findings (Wallace et al., 1998). This study show similarities with studies done elsewhere in LMICs and HICs as shown in a systematic review (Fiest et al., 2017), but it is inadvisable to compare estimates due to the varying methodological differences in definitions and case ascertainment, the dynamics of the recruitment strategy, the inherent differences in population and the size of population screened (Sander & Shorvon, 1987, Thurman et al., 2011).

The reason for the large difference in the incidence estimates compared to the prevalence estimates when Gwandu was compared to the other sites is not fully known, but it could be suggested that people with epilepsy may have higher mortality in Gwandu. This discrepancy between the higher incidence and appreciable low lifetime prevalence in low-income countries (LICs) led to the postulation that the low lifetime prevalence is largely due to premature mortality (Bell et al., 2014). Further suggesting that the mortality may be much higher in LMIC, or people may go into remission and are not picked during surveys (Bell et al., 2014). The large number of children in our study together with the discrepancy in incidence and prevalence may suggest higher childhood mortality in Gwandu (Doctor et al., 2011, Yaya et al., 2017), irrespective of the independent effect of premature mortality due to epilepsy. People with less severe epilepsy or those in remission may be less likely to disclose the disease for fear of stigmatization with no concurrent benefits. This might lead to under-ascertainment of cases when assessing the lifetime prevalence of epilepsy (Beghi & Hesdorffer, 2014). Under-ascertainment of epilepsy in lifetime prevalence studies may also occur when remission leads a person to conceal epilepsy due to stigma. Methodological issues are a source of heterogeneity in the existing studies, making it difficult to attribute any one cause to the differences between incidence and lifetime prevalence, and it is unlikely

that anyone study methodology can be applied to all settings (Beghi & Hesdorffer, 2014).

We combined data from the three sites to get a 'national' figure. The combined prevalence was lower than the reported median prevalence of 15.0 per thousand for sub-Saharan Africa (Preux & Druet-Cabanac, 2005). The combined figures should be interpreted with caution because of the heterogeneity between sites, in addition to the marked difference in the total number diagnosed with epilepsy between sites. Gwandu has a much larger number and may skew overall estimates towards its average. Stigma may have affected people's willingness to reveal their epilepsy status particularly in southern parts of Nigeria and may have contributed to the lower estimates. Stigma is an important factor in epilepsy and mental conditions in the country (Adewuya & Ola, 2005, Adewuya & Oseni, 2005, Sanya et al., 2005), reports mainly in the Southwest and anecdotal evidence indicates that culturally averse attitudes appear more entrenched among the Yoruba people of Southwest (Coker et al., 2018, Jegede, 2017). The effect of stigma on response to community-based study could be an area of further studies. Despite these inherent differences in stigma, the wide variation between the North and the South cannot be explained by chance alone. The variations observed between sites and the number recruited may be due to socioeconomic, cultural, environmental and genetic differences. Local differences in exposure to infections or parasites, the quality and access to maternal and child health services which depend on socioeconomic factors may play a role (Sander, 2003). Northern Nigeria has some of the poorest health indices in Nigeria, with deficient access to health care and poorer obstetric practices (Babalola & Fatusi, 2009). Primary health care and immunisation coverage in southern Nigeria is better than in the North (Gunnala et al., 2016). These indices are a function of educational attainment and economic capacity which are influenced by sociocultural and religious factors (Babalola & Fatusi, 2009, Uthman, 2009). The Oxford Poverty and Human Development Index (OPHI) report also corroborates these facts and showed that Kebbi State where

Gwandu is located has one of the worse multidimensional poverty index (MPI) (Alkire & Robles, 2017, Oxford Poverty and Human Development Initiative, 2017). MPI is a function of deprivation in education, health, living standard, income and employment. When we compared MPI between these three sites with our corresponding prevalence, we observed that MPI was directly proportional to the prevalence of epilepsy (Figure 9).



	MPI (%)	Prevalence (per 1,000)
Gwandu	86	17.7
Afikpo	56	4.8
Ijebu-Jesa	11	3.3

Figure 10: Comparing MPI with the prevalence from three sites

A presumed cultural reason for the lower prevalence of epilepsy in Ijebu-Jesa may due to the issues of a diagnostic label for epilepsy. One particular label is "*ogun oru*" (nocturnal warfare), a condition reported in southwest Nigeria which includes nocturnal seizures and other nighttime disturbances. It is common in females, attributed to

demonic possession of the body and psyche during sleep and perceived to be due to an underlying feud between "earthly" and "spiritual" interactions (Aina & Famuyiwa, 2007). It is cultural not considered an epileptic condition and therefore these individuals may have been missed during the census. Another possible reason for the high prevalence and incidence in Gwandu may be the role of genetics. This area of Northwest Nigeria has some of the highest consanguinity rates in Nigeria (Obembe et al., 2016). Some forms of epilepsy have a genetic background which is usually underestimated in routine clinical practice (Thomas & Berkovic, 2014). We cannot rule out the migration of people with epilepsy congregating in clusters for stigma reasons (Kassah, 2009, Newton & Garcia, 2012), which may explain why some communities of Gwandu have very high estimated prevalence. Irrespective of the reason for the higher epilepsy burden, temporal and spatial clustering is usually from a combination of genetics and shared environmental as well as infectious aetiologies (Hesdorffer et al., 2012). The influence of consanguinity and assortative mating on epilepsy could be an area of further research. Our study has shown that in Gwandu and its environs epilepsy should be considered a serious health issue and given the priority it deserves. The large variation in the number of cases identified between sites emphasizes the need for larger population-based study.

Strengths: This survey is the first to be conducted in a quasi-nationally representative sample, which allows for generalisability. It shows that one area is different from another. A standardized criterion for all definitions and classifications was used in addition to using a validated epilepsy screening questionnaire in the local languages (Thurman et al., 2011). The calculated prevalence was age-standardised and corrected for attrition and sensitivity of the screening tool. These adjustments are important to make a fairer comparison between groups with different age distributions (Chinnakali et al., 2012). During the fieldwork, concerted efforts were made to maintain the quality and integrity of the study, by prompt payment of stipends, providing transport allowance for the field workers and promoting good interpersonal relationships between

enumerators and investigators. Regular meetings and the use of mobile phone conversations between the teams to de-escalate difficult issues helped. The study also benefited from positive cooperation of traditional and spiritual leaders. The explanations of the process and importance of the research and assurances of confidentiality contributed to the successful conduct of the study.

Limitations: The door-to-door design despites its advantages had its inherent limitations and subjectivity. This study, unlike others, did not use the multiple-source case-ascertainment methods, which in addition to the traditional door-to-door survey uses the capture-recapture method and the key-informant approach (Pal et al., 1998, Debrock et al., 2000). The use of different methods simultaneously could have improved the efficiency of community screening. Recently, there has been a call to promote the use of mixed-method designs in implementation research and the challenges and complexity of implementing field research mean that the use of a single methodological approach is often inadequate (Palinkas et al., 2015). It would have been helpful to check the local health service records for any epilepsy cases seen previously. The poor primary and secondary healthcare record keeping however meant this method could not be useful.

The incidence rate in this study may be faulted, as the follow-up time is relatively short. One year is too short a period to get a reliable incidence estimate as the dynamics of the disease process over a short period has some uncertainty and reliable outcome assessment depends on whether or not the study end has been defined upfront. The exclusion of children less than six years of age may also have underestimated the burden of epilepsy. We followed this approach to address the concern of including children with febrile convulsions. Lastly, the lack of investigations like EEG and neuroimaging is also a limitation, but investigations are not a necessary prerequisite for the diagnosis of epilepsy (Pohlmann-Eden & Newton, 2008).

5.6 Conclusion

This chapter reports the findings of a door-to-door survey conducted to estimate the prevalence and incidence of epilepsy in three representative regions. The estimated prevalence and incidence in Gwandu northern Nigeria are much higher than in the two other sites in South Nigeria. Future research using the methods described can build on the present study to investigate epilepsy in other parts of Nigeria improving on the current response rate and the size of the enumerated communities. Our findings may represent a part of the epilepsy burden, as people with less severe epilepsy are more likely to present for assessment.

Chapter 6: Sociodemographic and clinical characteristics of active epilepsy cases

6.1 Abstract

Background: This chapter describes the sociodemographic and seizure characteristics of people with active epilepsy identified from the three rural areas of Nigeria. **Methods:** Those cases with active epilepsy identified and confirmed from the 2-stage screening process were selected. These cases were interviewed and examined by physicians. Data on sociodemographic and seizure characteristics were recorded using an epilepsy questionnaire. Largely descriptive analyses were done for comparing data between sites and to produce a pooled result from the three sites. **Results:** From the 254 people confirmed to have active epilepsy, 252 participated; 40 from Afikpo, 24 from Ijebu-Jesa and 188 from Gwandu. The median age and interquartile range (IQR) of subjects at time of recruitment was 18 (IQR: 11.0 – 25.0) years in Gwandu which was significantly younger compared to 25.5 (IQR: 19.5 – 41.1) years and 25 (IQR: 12.5 – 28.5) years in Afikpo and Ijebu-Jesa respectively ($P < 0.001$). The median age at seizure onset was 6 (IQR: 4 – 10) years and not statistically different between sites ($P = 0.359$). The median duration of epilepsy significantly varied across the centres, lowest in Gwandu (9.5 years) and highest in Afikpo (18.5 years). Generalised epilepsy was reported in 48.4% and focal epilepsies in 45.2%. Eighty (31.7%) subjects reported SE. Forty-four (17.5%) persons had varied degree of cognitive decline or learning difficulties significantly different across sites, highest in Afikpo compared to Gwandu ($P < 0.001$). Seizure-related injuries occurred in 63.9% of all participants. **Conclusions:** Despite the similarities in some characteristics, differences exist between these sites. The report of an earlier age of onset may suggest early perinatal injury from substandard obstetric practices and possibly genetic contributions especially from Gwandu in Northern Nigeria.

Keywords: Epilepsy, seizure, demographic, characteristic, gender.

6.2 Introduction

Epilepsy is now considered to be a multi-dimensional disorder (Yuen et al., 2018), with the tendency to have recurrent unprovoked seizures associated with long-term neurobiologic, cognitive and psychosocial implications (Fisher et al., 2014). Seizures are usually the most consequential manifestation and can either be motor, sensory, psychic or autonomic (Fisher et al., 2017). Clinical data on epilepsy in SSA are scarce and inconsistent and understanding seizure characteristics are often made more difficult as eyewitness reports are often lacking. The unpredictable and dramatic nature also makes reporting difficult. The individual who has repeatedly witnessed the patient's events is usually the most reliable person to provide an accurate description and history. Seizure descriptions by witnesses are, however, often inaccurate and widely varied (Mannan & Wieshmann, 2003); this is further compounded in sub-Saharan Africa by the absence of video-EEG data (Nowacki & Jirsch, 2017).

6.3 Methods

The onset, type and manifestations of seizures depend on the location (focus) and aetiology. Those with birth complications are likely to start earlier in life, followed by genetic epilepsies which are more likely to occur in the second or third decade of life and also in the first months or years depending on the mutation, while those with head injuries and other acquired brain conditions are more likely to start later in life (Sander & Shorvon, 1996). Little is known about the clinical manifestations of epilepsy in Nigeria (Ogunrin, 2006). The findings may or may not be similar to other community-based studies in SSA (Tekle-Haimanot et al., 1990, Kaiser et al., 2000, Munyoki et al., 2010, Kariuki et al., 2014). Any differences are likely due to genetic and aetiological factors, in addition to the variations in study design (Sander & Shorvon, 1996). Here, we report the sociodemographic and clinical characteristics of people with active epilepsy recruited from a door-to-door survey.

Subjects with active epilepsy were identified from a door-to-door cross-sectional study described in Chapter 5. Subjects were interviewed and examined in-depth by neurologists and a neuropsychiatrist. Data on sociodemographic and seizure characteristics were collected. These included ethnicity, religion, and educational attainment, marital and occupational status, and monthly income. The age of onset, seizure history, duration of epilepsy, seizure frequencies, presence of aura, post-ictal phenomena, seizure precipitants, seizure-related injuries, and other antecedent histories was also collected. Basic physical and neurological examinations were conducted. Any degree of learning or cognitive impairment was recorded as either present or absent as a full cognitive assessment was not done. This is because a full battery of neuropsychological examination takes time and beyond the scope of this work. A relative or caregiver with knowledge of the seizures accompanied the subjects for clarification. The research teams witnessed four seizures during the assessment (two persons each from Gwandu and Afikpo). Relatives were encouraged to use mobile phone cameras to capture seizure events and show the recordings to the research team. Parents or caregivers were interviewed if the participant was a child or cognitively impaired. All information was recorded in an epilepsy pro-forma (Preux, 2002). The collaborators at the sites reviewed all the cases and completed pro-forma; all were consultant neurologists or neuropsychiatrists. Lastly, the principal investigator also reviewed the pro-formas. The definition of *active epilepsy* was based on the recommendation by the International League Against Epilepsy (ILAE) Commission report on Epidemiology (Thurman et al., 2011). Where possible the cases confirmed were classified according to current International League Against Epilepsy (ILAE) recommendations for the clinical classification of seizures as either generalized, focal, combined, or unknown using the recently revised operational classification of seizure types by ILAE (Fisher et al., 2017). The *age of onset* was defined as the age of occurrence of first unprovoked seizure (Thurman et al., 2011). *Seizure frequency* was categorized as daily, weekly, monthly, every two to six months and yearly or longer.

Status epilepticus (SE) was described as seizures lasting more than 30 min or a succession of seizures without full recovery of consciousness (Trinka et al., 2015).

Statistical Analysis: All data were entered into Microsoft Excel 2010 and statistical analyses were performed using Stata version 15 (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). Data presented in this chapter are largely descriptive. The Chi-square test (or Fisher's exact) was used to compare categorical variables between sites. The continuous variables were non-normally distributed using the Shapiro-Wilk W test for normality. The non-parametric Kruskal-Wallis test was used to compare continuous variables across the three sites. The Wilcoxon Rank Sum test was used to compare variables between the two genders and age groups (< 18 and ≥ 18 years). A P-value of 0.05 was set as a cut-off for the level of significance.

6.4 Results

Of 254 subjects confirmed to have active epilepsy, 252 (49.2% females) were recruited into the study (no information was obtained in two persons in Afikpo). These included 40 (47.5% female) subjects from Afikpo, 24 (50.0% females) from Ijebu-Jesa and 188 (49.5% females) from Gwandu. Table 25 describes the sociodemographic characteristics of the three sites. The total median and interquartile range (IQR) of the age of all subjects from the three sites was 19 (IQR: 12.0 – 27.0) years. Those from Gwandu were significantly younger (P < 0.001). Figure 10, 11 and 12 displays the age group by total, centre and gender.

Table 25: Sociodemographic characteristics of recruited subjects

	Afikpo (n =40)	**Ijebu-Jesa (n=24)**	**Gwandu (n=188)**	**Total (N=252)**	**p-value***
Age (years)					
Median	25.5 (IQR:19.5 – 41.0)	25.0 (IQR:12.5 – 28.5)	18 (IQR:11.0 – 25.0)	19 (IQR: 12.0 – 27.0)	< 0.001
Gender					
Male	21 (52.5%)	12 (50.0%)	95 (50.5%)	128 (50.8%)	0.972
Female	19 (47.5%)	12 (50.0%)	93 (49.5%)	124 (49.2%)	
Religion					
Christianity	40 (100.0%)	20 (83.3%)	0 (0.0%)	60 (23.8%)	< 0.001
Islam	0 (0.0%)	4 (16.7%)	188 (100.0%)	192 (76.2%)	
Marital status					
Single	32 (80.0%)	16 (66.7%)	147 (78.2%)	195 (77.4%)	0.141
Married	7 (17.5%)	6 (25.0%)	37 (19.7%)	50 (19.8%)	
Divorced	0 (0.0%)	1 (4.2%)	4 (2.1%)	5 (2.0%)	
Widowed	1 (2.5%)	1 (4.2%)	0 (0.0%)	2 (0.8%)	
Education					
None or not in school	13 (32.5%)	3 (12.5%)	106 (56.4%)[#]	122 (48.4%)	< 0.001
Primary	16 (40.0%)	9 (37.5%)	57 (28.7%)	79 (31.4%)	
Secondary	9 (22.5%)	8 (33.3%)[#]	26 (13.8%)	43 (17.1%)	
Tertiary	2 (5.0%)	4 (16.7%)[#]	2 (1.1%)	8 (3.2%)	
Employment					
Unemployed[α]	19 (47.5%)	7 (29.2%)	78 (41.5%)	104 (41.3%)	< 0.001
Wage earner/civil servant	1 (2.5%)	1 (4.2%)	6 (3.2%)	8 (3.2%)	
Crafts or trademan/-woman	8 (20.0%)	6 (25.0%)	11 (5.8%)[#]	25 (9.9%)	
Farmer	1 (2.5%)	0 (0.0%)	40 (21.3%)[#]	41 (16.3%)	
Student	2 (5.0%)	1 (4.2%)	14 (7.5%)	17 (6.8%)	
Semi-skilled/labourer	9 (22.5%)	9 (37.5%)	39 (20.7%)	57 (22.6%)	

* P-value significance set at 0.05; [#]Shows were it is significant different from other cells after a post-hoc analysis using adjusted residuals for Chi-squared (or Fisher's exact) test or a one-way ANOVA with Bonferroni correction. [α] These unemployed people are excluded from both the cash economy or community based income.

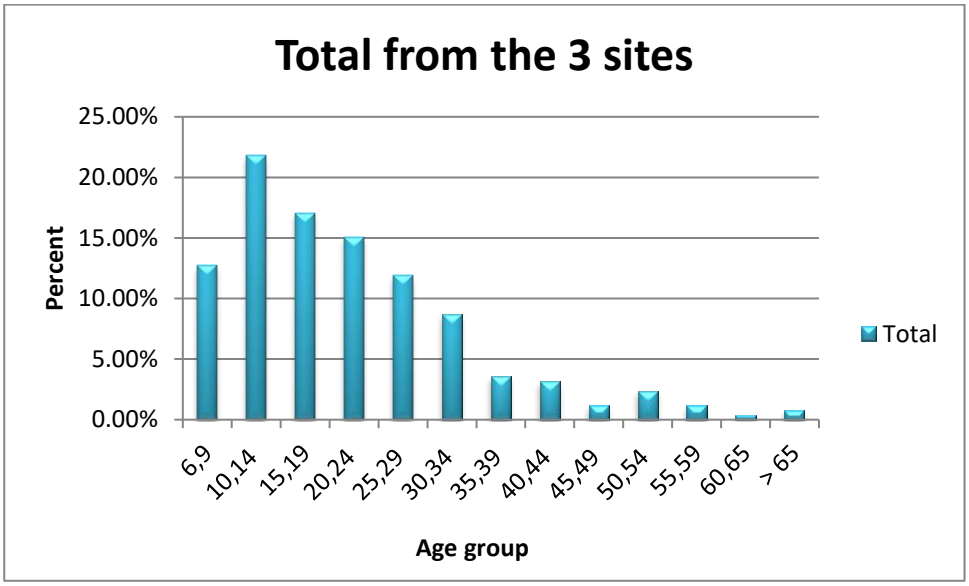


Figure 11: Age group of subjects recruited

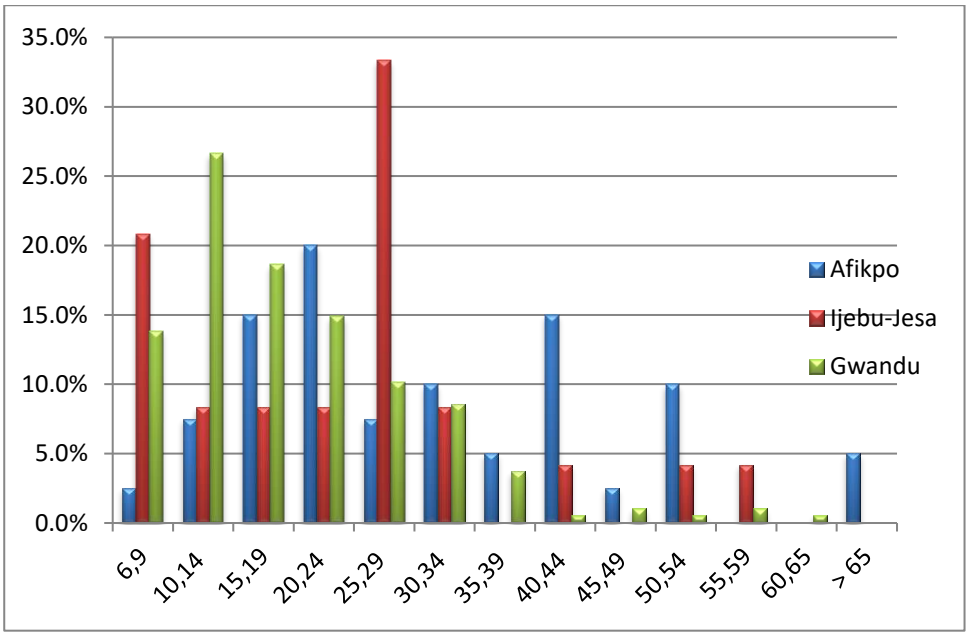


Figure 12: Age group by centres

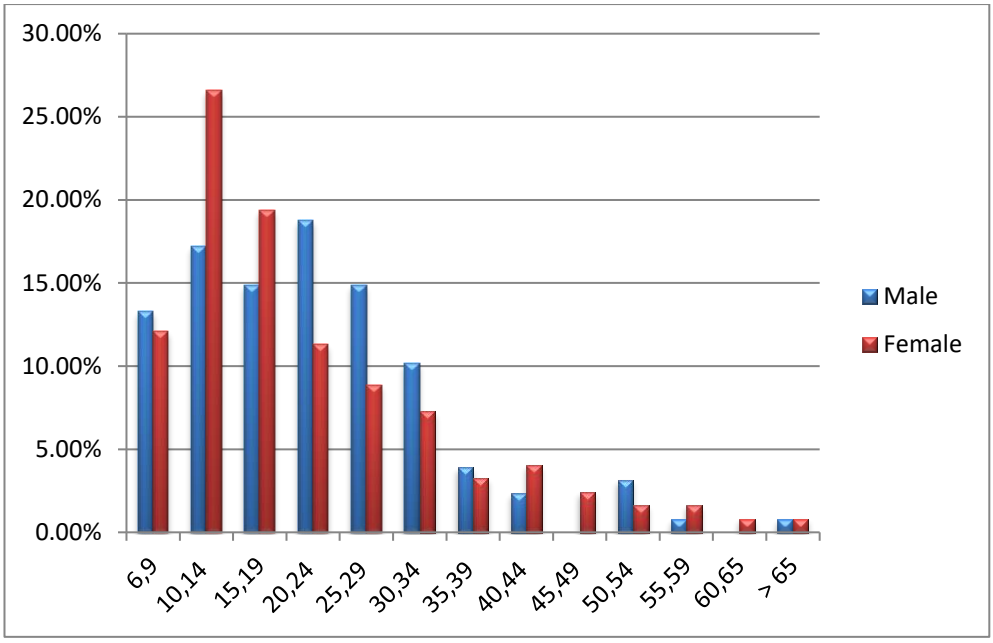


Figure 13: Age group of subjects recruited by gender

The gender distribution was not statistically significant across sites (P = 0.972). A significant difference in educational attainment was observed across sites (P < 0.001). More than half in Gwandu compared to a third in Afikpo and one-eighth in Ijebu Jesa did not have at least a primary education or were not attending school. There was a significant difference in employment rates (P < 0.001), with the unemployment rates higher in Afikpo and Gwandu. People in Gwandu were more likely to be farmers and those in Afikpo more likely to be involved with crafts or trade.

Table 26 shows the clinical and seizure characteristics of the subjects by the site. The combined median age of seizure onset was 6 (IQR: 4 – 10) years, with no significant difference between sites (P = 0.359). The median duration of epilepsy significantly varied across the sites, twice as long in Afikpo (18.5 years) compared to Gwandu (9.5 years) (P < 0.001). Primarily generalised epilepsy occurred in 122 (48%) and focal epilepsies in 114 (45%) of all those recruited from various sites, with no significant difference across the three sites (P = 0.617). There was also no significant difference in seizure types across sites (P = 0.396). The most common seizure type was

generalised motor (convulsive) seizure (39%), followed by focal seizures with impaired awareness (29%). About a third had more than one seizure type. Generalised non-motor occurred in 13.5% of individuals. Eighty (~ 32%) subjects in total reported having had SE, lowest in Afikpo (17.5%) and highest in Gwandu (35%), however, this difference was not statistically significant (P = 0.091). Emotional disturbance, lack of sleep and stopping ASM were the most common seizure precipitants. Cognitive deficit was recorded in 44 (17.5%) persons, significantly different across sites (P < 0.001); four times higher in Afikpo compared to Gwandu. Two (5%) cases had hemiparesis and one (2.5%) had cerebral palsy from Afikpo. Two (16.7%) cases with hemiparesis, another two with microcephaly, one (4%) each had bilateral lateral strabismus, hearing impairment, and monoparesis in Ijebu-Jesa. Three (1.6%) each had hemiparesis and cerebral palsy, and one (0.5%) was deaf and mute in Gwandu. Table 27 shows that seizure-related injuries occurred in 64% of all the subjects, this was statistically significant across sites (P=0.027), with higher rates of injuries in Afikpo (82.5%). Soft tissue, head, burns, fractures, eye and submersion injuries were significantly more common in subjects from Afikpo.

Table 26: Seizure history characteristics of recruited subjects

	Afikpo (n =40)	**Ijebu-Jesa (n=24)**	**Gwandu (n=118)**	**Total (N=252)**	**p-value***
Age at seizure onset (years)					
≤ 9	23 (57.5%)	18 (75.0%)	134 (71.3%)	175 (69.4%)	0.018
10 – 19	9 (22.5%)	3 (12.5%)	44 (23.4%)	56 (22.2%)	
20 – 29	4 (10.0%)	2 (8.3%)	5 (2.7%)[#]	11 (4.4%)	
30 – 39	4 (10.0%)[#]	0 (0.0%)	4 (2.1%)	8 (3.2%)	
≥ 40	0 (0.0%)	1 (4.2%)	1 (0.5%)	2 (0.8%)	
Median duration of epilepsy (years)					
	18.5 (IQR: 12.5 – 29.5)	12.5 (IQR: 4.0 – 24.5)	9.5 (IQR: 6.0 – 15.0)	11.0 (IQR: 6.0 – 18.0)	< 0.001
Duration of epilepsy (years)					
< 10	7 (17.5%)[#]	9 (37.5%)	94 (50.0%)[#]	110 (43.7%)	< 0.001
10 – 19	18 (45.0%)	8 (33.3%)	62 (33.0%)	88 (34.9%)	
20 – 29	5 (12.5%)	6 (25.0%)	26 (13.8%)	37 (14.7%)	
≥ 30	10 (25.0%)[#]	1 (4.2%)	6 (3.2%)	17 (6.7%)	
Type of epilepsy					
Focal	18 (45.0%)	11 (45.8%)	85 (45.2%)	114 (45.2%)	0.617
Generalised	17 (42.5%)	13 (57.2%)	92 (48.9%)	122 (48.4%)	
Combined focal and generalised	4 (10.0%)	0 (0.0%)	8 (4.3%)	12 (4.8%)	
Unknown	1 (2.5%)	0 (0.0%)	3 (1.6%)	4 (1.6%)	
Seizure type[§]					
Focal motor	4 (10.0%)	4 (16.7%)	18 (9.6%)	26 (10.3%)	0.396
Focal to bilateral tonic-clonic	5 (12.5%)	0 (0.0%)	12 (6.4%)	17 (6.8%)	
Focal with impaired awareness	9 (22.5%)	7 (29.2%)	57 (30.3%)	73 (29.0%)	
Generalised Motor	18 (45.0%)	9 (37.5%)	71 (37.5%)	98 (38.9%)	
Generalised Non-Motor	3 (7.5%)	4 (16.7%)	27 (14.4%)	34 (13.5%)	

Table 26: Seizure history characteristics of recruited subjects

	Afikpo (n =40)	**Ijebu-Jesa (n=24)**	**Gwandu (n=118)**	**Total (N=252)**	**p-value***
Unknown	1 (2.5%)	0 (0.0%)	3 (1.6%)	4 (1.6%)	
More than one seizure type	9 (22.5%)	6 (25.0%)	64 (34.0%)	78 (30.9%)	0.076
Seizure frequency					
Daily	22 (55.0%)[#]	4 (16.7%)	9 (4.8%)[#]	35 (14.0%)	< 0.001
Weekly	9 (22.5%)	3 (12.5%)	43 (23.1%)	55 (22.0%)	
Monthly	5 (12.5%)[#]	11 (45.8%)	83 (44.6%)	99 (39.6%)	
One in 2 to 6 months	2 (5.0%)[#]	4 (16.7%)	51 (27.4%)	57 (22.8%)	
Yearly	2 (5.0%)	2 (8.3%)	0 (0.0%)	4 (1.6%)	
Seizure timing					
Nocturnal	5 (12.5%)	4 (16.7%)	16 (8.5%)	25 (9.9%)	0.038
Early morning	6 (15.0%)	6 (25.0%)[#]	14 (7.5%)[#]	26 (10.3%)	
Afternoon	1 (2.5%)	2 (8.3%)	5 (2.7%)	8 (3.2%)	
Anytime	28 (70.0%)	12 (50.0%)[#]	150 (79.8%)	190 (75.4%)	
Unknown	0 (0.0%)	0 (0.0%)	3 (1.6%)	3 (1.3%)	
SE	7 (17.5%)	7 (29.2%)	66 (35.1%)	80 (31.7%)	0.091
Seizure precipitant[α]					
Emotional disturbance	23 (57.5%)[#]	2 (8.3%)	44 (23.4%)	69 (27.4%)	< 0.001
Alcohol	3 (7.5%)	2 (8.3%)	1(0.5%)[#]	6 (2.4%)	0.005
Lack of sleep	8 (20.0%)	5 (20.8%)	56 (29.8%)	69 (27.44%)	0.339
Flashing light	10 (25.0%)[#]	1 (4.2%)	15 (8.0%)	26 (10.3%)	0.008
Hyperventilation	9 (22.5%)[#]	2 (8.3%)	179 (9.0%)	28 (11.1%)	0.055
Menstruation	3 (7.5%)	2 (8.3%)	19 (10.1%)	24 (9.5%)	0.935
Stopping ASM	7 (17.5%)	9 (37.5%)	45 (23.9%)	61 (24.2%)	0.192
Pregnancy	1 (2.5%)	2 (8.3%)	3 (1.6%)	6 (2.3%)	0.112
Fever	1 (2.5%)	6 (25.0%)[#]	8 (4.3%)	15 (6.0%)	< 0.001
Learning difficulty or cognitive decline					
No	21 (52.5%)	19 (79.2%)	168 (89.4%)	208 (82.5%)	< 0.001
Yes	19 (47.5%)[#]	5 (20.8%)	20 (10.6%)[#]	44 (17.5%)	

* P-value significance set at 0.05; [#] shows where it is statistically different from other cells in a post-hoc analysis using adjusted residuals for Chi-squared (or Fisher's exact) test or a one-way ANOVA

Table 26: Seizure history characteristics of recruited subjects

	Afikpo (n =40)	**Ijebu-Jesa (n=24)**	**Gwandu (n=118)**	**Total (N=252)**	**p-value***

with Bonferroni correction; [§] some subjects had more than one seizure type and recorded as the main seizure types; [α] some had more than one precipitant; SE – status epilepticus.

Table 27: Seizure-related injuries across sites

	Afikpo (n =40)	**Ijebu-Jesa (n=24)**	**Gwandu (n=118)**	**Total (N=252)**	**p-value***
Seizure-related injury					
No	7 (17.5%)#	9 (37.5%)	75 (39.9%)	91 (36.1%)	0.027
Yes	33 (82.5%)#	15 (62.5%)	113 (60.1%)	161 (63.9%)	
Types of Injuries					
Bruises	18 (45.0%)	6 (25.0%)	70 (37.2%)	94 (37.3%)	0.277
Soft tissue	25 (62.5%)#	7 (29.2%)	35 (18.6%)	67 (26.6%)	< 0.001
Tongue	7 (17.5%)	6 (25.0%)	48 (25.5%)	61 (24.2%)	0.557
Head injury	21 (52.5%)#	5 (20.8%)	16 (8.5%)#	42 (16.7%)	< 0.001
Dental	4 (10.0%)	6 (25.0%)	23 (12.2%)	33 (13.1%)	0.178
Burns	10 (25.0%)#	2 (8.3%)	18 (9.6%)	30 (11.9%)	0.020
Fracture	13 (32.5%)#	1 (4.2%)	8 (4.3%)	22 (8.7%)	< 0.001
Eye	13 (32.5%)#	3 (12.5%)	1 (0.5%)	17 (6.8%)	< 0.001
Traffic injury	3 (7.5%)	1 (4.2%)	3 (1.6%)	7 (2.8%)	0.108
Submersion	3 (7.5%)#	1 (4.2%)	2 (1.1%)	6 (2.4%)	0.044

* P-value significance set at 0.05; # shows where it is statistically different from other cells and the average in a post-hoc analysis using adjusted residuals for Chi-squared test. Many of the subjects had more than one injury.

Table 28 reports the characteristics of the subjects by gender combining data from the three sites. There was no significant gender difference concerning subject's age, age at seizure onset, duration of epilepsy, and marital status. Females, however, were more likely to be unemployed compared to males (P = 0.013). There was a tendency for females to be uneducated compared to males, but this difference was not statistically significant (P = 0.163). There was a non-significant difference in epilepsy type between the two genders. More males reported focal epilepsy than females (50.8% versus 39.5%), while generalised epilepsy was commoner in females than males (52.4% versus 44.3%). SE and seizure-related injuries were more common among females but this was not statistically significant.

Table 28: Gender differences in sociodemographic and seizure characteristics

	Male (n = 128)	**Female (n = 124)**	**p-value**
Age (years)			
Median	20.0 (IQR: 12 – 26.5)	18 (IQR: 12 – 27.5)	0.377
Mean	21.5 ± 11.4	21.3 ± 13.3	0.905
Age at seizure onset (years)			
Median	6 (IQR: 3 – 10.5)	6 (IQR: 3 – 10.5)	0.620
Mean	8.6 ± 8.0	8.1 ± 7.8	0.636
Age at seizure onset (years)			
≤ 9	89 (69.5%)	86 (69.4%)	0.690
10 – 19	26 (20.3%)	30 (24.2%)	
20 – 29	6 (4.7%)	5 (4.0%)	
30 – 39	6 (4.7%)	2 (1.6%)	
≥ 40	1 (0.8%)	1 (0.8%)	
Duration of epilepsy (years)			
Median	11.5 (IQR: 6 – 19)	10 (IQR: 6 – 17)	0.588
Mean	12.9 ± 9.1	13.2 ± 11.0	
Marital status			
Single	103 (80.5%)	92 (74.2%)	0.232
Married	24 (18.8%)	26 (21.0%)	
Divorced	1 (0.8%)	4 (3.2%)	
Widower	0 (0.0%)	2 (1.6%)	
Education			
None	54 (42.2%)	68 (54.8%)	0.163
Primary	42 (32.8%)	37 (29.8%)	
Secondary	27 (21.1%)	16 (12.9%)	
Tertiary	5 (3.9%)	3 (2.4%)	
Employment			
Unemployed	41 (32.0%)	63 (50.8%)	0.013
Wage earner/civil servant	3 (2.3%)	5 (4.0%)	
Crafts or trade	11 (8.6%)	14 (11.3%)	
Farmer	26 (20.3%)	15 (12.1%)	
Student	12 (9.4%)	5 (4.0%)	
Semi-skilled/labourer	35 (27.3%)	22 (17.4%)	
Type of epilepsy			
Focal	65 (50.8%)	49 (39.5%)	0.277
Generalised	57 (44.3%)	65 (52.4%)	
Combined focal and generalised	5 (3.9%)	7 (5.7%)	
Unknown	1 (0.8%)	3 (2.4%)	

Table 28: Gender differences in sociodemographic and seizure characteristics

	Male (n = 128)	Female (n = 124)	p-value
Seizure type*			
Focal motor	14 (10.9%)	12 (9.7%)	0.684
Focal to bilateral tonic-clonic	9 (7.0%)	8 (6.5%)	
Focal with impaired awareness	41 (32.0%)	32(25.8%)	
Generalised Motor	49 (38.3%)	49 (39.5%)	
Generalised Non-Motor	14 (10.9%)	20 (16.1%)	
Unknown	1 (0.8%)	3 (2.4%)	
Reported status epilepticus	36 (28.1%)	44 (35.5%)	0.210
Seizure frequency n=186			
Daily	18 (14.3%)	17 (13.7%)	0.262
Weekly	33 (26.2%)	22 (17.7%)	
Monthly	49 (38.9%)	50 (40.3%)	
1 in 2 to 6 months	29 (18.3%)	34 (27.4%)	
Yearly	3 (2.4%)	1 (0.8%)	
Seizure timing			
Nocturnal	12 (9.4%)	13 (10.5%)	0.975
Early morning	14 (10.9%)	12 (9.7%)	
Afternoon	4 (3.1%)	4 (3.2%)	
Anytime	96 (75.0%)	94 (75.8%)	
Unknown	2 (1.6%)	1 (0.8%)	
Precipitant#			
Emotion	35 (27.3%)	34 (27.4%)	0.989
Alcohol	5 (3.1%)	1 (0.8%)	0.213
Lack of sleep	39 (30.5%)	30 (24.2%)	0.264
Flashing light	12 (9.4%)	14 (11.3%)	0.617
Hyperventilation	14 (10.9%)	14 (11.3%)	0.929
Menstruation	0 (0.0%)	23 (18.6%)	-
Stopping ASM	27 (21.1%)	34 (27.4%)	0.241
Pregnancy	0 (0.0%)	6 (4.8%)	-
Fever	8 (6.3%)	6 (4.8%)	0.625
Learning difficulty or cognitive decline			
No	105 (82.0%)	103 (83.1%)	0.829
Yes	23 (18.0%)	21 (16.9%)	
Seizure-related injury			
No	52 (40.6%)	39 (31.5%)	0.130
Yes	76 (59.4%)	85 (68.5%)	

***** Some had more than one seizure type, **#** some had more than one seizure precipitants

Table 29 shows sociodemographic and seizure characteristics by age groups (using 18 years as a cut-off) combining data from the three sites. The types of epilepsy were significantly different between the two age groups (P = 0.014). Adults were more likely to have focal epilepsies, while those younger were more likely to have generalised seizures. Older subjects are more likely to have daily seizures compared to younger subjects (P = 0.003). The frequency of SE did not differ between the two age groups.

Table 29: Age differences in sociodemographic and seizure characteristics

	< 18 years (n=108)	**≥ 18 years (n=144)**	**p-value**
Gender			
Female	48 (44.4%)	80 (55.6%)	0.081
Male	60 (55.6%)	64 (44.4%)	
Age at seizure onset (years)			
Median	4 (IQR: 2.5 – 7.0)	9.0 (IQR: 4 – 15.0)	< 0.0001
Age at seizure onset (years)			
≤1	12 (11.1%)	15 (10.4%)	< 0.0001
2 – 5	59 (54.6%)[#]	33 (22.9%)[#]	
6 – 9	25 (23.2%)	31 (21.5%)	
10 – 19	12 (11.1%)[#]	44 (30.6%)[#]	
20 – 29	0 (0.0%)	11 (7.6%)	
30 – 39	0 (0.0%)	8 (5.6%)	
≥ 40	0 (0.0%)	2 (1.4%)	
Duration of epilepsy (years)			
Median	6.0 (IQR: 3 – 9)	17 (IQR: 11 – 23)	< 0.0001
Mean	6.2 ± 3.6	18.2 ± 10.3	
Type of epilepsy			
Focal	39 (36.1%)[#]	75 (52.1%)[#]	0.014
Generalised	64 (59.3%)[#]	58 (40.3%)[#]	
Combined focal and generalised	3 (2.8%)	9 (6.3%)	
Unknown	2 (1.9%)	2 (1.4%)	
Reported status epilepticus	33 (30.6%)	47 (32.6%)	0.725
Seizure frequency n=186			
Daily	6 (5.6%)	29 (20.3%)	0.003
Weekly	24 (22.4%)	31 (21.7%)	
Monthly	42 (39.3%)	55 (39.9.3%)	

Table 29: Age differences in sociodemographic and seizure characteristics

	< 18 years (n=108)	**≥ 18 years (n=144)**	**p-value**
1 In 2 to 6 months	33 (30.8%)	24 (16.9%)	
Yearly	2 (1.9%)	2 (1.4%)	
Seizure timing			
Nocturnal	9 (8.3%)	16 (11.1%)	0.183
Early morning	8 (7.4%)	18 (12.5%)	
Afternoon	2 (1.9%)	6 (4.2%)	
Anytime	89 (82.4%)	101 (70.1%)	
Unknown	0 (0.0%)	3 (2.1%)	
Precipitant*			
Emotion	20 (18.5%)	49 (34.0%)	0.006
Alcohol	0 (0.0%)	6 (4.2%)	0.032
Lack of sleep	28 (25.9%)	41 (28.5%)	0.654
Flashing light	9 (8.3%)	17 (11.8%)	0.370
Hyperventilation	12 (11.1%)	16 (11.1%)	1.000
Menstruation	2 (1.9%)	22 (15.3%)	< 0.0001
Stopping ASM	20 (18.5%)	41 (28.5%)	0.068
Pregnancy	0 (0.0%)	6 (4.2%)	0.032
Fever	9 (6.3%)	5 (4.8%)	0.095
Learning difficulty or cognitive decline			
No	88 (81.5%)	120 (83.3%)	0.702
Yes	20 (18.5%)	24 (16.7%)	
Seizure-related injury			
No	44 (40.7%)	47 (32.6%)	0.185
Yes	64 (59.2%)	97 (67.4%)	

[#] Some had more than one seizure precipitants

6.5 Discussion

This chapter describes the sociodemographic and clinical features of people with active epilepsy from three geographic, ethnic and culturally diverse settings of Nigeria.

The median age of our subject at recruitment is similar to the multicentre study in 5 countries of SSA (Kariuki et al., 2014) but different from the UK General Practice Research Database (GPRD) (Wallace et al., 1998). The significant age and gender differences between sites was also observed in the multisite study (Kariuki et al.,

2014). A study in southwest Nigeria reported a female preponderance (Osuntokun et al., 1987a). The differences in religion, educational attainment and employment across sites as well as the gender differences reflect the cultural and socioeconomic realities of SSA (Mula & Sander, 2016, Quereshi et al., 2017). Generally, education attainment is poorer in people with epilepsy (Callaghan et al., 1992, Quereshi et al., 2017). Our finding of lower educational attainment in Gwandu has been highlighted (Oxford Poverty and Human Development Initiative, 2017). The reason for the disparity of education is multifactorial. Children are less likely to be enrolled in formal schools, but more likely to be enrolled in the preferred Qur'anic based education in Gwandu (Csapo, 1981, Umar, 2001, Antoninis, 2014). The diagnosis of epilepsy may independently affect school enrolment due to the current attitude of students and teachers (Owolabi et al., 2014). It could be argued that the subjects in Gwandu were significantly younger and may not be in school and more likely to have been picked during the screening exercise. However, only those above six years were recruited and are past the age of enrolment into primary schools.

This study did not show any difference in median age at onset of seizure across sites as reported in a previous study (Kariuki et al., 2014). The median age at seizure onset is similar to the rural Ethiopian study (Tekle-Haimanot et al., 1990), but lower than the findings in Agincourt South Africa, Ifakara Tanzania, Kintampo Ghana (Kariuki et al., 2014, Wagner et al., 2014) and Haydom northern Tanzania (Winkler et al., 2009b), while the findings in Iganga Uganda and Kilifi Kenya were lower than our findings (Kariuki et al., 2014). However, the estimates of the combined data from five sites were similar to our combined estimates (Kariuki et al., 2014). This study is also in keeping with findings of no gender difference in the age of seizure onset (Kariuki et al., 2014). Most people may confuse the age of onset with those of febrile seizures; however, an attempt was made to ask of onset of non-febrile seizures.

The median age of onset was similar in the three regions, but at the time of the study people in Gwandu were significantly younger in comparison to the other 2

communities. Hence, the median duration of epilepsy was shorter in Gwandu. This lower duration of epilepsy in Gwandu, in addition to the much higher incidence compared to the prevalence reported in the earlier chapter, may suggest higher premature mortality from epilepsy in Gwandu (Bell et al., 2014). Higher remission rate cannot be ruled out, neither can the effect of higher childhood mortality reported in Northwest region of Nigeria be excluded (Doctor et al., 2011, Bell et al., 2014, Yaya et al., 2017). These discrepancies and its possible relationship to premature mortality should be a focus for future studies.

This study reported almost equal proportion of focal and generalised epilepsies with no gender difference. A similar percentage was observed in the multicentre study (Kariuki et al., 2014) and the Haydom study (Winkler et al., 2009b). Two studies from the Hai district of Tanzania reported focal-onset seizures in 72% of those 15 years and above and 65.2% among children aged 6 – 14 years (Burton et al., 2012, Hunter et al., 2012). A Nigerian (Osuntokun & Odeku, 1970) and an Ethiopian study reported generalised convulsive epilepsy in about 80 to 90% of their subjects (Tekle-Haimanot et al., 1990). Convulsive seizures are most reliably reported because they are dramatic (Ngugi et al., 2013a). The questionnaires developed in those studies may have had a bias to recruit people with convulsive seizure (Osuntokun et al., 1982). It is likely that the high occurrence of cerebral pathology in older subjects may be responsible for the predominance of focal seizures in those above 18 years (Huang et al., 2016).

The seizure frequency findings in Ijebu-Jesa and Gwandu are consistent with findings from other African countries (Kariuki et al., 2014). SE reported in this study varied and was highest in Gwandu. The higher SE reported in Gwandu might be due to access to donations of ASM, a supply that is irregular. The percentage of subjects with SE in Ijebu Jesa was higher than an earlier in-hospital study (14.1%) in a tertiary hospital also serving Ijebu-Jesa (Olubosede et al., 2017). The burden of SE varies between centres and suggests poorly managed epilepsy. The high percentage may have been due to overestimation of the duration of seizures. SE outside of epilepsy in LMIC are

more likely to be due to malaria, meningitis and encephalopathies (Kariuki et al., 2015, Olubosede et al., 2017), while in HIC cerebrovascular disease is commoner (Neligan & Shorvon, 2010). The seizure-related injuries reported in this study appear much higher than those from HIC (Tiamkao & Shorvon, 2006, Nguyen & Tellez Zenteno, 2009) and Africa (Bifftu et al., 2017). A high rate of injury was reported in an in-hospital study among children in Southwest Nigerian, the high rate was despite the treatment in the majority being reported as satisfactory (Lagunju et al., 2016). A study from Southeast Nigeria reported a very high injury rate; all 87 participants except one had seizure-related injuries (Birinus et al., 2012). This study reported a significantly varied rate of cognitive deficit between sites, highest in Afikpo and lowest in Gwandu. It is expected that with the higher obstetric problems in Gwandu, there should have been a higher rate of learning difficulties compared to the other sites. Our inability to perform a standard cognitive assessment could have potentially affected the frequency and missed those with mild cognitive impairment. A higher proportion of people with epilepsy in Gwandu were young and not in school and any mild deficit may not have been apparent. Since several medical characteristics such as the type of epilepsy syndrome, seizure frequency, number and type of ASMs affect cognitive deficit, further studies with full neuropsychological assessment are needed to understand this important area. The higher rates of injuries, daily seizure frequency and the higher number of people with cognitive decline in Afikpo may suggest recruitment of more persons with severe epilepsy. SE and injuries usually reflect poor treatment which may be worse in Nigeria.

Strength: The strength of this study is the community-based approach. Hospital-based study designs often do not reflect the true nature of events and have a bias of recruiting more severe cases or those who are more educated or affluent as they are more likely to seek biomedical healthcare. Secondly, we compared data from three diverse regions of Nigeria; the difference noted in this study proves that clinical characteristics vary not

only across international and national boundaries but even within the same country (Bell et al., 2014).

Limitations: Firstly, a major limitation is that we cannot be completely confident of the accuracy of seizures description, frequency and timing, despite attempting to get reports from a close relative and eyewitness. A study looking at the accuracy of seizure frequency reporting, comparing parent and video-EEG (vEEG), observed that only 38% of seizures were correctly reported by parents, with a sensitivity of 43% and positive predictive value of 76% (Akman et al., 2009). Similarly, a study evaluating the accuracy of seizure description by relatives using vEEG (Rugg-Gunn et al., 2001), reported that a relative's description on admission had a median accuracy of only 26%. Even after viewing a video recording and recalling the events, the median accuracy was just 44.5% for convulsive episodes. The relatives and caregivers of participants were encouraged to use mobile phone cameras to record seizure events, but the compliance was low, as only one video recording was submitted during the entire study period. Some of the reasons given for the low compliance were poor understanding of the importance of seizure characterisation, a run-down battery of mobile phones from lack of electricity and some relatives felt that it was unfair to record a video when a person was suffering from a seizure. These challenges of getting accurate seizure reports and how it can be improved could be an area of research in SSA. Since proper seizure characterisation is important in deciding treatment, and because of the scarcity and cost of vEEG, cheaper automatic seizure detection techniques could be developed to help (Elger & Hoppe, 2018). Secondly, the nature of data gathering of past seizure events may be liable to recall bias. It has been demonstrated that the failure to recall accurately an event in epilepsy should not in any way invalidate a work (Neugebauer et al., 1994). Thirdly, the larger sample size in Gwandu may skew results towards its average. This is the reason why analyses were conducted for individual sites, before combining the data.

6.6 Conclusion

The findings show that the median age of onset was similar across sites, but the median age at the time of recruitment and the median duration of epilepsy varied between sites and were lowest in Gwandu, which may suggest higher premature mortality or remission. There was an almost equal proportion between focal and generalised epilepsy. The rate of SE and seizure-related injuries were high. Those younger than 18 years were more likely to have generalised seizures. The differences reported may be due to differences in the aetiology. Further analyses on some of the questions will be discussed in the case-control part of the study.

Chapter 7: The epilepsy treatment gap and determinants of access to care in Nigeria

7.1 Abstract

Background: The epilepsy treatment gap and associated factors are not well known in Nigeria. This chapter determined the prevalence of the epilepsy treatment gap and factors that determine access to care and adherence from three sites in Nigeria. **Methodology:** People with active epilepsy were recruited from a cross-sectional door-to-door survey. The sociodemographic and clinical characteristics, the pattern of access to care and treatment-related information were obtained using an epilepsy pro-forma. Active epilepsy was defined as seizures occurring within the past one-year period and/or currently on treatment. Epilepsy treatment gap was defined as the number of people with active epilepsy not on treatment (or not properly treated) divided by the total number of people with active epilepsy expressed as a percentage. Potential factors associated with access to medical care and adherence were examined using univariate and multivariate logistic regression. **Results:** From the three sites, 252 (40 from Afikpo, 24 from Ijebu-Jesa and 188 from Gwandu) subjects were recruited. Of this, 91% visited traditional or spiritual healers for treatment, while 73% first sought treatment from them. Only 57% ever sought medical care from a health facility. Approximately 68% reported not taking ASM in the last one month, including those who had never been on medication. Carbamazepine and phenobarbital were the commonest medication prescribed. The self-reported therapeutic gap was 83.3% (95% CI: 78.1, 87.7). When this was considered together with the diagnostic gap, the treatment gap rose to as high as 94.4% (95% CI: 90.9, 96.9) and this was not statistically different across sites. The potential factors associated with failure to access to care include: difficulty reaching a health facility (OR 0.33, 95% CI: 0.14, 0.75; P = 0.008), non-acceptance of diagnosis (OR 0.36, 95% 0.15, 0.85; P = 0.021), perceived stigma (OR 0.16, 95% CI: 0.04, 0.71; P = 0.016) and cultural belief (OR: 0.31, 95% CI:

0.16, 0.62; P = 0.001). While factors associated with non-adherence include: afternoon seizures (OR 0.006, 95% CI: 0.001, 0.58; P = 0.029) learning difficulty (OR 0.16, 95% CI: 0.03, 0.88; P = 0.035), difficulty reaching a health facility (OR 25.44, 95% CI: 0.88, 735.88; P = 0.059) and cultural belief (OR 28.68, 95% CI: 1.70, 483.97; P = 0.020). **Conclusion:** The treatment gap is high in Nigeria and ways to reduce it should be a priority. The current cultural belief can be modified through patient and community education and engagement. The potential factors identified could be addressed in outreach programs.

