Risk factors for 30-day in-hospital mortality for in-patient with stroke in sub-Saharan Africa: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction While individual studies have reported on in-hospital stroke mortality rates in sub-Saharan Africa (SSA), the estimates are highly variable and inconclusive, buttressing the need for precise and reliable estimations. To overcome these inconsistencies, a well-structured systematic review and meta-analytical models are necessary. However, to the best of our knowledge, there is no published systematic review and meta-analysis on risk factors for 30-day mortality for in-hospital patients with stroke in SSA.

Method and analysis We will include all retrospective and prospective facility-based observational studies reporting on the incidence and/or risk factors for in-hospital stroke mortality in SSA. Electronic databases such as PubMed, Google scholar and Africa Journal Online (AJOL) will be searched for potentially relevant studies on in-hospital stroke mortality and risk factors in SSA. The search will be limited to studies conducted from January 1990 to December 2020. Two independent authors will screen titles and abstract to find studies that meet the prespecified eligibility criteria for inclusion in the review. The incidence of 30-day in hospital stroke mortality will be pooled. Meta-regression will be used to assess the factors associated with in-hospital stroke mortality in SSA. If possible, subgroup analysis will be performed based on subregion, publication year and study design, and quality score to determine possible source of heterogeneity. If possible, a sensitivity analysis will be performed to determine the robustness of the estimates obtained from the meta-analysis.

Ethics and dissemination Ethical approval is not required as this is a secondary research and will use reported data in scientific literature. A full manuscript will be submitted to a reputable peer-review journal for publication.

INTRODUCTION

Stroke is a major cause of death and injury, and poststroke treatment costs are a significant economic burden worldwide. 1, 2 High-income countries have seen rapid and significant reduction in stroke incidence, and long-term survival as a result of expanded use of preventive therapies and significant decreases in premorbid risk factors. 3–5 Nonetheless, most sub-Saharan Africa countries (SSA) are unable to say same. 6

The incidence of stroke is rising in low-income and middle-income countries (LMICs) in SSA countries, and research has shown that between 2002 and 2020, stroke mortality in SSA was tripled. 7, 8 For instance, community-based SSA studies indicate that 5%–10% of all deaths are caused by stroke, partially due to poor health system and rising rates of hypertension. 9, 10 In addition, LMICs account for 85% of all stroke deaths, as well as 87% of total losses due to stroke measured in disability-adjusted life-years which total 72 million per year worldwide. 11

In SSA, epidemiological studies have shown that in-hospital stroke mortality rates varied from 18% in Ethiopia to 43% in Ghana. 8, 12 SSA countries have insufficient resources for acute medical and rehabilitation care for stroke, therefore, comprehensive and
pragmatic preventive efforts directed at risk factors are
of utmost importance to curtail the burden.13 In the
same vein, early intervention on in-patient with stroke
identified with a high risk of mortality may increase the
survival rate.14 It is, therefore, imperative to identify risk
factors for 30-day in-hospital mortality for in-patients
with stroke in SSA. The proportion of patients who die
within 30 days from the time of admission to the time
of death among all patients hospitalised with stroke is
referred to as 30-day in-hospital stroke mortality.

While individual studies have reported on in-hospital
stroke mortality rates in SSA, the estimates are highly
variable and inconclusive, buttressing the need for
precise and reliable estimations. To overcome these
inconsistencies, a well-structured systematic review and
meta-analytical models are necessary. However, to the
best of our knowledge, there is no published system-
atic review and meta-analysis on risk factors for 30-day
day mortality for in-hospital patients with stroke in SSA.

With this in mind, the study seeks to systematically
review empirical evidence on risk factors for 30-day
day mortality for in-hospital patients with stroke in SSA.
It is important for healthcare providers to learn about
the risk factors associated with in-hospital stroke 30-day
day mortality in order to prepare for future patient care as
well as to optimise hospital staffing and necessary skills
in SSA.

Review questions
► What is the incidence for 30-day mortality rates for
in-patients with stroke in SSA?
► What are the risk factors for 30-day mortality rates for
in-patients with stroke in SSA?

Objectives
► Primary objective: To determine the incidence for
30-day mortality rates for in-patients with stroke in SSA.
► Secondary objective: To assess the risk factors for
30-day mortality for in-patients with stroke in SSA.

METHODS

Patient and public involvement
Patients and/or the public were not involved in the
design, or conduct, or reporting, or dissemination
plans of this research.

