Stroke survivors in Low-and middle-income countries: A meta-analysis of prevalence and secular trends

Martinsixtus C. Ezejimofor* MPH[a]; Yen-Fu Chen PhD[a,e]; Ngianga-Bakwin Kandala PhD[a,b,d]; Benedeth C.Ezejimofor MD[a]; Aloysius C. Ezeabasili PhD[c] ; Saverio Stranges PhD[d] . Olalekan A.Uthman PhD[e, f]

[a]Division of Health Sciences, University of Warwick Medical School, Coventry, CV4 7AL, UK

[b]Northumbria University, Department of Mathematics and Information sciences, Faculty of Engineering and Environment, Newcastle upon Tyne, NE1 8ST, United Kingdom.

[c]School of the Built Environment, University of Salford, M5 4WT, UK

[d]Luxembourg Institute of Health (LIH), Department of Population Health, 1A-B, rue Thomas Edison, L-1445 Strassen, Luxembourg

[e]Warwick-Centre for Applied Health Research and Delivery (WCAHRD), Division of health Sciences, University of Warwick Medical School, Coventry, UK

[f]Liverpool School of Tropical Medicine, International Health Group, Liverpool, UK

Corresponding Author
Martinsixtus C. Ezejimofor
Division of Health Sciences
University of Warwick Medical School
University of Warwick
Coventry, CV4 7AL
United Kingdom.
Phone: +44(0)7944420045
Email: **m.c.ezejimofor@warwick.ac.uk**

ABSTRACT

Purpose

To provide an up-to-date estimate on the changing prevalence of stroke survivors, and examines the geographic and socioeconomic variations in low and middle-income countries (LMICs).

Methods

We searched MEDLINE, EMBASE, SCOPUS and Web of Science databases and systematically reviewed articles reporting stroke prevalence and risk factors from inception to July, 2015. Pooled prevalence estimates and secular trends based on random-effect models were conducted across LMICs, World Bank regions and income groups

Results

Overall, 101 eligible community-based studies were included in the meta-analysis. The pooled crude prevalence of stroke survivors was highest in Latin America and Caribbean (21.2 per 1000, 95% CI 13.7 to 30.29) but lowest in sub-Saharan Africa (3.5 per 1000, 95% CI 1.9 to 5.7). Steepest increase in stroke prevalence occurred in low-income countries, increasing by 14.3% annually while the lowest increase occurred in lower-middle income countries (6% annually), and for every 10 years increase in participants' mean age, the prevalence of stroke survivors increases by 62% (95% CI 6% to 147%).

Conclusion

The prevalence estimates of stroke survivors are significantly different across LMICs in both magnitude and secular trend. Improved stroke surveillance and care, as well as for better management of the underlying risk factors, primarily undetected or uncontrolled high blood pressure (HBP) are needed.

Key Words: Stroke Survivors, Prevalence, Secular trends; Low-and middle-income countries; World Bank regions

1.0 Introduction

Recent global estimates found that stroke ranked as the second commonest cause of death with 5.9 million stroke-related deaths in 2010 [1]. This number is expected to increase to 7.8 million by 2030 in the absence of significant global public health response [2]. Despite the infectious disease scourge, low-and middle-income countries (LMICs) account for over 78% disability adjusted life years (DALYs) from stroke, which is at least 7 times the DALYs lost in high-income countries [1]. Disentangling the drivers of global mortality and morbidity has led to targeted regional and national investments in cardiovascular health resulting in about 40% reduction of stroke burden between 1970 and 2008 in high income countries [3]. Surprisingly, the trend is the opposite in LMICs with a rise of over 100% of stroke prevalence within the same period [3]. The increase and changing pattern of stroke prevalence in LMICs has mostly been attributed to rapid economic development and combined effects of demographic (particularly population growth and ageing), epidemiological and nutritional transitions currently occurring [4]. As the global population older than 65 years of age continues to increase by approximately 9 million people per year in LIMCs, this predicts a higher stroke prevalence with increase burden particularly in Asia and Latin America [5].

Though there are existing reviews that had looked at prevalence of stroke in LMICs and regions such as Africa and Latin America [6-9], to the best of our knowledge there is no recent attempt to compile studies on stroke prevalence across different geographic regions in LMICs. Since the publication of these reviews, there have been an increasing number of new studies from these regions. This study therefore, aimed to provide more accurate estimates on the prevalence of stroke survivors and secular trends in LMICs in order to inform decision regarding policy responses and public health intervention across many geographic regions, socioeconomic and populations' subgroups.

2. Methods

2.1 Protocol and registration

This systematic review rational and methods were specified in advance and documented in a protocol which was published in the PROSPERO register (CRD42014015129) [10]

2.2 Search strategy and data extraction

We conducted a thorough literature search to identify relevant studies on stroke prevalence in LMICs. Electronic databases of MEDLINE, EMBASE, SCOPUS and Web of Science were searched from inception to July, 2015 without any language restriction. Relevant journals and reference lists of included primary articles were also scrutinized for additional studies that could have been omitted from the database searches. The following combinations of controlled review terms and keywords covering the study characteristics were used. These include: outcomes; "stroke", “cerebrovascular disease", “cerebrovascular accident", “brain infarction”, “brain stem infarctions”, “cerebral infarction,” study design; "surveillance”, “survey”, “population based”, “community based", and low-and middle-income countries; including all individual countries (Supplementary Table 1).

2.3 Data extraction and eligibility criteria

Three authors (ME, AE and EB) evaluated the eligibility of studies obtained from the literature search using a predefined protocol. They independently extracted, compared and merged the data on studies that met the selection criteria. In cases of discrepancy, agreement was reached by consensus. We included only community-based studies that reported prevalence of stroke ‘survivors’ and conducted in LMICs as defined by World Bank [11]. We also included only studies that used WHO’s definition of stroke, ‘‘rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting longer than 24 hour, unless interrupted by death, with no apparent cause other than that of vascular origin’’[12], however, we allowed less rigorous case ascertainment due to inadequate facilities in most LMICs. Studies that reported prevalence of stroke using some elements of the Sudlow–Warlow criteria [13] for stroke incidence were also included.

2.4 Assessment of methodological quality

Two authors (ME and AE) independently evaluated the methodological and reporting quality of each study using the modified version of Newcastle-Ottawa Scale (Supplementary Table 2). Essentially, we graded the risk of bias in each study as low, moderate, high or unclear according to five study areas namely; selection of participants (selection bias), sample size, detection instrument (outcome measurement tool), adjustment for confounding and (controlled) and detection accuracy. Publication bias using funnel plots and Egger’s test was also conducted on the pooled studies

2.5 Statistical analysis

For the meta-analysis, we first stabilized the raw prevalence of stroke from each study using the Freeman-Tukey variant of the arcsine square root transformed proportion [14] suitable for pooling. We used a DerSimonian-Laird random effects model [15] due to anticipated variations in study population, health care delivery systems and stage of epidemic transition. We performed leave-one-study-out sensitivity analysis to determine the stability of the results. This analysis evaluated the influence of individual studies by estimating the pooled stroke prevalence in the absence of each study [16]. We assessed heterogeneity among studies by inspecting the forest plots and using the chi-squared test for heterogeneity with a 10% level of statistical significance, and using the I^2 statistic where we interpret a value of 50% as representing moderate heterogeneity [17, 18]. We assessed the possibility of publication bias by evaluating a funnel plot for asymmetry. Because graphical evaluation can be subjective, we also conducted a Egger's regression asymmetry test [19] as formal statistical tests for publication bias.