Keywords: Epilepsy, Treatment gap, Access, Adherence, Nigeria

7.2 Introduction

Of the approximately 70 million people with epilepsy worldwide (Singh & Trevick, 2016), the current estimate is that 20% live in SSA (Prevett, 2013). People with epilepsy in SSA continue to experience a profound barrier to accessing quality health care with the majority not in either treatment or are inadequately treated (Meinardi et al., 2001, Mbuba et al., 2008). This epilepsy treatment gap remains high despite the efforts made by the WHO and other international organisations to bring epilepsy 'out of the shadow' by improving health care services, treatment and social acceptance (Reynolds, 2001). Studies have shown that with appropriate treatment about two-third of people with epilepsy could be seizure-controlled (Mattson et al., 1985, Goldenberg, 2010). Access to care is not easily measurable, and such measurements are insufficient to capture whether people receive effective care. Thus, the ability to give people with epilepsy standard care is dependent on the acceptable interaction between factors that determine access to care and adherence to treatment (Mbuba & Newton, 2009, Mbuba et al., 2012b, Bailie et al., 2015). A systematic review on the global disparity in the epilepsy treatment gap of LMICs and HICs showed that the treatment gaps commonly exceeded 50% to 75% in most LMICs, while the majority of HICs had gaps of less than 10% (Meyer et al., 2010). The treatment gap generally high in sub-Saharan varies widely between 23% and 100% (Ndoye et al., 2005, Edwards et al.,

2008, Simms et al., 2008, Koffi et al., 2009, Guinhouya et al., 2010, Amos & Wapling, 2011b, Ratsimbazafy et al., 2011, Mbuba et al., 2012b, Bora et al., 2015, Sebera et al., 2015, Hunter et al., 2016, Sokhi et al., 2016). The reasons for the high treatment gap in resource-limited settings are multifactorial, however the main attributing factors are inadequate skilled manpower, lack of basic primary care, cost of treatment and unavailability of ASMs which is significantly higher in rural dwellers (Mbuba et al., 2008, Carter et al., 2012, Meyer et al., 2012). The treatment gap is perpetuated by the current beliefs and cultural perceptions people have about epilepsy (Shorvon & Farmer, 1988). Most people would not even accept the diagnosis of epilepsy. The social acceptability is another dimension of access that is often neglected in epilepsy, as there must be a match between the sufferer's and health providers understanding of the condition (Dillip et al., 2012). Stigma also contributes to people's fear of accessing biomedical care (Mbuba et al., 2012b, O'Rourke & O'Brien, 2017). For those who access medical care, some have the idea that a finite short course of medication is sufficient to cure epilepsy (O'Rourke & O'Brien, 2017). In addition, due to the irregular and unpredictable nature of seizures, the expected benefit of ASMs or the detrimental effect of nonadherence is not immediately obvious (Faught, 2012). The effectiveness of epilepsy treatment also depends on the correct identification and diagnosis of the seizure type and the availability of potent medications as LMIC are prone to having substandard medications (Meyer et al., 2012).

It is not clear what the treatment gap and associated factors are in Nigeria. A literature search retrieved only three papers on the treatment gap in two rural communities limited by small sample size. These studies revealed an epilepsy treatment gap rate between 76% and 100% (Osuntokun et al., 1987a, Nwani et al., 2013, Eseigbe et al., 2014), and observed that cultural belief, weak health system and low SES were the most important determinants. A better understanding of the treatment gap and associated factors will ultimately help in making decisions about improving care standards. This study, therefore, was designed to determine the prevalence of epilepsy

treatment gap and treatment-related issues from three regions of Nigeria, in addition to evaluating factors that determine access to care and adherence.

7.3 Methodology

This is a population-based cross-sectional study conducted in Afikpo, Ijebu-Jesa and Gwandu located in the southeast, southwest and northwest Nigeria respectively. Subjects with active epilepsy were recruited from the prevalence study. The subjects underwent a detailed interview and evaluation by physicians. Information on basic sociodemographic, history on access to care, treatment history and referral pattern was acquired and recorded in the epilepsy questionnaire (Appendix 6).

Active epilepsy was defined as two or more unprovoked seizures and where persons are currently on treatment or whose seizures have occurred within the last one year period (Thurman et al., 2011). The *epilepsy treatment gap* was defined as the number of people with active epilepsy who are not on treatment or whose seizures are not been properly treated, expressed as a percentage of the total number with active epilepsy. It is recommended that the definition should include therapeutic and diagnostic deficits (Meinardi et al., 2001). In this study, the *therapeutic gap* was calculated as those who were not on treatment and were not adherent irrespective of who diagnosed the condition, while the treatment gap was calculated as the diagnostic plus therapeutic gap, including adherence based on the prescribed regimen (Mbuba et al., 2012b). Diagnostic gap was considered as those who had no access to a physician or a trained health personel to get a correct diagnosis (Berglund, 2014). Information was gathered on where subjects first sought help, how long it took to seek care, current treatment, the type and source of ASM and adherence to ASM. *Adherence* was defined as the extent to which a person follows the recommendations given by a health care provider (Kenreigh & Wagner, 2005). For this study, adherence was arbitrarily assessed when a person who is on ASM had missed three days or more in the last one month (Wang et al., 2003). *Seeking medical treatment* meant visiting formally recognised health facilities or hospital either public or private (Pariyo et al., 2009, Wandera et al., 2015).

The number of persons who have had a proper neurological consultation with investigations like EEG and neuroimaging was recorded. Learning difficulty was assessed historically by inquiry of parents or siblings when they had problems with following instruction, a problem with orientation and difficulty with learning in school. Subject's cultural beliefs on diagnosis and treatment, cultural attitudes and misconceptions were recorded as present or absent. *Perceived stigma* was defined as the measure of the extent to which people with epilepsy feel they are the victims of prejudice because epilepsy is culturally defined as undesirably different and was recorded as either present or absent (Jacoby & Austin, 2007). Questions related to stigma were adopted from the Kilifi Stigma Scale. It is a validated and culturally appropriate measure of stigma for an African setting (Mbuba et al., 2012a).

Factors that determine access to care were grouped into three based on the ILAE recommendation of the Andersen's behavioural model of health services use (Andersen, 1995, Thurman et al., 2011). The 'predisposing factors' (sociodemographic factors) included: age, gender, marital status, religion, cultural beliefs and attitudes to epilepsy. 'Health-need' factors that may reflect disease severity were recorded, which includes learning deficits, SE, and seizure-related injuries. 'Enabling factors' included: education, access to health insurance, distance to a health facility, monthly income, cost of medication and travel cost to a health facility in Naira (one US dollar ≈ 360 Naira). Cultural beliefs were measured as the perception and attitudes in interpreting or judging the causes of treatment of epilepsy based on the tradition or customary practices. Because most people do not accept the diagnosis of epilepsy and is a poorly understood factor in access to care, we added the question on "rejection of diagnosis" as a factor that determines access to care (Dillip et al., 2012). To calculate the distance to health facilities from their homes, the enumerators estimated a distance travelled by road. Ethical considerations are as previously documented.

Statistical analysis: All data were entered into Microsoft Excel 2010 and statistical analyses were performed using Stata version 15 (StataCorp. 2017. *Stata Statistical*

Software: Release 15. College Station, TX: StataCorp LLC). The continuous variables were skewed using the Shapiro-Wilk test. A one-way ANOVA with Bonferroni correction was used to compare means within and between the three sites, rather than do a "post hoc" analysis after Kruskal Wallis test (Cabin & Mitchell, 2000). The Pearson's chi-square test (or Fisher's exact) was used to compare categorical variables across the three sites. A post hoc analysis was done using the adjusted residuals to determine which groups differ from each other in a chi-square test for those that were statically significant at < 0.05 (adjusted residual > 3 is implicated in the statistical difference) (Sharpe, 2015). The *epilepsy treatment gap* was calculated as a percentage with their respective 95% confidence interval (95% CI) for each site and for the combined. In calculating the *epilepsy treatment gap*, we initially considered the *therapeutic gap* as those who are not on medication and not adherent irrespective of who diagnosed the individual. The treatment gap was also calculated as those who were not on treatment in the last one month. This includes those who had never been on treatment and those who had been on treatment but stopped up to a month. In addition, the treatment gap based on the ILAE commission definition of treatment gap which includes diagnostic and therapeutic gap was calculated (Meinardi et al., 2001). A univariate analysis was performed using a simple logistic regression to ascertain factors (predictor variables) associated with i) seeking medical care and ii) adherence to ASM (outcome variables) and were re-coded as a binary outcome (0 = No and 1 = Yes). To facilitate analysis, dummy predictor variables were created. Educational attainment was transformed into a binary variable, as those with at least primary education (6 years of education) or those without. Age was dichotomised into those < 18 years and ≥ 18 years. Some categorical variables were polychotomous (employment, epilepsy type, travel distance, travel cost and cost of ASM) and could not be converted to a binary variable. Marital status was recoded as single, married, divorced or widowed. Religion was categorized as Christianity or Islam, as most people in Nigeria tended to identify officially with one of the two religions even if they practised

in addition to some form of traditional beliefs. Data were analysed according to the sites of recruitment and combined to have a larger sample size of the representative population of Nigeria. After the univariate screening, variables with P-value < 0.2 were entered into a multivariable logistic regression model to identify independent predictors with P-value of < 0.05. The forward and backward process was also used to examine and verify predictors but was not relied on because of the limited power to select true variables and include noise variables in the final model especially for smaller sample sizes (Heymans et al., 2007). In dealing with missing data and to correct for the potential non-response bias that result in biased parameter estimates in logistic regression, multiple imputations by chained equation (MICE) were performed to get results with valid statistical inference. The MICE handles missing data by replacing missing values with multiple sets of simulated values to complete the data. It applies standard analyses to each completed dataset and adjusts the obtained parameter estimates for missing-data uncertainty (Rubin, 1996). Since the mechanism of missing-ness could not be known with all certainty and that all the possible mechanisms of missing-ness could have been at play, the imputation was done with no assumption about missing data mechanism using 25 imputations. The step-by-step process of the imputation scheme and subsequent analysis is shown in (Appendix 17).

7.4 Results

A total of 252 persons with active epilepsy were recruited from the door-to-door study. Table 30 shows how subjects access to care and treatment patterns. More subjects in Gwandu do not have at least a primary education or were not in school, compared the other sites (P < 0.0001). By the time of recruitment, 91% had seen traditional and/or spiritual healers for help, although this was slightly less common in Ijebu-Jesa, it was not statistically significant (P = 0.097). Overall, the majority (73%) sought help first from traditional and spiritual healers across sites. There was a significant difference in where people first sought help across sites (P < 0.0001), more people in Afikpo first sought help from a spiritual healer. Only 57.1% of subjects combined from the three sites

sought care from a formally recognised health facility, this was better in Ijebu-Jesa where only one-fifth of the subjects did not seek biomedical care (P = 0.057). There was a significant difference in time taken from the onset of seizures to seeking medical care across the three sites (P < 0.0001), with only about two-fifth attending a medical facility within the first year of onset of recurrent seizures. Almost all subjects in Afikpo and Ijebu-Jesa who sought medical care either were self-referred or were suggested by parent or relatives, and this varied across sites (P < 0.0001). Interestingly, 10.5% of subjects in Gwandu reported that a traditional or spiritual healer suggested they seek medical care. The median travel distance to health facility varied significantly between sites (0.0001), with a 20km median travel distance to a health facility in Gwandu, where subjects paid more for travel, however, this was not statistically different across sites (P = 0.277). Only one person in Afikpo (2.5%), two in Gwandu (1.1%) and none from Ijebu-Jesa reported having access to health insurance.

Looking at the past treatments with ASM, about half (51.6%) of the respondents in total reported having been on an ASM with no difference across sites. About a third reported taken ASM in last one month. Of those who reported their source of medication, the majority got their ASMs from registered pharmacies; a significant proportion purchased their medications from hawkers, with 18.5% from Gwandu getting their ASMs from donations. Carbamazepine was the most commonly used ASM by about three-fourth of persons who reported taken ASM, while 13.6% of people took phenobarbital. More than a third of persons in Afikpo did not know the name of the ASM they were taking compared to 10% in the other sites. Only about 6.9% were on polytherapy (two or more ASMs). Only 62 persons reported how much ASM costs per month. The median cost of ASM was highest in Afikpo compared to Ijebu-Jesa and Gwandu (P = 0.040). About two-third reported reduced seizures while on ASM. An estimated 16.7%, 5.0% and 1.1% had a neurological consultation in Ijebu-Jesa, Afikpo and Gwandu respectively (P = 0.001). Of all the persons recruited only one person in Afikpo had a neuroimaging

done and only 1.6% of all the persons had an EEG done, significantly higher in Ijebu-Jesa (P = 0.030).

Table 30: Access to care and treatment pattern for people with epilepsy across the three sites

	Afikpo [n = 40]	**Ijebu-Jesa [n =24]**	**Gwandu [n =188]**	**Total [n = 252]**	**P-value**
At least primary education or currently in school					
No	13 (32.5%)	3 (12.5%)	106 (56.4%)	122 (48.4%)	< 0.0001
Yes	27 (67.5%)	21 (87.5%)[#]	82 (43.6%)[#]	130 (51.6%)	
Where did you first seek help?					
Traditional healer	22 (55.0%)	8 (33.3%)	106 (56.7%)	136 (54.2%)	< 0.0001
Spiritual leader	16 (40.0%)[#]	5 (20.8%)	26 (13.9%)	47 (18.7%)	
District hospital	0 (0.0%)[#]	6 (25.0%)	49 (26.2%)	55 (21.9%)	
Primary health care	2 (5.0%)	3 (12.5%)[#]	1 (0.5%)[#]	6 (2.4%)	
Psychiatric hospital	0 (0.0%)	1 (4.2%)	5 (2.7%)	6 (2.4%)	
Tertiary healthcare	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (0.4%)	
Sought treatment from traditional and/or spiritual healer					
No	2 (5.0%)	5 (20.8%)	16 (8.5%)	23 (9.1%)	0.097
Yes	38 (95.0%)	19 (79.2%)	172 (91.5%)	229 (90.9%)	
Sought biomedical treatment					
No	20 (50.0%)	5 (20.8%)	83 (44.1%)	108 (42.9%)	0.057
Yes	20 (50.0%)	19 (79.2%)[#]	105 (55.9%)	144 (57.1%)	
Who suggested biomedical referral (n=145)					
Traditional or spiritual healer	0 (0.0%)	0 (0.0%)	11 (10.5%)	11 (7.6%)	< 0.0001
Primary care personnel	0 (0.0%)[#]	1 (5.3%)[#]	54 (51.4%)[#]	53 (37.9%)	
Self-referral	14 (66.7%)[#]	0 (0.0%)	15 (14.3%)	29 (20.0%)	
Parent or relative	7 (33.3%)	18 (94.7%)[#]	25 (22.8%)[#]	50 (34.5%)	
Time taken to seek medical care (n-143)					
< 1 month	5 (26.3%)	2 (10.5%)	11 (10.5%)	18 (12.6%)	< 0.0001
1 month - 1 year	4 (21.1%)	1 (5.3%)	37 (35.2%)[#]	42 (29.4%)	
1 year - 5 years	1 (5.3%)[#]	10 (52.6%)	41 (39.1%)	52 (36.4%)	
5 years - 10 years	2 (10.5%)	3 (15.8%)	0 (0.0%)	5 (3.5%)	
> 10 years	7 (36.8%)	3 (15.8%)	16 (15.2%)	26 (18.2%)	
Median estimated travel distance to health facility (km) (N=96)					

Table 30: Access to care and treatment pattern for people with epilepsy across the three sites

	Afikpo [n = 40]	**Ijebu-Jesa [n =24]**	**Gwandu [n =188]**	**Total [n = 252]**	**P-value**
	2 (IQR: 1.25 – 3.0)	3 (IQR: 1 – 10)	20 (IQR: 10 - 20) [#]	11 (IQR: 2 – 20)	0.0001
Median cost of transport to health facility (Naira[§]) (n=93)					
	200 (IQR: 50 – 500)	250 (IQR: 100 – 300)	300 (IQR: 150 – 800)	300 (IQR: 150 -800)	0.277
Access to Nigerian health insurance					
No	39 (97.5%)	24 (100.0%)	185 (98.4%)	248 (98.4%)	0.693
Yes	1 (2.5%)	0 (0.0%)	2 (1.1%)	3 (1.2%)	
Unsure	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.4%)	
Took antiseizure medication(s) (currently or previously)					
No	21 (52.5%)	15 (62.5%)	86 (45.7%)	122 (48.4%)	0.260
Yes	19 (47.5%)	9 (37.5%)	102 (54.3%)	130 (51.6%)	
On medication in the last one month (historically)					
No	28 (70.0%)	17 (70.8%)	125 (66.5%)	170 (67.5%)	0.851
Yes	12 (30.0%)	7 (29.2%)	63 (33.5%)	82 (32.5%)	
Currently on antiseizure medication(s) and adherent (historically)					
No	32 (80.0%)	19 (79.2%)	159 (84.6%)	210 (83.3%)	0.661
Yes	8 (20.0%)	5 (20.8%)	29 (15.4%)	42 (16.7%)	
Source of antiseizure medication(s) (n=130)					
Hawker	6 (37.5)	0 (0.0)	21 (19.4)	27 (20.1)	0.093
Registered pharmacy	9 (56.3)	8 (80.0)	44 (40.7)	61 (45.5)	
Hawker and pharmacy	0 (0.0)	0 (0.0)	5 (4.6)	5 (3.7)	
Hospital pharmacy	0 (0.0)	1 (10.0)	18 (16.7)	19 (14.2)	
Donation	1 (6.3)	1 (10.0)	20 (18.5)	21 (16.4)	
Type of antiseizure medication(s) taken (n=132)					
Phenobarbital	2 (10.5%)	1 (9.1%)	15 (13.5%)	18 (13.6%)	0.006
Carbamazepine	9 (47.4%)	8 (72.7%)	83 (74.8%)	100 (75.8%)	
Valproate	1 (5.3%)	1 (9.1%)	0 (0.0%)	2 (1.5%)	
Phenytoin	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.8%)	
Unknown	7 (36.8%)[#]	1 (10.0%)	12 (10.8%)	20 (15.1%)	

Table 30: Access to care and treatment pattern for people with epilepsy across the three sites

	Afikpo [n = 40]	**Ijebu-Jesa [n =24]**	**Gwandu [n =188]**	**Total [n = 252]**	**P-value**
Polytherapy (≥ 2 drugs) (n=130)					
No	17 (94.4%)	9 (90.0%)	97 (93.3%)	123 (93.1%)	0.902
Yes	1 (5.3%)	1 (1.1%)	7 (6.9%)	9 (6.9%)	
Median cost of antiseizure medication(s) per month (n=62)					
	4,500 (1,000 – 5,000)[#]	2,700 (2,000 – 6,000)	1,500 (1,000 – 2,500)	2,000 (1,250 – 2,700)	0.040
Reported that drugs are readily available (n=145)					
No	13 (68.4)	3 (30.0)	77 (66.4)	93 (64.1)	0.073
Yes	6 (31.6)	7 (70.0)	39 (33.6)	52 (35.9)	
Effect of antiseizure medication(s) on seizures (n=139)					
Stopped over 6 months	3 (17.7)	3 (30.0) [#]	7 (6.3) [#]	13 (9.4)	0.004
Reduced	8 (47.1) [#]	6 (60.0)	82 (73.2)[#]	96 (69.1)	
Same	2 (11.8)	1 (10.0)	20 (17.9)	23 (16.6)	
Worse	2 (11.8)	0 (0.0)	3 (2.7)	5 (3.6)	
Not sure	2 (11.8)	0 (0.0)	0 (0.0)	2 (1.4)	
Had a neurological consultation					
	2 (5.0)	4 (16.7)	2 (1.1)	8 (3.2)	0.001
Had EEG done					
	1 (2.5)	2 (8.3)	1 (0.5)	4 (1.6)	0.030
Had neuroimaging done (CT/MRI)					
	1 (2.5)	0 (0.0)	0 (0.0)	1 (0.4)	0.254

IQR – Interquartile range, [#] Shows which cell differs from another in a post-hoc analysis using adjusted residuals for chi-square (or Fisher's exact) test or a one-way ANOVA with Bonferroni correction where $P < 0.05$, [§] one US dollar ~ 360 Naira, EEG – Electroencephalography, CT – Computerised Tomography, Magnetic Resonance Imaging.

Table 31 summarises the therapeutic and treatment gap and their 95% CI from three sites. The therapeutic gap was high in all the three sites. When the diagnostic gap (diagnosed by a physician or trained personnel or access to speciality care) was considered, the treatment gap was found to be even higher. The treatment gap using a month as a cut-off was lower.

Table 31: The treatment gap across three sites

	Afikpo	**Ijebu-Jesa**	**Gwandu**	**Total**	**P-value**
Therapeutic gap	80.0 (64.3, 90.9)	79.2 (57.8, 92.9)	84.6 (78.6, 89.4)	83.3 (78.1, 87.7)	0.661
Treatment gap*	97.5 (86.8, 99.9)	87.5 (67.6, 97.3)	94.7 (90.4, 97.4)	94.4 (90.9, 96.9)	0.230
Treatment gap#	70.0 (53.5, 83.4)	70.8 (48.9, 87.4)	68.1 (60.9, 74.7)	66.5 (59.3, 73.2)	0.851

* Therapeutic + diagnostic gap (therapeutic gap = those not on treatment and not adherent, diagnostic gap = those diagnosed by physician or a trained healthworker). # Those who had not been on medication in the last one month, whether or not they have ever been on medication.

Table 32 reports the potentials factors for the treatment gap for those not on medications in the last one month. It showed that those with history of SE were 85% more likely to remain on treatment in the last one month (OR 0.15, 95% CI: 0.03, 0.94; P = 0.043). While those who pay more for their treatments were less likely to stop.

Twenty-one potential variables were studied as potential factors associated with failure to access care. Table 33 shows the univariate, multivariate analysis with and without multiple imputations combining data from three sites. The analysis for each of the sites is shown in Appendix 18. The univariate analysis from each of the site showed that people were less likely to seek treatment if they had negative cultural belief and misconceptions about epilepsy across sites. For most of the multivariate analysis, the

factors were mainly not significant for each site because of small sample sizes, some analyses were dropped because of collinearity and some cells were empty, this was more apparent in Ijebu-Jesa. When the data for the three sites were combined, eight factors (those with $P < 0.20$) were retained and included in the multivariable logistic regression. The multivariate analysis yielded five potential factors. After MI and controlling for age and gender significant effect on four potential factors was seen. Those who reported they had difficulty reaching a health facility were 67% less likely to attend biomedical care (OR 0.33, 95% CI: 0.14, 0.75; P = 0.008). The odds for seeking medical care was reduced by approximately 64% for those who never accepted or who rejected their diagnosis of epilepsy (OR 0.36, 95% 0.15, 0.85; P = 0.021). The odds of accessing medical care was reduced by 84% for those who reported perceived stigma, (OR 0.16, 95% CI: 0.04, 0.71; P = 0.016), whilst those with an aversive cultural belief were almost three times less likely to seek care (OR 0.31, 95% CI: 0.16, 0.62; P = 0.001). Factors such as education, type of epilepsy, seizure frequency, seizure-related injuries and the distance to health facility and cost were not significant predictors.

Table 32: Analysis of potential factors associated with treatment gap (using one month as a cut-off)

			Univariate Analysis		Multivariate Analysis	
	Not on treatment (n=170)	**On treatment (n=82)**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Age						
< 18 years	71 (41.8%)	37 (36.7%)	1.0			
≥ 18 years	99 (58.2%)	45 (63.3%)	1.15 (0.67, 1.95)	0.614	2.48 (0.56, 10.85)	0.227
Gender						
Female	85 (49.1%)	41 (50.0%)	1.0			
Male	88 (50.9%)	41 (50.0%)	0.95 (0.56, 1.62)	0.861	0.49 (0.12, 1.92)	0.303
Religion						
Christianity	43 (25.3%)	17 (20.7%)	1.0			
Islam	127 (74.7%)	65 (79.3%)	0.77 (0.41, 1.46)	0.426		
Marital status						
Single	137 (78.8%)	61 (74.4%)	1.0			
Married	32 (18.8%)	18 (22.0%)	0.81 (0.42, 1.55)	0.525		
Divorced	3 (1.8%)	2 (2.4%)	0.68 (0.11, 4.91)	0.680		
Widower	1 (0.6%)	1 (1.2%)	0.46 (0.03, 7.40)	0.580	-	-
At least primary education or in school						
No	84 (49.4%)	38 (46.3%)	1.0			
Yes	86 (50.6%)	44 (53.7%)	0.88 (0.52, 1.50)	0.648		
Employment or trade						
None	75 (44.1%)	29 (35.2%)	1.0			
Civil servant or wage earner	5 (2.9%)	3 (3.7%)	0.64 (0.14, 2.87)	0.564		
Crafts or trade	16 (9.4%)	9 (11.0%)	0.69 (0.27, 1.73)	0.462		
Subsistence farmer	24 (14.1%)	17 (20.7%)	0.55 (0.26, 1.16)	0.116		
Student	11 (6.4%)	6 (7.3%)	0.71 (0.24, 2.09)	0.534		
Others	39 (22.9%)	18 (22.0%)	0.84 (0.41, 1.69)	0.622		

Table 32: Analysis of potential factors associated with treatment gap (using one month as a cut-off)

			Univariate Analysis		Multivariate Analysis	
	Not on treatment (n=170)	**On treatment (n=82)**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Age of onset (years)						
< 1	19 (11.2%)	8 (9.8%)	1.0			
1 – 9	99 (58.2%)	49 (59.8%)	0.85 (0.35, 2.08)	0.723		
10 – 19	38 (22.4%)	18 (22.0%)	0.88 (0.33, 2.41)	0.817		
20 – 29	7 (4.1%)	4 (4.9%)	0.74 (0.17, 3.24)	0.686		
≥ 30	7 (4.1%)	3 (3.7%)	0.98 (0.20, 4.79)	0.983		
Duration of epilepsy (years)						
< 5	34 (20.0%)	12 (14.6%)	1.0			
5 – 10	52 (30.6%)	27 (32.9%)	0.68 (0.30, 1.52)	0.348		
11 – 20	48 (28.2%)	32 (39.0%)	0.52 (0.24, 1.17)	0.117		
21 – 30	25 (14.7%)	7 (8.5%)	1.26 (0.43, 3.66)	0.670		
≥ 31	11 (6.5%)	4 (4.9%)	0.97 (0.26, 3.63)	0.965		
Type of epilepsy						
Focal	70 (41.2%)	44 (53.7%)	1.0			
Generalised	88 (51.8%)	34 (41.5%)	1.63 (0.94, 2.81)	0.081	5.32 (0.91, 31.22)	0.064
Combined generalised and focal	10 (5.9%)	2 (2.4%)	3.14 (0.66, 15.02)	0.151	1.70 (0.11, 26.77)	0.705
Unknown	2 (1.2%)	2 (2.4%)	0.63 (0.09, 4.63)	0.648	-	-
Seizure frequency						
Daily	23 (13.6%)	12 (14.8%)	1.0			
Weekly	39 (23.1%)	16 (19.8%)	1.27 (0.51, 3.16)	0.604		
Monthly	63 (37.3%)	36 (44.4%)	0.91 (0.41, 2.05)	0.826		
1 in 2 to 6 months	44 (26.0%)	17 (21.0%)	1.35 (0.55, 3.30)	0.510		
Seizure timing						
Nocturnal	21 (12.4%)	4 (4.9%)	1.0			

Table 32: Analysis of potential factors associated with treatment gap (using one month as a cut-off)

			Univariate Analysis		Multivariate Analysis	
	Not on treatment (n=170)	**On treatment (n=82)**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Early morning	19 (11.2%)	7 (8.5%)	0.52 (0.13, 2.05)	0.347	0.35 (0.02, 6.92)	0.490
Afternoon	3 (1.8%)	5 (6.1%)	0.11 (0.02, 0.68)	0.017	0.09 (0.001, 6.81)	0.273
Anytime	125 (73.5%)	65 (79.3%)	0.37 (0.12, 1.11)	0.076	0.80 (0.06, 11.21)	0.866
Unknown	2 (1.2%)	1 (1.2%)	0.38 (0.03, 5.27)	0.472		
Reported status epilepticus						
No	124 (72.9%)	48 (58.5%)	1.0			
Yes	46 (27.1%)	34 (41.5%)	0.52 (0.30, 0.91)	0.022	0.15 (0.03, 0.94)	0.043
Learning difficulty						
No	144 (84.7%)	64 (78.1%)	1.0			
Yes	26 (15.3%)	18 (21.9%)	0.64 (0.33, 1.25)	0.194	0.26 (0.04, 1.84)	0.178
Reported difficulty with access to health care facility						
No	126 (74.1%)	64 (78.1%)	1.0			
Yes	44 (25.9%)	18 (21.9%)	1.24 (0.66, 2.32)	0.498		
Lack of medical personnel at health facility						
No	153 (90.0%)	76 (92.7%)	1.0			
Yes	17 (10.0%)	6 (7.3%)	1.41 (0.53, 3.71)	0.490		
Reported rejection of diagnosis of epilepsy						
No	142 (83.5%)	68 (82.9%)	1.0			
Yes	28 (16.5%)	14 (17.1%)	0.96 (0.47, 1.94)	0.904		
Reported having misconceptions of epilepsy						
No	114 (67.1%)	56 (68.3%)	1.0			
Yes	56 (32.9%)	26 (31.7%)	1.06 (0.60, 1.86)	0.845		
Reported perceived stigma						
No	159 (93.5%)	79 (96.3%)	1.0			

Table 32: Analysis of potential factors associated with treatment gap (using one month as a cut-off)

			Univariate Analysis		Multivariate Analysis	
	Not on treatment (n=170)	**On treatment (n=82)**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Yes	11 (6.5%)	3 (3.7%)	1.82 (0.49, 6.72)	0.368		
Lack of drugs at health facility						
No	145 (85.3%)	75 (91.5%)	1.0			
Yes	25 (14.7%)	7 (8.5%)	1.85 (0.76, 4.47)	0.173		
Cost of drugs						
No	127 (74.7%)	61 (74.4%)	1.0			
Yes	43 (25.3%)	21 (25.6%)	0.98 (0.53, 1.80)	0.957		
Rejection of treatment by subject or care-giver						
No	164 (96.5%)	80 (97.6%)	1.0			
Yes	6 (3.5%)	2 (2.4%)	1.46 (0.29, 4.71)	0.646		
Reported having negative cultural belief						
No	112 (65.9%)	60 (73.2%)	1.0			
Yes	58 (34.1%)	22 (26.8%)	1.41 (0.79, 2.53)	0.245		
Seizure-related injury						
No	66 (38.8%)	25 (30.5%)	1.0			
Yes	104 (61.2%)	57 (69.5%)	0.69 (0.39, 1.21)	0.198	3.31 (0.50, 22.02)	0.217
Access to the Nigerian health insurance						
No	170 (100.0%)	79 (96.3%)	1.0			
Yes	0 (0.0%)	3 (3.7%)	-	-		
Travel distance to health facility (km)						
≤ 1	11 (18.0%)	3 (8.6%)	1.0			
1.1 to 5	19 (31.2%)	8 (22.9%)	0.64 (0.14, 2.96)	0.576		
5.1 to 10	5 (8.2%)	2 (5.7%)	0.68 (0.09, 5.45)	0.718		
> 10	26 (42.6%)	22 (62.9%)	0.32 (0.08, 1.30)	0.112		

Table 32: Analysis of potential factors associated with treatment gap (using one month as a cut-off)

			Univariate Analysis		Multivariate Analysis	
	Not on treatment (n=170)	**On treatment (n=82)**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Cost of transport to health facility (Naira[§])						
< 200	21 (39.6%)	15 (37.5%)	1.0			
200 – 499	14 (26.4%)	7 (17.5%)	1.42 (0.46, 4.39)	0.534		
500 -1000	15 (28.3%)	14 (35.0%)	0.77 (0.29, 2.05)	0.594		
> 1000	3 (5.7%)	4 (10.0%)	0.54 (0.10, 2.75)	0.455		
Cost of antiseizure medication per month (Naira[§])						
< 1,000	8 (24.2%)	2 (6.9%)	1.0			
1,000 – 1,999	12 (36.4%)	7 (24.1%)	0.43 (0.07, 2.61)	0.321	0.21 (0.02, 2.09)	0.182
2,000 – 5,000	11 (33.3%)	12 (41.4%)	0.23 (0.04, 1.32)	0.099	0.05 (0.004, 0.60)	0.018
> 5,000	2 (6.1%)	8 (27.6%)	0.06(0.01, 0.56)	0.013	0.01 (0.00, 0.37)	0.012

*MICE – Multiple imputation by changed equation, OR – Odds ratio, CI – Confidence Interval. Some cells were omitted in the analysis because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Table 33: Analysis of potential factors determining access to care combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Sought medical care (n = 144)**	**Never sought medical care (n = 108)**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**
Age								
< 18 years	57 (39.6%)	51 (47.2%)	1.0 (Reference)					
≥ 18 years	87 (60.4%)	57 (52.8%)	1.37	0.225	1.40 (0.78, 2.51)	0.265	1.42 (0.68, 2.96)	0.346
Gender								
Female	69 (47.9%)	55 (50.9%)	1.0					
Male	75 (52.1%)	53 (49.1%)	0.89 (0.52, 1.50)	0.640	1.03 (0.58, 1.82)	0.926	0.90 (0.78, 1.68)	0.736
Religion								
Christianity	35 (24.3%)	25 (23.2%)	1.0					
Islam	109 (75.7%)	83 (76.8%)	0.94 (0.50, 1.75)	0.830				
Marital status								
Single	108 (75.0%)	87 (80.6%)	1.0		-	-		
Married	31 (21.5%)	19 (17.6%)	1.31 (0.70, 2.50)	0.400	-	-	1.65 (0.72, 3.78)	0.241
Divorced	3 (2.1%)	2 (1.8%)	1.21 (0.20, 7.39)	0.838	-	-	1.54 (0.18, 13.36)	0.694
Widower	2 (1.4%)	0 (0.0%)	-	-				
At least primary education or in school								

Table 33: Analysis of potential factors determining access to care combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Sought medical care (n = 144)**	**Never sought medical care (n = 108)**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**
No	110 (79.4%)	92 (85.2%)	1.0					
Yes	34 (23.6%)	16 (14.8%)	1.78 (0.92, 3.42)	0.086	0.82 (0.47, 1.46)	0.508	-	-
Employment or trade								
None	58 (38.9%)	46 (42.6%)	1.0					
Civil servant or wage earner	5 (3.5%)	3 (2.8%)	1.3 (0.30, 5.82)	0.712				
Crafts or trade	16 (17.4%)	9 (8.3%)	1.41 (0.57, 3.48)	0.456				
Subsistence farmer	26 (18.1%)	15 (13.9%)	1.37 (0.65, 2.89)	0.402				
Student	9 (6.3%)	8 (7.4%)	0.89 (0.32, 2.49)	0.828				
Others	30 (28.3%)	27 (25.0%)	0.88 (0.46, 168)	0.702				
Age of onset (years)								
$\leq$ 1	16 (11.1%)	11 (10.2%)	1.0					
1 – 9	81 (56.3%)	67 (62.0%)	0.83 (0.36, 1.91)	0.664				
10 – 19	32 (22.2%)	24 (22.2%)	0.92 (0.37, 2.33)	0.855				
20 – 29	8 (5.6%)	3 (2.8%)	1.83 (0.40, 8.50)	0.438				
$\geq$ 30	7 (4.9%)	3 (2.8%)	1.60 (0.34, 7.60)	0.551				
Duration of epilepsy (years)								
< 5	26 (18.1%)	20 (18.5%)	1.0					
5 – 10	44 (30.6%)	35 (32.4%)	0.97 (0.46, 2.01)	0.929				
11 – 20	46 (31.9%)	34 (31.5%)	1.04 (0.50, 2.16)	0.915				
21 – 30	20 (13.9%)	12 (11.1%)	1.28 (0.51, 3.23)	0.598				
$\geq$ 31	8 (5.6%)	7 (6.5%)	0.88 (0.27, 2.83)	0.829				
Type of epilepsy								
Focal	67 (46.5%)	47 (43.5%)	1.0					

Table 33: Analysis of potential factors determining access to care combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Sought medical care (n = 144)**	**Never sought medical care (n = 108)**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**
Generalised	67 (46.5%)	55 (50.9%)	0.85 (0.51, 1.43)	0.550				
Combined generalised and focal	8 (5.6%)	4 (3.7%)	1.40 (0.40, 4.93)	0.597				
Unknown	2 (1.4%)	2 (1.9%)	0.70 (0.40, 5.16)	0.728				
Seizure frequency								
Daily	20 (14.1%)	15 (13.9%)	1.0					
Weekly	34 (23.9%)	21 (19.4%)	1.21 (0.51, 2.87)	0.659				
Monthly	53 (37.3%)	46 (42.6%)	0.86 (0.40, 1.88)	0.713				
One in 2 to 6 months	35 (24.7%)	26 (24.1%)	1.01 (0.44, 2.34)	0.982				
Seizure timing								
Nocturnal	11 (7.6%)	14 (13.0%)	1.0					
Early morning	17 (11.8%)	9 (8.3%)	2.40 (0.78, 7.44)	0.128	2.50 (0.70, 8.90)	0.158	-	-
Afternoon	5 (3.5%)	3 (2.8%)	2.12 (0.41, 10.88)	0.367	3.28 (0.52, 20.79)	0.208	-	-
Anytime	109 (75.7%)	81 (75.0%)	1.71 (0.74, 3.97)	0.210	1.56 (0.59, 4.09)	0.366	-	-
Unknown	2 (1.4%)	1 (0.9%)	2.55 (0.20, 31.86)	0.469	2.59 (0.11, 59.08)	0.551	-	-
Reported status epilepticus								
No	94 (65.3%)	78 (72.2%)	1.0					
Yes	50 (34.7%)	30 (27.8%)	1.38 (0.80, 2.38)	0.242				
Learning difficulty								
No	102 (70.8%)	80 (74.1%)	1.0					
Yes	42 (29.2%)	28 (25.9%)	1.18 (0.67, 2.06)	0.570	1.82 (0.81, 4.08)	0.146	1.89 (0.84, 4.28)	0.126
Reported difficulty with access to health care facility								
No	114 (79.2%)	76 (70.4%)	1.0					
Yes	30 (20.8%)	32 (29.6%)	0.62 (0.35, 1.11)	0.110	0.42 (0.22, 0.80)	0.009	0.33 (0.14, 0.75)	0.008

Table 33: Analysis of potential factors determining access to care combining data from the three sites

			Univariate Analysis		Multivariate Analysis		Multivariate Analysis with MICE*	
Variables	**Sought medical care (n = 144)**	**Never sought medical care (n = 108)**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**
Reported rejection of diagnosis of epilepsy								
No	131 (91.0%)	79 (75.1%)	1.0					
Yes	13 (9.0%)	29 (26.9%)	0.27 (0.13, 0.55)	< 0.001	0.38 (0.17, 0.86)	0.020	0.36 (0.15, 0.85)	0.021
Reported having misconceptions of epilepsy								
No	110 (76.4%)	60 (65.6%)	1.0					
Yes	34 (23.6%)	48 (44.4%)	0.39 (0.23, 0.66)	0.001	0.50 (0.26, 0.97)	0.041	-	-
Reported perceived stigma								
No	140 (97.2%)	98 (90.7%)	1.0					
Yes	4 (2.8%)	10 (9.3%)	0.28 (0.09, 0.92)	0.036	0.32 (0.09, 1.15)	0.080	0.16 (0.04, 0.71)	0.016
Reported having negative cultural belief								
No	115 (79.9%)	57 (52.7%)	1.0					
Yes	29 (20.1%)	51 (47.2%)	0.28 (0.16, 0.49)	< 0.001	0.34 (0.18, 0.66)	0.001	0.31 (0.16, 0.62)	0.001
Seizure-related injury								
No	47 (36.2%)	44 (40.7%)	1.0					
Yes	97 (67.4%)	64 (59.3%)	1.42 (0.85, 2.38)	0.186	1.17 (0.64, 2.16)	0.609	-	-
Travel distance to health facility (km)								
≤ 1	13 (14.3%)	1 (20.0%)	1.0					
1.1 to 5	26 (28.6%)	1 (20.0%)	2.0 (0.11, 34.60)	0.634	-	-	-	-
5.1 to 10	7 (7.7%)	0 (0.0%)	-	-	-	-	-	-
> 10	45 (49.4%)	3 (60.0%)	1.15 (0.11, 12.05)	0.905	-	-	-	-
Cost of transport to health facility (Naira[§])								
< 200	34 (40.0%)	2 (25.0%)	1.0		-	-	1.0	-
200 – 499	19 (22.4%)	2 (25.0%)	0.56 (0.07, 4.29)	0.576	-	-	2.49 (0.67, 9.23)	0.170
500 -1000	25 (29.4%)	4 (50.0%)	0.37 (0.06, 2.17)	0.269	-	-	3.37 (0.74, 15.24)	0.113

Table 33: Analysis of potential factors determining access to care combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Sought medical care (n = 144)**	**Never sought medical care (n = 108)**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**	**OR (95% CI)**	**P-Value**
> 1000	7 (8.2%)	0 (0.0%)	-	-			4.90 (0.65, 37.14)	0.122

Some cells were omitted in the analysis because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Table 34 depicts the twenty-seven potential variables for non-adherence that were assessed. The analysis for each site is shown in Appendix 19. Many of these variables were dropped from analyses because of collinearity and empty cells. To get a more robust sample size, data from the three sites were combined (Table 34). Of the 27 potential predictors of adherence assessed in univariate analysis, 15 variables were retained and included in the multivariable logistic regression. The multivariate analysis yielded five significant factors. Those with seizures predominantly occur in the afternoons, learning deficit and seizure-related injury were more likely to be adherent, while those who reported difficulty reaching a health facility and those with averse cultural beliefs were more likely to be non-adherent. The final model with MI showed that seizure-related injury was dropped, with significant effects on the five potential factors. Those who had seizures in the afternoon were more likely to be adherent (OR 0.006, 95% CI: 0.001, 0.58; P = 0.029). Those with learning deficit were 84% more likely to be adherent on medication (OR 0.16, 95% CI: 0.03, 0.88; P = 0.035). Those who reported that they had difficulty reaching a health facility were twenty-five times more likely to be nonadherent (OR 25.44, 95% CI: 0.88, 735.88; P = 0.059). Subjects with averse cultural belief were more than twenty-eight times more likely to be nonadherent (OR 28.68, 95% CI: 1.70, 483.97; P = 0.020). This final model with MI brought in cost of medication as a factor on adherence (paying > 5,000 naira for medication, OR 0.005, 95% CI: 0.00, 0.99; P = 0.050). Factors such as marital status, religion, education, type of epilepsy, seizure frequency, and the distance to health facility or cost were not significant predictors. In all the analysis, some factors were dropped in the final model because of collinearity and small sample sizes in some cells.

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Age								
< 18 years	94 (44.8%)	14 (33.3%)	1.0					
≥ 18 years	116 (55.2%)	28 (66.7%)	0.62 (0.31, 1.24)	0.174	1.31 (0.39, 4.41)	0.662	0.86 (0.13, 5.85)	0.878
Gender								
Female	104 (49.5%)	24 (57.1%)	1.0					
Male	106 (50.5%)	18 (42.9%)	1.36 (0.70, 2.65)	0.368	1.35 (0.56, 3.24)	0.503	1.66 (0.37, 7.42)	0.502
Religion								
Christianity	48 (22.9%)	12 (28.6%)	1.0					
Islam	162 (77.1%)	30 (71.4%)	1.35 (0.64, 2.84)	0.429				
Marital status								
Single	167 (79.5%)	28 (66.7%)	1.0					
Married	39 (18.6%)	11 (26.2%)	0.59 (0.27, 1.30)	0.191	0.40 (0.13, 1.25)	0.114	0.32 (0.05, 2.09)	0.234
Divorced	3 (1.4%)	2 (4.8%)	0.25 (0.04, 1.57)	0.140	0.21 (0.02, 1.91)	0.167	0.18 (0.005, 6.49)	0.350
Widower	1 (0.5%)	1 (2.4%)	0.17 (0.01, 2.76)	0.211	-	-		
At least primary education or in school								
No	101 (48.1%)	21 (50.0%)	1.0					
Yes	109 (51.9%)	21 (50.0%)	1.08 (0.56, 2.09)	0.822				

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
Employment or trade								
None	88 (41.9%)	16 (38.1%)	1.0					
Civil servant or wage earner	6 (2.9%)	2 (4.8%)	0.54 (0.10, 2.95)	0.481				
Crafts or trade	21 (10.0%)	4 (9.5%)	0.95 (0.29, 3.15)	0.696				
Subsistence farmer	31 (14.8%)	10 (23.8%)	0.56 (0.23, 1.37)	0.207				
Student	13 (6.2%)	4 (9.5%)	0.59 (0.17, 2.04)	0.406				
Others	51 (24.3%)	6 (14.3%)	1.54 (0.57, 4.20)	0.393				
Age of onset (years)								
< 1	21 (10.0%)	6 (14.3%)	1.0					
1 – 9	124 (59.1%)	24 (57.1%)	1.48 (0.54, 4.04)	0.448				
10 – 19	48 (22.9%)	8 (19.1%)	1.71 (0.53, 5.56)	0.369				
20 – 29	9 (4.3%)	2 (4.8%)	1.29 (0.22, 7.63)	0.782				
≥ 30	8 (3.8%)	2 (4.8%)	1.14 (0.19, 6.88)	0.884				
Duration of epilepsy (years)								
< 5	42 (20.0%)	4 (9.5%)	1.0					
5 – 10	68 (32.4%)	11 (26.2%)	0.59 (0.18, 1.97)	0.390	0.62 (0.16, 2.41)	0.492	0.61 (0.09, 4.31)	0.619
11 – 20	62 (29.5%)	18 (42.9%)	0.33 (0.10, 1.04)	0.058	0.36 (0.08, 1.55)	0.170	0.22 (0.03, 1.74)	0.149

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
21 – 30	25 (11.9%)	7 (16.7%)	0.34 (0.09, 1.28)	0.111	0.58 (0.10, 3.33)	0.538	0.38 (0.03, 4.71)	0.452
≥ 31	13 (6.2%)	2 (4.8%)	0.62 (0.10, 3.77)	0.603	1.56 (0.11, 22.89)	0.746	0.61 (0.008, 44.97)	0.823
Type of epilepsy								
Focal	87 (41.4%)	27 (64.3%)	1.0					
Generalised	107 (51.0%)	15 (35.7%)	2.21 (1.11, 4.42)	0.024	1.80 (0.73, 4.45)	0.201	3.60 (0.85, 15.28)	0.082
Combined generalised and focal	12 (5.7%)	0 (0.0%)	-	-	-	-	-	-
Unknown	4 (1.9%)	0 (0.0%)	-	-	-	-	-	-
Seizure frequency								
Daily	28 (13.4%)	7 (17.1%)	1.0					
Weekly	46 (22.0%)	9 (21.9%)	1.28 (0.43, 3.81)	0.660				
Monthly	82 (39.2%)	17 (41.5%)	1.21 (0.45, 3.21)	0.708				
1 in 2 to 6 months	53 (25.4%)	8 (19.5%)	1.66 (0.54, 5.04)	0.374				
Seizure timing								
Nocturnal	24 (11.4%)	1 (2.4%)	1.0					
Early morning	23 (11.0%)	3 (7.1%)	0.32 (0.03, 3.30)	0.338	0.53 (0.04, 6.35)	0.613	0.62 (0.02, 20.15)	0.786
Afternoon	4 (1.9%)	4 (9.5%)	0.04 (0.003,	0.010	0.04 (0.003,	0.020	0.006 (0.001, 0.58)	0.029

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
			0.47)		0.60)			
Anytime	157 (74.8%)	33 (78.6%)	0.20 (0.03, 1.52)	0.119	0.31 (0.03, 2.85)	0.301	0.13 (0.006, 2.73)	0.190
Unknown	2 (1.4%)	1 (2.4%)	0.08 (0.03, 1.90)	0.119	0.31 (0.01, 12.17)	0.532	0.10 (0.00, 367.26)	0.578
Reported status epilepticus								
No	147 (70.0%)	25 (59.5%)	1.0					
Yes	63 (30.0%)	17 (40.5%)	0.63 (0.32, 1.25)	0.185	0.72 (0.30, 1.70)	0.450	0.50 (0.11, 2.26)	0.368
Learning difficulty								
No	179 (85.2%)	29 (69.1%)	1.0					
Yes	31 (14.8%)	13 (30.9%)	0.39 (0.18, 0.82)	0.014	0.28 (0.10, 0.76)	0.013	0.16 (0.03, 0.88)	0.035
Reported difficulty with access to health care facility								
No	154 (73.3%)	36 (85.7%)	1.0					
Yes	56 (26.7%)	6 (14.3%)	2.18 (0.87, 5.46)	0.095	3.03 (0.99, 9.34)	0.053	25.44 (0.88, 735.88)	0.059
Lack of medical personnel at health facility								
No	190 (90.5%)	39 (92.9%)	1.0					
Yes	20 (9.5%)	3 (7.1%)	1.37 (0.39, 4.83)	0.626				
Reported rejection of diagnosis of epilepsy								

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
No	172 (81.9%)	38 (90.5%)	1.0					
Yes	38 (18.1%)	4 (9.5%)	2.08 (0.71, 6.23)	0.182	1.23 (0.31, 4.86)	0.765	0.29 (0.02, 3.68)	0.340
Reported having misconceptions of epilepsy								
No	137 (65.2%)	33 (78.6%)	1.0					
Yes	73 (34.8%)	9 (21.4%)	1.95 (0.89, 4.30)	0.097	1.56 (0.52, 4.63)	0.431	2.46 (0.37, 16.36)	0.349
Reported perceived stigma								
No	196 (93.3%)	42 (90.7%)	1.0					
Yes	14 (6.7%)	0 (9.3%)	-	-	-	-	-	-
Lack of drugs at health facility								
No	183 (87.1%)	37 (88.1%)	1.0					
Yes	27 (12.9%)	5 (11.9%)	1.09 (0.39, 3.02)	0.866				
Cost of drugs								
No	156 (74.3%)	32 (76.2%)	1.0					
Yes	54 (25.7%)	10 (23.8%)	1.11 (0.51, 2.40)	0.796				
Rejection of treatment by subject or care-giver								
No	203 (96.7%)	41 (97.6%)	1.0					
Yes	7 (3.3%)	1 (2.4%)	1.41 (0.17,	0.749				

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
			11.80)					
Reported having negative cultural belief								
No	136 (64.8%)	36 (85.7%)	1.0					
Yes	74 (35.2%)	6 (14.3%)	3.26 (1.31, 8.11)	0.011	5.54 (1.60, 19.20)	0.007	28.68 (1.7, 483.97)	0.020
Seizure-related injury								
No	82 (39.1%)	9 (21.4%)	1.0					
Yes	128 (60.9%)	33 (78.6%)	0.43 (0.19, 0.94)	0.034	0.36 (0.13, 0.99)	0.047	0.22 (0.04, 1.34)	0.100
Access to the Nigerian health insurance								
No	209 (99.5%)	40 (95.2%)	1.0					
Yes	1 (0.5%)	2 (4.8%)	0.10 (0.01, 1.08)	0.058	Omitted		omitted	
Travel distance to health facility (km)								
≤ 1	12 (17.1%)	2 (7.7%)	1.0					
1.1 to 5	20 (28.6%)	7 (26.9%)	0.48 (0.08, 2.68)	0.400			0.30 (0.01, 7.80)	0.466
5.1 to 10	5 (7.1%)	2 (7.7%)	0.42 (0.05, 3.84)	0.440			0.53 (0.003, 85.77)	0.806
> 10	33 (47.1%)	15 (57.7%)	0.37 (0.07, 1.85)	0.224			0.04 (0.0007, 2.18)	0.113
Cost of transport to health facility (Naira[§])								

Table 34: Analysis of potential factors associated with adherence combining data from the three sites

			Univariate Analysis		**Multivariate Analysis**		**Multivariate Analysis with MICE***	
Variables	**Not adherent (n=210)**	**Currently on treatment and adherent n=42**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**	**Odds ratio (95%CI)**	**P-Value**
< 200	26 (40.6%)	10 (34.5%)	1.0					
200 – 499	15 (23.3%)	6 (20.7%)	0.96 (0.29, 3.18)	0.949			0.16 (0.006, 4.3)	0.268
500 -1000	20 (31.3%)	9 (31.0%)	0.85 (0.29, 2.50)	0.774			0.08 (0.002, 4.57)	0.216
> 1000	3 (4.7%)	4 (13.8%)	0.29 (0.05, 1.52)	0.143	Omitted		0.13 (0.004, 4.36)	0.250
Cost of antiseizure medication per month (Naira[§])								
< 1,000	9 (22.0%)	1 (4.8%)	1.0					
1,000 – 1,999	14 (34.1%)	5 (23.8%)	0.31 (0.03, 3.12)	0.321	Omitted		0.09 (0.002, 3.65)	0.197
2,000 – 5,000	13 (31.7%)	10 (47.6%)	0.14 (0.02, 1.34)	0.088			0.04 (0.001, 1.35)	0.072
> 5,000	5 (12.2%)	5 (23.8%)	0.11(0.01, 1.24)	0.074			0.005 (0.00, 0.99)	0.050

*MICE – Multiple imputation by changed equation, OR – Odds ratio, CI – Confidence Interval. Some cells were omitted in the analysis because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

7.5 Discussion

This study estimated the treatment gap and explored the determinants of access to care and adherence from three regions of Nigeria. The treatment gap was about 80% and when access to speciality care was considered it exceeded 90%. The high treatment gap reported in this study is congruent with figures from other Nigerian (Osuntokun et al., 1987a, Nwani et al., 2013, Eseigbe et al., 2014) and African studies (Kaiser et al., 1998b, Koffi et al., 2009, Guinhouya et al., 2010, Mbuba et al., 2012b). Some studies in Africa, however, reported a lower treatment gap (Ndoye et al., 2005, Simms et al., 2008, Amos & Wapling, 2011b, Ratsimbazafy et al., 2011, Hunter et al., 2016, Sokhi et al., 2016). A treatment gap of 63% and 38% were reported in the Chinese and Brazil demonstration projects (Wang et al., 2003, Li et al., 2007). The gap reported in HICs is generally below 10%. These variations in the treatment gap between studies simply reflect the interplay between various factors inherent to those regions (Meinardi et al., 2001, Meyer et al., 2010). These differences in gap between HIC and LMIC make the approach of access to care very different.

