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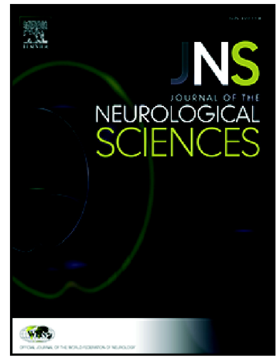

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Estimating the uptake of brain imaging and 30-days stroke mortality in Nigeria: A meta-analysis of hospital-based studies

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Abstract

Purpose: This study aims to estimate the computed tomography (CT) and Magnetic resonance imaging (MRI) uptake, stroke subtypes and 30-days case-fatality in Nigeria.

Methods: Stroke diagnosis and mortality data were identified from relevant databases. A random effect meta-analysis was conducted to obtain the pooled percentage uptake of CT/MRI, including 30-days case fatality and a meta-regression-like epidemiological model was applied on all data points.

Findings: A total of 24 studies involving 5874 stroke patients conducted in predominantly tertiary referral hospitals met the inclusion criteria. The pooled CT/MRI uptake in the last seven years was 46.66% (95% CI =15.35 to 77.98, 8 studies). There were significant variations in the prevalence of stroke subtypes. The pooled prevalence ischemic stroke was highest (55.32%, 95% CI 48.67 to 61.97, 16 studies), followed by intracerebral haemorrhage (ICH) (32.69%, 95% CI 25.54 to 39.83, 16 studies), subarachnoid haemorrhage (SAH) (3.76%, 95% CI 2.30 to 5.22, 14 studies). In addition, the stroke of undetermined aetiology was found to be 16.57% (95% CI, 7.44-25.70, 8 studies). Overall, the 24-hours, one-week and 30-days case-fatality from stroke were 10.84% (95% CI, 4.48-17.20), 24.62% (95% CI, 17.20-32.04) and 33.28% (95% CI, 27.80-38.77), respectively. There was a moderate negative correlation between prevalence of brain imaging uptake and ischaemic stroke, albeit not statistically significant (Spearman rho = 0.333, p-value = 0.412).

Conclusion: Uptake of CT/MRI procedure for stroke is poor in Nigeria. Although poverty, inaccessibility and influence of major risk factors remain pronounced, scaling up of effective strategies for stroke prevention and management should be a major public health policy priority in Nigeria.

Key Words: Stroke; computed tomography; Magnetic resonance imaging; Hospital-based study

1. Introduction

Stroke is the leading cause of death and disability worldwide. Current estimates found that about 15 million new acute strokes occur every year and about 51.0 million (46.6–57.3) disability adjusted life-years (DALY) were lost among 20 to 64 year-olds in 2013 [1]. In the past few decades, research evidence revealed a constant decrease in the incidence of stroke in high-income countries reaching up to 42% [2]. However, there has been a dramatic increase in stroke incidence of up to 100% in low- and middle-income countries (LMICs) where 85% of global deaths from stroke has occurred [1]. The burgeoning increase has been associated with socioeconomic, environmental and lifestyle factors [3-5].

In WHO African region, a systematic review evidence in 2013 reported 535,000 (87.0–625.3) new stroke cases and 2.09 million (2.06–4.93) stroke survivors suggesting an increase of 10.8% and 9.6% of incident stroke cases and stroke survivors respectively [5]. Specifically, recent evidence from hospital-based studies in Nigeria found that stroke accounted for more than 45% neurological admissions and 5-17% of medical deaths with about 2 out of every 5 cases dying within 30 days of onset [6]. This estimate is huge especially given the fact that the data does not include stroke patients from the local community who could not access neurological care due to prohibitive out-of-pocket expenses and distance to the urban hospital where such services could be purchased [7, 8].

Despite the upward trend in stroke mortality and even among those that could access hospital care in Nigeria, uptake of CT/MRI diagnostic and management procedures remain unknown. In the last few years, there has been a sharp rise in the establishment of tertiary hospitals across the states and geopolitical regions by both federal and state government aimed at strengthening the medical education curriculum in Nigeria [9]. Most of these tertiary referral hospitals have neurological departments equipped with functional stroke units and state of the art CT and MRI machines [9, 10]. However, there is no published systematic review or national survey estimates of the proportion of new and recurrent cases that have undergone CT scan and/or MRI in stroke diagnoses and management. In addition, no study has reported any national or regional estimates on the proportion of stroke subtypes or the percentage of 30-days stoke outcomes.

