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Review

Prevalence and burden of epilepsy in Nigeria: A systematic review and meta-analysis of community-based door-to-door surveys

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ABSTRACT

Background: Studies on prevalence of epilepsy in Nigeria yielded figures ranging between 3.1 and 37 per 1000, giving one of the widest variations in prevalence of epilepsy world over. In order to accurately estimate clinical and public health impacts of epilepsy in Nigeria, robust and reliable epidemiological data are required for an appropriate estimation of logistical, economical, and social impacts of epilepsy.
Objective: The objectives of the study were to determine, using meta-analysis, the prevalence of epilepsy by pooling data from community-based door-to-door surveys conducted in various parts of Nigeria, explore the existing variation in prevalence of epilepsy in Nigeria along geopolitical regions and settlement setting of the country, and then evaluate the burden of epilepsy in Nigeria.
Methods: Prevalence estimates were derived from a random effects meta-analysis of observational studies reporting the prevalence of epilepsy in Nigeria. The derived estimate for the prevalence of epilepsy was applied to the total populations in Nigeria to give an estimated burden of epilepsy in Nigeria.
Result: Nine community-based door-to-door surveys, with quality data from different regions in Nigeria, were included. I-squared (I^2) heterogeneity was 88.5%. Random effects model (REM) estimate of overall prevalence of epilepsy from the studies was 8 per 1000 (95% confidence interval (95% CI): 6–10). The prevalence was highest (11 per 1000) in the south western part of the country. It was also higher among the rural (15 per 1000 people) than the urban (6 per 1000) dwellers. The burden of epilepsy in Nigeria, based on the prevalence estimate was 1,280,000 persons (95% CI: 960,000–1,600,000 persons).
Conclusion: In Nigeria, the estimated prevalence of epilepsy is 8 per 1000 people indicating a substantial burden of the disease in the country.

1. Introduction

Epilepsy is one of the most prevalent noncommunicable neurological conditions affecting more than 70 million people worldwide most of whom live in developing countries. On the African continent, it affects 10,000,000 people directly from childhood to aging population [1]. It is an important cause of disability worldwide [2], and one of the most common noninfectious neurologic disease in developing African countries, Nigeria inclusive [3,4].

The exact prevalence of epilepsy in developing countries has been difficult to obtain. Consequently, there are marked variations in prevalence of epilepsy figures in different developing countries or even in different regions or neighboring geographical settings of the same country. The estimated prevalence of epilepsy in Africa is as high as 15 per 1000 [5], a figure that is about 3 times higher than the prevalence of epilepsy in the industrialized world [6].

In Nigeria, data on prevalence of epilepsy varied remarkably from one place to another with figures, obtained from population-based studies, ranging from 3.1 to 37 per 1000 [4,7–10]. This marked variation in prevalence estimates may be attributed to a wide variation in study design, risk factors, population demographics, case definitions, or case ascertainment. This discrepancy is also observed even in studies that employed similar methodologies as exemplified by two Nigerian studies with the same protocol that reported discordant prevalence of 5.3 and 37.0 per 1000 in Igbo-Ora and Aiyété respectively, two areas in south west Nigeria that were demographically similar, and from the same ethnic community 20 km apart from each other [3,4].

The wide variation in the estimates of prevalence from Nigeria, in contrast to what obtains in the developed countries, complicates the use of these data in estimating the number of people with epilepsy (PWE) who may benefit from treatment and in informing national public

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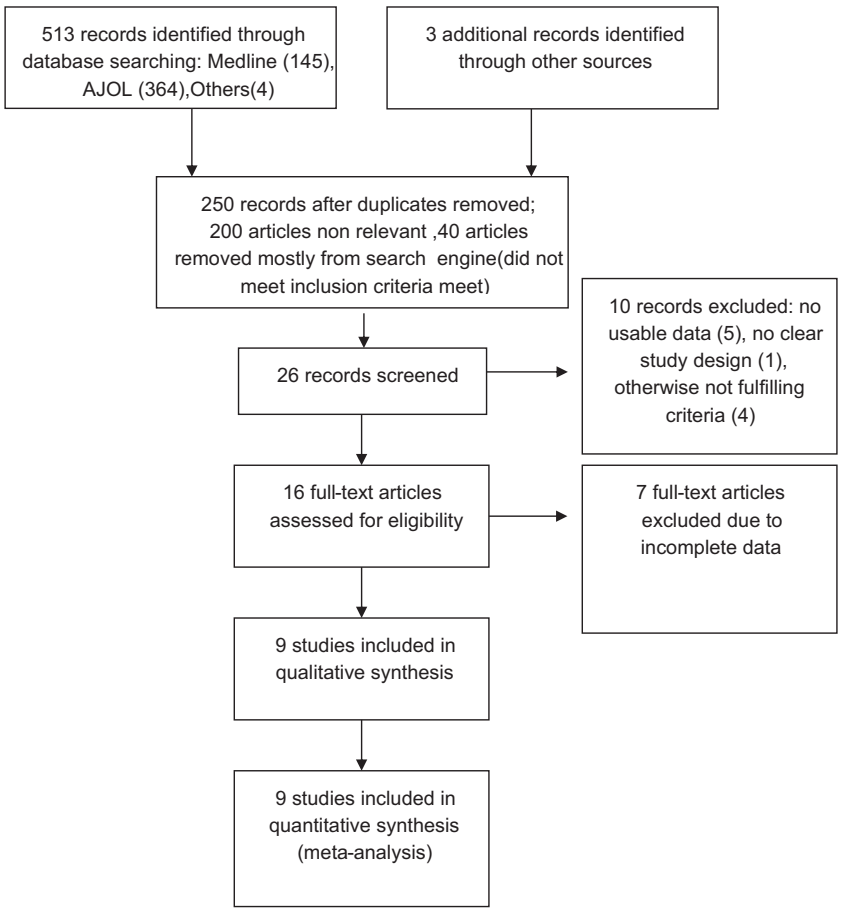

Fig. 1. Flow diagram of the process of article selection for the meta-analysis and review.

health policy. Furthermore, differences in prevalence figures could have implications for resource allocation in public health interventions.