This study adds to previous existing knowledge and observed that cultural beliefs and perceptions, perceived stigma and difficulty with access to a health facility were factors associated with failure to seek health care. Cultural beliefs were also a factor associated with failure to adhere to treatment. Seizures occurring in the afternoon, learning difficulty and paying more than 5,000 naira for medication were positive factors for adherence. Studies have shown that averse cultural beliefs and attitudes toward epilepsy are a major factor associated with failure to seek biomedical treatment and adherence (Meinardi et al., 2001, Mbuba et al., 2008, Kendall-Taylor et al., 2009, Mbuba et al., 2012b). In addition to the negative perception of epilepsy affecting access to care, perceived stigma adversely influences access to care. Stigma carries a profound psychosocial impact. This study shows that the rejection of a diagnosis of epilepsy was an important factor that limits access to care and adherence. This supports the findings from another study that social acceptability is an important but

neglected dimension of access to care (Dillip et al., 2012). In most parts of Africa, epilepsy is thought to be due to demon possession and the demon possession itself may be transferable. In addition, epilepsy itself is erroneously believed to be contagious. These and other factors lead to marginalisation in society, with a subsequent failure to access care (Atadzhanov et al., 2010). Cultural perception and stigma is one critical area that needs to be tackled to improve health-seeking behaviour and adherence. Community and patient education should be a priority. The Tanzanian study suggests that there must be a match between local and biomedical understandings of such problems to understand the concept of acceptability (Dillip et al., 2012). The wrong perceptions and beliefs about epilepsy, however, are not easily erased, as they are ingrained even among those who are supposedly literate and among health workers (Nyame & Biritwum, 1997, Ismail et al., 2005, Otte et al., 2013). A recent Cochrane review of intervention trials to improve adherence observed that mixed interventions of education and behavioural approaches showed improved adherence (Al-Aqeel et al., 2017). The health-seeking behaviour appeared to be better in Ijebu-Jesa. The educational attainment observed in Ijebu-Jesa may have had a positive influence; however, the multivariate analysis was not significant. The south-west of Nigeria where Ijebu-Jesa is located has better health and poverty indices, supporting the fact that education and a better socioeconomic situation is critical to improving access to care (Frizzell et al., 2011).

This study observed that in Gwandu some participants sought medical care by the positive prompting of spiritual and traditional healers. Why this is so, is not understood. The role that spiritual and traditional healers could play in improved standards of care would a productive area for future studies. This is important because traditional healers are revered in the majority of rural communities in Africa and are easily accessible (Kpobi et al., 2018). Traditional healers are often the first point of call (Boling et al., 2018), they have a role in the treatments of poorly understand medical conditions and their opinions and remedies are taking seriously (Kendall-Taylor et al., 2009). If

traditional healers understand that persons with epilepsy can be seizure-free due to biomedical treatment, they could help improve health-seeking behaviours. Studies have shown that it is possible to solicit the help of these traditional healers in improving access to care, by breaking down barriers of distrust and knowledge (Baskind & Birbeck, 2005, Mbuba & Newton, 2009, Njamnshi et al., 2010, Keikelame & Swartz, 2015).

This study observed that learning difficulty was surprisingly positively associated with adherence, but not a significant factor for seeking health care. Learning difficulties may suggest severer epilepsy and thus the need to take medication and receive support from caregivers. On the contrary, learning difficulty was associated with failure to seek biomedical treatment but not adherence in the Kenyan study (Mbuba et al., 2012b). This study was also at variance with a study in Californian children with learning difficulties, it was observed that better cognition was positively associated with medication levels suggesting better adherence, which may indicate cultural differences (Mitchell et al., 2000).

Unlike other studies, travel distance to health facilities was not a significant factor in this study (Mbuba et al., 2008, Mbuba et al., 2012b). Distance to a health facility was difficult to assess, as many people did not report the information. Some of the subjects in this study reported travelling to a farther health facility to access care. Anecdotal evidence, particularly from Southwest Nigeria, reported people travelling long distances to access health care where no one knows them in order to avoid stigmatization. A focus group discussion on women's perspectives on sociocultural aspects of epilepsy in Southwest Nigeria reported that women with epilepsy have more problems with accessing care. The study showed that families in urban areas send their affected children to grandparents living in rural areas to avoid stigma and neighbours knowing the diagnosis as it can impair the marriage prospects even for other siblings (Komolafe et al., 2012).

People in Gwandu seem to have poorer access to care, but they were more likely to have been on an ASM at some point in time and shorter time is taken to seek medical care. This may be due to donation of drugs (mainly carbamazepine) through a 'Zakat' committee (Zakat is a form of compulsory Islamic giving of a proportion of one's wealth to charity to benefit the poor and disabled in the communities). People had to, however, travel to the headquarters in Gwandu town to get about a month's dose. This may explain why the median travel distance to a health facility was higher. We are unsure of the regularity and how often people with epilepsy are able to access the medication. This is a commendable effort helping with epilepsy care that could be incorporated into the established biomedical health system, where people can be given the appropriate choice of medication and monitored. Health workers can be trained to render care in the existing health facility using simple treatment algorithm or a phone app (Feksi et al., 1991b, Coleman et al., 2002, Patterson et al., 2018). The role of health workers in providing care in primary health centres could be an area of study (Scott et al., 2001). Health workers can assist to operate mobile clinics as shown in the demonstration projects in some African countries (Nimaga et al., 2002, Boissy, 2005, Balogou et al., 2007). Strengthening the primary care could be an option, as the majority can be managed at the PHC as suggested by various recommendations (Meinardi et al., 2001, Birbeck et al., 2012b, Mbuba et al., 2012b) (Figure 13). This can work if various stakeholders participate in epilepsy care. The nurse-led epilepsy services could be a more efficient way to deliver care, as children with epilepsy and their families feel well supported through these services (Mantri, 2008). Nurses can help triage cases that need a referral to physicians, forming a bridge between primary and secondary care. Two Cochrane reviews suggest that the specialist epilepsy nurse have some evidence of benefit in people with epilepsy (Bradley et al., 2016, Fleeman & Bradley, 2018). This task-shifting and task-sharing model can help redistribute duties, strengthen and expand the health workforce and increase access to health care. A recent study from rural Ethiopia exploring a task-shared model by service-users and caregivers on

accessibility, experience and perceived impact of epilepsy treatment, observed that task-sharing improves accessibility and satisfaction with services, with a clear improvement in the perceived clinical and functional status of the majority of service-users (Catalao et al., 2018). A recent report from the mhGAP Epilepsy Program in Mozambique, show how task-shifting/sharing strategy can provide alternative pathways for delivering epilepsy care in the community and improve the epilepsy treatment gap (Dos Santos et al., 2019).

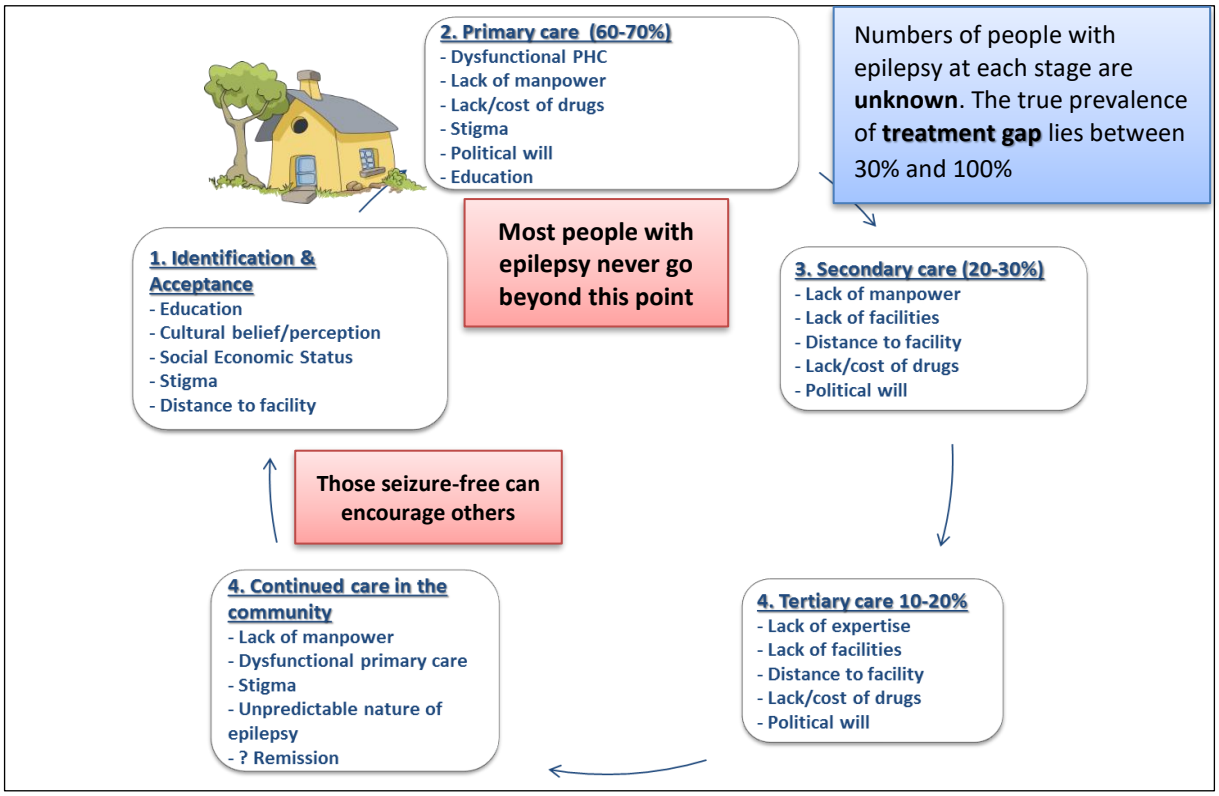


Figure 14: The treatment model and hindrances at each stage

These options and models can only function when governments are committed. Unlike other chronic health problems, epilepsy does not receive the priority it needs from the health-care system. The health care cost for treating epilepsy is mainly out-of-pocket and health insurance is almost non-existent in these rural areas as reported in this study. In the entire country, only about 3% of the population – mainly urban – have

access to the NHIS (Odeyemi & Nixon, 2013). The cost of treating epilepsy and the failure to be gainfully employed further impoverishes the sufferer, family and communities, leading to poor education, under-nutrition and raising the possibility of a link between early under-nutrition and development of epilepsy (Vaid et al., 2012). The introduction of the universal health coverage could be a way to improve accessible, affordable and quality health services without suffering financial hardship (Tangcharoensathien et al., 2015). NGOs and epilepsy charities could help with advocacy, soliciting local support and funding, counselling and providing educational materials for people with epilepsy, their families and the general public and volunteering with running epilepsy clinics (Bertolote, 1994, Chin, 2012). Government and NGOs need to develop a clear framework for the disability status of people with epilepsy and their constitutional right for health care like HIV and TB – which has improved stigma and access to care for these conditions. The profound negative perception and sociocultural issues in epilepsy, however, challenges the social model of disability which emphasizes social adaptation, inclusion, and empowerment (Hahn, 1988). Societal focus on the perceived unattractiveness and the unfavourable social attributes of people with epilepsy further worsens its functional impairments, vocational limitations and access to health care (Albert, 2004, Rhodes et al., 2008).

Strengths: The direct method for measuring treatment gap used in this study rather than the indirect method is a strength. The indirect method of using the Defined Daily Dose (DDD) based on the number of people treated for epilepsy and the amount of ASMs sold in a year cannot be relied on in Nigeria due to the absence of national figures (Ellison, 1989, Thurman et al., 2011). The logistic regression and multiple imputations used in this study provide a quantified value for the strength of association adjusting for other variables and handling missing values (Stuart et al., 2009). Using imputation reduces the bias missing data introduces and increases the efficiency in the analysis. It is important to note that whichever method is used for regression analysis it has its own limitations (Aggarwal & Ranganathan, 2017). To understand the reality of

how the interplay of these factors affects access to care or adherence in rural Africa, a qualitative analysis where each individual is interviewed to understand reasons in depth may be useful, and subsequent care tailored to individual need.

Limitations: In a complex study as this, it is difficult to evaluate all the underlying factors that determine access to care as they are interrelated. This study did not consider the effect of the quality, type and number of ASM on adherence, in addition to family-related factors (Yang et al., 2018). Whether people with epilepsy are more likely to adhere or not if the medications are effective could have been studied, but this was beyond the scope of this study. Previous studies have shown that a large percentage of ASMs in SSA are sub-standard (Otte et al., 2015, Jost et al., 2018). This could be an added reason for the treatment gap, as people will abandon treatment if the drugs are ineffective. Error in the type of medication prescribed is another important factor limiting care that was not studied (Feely, 1999). It was not possible to include SES and monthly income in the analysis as monthly income was difficult to quantify. In most parts of rural Nigeria income is not quite tangible and household assets are difficult to express in the form of currency especially in communal living. This difficulty in measuring household wealth in LMIC has previously been observed (Ward, 2014). Self-reported adherence used in this study is a major limitation. Self-reported adherence is a subjective method that is less reliable when compared to measuring serum levels of ASMs (Mbuba et al., 2012b). The direct method of measuring the serum level of ASM is expensive and beyond the scope of this study (Lam & Fresco, 2015).

A regression analysis was done for each site, but some cells had very few cases or were empty and the model became unstable and did not run at all, some had a wider confidence interval suggesting a small sample size or inconsistent data in certain categories. The sparse-data bias that may occur from a small sample size may be worse in Ijebu-Jesa with only 24 subjects, and real relationships may have been overlooked. Because of the small sample size, data from the three sites were

combined to get a nationally representative figure. Combining data from the sites has its own problem as the inherent difference cannot be assumed to be the same.

An influential report on the treatment gap suggests that surgical treatment should be considered an appropriate treatment (Meinardi et al., 2001). This work may differ from that view as most people in rural area of Nigeria do not receive basic care, and therefore those with refractory epilepsy and those requiring surgical treatment will be unknown.

7.6 Conclusion

This study reported a very high treatment gap. The negative cultural belief was a factor associated with failure to seek health care and adherence to treatment. This negative cultural attitude towards medical treatment of epilepsy requires community and patient education. The role that traditional healers, NGOs and the community can play in improving the negative cultural perception and care standards of people with epilepsy could be an area for future studies. Since trained physicians are scarce, primary health care workers could be trained to render care in the community.

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Chapter 8: A case-control study for potential risk factors of epilepsy in Nigeria

8.1 Abstract

Background: There is limited data on the risk factors for epilepsy in LMICs. This chapter aimed to determine potential risk factors and their contributions to epilepsy in three distinct regions of Nigeria. **Methodology:** This was a community-based case-control study. The recruited cases were people with active epilepsy identified from the door-to-door epilepsy survey. The control group consisted of more than twice as many unmatched persons who had never had non-febrile seizures, randomly selected from the same communities as the cases. A structured interview was conducted to collect sociodemographic and risk factor data using the epilepsy questionnaire for cases and a version for controls. To determine those factors associated with epilepsy, cases and controls were compared using univariate and multivariate logistic regression analyses to estimate odd ratios (ORs) and population attributable fractions (PAFs), and their 95% confidence interval (CI). The analyses were stratified based on age (children <16 years and adults ≥ 16 years) and performed for each site and pooled data. **Results:** There were 252 cases and 585 controls, with no significant age or gender differences. The most significant risk factors among children include: febrile seizures (OR 12.64, 95% CI: 4.75, 33.58; P = < 0.001), meningitis (OR 12.32, 95% CI: 1.84, 82.39; P = 0.010), poor perinatal (obstetric) care (OR 10.85, 95% CI: 3.98, 29.57; P = < 0.001), open defecation (OR 5.12, 95% CI: 1.67, 15.65; P = 0.004), measles (OR 4.50, 95% CI: 1.42, 14.27; P = 0.011) and family history in first-degree relatives (OR 3.08, 95% CI: 1.05, 8.99; P = 0.040). The significant factors among adults include: head injury (OR 14.36, 95% CI: 3.84, 53.63; P < 0.001), poor perinatal care (OR 12.09, 95% CI: 5.57, 26.24; P < 0.001), febrile seizures (OR 9.33, 95% CI: 4.57, 19.06; P < 0.001), family history in second-degree relatives (OR 7.00, 95% CI: 2.11, 23.21; P = 0.001) and consanguinity (OR 3.28, 95% CI: 1.74, 6.18; P < 0.001). The PAFs for these

individual factors were significantly high. Collectively, the PAF for the six most important factors in children was 74.0% (95% CI: 71.0, 76.0) and for the five in adults was 79.0% (75.0, 81.0). The ORs varied between individual sites; however, febrile seizures and poor perinatal care in adults were common to all the sites. **Conclusion:** This chapter has identified a variety of risk factors for epilepsy. The majority of the risk factors are potentially preventable if effective intervention strategies are put in place.

Keywords: Epilepsy, Risk factors, Associations, Odds ratio, Nigeria, Sub-Saharan Africa

8.2 Introduction

The reason for the high burden and associated risk factors in LMICs remains unclear (Sander, 2003, Beghi et al., 2019). To date, there are no cohort studies in SSA, but the few case-control studies have shown that epilepsy is associated with various infectious and non-infectious factors which vary between regions (Preux & Druet-Cabanac, 2005). There is a relationship between epilepsy and 'neurotrophic' parasites (Carpio et al., 2016), such as cysticercosis (Nicoletti et al., 2002, Nsengiyumva et al., 2003, Winkler et al., 2009a, Nitiema et al., 2012), onchocerciasis (Boussinesq et al., 2002, Pion & Boussinesq, 2012, Ngugi et al., 2013a, Kamuyu et al., 2014, Ae-Ngibise et al., 2015), toxoplasmosis (Ngugi et al., 2013a, Kamuyu et al., 2014, Ae-Ngibise et al., 2015) and toxocariasis (Nicoletti et al., 2002, Ngugi et al., 2013a, Kamuyu et al., 2014). The susceptibility to developing epilepsy following infestations with these parasites is determined by host immunity and genetic differences within the species, which vary between geographical locations (Edwards, 2003, Campbell et al., 2006, Jayaraman et al., 2011). Bacterial and viral agents causing meningitis have been implicated in epilepsy (Edmond et al., 2010, Ngugi et al., 2013a, Kamuyu et al., 2014, Ae-Ngibise et al., 2015). Occurrence of febrile seizures have also been found to be a major risk factor for developing epilepsy (Chungath & Shorvon, 2008, Dube et al., 2009). A United Kingdom prospective cohort reported that people who had febrile seizures had an approximately 10 times higher risk of developing epilepsy compared to the general

population over a 24 years follow-up (Neligan et al., 2012). In LMIC febrile seizures are common occurrences associated with acute febrile illnesses particularly malaria - which has been shown to increase the risk of developing epilepsy (Mung'ala-Odera et al., 2008, Prischich et al., 2008, Matuja & Fataki, 2011). There are various proposed mechanisms for people with febrile seizures developing epilepsy, but it may be due to either an already existing inherent susceptibility to seizures or brain damage from prolonged and recurrent febrile seizures (Ngoungou et al., 2006, Idro et al., 2008, Dube et al., 2009, Christensen & Eslick, 2015).

Non-infectious factors like family history (Matuja et al., 2001, Nsengiyumva et al., 2003, Edwards et al., 2008, Mung'ala-Odera et al., 2008, Ngugi et al., 2013a, Ae-Ngibise et al., 2015), head injury (Edwards et al., 2008, Ngugi et al., 2013a), poor obstetric care (Matuja et al., 2001, Edwards et al., 2008, Mung'ala-Odera et al., 2008, Ngugi et al., 2013a, Ae-Ngibise et al., 2015), substance abuse (Ngugi et al., 2013a, Ae-Ngibise et al., 2015) and malnutrition (Ngugi et al., 2013a, Ae-Ngibise et al., 2015) have been shown to be associated with epilepsy in SSA. There is a strong correlation between the prevalence of epilepsy and social deprivation (Morgan et al., 2000). Socioeconomically disadvantaged people in both LMICs and high income countries (HICs) are more likely to develop epilepsy due to an increased risk of exposures due to poverty-driven risk factors (Heaney et al., 2002).

The considerable variation in the strength of association between these risk factors and epilepsy could be attributed to differences in study design, population structure, environmental and genetic differences (Thurman et al., 2011). The role genetics has in epilepsy is yet to be fully understood. Some forms of epilepsy are likely to have a genetic basis, but the role of *de novo* mutagenesis appears underrated (Thomas & Berkovic, 2014). Inherent genetic differences also seem to predispose to epileptogenesis following various cerebral insults (Loscher & Brandt, 2010, Webster et al., 2017).

Most studies done in Nigeria regarding risk factors are cross-sectional and largely from the southwest region (Dada et al., 1969, Familusi & Sinnette, 1971, Osuntokun, 1972, Danesi, 1985, Osuntokun et al., 1987a, Ogunrin et al., 2013). The only two case-control studies conducted in Nigeria among hospital-based participants reported febrile convulsions, birth-related complications and family history as the most important factors associated with epilepsy (Ogunniyi et al., 1987, Ogunrin et al., 2014). These few case-controls studies are insufficient to make reasonable conclusions on risk factors for epilepsy (Preux & Druet-Cabanac, 2005). This study was conducted with the aim of assessing potential risk factors and their contributions to epilepsy in three distinct regions of Nigeria. This is valuable as determining the factors associated with epilepsy will be a useful first step for developing preventative modalities and determining the healthcare needs of those predisposed.

8.3 Methodology

This was a community-based observational study using an unmatched case-control design. The cases (n=252) were people with active epilepsy recruited from the cross-sectional door-to-door census, while the controls were those who had never had epilepsy (or recurrent non-febrile seizures). More than twice as many (n=585) unmatched controls as the cases were randomly selected from a representative sample frame of households across the communities who participated in the door-to-door census. They were selected from the same period and the same communities as the case population. A table of random numbers was used to select controls from households using the specific household census numbers. Subjects underwent a scheduled structured interview with information collected using the epilepsy questionnaire. A similarly modified version without epilepsy-specific questions for the control group. The sociodemographic information recorded includes age, gender, educational attainment, religion, marital status, employment and average monthly income, source of water supply, toilet facilities and consumption of pork. Other information examined includes childhood febrile seizures, perinatal care, family history

of epilepsy (among first- and second-degree relatives), sickle cell disease, meningitis, measles and head-injury before the onset of seizures. History of hypertension, diabetes, stroke, alcohol consumption and cigarette smoking (current and previous) were of interest among adults. The source of water was classified into tap (pump), well, flowing stream and pond water. Toilet facilities were classified into water-closet, pit latrine or open defecation. Open defecation was defined as the emptying of bowels in the open without the use of properly designed structures for handling human waste (Jones et al., 2012). A *first-degree relative* was defined as an individual's parents, siblings, or offspring, whereas second-*degree relative* was defined as an individual's grandparents, grandchildren, aunts, uncles, nephews, or nieces. Because of the likelihood of marriage among relatives in Nigeria, history of consanguineous marriage in the subject's parents was documented and defined as a union between second cousins or closer (Hamamy, 2012). A history of childhood febrile seizures was defined as seizures associated with a high fever between the ages of 6 months and 5 years (Capovilla et al., 2009). One way the community differentiated febrile seizure from other encephalopathic condition is how fast a child is awake after the seizure. Poor perinatal and obstetric care was defined as the presence of maternal or birth complications such as prolonged/obstructed delivery, eclampsia, apnoea or problems after delivery of the index subject and unsupervised home delivery. Attendance of a pregnant mother by a trained traditional birth attendant was not considered as poor obstetric practice (Kayombo, 2013). These histories were obtained from mothers where possible. History of sickle cell disease was based on previous diagnosis. Stroke was defined as a rapidly developing clinical signs of neurological dysfunction of vascular origin with symptoms persisting ≥ 24 hours or until death (Sacco et al., 2013). Meningitis was defined as an inflammation of the meninges, caused by a viral or bacterial infection, and marked by intense headache and fever, sensitivity to light, and neck stiffness (Overturf, 2005). Measles caused by a virus was defined as the presence of generalized maculopapular rash, fever, and at least one of the "3 Cs"

(cough, conjunctivitis, or coryza) (Hutchins et al., 2004). These infections are confirmed by means of microbiological or serological tests; however, most people in the communities can recognise them. The local terms for conditions such as meningitis and measles were verified by the research team to get accurate histories and hospital records were used were available. Additional information was obtained from the PHC workers living in these communities, as they know a lot about the health status of these individuals over the years. These factors were recorded as either present or absent; the response option 'unknown' was added where subjects were unsure. Children below six years were excluded to avoid including those with recurrent febrile seizures as epilepsy cases. Those who are not permanent residents, or recent migrants, were excluded. Ethical considerations were as previously documented and the study conducted according to the set standard of the declaration of Helsinki (Carlson et al., 2004).

Statistical analysis: Data were analysed using Stata 15 (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). Descriptive statistics were used to assess the distribution of the socio-demographic characteristics between cases and controls. A chi-squared (χ^2) test was used to compare categorical variables between cases and controls, and between sites. The Wilcoxon-rank sum test was used to compare continuous variables between the cases and controls and the Kruskal-Wallis test to compare between the three recruitment sites. A univariate analysis was performed using a simple logistic regression to ascertain factors associated with epilepsy. To understand the interplay and identify potential risk factors for epilepsy, covariates with higher P-value ($P > 0.2$) were removed and a multivariate logistic regression model fitted to get the most important factors adjusting for age and gender. The odds ratios (ORs) and their 95% CI were recorded. MICE was performed to deal with missing data and to correct for the potential non-response bias using 25 imputations. The systematic process of the imputations is shown in Appendix 20. To assess the public health impact and quantify the contribution of that factor to epilepsy,

the population attributable fraction (PAF) and their 95% CIs were calculated for each factor and a combination of factors using the '*punafcc*' command for case-control data that corresponds to the logistic regression (Newson, 2013). PAF assumes the proportional reduction in the disease that would occur if exposure to a risk factor were reduced to an alternative ideal exposure scenario (Mansournia & Altman, 2018). Data were analysed for the individual sites and then combined to get a pooled result. The analyses were stratified based on age into children (those below 16 years) and adults (those 16 years and above), as exposures to some risk factors differ with age (House et al., 1994). Those with P-values at < 0.05 were considered significant.

Table 35: Univariate analysis of the sociodemographic characteristics of subjects with epilepsy and controls by sites

	Afikpo			**Ijebu-Jesa**			**Gwandu**			**All sites**		
	Cases (n=40)	**Control (n=109)**	**P-value**	**Cases (n=24)**	**Control (n=82)**	**P-value**	**Cases (n=188)**	**Control (n=394)**	**P-value**	**Cases (n=252)**	**Control (n=585)**	**P-value**
Age (Years)												
Median (IQR)	25.5 (19.5 – 41.0)	28.0 (15.0-38.0)	0.339	25.0 (12.5 – 28.5)	29.5 (18.0 – 40.0)	0.051	18 (11.0 – 25.0)	17.0 (10.0 – 27.0)	0.959	19 (12 – 27)	19.0 (11.0 – 32.0)	0.355
Range	7 – 76	6 – 89		6 – 56	6 – 105		6 – 60	6 – 60		6 – 76	6 – 105	
Gender												
Male	21 (52.5%)	46 (42.2%)	0.263	12 (50.0%)	38 (46.9%)	0.790	95 (50.5%)	213 (54.1%)	0.425	128 (50.8%)	297 (50.9%)	0.987
Female	19 (47.5%)	63 (57.8%)		12 (50.0%)	43 (53.1%)		93 (49.5%)	181 (45.9%)		124 (49.2%)	287 (49.1%)	
Marital status												
Single	32 (80.0%)	61 (56.0%)	1.0 (ref)	16 (66.7%)	37 (45.1%)	1.0 (ref)	147 (78.2%)	266 (67.5%)	1.0 (ref)	194 (77.4%)	364 (62.2%)	1.0 (ref)
Married	7 (17.5%)	41 (37.6%)	0.015	6 (25.0%)	41 (50.0%)	0.041	37 (19.7%)	126 (32.0%)	0.003	50 (19.8%)	208 (35.6%)	<0.0001
Divorced	0 (0.0%)	0 (0.0%)	-	1 (4.2%)	2 (2.4%)	0.908	4 (2.1%)	1 (0.25%)	0.078	5 (2.0%)	3 (0.51%)	0.123
Widow(er)	1 (2.5%)	7 (6.4%)	0.233	1 (4.2%)	2 (2.4%)	0.908	0 (0.0%)	1 (0.25%)	-	2 (0.8%)	10 (1.71%)	0.206
Religion												
Christian	40 (100.0%)	101 (92.7%)	1.0 (ref)	20 (83.3%)	74 (89.2%)	1.0 (ref)	188 (100.0%)	394 (100.0%)	1.0 (ref)	60 (23.8%)	175 (29.9%)	1.0 (ref)
Muslim	0 (0.0%)	6 (5.5%)	-	4 (16.7%)	9 (10.8%)	0.445	0 (0.0%)	0 (0.0%)	-	192 (76.2%)	403 (68.8%)	0.058
Traditional	0 (0.0%)	2 (1.8%)	-	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	-	0 (0.0%)	6 (1.0%)	-
Others	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	-	0 (0.0%)	2 (0.3%)	-
Level of Education												
Uneducated	13 (32.5%)	7 (6.4%)	1.0 (ref)	3 (12.5%)	6 (7.3%)	1.0 (ref)	106 (56.4%)	104 (26.4%)	1.0 (ref)	122 (48.1%)	117 (20.0%)	1.0 (ref)
Primary	16 (40.0%)	31 (28.4%)	0.022	9 (37.5%)	17 (20.7%)	0.944	54 (28.7%)	184 (46.7%)	<0.0001	79 (31.5%)	232 (39.7%)	<0.0001
Secondary	9 (22.5%)	37 (33.9%)	0.001	8 (33.3%)	39 (47.6%)	0.269	26 (13.8%)	88 (22.3%)	<0.0001	43 (17.1%)	164 (28.0%)	<0.0001

Table 35: Univariate analysis of the sociodemographic characteristics of subjects with epilepsy and controls by sites

	Afikpo			**Ijebu-Jesa**			**Gwandu**			**All sites**		
	Cases (n=40)	**Control (n=109)**	**P-value**	**Cases (n=24)**	**Control (n=82)**	**P-value**	**Cases (n=188)**	**Control (n=394)**	**P-value**	**Cases (n=252)**	**Control (n=585)**	**P-value**
Tertiary	2 (5.0%)	34 (31.2%)	<0.0001	4 (16.7%)	20 (24.4%)	0.306	2 (1.1%)	18 (4.6%)	0.003	8 (3.2%)	72 (12.3%)	<0.0001
Employment or trade												
Unemployed	19 (47.5%)	10 (9.2%)	1.0 (ref)	7 (29.2%)	3 (3.7%)	1.0 (ref)	78 (41.5%)	63 (16.0%)	1.0 (ref)	104 (41.3%)	76 (13.0%)	1.0 (ref)
Civil servant or wage earner	1 (2.5%)	15 (13.8%)	0.002	1 (4.2%)	4 (4.9%)	0.089	6 (3.2%)	15 (3.8%)	0.027	8 (3.2%)	34 (5.8%)	<0.0001
Crafts or trade	8 (20.0%)	19 (17.4%)	0.009	6 (25.0%)	37 (45.1%)	0.001	11 (5.9%)	85 (21.6%)	<0.0001	25 (9.9%)	141 (24.1%)	<0.0001
Subsistence farmer	1 (2.5%)	11 (10.1%)	0.006	0 (0.0%)	8 (9.8%)	-	40 (21.3%)	92 (23.3%)	<0.0001	41 (16.3%)	111 (19.0%)	<0.0001
Student	2 (5.0%)	4 (3.7%)	0.160	1 (4.2%)	2 (2.4%)	0.273	14 (7.5%)	4 (1.0%)	0.079	17 (6.8%)	10 (1.7%)	0.611
Semi-Skilled and unskilled labourer	9 (22.5%)	50 (45.9%)	<0.0001	9 (37.5%)	28 (34.2%)	0.012	39 (20.7%)	135 (34.3%)	<0.0001	57 (22.6%)	213 (36.4%)	<0.0001
Access to health insurance												
No	39 (97.5%)	103 (98.1%)	1.0 (ref)	24 (100.0%)	77 (96.2%)	1.0 (ref)	186 (98.9%)	383 (98.5%)	1.0 (ref)	249 (98.8%)	563 (98.1%)	1.0 (ref)
Yes	1 (2.5%)	2 (1.9%)	0.822	0 (0.0%)	3 (3.8%)	0.336	2 (1.1%)	6 (1.5%)	0.645	3 (1.2%)	11 (1.9%)	0.457

8.4 Results

The sociodemographic characteristics of the cases and controls from each site and the total are presented in Table 35. A total of 252 (females 49.2%) cases and 586 (females 49.1%) controls (ratio of 1: 2.3) were recruited from the three sites. Figure 14 illustrates the skewed age distribution of cases and controls. Despite being unmatched there were no significant age or gender differences between the cases and controls. The cases were significantly less likely to be married compared to controls across sites. Apart from Ijebu-Jesa, those with epilepsy were significantly less likely to have received some education or to be in employment compared to controls. All the cases and controls were Muslims in Gwandu, while almost all were Christians in Afikpo and Ijebu-Jesa. The number of people with health insurance was extremely low (cases – 1.2% vs controls – 1.9%).

Table 36 displays the pooled analyses of factors for children. The multivariate analysis showed that febrile seizures had the largest odds ratio (OR 12.64, 95% CI: 4.75, 33.58; P < 0.001). Followed by meningitis (OR 12.32, 95% CI: 1.84, 82.39; P = 0.010), poor perinatal care (OR 10.85, 95% CI: 3.98, 29.57; P < 0.001), open defecation (OR 5.12, 95% CI: 1.67, 15.65; P = 0.004), measles (OR 4.50, 95% CI: 1.42, 14.27; P = 0.011) and family history in first-degree relatives (OR 3.08, 95% CI: 1.05, 8.99; P = 0.040). The analysis of the individual sites (details in Appendix 21) among children showed that measles (OR 42.52, 95% CI: 1.34, 1353.41; P = 0.034) was the most important factor in Afikpo, while febrile seizures (OR 33.61, 95% CI: 0.92, 1228.22); P = 0.056) and poor perinatal care (OR 16.43, 95% CI: 0.53, 511.98; P = 0.111) were most important in Ijebu-Jesa. Compared to controls, children with epilepsy in Ijebu-Jesa were four times more likely to have had a history of childhood measles; however, this was not statistically significant. It is important to note that these two sites have small numbers of cases that led to wide confidence intervals.

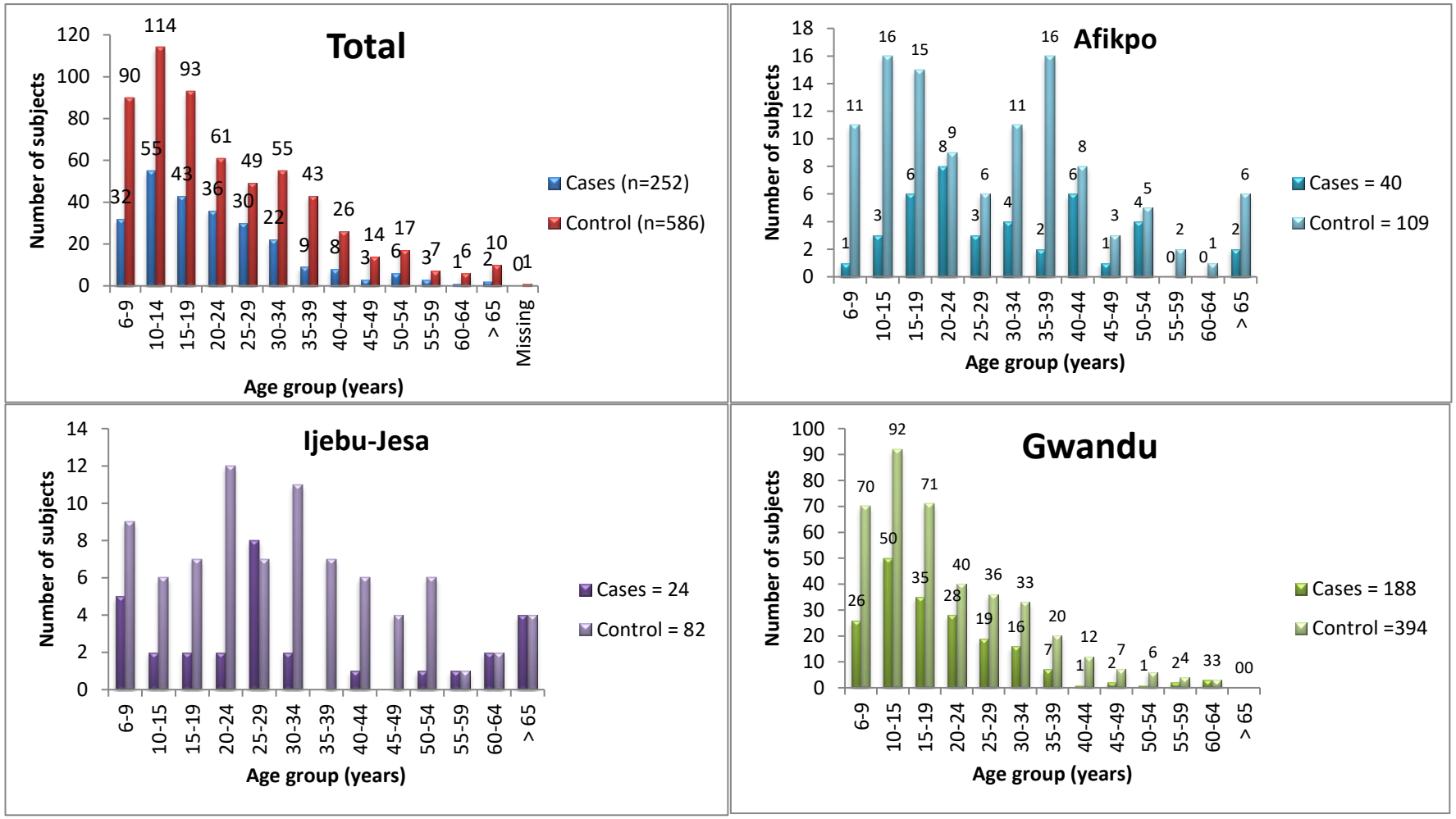

Figure 15: Age group of cases and controls total combined and by site

Table 36: Factors associated with epilepsy in children (< 16 years) combining all centres

Risk Factor	Children with active epilepsy (n=96)	Controls (n=226)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Age								
					1.10 (0.98, 1.25)	0.112	1.42 (0.86, 2.44)	0.192
Gender								
Male	43 (44.8%)	126 (55.8%)	1.0 (reference)					
Female	53 (55.2%)	100 (44.2%)	1.55 (0.96, 2.51)	0.072	1.28 (0.65, 2.55)	0.473	1.47 (0.75, 2.88)	0.257
Well water								
No	16 (16.8%)	68 (30.1 %)	1.0 (reference)					
Yes	79 (83.2%)	158 (69.9%)	2.13 (1.16, 3.90)	0.015	1.75 (0.72, 4.22)	0.215	1.40 (0.60, 3.25)	0.434
Stream water								
No	96 (100.0%)	223 (98.7%)	1.0 (reference)					
Yes	0 (0.0%)	3 (1.3%)	-	-				
Pond water								
No	96 (100.0%)	221 (97.8%)	1.0 (reference)					
Yes	0 (0.0%)	5 (2.2%)	-	-				
Use pit latrine								
No	23 (24.2%)	36 (17.3%)	1.0 (reference)					
Yes	72 (75.8%)	172 (82.7%)	0.66 (0.36, 1.18)	0.161	0.78 (0.29, 2.08)	0.616	1.01 (0.41, 2.49)	0.984
Open defecation								
No	80 (83.3%)	213 (94.3%)	1.0 (reference)					
Yes	16 (16.7%)	13 (5.6%)	3.28 (1.51, 7.12)	0.003	7.14 (1.95, 26.09)	0.003	5.12 (1.67, 15.65)	0.004
Pork consumption								
No	96 (100.0%)	224 (99.1%)	1.0 (reference)					
Yes	0 (0.0%)	2 (0.9%)	-	-				

Table 36: Factors associated with epilepsy in children (< 16 years) combining all centres

Risk Factor	Children with active epilepsy (n=96)	Controls (n=226)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Consanguineous parents								
No	64 (66.7%)	186 (82.7%)	1.0 (reference)					
Yes	32 (33.3%)	37 (16.4%)	2.51 (1.45, 4.36)	0.001	1.43 (0.60, 3.43)	0.416	1.26 (0.55, 2.87)	0.579
Unknown	0 (0.0%)	2 (0.9%)	-	-				
Poor perinatal care								
No	65 (68.4%)	217 (96.4%)	1.0 (reference)					
Yes	28 (29.5%)	8 (3.6%)	11.87 (5.21, 27.07)	<0.0001	9.01 (3.26, 24.95)	<0.0001	10.85 (3.98, 29.57)	<0.0001
Unknown	2 (2.1%)	0 (0.0%)	-	-	-	-	-	-
Family history of epilepsy (first-degree relative)								
No	67 (69.8%)	215 (95.6%)	1.0 (reference)					
Yes	29 (30.2%)	10 (4.4%)	9.31 (4.31. 20.08)	<0.0001	4.36 (1.30, 14.70)	0.017	3.08 (1.05, 8.99)	0.040
Family history of epilepsy (second-degree relative)								
No	72 (75.0%)	218 (96.9%)	1.0 (reference)					
Yes	24 (25.0%)	7 (3.1%)	10.38 (4.29, 25.10)	<0.0001	1.32 (0.35, 4.99)	0.678	1.80 (0.50, 6.50)	0.370
Febrile seizures								
No	57 (59.4%)	216 (96.0%)	1.0 (reference)					
Yes	39 (40.6%)	9 (4.0%)	16.42 (7.52, 35.87)	<0.0001	14.23 (5.07, 39.94)	<0.0001	12.64 (4.75, 33.58)	<0.0001
Measles								
No	76 (79.2%)	217 (96.4%)	1.0 (reference)					
Yes	20 (20.8%)	8 (3.6%)	7.14 (3.02, 16.88)	<0.0001	4.89 (1.44, 16.54)	0.011	4.50 (1.42, 14.27)	0.011
Meningitis								
No	91 (94.8%)	221 (99.1%)	1.0 (reference)					
Yes	5 (5.2%)	2 (0.9%)	6.07 (1.16, 31.86)	0.033	10.39 (1.54, 69.99)	0.016	12.32 (1.84, 82.39)	0.010
Head injury								
No	93 (96.9%)	223 (99.1%)	1.0 (reference)					

Table 36: Factors associated with epilepsy in children (< 16 years) combining all centres

Risk Factor	**Children with active epilepsy (n=96)**	**Controls (n=226)**	**Univariate analysis**	**P-value**	**Multivariate analysis**	**P-value**	**Multivariate analysis with MICE***	**P-value**
Yes	3 (3.1%)	2 (0.9%)	3.60 (0.59, 21.88)	0.165	0.23 (0.02, 2.33)	0.213	0.23 (0.02, 2.29)	0.208
Sickle cell disease								
No	95 (99.0%)	224 (99.6%)	1.0 (reference)					
Yes	1 (1.0%)	1 (0.4%)	2.36 (0.15, 38.09)	0.546				

* MICE – multiple imputation by chained equation, used to handle missing variable

The most important factors in Gwandu include: febrile seizures (OR 12.71, 95% CI: 4.24, 38.10; P = < 0.001), poor perinatal care (OR12.09, 95%CI: 3.76, 38.85; P < 0.001), meningitis (OR 8.13, 95% CI:1.00, 66.21; P = 0.050), measles (OR 6.65, 95% CI: 1.06, 41.72; P = 0.043), open defecation (OR 6.46, 95% CI: 1.69, 24.66; P = 0.006) and family history in first-degree relatives (OR 3.12, 95% CI: 0.99, 9.85; P = 0.052).

Table 37 shows that the most important factors associated with epilepsy in adults were head injury (OR 14.36, 95% CI: 3.84, 53.63; P < 0.001), poor perinatal care (OR 12.09, 95% CI: 5.57, 26.24; P < 0.001), febrile seizures (OR 9.33, 95% CI: 4.57, 19.06; P < 0.001), family history in second-degree relatives (OR 7.00, 95% CI: 2.11, 23.21; P = 0.001) and consanguinity (OR 3.28, 95% CI: 1.74, 6.18; P < 0.001). The analysis of the individual sites (Appendix 22) showed that in Afikpo, febrile seizures (OR 22.70, 95% CI: 2.88, 178.88; P = 0.003), poor perinatal care (OR 11.07, 95% CI: 1.27, 96.40; P = 0.029), head injury (OR 12.67, 95% CI: 0.81, 199.02; P = 0.071), and family history in second-degree relatives (OR 8.83, 95% CI: 0.40, 196.45; P = 0.169) were the most important factors. The administration of Ivermectin in the family was inversely associated with epilepsy in Afikpo (OR 0.05, 95% CI: 0.006, 0.42; P = 0.006). In Ijebu-Jesa poor perinatal care (OR 49.00, 95% CI: 3.37, 711.92; P = 0.004), family history in first-degree relatives (OR 11.85, 95% CI: 1.19, 118.50; P = 0.0.035) and febrile seizures (OR 11.19, 95% CI: 1.91, 65.44; P = 0.007) were important factors. The significant factors in Gwandu include head injury (OR 11.56, 95% CI: (1.67, 80.07); P < 0.013), poor perinatal care (OR 9.75, 95% CI: 3.62, 26.26; P < 0.001), febrile seizures (OR 9.13, 95% CI: 3.44, 24.25; P < 0.001), family history in second-degree relatives (OR 8.26, 95% CI: 1.74, 39.29; P = 0.008) and consanguinity (OR 3.69, 95% CI:1.78, 7.64; P < 0.001). Adults in Gwandu who reported measles, meningitis and family history in first-degree relatives had higher odds (OR > 2.0) for epilepsy; however, they were not statistically significant. Interestingly, the use of pit latrines was a negative factor in Gwandu but a positive one in Afikpo in univariate analysis, but turned out not

to be significant in the multivariate model. Twelve (16.9%) of the 71 adult female cases had a history of eclampsia [Afikpo (7.1%), Ijebu-Jesa (25.0%), Gwandu (18.4%)].

