

Stroke in Africa: a systematic review and meta-analysis of the incidence and case-fatality rates

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Title: Stroke in Africa: a systematic review and meta-analysis of the incidence and case-fatality rates

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Abstract

Background: The burden of stroke (a leading cause of disability and mortality) in Africa appears to be increasing, but a systematic review of the best available data to support or refute this observation is lacking.

Aim: To determine the incidence and one-month case-fatality rates from high-quality studies of stroke epidemiology among Africans.

Summary of review : We searched and retrieved eligible articles on stroke epidemiology among indigenous Africans in bibliographic databases (PubMed, ScienceDirect, Google Scholar and Cochrane library) using predefined search terms from the earliest records through January 2022. Methodological assessment of eligible studies was conducted using the Newcastle-Ottawa scale. Pooling of incidence and case-fatality rates was performed via generalized linear models (Poisson-Normal random-effects model).

Of the 922 articles retrieved, fourteen studies were eligible for inclusion. The total number of stroke cases was 5,104 (mean: 365 SD: 254) with a population denominator (total sample size included in population-based registries or those who agreed to participate in door-to-door community studies) of 3,638,304. The pooled crude incidence rate of stroke per 100,000 persons in Africa was 106.49 (95% CI 58.59–193.55), $I^2 = 99.6\%$. The point estimate of the crude incidence rate was higher among males, 111.33 (95% CI 56.31–220.12), $I^2 = 99.2\%$ than females, 91.14 (95% CI 47.09–176.37), $I^2 = 98.9\%$. One-month case-fatality rate was 24.45 (95% CI 16.84–35.50), $I^2 = 96.8\%$ with lower estimates among males, 22.68 (95% CI 18.62–27.63), $I^2 = 12.9\%$ than females, 27.57 (95% CI 21.47–35.40), $I^2 = 51.6\%$.

Conclusions: The burden of stroke in Africa remains very high. However, little is known about the dynamics of stroke epidemiology among Africans due to the dearth of high-quality evidence. Further continent-wide rigorous epidemiological studies and surveillance programs using the World Health Organization STEPwise approach to Surveillance (WHO STEPS) framework are needed.

Introduction

Stroke is a principal cause of disability and mortality worldwide¹⁻³, with significant increases in epidemiological burden in low- and middle-income countries (LMICs)⁴⁻⁶. Recent evidence suggests a rapidly growing burden of stroke in Africa with an annual age-adjusted incidence as high as 316 per 100,000 persons, an age-adjusted prevalence of up to 1,460 per 100,000 persons and a 3-year fatality rate of up to 84%⁵. Also, stroke and stroke-related disability accounted for 70% and 80% of all mortality in LMICs between 1970 and 2020⁵.

The case for the high burden of stroke in Africa is mounting, but large geographical regions of the continent are without high-quality incidence and case-fatality data. Also, the quality of earlier systematic reviews⁷ has been limited by the high heterogeneity across studies and deficiencies in standardized methods of evaluating stroke epidemiology. Many studies on stroke epidemiology among Africans were characterized by low statistical power and poor generalizability across the hugely-diverse African population. There are several stroke prevalence studies among Africans. However, they do not provide a clear picture of the African stroke landscape and have limited policy implications and priority settings related to interventions for stroke prevention, surveillance, acute care and rehabilitation among Africans⁶. Therefore, an estimate of the burden of stroke using high-quality stroke incidence studies in Africa is important, in the light of newer studies, to advance the understanding of stroke science and care in Africa. Thus, we pooled data from high-quality epidemiological stroke studies to determine the true stroke incidence and 30-day case-fatality rates among Africans.

Methods

This systematic review and meta-analysis were conducted in accordance with the MOOSE guidelines¹⁰ and reported using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) framework¹¹. The protocol was prospectively registered in PROSPERO¹².

Search Strategy and Study Selection

The search strategy used 'stroke' terms from the Cochrane Stroke Strategy 2020¹³ and an adapted filter¹⁴ to search for previously published reports on the epidemiology of stroke among indigenous Africans in MEDLINE (OVID), EMBASE (OVID), AJOL, EBSCO, Google Scholar, Cochrane Library, IMSEAR via Global Index Medicus, Science Citation Index Expanded (SCI-EXPANDED), Social Sciences Citation Index, and Arts &

Reference lists of retrieved studies were reviewed for additional studies.

Inclusion criteria

Studies were eligible based on the following criteria: population boundaries defined within Africa, prospective and consecutive recruitment, pre-specified sampling plan, complete community-based case-ascertainment of stroke (with multiple overlapping sources) or non-community-based case-ascertainment (acute hospital-based registry, rehabilitation-based registry), including case series and case-control studies. Studies were included if stroke was confirmed based on a predefined set of criteria, e.g. World Health Organization (WHO)¹⁶, or clinical criteria (confirmed by imaging, where possible), including cerebral infarction, intracerebral haemorrhage, subarachnoid haemorrhage or uncertain pathological subtypes with no restrictions on age, sex, degree of impairment post-stroke or interventions.