We explored the effect of study-level factors on the overall pooled stroke prevalence estimates using sub-group and meta-regression analyses. Univariate and multivariate random-effects logistic regression analyses were conducted to investigate the impact of study-level factors on the pooled stroke prevalence. Univariate random-effects logistic regression analyses were used to investigate the bivariate relationship between each study-level factors and prevalence of stroke estimates. Multivariate random-effects logistic regression analyses were carried out to determine which study-level factors were independently associated with prevalence of stroke estimates. Only factors statistically significant in the univariate models were included in the multivariate model. Meta-analysis results were reported as combined stroke prevalence with 95% confidence intervals (CIs), while meta-regression results are reported as odds ratio with 95% CIs. All P values are exact and P<.05 was considered significant. Analyses were conducted using Stata version 14 for Windows (Stata Corp, College Station, Texas). This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline [20, 21] PRISMA checklist is provided in the Supplementary Table 3.

2.6 Trend analysis

We examined time trends in the stroke prevalence estimates from 1970 to 2014 using Poisson regression models with the absolute cases of stroke as the outcome variable and the calendar year of the publication as the predictor. This method allows for estimation of time trends across individual calendar years to obtain average annual percentage change (AAPC), assuming that the rate of change is at a constant rate of the previous year [22]. The Poisson regression procedure fits a model of the following form:

$$\log\left(cases_y\right) = b_0 + b_1 y + \log(\,sample\,size) \qquad (1)$$

where *'cases'* equals number of stroke cases reported per year, log is the natural log, *b0* is the intercept, *b1* is the trend, *y* is the year – year is given as 0, 1, 2, … 14 (year 0 is 1970, year 1 is 1971, and so on to 2014), and log of 'sample size' was entered as the offset. The AAPC was calculated using the following formula:

$$AAPC = \left(e^{b_1} - 1\right) \times 100 \qquad (2)$$

3. Results

3.1 Study selection and characteristics of the included studies

The process of study selection is shown in Fig.1. Overall, the literature search of databases yielded 1,877 articles. The titles and abstracts of these were screened for relevance and 1,718 were excluded as duplicates, non-relevant titles and abstracts. 159 articles were selected for critical reading. In all, 101 articles with a total of 7,909,976 participants from 34 LMICs were included. The characteristics of the included studies are summarised in Supplementary Tables 4 to 10. The studies were published between 1970 and 2014, and sample size ranged from 500 to as much as 258,576. All the studies are community-based employing a door-to door, multi-stage or simple random sampling technique. Each of the study covered at least one part of the WHO STEPS stroke protocol for case ascertainment [23]. We found that 39 studies (38.6%) that employed cranial computed tomography (CT) or magnetic resonance imaging (MRI) have a low risk of bias in stroke diagnosis, while 62 (61.4%) studies were limited by availability of resources and neurological imaging, however, rigorous and detailed epidemiological exercise of self-reported diagnosis of stroke in these groups were validated through neurological examination by a specialist team. Most of the studies were conducted in a single site in the rural, urban settings or both. Only two studies were conducted in multiple sites in different countries [24, 25]. When reported, the mean age of participants ranged from 25 years to 78 years. The median percentage of male participants was 48% (range: 31% to

82%). The median percentage of participants with known hypertension was 36% (range: 6 to 71%).

3.2 Risk of bias of included studies

Summary of risk of bias assessment for each study is shown in Supplementary Table 11**.** The risk of bias in the selection of participants is low in most studies (n=98, 97%) and moderate in three studies (3%). The risk of bias due to sample size or number of participants included in the studies was low in most studies (n=83, 83%), high in seventeen studies (17%) and unclear in one study. The risk of detection bias due to inadequate outcome assessment was low, about three-quarter of the studies (n=77, 76%) and high in the remaining studies (n=24, 24%).

3.3 Variations in Stroke prevalence by geographical regions

3.3.1 East Asia and Pacific

Prevalence of stroke 'survivors' and 95% CIs from individual studies with a pooled estimate are shown in Fig.3 and Supplementary Fig. 1. The reported stroke prevalence ranged from 4.27 (per 1000 population) to as much as 162 (per 1000 population). The pooled prevalence ('annualised year average') of stroke for all studies yielded an estimate of 19.9 (95% 14.7 to 25.9 per 1000 population). There was no evidence of publication bias (P = 0.058 for Egger's regression asymmetry test). The results of leave-one-study-out sensitivity analyses showed that no study had undue influence on pooled stroke prevalence (Supplementary Fig. 3).

3.3.2 Europe and Central Asia

Prevalence of stroke 'survivors' and 95% CIs from individual studies with a pooled estimate are shown in Fig. 3 and Supplementary Fig. 4. The reported stroke prevalence ranged from 9 per 1000 population in Turkey to 33 per 1000 population in Romania. The pooled prevalence ('annualised year average') of stroke for all studies yielded an estimate of 19.5 (95% 3.2 to 49.1 per 1000 population).

3.3.3 Latin America and Caribbean

Prevalence of stroke 'survivors' and 95% CIs from individual studies with a pooled estimate are shown in Fig. 3 and Supplementary Fig. 5. The reported stroke prevalence ranged from 1.5 (per 1000 population) to as much as 54.2 (per 1000 population). The pooled prevalence ('annualised year average') of stroke for all studies yielded an estimate of 21.2 (95% 13.7 to 30.3 per 1000 population). There was no evidence of no evidence of publication bias (P = 0.053 for Egger's regression asymmetry test). The results of leave-one-study-out sensitivity analyses showed that no study had undue influence on pooled stroke prevalence (Supplementary Fig. 7).

3.3.4 Middle East and North Africa

Prevalence of stroke ‘survivors’ and 95% CIs from individual studies with a pooled estimate are shown in Fig. 3 and Supplementary Fig. 8. The reported stroke prevalence ranged from 1.20 (per 1000 population) to 10.8 (per 1000 population). The pooled prevalence (‘annualised year average’) of stroke for all studies yielded an estimate of 5·6 (95% 4.0 to 7.5 per 1000 population). There was no evidence of publication bias (P = 0.917 for Egger's regression asymmetry test). The results of leave-one-study-out sensitivity analyses showed that no study had undue influence on pooled stroke prevalence (Supplementary Fig. 10).

3.3.5 South Asia

Prevalence of stroke ‘survivors’ and 95% CIs from individual studies with a pooled estimate are shown in Fig.3 and Supplementary Fig. 11. The reported stroke prevalence ranged from 0.5 (per 1000 population) to as much as 191 (per 1000 population). The pooled prevalence (‘annualised year average’) of stroke for all studies yielded an estimate of 9.4 (95% 6.7 to 12.6 per 1000 population). There was no evidence of publication bias (P = 0.928 for Egger's regression asymmetry test). The results of leave-one-study-out sensitivity analyses showed that no study had undue influence on pooled stroke prevalence (Supplementary Fig. 13).

3.3.6 Sub-Saharan Africa

Prevalence of stroke ‘survivors’ and 95% CIs from individual studies with a pooled estimate are shown in Fig. 3 and Supplementary Fig. 14. The reported stroke prevalence ranged from 0.15 (per 1000 population) to as much as 24.2 (per 1000 population). The pooled prevalence (‘annualised year average’) of stroke for all studies yielded an estimate of 3.5 (95% 1.9 to 5.7 per 1000 population). There was no evidence of publication bias (P = 0.945 for Egger's regression asymmetry test). The results of leave-one-study-out sensitivity analyses showed that no study had undue influence on pooled stroke prevalence (Supplementary Fig. 16).

