A systematic evaluation of stroke surveillance studies in low- and middle-income countries

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ABSTRACT

Objective: Reliable quantification of the burden of stroke in low- and middle-income (LMI) countries is difficult as population-based surveillance reports are scarce and may vary considerably in methodology. We aimed to evaluate all available primary stroke surveillance studies by applying components of a benchmark protocol (WHO STEPwise approach to stroke surveillance) and quantify the reported burden of stroke in LMI settings.

Methods: Electronic databases Medline, Embase, Scopus, and Web of Knowledge were searched for population-based surveillance studies. Studies conducted in the LMI countries that reported on incident stroke were included. Data were extracted from each study using a prestructured format. Information on epidemiologic measures including crude and age-adjusted incidence rates, person-years, admission rates, case fatality rates, death certification, autopsy rates, measures of disability, and other study-specific information, in line with WHO STEPS stroke protocol, were recorded. Age-adjusted incidence rate data of stroke were combined using random-effects meta-analyses.

Results: We identified 7 studies that reported on burden of stroke in 9 LMI countries, including aggregate information from 1,711,372 participants collected over 5,240,923 person-years. The age-adjusted incidence rates across the LMI countries varied widely, with the burden of total first-ever strokes ranging from 41 to 909 events per 100,000 person-years.

Conclusions: Systematic evaluation of all available primary surveillance studies, particularly in the context of WHO STEPS guidelines, indicates inadequate adherence to standardized surveillance methodology in LMI countries. Incorporation of standardized approaches is essential to enhance generalizability and estimate stroke burden accurately in these resource-poor settings. *Neurology*® 2013;80:677-684

GLOSSARY

COI = cost of illness studies; **DALY** = disability-adjusted life-years; **LMI** = low and middle income; **mRS** = modified Rankin Scale.

Stroke remains a major cause of death and disability globally, claiming more lives each year than HIV-AIDS, tuberculosis, and malaria combined,¹⁻³ and accounting for 46.6 million disability-adjusted life-years (DALY) worldwide.⁴ In 2005, mortality due to stroke was 5.8 million and more than 85% of all stroke-related deaths were estimated to occur in low- and middle-income (LMI) countries.⁵⁻⁸ Accurate estimation of stroke burden in these settings is difficult due to shortage of resources to establish sustainable, reliable, and standardized surveillance systems essential to generate comparable data.

In this context, the WHO has devised a tool for stroke surveillance that comprises 6 modules arranged in 3 different “STEPS” based on the initial presentation and outcome of a stroke patient.⁹ As the hierarchy of the modules is climbed, the costs and complexity of data collection processes increases. In LMI countries, where resources are limited, the importance of seeking an optimum balance between feasibility and practicality is considered the mainstay of this system to gather stroke epidemiology data.⁹ Interpretation of available reports in LMI regions is also complicated as data

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collection methods vary widely across studies. Systematic assessment of these studies, particularly in the context of the WHO surveillance guidelines, could potentially help 1) collect more reliable stroke estimates in LMI countries, 2) allow international comparisons across populations, and 3) shape public health interventions and policies aimed to improve the prevention and management of stroke.

Therefore, the purpose of this review is to 1) systematically evaluate published studies on stroke surveillance in LMI countries in order to compare the strategies adopted by these studies with that of the stroke surveillance protocol proposed by WHO and 2) quantify the burden of first-ever stroke in LMI countries reported in available studies from these settings.

METHODS This review was conducted using a predefined protocol and in accordance with the PRISMA guidelines.

Search strategy. We conducted a systematic literature search to corroborate surveillance data and to identify candidate studies on stroke surveillance in LMI countries. A combination of controlled vocabulary and key words was used in the search strategy in the electronic databases Medline, Embase, Scopus, and Web of Knowledge, and no restrictions were placed by date of publication. The search strategy was restricted to English language. Stroke surveillance registries were also searched for local data. The computer-based searches combined search terms related to the surveillance (e.g., “population surveillance,” “surveillance,” “sentinel surveillance,” “survey”), outcome (e.g., “stroke,” “cerebrovascular disease”), and LMI

countries (e.g., “low- and middle-income countries” and “names of all LMI countries individually” [appendix e-1 on the *Neurology*® Web site at www.neurology.org]).