Exclusion criteria

Studies were excluded if they were case studies, randomised controlled trials, reviews, epidemiological reports from mixed populations (e.g. stroke and head injury) without specific results for the stroke population, cross-sectional or retrospective recruitment, qualitative assessment only, or adopted convenience sampling. All references were collated using EndNote¹⁵, and duplicates were removed using the EndNote automated function and then manually.

Data collection and analysis

Three independent reviewers (AO, OA and SJ) screened the title or abstract of all citations, two reviewers (SJ and RA) were randomly assigned to evaluate the selected citations and disagreements were resolved by recourse to a third reviewer (MH, CW and MO) to reach a consensus. The article with the most comprehensive dataset was selected when there were multiple articles from the same study population with evidence of overlapping data or identical participant characteristics. The search strategy and selection procedure are detailed in Figure 1.

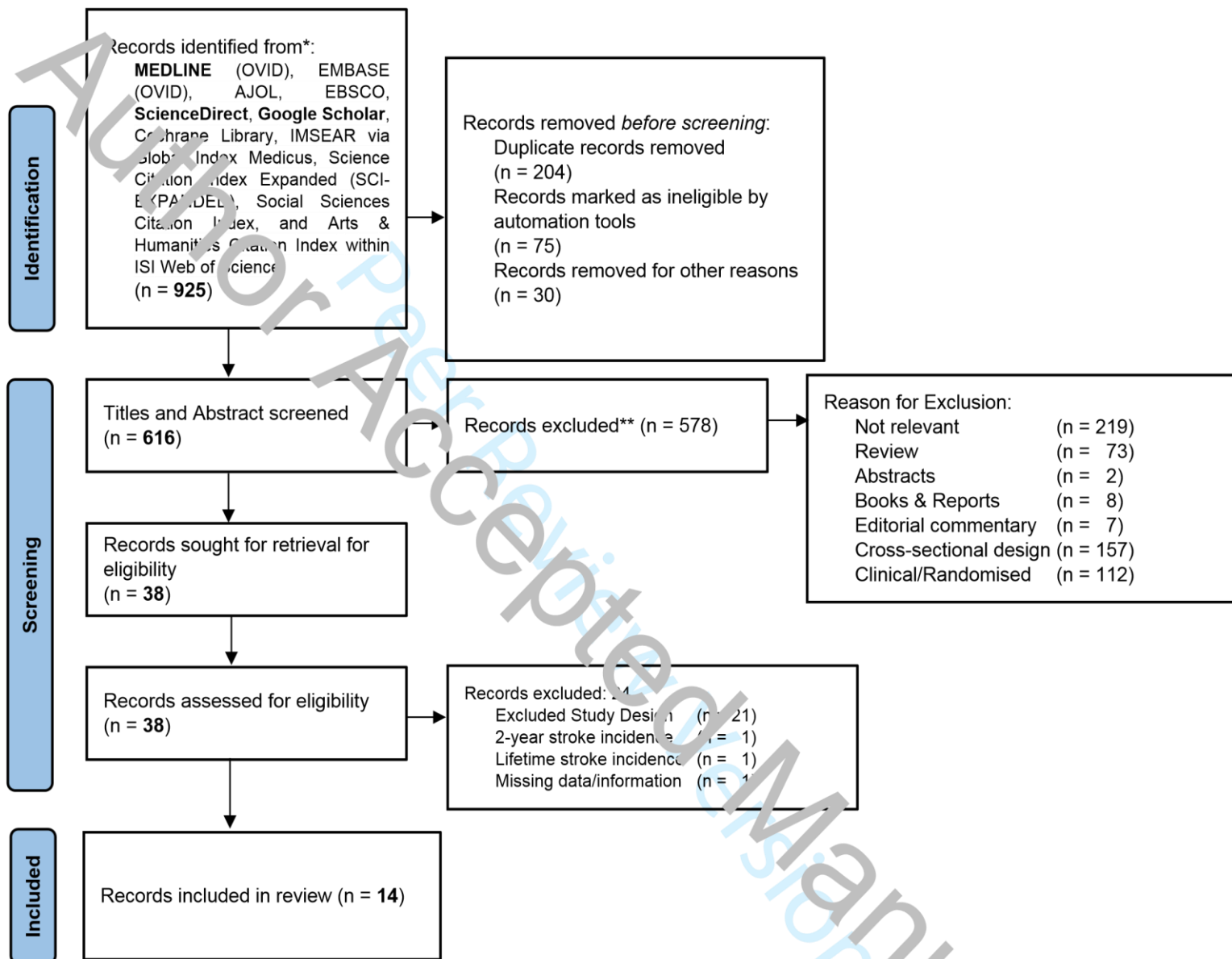


Figure 1: PRISMA flowchart of study selection

Data extraction was carried out independently by two reviewers (APO, OAA) using a previously designed proforma¹⁶, verified by another reviewer (SJ). The difference(s) was resolved in an organized discussion in the review team. Extracted data included; author, year, study name, sample characteristics (country, city, study period and design) and epidemiological data (number of stroke cases and subtype, age, crude incidence, one-month case-fatality rate [CFR]).