3.4 Variations in Stroke prevalence by country’s income categories

As shown in Fig. 3, the pooled prevalence stroke ‘survivors’ was highest in upper-middle income countries (20.9, 95% CI 17.0 to 25.2 per 1000, 57 studies) followed by lower middle-income countries (6.9, 95% CI 5.4 to 8.6 per 1000, 37 studies) and closely by low-income countries (6.0, 95% CI 2.1 to 11.8 per 1000, 7 studies).

3.5 Secular trend in the prevalence of stroke survivors

Secular trend in stroke prevalence by different geographic region is shown in Fig. 4. We observed a continuous increase in prevalence of stroke across all geographic regions. The increase is more pronounced in Latin America and Caribbean (trend = 0·157, p value = 0.0001) followed East Asia and Pacific (trend = 0.125, p value = 0.0001) and sub-Saharan Africa countries (trend = 0.113, p value = 0·0001), such that prevalence of stroke have been increasing annually by 17.0%, 13.3% and 12.0% respectively. As shown in Fig. 5, we observed a continuous increase in the stroke prevalence across the countries' income categories. Over the past three decades, the stroke prevalence has increased annually by 14.3% (trend = 0.134, p value = 0.0001) in low-incomes countries, by 12% in upper-middle income countries (trend = 0.113, p value = 0.0001) and by 5.8% in lower-middle income countries (trend = 0.057, p value = 0.0001). Though the prevalence of stroke has been lowest in low-income countries, over time, it recorded the steepest increase and have already overtaken the lower-middle and upper-middle-income countries.

3.6 Factors modifying prevalence of stroke estimates

The result of study-level factors associated with prevalence of stroke is shown in Table 1. In the adjusted analyses, study's geographic region, income category, publication year, participants' mean age, and percentage male were statistically significantly associated with stroke prevalence estimates. Prevalence estimates from East Asia and Pacific and Latin America and Caribbean were six times higher than those from sub-Saharan Africa. Similarly, stroke prevalence from upper-middle income countries was as four times as high as those from low-income countries. Stroke prevalence from urban areas was twice as high as those from rural areas. For every 10 years increase in participants' mean age, the stroke prevalence increases by 84% (OR = 1.84, 95% CI 1.46 to 2.32) (Supplementary Fig. 18). For every 10% increase in the percentage of male participants included in the study, the stroke prevalence decreases by 68% (OR = 0.32, 95% CI 0.22 to 0.47) (Supplementary Fig. 19). Variations in the mean age of the participants explained almost half of the between studies variation in stroke prevalence estimates (49%).

Year of publication, percentage male, and sample size each explained almost one-third in the between studies variation in stroke prevalence estimates. However, in the adjusted analysis, when all study-level factors that were significant in unadjusted analyses were controlled for statistically, only mean age of the participants remained statistically significant with the prevalence of stroke estimates (OR- 1.62, 95% CI 1.06 to 2.47).

4. Discussion

Stroke prevalence varied significantly across geographical regions in different time period. Low-income countries particularly in sub-Saharan African have low prevalence of stroke survivors. This may have been due to the high fatality rates from stroke owing to less investment in health care, increased poverty and co-morbidities like HIV/AIDS and Tuberculosis [26-28]. The early stage of epidemiological transition characterised by hypertensive heart disease and a huge proportion of haemorrhagic stroke disease are now occurring in these countries [29]. Pooled estimate of stroke in upper-middle-income countries is about 3-fold higher as against lower-middle-income or low-income countries. These differences are not surprising, however, the increasing levels of affluence and urbanization [30] and the rise in life expectancy [30] and associated risk factors [4, 25] particularly hypertension provide a plausible explanation. In fact, there is a large body of epidemiological evidence on the high prevalence of undetected or poorly managed hypertension in LMICs, which is likely to play a major role in the huge prevalence of stroke in these settings [25].

We observed a continuous increase in the stroke prevalence across the three countries' income categories. Over the past three decades, the stroke prevalence has increased annually by 14.3% (trend = 0.134, p value = 0.0001) in low-incomes countries, 12% in upper-middle income countries (trend = 0.113, p value = 0.0001) and by 5.8% in lower-middle income countries (trend = 0.057, p value = 0.0001). Though, the prevalence of stroke has been highest in upper-middle income countries, however, low-income countries record the steepest increase in stroke prevalence and projected to overtake both lower-middle and upper-middle- income countries. The changing prevalence of stroke survivors is quite revealing, and suggests a major epidemiological and demographic shift. Other common themes found within the periods indicate a low prevalent rate from 1970-1989, however, there are few exceptions where the rate had increased significantly and reached a plateau from 1983 and 1988 [31-33]. Between 1990 and 2007, data from China [34], Columbia [35, 36] and Romania [37] showed a net increase in prevalence. This increases several folds from 2010 to 2014 particularly in China [32, 38, 39] Brazil [30, 40, 41] and Cuba [42], suggesting a combination of rapid socioeconomic changes including increase in aging population, urbanization, and lifestyle factors. Latin America faces major demographic changes; the most important being urbanization (almost 90% of the population now live in urban areas) and aging; that is, the ratio of productive adults to elderly individuals is steadily shrinking [5, 8]. In Brazil for instance, socio-economic developments that have occurred over the past decades is well-known. Other factors may include access to vascular prevention strategies, exposure to risk factors and inequality to basic medical *care* particularly in the rural communities [41].

This review apart from the evidentiary underpinning of the significantly higher prevalence of stroke, revealed some important issues including the preponderance of traditional risk factors. For every 10 years increase in participants' mean age, the stroke prevalence increases by 62%. The pattern of age-specific increase in stroke prevalence is clearly marked within three age-brackets for both genders with available data**.** Our result show that Latin America and Caribbean region has the highest proportion of elderly (≥65 years) participants living in urban areas. This corroborated the recent evidence of epidemiological transition in Latin America toward older urban dwelling adults [8]. The higher proportion of stroke in upper-middle-income countries and urban settings compared to low-income countries and rural environments as shown in the present study and in previous reviews [6, 8, 43] are in line with convergence of increasing income level, urbanisation and cardio-vascular disease predictors.

The most recent reviews on stroke epidemiology were limited to 7 incidence studies in 9 LMICs [9]. Previous reviews had little representation of LMICs [44], others were based on regional [6, 8, 45-48], country [28, 49, 50] or population-specific analysis [28, 49, 50]. There are also global reviews of stroke with few studies in LMICs [1, 44]. Given the limited number of studies, geographical spreads and omission of important development indicators, it appears that these reports may not necessarily reflect the true prevalence estimate of stroke survivors in LMICs in the current epidemiological and demographic transitions. For instance, Feign and co-authors (2014), in a recent report on the global burden of stroke reported a prevalence estimates of 393.4/100,000 population in 2010[1]. The result was comparable with the current estimate, which further underpins a near representation of the size of the problem in LMICs. However, the minor differences may probably be due to the study periods, age groups and fewer data-points (the report provided data for only 34 population-studies for LMICs). In addition, the result of stroke prevalence in Africa reported a continentwide pooled estimate without due consideration of human development index and gross national income per capita estimates [6, 51]. Our study presents the most comprehensive and up-to-date review of stroke prevalence in LMICs. Moreover, the introduction of World Bank regions and income groups in our analytical model provided interesting dimension to warrant valid comparative estimate appropriate for public health policy interventions on the prevalence of stroke survivors within these jurisdictions.