Current guidelines on the diagnosis and management of stroke recommend CT scans and or MRI to distinguish stroke types and accurately triage patients, expedite clinical decision and improve outcomes particularly among patients with acute stroke [11]. Evidence found that increased stroke mortality and morbidity has been linked with specific stroke subtypes, with approximately 50% or higher for primary intracerebral haemorrhage and subarachnoid haemorrhage and about a quarter of ischemic strokes fatality within a month [12], options for increased CT/MRI uptake remains an important public health priority.

Recommendations on the management of acute stroke of unknown aetiology rely on existing epidemiological data in high-resource settings, such data may not be generalised or applicable in Nigeria [13]. With increased uncertainty among physicians and neurological specialists on how best to manage cases presenting with acute stroke when CT/MRI is unavailable to distinguish ischaemic from other stroke types, there is no documented national set protocol derived from locally available evidence for acute management of stroke patients at national and referral hospitals in Nigeria. This underscores the need for a quality review of hospital-based studies in Nigeria.

The aim of this study therefore, is to provide the accurate estimate of CT/MRI uptake for stroke including the proportions of different stroke sub-types and 30-days mortality among those presenting to tertiary referral hospitals in Nigeria. Suck knowledge would no doubt provide a realistic approach to reduce poor stroke outcomes such as cognitive impairment, physical disability and even death. In addition, to improve public health policy and clinical practice, the outcome would be relevant in addressing uncertainty about how best to manage patients with acute stroke of unknown aetiology particularly among those who cannot afford neuro-diagnostic test or residents in rural areas where CT/MRI is unavailable or inaccessible.

2. Methods

2.1. Search strategy

A literature search was performed in MEDLINE, EMBASE, African Index Medicus, African Journal Online (AJOL) and Google Scholar databases from 1980 to April 21, 2018, for relevant articles without any language restriction. We then supplemented the search by reviewing the reference lists of the retrieved articles and the latest reviews to identify additional studies that could have been omitted from the database searches. Authors of selected articles were contacted to provide specific or missing information regarding their studies. A literature search was performed using the following medical subject headings (MESH) and keywords; "Stroke" OR "cerebrovascular disease" OR "cerebrovascular accident" OR "brain infarction" OR "infarctions" OR "cerebral infarction" AND "reviews" OR "medical records evaluation" AND "hospital-based" OR "tertiary hospital" OR "teaching hospital" OR "national hospital" OR "federal medical centres" including all the states and their capitals in Nigeria.

2.2. Study eligibility criteria

We included studies that met all of the following criteria: (i) hospital-based studies on stroke conducted in any of the 36 states (including the federal capital territory Abuja) in Nigeria. (ii) Studies conducted among adults aged 18 years or more and reporting a diagnosis of stroke or different stroke subtypes using CT/MRI or other validated procedure [14-16]. (iii) Studies that used WHO definition of stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting longer than 24 hours, unless interrupted by death, with no apparent cause other than that of vascular origin" [16]. (iv) Studies providing information on hospitalisations or 30-days mortality for stoke. (v) Studies that provided the estimate of the different stroke subtypes or appropriates metrics for the estimation of the proportion of stroke subtypes and/or case-fatality estimates.

We excluded studies that met any of the following criteria; (i) Studies that were primarily on transient ischemic attack (TIA) or studies involving participant groups with a variety of conditions such as HIV/AIDS. (ii) Studies that were conducted on paediatric population or among populations. (iii) Hospital-based studies without clearly defined diagnostic criteria or study based solely on self-reports. (iv) Publications were expert opinions, commentaries, letters or editorials.

2.3. Data extraction and quality assessment

After eligibility evaluation by two authors (TB) and (ME), relevant data were abstracted systematically using piloted online data extraction form. The reviewers worked independently in the evaluation and extraction phase and in cases of discrepancy, an agreement was reached by consensus and by discussions with the third reviewer. Relevant study information extracted includes; author's name, publication date, study period, publication type, state, gender proportion, age-range, mean-age, case fatality, percentage of CT/MRI and sample size, diagnostic criteria/case ascertainment and proportion of 30-days mortality. For studies conducted on the same study site or hospital population or cohort, the first chronologically published study was selected, and all additional data from other studies were compared for consistency and included in the selected paper.

Two authors (ME and TB) independently evaluated the methodological and reporting quality of the individual studies using the modified version of Newcastle-Ottawa Scale [17]. In cases of discrepancy, agreement was reached by consensus.