Assessment of risk of methodological bias

The Newcastle–Ottawa scale was used to determine the risk of bias (see Supplementary Table 1)

Statistical Analysis

Using data reported in the original studies, we (re-)calculated crude incidence and one-month case-fatality rates along with 95% confidence intervals (95% CI). Then we performed meta-analyses for each outcome fitting a generalized linear model using Poisson-Normal random-effects models. To assess quantitative heterogeneity, we have performed a subgroup analysis by the sex and study setting (community-based, hospital-based, community- and hospital-based) for the overall incidence of stroke and fitted a series of meta-regressions using follow-up lengths as a fixed-effect covariate. We performed a formal homogeneity test and reported the proportion of variability attributable to heterogeneity rather than chance (I^2). Statistical analyses have been performed using the metafor package of the R software¹⁷.

Results

Study characteristics and epidemiological data from included reports

Of 925 records retrieved (Figure 1), fourteen reports¹⁸⁻³¹ from thirteen studies across nine African countries (Table 1) were included. We searched references of studies eligibility during screening and found no additional studies eligible for inclusion. The earliest record was from Benghazi, Libya, published in 1986, and the most recent report was from Akure, Nigeria, published in 2015. More than three-quarters of the studies were conducted in urban areas, with a minimum surveillance period of six months. Crude stroke incidence rates were reported in eight¹⁸⁻²⁵ reports, and six²⁶⁻³¹ of the ten articles on CFR^{18, 20, 22, 25-31} reported CFR only (Figure 2, Supplementary Table 2). Six reports were primarily community-based (i.e. recruitment of participants was in a

community-based setting)^{21-25, 27}, and eight were hospital-based (i.e. recruitment of participants was in a clinical setting)^{18-20, 26, 28-31}. The total number of recorded strokes was 2,568, with a population denominator (total sample included in population-based registries or those who agreed to participate in the door-to-door community studies) of 3,384,102 (see Supplementary Table 2). Five studies reported in-hospital 30-day CFR^{20, 22, 25, 28, 29}, two^{30, 31} reported results from verbal autopsies, and 1,013 deaths (out of 3,157 stroke events) were recorded within 30 days of stroke onset.

The crude annual incidence rate of stroke among Africans varied widely, from 25 (Danesi et al. in Lagos, Nigeria)²² to \approx 250 (Farghaly et al. in Al-Kharga District, Egypt)²⁴ per 100,000 persons. The point estimate of the sex-disaggregated crude incidence rate was generally higher among males, and the age-adjusted incidence rate ranged from 54 (Danesi et al. in Lagos, Nigeria)²² to 316 (Walker et al. in Dar-es-Salaam, Tanzania)²¹. There was considerable variation in the one-month CFRs from 4.0 (Okon et al. in Akure, Nigeria)²⁵ to \approx 50 (Damasceno et al. in Maputo, Mozambique)²⁰ per 100,000 stroke events.

Incidence studies

1	Ashok et al. 1986 ¹⁸	518,745	251,155 (48.4)		
2	Matenga et al. 1997 ¹⁹	887,768	NR		
3	Damasceno et al. 2010 ²⁰		NR	NR	
4	Walker et al. 2010 ²¹	159,814	82,242 (51.5)		
				56,517	28,654 (50.7)

Table 1. A summary of the characteristics of included studies on stroke epidemiology in Africa

Study and publication year	Study period	Country	Location	Population type	Study design	Duration of surveillance [†]	Frequency of surveillance	Population denominator	Female N (%)
	November 1983 – October 1984	Libya	Benghazi	Urban	Hospital-based registry	12	Continuous*		
	January – December 1991	Zimbabwe	Harare	Urban	Hospital-based registry	12	Continuous*		
	August 2005 – July 2006	Mozambique	Maputo	Urban	Hospital-based registry	12	Continuous*		
	June 2003 – June 2006	Tanzania	Hai Dar es Salaam	Urban & Rural	Community & Hospital-based registry	36	Continuous*		
	January – December 2007	Nigeria	Lagos	Urban	Community-based	12	Continuous*		
	July 2009 – January 2012	Egypt	Al Quseir	Urban	Community-based	30	Continuous*		
	June 2005 – May 2008	Egypt	Al-Kharga	Urban & Rural	Community-based	36	Continuous*		
	November 2010 – October 2011	Nigeria	Akure	Urban	Community-based registry	12	Continuous*		
5 Danesi et al.	February 2000 – February 2001 750,000 333,000 (44.4)	The Gambia	Banjul	Urban	Hospital-based registry	12	Quarterly		