Table 37: Factors associated with epilepsy in adults (≥16 years) combining all centres

Risk Factor	Adults with active epilepsy (n=156)	Controls (n=359)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Age								
					0.98 (0.96, 1.01)	0.163	0.92 (0.82, 1.03)	0.136
Gender								
Male	85 (54.5%)	171 (47.8%)	1.0 (reference)					
Female	71 (45.5%)	187 (52.2%)	0.76 (0.52, 1.11)	0.162	1.05 (0.61, 1.78)	0.865	1.00 (0.59, 1.69)	0.999
Well water								
No	41 (26.3%)	137 (38.2%)	1.0 (reference)					
Yes	115 (73.7%)	222 (61.8%)	1.73 (1.14, 2.62)	0.010	1.21 (0.65, 2.23)	0.550	1.23 (0.67, 2.26)	0.500
Stream water								
No	151 (96.8%)	351 (97.8%)	1.0 (reference)					
Yes	5 (3.2%)	8 (2.2%)	1.45 (0.47, 4.51)	0.518				
Pond water								
No	155 (99.4%)	359 (100%)	1.0 (reference)					
Yes	1 (0.6%)	0 (0.0%)	-	-				
Pit latrine								
No	44 (28.2%)	104 (30.6%)	1.0 (reference)					
Yes	112 (71.8%)	236 (69.4%)	1.12 (0.74, 1.70)	0.590				
Open defecation								
No	147 (94.2%)	336 (93.6%)	1.0 (reference)					
Yes	9 (5.8%)	23 (6.4%)	0.89 (0.40, 1.98)	0.783				
Pork consumption								
No	156 (100.0%)	348 (96.9%)	1.0 (reference)					
Yes	0 (0.0%)	11 (3.1%)	-	-				
Consanguineous parents								

Table 37: Factors associated with epilepsy in adults (≥16 years) combining all centres

No	104 (66.7%)	307 (86.0%)	1.0 (reference)					
Yes	52 (33.3%)	44 (12.3%)	3.49 (2.20, 5.52)	<0.0001	3.03 (1.60, 5.71)	0.001	3.28 (1.74, 6.18)	<0.0001
Unknown	0 (0.0%)	6 (1.7%)	-	-				
Poor perinatal care								
No	103 (66.0%)	346 (96.6%)	1.0 (reference)					
Yes	53 (34.0%)	12 (3.4%)	14.8 (7.64, 28.82)	<0.0001	11.01 (5.06, 23.95)	<0.0001	12.09 (5.57, 26.24)	<0.0001
Family history (first-degree relative)								
No	113 (72.4%)	348 (96.9%)	1.0 (reference)					
Yes	43 (27.6%)	11 (3.1%)	12.04 (6.00, 24.13)	<0.0001	2.39 (0.84, 6.80)	0.102	2.30 (0.83, 6.40)	0.110
Family history (second degree relative)								
No	118 (75.6%)	353 (98.3%)	1.0 (reference)					
Yes	38 (24.4%)	6 (1.7%)	18.95 (7.81, 45.95)	<0.0001	7.19 (2.07, 24.94)	0.002	7.00 (2.11, 23.21)	0.001
Febrile seizures								
No	91 (58.3%)	341 (95.0%)	1.0 (reference)					
Yes	65 (41.7%)	18 (5.0%)	13.53 (7.65, 23.95)	<0.0001	9.25 (4.42, 19.38)	<0.0001	9.33 (4.57, 19.06)	<0.0001
Measles								
No	114 (73.1%)	330 (91.9%)	1.0 (reference)					
Yes	42 (26.9%)	29 (8.1%)	4.19 (2.50, 7.04)	<0.0001	1.91 (0.84, 4.31)	0.121	1.43 (0.66, 3.10)	0.363
Meningitis								
No	137 (87.8%)	347 (96.7%)	1.0 (reference)					
Yes	19 (12.2%)	12 (3.3%)	4.01 (1.90, 8.48)	<0.0001	1.85 (0.54, 6.31)	0.327	1.33 (0.41, 4.27)	0.633
Head injury								
No	136 (87.2%)	354 (98.6%)	1.0 (reference)					
Yes	20 (12.8%)	5 (1.4%)	10.41 (3.83, 28.29)	<0.0001	12.44 (3.28, 47.19)	<0.0001	14.36 (3.84, 53.63)	<0.0001
Family history river blindness								
No	145 (93.0%)	335 (94.9%)	1.0 (reference)					
Yes	10 (6.4%)	15 (4.3%)	1.54 (0.68, 3.51)	0.304				
Unknown	1 (0.6%)	3 (0.8%)	0.77 (0.08, 7.46)	0.822				

Table 37: Factors associated with epilepsy in adults (≥16 years) combining all centres

Family history of Ivermectin use								
No	116 (74.4%)	273 (81.0%)	1.0 (reference)					
Yes	40 (25.6%)	62 (18.4%)	1.52 (0.97 2.39)	0.071	1.16 (0.59, 2.29)	0.660	1.07 (0.55, 2.10)	0.838
Unknown	0 (0.0%)	2 (0.6%)	-	-				
Hypertension								
No	150 (96.2%)	337 (93.9%)	1.0 (reference)					
Yes	6 (3.8%)	22 (6.1%)	0.61 (0.24, 1.54)	0.298				
Diabetes								
No	151 (96.8%)	348 (96.9%)	1.0 (reference)					
Yes	5 (3.2%)	11 (3.1%)	1.05 (0.36, 3.07)	0.932				
Sickle cell disease								
No	154 (98.7%)	356 (99.2%)	1.0 (reference)					
Yes	2 (1.3%)	3 (0.8%)	1.54 (0.25, 9.32)	0.638				
Stroke								
No	153 (98.1%)	353 (98.3%)	1.0 (reference)					
Yes	3 (1.9%)	6 (1.7%)	1.15 (0.28, 4.67)	0.841				
Smoking								
No	149 (95.5%)	339 (95.0%)	1.0 (reference)					
Yes	7 (4.5%)	18 (5.0%)	0.88 (0.36, 2.16)	0.788				
Alcohol consumption								
No	142 (91.0%)	316 (88.8%)	1.0 (reference)					
Yes	14 (9.0%)	39 (11.2%)	0.76 (0.41, 1.43)	0.403				
Eclampsia (females only – 71 cases)								
No	0 (0.0%)	0 (0.0%)	1.0					
Yes	12 (16.9%)	0 (0.0%)	-	-				

* MICE – multiple imputation by chained equation, used to handle missing variable

Table 38 and 39 displays the PAF for children and adults. Factors with significantly higher PAF in children across sites include febrile convulsion (38%), poor perinatal care (29%) and measles (18%). Family history of epilepsy for first- and second-degree relatives (39%), consanguinity (21%), open defecation (14%) and meningitis (4%) were important only in children from Gwandu. The use of well water by children gave a high PAF in Ijebu-Jesa (36%) and Gwandu (48%). The use of pit latrines contributed negatively to epilepsy in Gwandu and IJebu-Jesa, but positively in Afikpo with a high PAF of 41%. The highest PAF across sites for adults was febrile seizures (39%), followed by poor perinatal care (32%), family history (32%) and measles (21%). The PAF for consanguinity (36%) and meningitis (14%) was important for adults in Gwandu. The PAF for head injury was only significant in adults from Afikpo (18%) and Gwandu (10%). When the two vaccine-preventable diseases (measles and meningitis) were combined, the PAF was found to be 21% and 24% in children and adults respectively across sites. Comparing the ORs and PAFs showed that factors with smaller non-significant ORs resulted generally in a smaller or negative PAF. Collectively, the PAF for the six most important factors in children (febrile seizures, meningitis, poor perinatal care, open defecation, measles and family history first-degree relative) and the five in adults (head injury, poor perinatal care, febrile seizures, family history second-degree relative and consanguinity) based on their ORs accounted for 74.0% (95% CI: 71.0%, 76.0%) and 79.0% (95% CI: 75.0%, 81.0%) respectively.

Stroke, hypertension, diabetes, sickle cell disease, smoking and alcohol use were not associated with epilepsy in this study. Pork consumption was not an important factor as it was very rare among cases and controls.

Table 38: Population Attributable Fraction for potential risk factors of epilepsy in children

Risk Factors	Afikpo (95% CI)	Ijebu-Jesa (95% CI)	Gwandu (95% CI)	Total (95% CI)
Well water	0.00 (0.00, 0.00)	0.36 (-3.13, 0.90)	0.48 (0.00, 0.73)	0.44 (0.14, 0.63)
Stream water	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Pond water	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Use pit latrine	0.41 (0.08, 0.63)	-0.47 (-3.34, 0.50)	-3.51 (-10.03, -0.85)	-0.40 (-1.28, 0.14)
Open defecation	-0.03 (-0.51, 0.30)	0.09 (-0.07, 0.23)	0.14 (0.10, 0.17)	0.12 (0.08, 0.15)
Pork consumption	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Consanguineous parents	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.21 (0.12, 0.30)	0.18 (0.09, 0.25)
Poor perinatal care	0.00 (0.00, 0.00)	0.39 (0.30, 0.48)	0.31 (0.29, 0.33)	0.29 (0.27, 0.31)
Family history of epilepsy (1st degree relative)	0.00 (0.00, 0.00)	0.09 (-0.07, 0.23)	0.31 (0.28, 0.33)	0.27 (0.24, 0.29)
Family history of epilepsy (2nd degree relative)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.26 (0.24, .029)	0.23 (0.20, 0.25)
Febrile convulsions	0.00 (0.00, 0.00)	0.55 (0.48, 0.61)	0.40 (0.38, 0.42)	0.38 (0.36, 0.40)
Measles	0.26 (0.19, 0.32)	0.45 (0.17, 0.64)	0.16 (0.14, 0.17)	0.18 (0.15, 0.20)
Meningitis	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.04 (0.02, 0.06)	0.04 (0.03, 0.06)
Head injury	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.03 (0.02, 0.04)	0.02 (0.01, 0.04)

Sickle cell disease	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.01 (-0.01, 0.02)	0.006 (-.01, 0.018)
Measles and Meningitis	0.26 (0.19, 0.32)	0.57 (0.33, 0.73)	0.17 (0.15, 0.20)	0.21 (0.18, 0.23)
Family history 1st & 2nd degree relative	0.00 (0.00, 0.00)	0.09 (-0.07, 0.23)	0.39 (0.35, 0.42)	0.34 (0.31, 0.37)
[Febrile seizures, meningitis, poor perinatal care, open defecation, measles, family history1st]*				0.74 (0.71, 0.76)

*Summary population attributable fraction for the six most important factors in the multivariate analysis.

Table 39: Population Attributable Fraction for potential risk factors of epilepsy in adults

Risk Factor	Afikpo (95% CI)	Ijebu-Jesa (95% CI)	Gwandu (95% CI)	Total (95% CI)
Well	0.00 (0.00, 0.00)	0.51 (-0.16, 0.79)	0.30 (-0.26, 0.61)	0.31 (0.11, 0.47)
Stream	0.02 (-0.10, 0.12)	0.00 (0.00, 0.00)	0.01 (0 .003, 0.03)	0.01 (-0.02, 0.03)
Pond	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Pit latrine	0.20 (-0.01, 0.37)	0.08 (-0.36, 0.38)	-3.65 (-11.00, -0.80)	0.08 (-0.23, 0.31)
Open defecation	-0.05 (-0.29, 0.15)	0.03 (-0.05, 0.10)	0.00 (-0.04, 0.04)	-0.01 (-0.06, 0.04)
Pork consumption	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Consanguineous parents	0.02 (-0.02, 0.05)	0.00 (0.00, 0.00)	0.36 (0.29, 0.42)	0.24 (0.19, 0.28)
Poor perinatal care	0.28 (0.24, 0.31)	0.28 (0.26, 0.31)	0.33 (0.31, 0.35)	0.32 (0.30, 0.33)
Family history of epilepsy (1st degree relative)	0.22 (0.19, 0.25)	0.15 (0.01, 0.20)	0.28 (0.26, 0.30)	0.25 (0.24, 0.27)
Family history of epilepsy (2nd degree relative)	0.26 (0.24 0.28)	0.15 (0.10, 0.20)	0.23 (0.22, 0.25)	0.23 (0.22, 0.24)
Febrile convulsions	0.53 (0.50, 0.55)	0.31 (0.25, 0.37)	0.35 (0.33, 0.38)	0.39 (0.37, 0.40)
Measles	0.12 (0.07, 0.17)	0.20 (-0.08, 0.40)	0.25 (0.23, 0.28)	0.21 (0.17, 0.24)
Meningitis	-0.02 (-0.15, 0.10)	0.01 (-0.10, 0.11)	0.14 (0.12, 0.15)	0.09 (0.07, 0.11)
Head injury	0.18 (0.14, 0.22)	0.00 (0.00, 0.00)	0.10 (0.09, 0.12)	0.12 (0.10, 0.13)

Family history river blindness	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.03 (-0.03, 0.08)	0.02 (-0.02, 0.06)
Family history of Ivermectin use	-0.81 (-2.16, -0.04)	0.26 (0.13, 0.38)	0.22 (0.18, 0.25)	0.09 (0.01, 0.16)
Hypertension	-0.00 (-0.12, 0.10)	0.00 (0.00, 0.00)	-0.03 (-0.12, 0.04)	-0.02 (-0.08, 0.03)
Diabetes	0.06 (-0.006, 0.11)	0.00 (0.00, 0.00)	-0.02 (-0.08, 0.04)	0.001 (-0.03, 0.03)
Sickle cell disease	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.005 (-0.02, 0.03)	0.005 (-0.01, 0.019)
Stroke	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.02 (0.01, 0.03)	0.003 (-0.02, 0.03)
Smoking	-0.11 (-0.45, 0.15)	0.00 (0.00, 0.00)	0.03 (.007, 0.06)	-0.006 (-0.05, 0.04)
Alcohol intake	-0.06 (-0.37, 0.19)	-0.06 (-0.44, 0.22)	0.004 (-0.027, 0.03)	-0.03 (-0.10, 0.04)
Measles and meningitis	0.11 (-0.03, 0.23)	0.20 (-0.08, 0.40)	0.30 (0.27, 0.33)	0.24 (0.20, 0.27)
Family history 1st & 2nd degree relative	0.26 (0.24, 0.28)	0.24 (0.15, 0.31)	0.36 (0.34, 0.39)	0.32 (0.30, 0.34)
[Head injury, poor perinatal care, febrile seizures, family history 2nd, consanguinity]				0.79 (0.75, 0.81)

*Summary population attributable fraction for the five most important factors in the multivariate analysis.

8.5 Discussion

This study is the first community-based case-control study to report ORs and PAFs for factors associated with epilepsy from three regions of Nigeria and builds on previous studies (Ogunniyi et al., 1987, Ogunrin et al., 2014). The findings from this study showed that febrile seizures, poor perinatal care, family history of epilepsy and childhood measles were the most important factors in children and adults, while head injury was important in adults. Consanguinity in adults, and meningitis and open defecation in children were important and unique factors for epilepsy in Gwandu. A causal relationship cannot easily be inferred from a single study, but some of these factors had significantly large ORs and their corresponding PAFs reveal that they potentially contribute significantly to epilepsy. Consistent with previous community-based studies (Ogunniyi et al., 1987, Kannoth et al., 2009, Vozikis et al., 2012, Ogunrin et al., 2014), febrile seizures were a significant factor in this study for children and adults and across sites. A review of population-based studies reported a cumulative risk of developing epilepsy after febrile seizures between 2% and 7% mainly from HIC (Chungath & Shorvon, 2008). The Consequences of Prolonged Febrile Seizures in Childhood (FEBSTAT) study reported an association between febrile SE and hippocampal abnormalities. They observed that hippocampal damage could be a direct consequence of febrile SE in some, while in others a pre-existing hippocampal abnormality possibly increases the susceptibility for febrile seizures (Hesdorffer et al., 2016). Malaria and respiratory infections are usually the commonest identified aetiology associated with febrile seizures in SSA (Olubosede et al., 2015, Storz et al., 2015), and poor management may account for the high burden (Eseigbe et al., 2012). Prompt seizure treatment using standard pre-hospital treatment protocol of febrile seizures significantly leads to shorter seizure duration and better long-term outcomes (Seinfeld et al., 2014). Poor obstetric care was another significant factor for epilepsy in this study and in agreement with other SSA studies (Ogunniyi et al., 1987, Edwards et al., 2008, Mung'ala-Odera et al., 2008, Ngugi et al., 2013a, Ogunrin et al., 2014, Wagner et al.,

2014, Ae-Ngibise et al., 2015). Having access to antenatal care is a necessity, but the failure to use antenatal care is common among the rural, poor and less-educated, this is worse in Northern Nigeria (Fagbamigbe & Idemudia, 2015). The recognised factors influencing maternal health services utilization include affordability, availability and accessibility. The use of trained traditional birth attendants could help bridge the perinatal care gap (Babalola & Fatusi, 2009, Fagbamigbe & Idemudia, 2015). Similar to other studies from Africa (Matuja et al., 2001, Egeli et al., 2003, Nsengiyumva et al., 2003, Edwards et al., 2008, Mung'ala-Odera et al., 2008, Ngugi et al., 2013a, Wagner et al., 2014, Ae-Ngibise et al., 2015), family history of epilepsy was positively associated with epilepsy in this study. The positive family history reported from most studies could likely be due to shared socioeconomic and environmental risk factors (Ottman, 2005, Thomas & Berkovic, 2014). The majority of epilepsies are of complex genetic origin and since most people with epilepsy do not have an affected relative, *de novo* mutation needs to be considered (Shorvon, 2011, Hildebrand et al., 2013). One of the most common questions raised whilst in the field was whether epilepsy was hereditary; unfortunately, these questions have no clearcut answers and further studies are needed to make reasonable conclusions in SSA. The finding of a positive relationship between family history first-degree relatives in children and second-degree relatives in adults from Gwandu is an interesting finding. The reason for this is unclear. A plausible reason may be due to consanguinity being an important factor among adults in this study (Asadi-Pooya & Hojabri, 2005, Babtain, 2013). The effect of assortative mating may have also played a role (Millichap, 2006). The reason consanguinity was not important in children may be because it is a declining practice. A Jordanian study observed that although consanguinity is widely practised, it was not associated with increased risk of epilepsy (Daoud et al., 2003). The role consanguineous marriages and assortative mating may have on epilepsy could be an area for future studies.

Meningitis was important among individuals with epilepsy from Gwandu. Gwandu lies within the 'meningitis belt' of Africa (Figure 15) which has some of the highest incidence worldwide and meningococcal meningitis occurs in epidemics with severe consequences (Zunt et al., 2018).

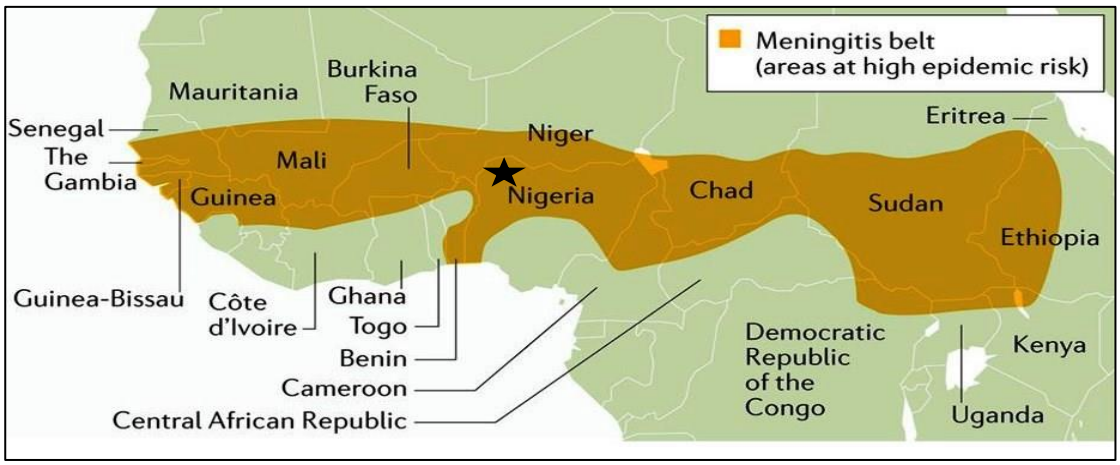

Figure 16: The Africa meningitis belt

It will be important to study whether there is a high incidence of epilepsy as sequelae of these epidemic waves, in addition to the influence of the microbiological strain. A mathematical transmission dynamic model was proposed to evaluate if vaccination schedules in line with meningococcal transmission patterns could be useful in reducing the incidence of meningitis (Mueller & Gessner, 2010). Similarly, measles is still endemic in Nigeria with continued resurgences due to chronic low routine immunisation coverage. Integrated Disease Surveillance and Response (IDSR) records of all states in Nigeria over a five-year period showed that the North-west region where Gwandu is located had some of the highest measles attack rates. The measles attack rate was lower in Ebonyi from the report, but it had one of the -highest recorded case fatality rates (Ibrahim et al., 2019). The link between measles and epilepsy is not entirely known, but it could be associated with febrile seizures, post-measles encephalitis,

measles inclusion body encephalitis or subacute sclerosing panencephalitis (SSPE) requiring further studies (Aarli, 1974, Fisher et al., 2015).

The two conditions (measles and meningitis) with PAF above 20% are vaccine-preventable. Vaccination as a factor associated with epilepsy was not a part of this study, some studies have shown that an incomplete immunisation history was a significant risk factor for epilepsy (Ogunniyi et al., 1987, Kannoth et al., 2009). Immunization rates in Nigeria are low, with about three out of four Nigerian children unlikely to have had basic routine immunisations; this is far worse in northern Nigeria, which has some of the poorest childhood vaccination rates worldwide (Abimbola et al., 2013). The greatest challenge to the acceptance of immunization is a religious one, especially amongst northern Nigerian Muslims. Ineffective primary health care services and the shortage of vaccines also affect coverage (Ophori et al., 2014). In 2013, nine female health workers were shot dead by Islamist extremists during a polio vaccination programme in northern Nigeria, further impeding and undermining coverage (https://www.theguardian.com/world/2013/feb/08/polio-workers-nigeria-shot-dead).

These attacks on health workers have continued.

Open defecation was found to be a significant factor among children from Gwandu. The role open defection has on epilepsy is not fully known, but poor sanitation is common in LMICs and is associated with cysticercosis and schistosomiasis implicated in epilepsy (Mara et al., 2010). Findings of epidemiological studies from rural India and Peru have shown that the practice of open defecation was common among people with epilepsy, however, these studies failed to identify a clear association (Koul et al., 1988, Moyano et al., 2014, Goyal et al., 2015).

It is possible that neurocysticercosis often goes undiagnosed because of the need for neuroimaging, which is not readily available in SSA (Hunter et al., 2012). Improved sanitation could contribute to a reduction in the prevalence of helminthic infestations through education and incentives to build and use toilets (Mara et al., 2010)**.** The use of well water in children appeared to be a positive factor for epilepsy in Gwandu and

Ijebu-Jesa, while the use of pit latrines was positively associated with epilepsy in Afikpo. The relationship between water sources or contaminated water sources with heavy metal and epilepsy is unclear (Sasmaz et al., 2003), and could be studied further.

This study has clearly shown that people with epilepsy are less likely to be married, employed or educated compared to controls. This social attainment is attributed to stigma and social ostracisation (Callaghan et al., 1992, Mula & Sander, 2016). Regarding education, a recent focus group discussion in the Hai district of Tanzania reported that learning difficulties and behavioural problems were the main barriers to educational attainment, in addition to parental stigmatization and teachers' knowledge gap on epilepsy care (Quereshi et al., 2017). SES as a factor for epilepsy was not studied. Most of the potential factors, such vaccine-preventable diseases, poor perinatal care, and poor sanitation observed in this study simply reflect poorer SES and are generally considered as markers of social deprivation and poverty (Świgost, 2017). The association between the prevalence of epilepsy and markers of social disadvantage has been shown in a study among incident cases attending general practices in southeast England and reported that epilepsy was strongly associated with socioeconomic deprivation; the most deprived fifth were 2.3 times more likely to have epilepsy than the least deprived fifth (Heaney et al., 2002). In this multivariate model monthly income was excluded as almost no control and very few cases agreed to answer the question. Employment and education as markers of SES were also not included in the regression model since these factors could be consequences of epilepsy rather than aetiological factors. The role SES has on epilepsy needs to be assessed in further studies and adjusted for in the analyses of risk factors. Assessing SES in rural Nigeria is complex because the traditional measures for assessing living standards such as income-based measures can be problematic due to the wide seasonal variation. Research summarising issues on the quality of income data in surveys expressed concerns that nonresponse is both common and predictable. They

noted that definitional issues, understanding concepts and terms, problems of recall, confusion and the underlying tendency to underestimate income were factors associated with incorrect income assessment. A single question covering all forms of income therefore is inadequate to assess income (Moore & Welniak, 2000). Consumption-based rather than monetary-based expenditure which is generally a more consistent predictor of SES could be used in future studies (Ward, 2014).

A Venn diagram (Figure 16) illustrates the distribution of the important risk factor and how they are shared across sites and their corresponding prevalence and incidence. Gwandu has much more positive risk factors compared to the other sites and may suggest poorer SES and explain the higher prevalence and incidence.

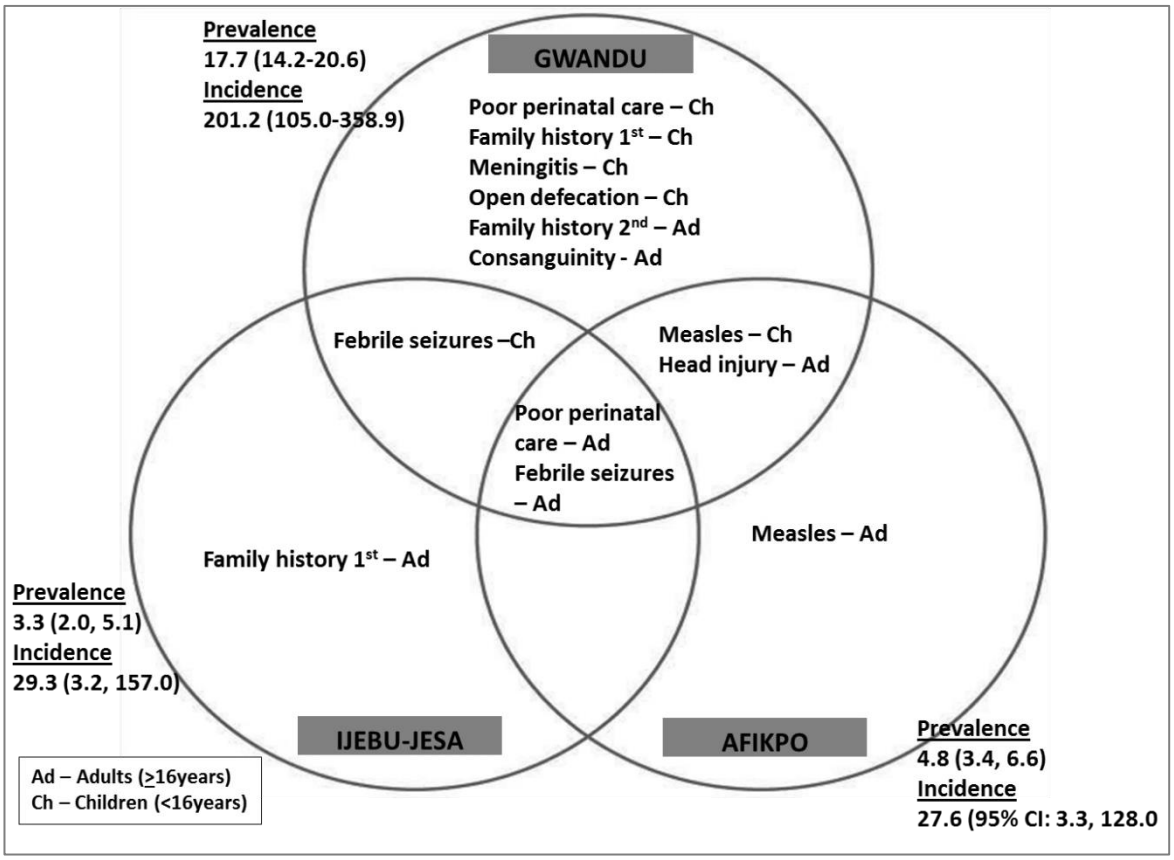

Figure 17: Venn diagram illustrating the distribution of important risk factors across sites

Pork consumption was rare and found not to be a factor for epilepsy in this study. The transmission of *Taenia solium* eggs which are needed for the establishment of neurocysticercosis is not entirely due to the presence, rearing pigs or consuming pork, but can also be due to poor sanitation and transmission from people with a previous contact to a tapeworm carrier (Maurice, 2014, Pal et al., 2000). We observed that the administration of ivermectin was inversely associated with epilepsy in Afikpo. The beneficial effect of ivermectin use against onchocerciasis and reduction in the prevalence of epilepsy is difficult to appreciate. The prevalence of onchocerciasis in Afikpo is unknown but may have been higher in the past due to its proximity to Cross River. A study in the neighbouring upper Imo river basin 15 years ago reported a high Onchocerca *volvulus* microfilariae rate of 37%, reaching 70% in those above 60 years of age (Uttah, 2010). Another study in the same communities reported a crude epilepsy prevalence of 1.2% and an O. *volvulus* microfilariae rate of 26.8% (Dozie et al., 2006). A recent study in the same communities 20 years after Community-Directed Treatment with Ivermectin (CDTI) observed a lower crude prevalence of epilepsy and onchocerciasis (Siewe et al., 2019). In certain areas of Uganda, epilepsy incidence significantly reduced years after the implementation of CDTI (Katabarwa et al., 2008). The effect of previous CDTIs in reducing the burden of epilepsy is difficult to corroborate as typical cases of onchocerciasis-related epilepsies were absent in our study. More studies are needed to understand the effect of previous helminthic control programmes on the lower prevalence in places like Afikpo and Ijebu-Jesa (Okorie et al., 2013). Gwandu with a higher prevalence and incidence is an agrarian society with numerous livestock (cows, goats, sheep, but not pigs). The infections with bovine tapeworm (Taenia *saginata*) transmitted through eating cysticerci (larval form) in undercooked beef is a more benign infection; it is not known to be implicated in epilepsy, unlike what is known to occur with the pig tapeworm (Taenia *solium*) in neurocysticercosis (Abba et al., 2010, Chesnais et al., 2018, Boulle et al., 2019). The communities in Gwandu are located along tributaries of a major river and are involved

in "*Fadama*" farming. *Fadama* is a Hausa word for a valley-bottom, flood plain, or lowland around a river that floods or becomes wet during the rainy seasons. Farmers usually produce vegetables during the dry and grains during the wetter seasons (Adesoji et al., 2006). Afikpo is also located near a major river, but are mainly involved in fishing. Studies on the role of helminthic infestations in epilepsy in these communities are needed. It is possible that these rivers are linked to helminthic infestations and tackling these parasites could possibly reduce the incidence of epilepsy (Pal et al., 2000).

Head injury was positively associated with epilepsy in adults from Gwandu and Afikpo. There have been reported an increase in the use of commercial motorbikes called 'Okada' in Nigeria (Olubomehin, 2012), with head injuries being the commonest and most consequential result of motorbike accidents (Solagberu et al., 2006, Nwadiaro et al., 2011). Studies in Nigeria have reported that seizures and epilepsy were common manifestations of these head injuries, and enforcement of wearing crash helmets would help (Ogunrin & Adeyekun, 2010, Rabiu & Adetunmbi, 2017).

This study provides no convincing evidence that hypertension and diabetes are associated with epilepsy. There is an upward trend for these conditions in urban areas but they are likely underreported in rural areas of Nigeria (Bello-Ovosi et al., 2018). Similarly, stroke was not associated with epilepsy, but with the upward trend in cardiovascular risk factors in SSA (Dewhurst & Walker, 2016), stroke might become an important factor for epilepsy in the future especially among the middle-aged and elderly (Stephen & Brodie, 2000). A relationship between alcohol consumption and smoking with epilepsy was not observed in this study. The religious inclinations of these sites may have been a reason for the lower frequency. Although not universal (Dworetzky et al., 2010), alcohol consumption has a strong and consistent association with provoked and unprovoked seizures as reported in a previous meta-analysis, with the probability of the onset of epilepsy increasing significantly with the amount of alcohol consumed daily (Samokhvalov et al., 2010). Eclampsia was reported among females in Ijebu-Jesa

and Gwandu. The odds ratios could not be calculated because of the empty cells. The long term effect of eclampsia as a risk factor for epilepsy in the child or mother is unknown (Watila et al., 2015).

This study has some strength. The community-based approach whereby the cases and controls were recruited from less biased settings compared to hospital-based studies is an advantage. This study not only calculated ORs, but PAFs which was able to give an idea on the likely contributions of these factors to epilepsy. PAF is of the most value from a public health perspective for preventable factors, since it assumes that if exposure to a risk factor is reduced, it will lead to a proportional reduction in the disease. Because PAF assumes a causal relationship between exposure and disease (Mansournia & Altman, 2018), there have been controversies over its interpretation (Rockhill et al., 1998). Firstly, it may wrongly over- or under-estimate the proportion of disease. Secondly, in causal partitioning, a large PAF may simply reflect a broad exposure rather than any valuable measure of causality, especially if it lacks strong biological assumptions. Thirdly, the cumulative PAF from individual exposures considered one at a time usually exceeds 100%. To avoid some of these pitfalls, surrogates for proximate exposures such as educational, employment and marital status were excluded in the computations for PAF and the multivariate analyses, since the cause-effect cannot be verified. This study is cautious on interpreting and equating PAF with causality especially for susceptibility attributes like family history and consanguinity that are difficult to explain (Rockhill et al., 1998).

Several limitations have been recognised in this study. Firstly, the inherent limitation of every case-control design, which includes selection and recall bias, is acknowledged. Since this study assesses factors retrospectively, there is great potential for a biased assessment of their presence and significance by those affected. Those with epilepsy are more likely to search their memories for a particular exposure and report in the affirmative than those without the condition. This systematic error may lead to wrong estimates of the association. However, a concerted effort was made to obtain

information in a structured manner; proxies were used to establish the correctness of information provided. Secondly, the choice of the controls will always be open to challenge since this study did not match them with the cases (Breslow & Day, 1980). Matching in case-control studies has an advantage of eliminating the influence of measurable confounders and improves study efficiency, but attempts to strictly match increases the vulnerability to overmatching and further introduces selection bias (Song & Chung, 2010). Random selection helps reduce bias, as in this study, and the analyses showed no significant difference between the age and gender of cases and controls. Thirdly, the sample size, particularly from Ijebu-Jesa and Afikpo, could be faulted, as they may be inadequate to provide reliable information about the importance of each risk factor. Since the cases were retrieved from the door-to-door census, it will be inappropriate to include cases from elsewhere. Some of the high ORs and wide margin of confidence observed in Afikpo and Ijebu-Jesa may be due to some cells having fewer cases. The larger sample size in Gwandu may also skew the results towards its average when the total was pooled. Fourthly, this study failed to assess some other risk factors. The lack of serological and neuroimaging tests to investigate parasitic infestation such as neurocysticercosis and onchocerciasis was a limitation. The medical records were not checked for the investigations, as they were not routinely available locally. Onchocerciasis may be important since Gwandu is located near a branch of the Zamfara River and Afikpo is located next to Cross River. Malaria was not included in this study as a risk factor for epilepsy, due to the lack of serological tests. Absence of neuroimaging also limited the investigations of strokes, brain tumours and space-occupying lesion as causes of epilepsy. In addition, substance abuse as a contributory factor in the development of epilepsy was not considered in this study. A previous Nigerian study showed no significant difference in the antecedent use of psychotropic drugs between cases and controls 30 years ago (Ogunniyi et al., 1987). However, it is becoming an increasing problem among adolescents and young adults in Nigeria (Odejide, 2006).

This study, like others, has reported considerable variation in risk factor estimates observed between the three different sites, and this may be due to variations in sample sizes, inherent biological and geographical differences in the population studied. Because of this, the extent to which the findings might be generalizable to other parts of Nigeria can be questioned. Epilepsy is considered multifactorial, and as such; it will be useful to understand how the various risk factors interact in the complex aetiology across sites; however this can more realistically be done using a cohort study. To reinforce the findings of this study, it is recommended that future studies should replicate these analyses in other regions of Nigeria, increasing the sample size, also looking at these and other potential risk factors. Case-control studies are still favoured as a preferred choice for epidemiological investigations in the absence of prospective cohort studies since they are easier to undertake (Breslow & Day, 1980, Sander, 2003). In conditions like epilepsy, the acquisition of a fairly appropriate number of cases in a cohort study may take a long time and the follow-up in a dynamic environment of a resource-poor setting may not really be feasible (Breslow & Day, 1980).

8.6 Conclusion

Febrile seizures, poor perinatal care, family history and measles were associated with epilepsy across the sites. Meningitis and open defecation were important factors in children, while consanguinity and head injury were important factors in adults. The substantial PAF for some factors suggests that if they can be prevented there would be a significant impact in reducing the development of epilepsy. Because of the many variables that can affect the development of epilepsy, this study suggests but does not prove causality, as the issue of establishing causality in epilepsy in LMIC is an ongoing process. Further studies are needed to better understand the causes of epilepsy in LMICs. Such finding would be useful for reducing the burden of epilepsy through education, cultural changes and targeted preventive interventions.

Chapter 9: Physician's perspective about epilepsy care in Nigeria

9.1 Introduction

People with epilepsy have the potential to lead productive lives when given quality health care and psychosocial support (England et al., 2012). This significantly varies between various regions of the world. There is growing evidence that the impact of health interventions is undermined by the poor quality of care in lower-income countries which is linked to failure to attain expected health-care improvements (Akachi & Kruk, 2017). This expected quality of care is basically dependent on the resources allocated, which is by far poorer in LMICs (Kruk et al., 2017). The quality of care is assessed by health care interventions provided and the outcome of treatment (Werner & Asch, 2007). Clinical performance measurements should be an important part of health care evaluation, but it is difficult in sub-Saharan Africa due to the lack of data.

In Nigeria, health care services for epilepsy are largely dysfunctional and inadequate, statistical information that will provide a complete picture is also unavailable (Abdulraheem et al., 2012). Nigeria lacks a unified model for epilepsy care and information that is available on epilepsy is not comparable across different geopolitical regions or over time (Gureje et al., 2015). It is important to have background information on what is available for epilepsy care. This part of my work describes information derived from health care providers in Nigeria.

9.2 Methodology

This was a descriptive study conducted among professional healthcare providers. Questionnaires were distributed during the Nigerian Society of Neurological Sciences (NSNS) meeting held between 11th and 13th July 2017 and the Association of Psychiatrists in Nigeria (APN) held between 20th and 24th of November 2017. These meetings were chosen because of the good representation of health personnel from various regions of Nigeria. It has in attendance neurologists, psychiatrists, specialist

(senior) registrars, and other physicians involved in providing neurological, psychiatric and by extension epilepsy services. In attendance are also members of the Nigerian League Against Epilepsy (NLAE). The questionnaire (Appendix 7) distributed was designed to acquire information on the geopolitical area of practice, area of specialisation, the setting of practice (rural or urban), years of practice, basic ASMs and diagnostic facilities available, number of people seen per week, challenges and suggestions. Permission to distribute the questionnaire was sought from the leadership of the societies. The National Health and Research Ethics Committee (NHREC) in Nigeria approved the study. **Statistical analysis:** All data were entered into STATA (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). Descriptive statistics were undertaken to produce summary measures.

9.3 Results

A total of 173 questionnaires were distributed, 115 at the NSNS and 58 at the APN meetings. Out of which 150 questionnaires were completed and returned, 99 (66%) from the NSNS and 51 (34%) from the APN, which gave a response rate of 86.1% and 87.9%. These included 71 (47.3%) neurologist, 66 (44.0%) psychiatrists and 9 (6.0%) neurosurgeons, with the majority (80.3%) practising exclusively in urban areas and in government-owned tertiary hospitals (92%). The Southwest region was the most represented (20%) and the Southeast being the least (Figure 17). Two-thirds reported being adult physicians, with 6.7% attending children only, while 22.7% see both (Table 40). About three-fourth reported that they frequently treat people with epilepsy. The median number of people seen per week was 5 (IQR: 3 – 10), with psychiatrists attending to more people per week, although not statistically significant (P = 0.435).

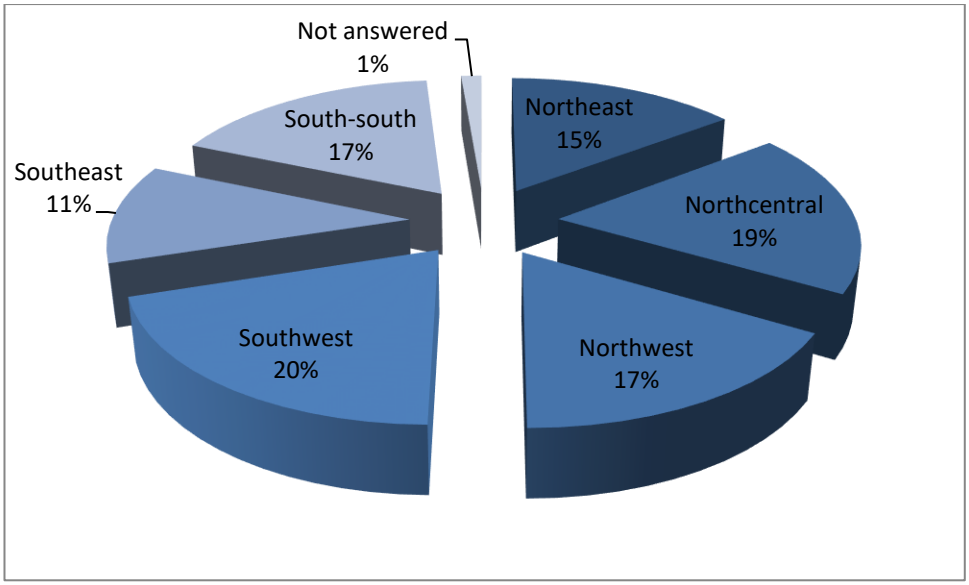

Figure 18: Geopolitical region of practice

Only 28% reported having had appropriate training in epilepsy. Almost all of them (95%) said this was through the residency programme in internal medicine (sub-speciality neurology) or psychiatry, with a few (2%) getting additional training from the International League Against Epilepsy's Virtual Epilepsy Academy (VIREPA) courses, international/local conferences and the International Brain Research Organisation (IBRO). About a third of responders were sometimes or often involved in epilepsy research, and 29.3% had publications related to epilepsy.

Figure 18 shows that only 5% reported having a qualified neurophysiologist and 8% had epilepsy nurses. About a third reported that training programs were somewhat or to a great extent available for their support staff. Concerning available equipment, 82% reported having basic EEG but only 4.7% reported having video-EEG and their median costs are shown in Table 41. Five of the older generation ASMs (Carbamazepine, Phenytoin, Diazepam, Valproate and Phenobarbital) were the most available, reported by more than 80% of responders (Figure 19), while diazepam and phenytoin injections were the most frequently used drugs for acute seizure treatment or SE (Figure 20).

Table 40: Background information on physicians interviewed

Place of practice*	
Rural	5 (3.3%)
Urban	114 (76.0%)
Both	23 (15.3%)
Not answered	8 (5.3%)
Specialty/designation	
Neurologists/senior registrar	71 (47.3%)
Psychiatrist/senior registrar	66 (44.0%)
Neurosurgeon/senior registrar	9 (6.0%)
Internal Medicine/senior registrar	6 (4.0%)
General physicians involved in epilepsy care	1 (0.7%)
Others (EEG technician and nurses)	3 (2.0%)
Area of Specialty	
Paediatrics	10 (6.7%)
Adults	100 (66.7%)
Both	34 (22.7%)
Not answered	6 (4.0%)
Type of hospital*	
Government-owned tertiary teaching hospital	138 (92.0%)
Government-owned secondary or general hospital	5 (3.3%)
Government-owned rural hospital	2 (1.3%)
Private hospital	19 (12.7%)
Duration of practice (years)	
< 10 years	90 (61.2%)
≥ 10 years	47 (36.8%)
Not answered	3 (2.0%)
How often do you treat people with epilepsy?	
Never	0 (0.0%)
Rarely	4 (3.2%)
Sometimes	25 (19.7%)
Quite often	68 (53.5%)
Very frequently	30 (23.6%)
Average number of patients attended per week	
Median (IQR) (98 responses)	5 (3 – 10)

By Neurologist (65 responses)	5 (3 – 8)
By Psychiatrist (33 responses)	6 (3 – 10)
What extent of formal training co you have in epilepsy care?	
To a great extent	41 (28.3%)
Somewhat	59 (40.7%)
Very little	33 (22.8%)
Not at all	11 (7.6%)
Have you been involved in epilepsy research?	
Often	18 (12.0%)
Sometimes	34 (22.7%)
Seldom	24 (16.0%)
Never	67 (44.7%)
Not answered	7 (4.7%)
Membership of professional international society	68 (46.9%)

*Some have more than one place of practice

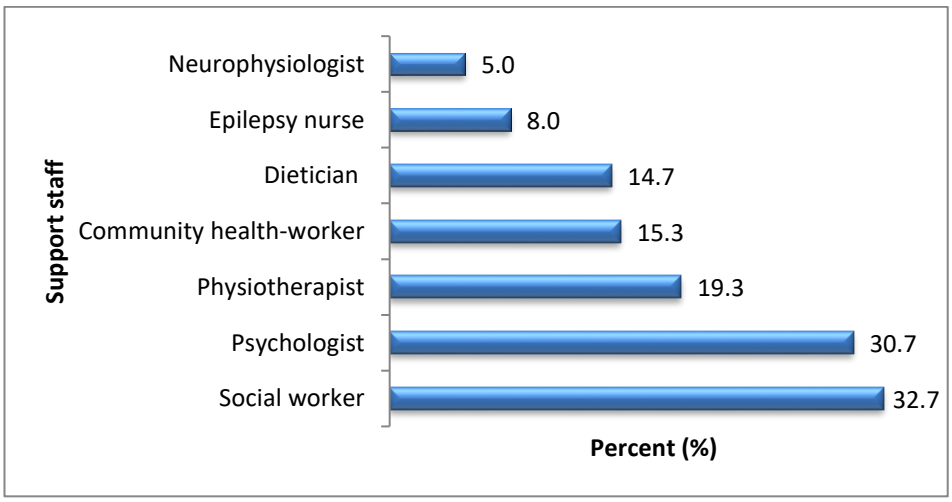

Figure 19: Supporting staff available

Table 41: Available facilities and training

Available equipment	
Basic EEG	122 (81.9%)
Video-EEG	7 (4.7%)
CT scan	102 (68.5%)
MRI scan	58 (38.9%)
The median cost of investigations (IQR) (Naira)	
Basic EEG	10,000 (6,000–10,000)
CT scan	35,000 (30,000–42,000)
MRI scan	65,000 (52,500–72,500)
Are training programs available for supporting staff in your centre?	
To a great extent	3 (2.1%)
Somewhat	46 (32.2%)
Very little	44 (30.8%)
Not at all	50 (35.0%)

One US dollar ~ 360 naira

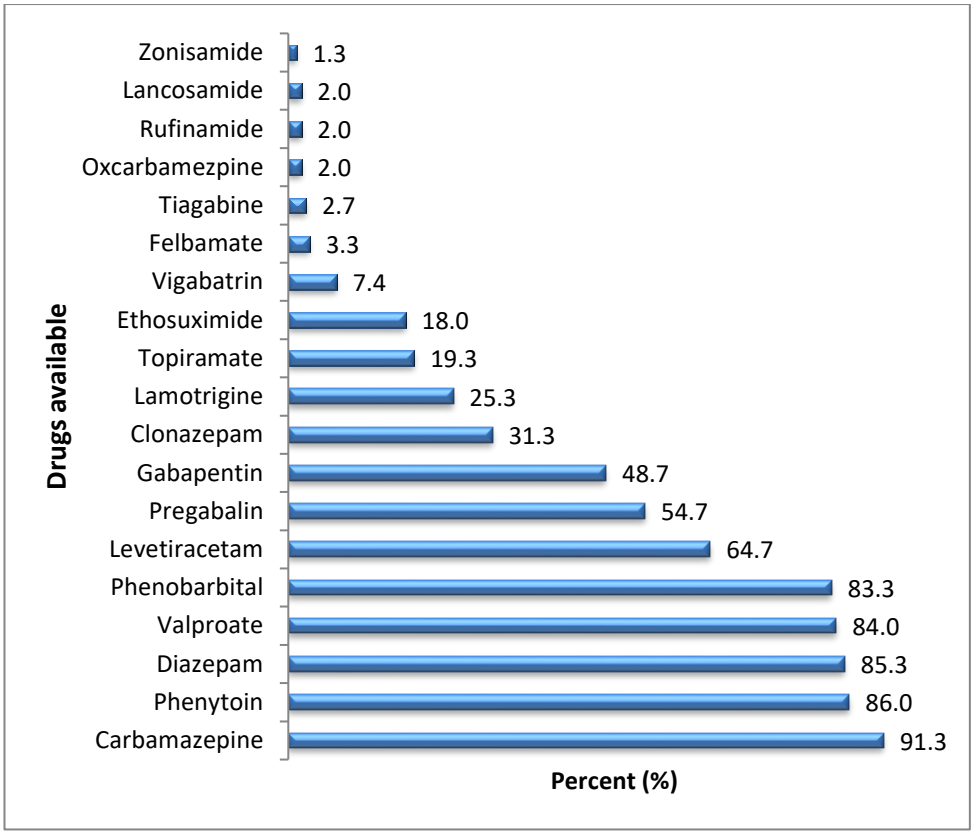

Figure 20: Antiseizure medications reported to be available

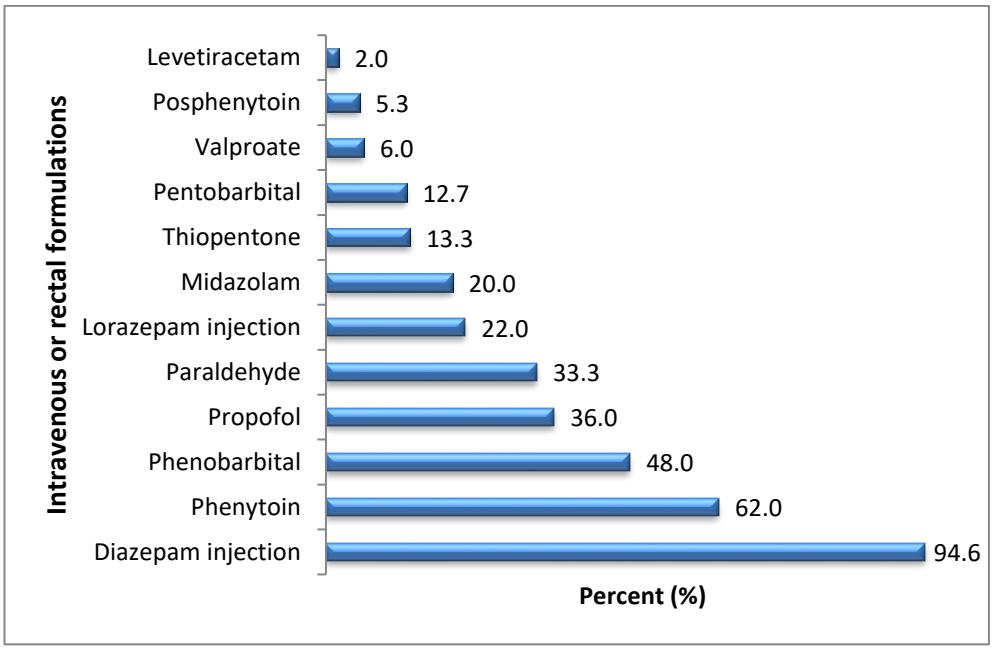

Figure 21: Intravenous or rectal formulations of antiseizure medications available

Table 42 shows the physician's view to epilepsy care in Nigeria. The majority reported that the support and care people with epilepsy receive was either poor to fair, with only 7.4% reporting it to be good. More than three-quarters reported that they were dissatisfied with the role of the Nigeria government in the care and support of people with epilepsy, only 4% reported they were satisfied. Only 9.3% reported being satisfied with the support from NGOs, with less than a quarter (22.7%) reporting they have an NGO involved with epilepsy care in their area of practice. Most physicians are of the opinion that people with epilepsy receive inadequate information about their condition. Only 16.0% reported that people with epilepsy in Nigeria receive adequate psychosocial support. Almost all are of the opinion that traditional and faith-based healers negatively affect people with epilepsy from seeking biomedical treatment and 74.7% are of the opinion that interacting and educating traditional healers will help individuals seek biomedical care. Epilepsy surgery is non-existent in Nigeria. About half of the respondents agree that epilepsy surgery was effective and 57.3% reported that that they will definitely or probably refer people for epilepsy surgery.