2.4. Statistical analysis

The overall percentage of CT/MRI uptake, 30-day mortality and the proportion of individual stroke subtypes were pooled using a meta-analysis. Before this, we first stabilized the raw proportions using the Freeman-Tukey variant of the arcsine square root transformed proportion suitable for pooling [23]. Thereafter, we used the DerSimonian and Laird random-effects model due to anticipated variations in the study population, settings, stroke treatment and management services to summarize the data [24]. We assessed the study heterogeneity by inspecting the forest plot and by using the I^2 statistics (we interpret a value of 50% as representing moderate heterogeneity) and the chi-squared test, to test subgroup differences. Meta-analysis results were reported as pooled CT/MRI proportions with 95% confidence intervals (CIs). All the results were presented with 95% confidence intervals (CIs) expressed in percentage. Spearman rank correlation was used to examine the correlation between CT/MRI uptake and stroke burden. All data analysis was conducted using Stata version 14 for Windows (Stata Corp, College Station, Texas). The study was conducted and reported in line with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guideline [18].

3. Results

3.1. Study selection

The search results from all the databases returned 1324 studies. After de-duplication, 1144 records remained. All the 1144 studies were screened by their titles and abstracts, leaving 38 full-text articles selected for critical reading after excluding 1106 studies. A further 14 studies were excluded. Six of these were reviews, two were studies conducted outside Nigeria, while six were community-based cross-section studies that investigated the prevalence of stroke in Nigeria. In all, 24 hospital-based studies that met the inclusion criteria were included in the meta-analysis. The flow diagram is shown in Fig. 1.

3.2. Characteristics of the included studies

The characteristics of the 24 studies included in the review are shown in Table 1. All studies included in the review were classified as being of moderate quality using the modified version of Newcastle-Ottawa Scale [17]. The study breakdown showed that the studies were conducted in all the regions (South-East, South-West, South-South, North-Central, North-East and North-West) across 14 states in Nigeria including the federal capital territory (FCT) Abuja (Fig. 2). South-West has the highest outputs (eight studies) while South East has the least (one study) (Fig. 2). Most studies (84.2%) were completed within a two-year period while the median study year from all data points was 2006. All the study (100%) were conducted in urban settings and in predominantly tertiary referral hospitals.

The included studies had about 5874 stroke cases. A significant difference between the sexes was observed (men: 53.51%), $P<0.02$. Most diagnoses were made on the entire study population with an overall mean age of 55.85 years and range 18-99 years. Only eight Studies [19-26] employed CT/MRI to diagnose and validate the different stroke subtypes, while 15 studies (Table 1) used validated instruments for diagnosis and to identify stroke subtypes [14-16]. Overall, there were estimated 5874 stroke cases diagnosed and differentiated into subtypes during the period.

3.3. Pooled estimates of brain imaging uptakes and stroke subtypes

Fig. 3 summarises the reported brain imaging uptakes and stroke subtypes across the six regions in Nigeria. Studies reporting stroke diagnosis during the study period found 8 studies conducted between 2011 and 2015 that provided data on CT/MRI uptake in Nigeria [19-26]. We found that the proportion of CT/MRI uptake varied widely across states and regions in Nigeria. In the last seven years, the percentage uptake for brain imaging using CT or MRI was generally high ranging from 96.7% (95% CI, 93.83-98.25), in the federal capital territory [20] to as low as 1.98% (95% CI, 0.54-6.93) in Ekiti state in South-western region [21]. The random-effect meta-analysis of CT/MRI uptake was 46.66% (95% CI, 15.35-77.98), $P = 0.000$ (eFig. 1).

Using a combination CT/MRI procedures and other widely adopted validated techniques we found about 14 studies which classified stroke into subtypes namely, brain ischemia, intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH) [10, 19-23, 25, 27-33]. Overall, the random effect meta-analysis of ischemic stroke was 55.32% (95% CI , 48.67-61.97), $P = 0.000$, (eFig. 2), while ICH was 32.69% (95% CI, 25.54-39.83), $P = 0.000$, (eFig. 3). Similarly, the random effect meta-analysis of SAH was 3.76% (95% CI, 2.30-5.22), $P = 0.00$, (eFig. 4). In addition, the pooled estimates of the stroke of undetermined aetiology were 16.57% (95% CI, 7.44-25.70), $P = 0.000$, (eFig. 5).

We found a moderate negative correlation between prevalence of brain imaging uptake and ischaemic stroke, albeit not statistically significant (Spearman rho = 0.333, p-value = 0.412) (Fig. 4). Such that, the burden of ischaemic stroke tended to be lower in areas with higher brain imaging uptake.