2013²²

6 El-Tallawy et al. 33,285 NR
2013²³

7 Farghaly et al. 62,583 30,418 (48.6)
2013²⁴

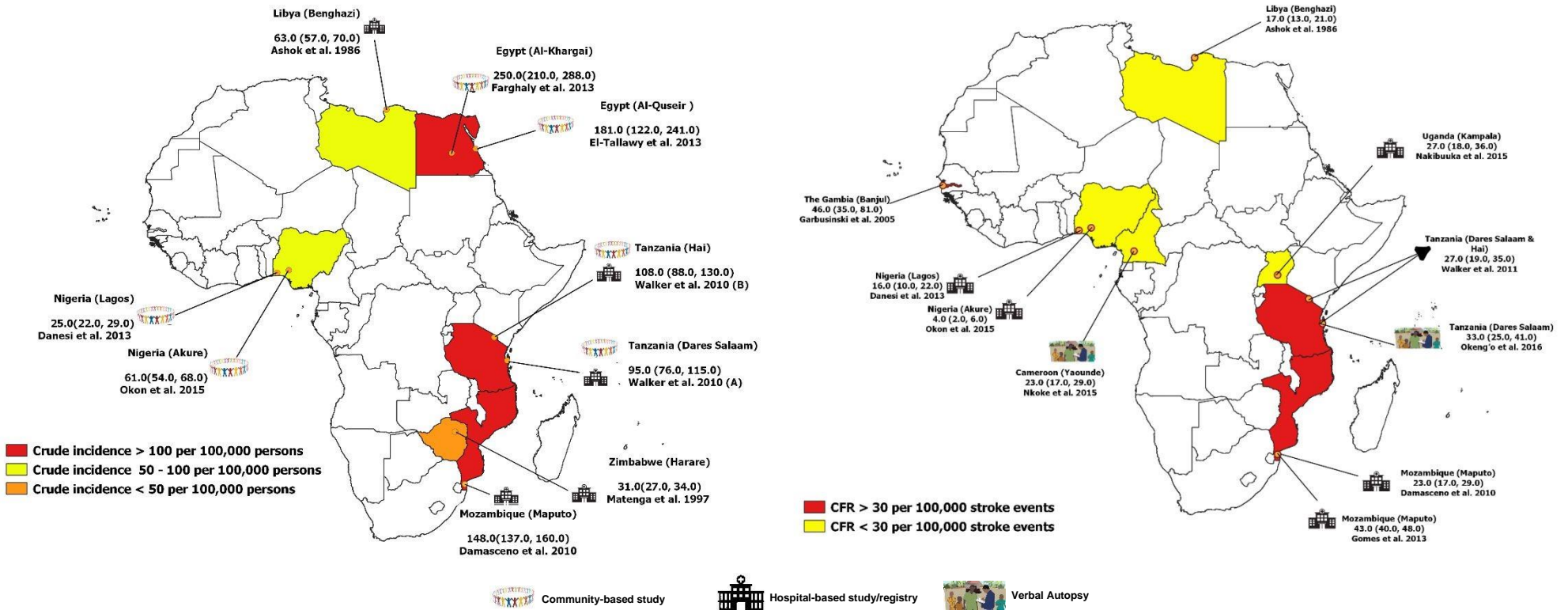
8 Okon et al. 2015²⁵ 491,033 245,835 (50.1)

Case fatality studies only

9 Garbusinski et al. NR NR
2005²⁶

10	Walker et al. 2011 ²⁷	June 2003 – June 2006	Tanzania	Hai Dar es Salaam	Urban & Rural	Community & Hospital-based registry	36-72	Post-stroke follow- up until June 2009	159, 814	
11	Gomes et al. 2013 ²⁸	August 2005 – July 2006	Mozambique	Maputo	Urban	Hospital-based registry	12	Continuous*	NR	NR
12	Nakibuuka et al. 2015 ²⁹	February – August 2014	Uganda	Kampala	Urban	Hospital-based registry	6	Continuous*	NR	NR
13	Nkoke et al. 2015 ³⁰	NR	Cameroon	Yaounde	Urban	Hospital-based registry	12	Monthly	NR	NR
14	Okeng'o et al. 2016 ³¹	January – June 2013	Tanzania	Dar es Salaam	Urban	Hospital-based registry	6	NR	NR	NR

†: duration of surveillance in months; NR: not reported.



A

B

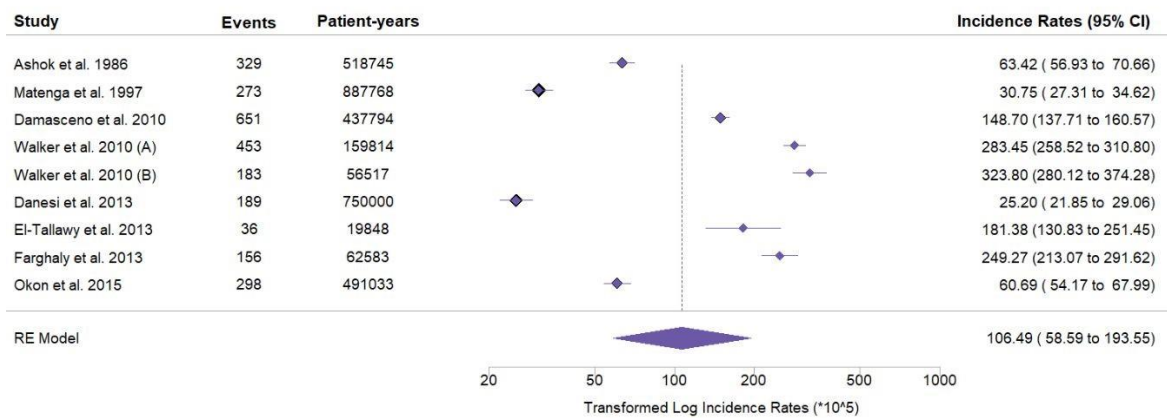
Figure 2: Location of studies assessing the crude incidence (A) and case-fatality rate – CFR (B) of stroke in Africa.