Thus, a reliable national prevalence rate of epilepsy is needed to judge the burden of epilepsy and to develop programs and priorities to tackle problems associated with epilepsy [11]. Furthermore, knowledge of a national estimate of epilepsy would be useful in the design and implementation of nationwide multisite prevalence studies on epilepsy.

A systematic review and meta-analysis of observational studies (Meta-analysis of Observational Studies in Epidemiology (MOOSE)) could help explain the variability in the existing literature, and through pooling of the available data, produce more precise prevalence estimates as the strength of a well conducted meta-analysis is in its ability to pool the results from the existing small studies that are possibly underpowered to detect a desired effect size (ES).

The current study, therefore, aimed to determine the prevalence of epilepsy by pooling data from community-based door-to-door surveys conducted in various parts of Nigeria, explore the existing variation in prevalence of epilepsy in Nigeria along geopolitical regions and settlement setting (rural versus urban) of the country, and evaluate the burden of epilepsy in Nigeria.

2. Methods

2.1. Literature search

An English-language literature search was conducted on PubMed, EMBASE, Institute for Scientific Researcher (ISI), African Journals Online (AJOL), African Index Medicus, databases, existing systematic reviews, specialty journals, websites, and other search engines such as Google. Reference lists of identified articles were also searched for relevant titles, and these were in turn searched online. Conduct and reporting of this study were in accordance with the guidelines on MOOSE and

Table 1
Characteristics of included studies in prevalence of epilepsy in Nigeria.

Author	Year of publication	Year of study	Cases	Total (study population)	Prevalence/100	[a]Region	Setting	[b]Survey method	Quality
Dada	1970	1970	34	2592	0.13	SW	Urban	Q + EEG	B
Oshuntokun et al.	1982	1982	33	903	3.7	SW	Rural	Q + EEG	B
Oshuntokun et al.	1987	1987	100	18,954	0.53	SW	Urban	Q + EEG	A
Longe et al.	1989	1989	18	2925	0.62	SS	Rural	Q + EEG	B
Osakwe et al.	2013	2010	52	2500	2.08	SE	Rural	Q	B
Osakwe et al.	2013	2010	28	6000	0.47	NC	Urban	Q	B
Mustapha et al.	2014	2013	10	2212	0.45	SW	Rural	Q + EEG + F	A
Nwani et al.	2015	2010	29	6800	9.43	SE	Urban	Q + EEG	A
Ezeala-Adikaibe et al.	2015	2013	49	8228	0.6	SE	Urban	Q + EEG	A

[a] Q — questionnaire, EEG — electroencephalography, F — focus group discussion.
[b] SW — South West, SS — South South, SE — South East, NC — North Central.