To date, the health priorities of many LMICs particularly in sub-Saharan Africa and south Asian countries remain infectious diseases mainly HIV/AIDS, Malaria and Tuberculosis [52-54]. This is in addition to high poverty, malnutrition, illiteracy, unsafe drinking water and social discrimination [55]. The economic impact of increased stroke survivors in our study would mean growing underinvestment and GDP loses reflecting increased loss in productivity and reduced labour efficiency in LMICs.

Cost for stroke survivors was estimated to be as high as $34 billion annually in the United States[56], and about 5% of total NHS cost amounting to £8.9billion in the UK [57]. Studies on the cost of stroke in LMICs are few and far between, in Togo for instance, the estimated direct cost per person stood at 936 Euros in only 17 days, about 170 times more than the average annual heath expenditure of a Togolese [58]. This does not include informal and indirect costs. Such financial outlay in stroke alone would foreclose the consideration of urgent priority public health issues in LMICs.

Consistent evidence from our study and elsewhere found that hypertension is the main risk factor of all stroke in LMICs and this is more prominent among the young adults who present with stroke unaware of their high blood pressure status [59]. With the steepest increase in the prevalence of stroke survivors taking place in LMICs particularly in low-income countries, options for urgent and improved surveillance and cost-effective prevention of major risk-factors such as hypertension remain an important public health priority. As a result of the double burden of communicable and non-communicable diseases in LMICs [60], it appears the estimates found in this study will continue in an upward trend with huge fatality due to policy alignment focusing on the prevention and control of infectious diseases including maternal, perinatal and nutrition related conditions.

While informative, the results of this meta-analysis should be interpreted with caution. First, in large continental region such as sub-Saharan Africa and Europe and Central Asia, there were insufficient studies to entirely represent the regions. In addition, we found significant difference related to study-level participants' characteristics, publication year, and study sample size. Nevertheless, the results of tests for publication bias provided evidence that we are unlikely to have missed studies that could have altered the meta-analyses results. The diagnosis of stroke in LMICs remains a huge challenge, hence, ascertainment of cases were not well defined across some studies and this has been reported previously [61]. We did not provide data on stroke-related disability or case-fatality. Although such data are important for health-care planning, such estimates may be unreliable due to conflicting information on causes of death, overlapping disabilities caused by disorders that accompany stroke in many older patients and the fact that majority of stroke survivors do not access the health service due to prohibitive out-of-pocket expenses, distance to urban hospital and lack of stroke functioning units in rural health care settings [44, 62]. Some hospital surveys in south Asia and sub-Saharan Africa have shown that CT scans for instance, were only conducted on less than half of patients presenting with stroke, and this is mainly among those that can afford it [62]. Nonetheless, we allowed studies showing quality methodological rigour including detailed epidemiological exercise in our final analysis.

Despite these limitations, the study's strengths are important. We conducted a meta-analysis as a preferable option for data synthesis, since qualitative or narrative synthesis can lead to misleading conclusions that should not be generalized beyond the scope of the analysis [63]. Comprehensive searches of databases were also conducted to ensure that all relevant publications were identified. We also reduced potential bias in the conduct of this review by having the authors independently scan through the search output and extract the data. In addition, we included only community-based studies and provided estimates on stroke prevalence trends. These provided additional information for local feedback on health system and public-health demands.

5. Conclusions

Our study findings provide contemporary estimates that reflect the significant prevalence of stroke survivors in LMICs. The socio-economic implication of stroke in LMICs is very high in terms of magnitude and secular trend. Though upper-middle income countries accounts for the largest prevalence of stroke, low-income countries have experienced the steepest increase in stroke prevalence over the last three decades, and are projected to overtake both lower-middle and upper-middle- income countries. The findings of the study will be useful for proper design of stroke screening (including high blood pressure and other predictors), treatment, rehabilitation, and related public health prevention strategies. Particular attention should be given to the large prevalence of undetected or uncontrolled high blood pressure [6, 25, 64], which is likely to play a major role in the observed secular trends in stroke prevalence across low-resource settings.

Conflict of interest

None

AUTHORS' CONTRIBUTIONS

All authors contributed to the study concept and design. Ezejimofor MC, Uthman OA, Ezejimofor BC, and Ezeabasili AC conducted literature search and collected data. Ezejimofor MC, Uthman OA, Chen Y-F, and Kandala N-B contributed to data and statistical analysis. Ezejimofor MC wrote the first draft and Stranges S, Kandala N-B, Uthman O, Ezeabasili AC and Chen Y-F provided critical revision and relevant intellectual content.

Acknowledgement

Ezejimofor MC acknowledges the support from Petroleum Technology development Fund (PTDF/OSS/663/12).

References

1. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al (2014) Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. Lancet 383(9913):245-255.
2. Strong K, Mathers C, Bonita R (2007) Preventing stroke: saving lives around the world. Lancet Neurol 6(2): 182-187.
3. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V (2009) Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 8(4):355-369.
4. Lloyd-Sherlock P (2010) Stroke in developing countries: epidemiology, impact and policy implications. Dev Policy Rev 28(6):693-709.
5. Mukherjee D, Patil CG (2011) Epidemiology and the global burden of stroke. World Neurosurg 76(6 Suppl):S85-90. doi: 10.1016/j.wneu.2011.07.023.
6. Adeloye D (2014) An Estimate of the Incidence and Prevalence of Stroke in Africa: A Systematic Review and Meta-Analysis. PLoS One 9(6): e100724. doi:10.1371/journal.pone.0100724
7. Connor MD, Walker R, Modi G, Warlow CP (2007) Burden of stroke in black populations in sub-Saharan Africa. Lancet Neurol 6(3):269-278.
8. Avezum Á, Costa-Filho FF, Pieri A, Martins SO, Marin-Neto JA (2015) Stroke in Latin America: Burden of Disease and Opportunities for Prevention. Glob Heart 10(4):323–331
9. Sajjad A, Chowdhury R, Felix JF, Ikram MA, Mendis S, Tiemeier H, et al (2013) A systematic evaluation of stroke surveillance studies in low-and middle-income countries. Neurology 80(7):677-684.
10. Ezejimofor M, Kandala N-B, Uthman O, et al (2015) Prevalence of stroke in low- and middle-income countries: a systematic review and meta-analysis. York, United Kingdom: Centre for Reviews and Dissemination: University of York doi:10.15124/CRD42014015129
11. World Bank Group. Countries and Economies. 2015. http://data.worldbank.org/country. Accessed 4 December 2015.
12. Sacco RL, Kasner SE, Broderick JP, et al (2013) An updated definition of stroke for the 21st century a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 44(7):2064-2089.