3.4. Pooled estimates of periodic stroke mortality

A total of 14 studies provided estimates on patients admitted to the hospital with stroke but died within 24-hours or 7-days or 30-days [19-22, 24-26, 30, 32, 34-38]. In the review, only three studies reported case fatality within 24-hours of hospital admission [19, 30, 32]. The random-effect meta-analysis of the proportion was 10.84% (95% CI, 4.48-17.20), $P = 0.000$ (eFig. 6). Similarly, we found only six studies that reported case fatality within one-week of hospital admission [22, 24, 30, 32, 35, 36]. The pooled random-effect estimates was 24.62% (95% CI, 17.20-32.04), $P = 0.000$, (eFig. 7). Overall, 14 studies reported case fatality within 30-days of hospital admission. The pooled random-effect estimates of the proportion were 33.28% (95% CI, 27.80-38.77), $P = 0.000$), (eFig. 8).

4. Discussion

4.1. Main findings

We presented evidence on the uptake of brain imaging for the diagnosis and management of stroke in Nigeria. To our knowledge, this is the first and most comprehensive review to date in Nigeria. The CT and MRI perfusion imaging remains an important approach in identifying a stroke and potential areas of reversible and salvageable brain tissue in the ischemic penumbra [39]. We found evidence of low to moderate percentage estimate of CT/MRI uptake from 2011-2015. There were obvious issues that point to the need for caution when using the pooled estimate. Among these are the fact that healthcare services including stroke diagnosis and management are not freely available in Nigeria unlike in most developed world. Hence, the percentage estimate was majorly for those who can afford the service. It may appears that majority of the cases that made it to the hospital and eventually undergo CT/MRI are severe cases. The wide variation in disposable income available to families to invest in healthcare [40] is a reflection of socio-economic inequality. This can be narrowed by policy makers by making CT/MRI available and affordable to patients at all levels

The low estimates are particularly important because the national health insurance scheme designed to insure a large number of Nigerians are yet to gain traction. [41]. Currently, 4.5 million people representing 3% of Nigeria's population are covered under the scheme [42]. This percentage is mainly in the formal sector and among the urban self-employed who can afford the premium contributions [40]. Nevertheless, the result of this study has clarified current uncertainty on the utilisation and the extent of diagnosis and evidence-based practice for stroke care in a lower-middle-income country like Nigeria. It is also important to note that the evidence is mainly from studies conducted across the tertiary facilities in the urban areas. This may provide an entry evidence of the demography of the patients, which favour mostly civil servants and those in the middle or upper-income thresholds living in the urban areas.

To accurately estimate the probable proportion of different stroke subtypes in the population, our analysis covered the first-ever strokes and all recurrent events. Our result showed that the pooled percentage estimates of ischemic stroke ranged from 48.67 % to 61.97% as against intracerebral haemorrhagic stroke, which ranged from 25.54-39.83%. We also found other rarer stroke types such as subarachnoid haemorrhage, which ranged from 2.30% to 5.22%. Consistent with previous studies conducted in African countries under the INTERSTROKE study [43] and previous review evidence from developing countries, [44] our findings showed that ischemic stroke was the most common of all stroke subtypes in this population.

The proportion of intracerebral haemorrhagic found in our study is comparable to review evidence from other developing countries particularly in sub-Saharan Africa [43]. However, our result is more than 2-fold higher when compared to the 9% in high-income countries [43, 45]. Although this stroke subtype is the most feared because of its high case-fatality rate and poor functional outcome, its high percentage could be attributed to potentially modifiable vascular risk factors which are the hallmark of epidemiological transition currently occurring [46]. This is also consistent with the finding in previous epidemiological studies conducted in Nigeria and other LMICs which found a very strong correlation with uncontrolled hypertension [43, 47-49].

We also found that the pooled percentage estimates of the stroke of undetermined aetiology ranged from 7.44 to 25.70%. This estimate is consistent with most reports from developing countries where there are huge delays before brain imaging could be carried out. It is understood that urgent identification and evaluation of stroke may lead to better outcomes among potentially reversible ischemia who may still benefit from intravenous, intra-arterial or mechanical reperfusion [39, 50]. In a recent study, it was found that more than 75% of CT failed to identify 75% of primary ICH, equivalent to 24 patients per 1000 (95% CI, 14 - 37) with mild strokes [51]. Evidence of delays led to the breakdown of the haematoma and subsequent disappearance of the characteristic hyper-density on CT. This has huge implication in terms of the accuracy of diagnosis and subsequent management of stroke patients particularly among those with minor stroke.