Crude incidence rate and 30-day CFR of Stroke in Africa

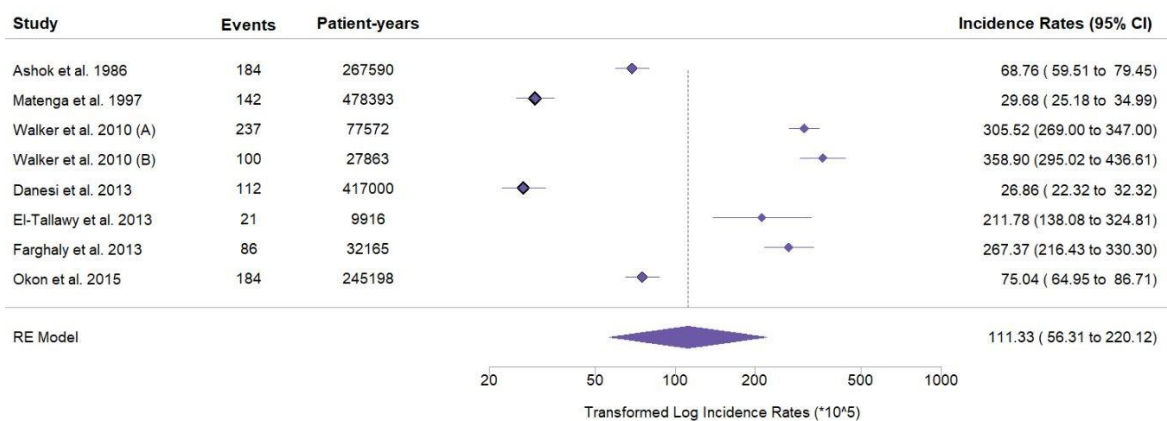
The pooled crude incidence rate of stroke (per 100,000 persons) from eight studies was 106.49 (95% CI: 58.59–193.55), $I^2 = 99.6\%$ (Figure 3). For studies reporting data by sex, the point estimate of the crude incidence rate was higher among males; 111.33 (95% CI: 56.31–220.12), $I^2 = 99.2\%$, than females; 91.14 (95% CI: 47.09–176.37), $I^2 = 98.9\%$. Also, meta-regression results revealed that stroke incidence rates increased by 1.17 per 100,000 per person for every month increase in the follow-up period (Supplementary Table 3). When we adjusted for the follow-up period, I^2 reduced from 99.6% to 98.3% in the overall pooled analyses. We performed subgroup analyses by study type (Figure 4) and found the pooled point estimate of the crude incidence of stroke was higher among community-based studies; 90.23 (95% CI: 37.03–219.88), $I^2 = 99.2\%$, than hospital-based studies; 66.19 (95% CI: 31.91–137.31), $I^2 = 99.4\%$, although the confidence intervals were largely overlapping. Furthermore, the pooled CFR of stroke (per 100,000 stroke events) from ten eligible studies was 24.45 (95% CI: 16.84–35.50), $I^2 = 96.8\%$ – Figure 5. The point estimate of the CFR was lower among males; 22.68 (95% CI 18.62 – 27.63), $I^2 = 12.9\%$ than females; 27.57 (95% CI 21.47 – 35.40), $I^2 = 51.6\%$.

Methodological assessment of risk of bias

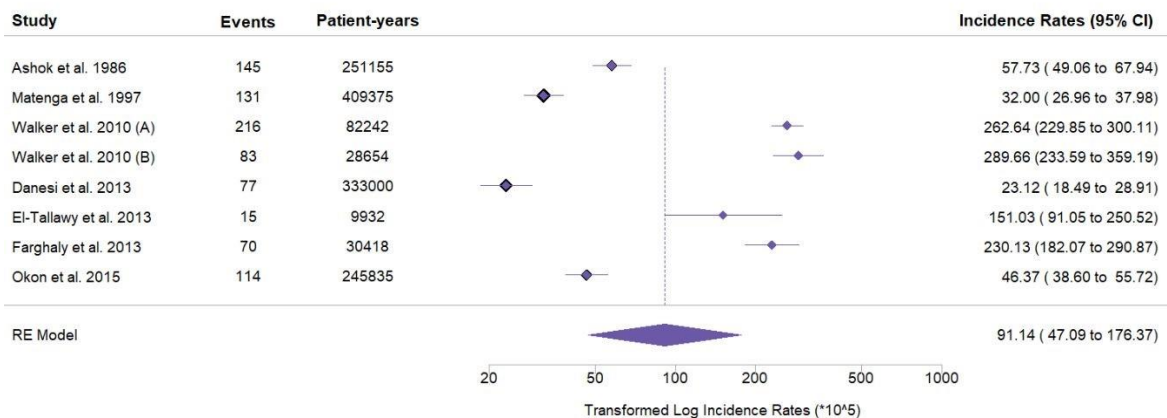
Most studies were rated as having a low risk of bias^{32, 33} (Supplementary Table 1). Most studies defined stroke using the WHO criteria^{19-23, 28-31}, but only two^{20, 28} were primarily guided by the WHO STEPwise approach to Surveillance (WHO STEPS) framework³⁴.