Ethics and dissemination
Ethical approval is not required as this is a secondary
research and will use reported data in scientific litera-
ture. A full manuscript will be submitted to a reputable
peer-review journal for publication.

Protocol registration and best practices
This systematic review and meta-analysis will follow strict
adherence to the guidelines of the Preferred Reporting
Items for Systematic Reviews and Meta-Analyses Proto-
cols (PRISMA-P) 15 (online supplemental file 2).

Eligibility

Types of studies
All retrospective and prospective facility-based observa-
tional studies reporting on incidence and/or risk
factors for in-hospital stroke mortality and case fatality in
SSA countries. Also, if any of the countries in SSA have
a public reporting of in-hospital 30-day mortality from
eventual published quality indicators, such outcome will
be included to help contribute to the identification and
understanding of risk factors. Animal studies, reviews,
commentaries, conference papers and letter to the editor
will be excluded.

Types of participants
Studies from SSA countries involving in-hospital patients
with stroke. The review will consider all age groups.

Types of outcome measures
The primary outcome is the in-hospital stroke 30-day
mortality in SSA and secondary outcome is the risk factors
for in-hospital mortality in SSA. However, if any study
reports on out-of-hospital mortality, it will be extracted
and reported separately.

Data source and search strategies
Primary electronic search in English on the incidence
and risk factors for in-hospital stroke case-fatality rate in
SSA will be conducted in MEDLINE via PubMed, Google
Scholar and AJOL. The search will be limited to studies
conducted from January 1990 to December 2020. Table
1 displays the main search term and approaches (online
supplemental file 1). The abstracts of all eligible papers
will then be reviewed and full articles will be accessed
through PubMed, Google Scholar, and AJOL. Reference
lists of papers that fulfil the eligibility requirements of the
study will be reviewed to identify additional studies not
included in our electronic search. To ensure that poten-
tial studies that will be missed by electronic searching are
included, experts will be consulted.

Screening and selecting studies
Two authors will screen titles and abstract independently
to find studies that meet the pre-specified eligibility
criteria for inclusion in the review. Full texts of all poten-
tially relevant studies will be accessed and assessed in
detail in a similar manner. A third reviewer will be avail-
able to resolve any discrepancies between the two inde-
dependent assessors. A screening guide will be used to
ensure that independent reviewers apply the selection
criteria reliably. Authors whose full-text documents are
not available via a variety of internet-based sources will be
contacted directly through the corresponding authors
to provide them to help make the final decision about
inclusion. If vital information needed to make the inclu-
sion decision is not obtained, the article will be excluded.
Mendeley reference manager will be used to deduplicate
studies.
are linked to or cause 30-day death among all patients hospitalised with stroke. In this study, a risk factor is defined as a set of variables that defined as the proportion or standardised hospital day mortality or death OR case-fatality.

Risk of bias and quality assessment
The Newcastle-Ottawa Quality Assessment tool adapted for cross-sectional studies will be used to assess the quality of the retrieved studies. The purpose of the assessment will be to determine the internal and external validity of the studies and to minimise risk of bias.

Data synthesis
Extracted data will be imported into Stata (V.16; Stata) from Microsoft excel 2013 for all analyses. The PRISMA flow chart (figure 1) will be used to summarised the selection process. When considerable homogeneity exists among the studies, the incidence of 30-day in-hospital stroke mortality in SSA will be pooled. This will be visually represented using the forest plot. The presence of heterogeneity among studies will be quantified by estimating variance using both Cochrane’s Q statistics and the I² statistics. The I² takes values between 0% and 100%, and a value of 0% indicates absence of heterogeneity. I² will be interpreted based on Higgins and Thompson classification, percentages of 25%, 50% and 75% will be considered as low, moderate and high heterogeneity, respectively.

Meta-regression will be used to assess the factors associated with in-hospital stroke 30-day mortality in SSA. If possible, subgroup analysis will be performed based on subregion (West Africa vs East Africa vs Southern Africa), publication year and study design (prospective vs retrospective), and quality score (low risk vs moderate risk vs high risk of bias) to determine possible source of heterogeneity.

If possible, a sensitivity analysis will be performed to determine the robustness of the estimates obtained from the meta-analysis. We will do sensitivity analysis on the quality of the studies included in the systematic review and meta-analysis, that is, studies with low quality score will initially be excluded to check their direction and impact on the overall (pooled) estimate and finally leave one out sensitivity analysis will be performed. Publication bias will be checked by the funnel plot and Egger’s test. Furthermore, trim and fill analysis will be used to adjust for publication bias using Duval and Tweedie’s method in case publication bias exist.