Table 42: Physicians view to epilepsy care

How do you rate the support and care people with epilepsy get in Nigeria?	
Very good	1 (0.7%)
Good	10 (6.7%)
Fair	53 (35.3%)
Poor	67 (44.7%)
Very poor	12 (8.0%)
Not answered	7 (4.7%)
How satisfied are you with the role the government is playing in the care and support of people with epilepsy?	
Very satisfied	3 (2.0%)
Satisfied	3 (2.0%)
Neither satisfied or unsatisfied	19 (12.7%)
Dissatisfied	84 (56.0%)
Very dissatisfied	36 (20.0%)
Not answered	5 (3.3%)
Do you know of any non-governmental organisation (NGO) involved with epilepsy care in your area of practice?	
Yes	34 (22.7%)
No	93 (62.0%)
Don't know	15 (10.0%
Not answered	8 (5.3%)
How satisfied are you with the role non-governmental organization(s) (NGOs) play in epilepsy care in your community?	
Very satisfied	2 (1.3%)
Satisfied	12 (8.0%)
Neither satisfied or unsatisfied	42 (28.0%)
Dissatisfied	68 (45.3%)
Very dissatisfied	20 (13.3%)
Not answered	6 (4.0%)
To what extent do you think people with epilepsy receive adequate information about	

their condition?	
To a great extent	6 (4.0%)
Somewhat	45 (30.0%)
Very little	75 (50.0%)
Not at all	20 (13.3%)
Not answered	6 (4.0%)
To what extent do you think people with epilepsy receive adequate psychosocial support?	
To a great extent	1 (0.7%)
Somewhat	23 (15.3%)
Very little	84 (56.0%)
Not at all	38 (24.3%)
Not answered	4 (2.7%)
To what extent do you think 'traditional' and 'spiritual' healers negatively affect access to biomedical care?	
To a great extent	112 (74.7%)
Somewhat	34 (22.7%)
Very little	0 (0.0%)
Not at all	1 (0.7%)
Not answered	3 (2.0%)
How useful do you think education of and interaction with traditional healers will help patients' health-seeking behaviour?	
Very useful	45 (30.0%)
Useful	67 (44.7%)
Not useful	35 (23.3%)
Not answered	3 (2.0%)
Epilepsy surgery availability	0 (0.0%)
Do you think surgical treatments are effective?	
Strongly agree	18 (12.0%)

Agree	58 (38.7%)
Not sure	42 (28.0%)
Disagree	2 (1.7%)
Strongly disagree	1 (1.3%).
Did not answer	29 (19.3%)
Will you refer a drug-resistant patient for surgical treatment?	
Definitely	30 (20.0%)
Probably	56 (37.3%)
Possibly	38 (25.3%)
Probably not	1 (1.3%)
Definitely not	0 (0.0%)
Did not answer	25 (16.7%))

The most important challenges to rendering standard epilepsy care reported include lack of knowledge, stigma and discrimination, lack and high cost of ASMs, counterfeit drugs, lack of infrastructure and equipment. In addition to, shortages of medical personnel with the 'brain drain' being a contributory factor, lack of specialist in epilepsy care, inadequate training of personnel, traditional practices, the negative influence of religion, government's failure to support epilepsy care, lack of social support and poverty. Some of the suggestions giving to improve epilepsy care include: increased participation from government and NGOs, improve health funding, more training of medical personnel, improve access and availability of ASMs, subsidize ASMs, improve individual and community education, formulate a national care guideline and create collaborations with foreign partners.

9.4 Discussion

This questionnaire-based study provides information on resources available for epilepsy care from members of two professional bodies. The number of psychiatrists and neurologist recruited in this study are at least a significant representative of various

regions. It is estimated that the number of qualified neurologists are just around one hundred in the entire country and that support staff are generally in short supply. This study shows that the southwest region had more responders, with the majority attending to adults and practising in urban areas and government-owned tertiary hospital. It is generally agreed that Southwest Nigeria has more physicians than other regions. Paediatric neurologists were far less in number than adult physicians in this study, this scarcity of paediatric neurologists compared to adult neurologists has been recognised in SSA (Wilmshurst et al., 2011, Wilmshurst et al., 2013). A recent review on diagnosis and management of children with epilepsy in Kenya observed that children continue to face a significant barrier to health care access, suggesting a multisector approach to improve outcomes (Samia et al., 2019).

This study observed a non-significant higher number of people seen by psychiatrists. In Nigeria, psychiatrists see more people with epilepsy due to accessibility and misconception about epilepsy being a mental illness (Nuhu et al., 2010, Gureje et al., 2015). The uneven distribution of physicians (urban versus rural) reported in this study was acknowledged in a recent systematic review of challenges in the Nigerian health sector and observed that the inequitable distribution of workforce remains a major challenge (Adeloye et al., 2017). The regional difference which is mainly due to the different approaches governments take in providing training, funding and organisation of health systems should be an area of focus, as understanding variations in care quality could be a way to identify drivers of performance (Kruk et al., 2017). Training of the workforce appears inadequate in this study. The overwhelming overburden of few health professionals and the available resources for training has been recognised as a challenge. Lack of opportunity for postgraduate training has also been recognised as an important 'push' factor for the 'brain drain' (Naicker et al., 2009). Poor remuneration and working conditions of health workers further worsens commitment and increases the 'brain drain' (Plotnikova, 2012).

There is an increasing interest in the use of non-physician led epilepsy clinic, especially nurse-led epilepsy clinics (Mantri, 2008). Our study, however, shows that trained epilepsy nurses were very few (8%) to implement such nurse-led programmes. The proportion of nurses compared to neuropsychologists and social workers is low. This may be due to the nurses' lack of interest in epilepsy care. An alternative to improving epilepsy care since the number of physicians and nurse cannot fill this gap, is the deployment of community health workers using the guidelines of the WHO mhGAP for managing mental, neurological and substance abuse in resource-poor areas (Dua et al., 2011, Keynejad et al., 2018). The physicians interviewed reported that the majority of people with epilepsy do not have adequate information about their condition nor receive sufficient psychosocial support. This lack of information regarding education, employment, family life and social life negatively affects the sufferer and their carers. The nurse-led system discussed above could incorporate education programme for those affected and their families. The public health system needs to invest in awareness programmes to increase knowledge and improve public perception leading to successful integration into the society (Mula & Sander, 2016). The role of education in improving the outcome of people with epilepsy could be an area for future work.

An interesting finding from this study is that about three-quarters of the respondents said they would be prepared to work with faith and traditional healers. The reason for such a high figure is unknown, but it may be due to the realisation that bridging the treatment gap cannot be achieved without engaging traditional healers. A Zambian study suggests that an important step to reducing the treatment gap in SSA is for physicians and traditional or faith-based healers to have a collaborative partnership (Baskind & Birbeck, 2005). It is encouraging to see from this study that physicians are willing to collaborate. Generally, modern medicine dismisses their usefulness, while traditional healers, on the other hand sometimes recognize that modern medicine has a role in treating seizures, especially when they are difficult to treat or occur within the context of certain conditions.

The most readily available drugs reported in this study are similar to the survey conducted in Zambia (Chomba et al., 2010). The older ASMs are cheaper, while the newer ones, the injectable and rectal formulations are scarce and expensive. Even the prices of originator brands compared to the lower-priced generics are expensive, raising the question of sub-standard drugs (Cameron et al., 2012). Improved access to ASMs should be a priority in line with the suggestions given. The issue of quality epilepsy care and access to ASMs falls within the "4 As" of Awareness, Availability, Accessibility and Affordability. However, a fifth-factor "Acceptability" is proposed as an important factor in the case of epilepsy care in SSA (Thomson et al., 2016). This study corroborates the finding of epilepsy surgery being non-existent in most countries of SSA (Wieser & Silfvenius, 2000). The priority for SSA, however, is ease of access to ASMs for the majority. It is important however to understand that improvements in quality of care for people with epilepsy do not have quick and easy solutions as many of the difficulties outlined above result from a multiplicity of factors particularly the limited funding by governments.

One important limitation of this study is that the findings are mainly from urban settings and likely to be poorer in rural settings because of the inequitable distribution of public resources. Primary care workers could have given reliable information on the true state of care from rural areas. This study did not assess the problems of diagnosis and factors affecting delays in initiation of treatment and assessment of pharmacies for the availability and cost of the drugs.

9.5 Conclusion

This study reports finding on epilepsy care from the perspective of the health care provider. Although the findings reflect more of the urban settings, it shows a significant deficit in workforce, training, facilities and available ASMs. With no quick fix solution for epilepsy care, it is important that all stakeholders must work together. Collaborations with international partners should be encouraged.

Chapter 10: Conclusions, Limitations and Future Work

10.1 Conclusions

This epidemiological work aimed to assess the standardised prevalence, incidence, risk factors, treatment gap and the extent of how factors influence access to care from three rural areas of Nigeria. The work revealed a widely varied prevalence and incidence between the north and the south of Nigeria, with the case-control components providing support for the association between epilepsy and febrile seizures, poor perinatal care, family history, meningitis, measles, open defecation and head injury. More of these factors were significant in the north. The strength of association evidenced by the significant PAF is underscored. As hypothesised the treatment gap which includes the diagnostic gap was high (> 90%). Negative cultural beliefs, perceived stigma, failure to accept epilepsy as a diagnosis and difficulty with access to a health facility appeared to be the most important factors associated with failure to seek biomedical care and adherence. This work also found that physicians experience significant deficiencies in workforce, training, facilities and treatment options. With the unique challenges of epilepsy in SSA, these results provide concrete background information that will be useful to improve the quality of epilepsy care in sub-Saharan Africa.

10.2 Limitations

It is important to highlight some of the limitations while interpreting the results. The main limitation is that the screening exercise engaged a small fragment of the population and may not reflect the true picture across the country. The door-to-door design has its limitation in screening people with epilepsy and this work could have in addition utilised the capture-recapture method and the key-informant approach, however, these methods require more time. The inter- and intra-observer variability in the administration of the questionnaire was not considered and the correction for sensitivity and attrition undertaken could have altered the estimates. The 1-year incidence rate could be faulted, as a year is too short to produce a reliable estimate.

The exclusion of children less than six years of age could have underestimated the burden; however, it was important not to include children with febrile seizures. The accuracy of seizures description was a major limitation in this work, leading to the failure to characterise epilepsy syndrome properly. The issues of recall bias in the case-control study could have affected the measures.

10.3 Future Works

It is worth noting that this is so far the largest epidemiological study on epilepsy in Nigeria. However, it is acknowledged that this research has generated many questions that are pertinent to answers. There are suggestions as to why a wide difference in prevalence and incidence was observed between the north and the south, but to elucidate them clearly would require larger prospective cohort studies to assess the variability and some of the unique risk factors observed. To curtail risk factors there is a need for intervention and preventive studies. Because of the importance of family history and consanguinity, there may be unique genetic causes of epilepsy in Nigeria which could be ascertained going forward. Stigma may have played a role in the varied prevalence estimates between sites and could be considered an area for future studies. Because of the difficulties we experienced with seizure characterisation, studies on the use of mobile phone cameras to record seizure events and seizure detection devices would improve this challenge in resource-limited settings. Studies on ways to improve the treatment gap by training community and allied health workers, improving access, availability and affordability of ASMs should be conducted in the future. The role of community engagement, use of mass media, and schools educational programmes could also be piloted to see if it improves public perception and a better outlook for people with epilepsy. Epilepsy care model tailored to the needs of particular communities should be developed as there is no “one size fits all” approach with this condition. Future work on improving the care of people with epilepsy would greatly improve if Nigeria adopts the WHO strategy. This utilises a six-building block strategy to help guide health professionals in the provision of health care (Figure

21). Setting clear and achievable goals that are sustainable is the way forward for a progressive approach to patient care (World Health Organization, 2010).

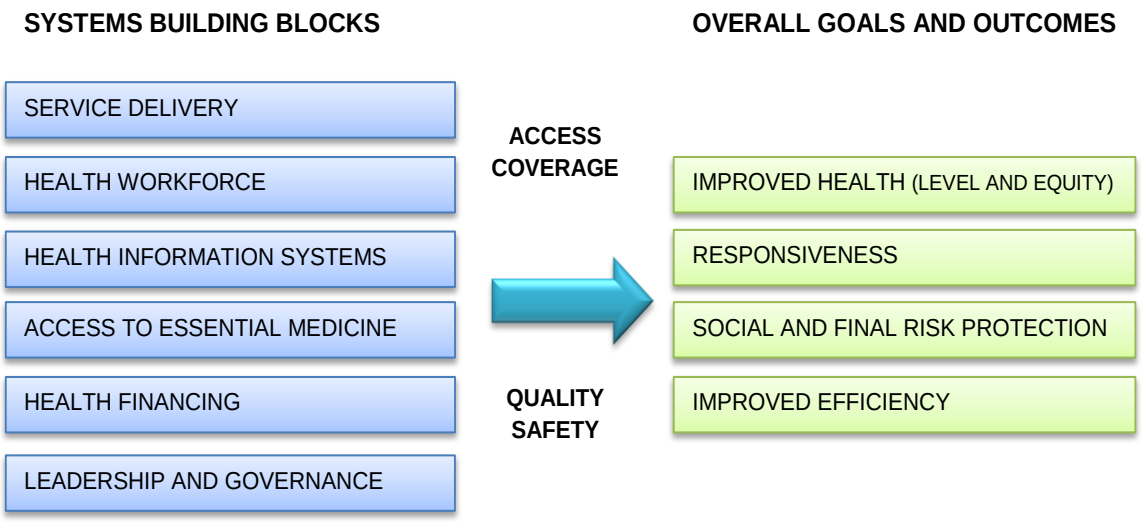

Figure 22: The six building blocks of a health system: aims and desirable attributes

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Appendices

Appendix 1

Details of Literature Search

1. Preliminary search terms developed are shown below, and was used for PUBMED, EMBASE and Web of Science databases.

((((epilepsy) OR epilep*)) AND ((healthcare OR neurologic services OR primary health care OR primary care OR tertiary care OR treatment program OR support OR service))) AND ((Africa OR Africa south of the sahara OR SSA OR Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cabo Verde OR Cameroon OR Central African Republic OR Chad OR Tchad OR Comoros OR Congo OR Republic of the Congo OR Democratic Republic of congo OR Cote d'Ivoire OR Djibouti OR Equatorial OR Guinea OR Eritrea OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR Sao Tome and Principe OR Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR South Sudan OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR Zambia OR Zimbabwe))

2. For Scopus and Cumulative Index to Nursing and Allied Health Literature (CINAHL)

   ''Epilepsy'' and ''Africa'' and ''Health care service''

3. For Open Grey and the Cochrane database

   ''Epilepsy'' and ''Africa''

4. For African Index Medicus (AIM)

   ''epilepsy''

Appendix 2

Search Detail

a. Pubmed search (May 2018)

Search	Query	Items found
#22	Search ((epilep*) AND ((((((((((((((((surg*) OR neurosurg*) OR operati*) OR surg* treatment) OR surg* procedure) OR disconnecti*) OR resecti*) OR neurostimulati*) OR stereotactic) OR vagus nerve stimulation) OR VNS) OR surg* outcome) OR surg* complication) OR surg* cost) OR presurg* evaluation) OR presurg* investigat*) OR quality of life) OR QOL)) AND ((Africa [TIAB] OR Asia[TIAB] OR Caribbean[TIAB] OR West Indies[TIAB] OR South America[TIAB] OR Latin America[TIAB] OR Central America[TIAB] OR ("afghanistan"[MeSH Terms] OR "afghanistan" [TIAB]) OR ("albania"[MeSH Terms] OR "albania"[TIAB]) OR ("algeria"[MeSH Terms] OR "algeria" [TIAB]) OR ("american samoa"[MeSH Terms] OR ("american"[TIAB] AND "samoa"[TIAB]) OR "american samoa"[TIAB]) OR ("angola"[MeSH Terms] OR "angola"[TIAB]) OR ("argentina"[MeSH Terms] OR "argentina"[TIAB]) OR ("armenia"[MeSH Terms] OR "armenia"[TIAB]) OR ("azerbaijan" [MeSH Terms] OR "azerbaijan"[TIAB]) OR ("bangladesh"[MeSH Terms] OR "bangladesh"[TIAB]) OR ("republic of belarus"[MeSH Terms] OR ("republic"[TIAB] AND "belarus"[TIAB]) OR "republic of belarus"[TIAB] OR "belarus"[TIAB]) OR ("belize"[MeSH Terms] OR "belize"[TIAB]) OR ("benin"[MeSH Terms] OR "benin"[TIAB]) OR ("bhutan"[MeSH Terms] OR "bhutan"[TIAB]) OR ("bolivia"[MeSH Terms] OR "bolivia"[TIAB]) OR ("bosnia and herzegovina"[MeSH Terms] OR ("bosnia"[TIAB] AND "herzegovina"[TIAB]) OR "bosnia and herzegovina"[TIAB]) OR ("botswana"[MeSH Terms] OR "botswana"[TIAB]) OR ("brazil"[MeSH Terms] OR "brazil"[TIAB]) OR ("bulgaria"[MeSH Terms] OR "bulgaria"[TIAB]) OR ("burkina faso"[MeSH Terms] OR ("burkina"[TIAB] AND "faso"[TIAB]) OR "burkina faso"[TIAB]) OR ("burundi"[MeSH Terms] OR "burundi"[TIAB]) OR ("cape verde"[MeSH Terms] OR ("cape"[TIAB] AND "verde"[TIAB]) OR "cape verde"[TIAB] OR ("cabo"[TIAB] AND "verde"[TIAB]) OR "cabo verde"[TIAB]) OR ("cape verde"[MeSH Terms] OR ("cape"[TIAB] AND "verde"[TIAB]) OR "cape verde"[TIAB]) OR ("cambodia"[MeSH Terms] OR "cambodia"[TIAB]) OR ("cameroon"[MeSH Terms] OR "cameroon"[TIAB]) OR ("cameroon"[MeSH Terms] OR "cameroon"[TIAB]) OR ("central african republic"[MeSH Terms] OR ("central"[TIAB] AND "african"[TIAB] AND "republic"[TIAB]) OR "central african republic"[TIAB]) OR ("chad"[MeSH Terms] OR "chad"[TIAB]) OR Tchad[TIAB] OR ("china"[MeSH Terms] OR "china"[TIAB]) OR ("colombia"[MeSH Terms] OR "colombia"[TIAB]) OR ("comoros"[MeSH Terms] OR "comoros"[TIAB]) OR ("congo"[MeSH Terms] OR "congo"[TIAB]) OR (Democratic[TIAB] AND Republic[TIAB] AND ("congo"[MeSH Terms] OR "congo"[TIAB])) OR ("costa rica"[MeSH Terms] OR ("costa"[TIAB] AND "rica"[TIAB]) OR "costa rica"[TIAB]) OR ("cote d'ivoire"[MeSH Terms] OR ("cote"[TIAB] AND "d'ivoire"[TIAB]) OR "cote d'ivoire"[TIAB]) OR ("cote d'ivoire"[MeSH Terms] OR ("cote"[TIAB] AND "d'ivoire"[TIAB]) OR "cote d'ivoire"[TIAB] OR ("ivory"[TIAB] AND "coast"[TIAB]) OR "ivory coast"[TIAB]) OR ("cuba"[MeSH Terms] OR "cuba"[TIAB]) OR ("djibouti"[MeSH Terms] OR "djibouti"[TIAB]) OR ("dominica"[MeSH Terms] OR "dominica"[TIAB]) OR ("dominican republic"[MeSH Terms] OR ("dominican"[TIAB] AND "republic"[TIAB]) OR "dominican republic"[TIAB]) OR ("ecuador"[MeSH Terms] OR "ecuador"[TIAB]) OR ("egypt"[MeSH Terms] OR "egypt"[TIAB]) OR ("el salvador"[MeSH Terms] OR ("el"[TIAB] AND "salvador"[TIAB]) OR "el salvador"[TIAB]) OR ("equatorial guinea"[MeSH Terms] OR ("equatorial"[TIAB] AND "guinea"[TIAB]) OR "equatorial guinea"[TIAB]) OR ("eritrea"[MeSH Terms] OR "eritrea"[TIAB]) OR ("ethiopia"[MeSH Terms] OR "ethiopia"[TIAB]) OR ("fiji"[MeSH Terms] OR "fiji"[TIAB]) OR ("gabon"[MeSH Terms] OR "gabon"[TIAB]) OR ("gambia"[MeSH Terms] OR "gambia"[TIAB]) OR	333

	("georgia (republic)"[MeSH Terms] OR ("georgia"[TIAB] AND "(republic)"[TIAB]) OR "georgia (republic)"[TIAB] OR ("georgia"[TIAB] AND "republic"[TIAB]) OR "georgia republic"[TIAB]) OR ("ghana"[MeSH Terms] OR "ghana"[TIAB]) OR ("grenada"[MeSH Terms] OR "grenada"[TIAB]) OR ("guatemala"[MeSH Terms] OR "guatemala"[TIAB]) OR ("guinea"[MeSH Terms] OR "guinea"[TIAB]) OR ("guinea-bissau"[MeSH Terms] OR "guinea-bissau"[TIAB] OR ("guinea"[TIAB] AND "bissau"[TIAB]) OR "guinea bissau"[TIAB]) OR ("guyana"[MeSH Terms] OR "guyana"[TIAB]) OR ("haiti"[MeSH Terms] OR "haiti"[TIAB]) OR ("honduras"[MeSH Terms] OR "honduras"[TIAB]) OR ("india"[MeSH Terms] OR "india"[TIAB]) OR ("indonesia"[MeSH Terms] OR "indonesia"[TIAB]) OR ("iran"[MeSH Terms] OR "iran"[TIAB]) OR ("iraq"[MeSH Terms] OR "iraq"[TIAB]) OR ("jamaica"[MeSH Terms] OR "jamaica"[TIAB]) OR ("jordan"[MeSH Terms] OR "jordan"[TIAB]) OR ("kazakhstan"[MeSH Terms] OR "kazakhstan"[TIAB]) OR ("kenya"[MeSH Terms] OR "kenya"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB] OR "kiribati"[TIAB]) OR (Democratic[TIAB] AND ("republic of korea"[TIAB] OR ("republic"[TIAB] AND "korea"[TIAB]) OR "republic of korea"[TIAB])) OR ("kosovo"[MeSH Terms] OR "kosovo"[TIAB]) OR ("kyrgyzstan"[MeSH Terms] OR "kyrgyzstan"[TIAB]) OR ("laos"[MeSH Terms] OR "laos"[TIAB]) OR ("lebanon"[MeSH Terms] OR "lebanon"[TIAB]) OR ("lesotho"[MeSH Terms] OR "lesotho"[TIAB]) OR ("liberia"[MeSH Terms] OR "liberia"[TIAB]) OR ("libya"[MeSH Terms] OR "libya"[TIAB]) OR ("macedonia (republic)"[MeSH Terms] OR ("macedonia"[TIAB] AND "(republic)"[TIAB]) OR "macedonia (republic)"[TIAB] OR "macedonia"[TIAB]) OR ("madagascar"[MeSH Terms] OR "madagascar"[TIAB]) OR ("malawi"[MeSH Terms] OR "malawi"[TIAB]) OR ("malaysia"[MeSH Terms] OR "malaysia"[TIAB]) OR ("indian ocean islands"[MeSH Terms] OR ("indian"[TIAB] AND "ocean"[TIAB] AND "islands"[TIAB]) OR "indian ocean islands"[TIAB] OR "maldives"[TIAB]) OR ("mali"[MeSH Terms] OR "mali"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB] OR ("marshall"[TIAB] AND "islands"[TIAB]) OR "marshall islands"[TIAB]) OR ("mauritania"[MeSH Terms] OR "mauritania"[TIAB]) OR ("mauritius"[MeSH Terms] OR "mauritius"[TIAB]) OR ("mexico"[MeSH Terms] OR "mexico"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB]) OR ("moldova"[MeSH Terms] OR "moldova"[TIAB]) OR ("mongolia"[MeSH Terms] OR "mongolia"[TIAB]) OR ("montenegro"[MeSH Terms] OR "montenegro"[TIAB]) OR ("morocco"[MeSH Terms] OR "morocco"[TIAB]) OR ("mozambique"[MeSH Terms] OR "mozambique"[TIAB]) OR ("myanmar"[MeSH Terms] OR "myanmar"[TIAB]) OR ("namibia"[MeSH Terms] OR "namibia"[TIAB]) OR ("nepal"[MeSH Terms] OR "nepal"[TIAB]) OR ("nicaragua"[MeSH Terms] OR "nicaragua"[TIAB]) OR ("niger"[MeSH Terms] OR "niger"[TIAB]) OR ("nigeria"[MeSH Terms] OR "nigeria"[TIAB]) OR ("pakistan"[MeSH Terms] OR "pakistan"[TIAB]) OR ("palau"[MeSH Terms] OR "palau"[TIAB]) OR ("panama"[MeSH Terms] OR "panama"[TIAB]) OR ("papua new guinea"[MeSH Terms] OR ("papua"[TIAB] AND "new"[TIAB] AND "guinea"[TIAB]) OR "papua new guinea"[TIAB]) OR ("paraguay"[MeSH Terms] OR "paraguay"[TIAB]) OR ("peru"[MeSH Terms] OR "peru"[TIAB]) OR ("philippines"[MeSH Terms] OR "philippines"[TIAB]) OR ("romania"[MeSH Terms] OR "romania"[TIAB]) OR ("russia"[MeSH Terms] OR "russia"[TIAB]) OR ("rwanda"[MeSH Terms] OR "rwanda"[TIAB]) OR ("samoa"[MeSH Terms] OR "samoa"[TIAB]) OR ("atlantic islands"[MeSH Terms] OR ("atlantic"[TIAB] AND "islands"[TIAB]) OR "atlantic islands"[TIAB] OR ("sao"[TIAB] AND "tome"[TIAB] AND "principe"[TIAB]) OR "sao tome and principe"[TIAB]) OR ("senegal"[MeSH Terms] OR "senegal"[TIAB]) OR ("serbia"[MeSH Terms] OR "serbia"[TIAB]) OR ("sierra leone"[MeSH Terms] OR ("sierra"[TIAB] AND "leone"[TIAB]) OR "sierra leone"[TIAB]) OR ("melanesia"[MeSH Terms] OR "melanesia"[TIAB] OR ("solomon"[TIAB] AND "islands"[TIAB]) OR "solomon islands"[TIAB]) OR ("somalia"[MeSH Terms] OR "somalia"[TIAB]) OR ("south africa"[MeSH Terms] OR ("south"[TIAB] AND "africa"[TIAB]) OR "south africa"[TIAB]) OR ("south sudan"[MeSH Terms] OR ("south"[TIAB] AND "sudan"[TIAB]) OR "south sudan"[TIAB]) OR ("sri lanka"[MeSH Terms] OR ("sri"[TIAB] AND "lanka"[TIAB]) OR "sri lanka"[TIAB]) OR ("saint lucia"[MeSH Terms] OR ("saint"[TIAB] AND "lucia"[TIAB]) OR "saint lucia"[TIAB] OR ("st"[TIAB] AND "lucia"[TIAB]) OR "st	

	lucia"[TIAB]) OR ("saint vincent and the grenadines"[MeSH Terms] OR ("saint"[TIAB] AND "vincent"[TIAB] AND "grenadines"[TIAB]) OR "saint vincent and the grenadines"[TIAB] OR ("st"[TIAB] AND "vincent"[TIAB] AND "grenadines"[TIAB]) OR "st vincent and the grenadines"[TIAB]) OR ("sudan"[MeSH Terms] OR "sudan"[TIAB]) OR ("suriname"[MeSH Terms] OR "suriname"[TIAB]) OR ("swaziland"[MeSH Terms] OR "swaziland"[TIAB]) OR ("syria"[MeSH Terms] OR "syria"[TIAB]) OR ("tajikistan"[MeSH Terms] OR "tajikistan"[TIAB]) OR ("tanzania"[MeSH Terms] OR "tanzania"[TIAB]) OR ("thailand"[MeSH Terms] OR "thailand"[TIAB]) OR ("timor-leste"[MeSH Terms] OR "timor-leste"[TIAB] OR ("east"[TIAB] AND "timor"[TIAB]) OR "east timor"[TIAB]) OR ("timor-leste"[MeSH Terms] OR "timor-leste"[TIAB] OR ("timor"[TIAB] AND "leste"[TIAB]) OR "timor leste"[TIAB]) OR ("togo"[MeSH Terms] OR "togo"[TIAB]) OR ("tonga"[MeSH Terms] OR "tonga"[TIAB]) OR ("tunisia"[MeSH Terms] OR "tunisia"[TIAB]) OR ("turkey"[MeSH Terms] OR "turkey"[TIAB]) OR ("turkmenistan"[MeSH Terms] OR "turkmenistan"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB] OR "tuvalu"[TIAB]) OR ("uganda"[MeSH Terms] OR "uganda"[TIAB]) OR ("ukraine"[MeSH Terms] OR "ukraine"[TIAB]) OR ("uzbekistan"[MeSH Terms] OR "uzbekistan"[TIAB]) OR ("vanuatu"[MeSH Terms] OR "vanuatu"[TIAB]) OR ("venezuela"[MeSH Terms] OR "venezuela"[TIAB]) OR ("vietnam"[MeSH Terms] OR "vietnam"[TIAB]) OR (("middle east"[MeSH Terms] OR ("middle"[TIAB] AND "east"[TIAB]) OR "middle east"[TIAB] OR ("west"[TIAB] AND "bank"[TIAB]) OR "west bank"[TIAB]) AND Gaza[TIAB]) OR ("yemen"[MeSH Terms] OR "yemen"[TIAB]) OR ("zambia"[MeSH Terms] OR "zambia"[TIAB]) OR ("zimbabwe"[MeSH Terms] OR "zimbabwe"[TIAB])))	
#21	Search (Africa [TIAB] OR Asia[TIAB] OR Caribbean[TIAB] OR West Indies[TIAB] OR South America[TIAB] OR Latin America[TIAB] OR Central America[TIAB] OR ("afghanistan"[MeSH Terms] OR "afghanistan"[TIAB]) OR ("albania"[MeSH Terms] OR "albania"[TIAB]) OR ("algeria"[MeSH Terms] OR "algeria"[TIAB]) OR ("american samoa"[MeSH Terms] OR ("american"[TIAB] AND "samoa"[TIAB]) OR "american samoa"[TIAB]) OR ("angola"[MeSH Terms] OR "angola"[TIAB]) OR ("argentina"[MeSH Terms] OR "argentina"[TIAB]) OR ("armenia"[MeSH Terms] OR "armenia"[TIAB]) OR ("azerbaijan"[MeSH Terms] OR "azerbaijan"[TIAB]) OR ("bangladesh"[MeSH Terms] OR "bangladesh"[TIAB]) OR ("republic of belarus"[MeSH Terms] OR ("republic"[TIAB] AND "belarus"[TIAB]) OR "republic of belarus"[TIAB] OR "belarus"[TIAB]) OR ("belize"[MeSH Terms] OR "belize"[TIAB]) OR ("benin"[MeSH Terms] OR "benin"[TIAB]) OR ("bhutan"[MeSH Terms] OR "bhutan"[TIAB]) OR ("bolivia"[MeSH Terms] OR "bolivia"[TIAB]) OR ("bosnia and herzegovina"[MeSH Terms] OR ("bosnia"[TIAB] AND "herzegovina"[TIAB]) OR "bosnia and herzegovina"[TIAB]) OR ("botswana"[MeSH Terms] OR "botswana"[TIAB]) OR ("brazil"[MeSH Terms] OR "brazil"[TIAB]) OR ("bulgaria"[MeSH Terms] OR "bulgaria"[TIAB]) OR ("burkina faso"[MeSH Terms] OR ("burkina"[TIAB] AND "faso"[TIAB]) OR "burkina faso"[TIAB]) OR ("burundi"[MeSH Terms] OR "burundi"[TIAB]) OR ("cape verde"[MeSH Terms] OR ("cape"[TIAB] AND "verde"[TIAB]) OR "cape verde"[TIAB] OR ("cabo"[TIAB] AND "verde"[TIAB]) OR "cabo verde"[TIAB]) OR ("cape verde"[MeSH Terms] OR ("cape"[TIAB] AND "verde"[TIAB]) OR "cape verde"[TIAB]) OR ("cambodia"[MeSH Terms] OR "cambodia"[TIAB]) OR ("cameroon"[MeSH Terms] OR "cameroon"[TIAB]) OR ("cameroon"[MeSH Terms] OR "cameroon"[TIAB]) OR ("central african republic"[MeSH Terms] OR ("central"[TIAB] AND "african"[TIAB] AND "republic"[TIAB]) OR "central african republic"[TIAB]) OR ("chad"[MeSH Terms] OR "chad"[TIAB]) OR Tchad[TIAB] OR ("china"[MeSH Terms] OR "china"[TIAB]) OR ("colombia"[MeSH Terms] OR "colombia"[TIAB]) OR ("comoros"[MeSH Terms] OR "comoros"[TIAB]) OR ("congo"[MeSH Terms] OR "congo"[TIAB]) OR (Democratic[TIAB] AND Republic[TIAB] AND ("congo"[MeSH Terms] OR "congo"[TIAB])) OR ("costa rica"[MeSH Terms] OR ("costa"[TIAB] AND "rica"[TIAB]) OR "costa rica"[TIAB]) OR ("cote d'ivoire"[MeSH Terms] OR ("cote"[TIAB] AND "d'ivoire"[TIAB]) OR "cote d'ivoire"[TIAB]) OR ("cote d'ivoire"[MeSH Terms] OR ("cote"[TIAB] AND "d'ivoire"[TIAB]) OR "cote d'ivoire"[TIAB] OR ("ivory"[TIAB] AND "coast"[TIAB])	1328064

	OR "ivory coast"[TIAB]) OR ("cuba"[MeSH Terms] OR "cuba"[TIAB]) OR ("djibouti"[MeSH Terms] OR "djibouti"[TIAB]) OR ("dominica"[MeSH Terms] OR "dominica"[TIAB]) OR ("dominican republic"[MeSH Terms] OR ("dominican"[TIAB] AND "republic"[TIAB]) OR "dominican republic"[TIAB]) OR ("ecuador"[MeSH Terms] OR "ecuador"[TIAB]) OR ("egypt"[MeSH Terms] OR "egypt"[TIAB]) OR ("el salvador"[MeSH Terms] OR ("el"[TIAB] AND "salvador"[TIAB]) OR "el salvador"[TIAB]) OR ("equatorial guinea"[MeSH Terms] OR ("equatorial"[TIAB] AND "guinea"[TIAB]) OR "equatorial guinea"[TIAB]) OR ("eritrea"[MeSH Terms] OR "eritrea"[TIAB]) OR ("ethiopia"[MeSH Terms] OR "ethiopia"[TIAB]) OR ("fiji"[MeSH Terms] OR "fiji"[TIAB]) OR ("gabon"[MeSH Terms] OR "gabon"[TIAB]) OR ("gambia"[MeSH Terms] OR "gambia"[TIAB]) OR ("georgia (republic)"[MeSH Terms] OR ("georgia"[TIAB] AND "(republic)"[TIAB]) OR "georgia (republic)"[TIAB] OR ("georgia"[TIAB] AND "republic"[TIAB]) OR "georgia republic"[TIAB]) OR ("ghana"[MeSH Terms] OR "ghana"[TIAB]) OR ("grenada"[MeSH Terms] OR "grenada"[TIAB]) OR ("guatemala"[MeSH Terms] OR "guatemala"[TIAB]) OR ("guinea"[MeSH Terms] OR "guinea"[TIAB]) OR ("guinea-bissau"[MeSH Terms] OR "guinea-bissau"[TIAB] OR ("guinea"[TIAB] AND "bissau"[TIAB]) OR "guinea bissau"[TIAB]) OR ("guyana"[MeSH Terms] OR "guyana"[TIAB]) OR ("haiti"[MeSH Terms] OR "haiti"[TIAB]) OR ("honduras"[MeSH Terms] OR "honduras"[TIAB]) OR ("india"[MeSH Terms] OR "india"[TIAB]) OR ("indonesia"[MeSH Terms] OR "indonesia"[TIAB]) OR ("iran"[MeSH Terms] OR "iran"[TIAB]) OR ("iraq"[MeSH Terms] OR "iraq"[TIAB]) OR ("jamaica"[MeSH Terms] OR "jamaica"[TIAB]) OR ("jordan"[MeSH Terms] OR "jordan"[TIAB]) OR ("kazakhstan"[MeSH Terms] OR "kazakhstan"[TIAB]) OR ("kenya"[MeSH Terms] OR "kenya"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB] OR "kiribati"[TIAB]) OR (Democratic[TIAB] AND ("republic of korea"[TIAB] OR ("republic"[TIAB] AND "korea"[TIAB]) OR "republic of korea"[TIAB])) OR ("kosovo"[MeSH Terms] OR "kosovo"[TIAB]) OR ("kyrgyzstan"[MeSH Terms] OR "kyrgyzstan"[TIAB]) OR ("laos"[MeSH Terms] OR "laos"[TIAB]) OR ("lebanon"[MeSH Terms] OR "lebanon"[TIAB]) OR ("lesotho"[MeSH Terms] OR "lesotho"[TIAB]) OR ("liberia"[MeSH Terms] OR "liberia"[TIAB]) OR ("libya"[MeSH Terms] OR "libya"[TIAB]) OR ("macedonia (republic)"[MeSH Terms] OR ("macedonia"[TIAB] AND "(republic)"[TIAB]) OR "macedonia (republic)"[TIAB] OR "macedonia"[TIAB]) OR ("madagascar"[MeSH Terms] OR "madagascar"[TIAB]) OR ("malawi"[MeSH Terms] OR "malawi"[TIAB]) OR ("malaysia"[MeSH Terms] OR "malaysia"[TIAB]) OR ("indian ocean islands"[MeSH Terms] OR ("indian"[TIAB] AND "ocean"[TIAB] AND "islands"[TIAB]) OR "indian ocean islands"[TIAB] OR "maldives"[TIAB]) OR ("mali"[MeSH Terms] OR "mali"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB] OR ("marshall"[TIAB] AND "islands"[TIAB]) OR "marshall islands"[TIAB]) OR ("mauritania"[MeSH Terms] OR "mauritania"[TIAB]) OR ("mauritius"[MeSH Terms] OR "mauritius"[TIAB]) OR ("mexico"[MeSH Terms] OR "mexico"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB]) OR ("moldova"[MeSH Terms] OR "moldova"[TIAB]) OR ("mongolia"[MeSH Terms] OR "mongolia"[TIAB]) OR ("montenegro"[MeSH Terms] OR "montenegro"[TIAB]) OR ("morocco"[MeSH Terms] OR "morocco"[TIAB]) OR ("mozambique"[MeSH Terms] OR "mozambique"[TIAB]) OR ("myanmar"[MeSH Terms] OR "myanmar"[TIAB]) OR ("namibia"[MeSH Terms] OR "namibia"[TIAB]) OR ("nepal"[MeSH Terms] OR "nepal"[TIAB]) OR ("nicaragua"[MeSH Terms] OR "nicaragua"[TIAB]) OR ("niger"[MeSH Terms] OR "niger"[TIAB]) OR ("nigeria"[MeSH Terms] OR "nigeria"[TIAB]) OR ("pakistan"[MeSH Terms] OR "pakistan"[TIAB]) OR ("palau"[MeSH Terms] OR "palau"[TIAB]) OR ("panama"[MeSH Terms] OR "panama"[TIAB]) OR ("papua new guinea"[MeSH Terms] OR ("papua"[TIAB] AND "new"[TIAB] AND "guinea"[TIAB]) OR "papua new guinea"[TIAB]) OR ("paraguay"[MeSH Terms] OR "paraguay"[TIAB]) OR ("peru"[MeSH Terms] OR "peru"[TIAB]) OR ("philippines"[MeSH Terms] OR "philippines"[TIAB]) OR ("romania"[MeSH Terms] OR "romania"[TIAB]) OR ("russia"[MeSH Terms] OR "russia"[TIAB]) OR ("rwanda"[MeSH Terms] OR "rwanda"[TIAB]) OR ("samoa"[MeSH Terms] OR "samoa"[TIAB]) OR ("atlantic islands"[MeSH Terms] OR ("atlantic"[TIAB] AND "islands"[TIAB]) OR "atlantic islands"[TIAB] OR ("sao"[TIAB] AND "tome"[TIAB] AND "principe"[TIAB]) OR	

	"sao tome and principe"[TIAB]) OR ("senegal"[MeSH Terms] OR "senegal"[TIAB]) OR ("serbia"[MeSH Terms] OR "serbia"[TIAB]) OR ("sierra leone"[MeSH Terms] OR ("sierra"[TIAB] AND "leone"[TIAB]) OR "sierra leone"[TIAB]) OR ("melanesia"[MeSH Terms] OR "melanesia"[TIAB] OR ("solomon"[TIAB] AND "islands"[TIAB]) OR "solomon islands"[TIAB]) OR ("somalia"[MeSH Terms] OR "somalia"[TIAB]) OR ("south africa"[MeSH Terms] OR ("south"[TIAB] AND "africa"[TIAB]) OR "south africa"[TIAB]) OR ("south sudan"[MeSH Terms] OR ("south"[TIAB] AND "sudan"[TIAB]) OR "south sudan"[TIAB]) OR ("sri lanka"[MeSH Terms] OR ("sri"[TIAB] AND "lanka"[TIAB]) OR "sri lanka"[TIAB]) OR ("saint lucia"[MeSH Terms] OR ("saint"[TIAB] AND "lucia"[TIAB]) OR "saint lucia"[TIAB] OR ("st"[TIAB] AND "lucia"[TIAB]) OR "st lucia"[TIAB]) OR ("saint vincent and the grenadines"[MeSH Terms] OR ("saint"[TIAB] AND "vincent"[TIAB] AND "grenadines"[TIAB]) OR "saint vincent and the grenadines"[TIAB] OR ("st"[TIAB] AND "vincent"[TIAB] AND "grenadines"[TIAB]) OR "st vincent and the grenadines"[TIAB]) OR ("sudan"[MeSH Terms] OR "sudan"[TIAB]) OR ("suriname"[MeSH Terms] OR "suriname"[TIAB]) OR ("swaziland"[MeSH Terms] OR "swaziland"[TIAB]) OR ("syria"[MeSH Terms] OR "syria"[TIAB]) OR ("tajikistan"[MeSH Terms] OR "tajikistan"[TIAB]) OR ("tanzania"[MeSH Terms] OR "tanzania"[TIAB]) OR ("thailand"[MeSH Terms] OR "thailand"[TIAB]) OR ("timor-leste"[MeSH Terms] OR "timor-leste"[TIAB] OR ("east"[TIAB] AND "timor"[TIAB]) OR "east timor"[TIAB]) OR ("timor-leste"[MeSH Terms] OR "timor-leste"[TIAB] OR ("timor"[TIAB] AND "leste"[TIAB]) OR "timor leste"[TIAB]) OR ("togo"[MeSH Terms] OR "togo"[TIAB]) OR ("tonga"[MeSH Terms] OR "tonga"[TIAB]) OR ("tunisia"[MeSH Terms] OR "tunisia"[TIAB]) OR ("turkey"[MeSH Terms] OR "turkey"[TIAB]) OR ("turkmenistan"[MeSH Terms] OR "turkmenistan"[TIAB]) OR ("micronesia"[MeSH Terms] OR "micronesia"[TIAB] OR "tuvalu"[TIAB]) OR ("uganda"[MeSH Terms] OR "uganda"[TIAB]) OR ("ukraine"[MeSH Terms] OR "ukraine"[TIAB]) OR ("uzbekistan"[MeSH Terms] OR "uzbekistan"[TIAB]) OR ("vanuatu"[MeSH Terms] OR "vanuatu"[TIAB]) OR ("venezuela"[MeSH Terms] OR "venezuela"[TIAB]) OR ("vietnam"[MeSH Terms] OR "vietnam"[TIAB]) OR (("middle east"[MeSH Terms] OR ("middle"[TIAB] AND "east"[TIAB]) OR "middle east"[TIAB] OR ("west"[TIAB] AND "bank"[TIAB]) OR "west bank"[TIAB]) AND Gaza[TIAB]) OR ("yemen"[MeSH Terms] OR "yemen"[TIAB]) OR ("zambia"[MeSH Terms] OR "zambia"[TIAB]) OR ("zimbabwe"[MeSH Terms] OR "zimbabwe"[TIAB]))	
#20	Search ((((((((((((((((surg*) OR neurosurg*) OR operati*) OR surg* treatment) OR surg* procedure) OR disconnecti*) OR resecti*) OR neurostimulati*) OR stereotactic) OR vagus nerve stimulation) OR VNS) OR surg* outcome) OR surg* complication) OR surg* cost) OR presurg* evaluation) OR presurg* investigat*) OR quality of life) OR QOL	332209
#19	Search QOL	31039
#18	Search quality of life	328872
#17	Search presurg* investigat*	1426
#16	Search presurg* evaluation	2757
#15	Search surg* cost	70567
#14	Search surg* complication	137468
#13	Search surg* outcome	585226
#12	Search VNS	1693
#11	Search vagus nerve stimulation	9477
#10	Search stereotactic	21939
#9	Search neurostimulati*	2240
#8	Search resecti*	264619
#7	Search disconnecti*	6321
#6	Search surg* procedure	1503557
#5	Search surg* treatment	2534001
#4	Search operati*	611212
#3	Search neurosurg*	259525
#2	Search surg*	3307001
#1	Search epilep*	152391

The search number (#) signifies the search term for each level and the search builds-up with increase in the number. Individual names for the LMICs were used for the search, in addition to the Medical Subject Heading (MeSH) terms for these countries. To focus the searches for these countries we searched within the title and abstract (TIAB).

b. Embase search (May 2018)

1	exp epilepsy/	208373
2	exp surgery/	4217302
3	exp neurosurgery/	230491
4	exp surgical technique/	1400852
5	disconnective surgery.mp.	48
6	resective surgery.mp.	1758
7	neurostimulation.mp. or exp nerve stimulation/	115145
8	exp vagus nerve stimulation/	8911
9	exp stereotactic treatment/ or exp stereotactic procedure/	38894
10	exp treatment outcome/	1389722
11	exp postoperative complication/	603617
12	exp "health care cost"/ or exp "cost benefit analysis"/	318322
13	exp preoperative evaluation/	92771
14	exp "quality of life"/	419286
15	exp middle income country/ or exp low income country/ or exp developing country/	91701
16	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	5657333
17	1 and 15 and 16	247

We used the Medical Subject Heading (MeSH) terms for LMICs rather than individual countries as used for PubMed search above. “exp” – signifies that the subject heading has been exploded, “mp” – signifies keyword search.

c. Global health archives (May 2018)

1	epilep*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1223
2	surg*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	11256
3	neurosurg*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	81
4	operati*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	17428
5	surg* treatment.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	868
6	surg* procedure.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	77
7	disconnecti*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	8
8	resecti*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1082
9	neurostimulati*.mp. [mp=abstract, title, original title, broad terms, heading	0

	words, identifiers, cabicodes]	
10	stereotactic.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1
11	vagus nerve stimulation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
12	VNS.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4
13	surgical complication.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	4
14	surgical outcome.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
15	surgical cost.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
16	presurgical evaluation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	1
17	presurgical investigation.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
18	quality of life.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	36
19	QOL.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	0
20	(Africa or Asia or Caribbean or West Indies or South America or Latin America or Central America).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	135552
21	(((Afghanistan or Albania or Algeria or American Samoa or Angola or Argentina or Armenia or Azerbaijan or Bangladesh or Belarus or Belize or Benin or Bhutan or Bolivia or Bosnia) and Herzegovina) or Botswana or Brazil or Bulgaria or Burkina Faso or Burundi or Cabo Verde or Cape Verde or Cambodia or Cameroon or Cameroon or Central African Republic or Chad or Tchad or China or Colombia or Comoros or Congo or Democratic Republic of Congo or Costa Rica or Cote d'Ivoire or Ivory Coast or Cuba or Djibouti or Dominica or Dominican Republic or Ecuador or Egypt or El Salvador or Equatorial Guinea or Eritrea or Ethiopia or Fiji or Gabon or Gambia or Georgia Republic or Ghana or Grenada or Guatemala or Guinea or Guinea-Bissau or Guyana or Haiti or Honduras or India or Indonesia or Iran or Iraq or Jamaica or Jordan or Kazakhstan or Kenya or Kiribati or Democratic republic of Korea or Kosovo or Kyrgyzstan or Laos or Lebanon or Lesotho or Liberia or Libya or Macedonia or Madagascar or Malawi or Malaysia or Maldives or Mali or Marshall Islands or Mauritania or Mauritius or Mexico or Micronesia or Moldova or Mongolia or Montenegro or Morocco or Mozambique or Myanmar or Namibia or Nepal).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	102527
22	(((((((Nicaragua or Niger or Nigeria or Pakistan or Palau or Panama or Papua New Guinea or Paraguay or Peru or Philippines or Romania or Russia or Rwanda or Samoa or Sao Tome) and Principe) or Senegal or Serbia or Sierra Leone or Solomon Islands or Somalia or South Africa or South Sudan or Sri Lanka or Saint Lucia or Saint Vincent) and the Grenadines) or Sudan or Suriname or Swaziland or Syria or Tajikistan or Tanzania or Thailand or East Timor or Timor-Leste or Togo or Tonga or Tunisia or Turkey or Turkmenistan or Tuvalu or Uganda or Ukraine or Uzbekistan or Vanuatu or Venezuela or Vietnam or West Bank) and Gaza) or Yemen or Zambia or Zimbabwe).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	2982

23	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	25648
24	20 or 21 or 22	160387
25	1 and 23 and 24	52

The names of the individual LMICs were used for the search. “mp” – signifies keyword search.

Search details from the WHO Global Health Index

(tw:(epilepsy)) AND (tw:(surgery)) AND (instance:"ghl") AND (db:("WPRIM" OR "LILACS" OR "IMEMR" OR "IMSEAR"))

- **d.** Latin American & Caribbean Health Sciences Literature (LILACS) = 305
- **e.** African Index Medicus (AIM) = 0
- **f.** Index Medicus for Eastern Mediterranean Region (IMEMR) = 45
- **g.** Index Medicus for South East Asian Region (IMSEAR) = 40
- **h.** Western Pacific Region Index Medicus (WPRIM) = 311
- **i.** African Journal Online (AJOL) = 3
- **j.** Others:= 29 (Mainly from google scholar and website search)

“tw” indicates a free text search in the title and abstract fields only, ghl – Global Health Index, db –database. Databases d, e, f, g and h were accessed via the WHO Global Health Index. In order not to miss relevant articles, we simplified the search and used few search terms.

Total = <u>1365</u>

Appendix 3

Training Manual for Enumerators

Registration/Attendance form

Enumerator's Training (Day 1/2)		**Date___/ ___/ _____**	
S/No	**Name**	**Designation**	**Signature**
1.			
2.			
3.			
4.			
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24.			
25.			

Training Outline **Training Date___/ ___/ _____**

S/No	Time	Activity (Day 1)	Facilitator/Responsible
1.	9:00 – 9:30 am	Arrival and Registration / Opening Prayers	Participants
2.	9:30 – 9:40 am	Opening Remark and Introduction	Principal investigator
3.	9:40 – 10:00 am	**Session 1:** Rationale and Objective of the rural epilepsy survey	
4.	10:00 – 10:45 am	**Session 2:** An overview of epilepsy & diagnosis	
5.	10:45 – 11:30 am	**Session 3:** Overview of the methodology of the rural survey	
6.	11:30 – 12:00 am	**Session 4:** Understanding the survey tools/ Role of the field staff	
7.	12:00 – 1:00 pm	**Session 5:** Enumerator's function and how to carry out the D2D survey	
8.	1:00 – 1:15 pm	Lunch Break	
9.	1:00 – 2:30 pm	**Session 6:** Group discussion of the survey instruments	
10.	2:30 – 3:30 pm	**Session 7:** Practice session/Role play/Practice of the D2D survey among participants	
11.	4:20 – 4:50 pm	**Session 8:** Field logistics and contract issues	
12.	4:15 – 5:00 pm	Wrap-up and Closing	

S/No	Time	Activity (Day 2)	Facilitator/Responsible
13.	9:00 – 12 noon	**Session 10:** Overview of the survey instruments	
14.	1:30 – 3:00 pm	**Session 11:** Field practice (at a pilot site) and how to refer a suspected person with epilepsy	

Introduction

This document aims to provide information and guidance on the conduct of the field study of the research titled “The Standard of care or people with epilepsy in sub-Saharan Africa: the case of Nigeria”. This research is part of a PhD research from the Institute of Neurology, University College London.