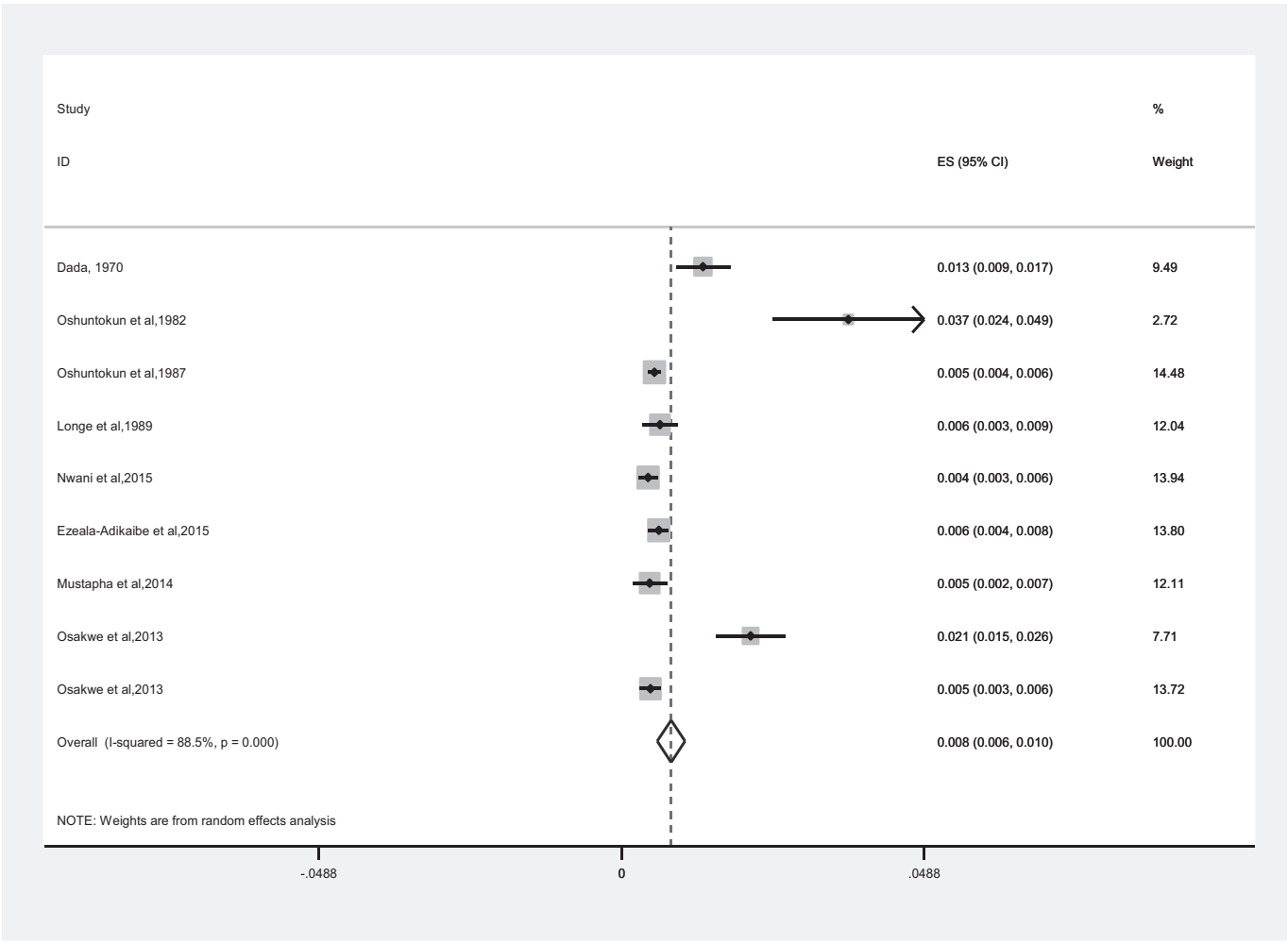

Fig. 2. Forest plot of studies included in meta-analysis with pooled epilepsy prevalence (ES values are approximated to 2 decimal places).

Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) respectively [12,13].

2.2. Search strategies

The database search was performed using the main search terms such as "Epilepsy", "Seizure disorder", "Prevalence" & "Nigeria" to identify relevant articles from April 1960, which is the year of independence in Nigeria, to April 2018. Where applicable, combined text words and Medical Subject Headings (MeSH) terminologies were used. Boolean operators were used to combine the search terms as necessary, and the MeSH tree was used to increase the specificity of the search terms in MEDLINE, EMBASE, and AJOL databases. The review question was broken down into search terms/elemental facets to develop a search strategy.

To make our searches more effective, a combination of these keywords was also explored. Titles and/or abstracts of the search results were screened to determine the relevance of the studies. Full texts of selected studies were also reviewed. (Search date 16/05/2018–18/06/2018). When required, we contacted the authors and also manually searched the reference lists of all identified publications and recent systematic reviews. Book chapters and review articles on the subject were also perused independently by two investigators on-screen to select potentially relevant studies. Studies that evaluated the prevalence of epilepsy were considered prima facie relevant.

3. Study selection

We included cross-sectional or prospective community-based or population-based studies measuring prevalence of epilepsy from any part of Nigeria. The estimate of the prevalence was obtained from papers that met the following criteria outlined:

3.1. Inclusion and exclusion criteria

A study was included if it reported prevalence or provided the denominator to allow recalculation of the presented or required estimates

Table 2
Summary of overall and subgroup analysis prevalence of epilepsy in Nigeria.

	Prevalence per 1000	95% confidence interval
Overall prevalence	8.0	6–10
Prevalence based on region		
South West	11	5–17
South South	6	3–9
South East	9	4–14
North Central	5	3–6
Prevalence based on setting		
Rural	11	6–24
Urban	6	4–7
Prevalence based on date		
<2010	12	6–17
≥2010	7	4–10

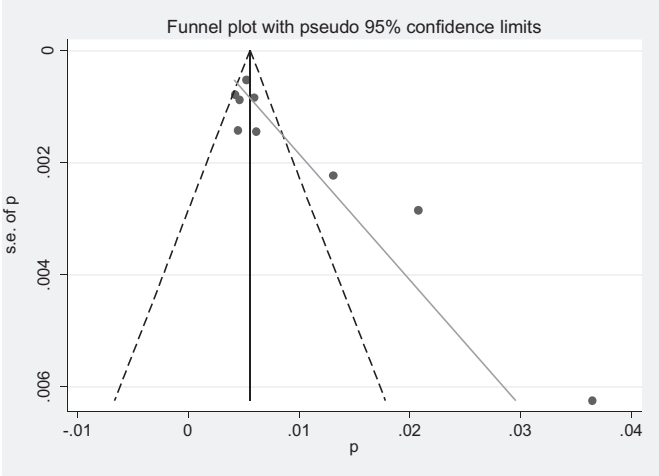

Fig. 3. Graphic representation of publication bias with funnel plot of included studies and representation of missing studies using trim and fill method.

and of epilepsy collected data using standardized previously validated questionnaires in door-to-door surveys and included a definition of epilepsy as two or more unprovoked seizures occurring at least 24 h apart.

A study was excluded if it examined only acute symptomatic seizures, specific seizure patterns, or epileptic syndromes. Hospital-based studies were excluded. Studies without identifiable origin or with inadequate data, i.e., did not report the prevalence or did not provide the denominator to allow recalculation of the presented or required estimates were also excluded.

