Implementing Stroke Unit Care in Selected Hospitals in Rwanda

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Abstract

Background: The burden of stroke in low-and middle-income countries (LMICs) has risen sharply in recent years and the rate of increase is set to accelerate due to socio-demographic and lifestyle changes related to the industrialization and a rise in many modifiable vascular disease risk factors.

Aims: The first aim was to establish, for countries like Rwanda, how much stroke is a major problem. The second aim was to explore whether the existing stroke services were well prepared. The third aim was to develop and implement a relevant service improvement in Rwanda.

Methods: First, I conducted systematic reviews of the literature on the epidemiology and impact of stroke, and the available stroke services in Africa. Second, I conducted a systematic review of the literature and analyzed the INTERSTROKE study data to identify the stroke key performance indicators (KPIs) that have been described in stroke care and assessed their association with patient outcomes. Finally, I selected the stroke unit care KPIs relevant to Rwandan and other LMIC settings, and used several strategies including site champions, provision of educational materials, feedback on usual care, training hospital staff on stroke KPIs, consensus discussions on service improvement by local staff, and discussions with the hospital directors to promote the implementation of the selected KPIs in two hospitals in Rwanda.

Results: Stroke was found to be common and important in Africa. However, the provision of stroke care was below the recommended standards. After adjustment for case mix and stroke onset-hospital arrival interval, I found a consistent trend of associations between my implementation intervention and improved delivery of stroke KPIs and patient outcomes.

Conclusion: Several common KPIs of stroke unit care can be implemented in hospitals in Rwanda. However, there are some major challenges that need to be addressed for optimal implementation of stroke unit care.

Chapter abstracts

Chapter 1: Epidemiology and impact of stroke in Africa: a systematic review of the literature

Background: Stroke is the second most common cause of death, and the third most common cause of disability-adjusted life-years (DALYs) worldwide, but there is limited information on the stroke burden in Africa.

Aim: To describe the epidemiology (incidence, prevalence, mortality, one month-case-fatality) and impact (disability, quality of life, and cost) of stroke in Africa.

Methods: I performed a systematic review which included full-text manuscripts published between January 1980 and June 2017 that described the epidemiology or impact of stroke. I searched Medline, Embase, PubMed, and African Journals Online (AJOL) databases, and screened references from bibliographies. There was no language restriction. To determine the estimates of stroke epidemiology and impact variables in Africa, the overall means with standard deviation (SD) were calculated.

Results: I identified 44 eligible studies among which 21 were hospital based and 23 were community based. The majority (30/44) of the studies were conducted in urban settings. Overall, the crude mean per 100,000 population was 122.4 (SD: 68.1) for the incidence, 539.1 (SD: 381.5) for the prevalence and 84.7 (SD: 30.15) for mortality. The age-adjusted mean per 100,000 population was 162.7 (SD: 117.5) for incidence, 788.3 (SD: 536.7) for the prevalence and 192.7(SD: 155.2) for mortality. The overall mean rate for stroke one-month case fatality was 30.4% (SD: 11.7%). It was also reported that 30.6% of stroke survivors had moderate or severe disability at one-year post stroke, and at 29 months post stroke, the stroke survivors in general had neither poor nor good quality of life (the mean for the health-related quality of life was 71%). The overall mean for the in-hospital care cost was found to be 1971 (SD: 1108) United States Dollars (USDs).

Conclusions: This review provides an overview of the epidemiology and impact of stroke in Africa, despite the paucity of available data. I found that stroke was common and important in Africa. Robust high-quality studies are needed to help policy makers and health care professionals to control the stroke burden in Africa. Appropriate preventive and therapeutic measures should be promoted to decrease the incidence of stroke, improve the outcomes, and maintain the survivors' quality of life in Africa.

Chapter 2: Stroke care in Africa: a systematic review of the literature

Background: Appropriate systems of stroke care are important to manage the increasing death and disability associated with stroke in Africa. Information on existing stroke services in African countries is limited.

Aim: To describe the status of stroke care in Africa.

Methods: I undertook a systematic search of the published literature to identify recent (January 1st, 2006-June 20th, 2017) publications that described stroke care in any African country.

Results: My initial search yielded 838 potential papers, of which 38 publications were eligible representing 14/54 African countries. Across the publications included for my review, the proportion of stroke patients reported to arrive at hospital within three hours from stroke onset varied between 10─43%. The median time interval between stroke onset and hospital admission was 31 hours. The reported proportions of stroke patients who received brain imaging within three hours of stroke onset varied between 0% and 13%, and the overall proportion of patients who received brain imaging varied between 13% and 36%. Only twenty-three stroke units in Africa were reported, and two studies indicated that stroke unit admission was associated with a decrease in in-patient case fatality rate of 17-30%. Access to in- and out-patient rehabilitation services was reported to be very low. Poor awareness of stroke signs and symptoms, shortages of medical transportation, health care personnel, and stroke units, and the high cost of brain imaging, thrombolysis, and outpatient physiotherapy rehabilitation services were reported as major barriers to providing best-practice stroke care in Africa.