Study selection. Identification of LMI countries was based on World Bank groups by income per capita. Income categories used were for 2006–2010 according to gross national income per capita.¹⁰ Studies were included that identified stroke as per WHO definition: a clinical syndrome characterized as “rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin.”⁹ Population-based surveillance studies recording incidence and case fatality were included in this review. Selection of studies and full eligibility criteria are presented in figure 1. We cross-referenced all articles selected to identify further relevant studies.

Data extraction. We extracted data from each study using a pre-structured format. Specific epidemiologic measures including crude incidence rates, person-years, age-adjusted incidence rates, hospital admission rates, case fatality rates, death certification, autopsy rates, and measures of disability were recorded. Incidence rates were age-standardized per 100,000 individuals by use of direct method using the WHO World Standard population.¹¹ Usage rates of MRI or CT scan in stroke diagnosis, determination of stroke subtype, and whether it was a first-ever or recurrent event were also extracted. We also recorded and compared the dates of publication, year in which surveillance was conducted, location, study duration, specific aims, and the strengths and limitations of each study.

Application and comparison of STEPS stroke surveillance criteria to each study. The WHO STEPS stroke surveillance protocol⁹ employs 3 steps for stroke surveillance as described below.

Step 1: Events in the hospital. Step 1 gives frequency of hospital admissions due to stroke. It consists of 3 modules that obtain core data. Module 1 includes basic history of the patient and records whether it is a first time or a recurrent stroke. Module 2 measures patient’s functional level and in-hospital medical treatment. Module

Figure 1 Flow diagram of literature search

*Studies were not available in the archives and no contact with the authors was established to retrieve full texts.

Table 1 Incidence rates and case fatality (%) of population-based studies

Country	Years	Study duration, y	Person-years	Age range	Total no. of incident strokes	Crude incidence of total strokes/100,000 (95% CI)
Nigeria	1971-1974	3	2,409,300	All	300	15 (13-17)
Mongolia	1971-1974	3	783,900	All	653	50 (46-54)
India (Rohtak)	1971-1974	1	124,700	All	82	27 (21-33)
Sri Lanka	1971-1974	1	562,400	All	163	24 (20-27)
Ukraine	2000	1	125,482	All	352	281 (248-313)
Georgia	2003	2.5	140,926	All	233	165 (144-186)
Brazil	2004	1	75,053	All	81	108 (84-131)
India (Mumbai)	2006	2	313,722	25->94	456	145 (132-159)
Bulgaria	2002	1	56,447	45-84	157	622 (560-690)
Tanzania	2003-2006	3	648,993	All	636	Urban: 107.9 (88.1-129.8); rural: 94.5 (76-115)
Country	Age-adjusted incidence of total first-ever strokes/100,000 (95% CI)	Hospital admission proportion, %	1-Month case fatality proportion, %	CT/MRI autopsy proportion, %	Timing of CT/MRI after stroke	Data of stroke types by age and sex
Nigeria	41 (36-45)	89	NR	NR	NR	Total strokes
Mongolia	78 (71-84)	51	NR	NR	NR	Total strokes
India (Rohtak)	48 (38-59)	55	NR	NR	NR	Total strokes
Sri Lanka	41 (35-47)	98	NR	NR	NR	Total strokes
Ukraine	238 (213-263)	66	23	41	NR	Total strokes
Georgia	103 (72-133)	66	35	66.7	NR	Total, IS, PICH, SAH
Brazil	130 (125-220)	100	19	100	2 days	Total, IS, PICH
India (Mumbai)	151 (137-165)	67	30	89	NR	Total strokes
Bulgaria	RM: 909 (712-1,105); UM: 597 (482-712); RF: 667 (515-818); UF: 322 (248-395)	46	35	36	1 week	Total strokes
Tanzania	Urban: 315.9 (281.6-352.3); rural: 108.6 (89.0-130.9)	32	NR	79	15 days	Total strokes

Abbreviations: CI = confidence interval; IS = ischemic stroke; NR = not reported; PICH = posterior intracerebral hemorrhagic stroke; RF = rural female; RM = rural male; SAH = subarachnoid hemorrhage; UF = urban female; UM = urban male.