3.2. Data extraction

We extracted data using a form designed to capture the information of interest from the articles for this review. Two investigators (OLF & ODS) selected and extracted all the data independently. From each included study, we obtained information on author, study setting, study type, study population, data collection and ascertainment method(s), and age of study subjects. All meta-analyses were carried out in STATA 12 (StataCorp, College Station, TX, U.S.A.).

3.3. Quality assessment and reporting format

This meta-analysis was done and reported according to specific guidelines/checklist: MOOSE [12] and PRISMA statements (Fig. 1) [13]. A 12-point scoring system was used to rate the quality of the articles extracted. The scoring was based on the modified Downs and Black checklist [14]. The modified checklist, which had been previously used and validated [15,16], comprises 12-point questions (objective of the study clearly described, study design clearly stated, participants representative of the population from which they were recruited, participants accrued during the same time period, modest sample size, management of missing data, age, gender, and other characteristics explored or reported). The other questions in the checklist included report of confounders, report on potential biases, and clear statement on outcome, i.e., prevalence. The assessment also included other items known to be associated with study quality. Two of the investigators independently conducted the scoring of the articles. We graded the quality of the studies into three levels (C (1–4), B (5–8), and A (9–12)) in increasing order of quality from C to A.

4. Data analysis

The primary outcome measure was the prevalence of epilepsy in Nigeria. The standard error of prevalence was determined by binomial probability distribution. The prevalence of epilepsy, which was expressed in percentage with their respective 95% confidence interval (95% CI), was calculated for each of the selected studies. The log of prevalence (logP) and the standard error of logP were computed for the respective studies. Meta-analyses were conducted for prevalence estimates. Given the inherent variability among observational studies, we combined results and obtained meta-analysis estimates using a random effects model (REM) by DerSimonian and Laird for estimate summary and 95% CIs from included studies [14].

Statistical heterogeneity was evaluated by conducting tests of between-study heterogeneity and I-squared (I^2) statistics with $I^2 >$ 50% denoting substantial heterogeneity, tau-squared (T^2), and Galbraith plot. Sensitivity analysis to examine the impact of specific publications on the overall prevalence was performed.

Subsequently, restricted scenario or subgroup analyses were performed on data derived from studies with similar characteristics. Publication bias and small study effect were assessed by visual inspection of funnel plots and by using Begg's adjusted rank correlation tests and

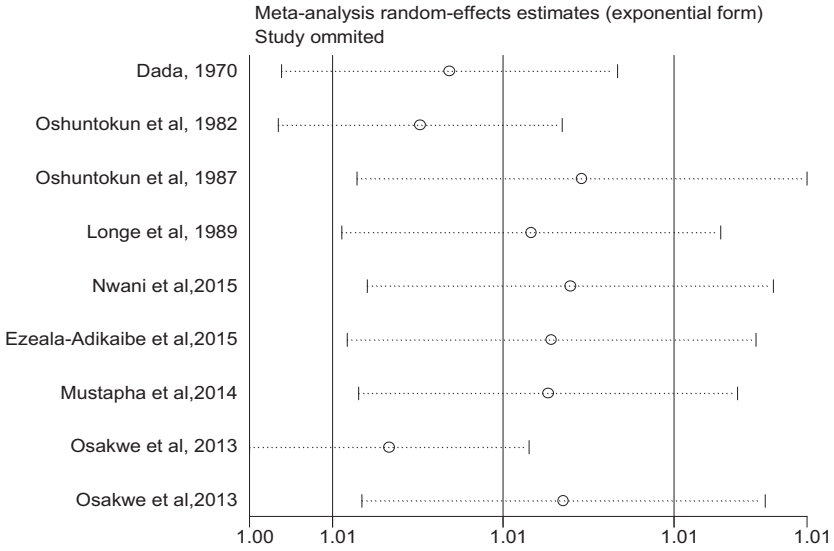

Fig. 4. Sensitivity analysis of the studies included in the meta-analysis.

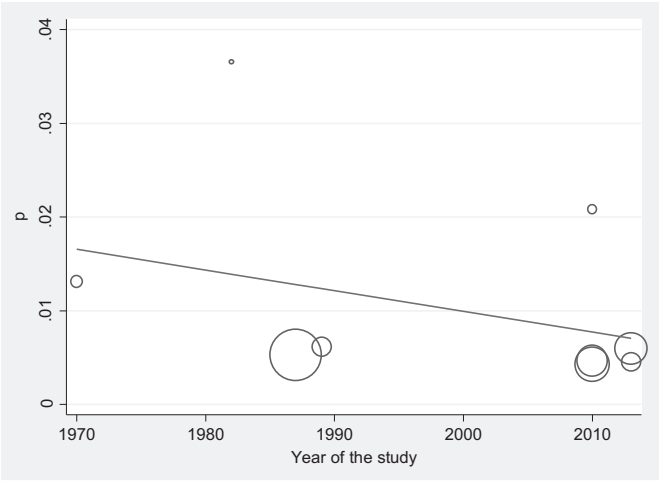

Fig. 5. Meta-regression plot showing the trend in epilepsy prevalence over the years.

Egger's regression asymmetry test [17,18]. Given the inconsistency detected in both tests [19], we also performed univariate, weighted, least-squares meta-regressions to identify study-level characteristics (mean or median age of participants and years of study) associated with prevalence. All analyses were carried out using Stata version 12.0 (Stata Corp., College Station, TX, USA).