Conclusions: This review provided an overview of stroke care in Africa and highlighted the paucity of available data. Stroke care in Africa usually fell below the recommended standards with variations across countries and settings. Combined efforts from policy makers and health care professionals in Africa are needed to improve, and ensure access to organised stroke care in as many settings as possible. Mechanisms to routinely monitor usual care (i.e. registries or audits) are also needed to inform policy and practice.

Chapter 3: Key performance indicators of quality stroke care and their association with patient outcomes: a systematic review of the literature and meta-analysis

Background: Translating research evidence into clinical practice often uses key performance indicators (KPIs) to monitor quality of care. However, information on KPIs for stroke care is limited.

Aims: To identify the stroke KPIs used in large registries, and to estimate their association with patient outcomes.

Methods: I sought publications of recent (January 2000-May 2017) national or regional stroke registers reporting the association of KPIs with patient outcome (adjusting for age and stroke severity). I searched Ovid Medline, Embase and PubMed and screened references from bibliographies. I used an inverse variance random effects meta-analysis to estimate associations (odds ratio; 95% Confidence Interval) with death or poor outcome (death or disability) at the end of follow up.

Results: I identified 30 studies (324,409 patients) eligible for the qualitative review. Among these, only 22 were eligible for the meta-analysis. The commonest KPIs were swallowing/nutritional assessment, stroke unit admission, antiplatelet use for ischemic stroke, brain imaging, anticoagulant use for ischemic stroke with atrial fibrillation, lipid management, deep vein thrombosis prophylaxis and early physiotherapy/mobilization. Lower case fatality was associated with swallow/nutritional assessment (OR: 0.78; 0.66-0.92), stroke unit admission (OR: 0.79; 0.72-0.87), antiplatelet use for ischemic stroke (OR: 0.61; 0.50-0.74), anticoagulant use for ischemic stroke with atrial fibrillation (OR: 0.51; 0.43-0.64), lipid management (OR: 0.52; 0.38-0.71), and early physiotherapy or mobilization (OR: 0.78; 0.67-0.91). Reduced poor outcome (death or disability) was associated with adherence to swallowing/nutritional assessment (OR: 0.58; 0.43-0.78) and stroke unit admission (OR: 0.83; 0.77-0.89). Adherence to several KPIs appeared to have an additive benefit.

Conclusions: I found that the most frequently reported KPIs for stroke care were swallowing assessment, stroke unit admission, antiplatelets for ischemic stroke, brain imaging, anticoagulants for ischemic stroke with atrial fibrillation, lipid management, deep vein thrombosis (DVT) prophylaxis, and early mobilization. Adherence to common KPIs was consistently associated with a lower risk of death or disability after stroke. Policy makers and health care professionals should implement and monitor those KPIs supported by good evidence.

Chapter 4: Stroke services in African and other low and middle-income countries in an international study

Background: Stroke key performance indicators (KPIs) have been used to monitor service improvement in high-income countries (HICs), but information regarding their utility in low and middle-income countries (LMICs) is limited.

Aims: To explore the association of recording of stroke KPIs with patient outcomes in LMICs, generally and African settings in particular.

Methods: I analysed data collected from the INTERSTROKE case control study (conducted between January 2007 and August 2015). I had full data for 12343 participants and analysed 9766 from LMICs. I calculated the odds ratios (OR) with 95% confidence intervals (CI) for the associations of KPIs with 30-day patient outcomes using univariate and multivariate regression analyses to account for patient casemix. I also used the Bonferroni correction method to control the familywise error rate and considered 0.006 as the p-value of significance.

Results: In LMICs, availability of a stroke unit (OR: 0.71, 0.60-0.83; p<0.0001) or a stroke specialist (OR: 0.74, 0.64-0.85; p<0.0001), receiving antiplatelet therapy for ischemic stroke (OR: 0.69, 0.56-0.85; p=0.001), and the availability of acute (OR: 0.70, 0.57-0.87; p=0.001) and post-discharge (OR: 0.41, 0.34-0.48; p<0.0001) rehabilitation were independently associated with lower risk for 30-day case fatality. Early brain imaging (OR: 0.71, 0.58-0.88; p=0.001) and stroke unit availability (OR: 0.62, 0.55-0.71; p<0.0001) were independently associated with lower risk of death or severe disability at 30 days. There was a dose dependent relationship of number of KPIs recorded with a better outcome. For the African countries alone, I had no enough evidence to show an association between any of the stroke KPIs investigated and patient outcomes.