The current analyses provide evidence that stroke patients cared for at most tertiary hospitals in Nigeria have higher 30-day mortality as compared to most estimate in LMICs. Specifically, our study found that one in three or 33.28% of stroke patients die within 30 days of admission. This estimate is comparable to recent results from sub-Saharan Africa where rates ranged from 25% to 41% [5, 52-55]. A breakdown of this evidence found that 30-days case fatality of 24.10% was found in Senegal [55]; 27-41% in Gambia [56], 26.8% in Uganda respectively [54], 25% in Congo-Brazzaville [52]; 26.8% in Cameroon [53] and 35% in Zimbabwe [57]. Our result is also higher than the estimates from the hospital-based INTERSTROKE study which found 22% in most African regions compared to 4% in high-income countries [43]. Even with this high estimate, the rate may be underreported as a significant number of the study did not follow-up patients particularly among those who left the hospital or refused to be admitted against specialist medical advice due to barriers related to high cost of hospital admission and care in Nigeria and other African countries [58-60].

Evidence found the high proportion of ICHs which has been associated with high lethality reported worldwide particularly among black race [44, 61]. Other factors that underline the significantly high case-fatality include; inadequate primary prevention of stroke [62-64], the shortage and prohibitive costs of medical-technical equipment, and the inadequacy of stroke specialist for investigations, emergency care and rehabilitation of stroke [65]. Apart from ageing, low socioeconomic status, huge delay associated with long distance to the hospital and co-morbidities including hypertension, HIV/AIDS, TB, diabetes mellitus remain important predictors of mortality [35, 66-70].

4.2. Study strengths and limitations

The overall strengths and limitations of this meta-analysis warrant careful consideration. Apart from a comprehensive search of databases to ensure that all relevant articles were identified, the review provided a clear and up-to-date evidence of stroke imaging uptake and outcomes in Nigeria. The findings revealed a low uptake of CT/MRI required for case ascertainment and specialist care in this population. This knowledge will no doubt be used as important estimate in public health policy planning of stroke services. Such services may be in the areas of increasing availability and affordability of CT/MRI services through healthcare subsidy toward individual insurance cover. The contribution of the study finding is worth mentioning in clinical practice as well. The knowledge of the estimates of stroke types and subtypes will make an important contribution in clinical decisions and managing patients with acute stroke of unknown etiology (which make up 16% of stroke types) or using validated instruments where CT/MRI services are lacking. This is in view of the fact that more than half of the cases are ischemic in nature while one in three stroke cases are heamoheagic stroke.

In addition, we included only hospital-based studies that constitute the best way to investigate or tract case-fatality of stroke in the absence of stroke registry in the communities. Although a standard systematic review approach was employed to locate all the relevant evidence for this review, there were insufficient published studies that entirely represent the states and regions in Nigeria. We found that the data reported in the included studies were all from tertiary hospitals. These hospitals were located in the cities and across the state capitals. These hospitals serve urban residents mostly. This implies that the data derived from them do not reflect the diverse Nigerian population among whom are those hard-to-reach residing in the rural and semi-rural areas. Caution, therefore, needs to be used in generalizing the results because our study findings may not be applicable to the entire region or communities that share a great diversity in socioeconomic and cultural features.

We are unable to investigate the relationship between CT/MRI uptake and case-fatality. This is due to fewer data points. A recent body of evidence suggests that under-reporting of stroke fatality could occur [4]. Such underreporting may be because no follow-up was undertaken to investigate the exact proportion of deaths outside the hospital setting particularly among those discharged or among those who refused to be admitted against specialist medical advice. In addition, the few available data are highly heterogeneous due to conflicting information on incidence and occurrence of total (first-ever and recurrent) stroke, causes of death, overlapping disabilities caused by disorders that accompany stroke in many older patients.

5. Conclusions

The review provides contemporary estimates that reflect the poor uptake of CT/MRI in case ascertainment across Nigerian cities. The current evidence provided interesting learning in view of the significantly higher burden of both infectious diseases and malnutrition and other non-communicable diseases recorded in this population. The study found that the pooled estimates of the percentage of ischemic stroke or stroke with unknown aetiology were higher compared to most counties in sub-Saharan Africa and other LMICs. In addition to the significantly high proportion of death that occurred in the first 30-days, the study revealed an increased proportion of haemorrhagic stroke that has been associated with increased case fatalities, particularly in high-income countries. Stroke data sourcing from rural areas remains an important research recommendation in view of the fact that deaths from stroke and other non-communicable disease are not known. Such research evidence would improve policy intervention and increase public health awareness particularly on stroke risk factors among vulnerable adults in these rural environment.