5. Results

Nine community-based studies [3,4,7,9,10,20–22] met the inclusion criteria for the meta-analysis. Table 1 shows the main characteristics of the studies included in the final analysis. They included studies from South East (SE), South West (SW), South South (SS), and North Central (NC) of Nigeria and as such can be considered to be fairly representative of Nigeria as a whole. The total number of participants was 51,114 in the 9 studies analyzed. Only one (11.1%) study was conducted on less than 2200 individuals, and 44.4% were conducted on more than 6000 individuals. Five (55.5%) of the studies were conducted in rural areas. The studies included in the analysis were all published after 1970, with 55.5% of the studies published after 2010.

5.1. Overall prevalence

All included studies were pooled for meta-analysis. The prevalence of epilepsy ranged from 0.31% (3.1 per 1000) to 3.7% (37 per 1000) among the studies analyzed. The pooled prevalence estimate for Nigeria was 0.8% (95% CI: 0.6–1.0%) (Fig. 2, Table 2). The measure of heterogeneity I^2 was 88.5% ($p = 0.000$). Publication bias was obtained on Egger's and Begg's testing (Begg's test, $p = 0.022$; Egger's test, $p = 0.007$). This finding was also evident in the funnel plot shown in Fig. 3. On sensitivity analysis, i.e., the weight of individual studies on the pooled summary effect, it showed that the prevalence estimate was dominated by Osuntokun et al. [3], Ezeala-Adikaibe et al. [8], Nwani et al. [9], and Osakwe et al. [10] studies (Fig. 4).

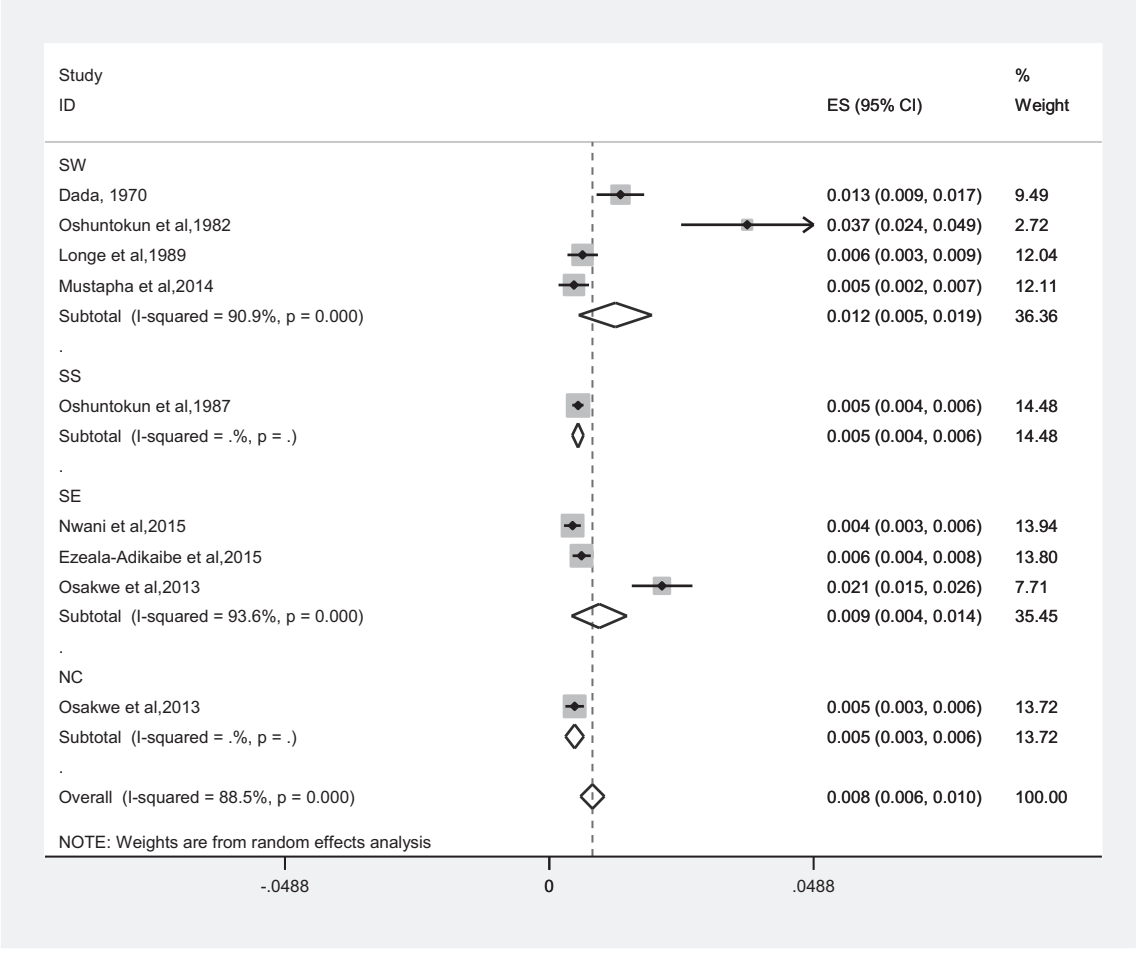

Fig. 6. Forest plot showing subgroup analysis by region. *SW — South West, SS — South South, SE — South East, NC — North Central.