3 consists of utilization of imaging facilities to classify the type of stroke.

Step 2: Fatal events in the community. Step 2 enables calculation of mortality rates. This records the stroke events that result in fatality but do not reach the health facility. Information about these events is gathered from death certificates or verbal autopsies (module 4). In countries where death certification is not used routinely or is uncertain in validity, verbal autopsies are used to ascertain the cause of death. Module 5 is the data collection from death records undergoing medical autopsies.

Step 3: Nonfatal events in the community. Step 3 provides incidence rates and case fatality. It represents the highest level of complexity in data collection. This involves medically recognizing all the stroke patients who are cared for entirely within the community and are not managed in the hospital at any time during or after the onset of stroke (module 6).

Depending on the availability of resources, layers of information can be built upon the basic framework of these 3 steps, adding detailed surveillance information in the form of modules.

The surveillance strategy and characteristics of each study were scrutinized and further divided to fit the guidelines proposed in the form of these 3 fundamental STEPS and various submodules of the WHO STEPS stroke surveillance protocol. Even if the study

was not based on the STEPS protocol, we used it as a template by which the methodology of each study was compared (table e-1 and table 1).

Statistical methods. Summary incidence rates (and corresponding 95% confidence intervals) were calculated by pooling the study-specific estimates using a random-effects model that included between-study heterogeneity (parallel analyses used fixed-effect models). Heterogeneity of findings across studies was primarily assessed by standard χ^2 tests and the I^2 statistic.¹² Additionally, further detailed assessments of heterogeneity were carried out by comparing results from studies subgrouped according to different study characteristics using meta-regression technique, and by performing sensitivity analyses to evaluate the influences of selected study or characteristics on the overall results. All statistical tests were 2-sided and used a significance level of $p < 0.05$. All analyses were performed using Stata release 11 (StataCorp, College Station, TX).

RESULTS Study selection and characteristics. The initial search yielded 76 articles, the titles and abstracts of which were reviewed, out of which 30 fit the inclusion criteria and were subjected to further review. After application of inclusion and exclusion criteria to the full texts of these

Figure 2 Descriptive protocol of an ideal stroke surveillance strategy adapted from WHO STEPwise approach to stroke surveillance

ER = emergency room; GP = general practitioner; NIHSS = NIH Stroke Scale.

articles, we included a total of 7 articles in this review (figure 1). Their summary characteristics are provided in table e-1 and table 1. According to the WHO regions, within the LMI countries, surveillance of stroke has been undertaken (and published) in Sri Lanka and India (South Asia)^{13,14}; Ukraine, Georgia, and Bulgaria (Europe)^{15–17}; Brazil (South America)¹⁸; Mongolia (Western Pacific)¹³; Nigeria (West Africa)¹³; and Tanzania (East Africa).¹⁹ The majority of the included studies were conducted primarily in urban populations, with only 2 studies (Powles et al.¹⁷ [Bulgaria] and Walker et al.¹⁹ [Tanzania]) that included both urban and rural participants. Most studies restricted their study population to the 45–85 years age group, in which most strokes typically occur (population at risk).