In all, the findings of the study will be useful for proper stroke treatment, rehabilitation, and related public health prevention strategies. Particular attention should be given to stroke of undetermined aetiology which requires a huge investment that would reduce slow decisions and delays within stroke patients' route to the tertiary facilities equipped with neurological services.

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Author's contributions: TB and ME conceptualized the study and conducted the literature review for all databases. ME and OU performed all statistical analyses. ME and TB drafted the paper. OU provided useful additional intellectual content into the draft and contributed to the writing of the final version of the paper.

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List of Table

Lists of Figures

ONLINE ONLY FIGURES (SUPPLEMENTARY DATA) - e-Components

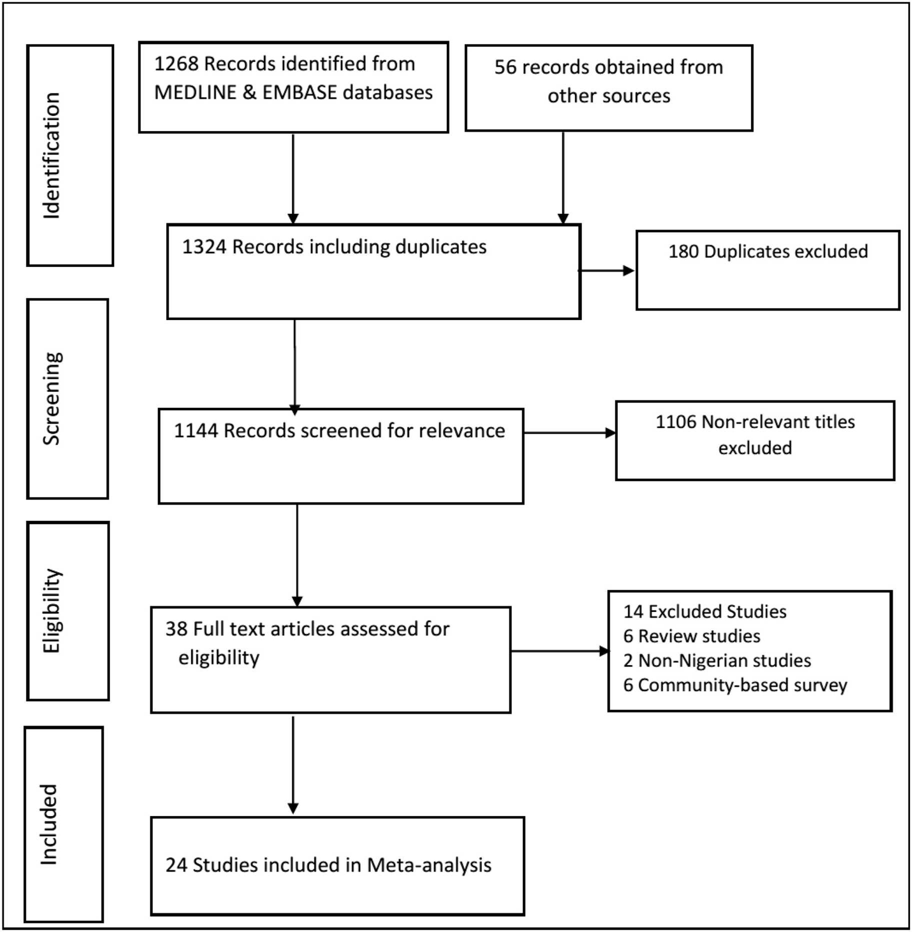

Identification
1268 Records identified from MEDLINE & EMBASE databases
56 records obtained from other sources
1324 Records including duplicates
180 Duplicates excluded
Screening
1144 Records screened for relevance
1106 Non-relevant titles excluded
Eligibility
38 Full text articles assessed for eligibility
14 Excluded Studies
6 Review studies
2 Non-Nigerian studies
6 Community-based survey
Included
24 Studies included in Meta-analysis