Meta-regression of prevalence and year of the studies, ranging from 1970 to 2013 had a slope coefficient of −0.00022 (95% CI: −0.00073 to 0.00029, p = 0.135) in the 9 studies (Fig. 5) depicting that the prevalence of epilepsy decreases by 2.2×10^{-4} per year, but this relationship was not statistically significant.

Assuming Nigeria has an estimated population of 160 million people [23], the overall burden of epilepsy, based on our estimates, was 1,280,000 persons (95% CI: 960,000–1,600,000 persons).

5.2. Subgroup analysis

As a sequel to the heterogeneity recorded in the overall meta-analysis, which could be partly explained by different study populations in the composite studies, we performed a subgroup analysis by the geopolitical regions of Nigeria where the studies were conducted, the settings (rural or urban), and date of the study (before and after 2010). The subgroup analysis along geopolitical regions of Nigeria showed that the prevalence of epilepsy was 1.1% (95% CI: 0.5%, 1.7%) in SW, 0.6% (95% CI: 0.3%, 0.9%) in SS, 0.9% (95% CI: 0.4%, 1.4%) in SE, and 0.5% (95% CI: 0.3%, 0.6%) in NC (Table 2, Fig. 6). Stratified analysis across settlement settings (rural versus urban) showed that the prevalence of epilepsy in urban setting was 0.6% (95% CI: 0.4%, 0.7%) whereas the prevalence in the rural setting was 1.5% (95% CI: 0.6%, 2.4%) (Table 2, Fig. 7). When the analysis was conducted based on studies conducted before and after 2010, the prevalence of epilepsy was 1.2% (95% CI: 0.6%, 1.7%) and 0.7% (95% CI: 0.4%, 1.0%) respectively (Table 2, Fig. 8).

6. Discussion

In 2011, the consensus at the United Nations high-level meeting on the prevention and control of noncommunicable diseases (NCDs) was that NCDs were the universal leading causes of death and that the burden of NCDs is fast growing at an alarming rate [24]. Noncommunicable diseases are expected to account for the death of over 50 million persons annually by the year 2030 [24]. Low- and middle-income countries (LMICs) that lack the resources, amenities, and infrastructure to cope with NCDs are expected to bear the brunt of these diseases [25,26]. As epilepsy is one of the most common NCD of neurologic origin, accurate estimation of its prevalence and burden has, therefore, become imperative for both monitoring and policy development in order to combat the menace [24,27].

The estimated overall prevalence of epilepsy generated by pooling data from nine community-based studies in Nigeria is 8 per 1000 people. All the data pooled in this meta-analysis were derived from door-to-door community-based surveys that are considered to be the best available method for obtaining prevalence of disease data [28]. It is crucial that in a true prevalence study on epilepsy, the study population of interest should be representative of the general population with epilepsy, regardless of whether the study aims to cover all forms of epilepsy