Training workshop purpose and objectives

The purpose of this workshop is to prepare the data collection teams to carry out the data collection. This training manual presents in brief the overall objectives, contents, tools and approaches of how the field enumerators will be trained for the field surveys for epidemiological study of epilepsy in three regions of Nigeria. The training is to ensure the quality and reliability of data acquired from the field. It is also to ensure that the methodology and data acquisition is uniform and comparable between the various centres. This guide therefore is aimed at providing that comprehensive guide to provide quality training to the field enumerators. The content of the training includes the following among others:

- The background and objectives of the community-based survey of epilepsy
- An overview of epilepsy & diagnosis
- Overview of the methodological approach used for the study
- Familiarization with the survey instruments
- The role and conduct of the field enumerators
- Detailed review of the survey instrument
- Field practice (site visit) and feedback

The Background and objective for the field survey in epilepsy. (Session 1)

- Epilepsy is a brain disorder that affects approximately 50 million people worldwide, with about 80% living in the low- and middle-income countries (LMIC).
- This higher burden in LMIC and particularly sub-Saharan Africa (SSA) is likely due to the increased higher incidence of malaria, neurocysticercosis, road traffic injuries, birth-related injuries, poorer medical infrastructure, and the problems of availability of preventative health programmes and accessible care.
- Because the manifestations of epilepsy are dramatic and unpredictable, it is still a neglected, misunderstood and highly stigmatizing condition especially in the SSA.

- In most parts of Nigeria the numbers of people with epilepsy are not known; and the few studies conducted have shown a wide variability.
- Assuming a conservative estimate that about 1% of Nigerians are affected, it means that almost 2 million Nigerians have epilepsy.
- Over the years, epidemiological studies in low- and middle-income (LMIC) have been centred on the community approach, with studies showing that the door-to-door (D2D) method is preferable in resource-poor regions of the world.
- Because most projects of this nature cannot cover the entire country, a representative population of Nigerians, especially from rural and sub-urban populations are selected. The findings from the few select are then extrapolated to the entire population. The few found to have epilepsy have the privilege to be studied.
- The objective of the survey is to obtain data on epilepsy from 3 regions of Nigeria (Oriade LGA in Osun State. Gwandu LGA in Sokoto State, and Afikpo LGA in Ebonyi State.
- It is expected that the entire communities of Ijebu Jesa (approx. 5,000 household) will be screened from Oriade LGA.

An overview of epilepsy & diagnosis (Session 2) (Fisher et al., 2005)

Definition of epilepsy

a. Conceptual definition

A disorder characterized by an enduring predisposition to generate epileptic seizures and by neurobiologic, cognitive, psychological and social consequences of this condition. The definition requires the occurrence of at least one epileptic seizure.

b. Operational definition

Epilepsy is defined in practice as two or more unprovoked seizures occurring at least 24 h apart. (*This definition will be used for this rural survey*)

What is a seizure?

- It is a transient occurrence of signs and/or symptoms due to abnormal excessive electrical discharges in a group of brain cells.
- Different parts of the brain can be the site of such discharges.
- These signs or symptoms include sudden and transitory abnormal events such as alterations of consciousness, or involuntary motor, sensory, autonomic, or psychic events perceived by the patient or an observer.

- Seizures can vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions.
- Seizures can also vary in frequency, from less than 1 per year to several per day.

Video Session: What is and what is not a seizure?

- Here we will show videos to help understanding.

Diagnosis

One seizure does not signify epilepsy.

- Has the subject had more than one ($\geq$ 2) unprovoked seizure?
- Does the subject have a diagnosis of an epilepsy syndrome?
- Does the subject have any associated neurobiologic, cognitive, psychological, and/or social disturbances?

Management

Epilepsy can be managed using drugs, surgery and other adjuvant therapy. There have been many advances in treating epilepsy. In Western countries, many of these treatments are unavailable in Nigeria. However, antiepileptic drugs (ASMs) available are still very useful in making majority of PWE seizure-free or at least significantly reduce seizure frequency. The good news is that studies have shown that community-based rehabilitation (CBR) services where allied health care workers can render care are effective.

Methodological Approach

This section will highlight the methods of data collection.

i. **The survey consists of a 2-step process.**
    a. The initial D2D survey is the first step of screening those with suspected epilepsy (2 or more seizures) in the community. Those suspected will be invited to the nearest hospital.
    b. The second stage to confirm those who have epilepsy from the people above, and they undergo a recruitment process in the designated hospital/health centre.

The most important is the first step that the enumerators are fully involved is using the 10-item epilepsy-screening questionnaire.

Why a D2D approach in epilepsy?

1. Cultural and religious belief that epilepsy is not a bodily disease, but rather a 'spiritual' condition. Therefore, they remain within the community and may never access health care.
2. Poverty and ignorance
3. Stigma-related. They are ashamed to access care.
4. Community perception.
5. Other issues of access to care. Like unavailable neurological care, distance to care, poor roads, etc.
6. It is less expensive.

These and other reasons will make sufferers remain 'hidden' in the community. Therefore, a D2D approach will be more appropriate.

Understanding the survey tools

The Survey Instruments: This section simply describes the field survey instrument to highlight the various sections and the kind of information it seeks to obtain.
The hard copy of the survey instrument would be given to the participants and the facilitator will also project various sections to explain what is required and the kind of information that each section seeks to elicit.

The enumerator will receive and use:

1. **Household census form:** to be completed based on the interview with the household head.
2. **Epilepsy screening questionnaire (The translated versions)**: This questionnaire is to screen those with suspected epilepsy. Should there be someone with a positive answer, the questionnaire should be personalised for that person(s).
3. **Hospital Invitation Card:** to invite suspected cases of epilepsy to the health centre where they are further screened.
4. **Second Stage of Epilepsy Screening:** A further stage of screening to determine and confirm those with epilepsy. To be done by a physician or a trained personnel.

5. **Epilepsy Questionnaire:** This will be used to recruit and get information from confirmed people with epilepsy at the health-centre. This form will also be completed by a physician or trained personnel.
6. **Epilepsy Questionnaire for controls:** Used to recruit and get information from people that do not have epilepsy. The controls will be determined through a randomisation process.

The Role and Conduct of the Field Enumerators

This section discusses in specific details the roles of field enumerators and other staff.

a. The Profile of the Field Enumerators/staff

A field enumerator should have the following minimum qualifications:

i. Since the official **language** of communication in Nigeria is English Language, the enumerator should have the necessary literacy skills that make it possible to understand the training process and what is required for the assignment.

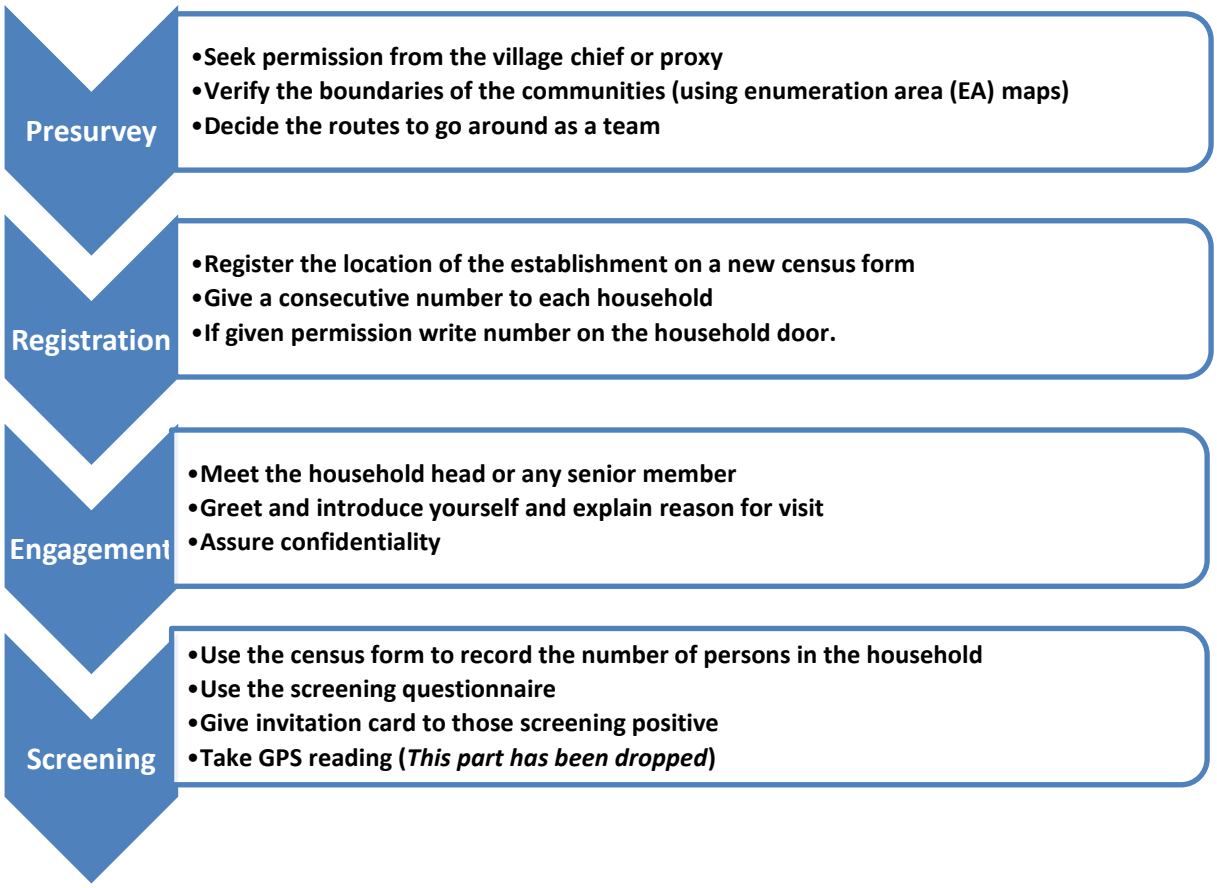
ii. Must be conversant with the language of the respondents – **Yoruba, Igbo or Hausa**

iii. **Previous experience** in surveys is necessary for an interviewer to appreciate some of the issues discussed during training.

iv. Should understand cultural aspects of the communities. Since this survey is cross ethnic, the heterogeneous nature of the Nigerian cultural and ethnic landscape should be considered.

b. Enumerator's functions

- Study and understand how to complete the survey in an appropriate manner.
- Write in clear and understandable manner on the survey forms by using capital letters.
- Check that materials needed to carry out the survey is sufficient and appropriate.
- Carry out the survey personally to each selected, avoiding the presence of external people and follow instructions given;
- Introduce themselves, explaining who they are and the purpose of the survey in a manner that facilitates the participation of households in the survey
- Ask questions in a clear and kind manner and write down the answers in a clear way.
- Double check and revise the survey at the end of the day in order to correct mistakes and sign off on completed surveys as verification of the accuracy of the survey.



Practice session/Role play

- Discuss what is seizures and epilepsy
- Discuss how to diagnose epilepsy
- Revise and identify the survey instruments
- Practice using the instruments
- Do a mock play of conducting a D2D survey

Enumerator's function and how to carry out the D2D survey

a. Survey team and their functions

i. Enumerators

- Primary role is to collect household-level data, by carrying out interview with household heads or a representative, under the leadership of the team leaders.
- They must be certain that the information they are collecting is accurate.
- They need to check that the data is consistent and that all survey tools are adequately completed.
- Enumerators must crosscheck forms upon survey completion and sign the forms verifying the accuracy of the survey.

- If data is found to be inaccurate, enumerators will be required to return to the household to collect accurate information.

ii. Team leaders/research assistant

- Team leaders are responsible for coordinating their survey team, checking the work done by enumerators and interacting with survey coordinators about any problems or needs that arise. Every day the team leaders must do a series of checks on every survey to ensure that the surveys were done properly and are not missing any information. The team leaders must sign the survey verifying its accuracy. If surveys are inaccurate or are missing information, they must send the enumerator back to the household to complete the information. Only when the survey is done should they sign off on the survey. Team leaders are also responsible for carrying out the community surveys. One of the team leaders will be assigned to coordinate the activities of the survey teams and report to coordinators on any issues/problems that arise.

iii. Coordinators

- **The Principal investigator** (PI) is the overall study coordinator who is responsible for providing liaison between University College London, the FMOH, OAUTH Ife, FTHE Abakiliki, UDUTH Sokoto, and UMTH Maiduguri. Making administrative arrangements and providing logistical support. The PI will make sure the teams have all the items needed and work in the field with other survey teams
- Each research site will have a **survey coordinator** who will be working out in the field with the survey teams, and will provide a schedule of the enumerators and household visits over the course of the survey developed in consultation with the local communities. The survey coordinator will be responsible for tracking the progress of the survey implementation by number, checking that completed surveys have been signed off by the enumerator and team leader.

b. Step-by-step process for the enumeration

(1) Meet the village chief or proxy, explain the purpose of your visit, and ask permission to conduct the research. Also verify the boundaries of the communities if possible.

(2) Use the EA map and decide the routes to go around the village to visit all the houses. Make sure you follow the route.

(3) When you come to a household; register the location of the establishment on a new census form that will be used for that establishment. Give a consecutive number to each household starting from 1.

(4) Meet the household head or any senior member, someone who can answer the questions.

(5) After a greeting, introduce yourself saying that you have come to ask about some medical conditions. Explain that the statistics produced will be essential for this certain groups.

(6) You must assure him/her that all the information you receive will be used only for purpose of the research and will be kept confidential.

(7) In case of absence or refusal, just record on the census form.

(8) After the owner (or his proxy) agrees to cooperate, use the census form and ask about number of persons in the household one by one, and enter the answers to the assigned space on the form.

(9) Record the household ID with a marker on the doorpost or signpost (if permission is granted).

(10) Now use the screening questionnaire to screen those with suspected epilepsy

(11) Fill in a separate form for everyone screening positive

(12) For those with positive answer (Q2 to Q10), give an invitation form to the health centre.

(13) Take a GPS reading *(This part has been dropped)*

(14) Once finished he/she will thank the person.

(15) When finished for that day register the location (landmark) where to continue the next day.

c. Revision

1. At the end of the interview and before taking leave, the enumerator should double check that all questions are properly answered and all relevant forms are filled.
2. If not then enumerator should go back and ask again.
3. Before submitting the survey forms to the team leaders, enumerators must check carefully that nothing is missing and there are no mistakes.
4. The team leader, who gets the survey, will check nothing is missing, everything is clear and understandable and there are no mistakes.

5. If there are problems with the survey, he/she will give it back to the enumerators who will go back to the household with a detailed list of what needs to be corrected.

Group discussion of the survey instruments

Detailed review of the Survey Instrument: This section will take a detailed step-by-step and section-by-section review of the survey instrument. The intention is to achieve uniform understanding of every section, word and the intended data it seeks to elicit. The overall aim is to keep all the participants on the same page with respect to the meaning and the kind of data required from the field.

Practice of the D2D survey among participants

i. How to carry out the interview

- The enumerator should identify the selected household
- Identify the head of the household or the next senior member or substitute that can give answers
- The enumerator should establish a clear relationship with the interviewee without making them suspicious.
- For this reason, the first impression is very important. When they meet, the interviewer is the first to start talking informally; introducing his/her name, for what organization is he/she working for and what the purpose of the visit is.
- The survey question are directed to the head of households but is meant to inquire about the entire family.
- It is a face-to-face interview and information is gotten directly from the person being interviewed.
- It should be a normal, smooth conversation between two persons, in a manner that does not influence or lead the answers, nor get external suggestion from other people.

  For example - “Good morning my name is ..... and I am from OAUTH/UDUTH/FETHA working on a project that helps to understand a health condition in rural area. We need you to provide some information that is very important for the purpose of this project. Would you be available to answer some questions?”
- It is very important that the interview is carried out privately without external presence or influences since other people could bias the output and thus the result of the survey.
- Before starting the first question it is very important to explain the importance of confidentiality

- The only reason we collect names is that so we can return for a visit later. For the purpose of the project and statistical analysis, names will not be used.
- There are no right or wrong answers to the questions
- It is essential that the enumerator maintain neutrality without interpreting the questions in his/her own way.
- Each question must be read exactly as it is written since a slight different word might change the meaning and induce a different reaction and answer.
- The respondents should be given time to understand the questions and answer. The enumerator should not suggest answers.

ii. Mock interviews [Interviewing each other]

- The enumerators will model interviews in the class.
- The demonstration will help enumerators get acquainted with the screening questionnaire and how to keep the interview flowing.
- One participant interviews another. The respondent can answer truthfully or play the role of a fictitious person.
- The participants should watch an interviewer-respondent pair and take notes about issues that arise.

Field practice (at a pilot site) and how to refer a suspected person with epilepsy

- This section provides hands-on experience to the participants. They will be grouped into a team of twos and sent randomly to households selected for the training.
- The essence is to shift from theory to practice.
- It is expected that such an exercise will highlight among other things, the length of time it takes to complete a questionnaire and the possible challenges associated with administering the field instrument.

Feedback on the practice sessions

- The feedback report will highlight grey areas that may be clarified and areas that may not be applicable to our environment.
- The information from it may help modify instrument and adapt it to suit cultural peculiarities of the particular environment.

Things You Must Do

- You must ask the questions exactly the same way to each respondent and in the same order in which they are presented in the questionnaire
- You must make every effort to carefully enter the data into the tablet, and try to avoid damage to the tablet by taking care of it.
- You need to review each questionnaire in the evening together with the Field Supervisor and make any corrections.
- You must be punctual in keeping all appointments made.
- You are solely responsible for all documents issued to you in connection with the survey, and you must ensure that they are secure at all times
- Dress appropriately

Things You Must Not Do

- You must not solicit or permit any unauthorized person to assist you with your work.
- You must not combine with the survey work any canvassing for personal gains, religious, political party or any other organization.
- You should never become involved in religious or political discussions while you are working.

Field logistics and contract issues

NOTE: Emphasis should be on quality not quantity, following best global practices.

- Contract terms
- Where to get what?
- Who to report to?
- When does the field survey starts and ends?
- What next?

Appendix 4

Household census form

State: ________________ LGA: _______________ Village: ______________ Community: ________________
Name(s) of Enumerators: i)_______________________ ii) _______________________ Date:_ _ / _ _ / _ _ _ _

S/No.	Household ID number	Total number in household		From the oldest write the age										
				1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	Number deceased (age & sex), since last census (2006)
			Male =											
			Female =											
			Male =											
			Female =											
			Male =											
			Female =											
			Male =											
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			Male =											
			Female =											
			Male =											
			Female =											

Appendix 5

Identification / Invitation slip

ID/HOSPITAL INVITATION CARD

Standard of care for people with epilepsy in Sub-Saharan Africa: the case of Nigeria

State: _____ Village_____ Community_____

Household ID number: _____ Serial number:_____

Date of survey:_ _ / _ _ / _ _ _ _

Patient code/Initials: _____

Age: _____

Sex: _____

Hospital or Health centre invited to: _____

Name(s) of Enumerators_____

Contact number at the hospital invited: _ _ _ _ _ _ _ _ _ _ _

Appendix 6

Epilepsy Questionnaire (cases)

Household ID number:_____ Serial number:_____ Date:_ _ / _ _ / _ _ _ _			
Name(s) of Physician: _____			
Has consent been granted? *		☐ Yes	☐ No

Section A: SOCIO-DEMOGRAPHIC CHARACTERISTICS				
Subject Initials: _____				DOB:_ _ /_ _ /_ _ _ _
Age:_____ years	Address (nearest landmark):_____			
Gender	☐ Male	☐ Female	☐ Others	
Subject's/parents cell phone	__ __ __ __ __ __ __ __ __ __ __			
Place of birth: _____	Ethnic group _____			
Religion:	☐ Christianity	☐ Islam	☐ Traditional	☐ Non/Others
Marital status	☐ Single	☐ Married	☐ Divorced	☐ Widow(er)
If married, is it consanguineous (married to a blood-relation)			☐ Yes	☐ No
Sleeping area	☐ Sleeps alone		☐ Share a bedroom, but sleeps On separate beds	
	☐ Share a bedroom, but sleeps on separate beds		☐ Share a bed with someone	
	☐ Share a dwelling but have separate bedrooms		☐ Stays alone in a different residence	
Highest educational attainment	☐ None	☐ Primary	☐ Secondary	☐ Tertiary
Employment or trade	☐ Wage earner or civil servant	☐ Crafts or Trade	☐ Farmer	☐ Student
	☐ unemployed	☐ Labourer	☐ others	
Average income per month _____ (Naira)				
Living area:		☐ Rural	☐ Semi-urban	☐ Urban
Water source	☐ Tap/pump	☐ Well	☐ Stream/river	☐ Pond

	☐ Others	Specify_____		
Waste management	☐ Water closet	☐ Pit latrine	☐ Bush (open defecation)	
	☐ Others	Specify _____		
Staple food	☐ Cereals (rice, corn, millet, etc)	☐ Tubers (yams/cassava)	☐ Leafy vegetables	☐ Dairy products (milk. Butter)
	☐ Beef	☐ Pork	☐ Fish	☐ Lamb/goat
Additional Information……				

Section B: GYNAECOLOGICAL AND OBSTETRIC HISTORY [if subject is female, if not go to next section]			
Age of Menarche: _____ Years	Last menstrual period:	_ _/ _ _ / _ _ _ _	
Number of Pregnancy(ies): _____	Number of Miscarriage(s)	_____	
Number of live-birth(s) _____	Past history of eclampsia	☐	☐
Any child (children) with epilepsy	☐ No	☐ Yes	☐ Unknown
Additional Information……			

Section C: CHILDHOOD HISTORY and IF SUBJECT IS A CHILD			
Name of next of kin:_____			
Relationship of next of kin if completing questionnaire:_____			
Primary Caretaker Cell Phone: _____			
Consanguineous parents?	☐ No	☐ Yes	☐ Unknown
Birth history:	☐ Full-term	☐ Premature	☐ Post-term
Birth weight: ☐ Normal	☐ Low	☐ High	☐ Unknown
Any maternal birth complications?	☐ No	☐ Yes	☐

(prolonged/obstructed delivery, CS, etc)			Unknown
Any complications at birth? (Breathing difficulty, resuscitation, etc)	☐ No	☐ Yes	☐ Unknown
If Yes (specify) _____			
Is the child in school?	☐ No	☐ Yes	☐ Unknown
If not in school, is it because of epilepsy?	☐ No	☐ Yes	☐ Unknown
What academic level is the child?	☐ Primary	☐ Secondary	☐ Post-secondary
Are there any learning difficulties or disability(ies)?	☐ No	☐ Yes	☐ Unknown
If Yes (specify disability(ies) _____			

Section D: NATURAL HISTORY OF THE SEIZURE DISORDER			
Age at first seizure? _____ Years		Date of last seizures?	_ _/ _ _ / _ _ _ _
Has the subject had any seizure in the last 2 years?	☐ No	☐ Yes	☐ Unknown
Has the subject had any seizure in the last 12 months?	☐ No	☐ Yes	☐ Unknown
Average seizure frequency?	_____ per day _____ every 2 to 3 months	_____ per week _____ every 6 months	_____ per month _____ every 6 months
Seizure timing?	☐ Nocturnal	☐ Early morning	☐ Afternoon
	☐ Anytime	☐ Unknown	
Additional Information…… .			

Section E: HISTORY – SEIZURE TYPE			
Does the subject have a history of?			
Generalised tonic-clonic seizures?	☐ No	☐ Yes	☐

			Unknown
Generalised myoclonic seizures?	☐ No	☐ Yes	☐ Unknown
Generalised atonic seizures?	☐ No	☐ Yes	☐ Unknown
Absences?	☐ No	☐ Yes	☐ Unknown
Simple partial seizures?	☐ No	☐ Yes	☐ Unknown
Complex partial seizures?	☐ No	☐ Yes	☐ Unknown
Partial seizures with secondary generalisation?	☐ No	☐ Yes	☐ Unknown
Seizure type difficult to classify?	☐ No	☐ Yes	☐ Unknown
Status epilepticus?	☐ No	☐ Yes	☐ Unknown
Other generalized seizures?	☐ No	☐ Yes	☐ Unknown
If yes above; specify _____			
If focal; where does the seizure start? _____			
Is the subject aware of his/her surrounding during the episode?		☐ No	☐ Yes
Additional Information…… .			

Section F: HISTORY – PRECIPITATING FACTORS			
Emotions?	☐ No	☐ Yes	☐ Unknown
Alcohol?	☐ No	☐ Yes	☐ Unknown
Sleep?	☐ No	☐ Yes	☐ Unknown
Lack of sleep?	☐ No	☐ Yes	☐ Unknown
Flashing lights?	☐ No	☐ Yes	☐

			Unknown
Hyperventilation?	No	Yes	Unknown
Menstruation?	No	Yes	Unknown
Stopping the antiepileptic drugs?	No	Yes	Unknown
Pregnancy?	No	Yes	Unknown
Specify other precipitating factor(s) not listed _____			
Additional Information…… .			

Section G: HISTORY – POSSIBLE AETIOLOGY(IES)			
Family history of epilepsy? 1st degree relative	No	Yes	Unknown
Family history of epilepsy? 2nd degree relative	No	Yes	Unknown
Family history febrile convulsions?	No	Yes	Unknown
Measles?	No	Yes	Unknown
Meningitis?	No	Yes	Unknown
Head injury before onset of seizures?	No	Yes	Unknown
Does the subject have any neurological deficit?	No	Yes	Unknown
If yes; what deficit? _____			
Was the subject on any long term medication before onset of seizures?	No	Yes	Unknown
If yes, specify the type of drug _____			
Have you been treated for river blindness in the past?	No	Yes	Unknown
Have you received Ivermectin (Mectizan) in the past?	No	Yes	Unknown

Are all siblings healthy?	☐ No	☐ Yes	☐ Unknown
If No above, specify ill health _____			
Additional Information…… .			

Section H: PAST MEDICAL HISTORY		
Apart from seizures what other medical problems do you have?		
Hypertension	☐ No	☐ Yes
Blackouts	☐ No	☐ Yes
Diabetes	☐ No	☐ Yes
Sickle cell disease	☐ No	☐ Yes
Stroke	☐ No	☐ Yes
Do you smoke cigarette?	☐ No	☐ Yes
If yes, specify number of sticks per day. _____		
Do you drink alcoholic beverages? ☐ No	☐ Yes	☐ Unknown
If yes, specify number of bottles or amount per week. _____		
Additional Information…… .		

Section I: CLINICAL EXAMINATION			
What is the general health of the subject?	☐ Good	☐ Average	☐ Poor
Height: _____Meters		Weight:	_____ Kg
Neurological Examination	☐ Normal	☐ Abnormal	☐ Not done
If the neurological examination is abnormal, what is the exact diagnosis (Focal neurological deficit)? _____ _____			
Any other abnormal examination, specify_____			
Additional Information…… .			

Section J: TREATMENT HISTORY and REFERRAL PATTERN			
Have you even seen a traditional or spiritual healer?		☐ No	☐ Yes
Where did you go first to seek help when you started having the fits?	☐ Traditional healer	☐ Spiritual leader	☐ Primary health care
	☐ Psychiatric hospital	☐ Tertiary healthcare	☐ None
If you saw a traditional healer or spiritual leader what was done to you then? _____			
Have you attended a hospital in the past?		☐ No	☐ Yes
Who referred you to the hospital?	☐ Traditional healer or spiritualist	☐ Primary care personnel	☐ Self-referral
	☐ Parent or relative		
How long did it take you to go to the hospital, from seizure onset?			_____ _ days
What is the approximate distance from where you reside to the hospital?			_____ _ Km
How long does it take you in Minutes/hours to reach the hospital?			_____ _
Means of transportation			_____ _
Average cost of transportation (Naira)			N_____ __
Are you on health insurance?	☐ No	☐ Yes	☐ Unknown
Is the subject on any ASM medication?	☐ No	☐ Yes	☐ Unknown
Who prescribes the ASM?	☐ Self	☐ Physician	☐ Pharmacy attendant
	☐ Nurse	☐ Relative or friend	☐ Others
Source of medication prescriber (self, physician, nurse, pharmacy attendant, relative or friend), compliance	☐ Hawker	☐ Registered pharmacy	☐ hospital pharmacy
	☐ donation	☐ Others	☐

			Polytherapy > 2 drugs
Which ASM(s) are you taking? _____			
Have you missed any dose in the past 1 month (≥ 3 doses)		☐ No	☐ Yes
Not on medication in the past 1 month		☐ No	☐ Yes
Are the drugs readily available?		☐ No	☐ Yes
Since starting medication, what has been effect of ASM on seizure frequency	☐ Stopped	☐ Reduced	☐ Same
	☐ worse	☐ don't know	____ per month/year
Any symptoms/side effects while taking the drugs? _____			
What is the cost of treatment per month? N_____			
If not on any treatment. What is the reason?			
☐ Lack of access to health care	☐ Lack of medical personnel	☐ Rejection of diagnosis by patient or relative	☐ Patient's misconception	☐ Stigma
☐ Unavailability of drugs	☐ Cost of drugs	☐ Rejection of treatment by patient	☐ Cultural belief (Your traditional belief)	☐ Others specify
Have you had any access to specialised neurological care (neurologist consultation, neurophysiology, neuroimaging)?		☐ No	☐ Yes
Additional Information……. Cultural belief (e.g in our culture it is caused by demon possession, can only be cured by exorcism)			

Section K: INVESTIGATIONS HISTORY			
Was an EEG ever done?	☐ No	☐ Yes	☐ Unknown
Was a CT or MRI ever done?	☐ No	☐ Yes	☐ Unknown
Have you had any access to specialised neurological care (neurologist consultation, neurophysiology, neuroimaging)?		☐ No	☐ Yes
Additional Information…….			

Section L: PATIENT'S SATISFACTION (For those receiving/attending hospital)			
Overall, how satisfied are you with your epilepsy care?	☐ No	☐ Yes	☐ Unknown
How would you rate the services provided for you in the hospital?	☐ Bad	☐ Good	☐ Unknown
Have you been provided with any resources or information to learn about epilepsy?	☐ No	☐ Yes	☐ Unknown
Did you receive any disability benefit?	☐ No	☐ Yes	☐ Unknown
Do you think a social group or an epilepsy association will be useful?	☐ No	☐ Yes	☐ Unknown
What suggestions do you have for improved care of people with epilepsy? _____ _____ _			
Additional Information…… .			

Section M: STIGMA-RELATED QUESTION – Patient's view				
Do you think that people think less of you because of epilepsy?	☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Do you think you have been gossiped about?	☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Do you think that the people are afraid to come close to you?	☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Have you ever been teased, bullied or harassed because of epilepsy?	☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Have you felt that you have been treated unfairly or that your rights have been denied because of epilepsy?	☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Have your experiences with stigma affected your recovery?	☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always

Has your epilepsy caused you to think less of yourself think less about yourself or your abilities?				
☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Has epilepsy affected your ability to make or keep friends?				
☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Has epilepsy affected your ability to interact with your family?				
☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Has epilepsy affected your satisfaction or quality of life?				
☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Do you avoid situations that may be stigmatizing to you? Like social gathering				
☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always
Do you think your epilepsy can be an obstacle to you having children?		☐ Yes	☐ No	☐ Unsure
Do you think your epilepsy can be an obstacle to you marrying?		☐ Yes	☐ No	☐ Unsure
Do you think you have been treated negatively in the hospital because of epilepsy?		☐ Yes	☐ No	☐ Unsure
Have you been denied admission into a school because of epilepsy?		☐ Yes	☐ No	☐ Unsure
Have you been verbally insulted, harassed or threatened?		☐ Yes	☐ No	☐ Unsure
Have you been physically abused because of epilepsy?		☐ Yes	☐ No	☐ Unsure
Have you been denied a job or employment because of epilepsy?		☐ Yes	☐ No	☐ Unsure
Additional Information…… .				

N: INJURY-RELATED HISTORY				
Have you ever experienced any injury (ies) from seizures?		☐ Yes	☐ No	☐ Unsure
Type of injury? Tick as many applicable				
☐ Dental	☐ Tongue	☐ Fracture	☐ head injury	☐ burn

injury	laceration			
☐ Submersion in water	☐ Road traffic accident	☐ Soft tissue injury	☐ Bruise, laceration, cut to skin	☐ Eye injury
☐ Joint dislocation	☐ Abdominal injury	☐ Others Specify:_____		
Frequency of injury				
☐ Once	☐ 2 to 3 times	☐ 4 to 5 times	☐ >5 times	☐ Unsure
Additional Information……				

Appendix 7

Physician's perspective about epilepsy care in Nigeria

INFORMATION PAGE

Hello,

My name is Dr Musa M. Watila a PhD student with the UCL Institute of Neurology, UK. I am a member of the Nigerian Society of Neurological Sciences and the Nigerian League Against Epilepsy. My research is on the ''standard of care for people with epilepsy in Sub-Saharan Africa: the case of Nigeria''. I will like to invite you to participate in a survey looking at the ''physician's perspective about epilepsy care in Nigeria''. The aim is to have an overview of the nature of epilepsy care and what is available from a medical practitioner's point of view, in addition to understanding the obstacles and difficulties in delivering standard epilepsy care. The questions are easy to answer and if you are not comfortable answering any question or it does not apply to your practice, you can skip it and move to the next. Multiple choices are provided for speed and ease of completion, you have few places to write comments.

Your participation is voluntary. Information you give us will be confidential and would be used only for the purpose of this study.

If would like to know more, please contact me (musa.watila.12@ucl.ac.uk) or my supervisor Professor Ley Sander (lsander@ucl.ac.uk).

Thank you for your time and participation.

Sincerely,

Dr Musa M. Watila
NIHR UCLH Biomedical Research Centre, UCL Institute of Neurology, London WC1N 3BG.
Epilepsy Society, Chalfont Centre for Epilepsy, Chalfont St Peter SL9 0RJ, UK.
University of Maiduguri, Borno State, Nigeria

1. Geopolitical zone of practice (Select one option)

☐ North-east ☐ North-central ☐ North-west
☐ South-west ☐ South-east ☐ South-south

2. Specialty/Designation (Select one option)

☐ Neurologists ☐ Psychiatrist ☐ Neurosurgeon ☐ Internal Medicine

☐ Specialist (senior) registrar in Neurology ☐ Specialist (senior) registrar in psychiatry

☐ Specialist (senior)registrar in Neurosurgery ☐ Specialist (senior)registrar in Internal medicine

☐ Registrar ☐ General physicians involved in epilepsy care ☐ Medical officer

☐ Doctoral/post-doctoral personnel ☐ Other (Please specify)- …… _____

3. Area of Specialisation (Select one option)

☐ Paediatric doctor ☐ Adult doctor ☐ Both Paediatric and adult

4. Setting of Practice - 1 (Select one option)

☐ Rural ☐ Urban ☐ Both

5. Setting of Practice - 2 (tick as many applicable)

☐ Government owned tertiary teaching hospital ☐ Government owned secondary (district) hospital ☐ Government owned rural/primary care ☐ Private owned hospital
☐ Specialist epilepsy care - Government/public owned ☐ Specialist epilepsy care - Private owned

6. How often do you attend to or treat children or adults with epilepsy? (Select one option)

☐ Never
☐ Rarely
☐ Sometimes
☐ Quite often
☐ Very frequently

8. Do you have a formal training in epileptology/epilepsy care? (Select one option)

☐ To a Great Extent
☐ Somewhat
☐ Very Little
☐ Not at All
☐ Give an example of training _____

8. How many years have you been involved in rendering epilepsy care? (Select one

option)

☐ < 5 years ☐ 5 to 9 years ☐ 10 to 14 years

☐ 15 to 19 years ☐ 20 to 24 years ☐ > 25 years

9. On average how many epilepsy patients do you attend to in a week?

_____

10. What antiepileptic drugs are readily available to patients in your locality? (tick as many)

- ☐ Phenobarbitone
- ☐ Phenytoin
- ☐ Carbamazepine
- ☐ Oxcarbamezpine
- ☐ Sodium valproate
- ☐ Lamotrigine
- ☐ Topiramate
- ☐ Levetiracetam
- ☐ Clobazam
- ☐ Tiagabine
- ☐ Clonazepam
- ☐ Diazepam
- ☐ Nitrazapam
- ☐ Zonisamide
- ☐ Rufinamide
- ☐ Ethosuxumide
- ☐ Vigabatrin
- ☐ Pregabalin
- ☐ Gabapentin
- ☐ Felbamate
- ☐ Lancosimide
- ☐ Pyridoxine
- ☐ Acetazolamida
- ☐ ACTH
- ☐ Other (Please specify) _____

11. Which of these facilities do you have functioning in your centre? (tick as many available)

- ☐ EEG
- ☐ EEG telemetry
- ☐ CT machine
- ☐ MRI machine
- ☐ SPECT
- ☐ PECT

12. What is the average cost of a routine EEG investigation? (In Naira)

_____

13. What is the average cost of CT head investigation? (In Naira)

_____

14. What is the average cost of an MRI Brain? (In Naira)

_____

15. Is epilepsy surgery offered to patients in your centre? (Select one option)

- ☐ Yes Please specify procedure(s) _____
- ☐ No
- ☐ Don't know

16. To what extent do you agree that surgical treatments for epilepsy are effective? (Select one option)

- ☐ Strongly Agree
- ☐ Agree
- ☐ Undecided
- ☐ Disagree
- ☐ Strongly Disagree
- ☐ If 'No' (Please specify why) _____

17. Will you refer a patient with intractable epilepsy for surgery? (Select one option)

- ☐ Definitely
- ☐ Probably
- ☐ Possibly
- ☐ Probably Not
- ☐ Definitely Not

18. Have you ever referred a patient for epilepsy surgery? (Select one option)

- ☐ Yes
- ☐ No
- ☐ Don't know
- ☐ If 'yes' (Please specify where) _____

19. If you do not offer epilepsy surgery. What is (are) the limiting factors in your centre?

- ☐ Lack of trained personnel
- ☐ Lack of Infrastructure
- ☐ Cost of surgery
- ☐ Electricity supply
- ☐ Brain drain
- ☐ Political will
- ☐ Others (Please specify) _____

20. Which of these alternative treatment(s) do you have experience with in your centre?

- ☐ Vagus nerve stimulation
- ☐ The ketogenic diet
- ☐ Deep brain stimulation
- ☐ Trigeminal nerve stimulation

21. Are these alternative treatment options effective? (Select one option)

- ☐ Very effective
- ☐ Somewhat effective
- ☐ Undecided
- ☐ Unlikely to be effective
- ☐ Not effective

22. Do you have the drugs to manage status epilepticus readily available? (Select one option)

- ☐ Yes
- ☐ No
- ☐ Don't know

23. Which of these drugs for treating Status epilepticus is (are) readily available? (tick as many available)

- ☐ Diazepam
- ☐ Lorazepam
- ☐ Midazolam
- ☐ IV phenytoin

- ☐ IV fosphenytoin
- ☐ IV Phenobarbtal
- ☐ IV Pentobarbital
- ☐ IV valproate
- ☐ IV levetiracetam
- ☐ IV paraldehyde
- ☐ Thiopentone
- ☐ IV Thiamine
- ☐ Propofol
- ☐ Ketamine

24. Which of these health care personnel are involved with epilepsy care in your centre? (tick as many available)

- ☐ Neurologist
- ☐ Psychiatrist
- ☐ Neurosurgeon
- ☐ Specialist (senior) registrar in Neurology
- ☐ Specialist (senior) registrar in psychiatry
- ☐ Specialist registrar in Neurosurgery
- ☐ General physicians involved in epilepsy care
- ☐ Epilepsy specialist nurse
- ☐ Psychologist
- ☐ Physiotherapy
- ☐ Dietician
- ☐ Social worker
- ☐ Community health worker
- ☐ Others

25. Are training programs available for health care personnel in epileptology in your centre? (Select one option)

- ☐ To a Great Extent
- ☐ Somewhat
- ☐ Very Little
- ☐ Not at All
- ☐ Give example of type of training …… _____

26. Do you belong to an international epilepsy or neurological society? (Select one option)

- ☐ Yes

- No
- Don't know
- if yes, please specify society _____

27. How often are you involved in epilepsy research? (Select one option)

- Often
- Sometimes
- Seldom
- Never
- If yes give example _____

28. Do you have publications related to epilepsy? (Select one option)

- Yes
- No
- Don't know

29. In general, how do you rate the support and care people with epilepsy get in Nigeria? (Select one option)

- Very Good
- Good
- Fair
- Poor
- Very poor

30. Are you satisfied with the role the government is playing in the care and support of PWE? (Select one option)

- Very satisfied
- Satisfied
- Neither
- Dissatisfied
- Very dissatisfied

31. How satisfied are you with role non-governmental organization(s) (NGOs) play in epilepsy care in your community? (Select one option)

- Very satisfied
- Satisfied
- Neither
- Dissatisfied
- Very dissatisfied

32. Do you know of any non-governmental organisation (NGO) involved with epilepsy care in your area of practice? (Select one option)

- Yes

- No
- Don't know

34. To what extent people with epilepsy receive adequate information about their condition?
(Select one option)

- To a Great Extent
- Somewhat
- Very Little
- Not at All

35. To what extent do you think people with epilepsy in Nigeria receive adequate psychosocial support?
(Select one option)

- To a Great Extent
- Somewhat
- Very Little
- Not at All

36. To what extent do you think the rights of people with epilepsy are denied? (Select one option)

- To a Great Extent
- Somewhat
- Very Little
- Not at All

37. How often do you think people with epilepsy attend 'traditional healers' before seeking treatment in hospitals? (Select one option)

- Always
- Very Frequently
- Occasionally
- Rarely
- Very Rarely
- Never

38. To what extent do you think 'traditional' and 'spritual' healers negatively affect people with epilepsy from seeking medical treatment? (Select one option)

- To a Great Extent
- Somewhat
- Very Little
- Not at All

39. How useful do you think education of and interaction with traditional healers will help patients' health-seeking behaviour? (Select one option)

- Very useful
- Useful
- Moderately useful
- Slightly useful
- Not useful

40. How likely will you be willing to work together with a 'traditional healer' regarding epilepsy care? (Select one option)

- Not likely
- Somewhat likely
- Very likely

42. What are some of the most important challenges to epilepsy care in Nigeria? You can list up to 5 challenges starting with the one you think is most important?

_____
_____

43. What suggestions do you have in improving epilepsy care in Nigeria?

_____
_____

Appendix 8

Ethical Approvals

UCL RESEARCH ETHICS COMMITTEE
OFFICE FOR THE VICE PROVOST RESEARCH

5th March 2018

Professor Sander
Department of Clinical and Experimental Epilepsy
Institute of Neurology
UCL

Dear Professor Sander

Notification of Ethics Approval with Provisos
Project ID/Title: 11229/001: Standard of care for people with epilepsy in sub-Saharan Africa. The case of Nigeria

Further to your satisfactory responses to the Committee's comments, I am pleased to confirm in my capacity as Joint Chair of the UCL Research Ethics Committee (REC) that the data collection element of your study has been ethically approved by the UCL REC until **5th March 2019.**

Ethical approval is subject to the following conditions.

Notification of Amendments to the Research
You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form'
http://ethics.grad.ucl.ac.uk/responsibilities.php

Adverse Event Reporting – Serious and Non-Serious
It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Final Report
At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research i.e. issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.

1

National Health Research Ethics Committee of Nigeria (NHREC)

Promoting Highest Ethical and Scientific Standards for Health Research in Nigeria

Federal Ministry of Health

NHREC Protocol Number NHREC/01/01/2007-4/12/2017
NHREC Approval Number NHREC/01/01/2007-26th/02/2018
Date: 26th February, 2018

Re: Standard of care for people with epilepsy in Sub-Saharan Africa: The case of Nigeria

Health Research Ethics Committee (HREC) assigned number: NHREC/01/01/2007

Name of Student Investigator: Dr. Watila M. Musa
Address of Student Investigator: Institute of Neurology
University College London
Queen's Square, London, UK.
E-mail: watilamusa@yahoo.com,
Tel: +447586535394 (UK MOBILE); +2348076260351

Date of receipt of valid application: 4-12-2017
Date when final determination of research was made: 26-02-2018

Notice of Continuing Review and Approval

This is to inform you that the research described in the submitted protocol the consent forms, advertisements and other participant information materials have been reviewed and *expedited committee approval by the National Health Research Ethics Committee for the study to continue for another one year.*

The approval for this study is from 26/02/2018 to 25/02/2019. If there is delay in starting the research, please inform the HREC so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the HREC assigned number and duration of HREC approval of the study.* In multiyear research, endeavour to submit your annual report to the HREC early in order to obtain renewal of your approval and avoid disruption of your research.

The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the HREC. No changes are permitted in the research without prior approval by the HREC except in circumstances outlined in the Code. The HREC reserves the right to conduct compliance visit your research site without previous notification.

Signed

[redacted]

Professor Zubairu Iliyasu MBBS (UniMaid), MPH (Glasg.), PhD (Shef.), FWACP, FMCPH
Chairman, National Health Research Ethics Committee of Nigeria (NHREC)

Department of Health Planning, Research & Statistics
Federal Ministry of Health
11th Floor, Federal Secretariat Complex Phase III
Ahmadu Bello Way, Abuja

Tel: +234-09-523-8367
E-mail: chairman@nhrec.net, secretary@nhrec.net,
deskofficer@nhrec.net,
URL: http://www.nhrec.net,

Appendix 9

Patient Information Sheet for adult participants (a modified one for minors or cognitively impaired)

Nigerian Health and Research Ethics Committee (NHREC) Approval ID Number: _____

UCL Research Ethics Committee Approval ID Number: _____

Title of Study: Standard of care for people with epilepsy in Sub-Saharan Africa: the case of Nigeria

Department: Department of clinical and experimental epilepsy, UCL IoN.

Name and Contact Details of the Researcher(s):_____

Name and Contact Details of the Principal Researcher:_____

You have been invited to participate in a research project that will help us understand more about epilepsy in Nigeria. Before you make your decision to participate, we wish to inform you about what the research is all about. You will be given a copy of the information sheet. If there is anything you do not understand, you can ask a member of the team to read and explain it in the language you know.

Purpose:
This study will be useful in understanding the number of people with epilepsy, the characteristics and issues of management. However, one important thing we do know is that people with epilepsy can be managed properly and do get better.

Participants:
You will be included in this study because you have or suspected to have epilepsy and live in this part of Nigeria.

Do I have a choice to participate or not?
You have freewill to participate or decline. If you agree to take part in the study, we will give you a consent form to read and sign. If you do you not wish to participate, it will in no way affect your treatment.

Procedures if you agree to participate:
While conducting the study, a member of the team will ask you some questions regarding your health, and carry out a physical examination if needs be. None of our procedure are harmful. All the information you give us and the result of the test will be stored in a file and also the principal investigators computers and analysed, the information will be kept confidential and would be used only for the purpose of this study. No other use will be made of them without your written permission.

Study Benefits:
This study will provide an opportunity for your condition to be evaluated extensively. If you require treatment, we will send you to where you can get help and compensate for your journey.

Is there any harm from the study?
Apart from the discomfort and the time spent coming to the health centre, taking a history and performing a physical examination, we do not anticipate any harm from the study. We understand that you may feel some distress with the questions asked, we assure you that we are here to give you the necessary help.

What if something goes wrong?
If you have any complaint or something serious happens related to the study you should contact Dr Musa Watila or any member of the team.

Who is (are) responsible for the study and funding?

Professor Ley Sander is the overall supervisor and the guarantor for the study. Dr. Musa Watila is also an investigator; he is a registered doctor and Neurologist with the Medical and Dental Council of Nigeria. He is currently doing a PhD with the UCL. The Commonwealth Scholarship Commission UK is funding the research.

Who has approved the Study?
The National Health and Research Ethics Committee of Nigeria (FMOH) and the UCL Research Ethics Committee UK have given their approvals.

What will happen to the results of the study?
The results will be published in a thesis and journal. A copy of the results will be made available at the nearest health centre to you. You will not be identified in any of the report or publication. Depending on the results you may be called in the future for a subsequent research. The data controller for this project will be UCL. The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data and your personal data will be processed for the purposes as outlined.

Who to contact for further information?
You are free to ask any question regarding the study. If you need any further information please contact any of the team members below.

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Dr. Morenikeji Komolafe – OAUTH, +2348034036351

Dr Igwe Stanley – FTHA, +23480605728882

Thank you for reading this information sheet and for considering to take part in this research study.

Appendix 10

Consent form (this was modified to an assent form for children)

(If subject is < 18 years and married or lives alone or independent; this form should be given)

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

If the subject cannot read nor has problem with understanding, the consent form should be read and explained to them in the language they understand by a team member.

Title of Study: Standard of care for people with epilepsy in Sub-Saharan Africa: the case of Nigeria

Department: Department of clinical and experimental epilepsy, UCL IoN.

Name and Contact Details of the Researcher(s):_____

Name and Contact Details of the Principal Researcher: Prof Ley Sander, Department of clinical and experimental epilepsy, UCL IoN.

This study has been approved by the Nigerian Health and Research Ethics Committee (NHREC) Approval ID Number: _____

This study has been approved by the UCL Research Ethics Committee: Project ID number: _____

Thank you for considering taking part in this research. The research must be explained to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes means that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element that I may be deemed ineligible for the study.

		Tick Box
1.	*I confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction *and would like to take part in* *(please tick one or more of the following)* - *an individual interview* - *an examination*	
2.	*I understand that I will be able to withdraw my data at any time during the study, but before data is analysed.	
3.	*I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be handled in accordance with all applicable data protection legislation.	
4.	*I understand that all personal information will remain confidential and that all efforts will be made to ensure I cannot be identified. I understand that my data gathered in this study will be stored anonymously and	

	securely. It will not be possible to identify me in any publications.	
5.	*I understand that my information may be subject to review by responsible individuals from the UCL for monitoring and audit purposes.	
6.	*I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason, without affecting the care I receive. I understand that if I decide to withdraw, any personal data I have provided up to that point will be deleted unless I agree otherwise.	
7.	I understand the potential risks of participating and the support that will be available to me should I become distressed during the course of the research.	
8.	I understand the direct/indirect benefits of participating.	
9.	I understand that the data will not be made available to any commercial organisations but is solely the responsibility of the researcher(s) undertaking this study.	
10.	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
11.	I agree that my anonymised research data may be used by others for future research.	
12.	I understand that the information I have submitted will be published as a report and I wish to receive a copy of it. Yes/No	
13.	I hereby confirm that I understand the inclusion criteria as detailed in the Information Sheet and explained to me by the researcher.	
14.	I agree that my doctors may be contacted if any unexpected results are found in relation to my health.	
15.	I am aware of who I should contact if I wish to lodge a complaint.	
16.	I voluntarily agree to take part in this study.	
17.	I would be happy for the data I provide to be archived at UCL institute of Neurology.	
18.	I understand that my personal data will be transferred to the UCL institute of neurology for analysis and the following safeguards will be put in place: Only the principal investigator and co-principal investigators will have access to the data. We will anonymize all data by removing identifiable information. All data will be stored in password protected computer(s). All hard copies of patient information will be kept safe and locked.	