13. Sudlow C, Warlow C (1997) Comparable studies of the incidence of stroke and its pathological types results from an international collaboration. Stroke 28(3):491-499.
14. Miller JJ (1978) The inverse of the Freeman–Tukey double arcsine transformation. Am Stat 32(4):138-138
15. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Contemp Clin Trials 7(3): 177-188.
16. Normand SL (1999) Meta-analysis: formulating, evaluating, combining, and reporting. Stat Med 18(3):321-359.
17. Higgins JP (2002) Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 21(11): 1539-1558.
18. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327(7414): 557-560.
19. Egger M, Smith GD, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315(7109):629-634.
20. Liberati A, Altman DG, Tetzlaff J, Cynthia M, Peter G, John I, et al (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med 151(4):65-94.
21. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 151(4): 264-269.
22. Clegg LX, Hankey BF, Tiwari R, Feuer EJ, Edwards BK (2009)Estimating average annual per cent change in trend analysis. Stat Med 28(29):3670–82.
23. World Health Organization (2005) WHO STEPS Stroke Manual: The WHO STEPwise approach to stroke surveillance. http://www.who.int/chp/steps/stroke/manual/en/ Accessed 15 June 2015.
24. Van Minh H, Ng N, Juvekar S, Abdur R, Ali A, Abdullahel H et al (2008) Self-reported prevalence of chronic diseases and their relation to selected sociodemographic variables: a study in INDEPTH Asian sites, 2005. Prev Chronic Dis 5(3):86-99.
25. Ferri CP, Schoenborn C, Kalra L, Acosta D, Guerra M, Huang Y et al (2011) Prevalence of stroke and related burden among older people living in Latin America, India and China. J Neurol Neurosurg Psychiatry 82(10):1074-1082

26. Abd-Allah F, Moustafa RR (2014) Burden of stroke in Egypt: current status and opportunities. Int J Stroke 9(8):1105-1108.
27. Anand K, Chowdhury D, Singh K, Pandav C, Kapoor S (2001) Estimation of mortality and morbidity due to strokes in India. Neuroepidemiology 20(30):208-211.
28. Wahab KW (2008) The burden of stroke in Nigeria. Int J Stroke 3(4):290-292.
29. Cappuccio FP (2004) Commentary: Epidemiological transition, migration, and cardiovascular disease. Int J Epidemiol 33(2):387-388
30. Copstein L, Fernandes JG, Bastos GAN (2013) Prevalence and risk factors for stroke in a population of Southern Brazil. Arq Neuropsiquiatr 71(5):294-300.
31. Li S-c, Schoenberg BS, Wang C-c, Cheng X-m, Bolis C, Wang K-j (1985) Cerebrovascular disease in the People's Republic of China Epidemiologic and clinical features. Neurology 35(12): 1708-1713
32. Wang C, Cheng X, Li S, Bolis C, Schoenberg B (1983). Epidemiology of cerebrovascular disease in an urban community of Beijing, People's Republic of China. Neuroepidemiology 2(3-4): 121-134.
33. Bharucha NE, Bharucha EP, Bharucha AE, Bhise AV, Schoenberg BS (1988). Prevalence of stroke in the Parsi community of Bombay. Stroke 19(1):60-62.
34. He Y, Jiang B, Wang J, Feng K, Chang Q, Fan L et al (2006) Prevalence of the Metabolic Syndrome and its Relation to Cardiovascular Disease in an Elderly Chinese Population. J Am Coll Cardiol 47(8):1588-1594.
35. Pradilla A, Vesga A, Boris E, León-Sarmiento FE (2003). National neuroepidemiological study in Colombia (EPINEURO). Rev Panam Salud Públi 14(2):104-111.
36. Pradilla AG, Vesga AB, León-Sarmiento F (2002) [Study of neurological diseases prevalence in Aratoca, a rural area of eastern Colombia]. Rev Med Chil 130 (2):191-199.
37. Florescu M, Margulescu A, Florian A (2007) Prevalence and control of cardiovascular risk factors in Romania cardio-zone national study. Maedica 2(4):278-288.
38. Dong Y LS, Zhao-Qiang S (2010). Investigation on prevalence of stroke in rural old groups of Liaoning province. Shanxi Medical Journal 39:404-406.
39. Wang Y, S. Huang S, Tang J-L (2012) Prevalence of Chronic Diseases and Influencing Factors Among Middle-aged and Senior Adults Aged over 50 in Rural Areas of Rushan City, 2009 [J]. Preventive Medicine Tribune 4:007.

40. Abe IM, Lotufo PA, Goulart AC, Bensenor IM (2014). Stroke prevalence in a poor neighbourhood of São Paulo, Brazil: applying a stroke symptom questionnaire. Int J Stroke 6(1): 33-39.
41. Fernandes TG, Benseñor IM, Goulart AC, Tavares BM, Alencar AP, Santos IS et al (2014) Stroke in the Rain Forest: Prevalence in a Ribeirinha Community and an Urban Population in the Brazilian Amazon. Neuroepidemiology 42(4):235-242.
42. Moreno C. Prevalence of stroke and associated risk factors in older adults in Havana City and Matanzas Provinces, Cuba (10/66 population-based study). MEDICC Rev 12(3):20-26.
43. Liu M, Wu B, Wang WZ, Lee LM, Zhang SH, Kong LZ (2007). Stroke in China: epidemiology, prevention, and management strategies. Lancet Neurol 6(5):456-464
44. Feigin VL, Lawes CM, Bennett DA, Anderson CS (2003) Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol 2(1):43-53.
45. Burke TA, Venketasubramanian RN (2006) The epidemiology of stroke in the East Asian region: a literature-based review. Int J Stroke 1(4):208-215.
46. Lavados PM, Hennis AJ, Fernandes JG, Medina MT, Legetic B, Hoppe A et al (2007) Stroke epidemiology, prevention, and management strategies at a regional level: Latin America and the Caribbean. Lancet Neurol 6(4):362-372.
47. Pandian JD, Sudhan P (2013) Stroke epidemiology and stroke care services in India. JOS 15(3): 128-134.
48. Saposnik G, Del Brutto OH (2003). Stroke in South America A Systematic Review of Incidence, Prevalence, and Stroke Subtypes. Stroke 34(9):2103-2107
49. Tse LA, Fang XH, Wang WZ, Qiu H, Yu IT (2012). Incidence of ischaemic and haemorrhagic stroke and the association with smoking and smoking cessation: a 10-year multicentre prospective study in China. Public Health 126(11):960-966.
50. Xu G, Ma M, Liu X, Hankey GJ (2013) Is there a stroke belt in China and why? Stroke 44(7): 1775-1783.
51. Owolabi MO, Akarolo-Anthony S, Akinyemi R, Arnett D, Gebregziabher M, Jenkins C et al (2015) The burden of stroke in Africa: a glance at the present and a glimpse into the future: review article. Cardiovasc J Afr 26:27-38. doi: 10.5830/CVJA-2015-038.
52. Bishwajit G, Ide S, Ghosh S (2014) Social Determinants of Infectious Diseases in South Asia. International Scholarly Research Notices 2014:1-10. doi:10.1155/2014/135243

53. Beaglehole R, Bonita R, Alleyne G, Horton R, Li L, Lincoln P et al (2011) UN high-level meeting on non-communicable diseases: addressing four questions. Lancet 378(9789):449-455.
54. Chan KY, Davies Adeloye LG, Kolčić I, Marušić A (2012) How big is the 'next big thing'? Estimating the burden of non–communicable diseases in low–and middle–income countries. J Glob Health 2(2): 020101. doi: 10.7189/jogh.02.020101
55. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ (2006) Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 367(9524):1747-1757.
56. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M et al (2015) Heart disease and stroke statistics-2015 update: a report from the american heart association. Circulation 131(4): e29-322. doi: 10.1161/CIR.0000000000000152
57. Saka Ö, McGuire A, Wolfe C (2009) Cost of stroke in the United Kingdom. Age Ageing 38(1):27-32.
58. Guinhouya K, Tall A, Kombate D, Kumako V, Apetse K, Belo M et al (2010) [Cost of stroke in Lome (Togo).]. Sante (Montrouge, France). doi: 10.1684/san.2010.019
59. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P et al (2010) Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. Lancet 376(9735):112-123
60. Remais JV, Zeng G, Li G, Tian L, Engelgau MM (2012) Convergence of non-communicable and infectious diseases in low-and middle-income countries. International journal of epidemiology 42(1):221-227. doi: 10.1093/ije/dys135
61. Bennett DA (2011) Methodology of the global and regional burden of stroke study. Neuroepidemiology 38(1):30-40.
62. Kengne AP, Anderson CS (2006) The neglected burden of stroke in Sub-Saharan Africa. Int J Stroke 1(4):180-190.
63. Ioannidis J, Patsopoulos N, Rothstein H (2008) Reasons or excuses for avoiding meta-analysis in forest plots: Heterogeneous data are a common problem in meta-analysis. BMJ 336(7658): 1413–1415
64. Adeloye D, Basquill C, Aderemi AV, Thompson JY, Obi FA (2015) An estimate of the prevalence of hypertension in Nigeria: a systematic review and meta-analysis. Journal of hypertension 33(2):230-242.