Comparison with WHO STEPS surveillance protocol. We applied the 3-step WHO STEPwise approach

(figure 2) to optimize stroke surveillance for LMI countries to individual studies (table e-1 and table 1). All studies covered at least one part of the STEPS approach, but beyond that adherence to the STEPS protocol was patchy. Dalal et al.¹⁴ based in urban India was the only study that incorporated the STEPS stroke surveillance protocol exclusively as its operational protocol. All studies established surveillance sites at local hospitals. Although patient core data, functional assessment, and medical treatment were recorded comprehensively, the majority of these studies were generally limited by resources or availability of neuroimaging to adequately classify and validate stroke subtypes. CT scanning rates varied substantially in these studies (ranging from 0% to 100%). Minelli et al.¹⁸ was the only study that performed CT scan on all of its recruited participants. By contrast, Aho et al.¹³ state that they did not have any

Figure 3 Features of studies included in the review

Study	LMI country	Events in hospital							Fatal events in the community			Non-fatal events in the community		
		First time stroke	Imaging to confirm stroke	Type of stroke	Recurrent stroke	10 day vital status	1 month case fatality	Death certificates	Verbal autopsy	Medical autopsy	6 month mortality	Disability assessment	Barthel Index	mRS
Aho et al	Nigeria	●	○	●	●	●	●	●	○	●	●	●	○	○
	Mongolia	●	○	●	●	●	●	●	○	●	●	●	○	○
	India	●	○	●	●	●	●	●	○	●	●	●	○	○
	Sri Lanka	●	○	●	●	●	●	●	○	●	●	●	○	○
Dalal et al	India	●	●	●	○	○	●	●	○	○	○	●	○	●
Mihalka et al	Ukraine	●	●	●	○	●	●	●	○	●	○	○	○	○
Tsiskaridze et al	Georgia	●	●	●	○	●	●	●	●	○	○	○	○	○
Powles et al	Bulgaria	●	●	●	○	●	●	●	○	●	○	○	○	○
Minelli et al	Brazil	●	●	●	○	●	●	●	○	○	●	○	●	○
Walker et al	Tanzania	●	●	●	●	●	●	●	●	●	●	○	○	○

- Relevant data collected in the study
- Relevant data not collected in the study

LMI = low and middle income; mRS = modified Rankin Scale.

access to CT scan facilities to enroll imaging-confirmed strokes at any of the participating centers due to unavailability (table e-1 and figure 3).

All studies recorded 1-month case fatality data and 3^{13,18,19} followed up patients for 6-month case fatality. While disability assessments were not adequately determined in the majority of studies, Minelli et al.¹⁸ and Dalal et al.¹⁴ were notable exceptions; they used Barthel scale for disease prognosis and modified Rankin Scale (mRS) score at day 28 to predict long-term disability, respectively. Death certification and autopsy records were screened efficiently for mortality data in all studies. WHO-validated verbal autopsy method to ascertain fatal outcomes in LMI settings were employed by 2 studies.^{16,19} The most complex level of data collection for nonfatal events in the community remained a challenge in all included studies, although efforts were taken to contact local general practitioners and community health workers in some studies. The door-to-door survey method, typically aiming to provide prevalence data of stroke, was used by Tsiskaridze et al.¹⁶ Walker et al.¹⁹ aimed to raise awareness of stroke and potential preventative and treatment measures in the general population in order to enhance overall stroke recognition.

Burden of stroke in LMI countries. In aggregate, included studies in this review involved 3,113 incident stroke events collected over 5,240,923 person-years from 1,711,372 participants. While all 7 studies

investigated the incidence of first-ever stroke (figure 4; figure e-1), only 2^{13,19} provided additional data on recurrent stroke events. Based on WHO global regions, age-adjusted stroke incidence rates are presented in figure 4 and table 1. Only 2 studies gathered surveillance data differentiating between urban and rural settings.^{17,19} The age-adjusted incidence rates were approximately 3 times higher in the urban population of Tanzania (315.9 per 100,000 person-years) than the rural population (108.6 per 100,000 person-years). By contrast, in Bulgaria, stroke incidence estimate in the urban residents was almost half (919 per 100,000 person-years) compared to their rural counterpart (1,576 per 100,000 person-years). Combined age-adjusted incidence rate, based on all 9 LMI countries, was 165.8 per 100,000 person-years (figure 4). Upon removal of the estimates from Bulgaria (i.e., the only study based on restricted age bands) in the sensitivity analyses, the age-adjusted incidence rate was reduced to 100.45 per 100,000 person-years (figure e-1). There was evidence of substantial heterogeneity across studies in both main and sensitivity analyses (I^2 estimates >50% and $p < 0.001$). In the subsequent subgroup analyses, conducted to explain the observed overall heterogeneity, there were important differences in the estimates across several study-level characteristics. For instance, studies published after 2005 (i.e., year when WHO STEPS was formally operationalized), studies that had lower hospital admissions, and those that had lower case fatality and higher CT/