If you would like your contact details to be retained so that you can be contacted in the future by UCL researchers who would like to invite you to participate in follow up studies to this project, or in future studies of a similar nature, please tick the appropriate box below.

Yes, I would be happy to be contacted in this way

No, I would not like to be contacted

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of witness (If applicable)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

Appendix 11

The Translated Epilepsy Screening Questionnaires

a. Igbo version

Household ID number:_____ Serial number:_____ Date:_ _ / _ _ / _ _ _ _		
Name(s) of Enumerators: 1. _____ 2. _____		
Horo Aziza [✓]	*Mba*	*Ee*
1. inwetula oria ukwu na aka ima jijiji nke na inweghi ike ijide onwe gi?		
2. Onwutula mgbe imataghi onwe gi, da na ala ihu agbaruo gi?		
3. Onwetula mgbe inweturula oria nke mere gi ida na ala tabisie ire gi?		
4. Onwetula mgbe inweturula oria nke mere gi ida na ala baa onwe gi mamiri?		
5. Onwetula mgbe inweturula oria neme otu aka gi, otu ukwu gi ma obu ihu gi ima jijiji nwa obere oge?		
6. Onwetula mgbe inweturula oria nke mere gi amatazigi gburugburu ebe ino ma nuwazie isi ojoo?		
7. Onwere mgbe obula na mgbe idi ntakiri ina eche oke echiche ma obu na ele anya puru iche karia umu ntakiri ndi uzo?		
8. Ngwa-ngwa itetara na ura na ututu ma obu na ehihe, onwetula mgbe ichoputara na ahu na ama gi jijiji ma obu ihe idanarigi na aka na amaghi ama?		
9. Onwere mgbe obula agwaturula gi na inwere oria akwukwu ma obu ihe yiri ya, ma obu inutu ogwu akwukwu ma obu nke yiri ya?		

b. Yoruba version

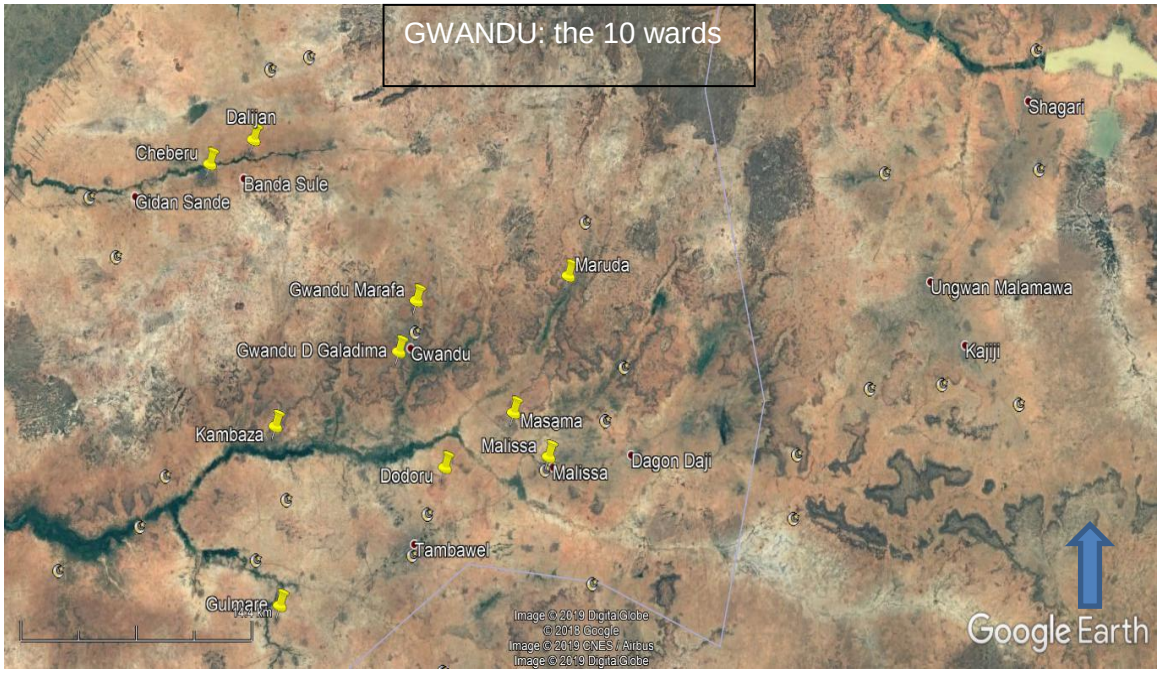
Household ID number:_____ Serial number:_____ Date:_ _ / _ _ / _ _ _ _		
Name(s) of Enumerators: 1. _____, 2. _____		
Jowo dahun awon Ibeere wonyi: ✓	Beeko	Beeni*
1. Nję o ti fi igba kan ni aisan ese tabi owo to ngbon-riri ti e kole dekun re?		
2. Nję o ti daku tabi subu lule ti o si funfun ni'gba kan ri?		
3. Nję o fi igbakan ni ikolu ti o mu o subu lulę ti o si ge ahon rę ję?		
4. Nję o ti fi igbakan ni ikolu ti o mu o subu, ti o si to sara laimo?		
5. Nję o ti fi igbakan ni ikolu ranpę to mu o maagbon-pipi l'apa kan, l'ęsę kan tabi l'oju?		
6. Nje o ti fi igbakan ni ikolu ti o mu ma mo ibi ti o wa tabi ti o mu o n gbo oorun abami?		
7. Nję, nigba ewe, o ti fi igbakan ma n lá álà ọ̀sán gan tabi ma wo bọọn?		
8. Nję o ti se akiyesi ri pe nigbati o ji lati oju orun, yala ni aaro ni abi ni osan, o wa ni airorun tabi ti ara rę ngbon-riri to bęę ti nkan jabo tabi fo danu lowo rę?		
9. Nję won so fun o ri pe o ni aisan giri tabi o fi igbakan lo oogun giri ri?		

c. Hausa version

Household ID number:_____ Serial number:_____ Date:_ _ / _ _ / _ _ _ _		
Name(s) of Enumerators: 1. _____, 2. _____		
Zabi daya ✓	Babu	a
1. Ka/Kin taba samun jijjigan ko motsin hannuwa ko kafafuwa da bashi da ikon dainawa da kanshi?		
2. Ka/Kin taba fadi ko ka/kin yi dogon suma kuma sai jiki yayi fari fat?		
3. Ka/Kin taba fadi ka/kin cije harshen ka/ki?		
4. Ka/Kin taba shiga wani yanayi na faduwa da sakar fistari ba tare da tsanin ka/ki ba?		
5. Ka/Kin taba samun jijjigan bangaren jiki kaman hannu, kafa ko fuska?		
6. Ka/Kin taba fita daga cikin hayyacin ka/ki, sannan ka/kin ji wani wari/kamshi?		
7. Shin, a lokacin da Kake/Ki ke yaranta ka/kin taba shiga yanayin da za ka/ki yi shuru ka/ki kalli wuri guda fiye da sauran yara?		
8. Jim kadan bayan tashi daga barci, ko da safe ko bayan wani ɗan rurumi ka/kin taba lura ka/ki na yawan yar da abun da Ka/Ki ke rike da shi ba tare da niyan yar da shi ba?		
9. An taba gaya ma Ka/Ki cewa kana/kina da bugun tsunsu ko ka/kin taba shan maganin cutar farfadiya?		

Appendix 12

Google earth maps showing location of these wards




IJEBU-JESA
Iwoye
Ijebu Jesa
1135 m
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Image © 2019 DigitalGlobe

Appendix 13

Performance and positive response rates to individual 9-item screening questions for the three sites

	Afikpo (Igbo questionnaire)			Ijebu-Jesa (Yoruba questionnaire)			Gwandu (Hausa questionnaire)		
Questions	**Number of positive responses**	**% of total population (N=15,738)**	**% of those screening positive (Stage 1) (n=104)**	**Number of positive responses**	**% of total population (N=10,316)**	**% of those screening positive (Stage 1) (n=121)**	**Number of positive responses**	**% of total population (N=16,373)**	**% of those screening positive (Stage 1) (n=384)**
1. Have you or anyone in this household ever had attacks of twitching, jerking or shaking of the arms or legs which you/they could not control?	79	0.50	76.0	60	0.58	50.0	162	0.99	42.2
2. Have you or anyone in this household ever lost consciousness; or fallen and become pale?	59	0.38	56.7	31	0.30	25.6	83	0.51	21.6
3. Have you or anyone in this household ever had attacks in which you/they fall and bite your tongue?	38	0.24	36.5	12	0.12	9.9	114	0.70	29.7
4. Have you or anyone in this household ever had attacks in which you/they fall and lose control of your/their bladder?	48	0.31	46.2	12	0.12	9.9	70	0.43	18.2
5. Have you or anyone in this household ever had brief attacks of shaking or trembling in one arm or leg, or face?	47	0.30	45.2	30	0.29	24.8	140	0.86	36.5

6. Have you or anyone in this household ever had attacks in which you/they lose contact with your/their surroundings and experience abnormal smells?	32	0.20	30.8	15	0.15	12.4	75	0.46	19.5
7. Did you or anyone in this household when you/they were a small child, daydream or stare into space more than other children?	38	0.24	36.5	16	0.16	13.2	106	0.65	27.6
8. Shortly after waking up, either in the morning or after a nap have you or anyone in this household ever noticed uncontrolled jerking or clumsiness, such as dropping things or things suddenly "flying" from your/their hands?	39	0.25	37.5	21	0.20	17.4	105	0.64	27.3
9. Have you or anyone in this household ever been told that you/they have or have had epilepsy or epileptic fits, or have taken medication for seizures/epilepsy?	41	0.26	39.4	58	0.56	47.9	131	0.80	34.1
Percentages are those of the previous column									

Appendix 14

A detailed population of persons screened and outcome of screening by ward/enumeration area

Local Government Area	Wards/ Communities	Number of households visited (%)	Number of people enumerated (6 years & above)	Female	Number positive 1st stage	Number responded for 2nd stage	Confirmed
Afikpo North	**Ohaisu (All)**	1,920 (56.8%)	9,459 (60.1%)	4,792 (50.7%)	67 (0.7%)	47 (70.1%)	31 (66.0%)
	Amangbala	519 (15.4%)	2,444	1,176 (48.1%)	22 (0.9%)	16 (72.7%)	10 (62.5%)
	Amachi	479 (14.2%)	1,755	955 (54.4%)	14 (0.8%)	6 (42.9%)	6 (100.0%)
	Amachara	220 (6.5%)	1,267	648 (52.0%)	2 (0.2%)	2 (100%)	2 (100.0%)
	Ngodo	264 (7.8%)	1,247	672 (53.9%)	24 (1.9%)	19 (79.2%)	11 (57.9%)
	Ukpa	438 (13.0%)	2,746	1,341 (48.8%)	5 (0.2%)	3 (60.0%)	2 (66.7%)
	Nkpoghoro (All)	1,458 (43.2%)	6,279 (39.9%)	3,227 (51.4%)	37 (0.6%)	14 (37.8%)	12 (85.7%)
	Ndibe	317 (9.4%)	1,421	762 (53.6%)	12 (0.8%)	4 (33.3%)	4 (100.0%)
	Amankwo	272 (8.1%)	1,118	570 (51.0%)	3 (0.3%)	0 (0%)	0 (0.0%)
	Amaobolobo	116 (3.4%)	451	223 (49.4%)	2 (0.4%)	0 (0%)	0 (0.0%)
	Amauzu	224 (6.6%)	889	435 (48.9%)	14 (1.6%)	10 (71.4%)	7 (70.0%)
	Amaoku	134 (4.0%)	603	334 (55.4%)	6 (1.0%)	1 (16.7%)	1 (100.0%)
	Amangwu	133 (3.9%)	708	369 (52.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Amaekwu	262 (7.8%)	1,089	534 (49.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Afikpo (Total)	3,378	15,738	8,019 (50.9%)	104 (0.66%)	61 (58.7%)	43 (70.5%)
Gwandu	Cheberu	295 (9.6%)	1,752	852 (48.6%)	65 (3.7%)	31 (47.7%)	23 (74.2%)
	Dalijan	298 (9.7%)	1,890	904 (47.8%)	47 (2.5%)	32 (68.1%)	24 (75.0%)
	Dodoru	314 (10.2%)	1,832	854 (46.6%)	37 (2.0%)	37* (94.6%)	34 (91.9%)
	Gulmare	305 (9.9%)	1,261	614 (48.7%)	23 (1.8%)	9 (39.1%)	7 (77.8%)
	Gwandu Dangidan Galadima	300 (9.8%)	1,401	749 (53.5%)	44 (3.1%)	36 (81.8%)	26 (72.2%)
	Gwandu Marafa	299 (9.7%)	1,434	686 (47.8%)	39 (2.7%)	33 (84.6%)	21 (63.6%)
	Kambaza	307 (10.0%)	1,880	910 (48.4%)	31 (1.7%)	20 (64.5%)	12 (60.0%)
	Malisa	349 (11.4%)	1,986	968 (48.7%)	38 (1.9%)	25 (65.8%)	17 (68.0%)
	Maruda	303 (9.9%)	1,505	760 (50.5%)	32 (2.1%)	31 (96.9%)	26 (83.9%)
	Masama	305 (9.9%)	1,432	579 (40.4%)	28 (2.0%)	24 (85.7%)	21 (87.5%)
	Gwandu (total)	3,075	16,373	7,876 (48.1%)	384 (2.4%)	278 (72.4%)	211 (75.9%)
Oriade	**Ijebu-Jesa (total)[§]**	3,996	10,316	5,398 (52.3%)	121 (1.2%)	104 (86.5%)	26 (25.0%)

*Afikpo has two main wards (Ohaisu and Nkpoghoro) that consist of 12 wards. *35 persons from the original responded, 2 additional persons who were not screened in the first stage reported for second stage screening. [§] Ijebu-Jesa is considered a single ward in Oriade local government area. Although it has a clear boundary with neighboring wards. It has 166 small .enumeration area. It is supposed to have 16 communities but we were unable to get clear demarcations. Percentages are those of the previous column.*

Appendix 15

Possible reason or medical conditions of those not screening positive at stage 2

Diagnosis	Afikpo (N=18)	Ijebu-Jesa (N=78)	Gwandu (N=67)
Essential tremor	3	1	3
Febrile seizure(s)	1	10	19
Parkinson's disease	3	1	4
Other movement disorder	1	0	2
Paraesthesia	-	-	0
?Drop attack	-	0	2
Diabetic neuropathy (Paraesthesia)	3	-	1
Single seizure	1	2	10
Syncope	-	1	2
Musculoskeletal (joint problems)	-	2	-
Respiratory (tuberculosis)	-	1	-
Hypertension	1	-	-
Stroke	1	-	-
Eclampsia	-	-	6
Sleep disturbance	-	-	2
Family history only	-	1	1
Unknown (or false response*)	1	57	15
*Some persons attended the second stage just because they heard some medical personnel where in town			

Appendix 16

a. Results of prevalence of active epilepsy in Africa and where our estimates lie

Author-Date	Region/community	Country	Age	Prevalence *
Prischich (2008)	Littoral Province	Cameroon	All ages	105
Sebera et al., 2015	-	Rwanda	All ages	41
Osuntokun et al., 1982	Aiyete (pilot study)	**Nigeria**	**All ages**	**37**
Almu (2006)	Zay Society Rift Valley	Ethiopia	All ages	29.5
Osakwe et al., 2014	Ochiohu, Izzi LGA, Ebonyi	**Nigeria**	**All ages**	**20.8**
PRESENT STUDY	**10 wards in Gwandu LGA Kebbi State**	**Nigeria**	**≥ 6 years**	**17.7**
Balogou (2007)	Batamariba district	Togo	All ages	15.7
Farnarier et al., 2000	Tyenfala & Baguineda	Mali	-	13.4
Birbeck (2004)	Chikankata	Zambia	All ages	12.5
Rwiza (1992) 1994	Ulanga district	Tanzania	All ages	12.1
Mungala-Odera(2006)	Kilifi district	Kenya	Children	11
Khedr (2013)	Assiut governorate	Egypt	All ages	9.3
Winkler (2009)	Haydom district	Tanzania	All ages	8.7
Dent (2005)	Nachingwea district	Tanzania	All ages	8.6
Yemadje (2012)	12 regions	Benin	All ages	8.1
Avode (2003)	Cotonou	Benin	Children & adolescents	7.9
Simms (2008)	National sample	Rwanda	All ages	7
Christianson (2000)	Bushbuckridge Northern Province	South Africa	Children	6.7
Longe and Osuntokun (1989)	Udo	**Nigeria**	**All ages**	**6.2**
Ezeala-Adikaibe et al., 2016	Agu-Abor and Ugbodogwu Enugu	**Nigeria**	**All ages**	**6**
Osuntokun et al. 1987a, Osuntokun et al. 1987b	Igbo-Ora	**Nigeria**	**All ages**	**5.3**
Tekle-Haimanot (1990)	Central region of Shoa	Ethiopia	All ages	5.2
El Tallawy (2013)	Al Kharga district	Egypt	All ages	5.0
PRESENT STUDY	**Ohaisu and Nkpoghoro communities of Afikpo North LGA, Ebonyi State**	**Nigeria**	**≥ 6 years**	**4.8**
Osakwe et al., 2014	Ogobia , Otukpo LGA, Benue State	**Nigeria**	**All ages**	**4.7**
Mustapha et al. (2014), Mustapha and Preux (2015)	Ilie	**Nigeria**	**All ages**	**4.5**
Coleman (2002)	Farafenni district	Gambia	All ages	4.3
Nwani (2013)	Ukpo, Anambra State	**Nigeria**	**All ages**	**4.3**
Attia-Romdhane (1993)	Kelibia	Tunisia	All ages	4.2
Ngugi (2013)	Ifakara	Tanzania	All ages	3.9

Nitiema (2012)	Batondo, Nyonyogo, and Pabré villages	Burkina Faso	All ages	3.9
Kaamugisha (1988)	Nakuru Municipality	kenya	All ages	3.6
PRESENT STUDY	**Ijebu-Jesa, Oriade LGA Osun State**	**Nigeria**	**≥ 6 years**	**3.3**
Ngugi (2013)	Kilifi district	Kenya	All ages	3.0
Ngugi (2013)	Agincourt	South Africa	All ages	3.0
Edwards (2008)	Kilifi district	Kenya	All ages	2.9
Ngugi (2013)	Kilifi district	Kenya	All ages	2.9
Burton et al., 2012	Hai district	Tanzania	All ages	2.9
Hunter (2012)	Hai district	Tanzania	All ages	2.8
Ngugi (2013)	Iganga-Mayuge	Uganda	All ages	2.4
Ngugi (2013)	Kintampo	Ghana	All ages	2.2

***** The prevalence is sorted from the highest to the lowest. We acknowledge that we may have missed some prevalence studies in Africa during our search.

b. Results of lifetime prevalence of epilepsy in Africa and where our estimates lie.

Author-Date	Region/community	Country	Age	Prevalence
Njamnshi (2007)	Bilomo village	Cameroon	All ages	49.0
Colebunders et al., 2016	Dingila	Congo DRC	All ages	29.0
Colebunders et al., 2016	Titule I and II	Congo DRC	All ages	23.0
Debrock (2000)	Yevié and Zinvié-Zoumé	Benin	Children & adolescents	21.1
PRESENT STUDY	**10 wards in Gwandu LGA Kebbi State**	**Nigeria**	**≥ 6 years**	**19.8**
Ndoye (2005)	Pikine	Senegal	All ages	14.2
Khedr (2013)	Assiut	Egypt	All ages	12.7
Rwiza (1992) 1994	Ulanga	Tanzania	All ages	11.4
Winkler (2009)	Haydom	Tanzania	All ages	11.2
Houinato (2013)	Djidja community	Benin	All ages	10.5
Couper (2002)	Kwazulu Natal	South Africa	Children	9.0
Druet-Cabanac (1998)	Ngaoundaye	Central African Republic	All ages	7.8
Christianson (2000)	Bushbuckridge	South Africa	Children	7.3
Mahmoud (2009)	El-Minia City	Egypt	Children	7.2
Tamrat (2001)	Dabat	Ethiopia	All ages	7.1
El Tallawy (2010)	Al Kharga	Egypt	All ages	7.0
Adoukonou et al., 2013	Tourou	Benin	All ages	7.0
El Tallawy (2013)	Al Kharga	Egypt	All ages	6.8
El Tallawy (2013)	Al Quseir City	Egypt	All ages	5.5
Bondestam (1990)	Zanzibar	Tanzania	All ages	4.9
PRESENT STUDY	**Ohaisu and Nkpoghoro, Ebonyi State**	**Nigeria**	**≥ 6 years**	**4.8**
Nitiema (2012)	Batondo, Nyonyogo and Pabré	Burkina Faso	All ages	4.5
Talaat (2009)	El Manyal Island	Egypt	Children & adolescents	4.4
Snow (1994)	Kilifi district	Kenya	Children	4.0
PRESENT STUDY	**Ijebu-Jesa, Oriade LGA Osun State**	**Nigeria**	**≥ 6 years**	**3.6**
Duggan, 2010	Rukungiri District	Uganda	Children	2.0

***** The prevalence is sorted from the highest to the lowest. We acknowledge that we may have missed some prevalence studies in Africa during our search.

Appendix 17

The multiple imputations scheme

misstable summarize

Variable	Obs-	Obs>.	Obs<.	Unique values	Min	Max
Distance_to_facility_Km	156	96		19	0	100
Transport cost	159	93		20	30	2500
Cost of ASM	190	62		23	0	15000
Seizure frequency_CAT	2	250		5	1	5

Missing variables and predictive model type for imputation								
S/No	**Variable**	**Type**	**Number**	**Number missing**	**% missing**	**Predictive model type for imputation**	**Predictor variables for**	
							Access to care	**Adherence**
1.	Agecat18	Dichotomous	252	NIL	-		✓	✓
2.	Religion	unordered categorical	252	NIL	-		✓	✓
4	Gender	Dichotomous	252	NIL	-		✓	✓
5	Marital status	unordered categorical	252	NIL	-		✓	✓
6	At least primary education	Dichotomous	252	NIL	-		✓	✓
7	Employment	ordered categorical	252	NIL	-		✓	✓
8	Duration of epilepsy	ordered categorical	252	NIL	-		✓	✓
9	Seizure timing	ordered categorical	252	NIL	-		✓	✓
10	Status epilepticus	Dichotomous	252	NIL	-		✓	✓
13	Learning difficulty	Dichotomous	252	NIL	-		✓	✓
15	Health insurance	Dichotomous	252	NIL	-		✓	✓
16	Rejection of diagnosis	Dichotomous	252	NIL	-		✓	✓
17	Patient misconception	Dichotomous	252	NIL	-		✓	✓
18	Stigma	Dichotomous	252	NIL	-		✓	✓
18	Unavailability of drugs	Dichotomous	252	NIL	-		×	✓
19	Lack of medical personnel	Dichotomous	252	NIL	-	-	×	✓
20	Cost of drugs	Dichotomous	252	NIL	-		×	✓
21	Rejection of treatment by patient	Dichotomous	252	NIL	-		×	✓
22	Cultural belief	Dichotomous	252	NIL	-		✓	✓
24	Seizure-related injury	Dichotomous	252	NIL	-		✓	✓
25	Type of epilepsy	unordered categorical	252	NIL	-	Multinomial logistic regression (mlogit)	✓	✓
26	Distance to facility_km	Ordered categorical	96	156	61.9	Ordered logistic regression (ologit)	✓	✓
28	Transport cost hospital	Ordered categorical	93	159	63.1	Ordered logistic regression (ologit)	✓	✓
29	Cost of ASM	Ordered categorical	62	190	75.4	Ordered logistic	×	✓

						regression (ologit)		
30	Seizure frequency_CAT	Ordered categorical	250	2	0.8	Ordered logistic regression (ologit)	✓	✓

1. STATA COMMAND - ACCESS TO CARE (for TABLE 3)

- mi set wide
- mi register imputed distance_kmCAT transportcostCAT seizurefrequency_CAT
- mi register regular attendedhospital agecat18yrs gendercat religion maritalstatus atleastprimary employmentCAT ageatonsetCAT durationofepilepsyCAT EpilepsytypeCAT seizuretiming se cognitivedecline lackofaccesstohealthcare rejectionofdiagnosisbypatientorr patientsmisconception stigma culturalbelief injury
- mi impute chained (ologit) distance_kmCAT transportcostCAT seizurefrequency_CAT = attendedhospital agecat18yrs gendercat religion maritalstatus atleastprimary employmentCAT ageatonsetCAT durationofepilepsyCAT EpilepsytypeCAT seizuretiming se cognitivedecline lackofaccesstohealthcare rejectionofdiagnosisbypatientorr patientsmisconception stigma culturalbelief injury, add(25) augment

2. STATA COMMAND - ADHERENCE (for TABLE 4)

- mi set wide
- mi register imputed distance_kmCAT transportcostCAT costofASM_CAT seizurefrequency_CAT
- mi register regular notAdherent agecat18yrs gendercat religion maritalstatus atleastprimary employmentCAT ageatonsetCAT durationofepilepsyCAT EpilepsytypeCAT seizuretiming se cognitivedecline lackofaccesstohealthcare lackofmedicalpersonnel rejectionofdiagnosisbypatientorr patientsmisconception stigma unavailabilityofdrugs costofdrugs rejectionoftreatmentbypatient culturalbelief injury healthinsurance
- mi impute chained (ologit) distance_kmCAT transportcostCAT costofASM_CAT seizurefrequency_CAT = notAdherent agecat18yrs gendercat religion maritalstatus atleastprimary employmentCAT ageatonsetCAT durationofepilepsyCAT seizuretiming se cognitivedecline lackofaccesstohealthcare lackofmedicalpersonnel rejectionofdiagnosisbypatientorr patientsmisconception unavailabilityofdrugs costofdrugs rejectionoftreatmentbypatient culturalbelief injury, add(25) augment

Appendix 18

Analysis of possible factors determining access to care in AFIKPO

Variables	Sought medical care [n = 20]	Never sought care [n = 20]	Univariate Analysis OR (95%CI)	P-value	Multivariate Analysis OR (95%CI)	P-value
Age						
< 18 years	4 (20.0%)	5 (25.0%)	1.0 (Reference)			
≥ 18 years	16 (80.0%)	15 (75.0%)	1.33 (0.30, 5.92)	0.705		
Gender						
Female	11 (55.5%)	10 (50.0%)	1.0			
Male	9 (45.0%)	10 (50.0%)	0.82 (0.24, 2.84)	0.752		
Religion						
Christianity	20 (100.0%)	20 (100.0%)	1.0			
Islam	0 (0.0%)	0 (0.0%)	1.0 (0.54, 1.86)	1.000		
Marital status						
Single	17 (85.0%)	15 (75.0%)	1.0			
Married	2 (10.0%)	5 (25.0%)	0.35 (0.06, 2.10)	0.252		
Divorced	0 (0.0%)	0 (0.0%)	-	-		
Widower	1 (5.0%)	0 (0.0%)	-	-		
At least primary education or in school						
No	6 (30.0%)	7 (35.0%)	1.0			
Yes	14 (70.0%)	13 (65.0%)	1.26 (0.33, 4.73)	0.736		
Employment or trade						
None	9 (45.0%)	10 (50.0%)	1.0			
Civil servant or wage earner	0 (0.0%)	1 (5.0%)	-	-		
Crafts or trade	3 (15.0%)	5 (25.0%)	0.67 (0.12, 3.61)	0.638		
Subsistence farmer	1 (5.0%)	0 (0.0%)	-	-		
Student	1 (5.0%)	1 (5.0%)	1.11 (0.06, 20.49)	0.944		
Others	6 (30.0%)	3 (15.0%)	2.22 (0.43, 11.60)	0.344		
Age of onset (years)						
< 1	7 (35.0%)	5 (25.0%)	1.0			
1 – 9	6 (30.0%)	5 (25.0%)	0.86 (0.16, 4.47)	0.855		
10 – 19	3 (15.0%)	6 (30.0%)	0.36 (0.06, 2.16)	0.262		
20 – 29	2 (10.0%)	2 (10.0%)	0.71 (0.07, 6.92)	0.772		
≥ 30	2 (10.0%)	2 (10.0%)	0.71 (0.07, 6.92)	0.772		
Duration of epilepsy (years)						
< 5	1 (5.0%)	3 (15.0%)	1.0			
5 – 10	3 (15.0%)	1 (5.0%)	9.00 (0.37, 220.93)	0.178	-	
11 – 20	8 (40.0%)	10 (50.0%)	2.40 (0.52, 2.33)	0.483	2.06 (0.05, 92.72)	0.711
21 – 30	2 (10.0%)	2 (10.0%)	3.00 (0.15, 59.88)	0.472	2.53 (0.04, 172.32)	0.666
≥ 31	6 (30.0%)	4 (20.0%)	4.50 (0.34, 60.15)	0.256	6.23 (0.18, 217.82)	0.313
Type of epilepsy						
Focal	10 (50.0%)	8 (40.0%)	1.0			
Generalised	7 (35.0%)	10 (50.0%)	0.56 (0.15, 2.14)	0.397		
Combined generalised and focal	3 (15.0%)	1 (5.0%)	2.40 (0.21, 27.71)	0.483		
Unknown	0 (0.0%)	1 (5.0%)	-	-		
Seizure frequency						
Daily	11 (55.0%)	11 (55.0%)	1.0			
Weekly	4 (20.0%)	5 (25.0%)	0.8 (0.17, 3.80)	0.779		
Monthly	3 (15.0%)	2 (10.0%)	1.50 (0.21, 10.81)	0.687		
One in 2 to 6 months	2 (10.0%)	2 (10.0%)	1.0 (0.06, 18.08)	1.000		
Seizure timing						
Nocturnal	0 (0.0%)	5 (25.0%)	1.0			
Early morning	2 (10.0%)	4 (20.0%)	0.28 (0.04, 1.79)	0.178	0.30 (0.02, 4.42)	0.379
Afternoon	0 (0.0%)	1 (5.0%)	-	-	-	-

Anytime	18 (90.0%)	10 (50.0%)§	-	-	-	-
Unknown	0 (0.0%)	0 (0.0%)	-	-	-	-
Reported status epilepticus						
No	13 (65.0%)	20 (100.0%)	1.0			
Yes	7 (35.0%)	0 (0.0%)	-	-		
Learning difficulty						
No	9 (45.0%)	12 (60.0%)	1.0			
Yes	11 (55.0%)	8 (40.0%)	1.83 (0.52, 6.43)	0.344		
Reported difficulty with access to health care facility						
No	17 (85.0%)	20 (100.0%)	1.0			
Yes	3 (15.0%)	0 (0.0%)	-	-		
Reported rejection of diagnosis of epilepsy						
No	20 (100.0%)	13 (65.0%)	1.0			
Yes	0 (0.0%)	7 (35.0%)	-	-		
Reported having misconceptions of epilepsy						
No	13 (65.0%)	3 (15.0%)	1.0			
Yes	7 (35.0%)	17 (85.0%)	0.10 (0.02, 0.44)	0.003	0.25 (0.01, 5.66)	0.380
Reported perceived stigma						
No	19 (95.0%)	19 (95.0%)	1.0			
Yes	1 (5.0%)	1 (5.0%)	1.0 (0.06, 17.18)	1.000		
Reported having negative cultural belief						
No	16 (80.0%)	5 (25.0%)	1.0			
Yes	4 (20.0%)	15 (75.0%)	0.08 (0.02, 0.37)	0.001	0.17 (0.01, 3.06)	0.232
Seizure-related injury						
No	3 (15.0%)	4 (20.0%)	1.0			
Yes	17 (85.0%)	16 (80.0%)	1.42 (0.27, 7.34)	0.678		
Travel distance to health facility (km) (n = 20)						
≤ 1	5 (26.3%)	0 (0.0%)	1.0			
1.1 to 5	13 (68.4%)	1 (100.0%)	-	-		
5.1 to 10	1 (5.3%)	0 (0.0%)	-	-		
> 10	0 (0.0%)	0 (0.0%)	-	-		
Cost of transport (Naira[§]) (n =14)						
< 200	6 (46.2%)	1 (100.0%)	1.0			
200 – 499	2 (15.4%)	0 (0.0%)	-	-		
500 -1000	4 (30.8%)	0 (0.0%)	-	-		
> 1000	1 (7.7%)	0 (0.0%)	-	-		

OR – Odds ratio, CI – Confidence Interval. Some cells were omitted because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Analysis of possible factors determining access to care in IJEBU-JESA

Variables	Sought medical care [n = 19]	Never sought care [n = 5]	Univariate Analysis OR (95%CI)	Univariate Analysis P-value	Multivariate Analysis OR (95%CI)	Multivariate Analysis P-value
Age						
< 18 years	7 (36.8%)	1 (20.0%)	1.0 (Reference)			
≥ 18 years	12 (63.2%)	4 (80.0%)	0.43 (0.04, 4.64)	0.486		
Gender						
Female	10 (52.6%)	2 (40.0%)	1.0			
Male	9 (47.4%)	3 (60.0%)	0.60 (0.08, 4.45)	0.617		
Religion						
Christianity	15 (79.0%)	5 (100.0%)	1.0			
Islam	4 (21.0%)	0 (0.0%)	-	-		
Marital status						
Single	15 (79.0%)	1 (20.0%)	1.0			
Married	3 (15.8%)	3 (60.0%)	0.07 (0.01, 0.88)	0.040	-	-
Divorced	0 (0.0%)	1 (20.0%)	-	-		
Widower	1 (5.3%)	0 (0.0%)	-	-		
At least primary education or in school						
No	3 (15.8%)	0 (0.0%)	1.0			
Yes	16 (84.2%)	5 (100.0%)	-	-		
Employment or trade						
None	5 (26.3%)	2 (50.0%)	1.0			
Civil servant or wage earner	1 (5.3%)	0 (5.0%)	-	-		
Crafts or trade	6 (31.6%)	0 (25.0%)	-	-		
Subsistence farmer	0 (0.0%)	0 (0.0%)	-	-		
Student	0 (0.0%)	1 (0.0%)	-	-		
Others	7 (36.8%)	2 (5.0%)	1.40 (0.14, 13.57)	0.772		
Age of onset (years)						
< 1	6 (31.6%)	1 (20.0%)	1.0			
1 – 9	8 (42.1%)	3 (60.0%)	0.44 (0.04, 5.40)	0.525		
10 – 19	3 (15.8%)	0 (0.0%)	-	-		
20 – 29	2 (10.3%)	0 (0.0%)	-	-		
≥ 30	0 (0.0%)	1 (20.0%)	-	-		
Duration of epilepsy (years)						
< 5	5 (26.3%)	1 (20.0%)	1.0			
5 – 10	3 (15.8%)	1 (20.0%)	0.60 (0.03, 13.58)	0.748		
11 – 20	7 (36.8%)	0 (0.0%)	-	-		
21 – 30	3 (15.8%)	3 (60.0%)	0.20 (0.01, 2.91)	0.239		
≥ 31	1 (5.3%)	0 (0.0%)	-	-		
Type of Epilepsy						
Focal	8 (42.1%)	3 (60.0%)	1.0			
Generalised	11 (57.9%)	2 (40.0%)	2.06 (0.28, 15.36)	0.480		
Combined generalised and focal	0 (0.0%)	0 (0.0%)	-	-		
Unknown	0 (0.0%)	0 (0.0%)	-	-		
Seizure frequency						
Daily	3 (15.8%)	1 (0.0%)	1.0	-		
Weekly	3 (47.4%)	0 (40.0%)	-	-		
Monthly	9 (15.8%)	2 (20.0%)	1.50 (0.10, 23.07)	0.771		
One in 2 to 6 months	4 (5.3%)	2 (20.0%)	0.67 (0.04, 11.28)	0.779		
Seizure timing						
Nocturnal	3 (15.8%)	1 (20.0%)	1.0			
Early morning	5 (26.3%)	1 (20.0%)	1.67 (0.04, 1.79)	0.748		
Afternoon	2 (10.5%)	0 (0.0%)	-	-		
Anytime	9 (47.4%)	3 (60.0%)§	1.00 (0.07, 13.64)	1.000		
Unknown	0 (0.0%)	0 (0.0%)	-	-		

Reported status epilepticus						
No	13 (68.4%)	4 (80.0%)	1.0			
Yes	6 (31.6%)	1 (20.0%)	1.85 (0.17, 20.25)	0.616		
Learning difficulty						
No	14 (73.7%)	5 (100.0%)	1.0			
Yes	5 (26.3%)	0 (0.0%)	-	-		
Reported difficulty with access to health care facility						
No	17 (89.5%)	3 (60.0%)	1.0			
Yes	2 (10.5%)	2 (40.0%)	0.18 (0.02, 1.78)	0.142	-	-
Reported rejection of diagnosis of epilepsy						
No	15 (100.0%)	5 (100.0%)	1.0			
Yes	4 (0.0%)	0 (0.0%)	-	-		
Reported having misconceptions of epilepsy						
No	14 (73.7%)	3 (60.0%)	1.0			
Yes	5 (26.3%)	2 (40.0%)	0.54 (0.07, 4.20)	0.553		
Reported perceived stigma						
No	18 (94.7%)	3 (60.0%)	1.0			
Yes	1 (5.3%)	2 (40.0%)	0.08 (0.006, 1.23)	0.071	-	-
Reported having negative cultural belief						
No	15 (79.0%)	4 (80.0%)	1.0			
Yes	4 (21.0%)	1 (20.0%)	1.07 (0.09, 12.40)	0.959		
Seizure-related injury						
No	6 (31.6%)	3 (60.0%)	1.0			
Yes	13 (64.8%)	2 (40.0%)	3.25 (0.43, 24.84)	0.256		
Travel distance to health facility (km) (n =17)						
≤ 1	5 (29.4%)	0 (0.0%)	1.0			
1.1 to 5	4 (23.5%)	0 (0.0%)	-	-		
5.1 to 10	4 (23.5%)	0 (0.0%)	-	-		
> 10	4 (23.5%)	0 (0.0%)	-	-		
Cost of transport to health facility (Naira[§]) (n =9)						
< 200	3 (33.3%)	0 (0.0%)	1.0			
200 – 499	4 (23.5%)	0 (0.0%)	-	-		
500 -1000	1 (11.1%)	0 (0.0%)	-	-		
> 1000	1 (11.1%)	0 (0.0%)	-	-		

OR – Odds ratio, CI – Confidence Interval. Some cells were omitted because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Analysis of possible factors determining access to care in GWANDU

Variables	Sought medical care [n = 105]	Never sought care [n = 83]	Univariate Analysis OR (95%CI)	P-value	Multivariate Analysis OR (95%CI)	P-value
Age						
< 18 years	46 (43.8%)	45 (54.2%)	1.0 (Reference)			
≥ 18 years	59 (56.2%)	38 (45.8%)	1.52 (0.85, 2.71)	0.157	5.89 (0.51, 70.14)	0.154
Gender						
Female	54 (51.4%)	41 (49.4%)	1.0			
Male	51 (48.6%)	42 (50.6%)	0.92 (0.52, 1.64)	0.782		
Religion						
Christianity	0 (0.0%)	0 (0.0%)	1.0			
Islam	105 (100.0%)	83 (100.0%)	-	-		
Marital status						
Single	76 (72.4%)	71 (85.5%)	1.0			
Married	26 (24.8%)	11 (13.3%)	2.2 (1.01, 4.80)	0.045	-	-
Divorced	3 (2.9%)	1 (1.2%)	2.8 (0.28, 27.6)	0.377	-	-
Widower	0 (5.0%)	0 (0.0%)	-	-		
At least primary education or in school						
No	61 (58.1%)	45 (54.2%)	1.0			
Yes	44 (41.9%)	38 (45.8%)	0.85 (0.48, 1.53)	0.594		
Employment or trade						
None	44 (41.9%)	41.0 (50.0%)	1.0			
Civil servant or wage earner	4 (3.8%)	2 (2.4%)	1.54 (0.27, 8.94)	0.627		
Crafts or trade	7 (6.7%)	4 (4.8%)	1.35 (0.37, 5.00)	0.651		
Subsistence farmer	25 (23.8%)	15 (18.1%)	1.29 (0.59, 2.81)	0.526		
Student	8 (7.6 %)	6 (7.2%)	1.03 (0.33, 3.25)	0.959		
Others	17 (16.2%)	22 (26.5%)	0.60 (0.28, 1.30)	0.192		
Age of onset (years)						
< 1	3 (2.9%)	5 (6.0%)	1.0			
1 – 9	67 (63.8%)	59 (71.1%)	1.89 (0.43, 8.26)	0.396		
10 – 19	26 (24.8%)	18 (21.7%)	2.41 (0.51, 11.37)	0.267		
20 – 29	4 (3.8%)	1 (1.2%)	6.67 (0.49, 91.33)	0.155	-	-
≥ 30	5 (4.8%)	0 (0.0%)				
Duration of epilepsy (years)						
< 5	20 (19.1%)	16 (19.3%)	1.0			
5 – 10	38 (36.2%)	33 (39.8%)	0.92 (0.41, 2.06)	0.842		
11 – 20	31 (29.5%)	24 (28.9%)	1.03 (0.44, 2.41)	0.939		
21 – 30	15 (14.3%)	7 (8.4%)	1.71 (0.56, 5.21)	0.342		
≥ 31	1 (1.0%)	3 (3.6%)	0.27 (0.03, 2.82)	0.272		
Type of epilepsy						
Focal	49 (46.7%)	36 (43.4%)	1.0			
Generalised	49 (46.7%)	43 (51.8%)	0.84 (0.46, 1.51)	0.558		
Combined generalised and focal	5 (4.8%)	3 (3.6%)	1.22 (0.27, 5.45)	0.791		
Unknown	2 (1.9%)	1 (1.2%)	1.47 (0.13, 16.84)	0.757		
Seizure frequency (n = 186)						
Daily	6 (5.8%)	3 (3.6%)	1.0			
Weekly	27 (26.2%)	16 (19.3%)	0.84 (0.18, 3.84)	0.826		
Monthly	41 (39.8%)	42 (50.6%)	0.49 (0.11, 2.08)	0.333		
1 in 2 to 6 months	29 (28.2%)	22 (26.5%)	0.66 (0.15, 2.93)	0.584		
Seizure timing						
Nocturnal	8 (7.2%)	8 (9.6%)	1.0			
Early morning	10 (9.5%)	4 (2.8%)	2.50 (0.55, 11.41)	0.237		
Afternoon	3 (2.9%)	2 (2.4%)	1.50 (0.20, 11.54)	0.697		
Anytime	82 (78.1%)	68 (81.9%)	1.21 (0.43, 3.38)	0.722		

Unknown	2 (1.9%)	1 (1.2%)	2.00 (0.15, 26.73)	0.600		
Reported status epilepticus						
No	68 (64.8%)	54 (65.1%)	1.0			
Yes	37 (35.2%)	29 (34.9%)	1.01 (0.88, 1.80)	0.966		
Learning difficulty						
No	94 (89.5%)	74 (89.2%)	1.0			
Yes	11 (10.5%)	9 (10.8%)	0.96 (0.38, 2.44)	0.935		
Reported difficulty with access to health care facility						
No	80 (76.2%)	53 (63.9%)	1.0			
Yes	25 (23.8%)	39 (36.1%)	0.55 (0.29, 1.04)	0.066	0.51 (0.06, 4.68)	0.555
Reported rejection of diagnosis of epilepsy						
No	96 (91.4%)	61 (73.5%)	1.0			
Yes	9 (8.6%)	22 (26.5%)	0.26 (0.11, 0.60)	0.002	-	-
Reported having misconceptions of epilepsy						
No	83 (79.1%)	54 (65.1%)	1.0			
Yes	22 (20.9%)	29 (34.9%)	0.49 (0.26, 0.95)	0.034	-	-
Reported perceived stigma						
No	103 (98.1%)	76 (91.6%)	1.0			
Yes	2 (1.9%)	7 (8.4%)	0.21 (0.04, 1.04)	0.056	-	-
Reported having negative cultural belief						
No	84 (80.0%)	48 (57.8%)	1.0			
Yes	21 (20.0%)	35 (42.2%)	0.34 (0.12, 0.65)	0.001	2.08	0.559
Seizure-related injury						
No	38 (36.2%)	37 (44.6%)	1.0			
Yes	67 (63.8%)	46 (55.4%)	1.42 (0.78, 2.55)	0.244		
Travel distance to health facility (km)						
≤ 1	3 (5.5%)	1 (25.0%)	1.0			
1.1 to 5	9 (16.4%)	0 (0.0%)	-	-		
5.1 to 10	2 (3.6%)	0 (0.0%)	-	-		
> 10	41 (74.5%)	3 (75.0%)	4.55 (0.36, 58.27)	0.244		
Cost of transport to health facility (Naira[§])						
< 200	25 (39.7%)	1 (14.3%)	1.0			
200 – 499	13 (20.6%)	2 (28.6%)	0.26 (0.02, 3.14)	0.286	1.12 (0.05, 23.67)	0.944
500 -1000	20 (31.8%)	4 (57.1%)	0.20 (0.02, 1.93)	0.164	1.25 (0.07, 21.26)	0.879
> 1000	5 (7.9%)	0 (0.0%)	-	-	-	-

OR – Odds ratio, CI – Confidence Interval. Some cells were omitted because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Appendix 19

Factors associated with being on treatment and adherence to ASMs for AFIKPO

Variables	Not adherent (n=32)	Currently on treatment and adherent (n=8)	Univariate Analysis OR (95%CI)	P-value	Multivariate Analysis OR (95%CI)	P-value
Age						
< 18 years	7 (21.9%)	2 (25.0%)	1.0			
≥ 18 years	25 (78.1%)	6 (75.0%)	1.19 (0.20, 7.25)	0.850	2.2 (0.19, 26.11)	0.532
Gender						
Female	15 (46.9%)	6 (75.0%)	1.0			
Male	17 (53.1%)	2 (25.0%)	3.40 (0.59, 19.46)	0.169	7.27 (0.48, 109.16)	0.151
Religion						
Christianity	32 (100.0%)	8 (100.0%)	1.0			
Islam	0 (0.0%)	0 (0.0%)	-	-		
Marital status						
Single	24 (75.0%)	8 (100.0%)	1.0			
Married	7 (21.9%)	0 (0.0%)	-	-		
Divorced	0 (0.0%)	0 (0.0%)	-	-		
Widower	1 (3.1%)	0 (0.0%)	-	-		
At least primary education or in school						
No	11 (35.4%)	2 (25.0%)	1.0			
Yes	21 (65.6%)	6 (75.0%)	0.64 (0.11, 3.69)	0.614		
Employment or trade						
None	15 (46.9%)	4 (50.0%)	1.0			
Civil servant or wage earner	1 (3.1%)	0 (0.0%)	-	-		
Crafts or trade	8 (25.0%)	0 (0.0%)	-	-		
Subsistence farmer	1 (3.1%)	0 (0.0%)	-	-		
Student	0 (0.0%)	2 (25.0%)	-	-		
Others	7 (2.9%)	2 (25.0%)	0.93 (0.14, 3.63)	0.944		
Age of onset (years)						
< 1	9 (28.1%)	3 (37.5%)	1.0			
1 – 9	8 (25.0%)	3 (37.5%)	0.89 (0.14, 5.72)	0.901		
10 – 19	9 (28.1%)	0 (0.0%)	-	-		
20 – 29	3 (9.4%)	1 (12.5%)	1.0 (0.07, 13.64)	1.000		
≥ 30	3 (9.4%)	1 (12.5%)	1.0 (0.07, 13.64)	1.000		
Duration of epilepsy (years)						
< 5 years	4 (12.5%)	0 (0.0%)	1.0			
5 – 10 years	3 (9.4%)	1 (12.5%)	0.33 (0.02, 7.14)	0.482		
11 – 20 years	13 (40.6%)	5 (62.5%)	0.29 (0.03, 2.91)	0.292		
21 – 30	3 (9.4%)	1 (12.5%)	0.33 (0.02, 7.14)	0.482		
≥ 31	9 (28.1%)	1 (12.5%)	-	-		
Type of epilepsy						
Focal	12 (37.5%)	6 (75.0%)	1.0			
Generalised	15 (46.9%)	2 (25.0%)	3.75 (0.64, 22.04)	0.114	3.30 (0.38, 28.92)	0.281
Combined generalised and focal	4 (12.5%)	0 (0.0%)	-	-	-	-
Unknown	1 (3.1%)	0 (0.0%)	-	-	-	-
Seizure frequency						
Daily	16 (50.0%)	6 (75.0%)	1.0			
Weekly	8 (25.0%)	1 (12.5%)	3.0 (0.31, 29.35)	0.345		
Monthly	4 (12.5%)	1 (12.5%)	1.5 (0.14, 16.27)	0.739		
1 in 2 to 6 months	4 (12.5%)	0 (0.0%)	-	-		
Seizure timing						
Nocturnal	5 (15.6%)	0 (0.0%)	1.0			
Early morning	5 (15.6%)	1 (12.5%)	1.36 (0.13, 14.00)	0.794		
Afternoon	0 (0.0%)	1 (12.5%)	-	-		

Anytime	22 (68.8%)	6 (75.0%)	-	-		
Unknown	0 (0.0%)	0 (0.0%)	-	-		
Reported status epilepticus						
No	28 (87.5%)	5 (62.5%)	1.0			
Yes	4 (12.5%)	3 (37.5%)	0.23 (0.40, 1.40)	0.113	0.09 (0.004, 2.23)	0.142
Learning difficulty						
No	18 (56.3%)	3 (37.5%)	1.0			
Yes	14 (43.7%)	5 (62.5%)	0.47 (0.9, 2.29)	0.348	0.84 (0.12, 6.14)	0.864
Reported difficulty with access to health care facility						
No	29 (90.6%)	8 (0.0%)	1.0			
Yes	3 (9.4%)	0 (0.0%)	-	-		
Lack of medical personnel at health facility						
No	32 (100.0%)	8 (100.0%)	1.0			
Yes	0 (0.0%)	0 (0.0%)	-	-		
Reported rejection of diagnosis of epilepsy						
No	25 (78.1%)	8 (100.0%)	1.0			
Yes	7 (21.9%)	0 (0.0%)				
Reported having misconceptions of epilepsy						
No	11 (34.4%)	5 (62.5%)	1.0			
Yes	21 (65.6%)	3 (37.5%)	3.18 (0.64, 15.86)	0.158	1.40 (0.16, 12.46)	0.761
Reported perceived stigma						
No	30 (93.8%)	8 (100.0%)	1.0			
Yes	2 (6.2%)	0 (0.0%)	-	-	-	-
Lack of drugs at health facility						
No	31 (96.9%)	8 (100.0%)	1.0			
Yes	1 (3.1%)	0 (0.0%)	-	-		
Cost of drugs						
No	26 (81.3%)	8 (100.0%)	1.0			
Yes	6 (18.7%)	0 (0.0%)	-	-		
Rejection of treatment by subject or care-giver						
No	30 (93.8%)	8 (100.0%)	1.0			
Yes	2 (6.2%)	0 (0.0%)	-	-		
Reported having negative cultural belief						
No	16 (50.0%)	5 (62.5%)	1.0			
Yes	16 (50.0%)	3 (37.5%)	1.67 (0.34, 8.18)	0.529		
Seizure-related injury						
No	6 (18.8%)	1 (12.5%)	1.0			
Yes	26 (81.2%)	7 (87.5%)	0.62 (0.06, 6.03)	0.680		
Access to the Nigerian health insurance						
No	32 (100.0%)	7 (87.5%)	1.0			
Yes	0 (0.0%)	1 (12.5%)	-	-	-	-
Travel distance to health facility (km)						
≤ 1	4 (26.7%)	1 (20.0%)				
1.1 to 5	10 (66.7%)	4 (80.0%)	0.63 (0.05, 7.46)	0.710		
5.1 to 10	1 (6.7%)	0 (0.0%)	-	-		
> 10	0 (0.0%)	0 (0.0%)	-	-		
Cost of transport to health facility (Naira[§])						
< 200	5 (50.0%)	2 (50.0%)	1.0			
200 – 499	1 (10.0%)	1 (25.0%)	0.40 (0.02, 10.02)	0.577		
500 -1000	3 (30.0%)	1 (25.0%)	1.2 (0.07, 19.63)	0.898		
> 1000	1 (10.0%)	0 (0.0%)	-	-		
Cost of antiseizure medication per month (Naira[§])						
< 1,000	1 (25.0%)	0 (0.0%)	-	-		
1,000 – 1,999	1 (25.0%)	0 (0.0%)	-	-		
2,000 – 5,000	2 (50.0%)	1 (50.0%)	-	-		
> 5,000	0 (0.0%)	1 (50.0%)	-	-		