TABLE

Table 1 Results of meta-regression analyses

	Unadjusted (Univariate)			Adjusted (Multivariate)*	
Variable	**OR (95% CI)**	**P-value**	**R2**	**OR (95% CI)**	**P-value**
Region			17.1		
East Asia & Pacific	5.95 (2.43 to 14.59)	0.0001		2.03 (0.37 to 11.11)	0.395
Europe & central Asia	7.01 (1.00 to 48.73)	0.049		1.19 (0.17 to 8.42)	0.858
Latin America & Caribbean	6.11 (2.54 to 14.69)	0.000		1.83 (0.37 to 9.12)	0.442
Middle East & North Africa	2.05 (0.67 to 6.32)	0.207		1.29 (0.18 to 9.40)	0.791
South Asia	2.39 (0.94 to 6.05)	0.066		5.21 (0.86 to 31.36)	0.069
Sub-Saharan Africa	1 (reference)			1 (reference)	
Country income			16.4	ni	
Low	1 (reference)			1 (reference)	
Low-middle	1.25 (0.43 to 3.59)	0.677		3.19 (0.54 to 18.83)	0·187
Upper-middle	3.94 (1.14 to 10.98)	0.009		3.12 (0.49 to 19.92)	0.213
Study design			0.0	ni	
Cohort	1 (reference)				
Cross-sectional	0.94 (0.31 to 2.80)	0.910			
Setting			2.9	ni	
Rural	1 (reference)				
Urban	2.13 (1.09 to 4.18)	0.028			
Rural & urban	1.34 (0.68 to 2.94)	0.393			
Publication year	1.08 (1.06 to 1.11)	0.0001	28.0	1.04 (0.92 to 1.16)	0.523
Sample size (log)	0.65 (0.57 to 0.75)	0.0001	28.6	0.96 (0.61 to 1.50)	0.839
Mean age (per 10 year)	1.84 (1.46 to 2.32)	0.0001	49.2	1.62 (1.06 to 2.47)	0.027
Percentage male (per 10%)	0.32 (0.22 to 0.47)	0.0001	30.4	0.77 (0.37 to 1.61)	0.462
Hypertensive (per 10%)	1.29 (0.98 to 1.68)	0·.064	11·.3	ni	
Smokers (per 10%)	1.52 (0.87 to 2·.68)	0.131	9.7	ni	

ni: not included, OR: Odds ratio; CI: Confidence Interval
*Explained variance (52.5%)