Figure 4 Age-adjusted incidence rates (95% confidence interval) for incident stroke in low- and middle-income countries, based on available studies

From random-effects meta-analyses. RM=Rural male; RF=Rural female; UM=Urban male; UF=Urban female; U=Urban; R=Rural

Random-effects meta-analyses of age-adjusted incidence rates in low- and middle-income countries included in this review. Studies included in this meta-analysis collected stroke incidence data on all ages in their respective populations except for Bulgaria and Mumbai, which were based on restricted age bands. Age bands for each study: Ukraine: 0-44, 45-54, 55-64, 65-74, 75-84, ≥ 85 ; Georgia: 0-44, 45-54, 55-64, 65-74, 75-84, ≥ 85 ; Bulgaria: 45-54, 55-64, 65-74, 75-84; Brazil: <45 , 45-54, 55-64, 65-74, ≥ 75 ; India (Rohtak): ≤ 44 , 45-54, 55-64, 65-74, ≥ 75 ; India (Mumbai): 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85- >94 ; Sri Lanka: ≤ 44 , 45-54, 55-64, 65-74, ≥ 75 ; Mongolia: ≤ 44 , 45-54, 55-64, 65-74, ≥ 75 ; Tanzania: 0-44, 45-54, 55-64, 65-74, 75-84, ≥ 85 ; Nigeria: ≤ 44 , 45-54, 55-64, 65-74, ≥ 75 . CI = confidence interval.

MRI autopsy proportions tended to have significantly higher stroke incidence rates (metaregression $p < 0.05$ for all; figure e-2).

DISCUSSION This comparative review is the first attempt to systematically compare the methodology used across published primary reports of stroke surveillance studies. In context of the WHO STEPS stroke surveillance protocol as a benchmark approach especially in the LMI countries revealed a lack of standardized approach toward stroke surveillance. Additionally, evidence from these population-based surveillance studies showed that the apparent discordance in the burden of incident stroke events across the LMI countries can be due to inherent differences in the population groups involved and potentially to the large variations in the underlying methods used. For instance, the age-adjusted rate of new stroke events in Bulgaria was much higher

than that of other countries. It is possible that this resulted from an apparent “hot pursuit” nature of this study that adopted a more vigorous approach and restricted age bands.

Furthermore, our subgroup analyses provide further support toward the potential role of heterogeneity between the studies that might affect the true disease burden estimates of stroke in the LMI countries. It is likely that the burden of stroke is underestimated in the LMI countries, as there have been few large-scale systematic efforts to monitor the actual occurrence of cerebrovascular diseases in these settings. Limited numbers of nationally representative surveys, lack of adherence to standardized optimum protocols, and limited disability information in the LMI countries have meant that conventional disease burden estimates have had to be derived from statistical modeling studies.^{20,21} Ability to accurately quantify the disease and causative risk factors

for stroke will make the development of locally appropriate prevention and treatment strategies easier to shape and the data collected more reliable.

In our review, most primary LMI countries studies only recorded hospital morbidity and mortality of acute stroke, which makes accurate estimation of the burden of disease at a population level difficult. While hospital-based data collection has shown to be feasible and easy to accrue in the LMI nations,⁷ their interpretation can only be used to characterize patients who were admitted to a specific health facility. Hospitalization rates in LMI countries differ due to access barriers and hospital patient samples may not be representative of the population. These rates vary among urban and rural populations, and between countries, making meaningful comparisons difficult to achieve. Hospital-based studies are also more likely to underdiagnose minor strokes. Linking up hospital events to death certificates in order to record cause-specific mortality is another challenge in LMI countries, as the majority of these countries do not have comprehensive certification of death. The data that are available are difficult to use for cross-national comparison since they often use different methods, varying criteria, and time periods.