OR – Odds ratio, CI – Confidence Interval. Some cells were omitted because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Factors associated with being on treatment and adherence to ASMs for IJEBU-JESA

Variables	Not adherent (n=19)	Currently on treatment and adherent (n=5)	Univariate Analysis OR (95%CI)	P-value	Multivariate Analysis OR (95%CI)	P-value
Age						
< 18 years	7 (36.8%)	1 (20.0%)	1.0			
≥ 18 years	12 (63.2%)	4 (80.0%)	0.43 (0.04, 4.64)	0.486		
Sex						
Female	12 (63.2%)	0 (0.0%)	1.0			
Male	7 (36.8%)	5 (100.0%)	-	-	-	-
Religion						
Christianity	16 (84.2%)	4 (80.0%)	1.0			
Islam	3 (15.8%)	1 (20.0%)	0.75 (0.06, 9.27)	0.823		
Marital status						
Single	13 (68.4%)	3 (60.0%)	1.0			
Married	5 (26.3%)	1 (20.0%)	1.15 (0.10, 13.88)	0.910		
Divorced	1 (5.3%)	0 (0.0%)	-	-		
Widower	0 (0.0%)	1 (20.0%)	-	-		
At least primary education or in school						
No	16 (84.2%)	0 (0.0%)	1.0			
Yes	3 (15.8%)	5 (100.0%)	-	-		
Employment or trade						
None	5 (46.9%)	2 (40.0%)	1.0			
Civil servant or wage earner	0 (3.1%)	1 (20.0%)	-	-		
Crafts or trade	5 (25.0%)	1 (20.0%)	2.0 (0.13, 29.81)	0.615		
Subsistence farmer	0 (0.0%)	0 (0.0%)	-			
Student	1 (3.1%)	0 (0.0%)	-			
Others	8 (0.0%)	1 (20.0%)	3.2 (0.23, 45.19)	0.389		
Age of onset (years)						
< 1 year	5 (26.3%)	2 (40.0%)	1.0			
1 – 9 years	10 (52.6%)	1 (20.0%)	4.0 (0.29, 55.47)	0.301		
10 – 19 years	2 (10.5%)	1 (20.0%)	1.19 (0.04, 14.64)	0.880		
20 – 29	1 (5.3%)	1 (20.0%)	0.4 (0.02, 10.01)	0.577		
≥ 30	1 (5.3%)	0 (0.0%)	-	-		
Duration of epilepsy (years)						
< 5 years	5 (26.3%)	1 (20.0%)	1.0			
5 – 10 years	3 (15.8%)	1 (20.0%)	0.60 (0.03, 13.58)	0.748		
11 – 20 years	5 (26.3%)	2 (40.0%)	0.50 (0.03, 7.45)	0.615		
21 – 30	6 (31.6%)	0 (0.0%)	-	-		
≥ 31	0 (0.0%)	1 (20.0%)	-	-		
Type of epilepsy						
Focal	8 (42.1%)	3 (60.0%)	1.0			
Generalised	11 (57.1%)	2 (40.0%)	0.60 (0.03, 13.58)			
Combined generalised and focal	0 (0.0%)	0 (0.0%)	-	-	-	-
Unknown	0 (0.0%)	0 (0.0%)	-	-	-	-
Seizure frequency						
Daily	3 (15.8%)	1 (20.0%)	1.0			
Weekly	3 (15.8%)	0 (0.0%)	-	-		
Monthly	9 (47.4%)	2 (40.0%)	1.5 (0.10, 16.27)	0.771		
1 in 2 to 6 months	4 (21.0%)	2 (40.0%)	0.67 (0.04, 11.29)	0.779		
Seizure timing						
Nocturnal	3 (15.8%)	1 (20.0%)	1.0			
Early morning	6 (31.6%)	0 (0.0%)				
Afternoon	1 (5.3%)	1 (20.0%)	0.33 (0.009, 11.94)	0.547		
Anytime	9 (47.4%)	3 (60.0%)	1.0 (0.07, 13.64)	1.000		
Unknown	0 (0.0%)	0 (0.0%)	-	-		
Reported status epilepticus						
No	13 (68.4%)	4 (80.0%)	1.0			

Yes	6 (31.5%)	1 (20.0%)	1.85 (0.17, 20.25)	0.616
Learning difficulty				
No	15 (79.0%)	4 (80.0%)	1.0	
Yes	4 (21.0%)	1 (20.0%)	1.07 (0.09, 12.40)	0.959
Reported difficulty with access to health care facility				
No	15 (79.0%)	5 (100.0%)	1.0	
Yes	4 (21.0%)	0 (0.0%)	-	-
Lack of medical personnel at health facility				
No	18 (94.7%)	5 (100.0%)	1.0	
Yes	1 (5.3%)	0 (0.0%)	-	-
Reported rejection of diagnosis of epilepsy				
No	15 (79.0%)	5 (100.0%)	1.0	
Yes	4 (21.0%)	0 (0.0%)	-	
Reported having misconceptions of epilepsy				
No	12 (63.2%)	5 (100.0%)	1.0	
Yes	7 (36.8%)	0 (0.0%)	-	-
Reported perceived stigma				
No	13 (68.4%)	5 (100.0%)	1.0	
Yes	6 (31.5%)	0 (0.0%)	-	-
Lack of drugs at health facility				
No	17 (89.5%)	5 (100.0%)	1.0	
Yes	2 (10.5%)	0 (0.0%)	-	-
Cost of drugs				
No	18 (94.7%)	5 (100.0%)	1.0	
Yes	1 (5.3%)	0 (0.0%)	-	-
Rejection of treatment by subject or care-giver				
No	17 (89.5%)	5 (100.0%)	1.0	
Yes	2 (10.5%)	0 (0.0%)	-	-
Reported having negative cultural belief				
No	14 (73.7%)	5 (100.0%)	1.0	
Yes	5 (26.3%)	0 (0.0%)	-	-
Seizure-related injury				
No	8 (42.1%)	1 (20.0%)	1.0	
Yes	11 (57.9%)	4 (80.0%)	0.34 (0.03, 3.69)	0.378
Access to the Nigerian health insurance				
No	19 (100.0%)	5 (100.0%)	1.0	
Yes	0 (0.0%)	0 (0.0%)	-	-
Travel distance to health facility (km)				
≤ 1	5 (41.7%)	0 (0.0%)		
1.1 to 5	3 (25.0%)	1 (20.0%)	3.0 (0.15, 59.89)	0.472
5.1 to 10	2 (16.7%)	2 (40.0%)	1.0 (0.06, 15.99)	1.000
> 10	2 (16.7%)	2 (40.0%)	-	-
Cost of transport to health facility (Naira[§])				
< 200	5 (50.0%)	1 (25.0%)	1.0	
200 – 499	1 (10.0%)	2 (50.0%)	0.5 (0.02, 11.09)	0.661
500 -1000	3 (30.0%)	0 (0.0%)		
> 1000	1 (10.0%)	1 (25.0%)	-	-
Cost of antiseizure medication per month (Naira[§])				
< 1,000	0 (0.0%)	0 (0.0%)	-	-
1,000 – 1,999	1 (25.0%)	0 (0.0%)	0.13 (0.005, 3.22)	-
2,000 – 5,000	1 (25.0%)	4 (80.0%)	-	-
> 5,000	2 (50.0%)	1 (20.0%)	-	-

OR – Odds ratio, CI – Confidence Interval. Some cells were omitted because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Factors associated with being on treatment and adherence to ASMs for GWANDU

Variables	Not adherent (n=159)	Currently on treatment and adherent (n=29)	Univariate Analysis OR (95%CI)	Univariate Analysis P-value	Multivariate Analysis OR (95%CI)	Multivariate Analysis P-value
Age						
< 18 years	80 (50.3%)	11 (37.9%)	1.0			
≥ 18 years	79 (49.7%)	18 (62.1%)	0.60 (0.27, 1.36)	0.223	4.75 (0.38, 59.55)	0.227
Gender						
Female	77 (48.4%)	18 (62.1%)	1.0			
Male	82 (51.6%)	11 (37.9%)	1.74 (0.77, 3.93)	0.180	18.08 (2.21, 147.79)	0.007
Religion						
Christianity	159 (100.0%)	29 (100.0%)	1.0			
Islam	0 (0.0%)	0 (0.0%)	-	-		
Marital status						
Single	130 (75.0%)	17 (58.6%)	1.0			
Married	27 (17.0%)	10 (34.5%)	0.35 (0.15, 0.85)	0.021		
Divorced	2 (1.3%)	2 (6.9%)	0.13 (0.02, 0.99)	0.049		
Widower	0 (0.0%)	0 (0.0%)	-	-		
At least primary education or in school						
No	87 (54.7%)	19 (65.5%)	1.0			
Yes	72 (45.3%)	10 (34.5%)	1.57 (0.69, 3.60)	0.283		
Employment or trade						
None	68 (42.8%)	10 (34.5%)	1.0			
Civil servant or wage earner	5 (3.1%)	1 (3.4%)	0.74 (0.08, 6.96)	0.789		
Crafts or trade	8 (5.0%)	3 (10.3%)	0.39 (0.09, 1.73)	0.216		
Subsistence farmer	30 (18.9%)	10 (34.5%)	0.44 (0.17, 1.17)	0.100		
Student	12 (7.6%)	2 (6.9%)	0.88 (0.17, 4.54)	0.881		
Others	36 (22.6%)	3 (10.3%)	1.76 (0.46, 6.82)	0.410		
Age of onset (years)						
< 1 year	7 (4.4%)	1 (3.4%)	1.0			
1 – 9 years	106 (66.7%)	20 (69.0%)	0.76 (0.09, 6.49)	0.800		
10 – 19 years	37 (23.3%)	7 (24.1%)	0.76 (0.08, 7.13)	0.806		
20 – 29	5 (3.1%)	0 (0.0%)	-	-		
≥ 30	4 (2.5%)	1 (3.5%)	0.57 (0.03, 11.85)	0.718		
Duration of epilepsy (years)						
< 5	33 (27.8%)	3 (0.0%)	1.0			
5 – 10	62 (39.0%)	9 (12.5%)	0.63 (0.16, 2.47)	0.504		
11 – 20	44 (27.7%)	11 (62.5%)	0.36 (0.09, 1.41)	0.143		
21 – 30	16 (10.1%)	6 (2.5%)	0.24 (0.05, 1.10)	0.066		
≥ 31	4 (2.5%)	0 (0.0%)	-	-		
Type of epilepsy						
Focal	67 (42.1%)	18 (62.1%)	1.0			
Generalised	81 (50.9%)	11 (37.9%)	1.98 (0.87, 4.48)	0.102		
Combined generalised and focal	8 (5.0%)	0 (0.0%)	-	-	-	-
Unknown	3 (1.9%)	0 (0.0%)	-	-	-	-
Seizure frequency						
Daily	9 (5.7%)	0 (0.0%)	1.0			
Weekly	35 (22.1%)	8 (28.6%)	0.58 (0.19, 1.84)	0.357		
Monthly	69 (43.7%)	14 (50.0%)	0.66 (0.24, 1.84)	0.423		
1 in 2 to 6 months	45 (28.5%)	6 (21.4%)	omitted	-		
Seizure timing						
Nocturnal	16 (10.1%)	0 (0.0%)	1.0			
Early morning	12 (7.6%)	2 (6.9%)	3.0 (0.18, 50.78)	0.447		
Afternoon	3 (1.9%)	2 (6.9%)	0.75 (0.04, 14.97)	0.851		
Anytime	126 (79.2%)	24 (82.8%)	2.6 (0.23, 30.11)	0.438		
Unknown	2 (1.3%)	1 (3.4%)	omitted	-		

Reported status epilepticus						
No	106 (66.7%)	16 (55.2%)	1.0			
Yes	53 (33.3%)	13 (44.8%)	0.62 (0.28, 1.37)	0.236		
Learning difficulty						
No	146 (91.8%)	22 (75.9%)	1.0			
Yes	13 (8.2%)	7 (24.1%)	0.28 (0.10, 0.78)	0.015		
Reported difficulty with access to health care facility						
No	110 (69.2%)	23 (79.3%)	1.0			
Yes	49 (30.8%)	6 (20.7%)	1.71 (0.65, 4.46)	0.274		
Lack of medical personnel at health facility						
No	140 (88.1%)	26 (89.7%)	1.0			
Yes	19 (11.9%)	3 (10.3%)	1.17 (0.32, 4.26)	0.805		
Rejection of diagnosis by patient or relative						
No	132 (83.0%)	25 (86.2%)	1.0			
Yes	27 (17.0%)	4 (13.8%)	1.28 (0.41, 3.97)	0.671		
Reported having misconceptions of epilepsy						
No	114 (71.7%)	23 (79.3%)	1.0			
Yes	45 (28.3%)	6 (20.7%)	1.51 (0.58, 3.96)	0.399		
Reported perceived stigma						
No	150 (94.3%)	29 (100.0%)	1.0			
Yes	9 (5.7%)	0 (0.0%)	-	-	-	-
Lack of drugs at health facility						
No	135 (84.9%)	24 (82.8%)	1.0			
Yes	24 (15.1%)	5 (17.2%)	0.85 (0.30, 2.46)	0.769		
Cost of drugs						
No	112 (70.4%)	19 (65.5%)	1.0			
Yes	47 (29.6%)	10 (34.5%)	0.80 (0.34, 1.84)	0.569		
Rejection of treatment by subject or care-giver						
No	156 (98.1%)	28 (96.5%)	1.0			
Yes	3 (1.9%)	1 (3.5%)	0.54 (0.05, 5.36)	0.598		
Reported having negative cultural belief						
No	106 (66.7%)	26 (89.7%)	1.0			
Yes	53 (33.3%)	3 (10.3%)	4.33 (1.25, 14.97)	0.020	10.51 (1.07, 103.43)	0.044
Seizure-related injury						
No	68 (42.8%)	7 (24.1%)	1.0			
Yes	91 (57.2%)	22 (75.9%)	0.43 (0.17, 1.05)	0.065		
Access to the Nigerian health insurance						
No	158 (99.4%)	28 (96.6%)	1.0			
Yes	1 (0.6%)	1 (3.4%)	0.18 (0.01, 2.92)	0.226	-	-
Travel distance to health facility (km)						
≤ 1	3 (7.0%)	1 (6.3%)				
1.1 to 5	7 (16.3%)	2 (12.5%)	1.17 (0.07, 18.35)	0.913		
5.1 to 10	2 (4.7%)	0 (0.0%)	-	-		
> 10	31 (72.1%)	13 (81.2%)	0.79 (0.08, 8.37)	0.848		
Cost of transport to health facility (Naira[§])						
< 200	19 (38.8%)	7 (33.3%)	1.0			
200 – 499	12 (24.5%)	3 (14.3%)	1.47 (0.38, 6.83)	0.620		
500 -1000	16 (32.7%)	8 (38.1%)	0.74 (0.22, 2.48)	0.622		
> 1000	2 (4.1%)	3 (14.3%)	0.25 (0.03, 1.79)	0.166		
Cost of antiseizure medication per month (Naira[§])						
< 1,000	8 (24.2%)	1 (7.1%)	1.0	-		
1,000 – 1,999	12 (36.4%)	5 (35.7%)	0.3 (0.03, 3.07)	0.310		
2,000 – 5,000	10 (30.3%)	5 (35.7%)	0.25 (0.2, 2.59)	0.246		
> 5,000	3 (9.1%)	3 (21.4%)	0.125 (0.01, 1.72)	0.120		

OR – Odds ratio, CI – Confidence Interval. Some cells were omitted because of collinearity and small sample size in a cell. [§] one US dollar ~ 360 Naira

Appendix 20

The multiple imputations scheme for the case-control study

misstable summarize if cascon==0 (Controls only)

Variable	Obs-	Obs>.	Obs<.	Unique values	Min	Max
Age		1	585	65	6	105
Gender		2	584	2	0	1
Marital status		1	585	4	0	3
Education		1	585	4	0	3
At least primary education		1	585	2	0	1
Income per month		586	0	0	-	-
Tap/pump		2	584	2	0	1
Well		1	585	2	0	1
Stream		1	585	2	0	1
Ponds		1	585	2	0	1
Water closet		1	585	2	0	1
Pit latrine		38	548	2	0	1
Open defcation		1	585	2	0	1
Pig/Pork		1	585	2	0	1
Consanguinity		3	583	3	0	2
Poor perinatal care		2	584	3	0	2
Family history 1st degree		2	584	2	0	1
Family history 2nd degree		2	584	2	0	1
Febrile seizures		2	584	2	0	1
Measles		2	584	2	0	1
Meningitis		4	582	2	0	1
Head injury		2	584	2	0	1
River blindness family history		12	574	3	0	2
Ivermectin use		32	554	3	0	2
Hypertension		2	584	2	0	1
Diabetes		2	584	2	0	1
Sickle cell disease		2	584	2	0	1
Stroke		2	584	2	0	1
Smoking		5	581	2	0	1
Alcohol intake		6	580	3	0	2
AgeCAT16yrs		1	585	2	0	1

misstable summarize if cascon==1 (Cases only)

Variable	Obs-	Obs>.	Obs<.	Unique values	Min	Max
Income per month		222	30	19	0	90000
Well		1	251	2	0	1
Pit latrine		1	251	2	0	1
Poor perinatal care		1	251	3	0	2

misstable summarize **(TOTAL case and control combined)**

Variable	Obs-	Obs>.	Obs<.	Unique values	Min	Max
Age		1	837	65	6	105
Gender		2	836	2	0	1
Marital status		1	837	4	0	3
Education		1	837	4	0	3
At least primary education		1	837	2	0	1
Income per month		808	30	19	0	90000
Tap/pump		2	836	2	0	1
Well		2	836	2	0	1
Stream		1	837	2	0	1
Ponds		1	837	2	0	1
Water closet		1	837	2	0	1
Pit latrine		39	799	2	0	1
Open defecation		1	837	2	0	1
Pig/Pork		1	837	2	0	1
Consanguinity		3	835	3	0	2
Poor perinatal care		3	835	3	0	2
Family history 1st degree		2	836	2	0	1
Family history 2nd degree		2	836	2	0	1
Febrile seizures		2	836	2	0	1
Measles		2	836	2	0	1
Meningitis		4	834	2	0	1
Head injury		2	836	2	0	1
River blindness family history		12	826	3	0	2
Ivermectin use		32	806	3	0	2
Hypertension		2	836	2	0	1
Diabetes		2	836	2	0	1
Sickle cell disease		2	836	2	0	1
Stroke		2	836	2	0	1
Smoking		5	833	2	0	1
Alcohol intake		6	832	3	0	2
AgeCAT16yrs		1	837	2	0	1

Missing variables and predictive model type for imputation								
S/No	**Variable**	**Type**	**Number**	**Number missing**	**% missing**	**Predictive model type for imputation**	**Predictor variables for**	
							< 16 years	**≥ 16 years**
	AgeCAT	ordered categorical	837	1	0.1	Ordered logistic regression (ologit)		
4	Gender	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
3.	Marital status	unordered categorical	837	1	0.1	Multinomial logistic regression (mlogit)	✓	✓
5	Education	ordered categorical	837	1	0.1	Ordered logistic regression (ologit)	✓	✓
6	At least primary education	Dichotomous	837	1	0.1	Logistic regression (logit)	✓	✓
7	Income per month*	Continuous	30	808	96.4	-	-	-
8	Tap/pump	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
9	Well	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
10	Stream	Dichotomous	837	1	0.1	Logistic regression (logit)	✓	✓
13	Ponds	Dichotomous	837	1	0.1	Logistic regression (logit)	✓	✓
15	Water closet	Dichotomous	837	1	0.1	Logistic regression (logit)	✓	✓
16	Pit latrine	Dichotomous	799	39	4.7	Logistic regression (logit)	✓	✓
17	Open defecation	Dichotomous	837	1	0.1	Logistic regression (logit)	✓	✓
18	Pig/Pork	Dichotomous	837	1	0.1	Logistic regression (logit)	✓	✓
19	Consanguinity	unordered categorical	835	3	0.4	Multinomial logistic regression (mlogit)	✓	✓
20	Poor perinatal care	unordered categorical	835	3	0.4	Multinomial logistic regression (mlogit)	✓	✓
21	Family history 1st degree	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
22	Family history 2nd degree	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
24	Febrile seizures	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
25	Measles	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
26	Meningitis	Dichotomous	834	4	0.5	Logistic regression (logit)	✓	✓
28	Head injury	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
29	River blindness	Unordered	826	12	1.4	Multinomial	×	✓

	(family history)	categorical				logistic regression (mlogit)		
30	Ivermectin use	Unordered categorical	806	32	3.8	Multinomial logistic regression (mlogit)	×	✓
31	Hypertension	Dichotomous	836	2	0.2	Logistic regression (logit)	×	✓
32	Diabetes	Dichotomous	836	2	0.2	Logistic regression (logit)	×	✓
33	Sickle cell disease	Dichotomous	836	2	0.2	Logistic regression (logit)	✓	✓
34	Stroke	Dichotomous	836	2	0.2	Logistic regression (logit)	×	✓
35	Smoking	Dichotomous	833	5	0.6	Logistic regression (logit)	×	✓
36	Alcohol intake	Ordered categorical	832	6	0.7	Ordered logistic regression (ologit)	×	✓
41	AgeCAT16yrs	Dichotomous	837	1	0.1	Ordered logistic regression (ologit)	✓	✓
* Income was not used in the analysis as the controls did not answer the question. Those with just one missing were not included in the imputation								

STATA COMMAND – case-control (for tables of age < 16yrs)

- mi set wide
- mi register imputed gendercat taporpump well pitlatrine consanguineousparents poorperinatal familyhistory1st familyhistory2nd febrileconvul measles meningitis headinjury scd
- mi register regular cascon ageCAT stream ponds watercloset open-defecation pork
- mi impute chained (logit) gendercat taporpump well pitlatrine familyhistory1st familyhistory2nd febrileconvul measles meningitis headinjury scd (mlogit) consanguineousparents poorperinatal = cascon ageCAT stream ponds watercloset open-defecation pork, add(25) augment
- mi estimate, or mcerror cformat(%8.4f): logit cascon ageCAT gendercat stream ponds watercloset open-defecation pork taporpump well pitlatrine familyhistory1st familyhistory2nd febrileconvul measles meningitis headinjury scd i.consanguineousparents i.poorperinatal

STATA COMMAND – case-control (for tables of age ≥ 16yrs)

- mi set wide
- mi register imputed gendercat taporpump well pitlatrine consanguineousparents poorperinatal familyhistory1st familyhistory2nd febrileconvul measles meningitis headinjury riverblind ivermectin hypertension diabetes scd stroke smoking alcoholintake
- mi register regular cascon stream ponds watercloset open-defecation pork
- mi impute chained (logit) gendercat taporpump well pitlatrine consanguineousparents poorperinatal familyhistory1st familyhistory2nd febrileconvul measles meningitis headinjury riverblind ivermectin hypertension diabetes scd stroke smoking alcoholintake = cascon ageCAT stream ponds watercloset open-defecation pork, add(25) augment

Appendix 21

Factors associated with epilepsy for the three sites

Factors associated with epilepsy in children (<16 years) for Afikpo

Risk Factor Total 838	Children with active epilepsy (n=7)	Controls* (n=30)	Univariate analysis**	P-value	Multivariate analysis**	P-value	Multivariate analysis with MICE**	P-value
Age								
				0.098	1.62 (0.98, 2.66)	0.059	5.77 (0.79, 42.12)	0.084
Gender								
Male	2 (28.6%)	10 (33.3%)	1.0 (reference)					
Female	5 (71.4%)	20 (66.7%)	1.25 (0.21, 7.62)	0.809	0.64 (0.05, 8.97)	0.737	0.70 (0.05, 9.09)	0.784
Well water								
No	7 (100.0%)	30 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Stream water								
No	7 (100.0%)	29 (96.7%)	1.0 (reference)					
Yes	0 (0.0%)	1 (3.3%)	-	-				
Pond water								
No	7 (100.0%)	30 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Pit latrine								
No	3 (42.9%)	22 (73.3%)	1.0 (reference)					
Yes	4 (57.1%)	8 (26.7%)	3.67 (0.67, 20.10)	0.135	1.00 (0.06, 15.84)	1.000	0.74 (0.05, 12.10)	1.000
Open defecation								
No	6 (85.7%)	25 (83.3%)	1.0 (reference)					
Yes	1 (14.3%)	5 (16.7%)	0.83 (0.08, 8.52)	0.634				
Pork consumption								
No	7 (100.0%)	29 (96.3%)	1.0 (reference)					
Yes	0 (0.0%)	1 (3.3%)	-	-				
Consanguineous parents								
No	7 (100.0%)	27 (93.1%)	1.0 (reference)					
Yes	0 (0.0%)	2 (6.9%)	-	-				
Poor perinatal care								
No	7 (100.0%)	29 (96.3%)	1.0 (reference)					
Yes	0 (0.0%)	1 (3.3%)	-	-				
Unknown		-	-	-				

Family history of epilepsy (first-degree relative)								
No	7 (100.0%)	30 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Family history of epilepsy (second-degree relative)								
No	7 (100.0%)	30 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Febrile seizures								
No	7 (100.0%)	29 (96.3%)	1.0 (reference)					
Yes	0 (0.0%)	1 (3.3%)	-	-				
Measles								
No	5 (71.4%)	29 (96.3%)	1.0 (reference)					
Yes	2 (28.6%)	1 (3.3%)	11.6 (0.88, 153.28)	0.063	50.49 (1.42, 1799.38)	0.031	42.52 (1.34, 1353.41)	0.034
Meningitis								
No	7 (100.0%)	30 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Head injury								
No	7 (100.0%)	29 (96.3%)	1.0 (reference)					
Yes	0 (0.0%)	1 (3.3%)	-	-				
Sickle cell disease								
No	7 (100.0%)	30 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-					

* MICE – multiple imputation by chained equation, used to handle missing variable

Factors associated with epilepsy in children (less than 16 years) for Ijebu-Jesa

Risk Factor	People with active epilepsy* (n=7)	Controls* (n=18)	Univariate analysis**	P-value	Multivariate analysis**	P-value	Multivariate analysis with MICE**	P-value
Age					0.74 (0.36, 1.50)	0.403	0.33 (0.03, 3.93)	0.381
Gender								
Male	3 (42.9%)	10(46.3%)	1.0 (reference)		-			
Female	4 (57.1%)	8 (53.7%)	1.67 (0.29, 9.71)	0.570	0.70 (0.03, 14.63)	0.816	0.72 (0.03, 15.15)	0.834
Well water								
No	1 (14.3%)	4 (22.2%)	1.0 (reference)					
Yes	6 (85.7%)	14 (77.8%)	1.71 (0.13, 98.29)	0.656				
Stream water								
No	7 (100.0%)	16 (88.9%)	1.0 (reference)					
Yes	0 (0.0%)	2 (11.1%)	-	-				
Pond water								
No	7 (100.0%)	18 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-					
Pit latrine								
No	4 (57.1%)	7 (38.9%)	1.0 (reference)					
Yes	3 (42.9%)	11 (68.1%)	0.48 (0.08, 2.81)	0.413				
Open defecation								
No	6 (85.7%)	17 (94.4%)	1.0 (reference)					
Yes	1 (14.3%)	1 (5.6%)	2.83 (0.15, 52.74)	0.485				
Pork consumption								
No	7 (100.0%)	17 (94.4%)	1.0 (reference)					
Yes	0 (0.0%)	1 (5.6%)	-	-				
Consanguineous parents								
No	6 (85.7%)	18 (100.0%)	1.0 (reference)					
Yes	1 (14.3%)	0 (0.0%)	-	-				
Poor perinatal care								
No	4 (57.1%)	16 (94.1%)	1.0 (reference)					
Yes	3 (42.9%)	1 (5.9%)	12.0 (0.97, 148.32)	0.053	18.66 (0.60, 583.81)	0.096	16.43 (0.53, 511.98)	0.111
Unknown	-	-	-	-				
Family history of epilepsy (first-degree relative)								
No	6 (85.7%)	17 (94.4%)	1.0 (reference)					
Yes	1 (14.3%)	1 (5.6%)	2.83 (0.15, 52.74)	0.485				
Family history of epilepsy (second-degree relative)								
No	7 (100.0%)	18 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Febrile seizures								
No	3 (42.9%)	17 (94.4%)	1.0 (reference)					
Yes	4 (57.1%)	1 (5.6%)	22.67 (1.84, 279.37)	0.015	28.12 (0.64, 1243.79)	0.084	33.61 (0.92, 1228.22)	0.056

Measles								
No	3 (42.9%)	14 (77.8%)	1.0 (reference)					
Yes	4 (57.1%)	4 (22.2%)	4.67 (0.72, 30.10)	0.105	2.73 (0.10, 73.86)	0.551	3.97 (0.11, 149.73)	0.456
Meningitis								
No	6 (85.7%)	18 (100.0%)	1.0 (reference)					
Yes	1 (14.3%)	0 (0.0%)	-	-				
Head injury								
No	7 (100.0%)	18 (100.0%)	1.0 (reference)	-				
Yes	0 (0.0%)	0 (0.0%)	-	-				
Sickle cell disease								
No	7 (100.0%)	18 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				

* MICE – multiple imputation by chained equation, used to handle missing variable. Some did not run because of failure to converge, possibly because of sample size.

Factors associated with epilepsy in children (less than 16 years) Gwandu

Risk Factor Total 838	People with active epilepsy (n=82)	Controls (n=178)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Age								
					1.12 (0.96, 1.32)	0.139	1.18 (0.63, 2.23)	0.608
Gender								
Male	38 (50.5%)	106 (59.6%)	1.0 (reference)					
Female	44 (49.5%)	72 (40.4%)	1.70 (1.01, 2.89)	0.047	1.26 (0.54, 2.93)	0.596	1.61 (0.75, 3.45)	0.224
Well water								
No	8 (9.9%)	34 (19.1%)	1.0 (reference)					
Yes	73 (90.1%)	144 (80.9%)	2.15 (0.95, 4.89)	0.067	3.77 (0.56, 25.51)	0.174	3.25 (0.70, 15.17)	0.133
Stream water								
No	82 (98.9%)	178 (99.7%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Pond water								
No	82 (98.9%)	173 (97.2%)	1.0 (reference)					
Yes	0 (0.0%)	5 (2.8%)	-	-				
Pit latrine								
No	19 (19.8%)	7 (4.4%)	1.0 (reference)					
Yes	65 (80.2%)	153 (95.6%)	0.19 (0.07, 0.47)	<0.0001	0.49 (0.10, 2.52)	0.396	0.82 (0.24, 2.78)	0.746
Open defecation								
No	68 (82.9%)	171 (96.1%)	1.0 (reference)					
Yes	14 (17.1%)	7 (3.9%)	5.03 (1.95, 13.00)	0.001	19.33 (2.86, 130.78)	0.002	6.46 (1.69, 24.66)	0.006
Pork consumption								
No	82 (98.9%)	178 (99.7%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-					
Consanguineous parents								
No	51 (62.2%)	141 (79.2%)	1.0 (reference)					
Yes	31 (37.8%)	37 (21.8%)	2.32 (1.30, 4.12)	0.004	1.02 (0.37, 2.85)	0.966	1.03 (0.42, 2.54)	0.950
Poor perinatal care								
No	54 (66.7%)	172 (96.6%)	1.0 (reference)					
Yes	25 (30.9%)	6 (3.4%)	13.27 (5.17, 34.04)	<0.0001	10.00 (2.76, 36.23)	<0.0001	12.09 (3.76,38.85)	<0.0001
Unknown	2 (2.5%)	0 (0.0%)	-	-	-	-	-	
Family history of epilepsy (first-degree relative)								
No	54 (65.9%)	168 (94.9%)	1.0 (reference)					
Yes	28 (34.1%)	9 (5.1%)	9.68 (4.30, 21.78)	<0.0001	6.46 (1.54, 27.09)	0.011	3.12 (0.99, 9.85)	0.052
Family history of epilepsy (second-degree relative)								
No	58 (70.7%)	170 (96.1 %)	1.0 (reference)					
Yes	24 (29.3%)	7 (3.9%)	10.05 (4.11, 24.55)	<0.0001	1.21 (0.27, 5.40)	0.799	1.59 (0.41, 6.08)	0.500
Febrile seizures								
No	47 (57.3%)	170 (95.4%)	1.0 (reference)					
Yes	35 (42.7%)	7 (4.6%)	18.09 (7.55, 43.32)	<0.0001	15.26 (4.36, 53.44)	<0.0001	12.71 (4.24, 38.10)	<0.0001
Measles								

No	68 (82.9%)	174 (98.3%)	1.0 (reference)					
Yes	14 (17.1%)	3 (1.7%)	11.94 (3.33, 42.86)	<0.0001	6.15 (0.90, 42.14)	0.064	6.65 (1.06, 41.72)	0.043
Meningitis								
No	78 (95.1%)	173 (98.9%)	1.0 (reference)					
Yes	4 (4.9%)	2 (1.1%)	4.44 (0.79, 24.73)	0.089	5.81 (0.68, 49.57)	0.107	8.13 (1.00, 66.21)	0.050
Head injury								
No	79 (96.3%)	176 (99.4%)	1.0 (reference)					
Yes	3 (3.7%)	1 (0.6%)	6.68 (0.68, 65.25)	0.102	0.20 (0.007, 5.62)	0.346	0.34 (0.02, 6.29)	0.470
Sickle cell disease								
No	81 (89.8%)	176 (99.4%)	1.0 (reference)					
Yes	1 (1.2%)	1 (0.6%)	2.17 (0.13, 35.17)	0.585				

* MICE – multiple imputation by chained equation, used to handle missing variable

Appendix 22

Factors associated with epilepsy in adults (≥ 16 years) for Afikpo

Risk Factor Total 838	People with active epilepsy (n=33)	Controls (n=79)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Age								
	32 (20.0 – 43.0)	35.0 (23.0- 42.0)	0.99 (0.97, 1.02)	0.643	1.00 (0.95, 1.05)	0.898	1.05 (0.79, 1.38)	0.746
Gender								
Male	19 (57.6%)	36 (45.6%)	1.0 (reference)					
Female	14 (42.4%)	43 (54.4%)	0.62 (0.27, 1.40)	0.248	0.69 (0.15, 3.05)	0.622	0.68 (0.15, 3.02)	0.615
Well water								
No	26 (78.8%)	79 (100.0%)	1.0 (reference)					
Yes	7 (21.2%)	0 (0.0%)	-	-				
Stream water								
No	30 (90.9%)	73 (92.4%)	1.0 (reference)					
Yes	3 (9.1%)	6 (7.6%)	1.21 (0.29, 5.18)	0.791				
Pond water								
No	33 (100.0%)	79 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Pit latrine								
No	19 (57.6%)	57 (72.2%)	1.0 (reference)					
Yes	14 (42.4%)	22 (27.8%)	1.91 (0.82, 4.45)	0.135	2.14 (0.37, 12.31)	0.393	2.16 (0.38, 12.35)	0.385
Open defecation								
No	28 (84.9%)	64 (81.0%)	1.0 (reference)					
Yes	5 (15.1%)	15 (19.0%)	0.76 (0.25, 2.30)	0.630				
Pork consumption								
No	33 (100.0%)	76 (96.2%)	1.0 (reference)					
Yes	0 (0.0%)	3 (3.8%)	-	-				
Consanguineous parents								
No	32 (97.0%)	72 (91.1%)	1.0 (reference)					
Yes	1 (3.0%)	1 (0.9%)	2.25 (0.14, 37.11)	0.571				
Unknown	0 (0.0%)	6 (7.6%)	-	-				
Poor perinatal care								
No	23 (69.7%)	76 (96.2%)	1.0 (reference)					
Yes	10 (30.3%)	3 (3.8%)	11.01 (2.79, 43.43)	0.001	10.69 (1.24, 91.87)	0.031	11.07 (1.27, 96.40)	0.029
Family history of epilepsy (first-degree relative)								
No	25 (75.8%)	77 (97.5%)	1.0 (reference)					
Yes	8 (24.2%)	2 (2.5%)	12.32 (2.45, 61.87)	0.002	Failed		Failed	
Family history of epilepsy (second-degree relative)								
No	24 (72.7%)	78 (98.7%)	1.0 (reference)					

Yes	9 (27.3%)	1 (1.3%)	29.25 (3.52, 242.72)	0.002	9.83 (0.45. 216.13)	0.147	8.83 (0.40, 196.45)	0.169
Febrile seizures								
No	15 (45.5%)	76 (96.2%)	1.0 (reference)					
Yes	18 (54.5%)	3 (3.8%)	30.4 (7.95, 116.31)	<0.0001	21.44 (2.81, 163.64)	0.003	22.70 (2.88, 178.88)	0.003
Measles								
No	28 (84.8%)	76 (96.2%)	1.0 (reference)					
Yes	5 (15.2%)	3 (3.8%)	4.52 (1.01, 20.18)	0.048	1.72 (0.12, 24.82)	0.691	1.72 (0.12, 25.45)	0.693
Meningitis								
No	31 (93.9%)	73 (92.4%)	1.0 (reference)					
Yes	2 (6.1%)	6 (7.6%)	0.78 (0.15, 4.11)	0.774				
Head injury								
No	26 (78.8%)	76 (96.2%)	1.0 (reference)					
Yes	7 (21.2%)	3 (3.8%)	6.82 (1.64, 28.33)	0.008	11.89 (0.78, 180.95)	0.075	12.67 (0.81, 199.02)	0.071
Family history river blindness								
No	33 (100.0%)	74 (93.7%)	1.0 (reference)					
Yes	0 (0.0%)	4 (5.1%)	-	-				
Unknown	0 (0.0%)	1 (1.3%)	-	-				
Family history of Ivermectin use								
No	28 (84.9%)	37 (46.8%)	1.0 (reference)					
Yes	5 (15.1%)	42 (53.2%)	0.16 (0.06, 0.45)	0.001	0.05 (0.01, 0.30)	0.007	0.05 (0.006, 0.42)	0.006
Unknown	0 (0.0%)	0 (0.0%)	-	-				
Hypertension								
No	31 (93.9%)	74 (93.7%)	1.0 (reference)					
Yes	2 (6.1%)	5 (6.3%)	0.95 (0.18, 5.19)	0.957				
Diabetes								
No	30 (90.9%)	76 (96.2%)	1.0 (reference)					
Yes	3 (9.1%)	3 (3.8%)	2.53 (0.48, 13.26)	0.271				
Sickle cell disease								
No	33 (100.0%)	79 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-					
Stroke								
No	33 (100.0%)	74 (93.7%)	1.0 (reference)					
Yes	0 (0.0%)	5 (6.3%)						
Smoking								
No	32 (97.0%)	68 (87.2%)	1.0 (reference)					
Yes	1 (3.0%)	10 (12.8%)	0.21 (0.03, 1.73)	0.148				
Alcohol consumption								
No	25 (75.8%)	56 (71.8%)	1.0 (reference)					
Yes	8 (24.2%)	22 (28.2%)	0.81 (0.32, 2.08)	0.668				
Eclampsia (female cases = 14)								
No	0 (0.0%)	0 (0.0%)	1.0 (reference)					
Yes	1 (7.1%)	0 (0.0%)	-	-				

* MICE – multiple imputation by chained equation, used to handle missing variable

Factors associated with epilepsy in adults (16 years and above) by sites Ijebu_Jesa

Risk Factor	Adults with active epilepsy (n=17)	Controls (n=63)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Age								
	26.0 (25.0 – 31.0)	33 (24.5 – 45.5)	0.96 (0.91, 1.00)	0.078	0.97 (0.90, 1.04)	0.432	0.89 (0.62, 1.28)	0.546
Gender								
Male	9 (52.9%)	28 (44.4%)	1.0 (reference)					
Female	8 (47.1%)	35 (55.6%)	0.71 (0.24, 2.08)	0.534	1.44 (0.28, 7.54)	0.663	1.07 (0.24, 4.76)	0.928
Well water								
No	3 (17.7%)	23 (35.9%)	1.0 (reference)					
Yes	14 (82.3%)	41 (64.1%)	2.62 (0.68, 10.07)	0.162	1.79 (0.24, 13.39)	0.569	2.77 (0.44, 17.35)	0.275
Stream water								
No	17 (100.0%)	63 (98.4%)	1.0 (reference)					
Yes	0 (0.0%)	1 (1.6%)	-	-				
Pond water								
No	17 (100.0%)	64 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-					
Pit latrine								
No	10 (58.8%)	41 (64.1%)	1.0 (reference)					
Yes	7 (41.2%)	23 (35.9%)	1.25 (0.42, 3.72)	0.691				
Open defecation								
No	16 (94.1%)	62 (96.9%)	1.0 (reference)					
Yes	1 (5.9%)	2 (3.1%)	1.94 (0.17, 22.74)	0.599				
Pork consumption								
No	17 (100.0%)	56 (87.5%)	1.0 (reference)					
Yes	0 (0.0%)	8 (12.5%)	-	-				
Consanguineous parents								
No	17 (100.0%)	61 (98.4%)	1.0 (reference)					
Yes	0 (0.0%)	1 (1.6%)	-	-				
Unknown	0 (0.0%)	0 (0.0%)	-	-				
Poor perinatal care								
No	12 (70.6%)	62 (98.4%)	1.0 (reference)					

Yes	5 (29.4%)	1 (1.6%)	25.83 (2.77, 241.27)	0.004	34.44 (2.32, 511.97)	0.010	49.00 (3.37, 711.92)	0.004
Family history of epilepsy (first-degree relative)								
No	14 (82.4%)	62 (96.9%)	1.0 (reference)					
Yes	3 (17.6%)	2 (3.1%)	6.64 (1.01, 43.57)	0.048	14.57 (1.01, 210.17)	0.049	11.85 (1.19, 118.50)	0.035
Family history of epilepsy (second-degree relative)								
No	14 (82.4%)	62 (96.9%)	1.0 (reference)					
Yes	3 (17.6%)	2 (3.1%)	6.64 (1.01, 43.57)	0.048	2.45 (0.14, 42.93)	0.539	1.46 (0.12, 17.92)	0.766
Febrile seizures								
No	11 (64.7%)	60 (93.7%)	1.0 (reference)					
Yes	6 (35.3%)	4 (6.3%)	8.18 (1.98, 33.82)	0.004	8.29 (1.27, 53.94)	0.027	11.19 (1.91, 65.44)	0.007
Measles								
No	10 (58.8%)	47 (73.4%)	1.0 (reference)					
Yes	7 (41.2%)	17 (26.6%)	1.94 (0.63, 5.89)	0.245				
Meningitis								
No	16 (94.1%)	61 (95.3%)	1.0 (reference)					
Yes	1 (5.9%)	3 (4.7%)	1.27 (0.12, 13.05)	0.840				
Head injury								
No	16 (94.1%)	64 (100.0%)	1.0 (reference)	-				
Yes	1 (5.9%)	0 (0.0%)	-	-				
Family history river blindness								
No	15 (88.2%)	58 (100.0%)	1.0 (reference)					
Yes	2 (11.8%)	0 (0.0%)						
Unknown	-	-						
Family history of Ivermectin use								
No	11 (64.7%)	35 (85.7%)	1.0 (reference)					
Yes	6 (35.3%)	5 (11.9%)	3.93 (1.00, 15.34)	0.050	3.71 (0.59, 23.51)	0.164	2.52 (0.43, 14.77)	0.305
Unknown	0 (0.0%)	1 (2.4%)	-	-				
Hypertension								
No	17 (100.0%)	62 (96.8%)	1.0 (reference)					
Yes	0 (0.0%)	2 (3.1%)	-	-				
Diabetes								
No	17 (100.0%)	64 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-	-				
Sickle cell disease								

No	17 (100.0%)	64 (100.0%)	1.0 (reference)	
Yes	0 (0.0%)	0 (0.0%)	-	-
Stroke				
No	17 (100.0%)	64 (100.0%)	1.0 (reference)	
Yes	0 (0.0%)	0 (0.0%)	-	-
Smoking				
No	17 (100.0%)	60 (95.2%)	1.0 (reference)	
Yes	0 (0.0%)	3 (4.8%)	-	-
Alcohol consumption				
No	14 (82.4%)	49 (77.8%)	1.0 (reference)	
Yes	3 (17.6%)	14 (22.8%)	0.75 (0.19, 2.98)	0.683
Eclampsia (female cases = 8)				
No	0 (0.0%)	0 (0.0%)	1.0 (reference)	
Yes	2 (25.0%)	0 (0.0%)	-	-

* MICE – multiple imputation by chained equation, used to handle missing variable

Factors associated with epilepsy in adults (16 years and above) by sites Gwandu

Risk Factor	Adults with active epilepsy (n=106)	Controls (n=216)	Univariate analysis	P-value	Multivariate analysis	P-value	Multivariate analysis with MICE*	P-value
Age								
					0.96 (0.92, 1.00)	0.036	0.83 (0.69, 0.99)	0.041
Gender								
Male	57 (53.7%)	107 (49.5%)	1.0 (reference)					
Female	49 (46.2%)	109 (50.5%)	0.84 (0.53, 1.34)	0.475	0.77 (0.38, 1.55)	0.467	0.86 (0.44, 1.70)	0.674
Well water								
No	12 (11.3%)	35 (16.2%)	1.0 (reference)					
Yes	94 (88.7%)	181 (83.8%)	1.51 (0.75, 3.05)	0.246				
Stream water								
No	104 (98.1%)	215 (99.5%)	1.0 (reference)					
Yes	2 (1.9%)	1 (0.5%)	4.13 (0.37, 46.11)	0.249				
Pond water								
No	105 (99.1%)	216 (100.0%)	1.0 (reference)					
Yes	1 (0.9%)	0 (0.0%)						
Pit latrine								
No	15 (14.2%)	6 (3.1%)	1.0 (reference)					
Yes	91 (85.8%)	191 (96.9%)	0.19 (0.07, 0.51)	0.001	0.17 (0.05, 0.61)	0.007	0.56 (0.20, 1.52)	0.254
Open defecation								
No	103 (97.2%)	210 (97.2%)	1.0 (reference)					
Yes	3 (2.8%)	6 (2.8%)	1.02 (0.25, 4.16)	0.979				
Pork consumption								
No	106 (100.0%)	216 (100.0%)	1.0 (reference)					
Yes	0 (0.0%)	0 (0.0%)	-					
Consanguineous parents								
No	55 (51.9%)	174 (80.6%)	1.0 (reference)					
Yes	51 (48.1%)	42 (19.4%)	3.84 (2.31, 6.39)	<0.0001	3.54 (1.69, 7.45)	0.001	3.69 (1.78, 7.64)	<0.0001
Unknown	0 (0.0%)	0 (0.0%)	-	-				
Poor perinatal care								
No	68 (64.2%)	208 (96.3%)	1.0 (reference)					
Yes	38 (35.8%)	8 (3.7%)	14.53 (6.46, 32.66)	<0.0001	8.19 (2.99, 22.45)	<0.0001	9.75 (3.62, 26.26)	<0.0001

Factors associated with epilepsy in adults (16 years and above) by sites Gwandu

Family history of epilepsy (first-degree relative)								
No	74 (69.8%)	209 (96.8%)	1.0 (reference)					
Yes	32 (30.2%)	7 (3.2%)	12.91 (5.47, 30.50)	<0.0001	3.52 (0.86, 14.43)	0.080	2.04 (0.57, 7.34)	0.275
Family history of epilepsy (second-degree relative)								
No	80 (75.5%)	213 (98.6 %)	1.0 (reference)					
Yes	26 (24.5%)	3 (1.4%)	23.08 (6.80, 78.35)	<0.0001	6.38 (1.31, 31.13)	0.022	8.26 (1.74, 39.29)	0.008
Febrile seizures								
No	65 (71.7%)	20 (94.9%)	1.0 (reference)					
Yes	41 (28.3%)	11 (5.1%)	9.08 (4.12, 20.00)	<0.0001	8.21 (2.94, 22.96)	<0.0001	9.13 (3.44, 24.25)	<0.0001
Measles								
No	76 (76.6%)	207 (98.6%)	1.0 (reference)					
Yes	30 (23.4%)	9 (1.4%)	9.08 (4.98, 18.89)	<0.0001	2.40 (0.75, 7.66)	0.141	2.26 (0.73, 7.02)	0.159
Meningitis								
No	90 (84.9%)	213 (98.2%)	1.0 (reference)					
Yes	16 (15.1%)	3 (1.3%)	12.62 (3.59, 44.39)	<0.0001	1.81 (0.32, 10.25)	0.500	2.19 (0.41, 11.75)	0.362
Head injury								
No	94 (88.7%)	214 (99.1%)	1.0 (reference)					
Yes	12 (11.3%)	2 (0.9%)	13.66 (3.00, 62.23)	0.001	11.96 (1.74, 82.40)	0.012	11.56 (1.67, 80.07)	0.013
Family history river blindness								
No	97 (91.5%)	203 (94.0%)	1.0 (reference)					
Yes	8 (7.6%)	11 (5.1%)	1.52 (0.59, 3.91)	0.382				
Unknown	1 (0.9%)	2 (0.9%)	1.04 (0.09, 11.68)	0.971				
Family history of Ivermectin use								
No	77 (72.6%)	200 (92.6%)	1.0 (reference)					
Yes	29 (27.4%)	15 (6.9%)	5.02 (2.55, 9.88)	<0.0001	2.02 (0.73, 5.56)	0.175	2.15 (0.80, 5.77)	0.129
Unknown	0 (0.0%)	1 (0.3%)	-	-				
Hypertension								
No	102 (96.2%)	201 (93.1%)	1.0 (reference)					
Yes	4 (3.8%)	15 (6.9%)	0.53 (0.17, 1.62)	0.264				
Diabetes								
No	104 (98.1%)	208 (96.3%)	1.0 (reference)					
Yes	2 (1.9%)	8 (3.7%)	0.50 (0.10, 2.40)	0.386				
Sickle cell disease								

Factors associated with epilepsy in adults (16 years and above) by sites Gwandu

No	104 (98.1%)	213 (98.2%)	1.0 (reference)	
Yes	2 (1.9%)	3 (1.3%)	1.37 (0.22, 8.30)	0.735
Stroke				
No	104 (98.1%)	213 (98.6%)	1.0 (reference)	
Yes	2 (1.9%)	3 (1.4%)	6.26 (0.64, 60.93)	0.114
Smoking				
No	100 (94.3%)	211 (97.7%)	1.0 (reference)	
Yes	6 (5.7%)	5 (2.3%)	2.53 (0.75, 8.49)	0.133
Alcohol consumption				
No	103 (97.2%)	211 (98.2%)	1.0 (reference)	
Yes	3 (2.8%)	3 (1.4%)	1.17 (0.32, 4.26)	0.808
Eclampsia (female cases = 49)				
No	0 (0.0%)	0 (0.0%)	1.0 (reference)	
Yes	9 (18.4%)	0 (0.0%)	-	-

* MICE – multiple imputation by chained equation, used to handle missing variable