Figure 1

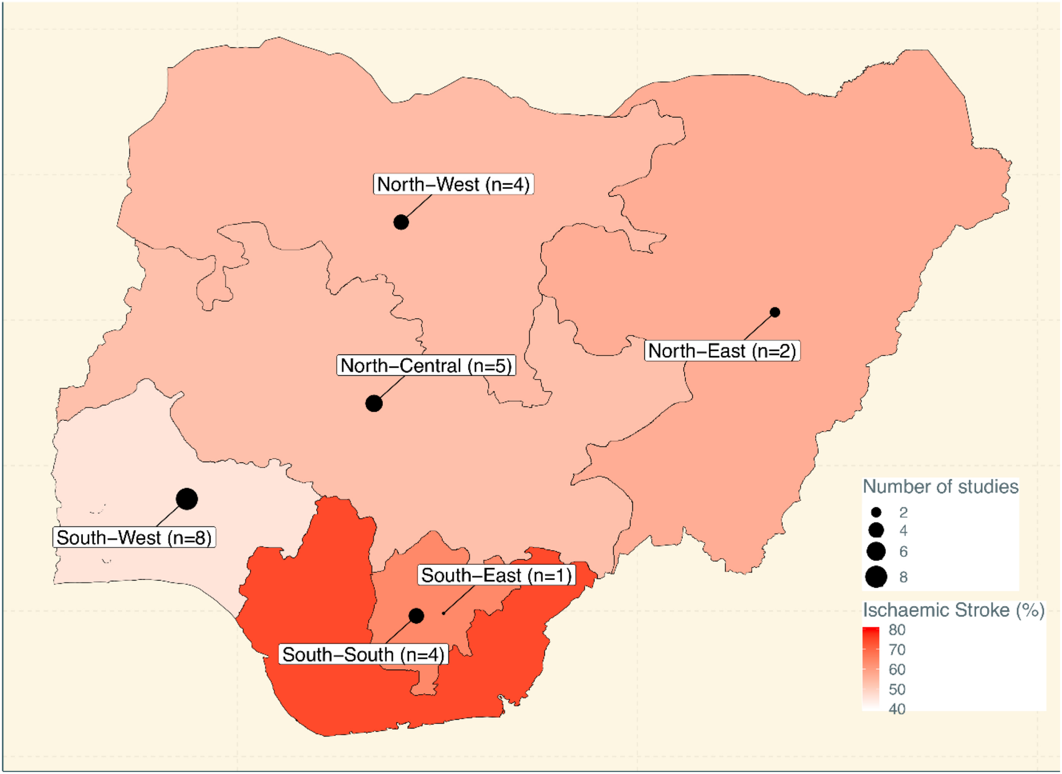

North–West (n=4)
North–Central (n=5)
North–East (n=2)
South–West (n=8)
South–East (n=1)
South–South (n=4)
Number of studies
2
4
6
8
Ischaemic Stroke (%)
80
70
60
50
40