Disability remains an important attribute resulting from cerebrovascular disease and has enormous economic implications.²² DALYs provide a useful indication of economic and social burden of the disease as this records both morbidity and mortality.^{23–25} Several measures of disability assessment such as in-hospital disability scales (NIH Stroke Scale and Glasgow Coma Scale) and postacute event disability scales (Barthel Index and mRS) have been formulated which provide disability scales encompassing the time of stroke onset and admission to the health care facility until the time of discharge and long-term disability ascertainment. In future studies, attention should be paid to inclusion of DALYs along with mortality and case fatality estimates.

It is well established that the rising burden of stroke in the LMI countries poses a high economic burden on the society as the event is typically followed by an array of expensive diagnostic measures, long hospital stays, and often requires long-term rehabilitation.²⁶ One method to estimate this associated financial burden is through cost of illness studies (COI).²⁷ COI use prevalence and incidence data from surveillance studies to compose models in estimating costs. An earlier review estimated economic losses in 23 LMI countries to be approximately \$84 billion in economic output in 2006–2015 from coronary disease, stroke, and diabetes combined.²⁸ However, no such study is currently available to quantify economic losses attributed to stroke alone. Therefore, accurate cerebrovascular disease burden estimation (a prerequisite for reliable economic assessment) would help inform health policy in the LMI countries.

Strengths of our study include its systematic approach. Additionally, we relied exclusively on “nationally conducted” population-based surveillance studies that use “reported” (rather than “estimated” national data from the global burden of disease study) data that give a more indubitable reflection of the actual burden of stroke in LMI countries. We have included studies that conducted national surveillances of stroke in their representative population subsets that varied considerably in methodology, outcomes ascertained, and population settings. Some limitations merit careful consideration: as countries have gone through economic metamorphoses in the past decades, e.g., Russia, there may be some discrepancies between their current economic status and their status at the time the study was conducted. In order to minimize the disconformities, we adhered to the categorization of the economic status of countries according to the 2006–2010 World Bank classification.¹⁰ In our study, comparison has been made with the WHO STEPS stroke surveillance protocol as an operational guideline to collect stroke surveillance data in the LMI settings; however, there are other processes such as census data, from which burden of stroke can also be ascertained that could have not been sufficiently covered by the search strategy implemented in our review and limited the scope of our findings.

This study systematically evaluates the methodology protocols adopted for stroke surveillances and compared the available surveillance studies to generate an overall comparative scenario. Available literature generally indicates lack of standardized surveillance systems in LMI countries. Although primary surveillance studies have been conducted in most global regions, they remain difficult to compare across nations or regions due to heterogeneity in underlying methodologies. If a more standardized benchmark approach for stroke surveillance was adopted, better estimates of the current and future burden of stroke would become available, which could inform future health policy. As resources are limited in LMI countries, it might be considered to focus on establishing sustainable systems to gather reliable and accurate data on stroke mortality and risk factors shared by other noncommunicable diseases. Wider application of comprehensive and practical, yet feasible surveillance protocols such as WHO STEPS stroke surveillance protocol could potentially maximize available local resources and produce comparable data to help shape effective stroke reduction programs and policies in resource-poor settings.

AUTHOR CONTRIBUTIONS

Ayesha Sajjad had the idea for the study. She did the literature searches and data extraction and drafted the manuscript. She is the guarantor of this study. Jonathon Mant revised the manuscript and was involved in the conception and design of the study. Rajiv Chowdhury revised the manuscript and did the analysis. Janine Felix revised the manuscript and contributed to the scientific content of the paper. Mohammad Arfan

Ikram revised the manuscript and contributed to the scientific content of the paper. Shanthi Mendis revised the manuscript and contributed to the scientific content of the paper. Henning Tiemeier revised the manuscript and contributed to the scientific content of the paper. Oscar H. Franco was involved in the design of the study and contributed to the critical revision of the manuscript before publication.

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