A



B



C

Figure 3: Forest plots on the pooled crude annual incidence rates of stroke per 100,000 persons in the overall population (A), among males (B) and females (C) in Africa.

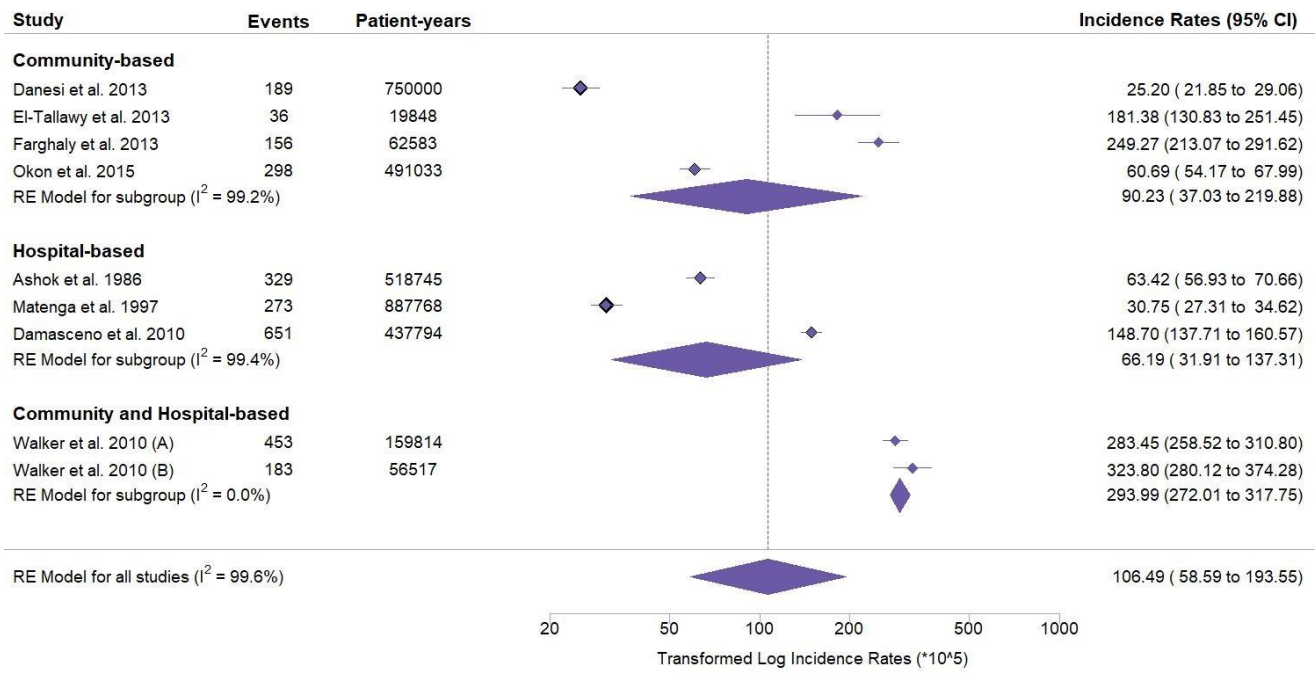
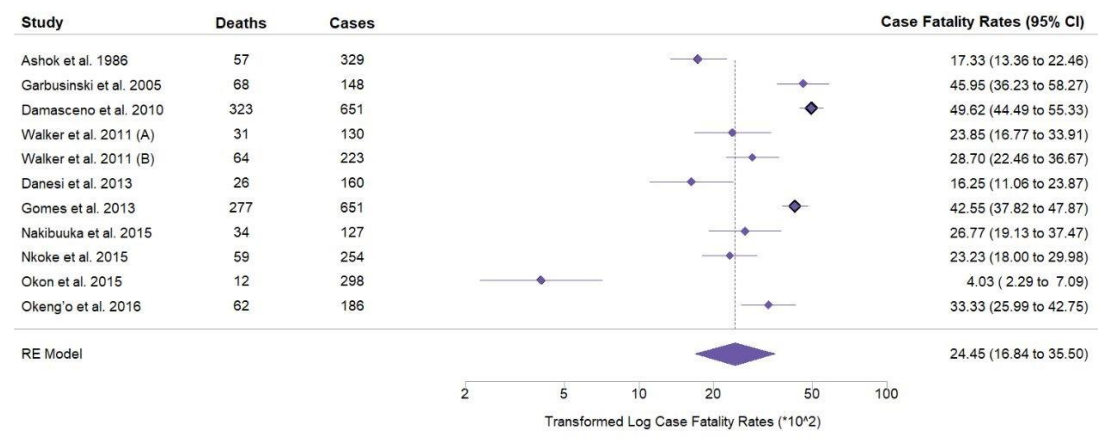
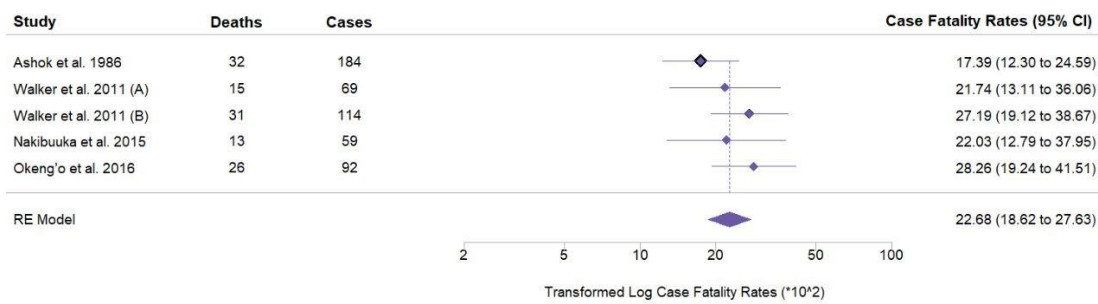