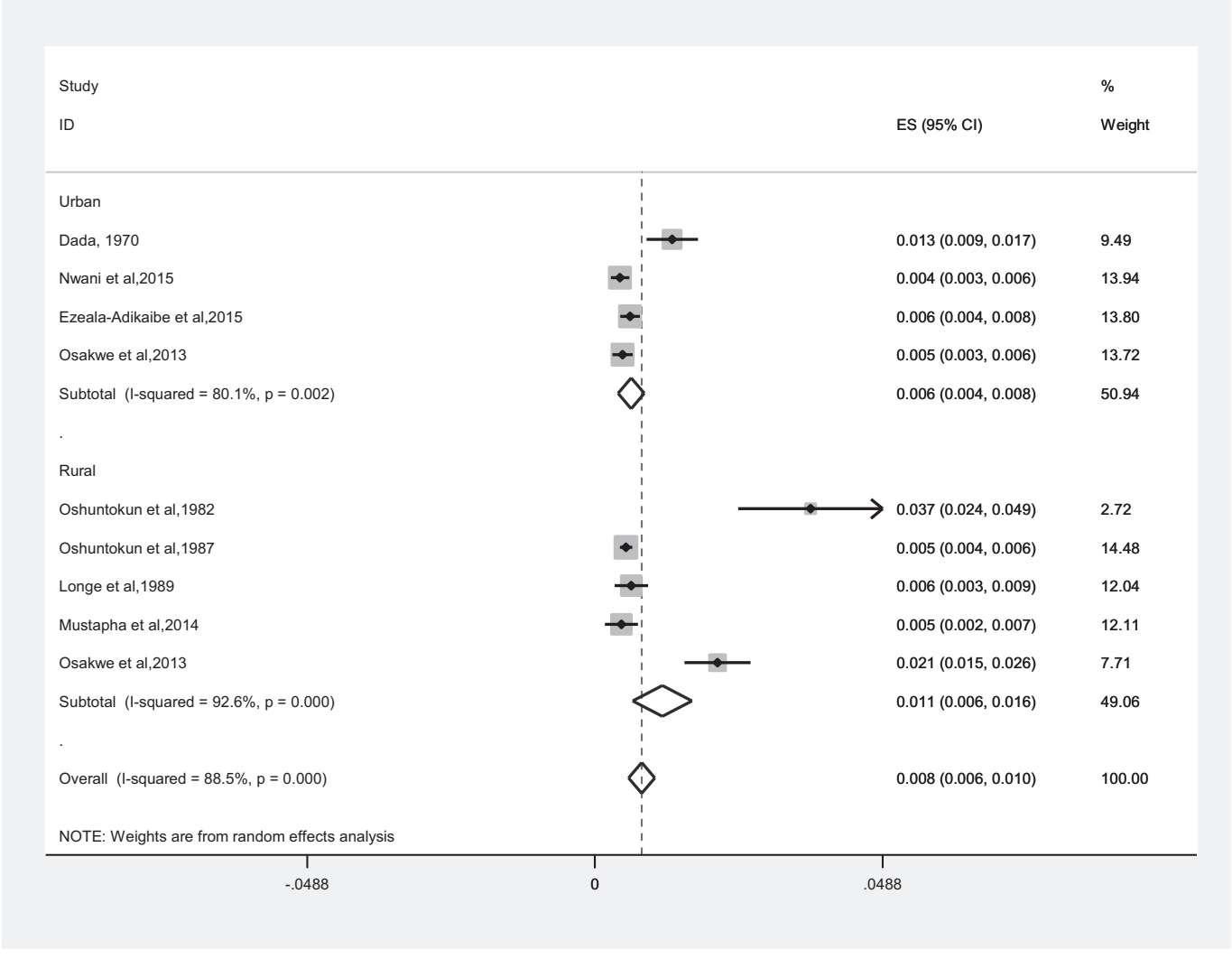

Fig. 7. Forest plot showing subgroup analysis by setting (rural vs urban).

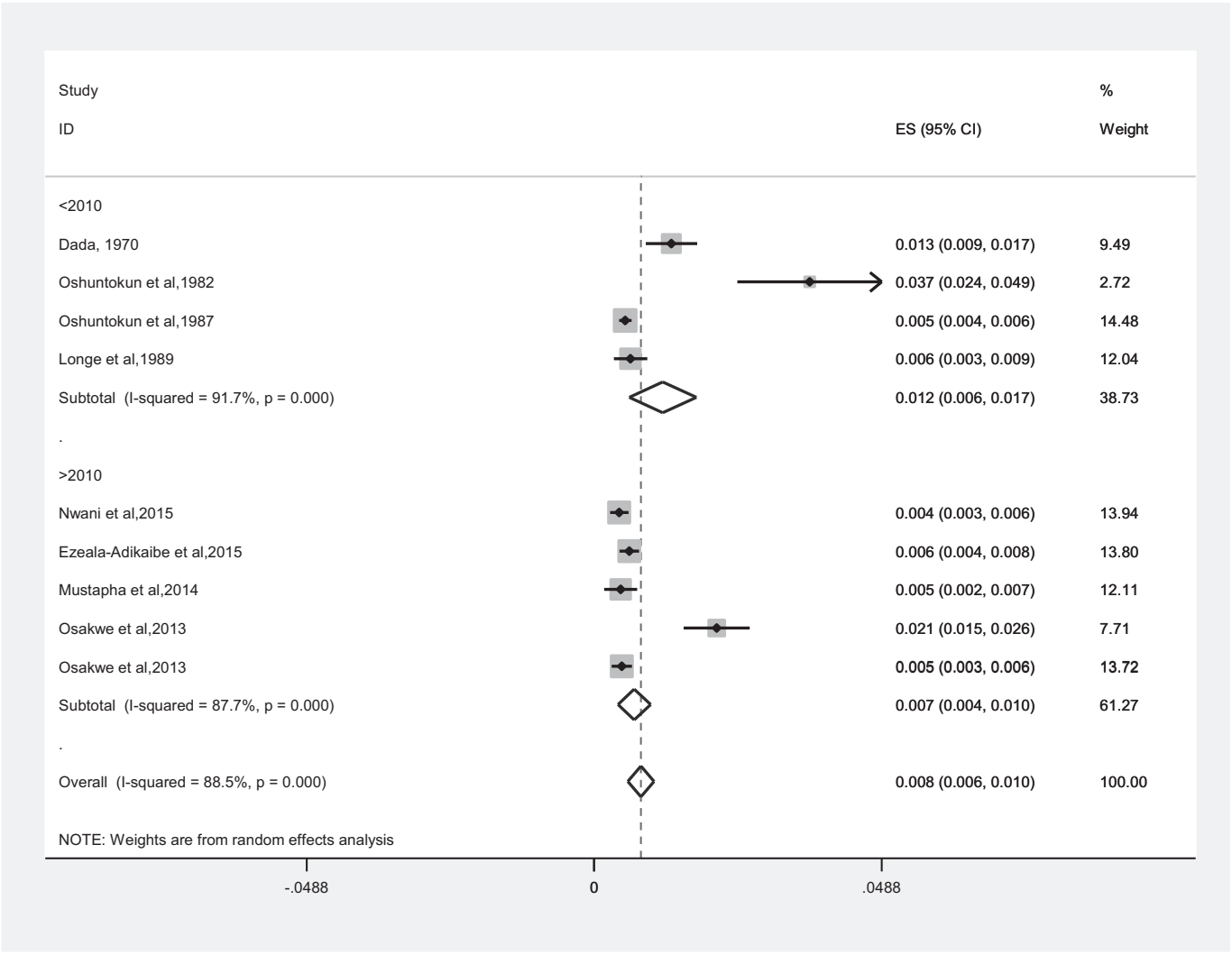

Fig. 8. Forest plot showing subgroup analysis by year of the study (before and after 2010).

or only specific forms or age groups. Studies using multiple sources for identification will identify the vast majority of persons with epilepsy and can be considered community-based and, thus, representative of the general population with epilepsy [29].