Figure 2

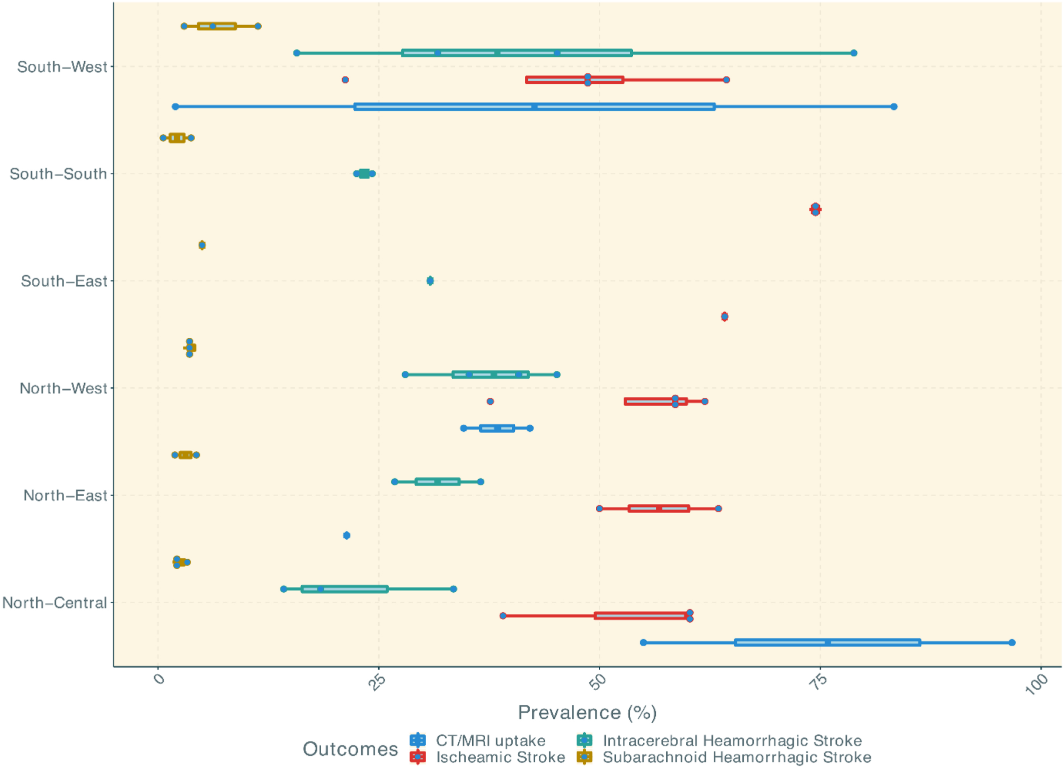
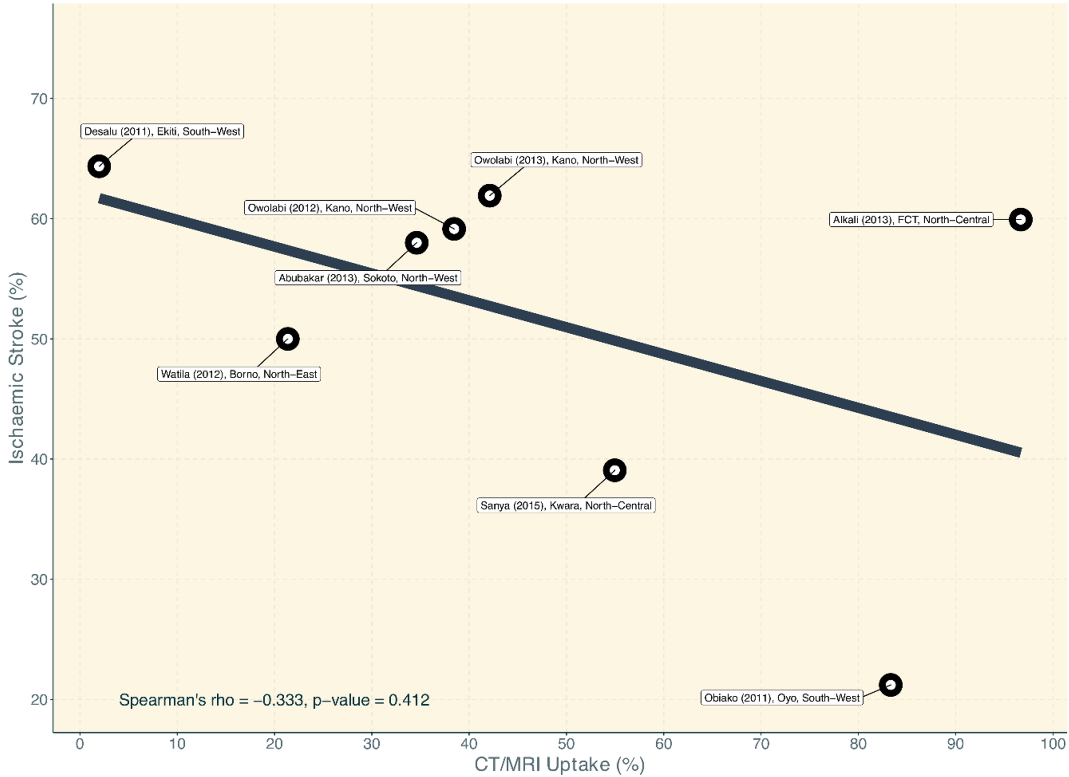

South−West
South−South
South−East
North−West
North−East
North−Central
0
25
50
75
100
Prevalence (%)
Outcomes
CT/MRI uptake
Ischeamic Stroke
Intracerebral Heamorrhagic Stroke
Subarachnoid Heamorrhagic Stroke

Figure 3



Desalu (2011), Ekiti, South–West
Owolabi (2013), Kano, North–West
Owolabi (2012), Kano, North–West
Alkali (2013), FCT, North–Central
Abubakar (2013), Sokoto, North–West
Watila (2012), Borno, North–East
Sanya (2015), Kwara, North–Central
Obiako (2011), Oyo, South–West
Spearman's rho = –0.333, p–value = 0.412
Ischaemic Stroke (%)
CT/MRI Uptake (%)
20
30
40
50
60
70
0
10
20
30
40
50
60
70
80
90
100

Figure 4