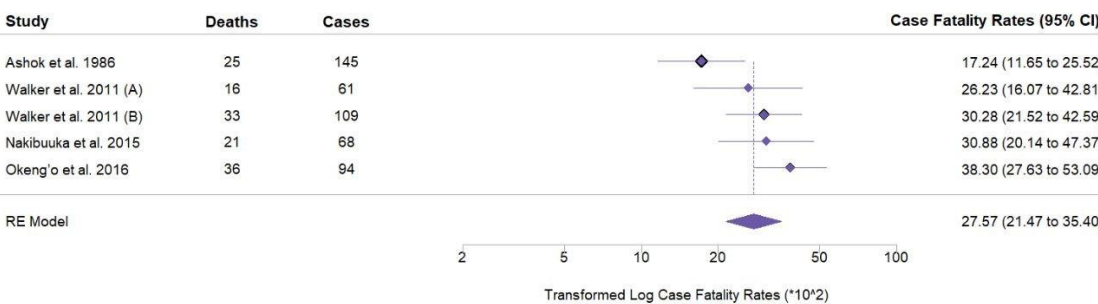
Figure 4: Forest plots on the pooled crude annual incidence rates of stroke per 100,000 persons stratified by study setting (community-based, hospital-based, community- and hospital-based).



A



B



C

Figure 5: Forest plots on the pooled 30-day case-fatality rate of stroke per 100,000 events in the overall population (A), among males (B) and females (C) in Africa.

Discussion

This systematic review pooled epidemiological data on stroke incidence rates and CFR from high-quality studies conducted in thirteen locations across ten countries (out of a total of 54 countries) in Africa, leaving most of the world's second-most populous continent short of high-quality data vital for evidence-based decision-making to prevent, track and manage stroke. The most recent review was conducted about ten years ago and published in 2013⁷. In addition, most reports estimating CFR among Africans^{20, 22, 25, 28, 29, 35} primarily used hospital mortality data, limiting the generalisability of the CFR estimates. This limits our ability to track changes in stroke epidemiology and outcome across the countries of Africa and to infer benefit or harm from changes in health policy, investment, or new prevention and treatment strategies. While these findings offer some insights into the epidemiology of stroke in Africa, the heterogeneity of data, from selected populations, within only ten (of 54) African countries from studies conducted well over seven years ago limit their usefulness. This review highlights the paucity of available data. However, there are promising prospects for ongoing stroke epidemiological studies in Africa³⁶.

Our meta-analysis revealed that the crude incidence rate of stroke in Africa was ≈ 106 per 100,000 per year, with a higher point estimate of crude incidence rate among males than females, similar to the Global Burden of Disease (GBD) study for LMICs³ except for China^{2 37}. This pooled estimate was lower than that reported in a meta-analysis in 2014⁷ and the GBD stroke study³ in sub-Saharan Africa. This observation was comparable to estimates from Asia (116-438 per 100,000 per year)^{16, 38} and the 2022 global stroke fact sheet³⁹. However, stroke incidence rates appear higher in Europe (219 per 100,000 per year)⁴⁰. The reasons for these differences, particularly in relation to the modelling-based GBD estimates, are multifaceted⁴¹ and might be related to the vast difference in age structure in Europe (with a more ageing population) vs Africa.