In event where meta-analysis is not possible due to considerable heterogeneity and low-quality studies, narrative systematic review will be presented.

Data extraction and management
Two independent assessors will extract the data from the eligible published articles using a pretested and standardised excel spreadsheet. Data such as the first author’s name, year of publication, study country, study design, sample size, mortality rate, risk factors for in-hospital stroke case-fatality, severity measure, type of stroke as well as the demographic information (ie, sex, age, etc) will be extracted. Missing data will be addressed by contacting the corresponding author for insufficient or unclear data. If possible, corresponding authors will be asked to provide us with the raw data to extract the missing data.

Outcome and operationalisation
A 30-day in-hospital stroke mortality is operationally defined as the proportion or standardised hospital mortality based on the number of patients who die within 30 days from the time of admission to the time of death among all patients hospitalised with stroke. In this study, a risk factor is defined as a set of variables that are linked to or cause 30-day death in hospitalised stroke patients in SSA. For example, patient-related factors that may increase mortality in stroke include poor control of major risk factors to stroke such as hypertension, obesity, smoking, heart disease and diabetes. Hospital-related factors such as availability of a stroke unit, availability of an intensive care unit and the capacities of the emergency unit. Treatment delays (ie, waiting times, time to get to hospital from onset of symptoms). The severity of stroke and length of stay may also influence 30-day mortality, etc.

### Table 1

<table>
<thead>
<tr>
<th>Search #</th>
<th>Search term</th>
</tr>
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<tbody>
<tr>
<td>1)</td>
<td>In-hospital OR in-patient</td>
</tr>
<tr>
<td>2)</td>
<td>Stroke OR cerebrovascular accident OR CVA OR cerebral infarction OR Ischemic stroke OR Lacunar stroke OR cerebral hemorrhage OR haemorrhagic stroke</td>
</tr>
<tr>
<td>3)</td>
<td>1 AND 2</td>
</tr>
<tr>
<td>4)</td>
<td>Mortality OR 30-day mortality OR death OR case-fatality</td>
</tr>
<tr>
<td>5)</td>
<td>3 AND 4</td>
</tr>
<tr>
<td>6)</td>
<td>risk factors OR associated factors</td>
</tr>
<tr>
<td>7)</td>
<td>5 OR 6</td>
</tr>
<tr>
<td>8)</td>
<td>sub-Saharan Africa</td>
</tr>
<tr>
<td>9)</td>
<td>Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cameroon OR Cape Verde OR Central African Republic OR Chad OR Comoros OR Congo OR Cote d’Ivoire OR Djibouti OR Equatorial Guinea OR Ethiopia OR Gabon OR The Gambia OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR Sao Tome and Principe OR Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR Zaire OR Zambia OR Zimbabwe</td>
</tr>
<tr>
<td>10)</td>
<td>8 OR 9</td>
</tr>
<tr>
<td>11)</td>
<td>Limit to January, 1990-December,2020</td>
</tr>
<tr>
<td>12)</td>
<td>Limit to Humans</td>
</tr>
<tr>
<td>13)</td>
<td>10 AND 11 AND 12</td>
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</tbody>
</table>
Grading the quality of evidence
The quality of evidence for all studies will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group methodology. The following domains will be assessed: risk of bias, consistency, directness, precision, publication bias and additional points. The assessments will be classified into four levels: high, moderate, low or very low. Two independent reviewers will assess the GRADE and disagreement will be resolved through discussion.

Expected key results and discussion
Globally, stroke is the third leading cause of death. The bulk of these deaths from strokes are found in LMICs. In these nations, deaths account for up to 87% of all stroke fatalities. This elevated death toll is much greater in SSA. To the best of the authors’ knowledge, there is no comprehensive systematic review and meta-analysis on in-hospital stroke case fatality exist in SSA. Hence, the primary aim of this review is to determine the incidence of in-hospital stroke 30-day mortality in SSA. Secondary objective is to assess the risk factors for in-hospital stroke mortality in SSA.

Acknowledgements Sincere thanks to Nana Abena Nyamedo Yeboah for critical reading of the manuscript and comments.

Contributors MA conceived the study, drafted the manuscript, critically revised the manuscript for methodological and intellectual content. COY drafted the manuscript, critically revised the manuscript for methodological and intellectual content. LA critically revised the manuscript for methodological and intellectual content. All authors approved the final manuscript. MA is the guarantor of the review.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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