Fig. 1. Study selection process and flow

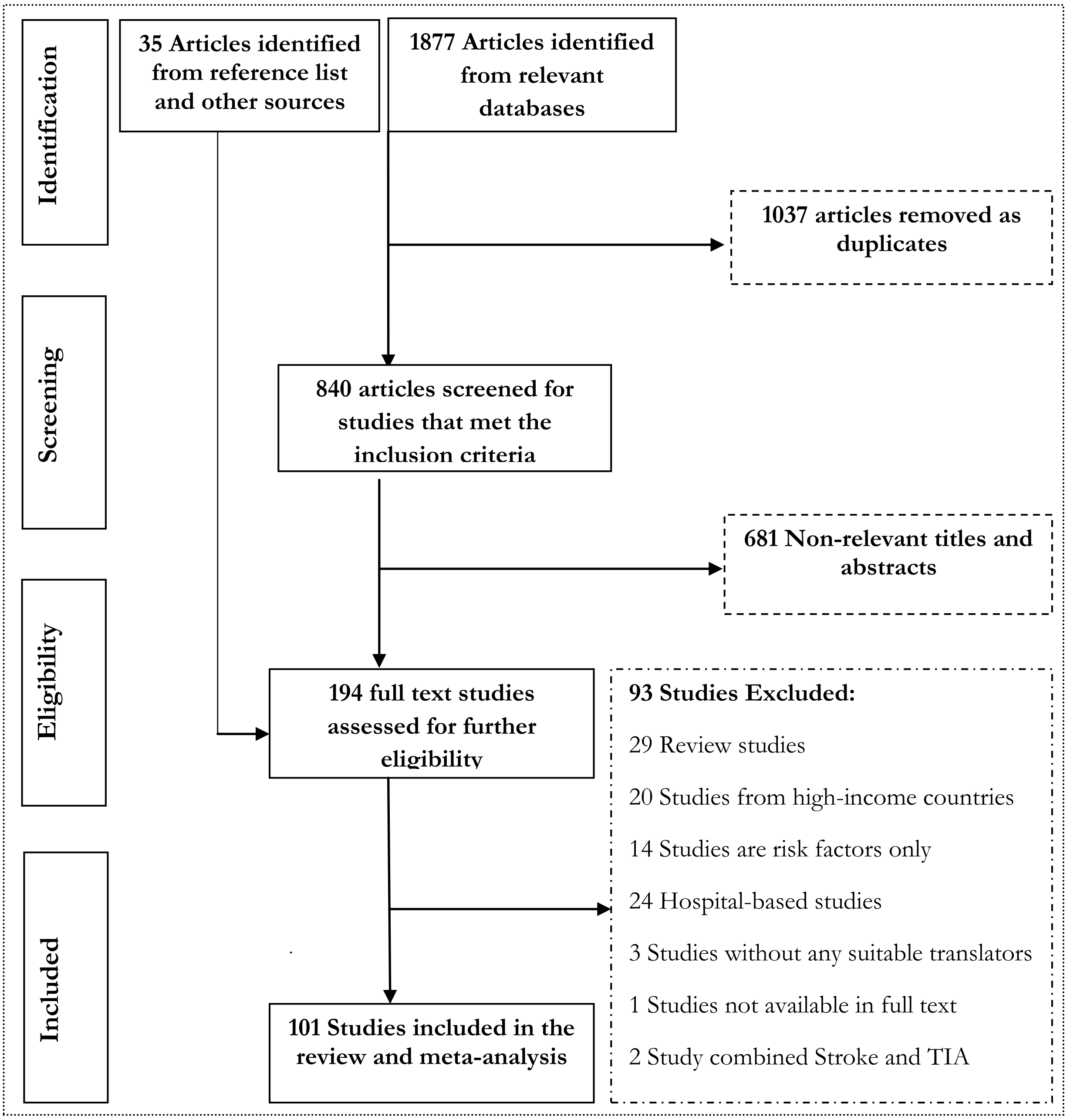


Fig. 2. **Study selection process and flow**

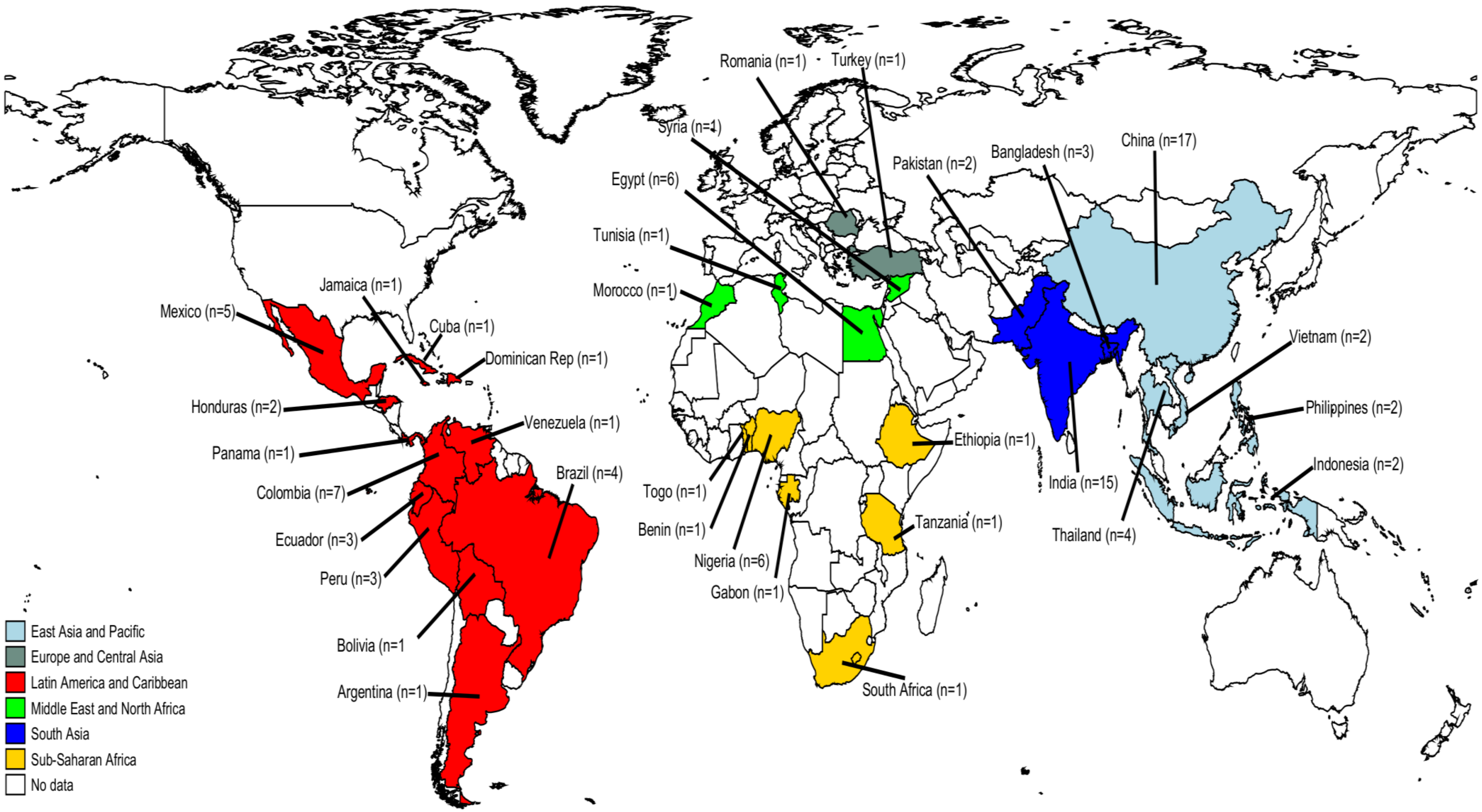


Fig. 3. Pooled stroke prevalence by different subgroups

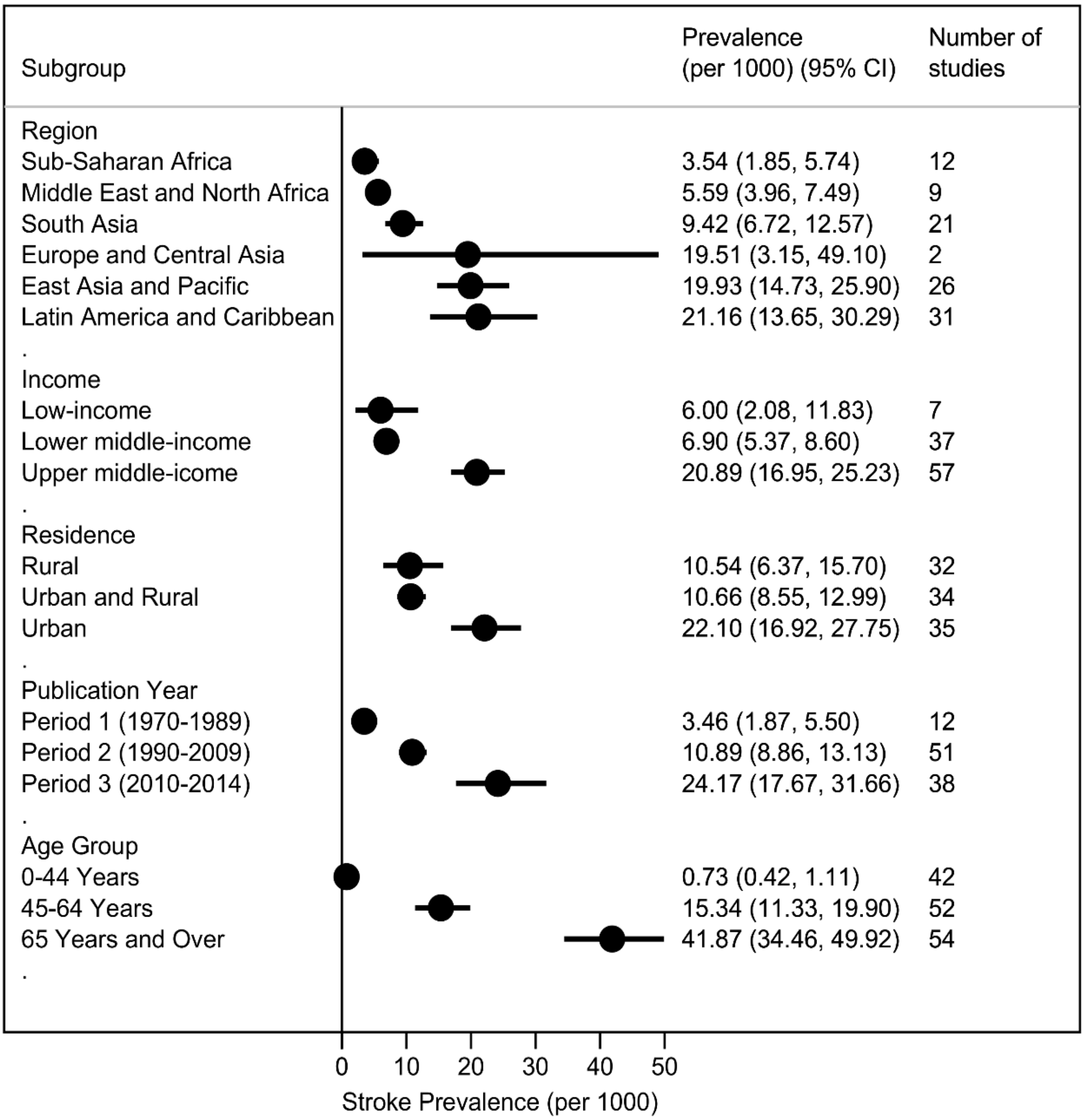


Fig. 4. Secular trends in prevalence of stroke survivors by different geographic

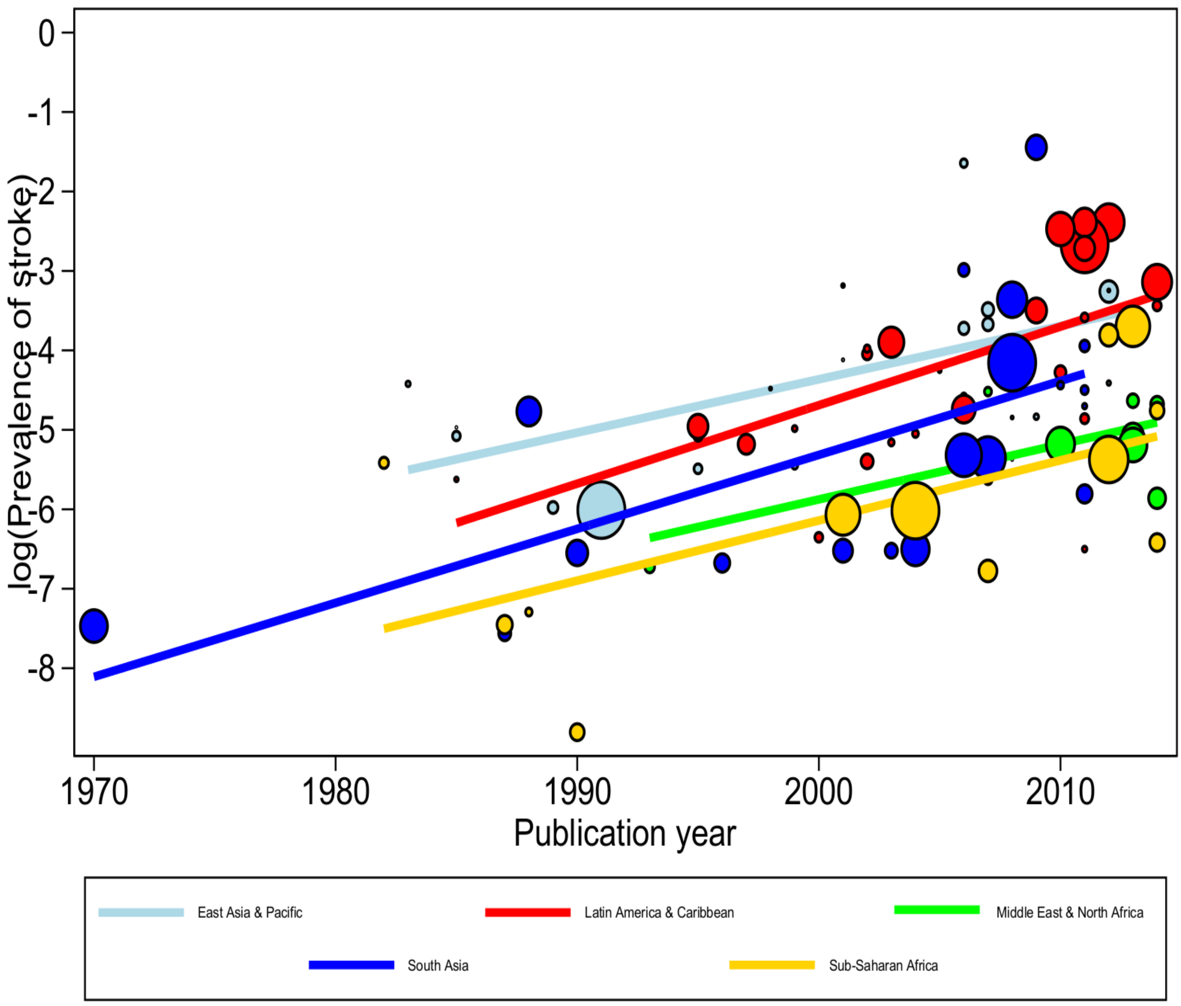
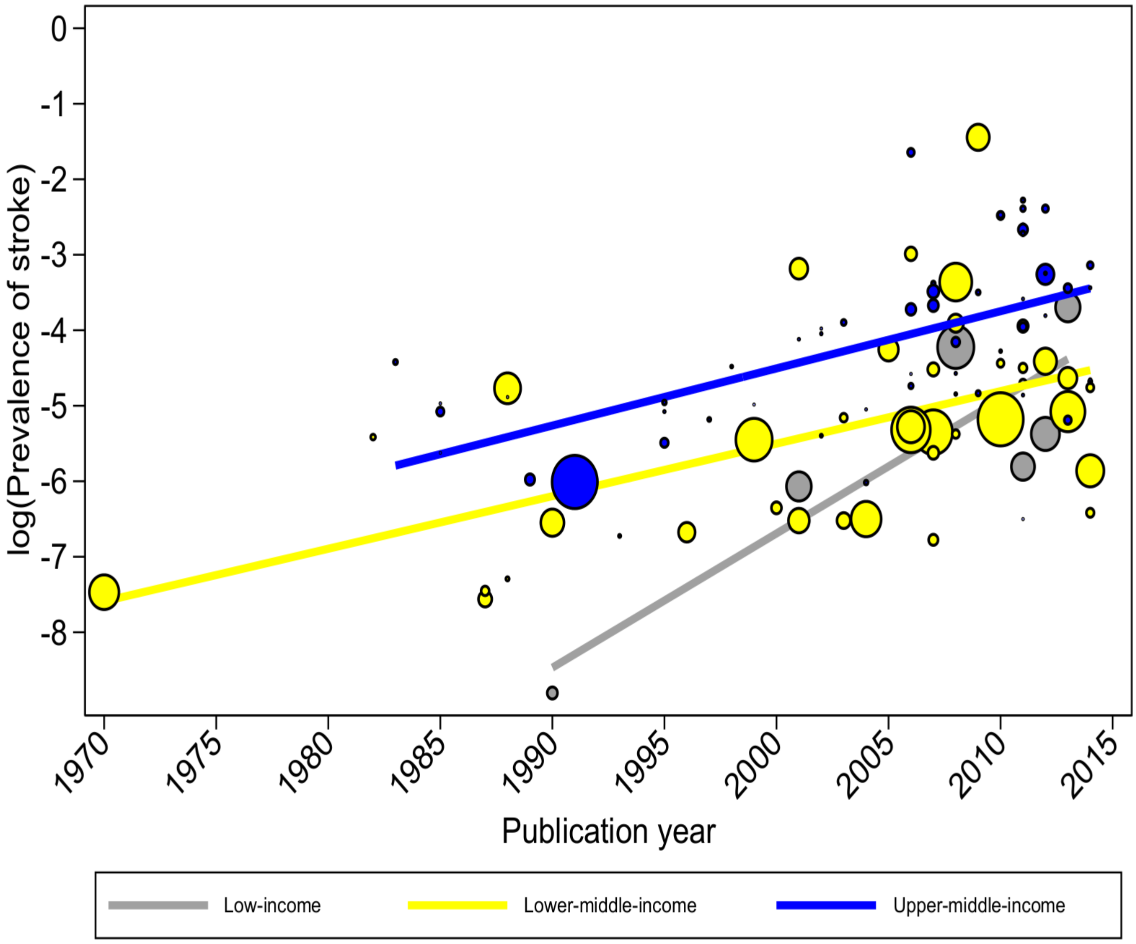


Fig. 5. Secular trends in prevalence of stroke survivors by country's income category



Highlights

- 101 community-based studies were identified and included in meta-analysis
- Stroke survivors differ significantly in both magnitude and secular trend in LMICs
- Highest annual increase of 14.3% occurred in low-income countries
- Stroke surveillance and management of undetected or uncontrolled HBP should remain public health priority