Furthermore, we found country-level differences in stroke burden in Africa. For example, reports from East and North African countries presented higher estimates compared to those from West Africa. The GBD estimates for East and West Africa were comparable, but reports from North Africa presented higher estimates for stroke burden. Methodological differences in design arising from multifaceted limitations detailed in an earlier report⁴² might account for these differences. Apart from methodological differences, the differential rates between North and Sub-saharan Africa are likely attributable to the substructural population and demographic differences between North Africa (which has a higher proportion of older persons – 60 years and above) vs sub-Saharan Africa and regional differences in the profile of stroke risk factors^{3, 5, 43}. Also, the sparse contribution of African

data to the GBD study, poor stroke literacy, diverse socio-cultural barriers and ethnic differences across African countries and the lack of rigorous community-based and institutional surveillance infrastructure, including neuroimaging for stroke care to promote detection, prognosis, and timely interventions are additional reasons for these differences.

Pooled CFR revealed that one in every four strokes in Africa is likely to be fatal within the first month. This is similar to a 24% estimate reported in an earlier review³⁵. Also, our observation is comparable to the 36% global CFR reported in the GBD study³ and India¹⁶. The point estimate of the pooled CFR was comparatively lower among males than females, contrary to observations in other reports^{3, 16}. Several factors account for these differences; the paucity of data and lack of stroke surveillance sites in Africa limit the generalisability of these estimates. Also, timely emergency care (critical to mortality reduction) is grossly deficient in Africa and reduced women's access to hospital care⁴⁴. In addition, there is a significant deficit of well-coordinated and holistic stroke care program(s), including the lack of public awareness, primary prevention, acute management and post-stroke management, in many African countries⁴⁵⁻⁴⁷.

Some notable studies on stroke epidemiology among Africans⁴⁸⁻⁵⁰ were omitted in this systematic review primarily due to missing details, uncertainties in reporting and other methodological issues previously identified in stroke incidence studies in Africa⁴². We intentionally and prospectively limited our review to studies whose design is close to an ideal stroke incidence study in design and rigour⁵¹. While such stringent criteria are necessary for comparing similar studies, they can be problematic in regions like Africa, where limited funding, infrastructure, capacity, and access to diagnostic and time-dependent resources to execute comprehensive stroke epidemiological and surveillance studies effectively make conducting any studies almost impossible. The stroke community must not equate resource constraints with 'lesser quality' research. However, this means that understanding is limited regarding the epidemiological dynamics of stroke among Africans.

In the light of the current understanding of stroke presentation in clinical settings among Africans, our findings on stroke epidemiology are likely to be conservative. Future studies should consider recruitment guidelines outlined in the WHO STEPS framework³⁴ to identify stroke cases outside a hospital-based setting, including a range of community-based ascertainment strategies. Also, national and regional population-based stroke registries and surveillance sites (in the context of epidemiological, clinical and public health studies) across Africa for early treatment, prevention, and management of stroke and other non-communicable diseases (NCDs) are long overdue. The African Stroke Organization promoted these ideals in its current conceptual framework⁵².

The third goal of the African Union AGENDA 2063 outlined the importance of ensuring healthy livelihoods and well-being for all Africans by 2063³. Our study aligns with this goal by providing evidence-based data for policy guidelines for Africans to achieve their full potential, free of stroke - the most prominent cause of disability and mortality among Africans. Further, our review does offer unique insights into the epidemiology of stroke among Africans. Stroke studies are capital-intensive, and there is a considerable deficit of high-quality studies, even over the 40 years since the first incidence study on stroke in Africa was reported in Ibadan, Nigeria⁴⁸. Our study is a clarion call, setting an agenda for a multi-stakeholder approach for health system financing, supportive grants, capacity-building, and mobilizing infrastructure for addressing stroke and non-communicable diseases among Africans. The current health infrastructure in most African countries delimits local researchers' efforts to conduct high-quality epidemiological and surveillance studies in a community setting. To that effect, we propose a bolstering of health-system engagement aimed at mobilizing and incentivizing communities to stimulate efforts at reporting stroke and NCDs for early prevention and management. Culturally-sensitive interventions including stroke education strategies are also necessary to overcome structural and cultural barriers to stroke surveillance and prevention.

Our findings did not account for the age-standardized incidence rate of stroke. It is important to discern the age group at the highest risk of stroke for prioritizing intervention. Adjusting our estimates for the follow-up period revealed a slight reduction in heterogeneity, yet substantial heterogeneity persisted. The diverse but considerable differences in ethnicity, the year the study was conducted, recruitment strategy differences in definitions/methods of stroke diagnosis, associated differences in care, age, and follow-up period, to mention a few, likely account for the heterogeneity observed in this systematic review. It is worth noting that this systematic review and meta-analysis aimed not only to provide an overall estimate of stroke incidence and CFR in Africa but also to itemize gaps in data coverage and limitations that could be used to inform future stroke epidemiological studies in Africa. True to our observation, several gaps worth considering when designing future studies were described. Despite the excellent quality rating of most of the included studies, salient details such as a follow-up strategy for most stroke incidence studies were missing, and most studies only reported in-hospital CFR. There is a paucity of epidemiological stroke studies in terms of rigour and quality in Africa. The burden of stroke among Africans is still predominantly very high. Continent-wide rigorous epidemiological studies and surveillance programs using the WHO STEPS framework is long overdue.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest.

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