The figure (8 per 1000) obtained in the current study is comparable with the figures reported in other developing countries. Prevalence of 10 per 1000 was reported in Pakistan [30–32], 9.3/1000 in Egypt [33], and 10–12 per 1000 in Bangladesh [34]. The prevalence of epilepsy obtained through meta-analysis of twenty studies in India was 5 per 1000 [11]. However, Gu et al., in a meta-analysis of pooled data from 38 studies on epilepsy, showed that the overall prevalence of epilepsy in the People's Republic of China was 2.89‰ [35]. The figure obtained in our study is significantly higher than that obtained in the People's Republic of China. It is, however, worthy of note that the studies selected for meta-analysis in the China study are more heterogeneous. In contrast to our study, in which only population-based surveys were selected, some of the individual studies in the China study meta-analysis were conducted on only pediatric age group while some were carried out only in the adult age group.

Lower figures were reported in developed countries; in North America, the age-adjusted prevalence ranged from 5.1% to 7.1% per 1000 [36,37] while in Europe, the prevalence rate of epilepsy in all ages ranged from 3.3 to 7.8% per 1000 [29]. The higher prevalence rate obtained in the current meta-analysis compared with the figures in developed countries is not surprising given the extreme conditions of poverty that facilitate transmissions of parasitic and bacterial infections as well as poor antenatal, delivery, and general healthcare that ultimately engendered epilepsy in resource-poor countries like Nigeria. It is for the same reasons that sub-Saharan Africa account for 80% of global patients with epilepsy [38].

On the other hand, the higher prevalence of epilepsy in Nigeria may indicate that it is necessary to improve the health service system, such as effective primary healthcare programs to combat the risk factors for epilepsy like childhood infections and poor obstetrics care covering both rural and urban communities in the country. The skewed funnel plot found in this study suggests publication bias that may be due to a wide variability in the reported prevalence of epilepsy in Nigeria, methodological differences, and gaps for unreported prevalence. Nevertheless, these have been adjusted for by the "filled" data points derived from the trim and fill method.

The presence of variation in true effect sizes underlying the different composite studies in this analysis is largely unavoidable in a meta-analysis of epidemiological studies, as multiple studies, performed by different teams in different places with different methods, all ended up estimating the same underlying parameter [39,40].

Reasons for the heterogeneity observed in this analysis would include the use of different survey methods, varying screening tools, and different case ascertainment standards.

In this study, several attempts were made to mitigate the effect of possible methodological variation of the component studies. We

explored within and in-between studies variation by using REM for analysis of the pooled data, quantification of the magnitude of the heterogeneity, conduction of sensitivity analysis, and subgroup analysis.

Nigeria is inhabited by people of different ethnicity with different beliefs and sociocultural practices. Subgroup analysis by geopolitical regions in Nigeria showed that South West Nigeria had the highest epilepsy prevalence. This finding may not be unconnected with higher number of studies from south west part of Nigeria included in the analysis. The lowest prevalence in this study, which was observed in the North Central region, could be a reflection of a fewer number of studies from the region that merited inclusion in the meta-analysis [11].

Our study showed that the prevalence of epilepsy in rural settings in Nigeria was 2.5 times higher than in urban/semiurban settings. This finding, which is in agreement with the report of Gu et al. in a meta-analysis of prevalence of epilepsy in China [35], is a common occurrence in developing countries [41]. However, it contrasts with the reports from Pakistan [42], India [43], Chile [44], and Italy [45] that indicated that the prevalence was higher in urban than in rural areas. The difference between the prevalence of epilepsy in rural and urban settings could be attributed to the inadequacy of healthcare services for identification and handling of the risk factors as well as lack of prompt diagnosis and management of risk factors for epilepsy in the rural areas.

Pooled data from studies carried out before 2010 (1970–1989) yielded a higher prevalence than those conducted after 2010 in Nigeria. The former group of studies were conducted more than three decades before the latter group of studies; improvement in healthcare services, improved health awareness, establishment of primary healthcare programs, increasing effort towards prevention of risk factors for epilepsy in the communities like childhood infections, and a better obstetrics care could have accounted for the reduced prevalence of epilepsy seen in the pooled data from studies after 2010.

The limitations of this meta-analysis include the absence of studies from North West and North East regions of Nigeria, relative scarcity of community-based epilepsy prevalence studies in Nigeria, lack of uniform screening instruments, and the presence of methodological issues such as varying diagnostic tools and divergent study designs that might have influenced the prevalence figure obtained in the composite studies. The possibility of underestimation by the individual studies selected for this meta-analysis cannot be overemphasized as epilepsy-associated stigma, which might have resulted in denial of having the disorder, could influence the outcome of prevalence epilepsy in the study communities.

It is, however, worthy of note that this study does not, in any way, underestimate the fact that only a large representative rigorous national epidemiological study conducted at the same time can give a more reliable overall prevalence of epilepsy in Nigeria. However, in the absence of such a national survey, a meta-analysis of all the observational studies cutting across most, if not all, the geopolitical zones of Nigeria, provides the best evidence and, hence, could be of use in planning prevention and treatment of epilepsy in Nigeria.

7. Conclusion

This study showed that overall prevalence estimate of epilepsy in Nigeria is 8 per 1000 people. This prevalence, which is associated with high burden, is 2.5 times higher in rural compared with urban communities and varies slightly across the geopolitical zones of Nigeria. The need for an intensive effort towards prevention and treatment of epilepsy cannot be overemphasized.

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Conflict of interest

The authors declared no conflict of interest.

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