Conclusions: In LMICs, achieving several common KPIs was associated with a statistically significant reduction in post-stroke death or disability. Policy makers and health care professionals should be encouraged to implement the commonly established stroke KPIs even in settings with limited resources.

Chapter 5: Implementing stroke unit care in Rwanda: a two-hospital before and after implementation trial

Background: Stroke unit care has become established as the central component of a modern stroke service to improve patient outcomes, but it requires several resources. This raises the question of whether stroke unit care is feasible and applicable to low and middle-income country settings.

Aims: To explore the feasibility and effectiveness of implementing stroke unit care in selected hospitals in Rwanda.

Methods: I used a before and after implementation trial design. The clinical intervention consisted of 11 key stroke unit care elements that were identified from the results of chapters three and four, the World Stroke Organisation (WSO) recommendations and the Rwandan clinical guidelines. The implementation intervention consisted of identification of site champions, provision of educational materials, face-to-face educational seminar (including feedback on usual care, training on stroke KPIs and local consensus discussions), and discussions with the study hospital directors.

Results: Overall, after case mix adjustment for stroke severity (using six simple variables), stroke type and stroke onset-hospital arrival interval, I found a consistent trend of associations between the intervention and an increase in participants who received the KPIs investigated and an increase in better patient outcomes. However, the results were statistically significant for only the use of standardized assessment tools (OR: 2.98, 1.36-6.51; p=0.006), swallowing assessment recorded (OR: 5.73, 2.08-15.74; p=0.001), mobilization recorded (OR: 2.30, 1.16-4.56; p=0.017) and multidisciplinary team meetings recorded (OR: 9.04, 2.74-29.86; p<0.0001). Survival in hospital (OR: 2.97, 1.25-7.05; p=0.014) and at three months post stroke (OR: 2.30, 1.10-4.78; p=0.026) significantly improved.

Conclusions: Several common KPIs for stroke unit care can be implemented in two selected hospitals in Rwanda although there were limited resources, and some important KPIs such as geographic stroke unit and thrombolysis could not be implemented. The data also suggested that there may be improved patient outcomes. There is a need for combined efforts to continue improving the implementation of stroke KPIs including those that are not yet initiated like a geographic stroke unit.

Chapter 6: Final discussion

In this final chapter, I aim to discuss to what extent the aims of the thesis have been achieved, the contributions made by this thesis and future work.

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List of publications and presentations

Parts of this work have been published in scientific journals, on which I am first author. This thesis contains extracts of the following:

- '***Association between patient outcomes and key performance indicators of stroke care quality: a systematic review and meta-analysis'***, published in the October 2017 issue of European Stroke Journal (Urimubenshi G, Langhorne P, Cadilhac DA, Kagwiza NJ, Wu O).
- '***Stroke care in Africa: A systematic review of the literature'***, published in the April 2018 issue of International Journal of Stroke (Urimubenshi G, Cadilhac DA, Kagwiza NJ, Wu O, Langhorne P).

Also, parts of this work have been presented in scientific conferences, on which I am first author:

- '***Key performance indicators of quality stroke care and their association with patient outcomes: a systematic literature review'***, presented as '**poster**' during the 3rd European Stroke Organization Conference (ESOC), Prague, Czech Republic, May 2017 (Urimubenshi G, Langhorne P, Cadilhac DA). The abstract has been published in the May 2017 issue of European Stroke Journal.
- '***Association between stroke care key performance indicators and patient outcomes in low and middle-income countries in the INTERSTROKE study'***, presented as '**oral presentation'** during the 11th World Stroke Organization Conference (WSOC), Montreal, Canada, October 2018 (Urimubenshi G, Langhorne P, O'Donnell MJ, Chin SL, Yusuf S, on behalf of the INTERSTROKE investigators). The abstract has been published in the October 2018 issue of International Journal of Stroke.
- '***Experience from a stroke unit implementation project'***, presented as '**invited speaker**' during the 11th WSOC, Montreal, Canada, October 2018 (Urimubenshi G).
- ***Implementation of stroke unit care in low income countries – tales from Rwanda'***, presented as '**invited speaker'** during the 5th ESOC, Milan, Italy, May 2019 (Urimubenshi G).

I made editorial changes of the publications for inclusion in this thesis. The publications can be found in the appendix 6.1.

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I thank Dr Jackie Bosch and the whole team for the Organized Stroke Care Across Income Levels (OSCAIL) study for advising and supporting me to efficiently carry out the research contained in this thesis. The generosity of the research participants in accepting to take part in my study was a constant reminder of my purpose and duty as a researcher to identify the appropriate strategies to respond to the growing burden of stroke in LMICs.

Finally, I would like to thank the University of Glasgow, the Government of Rwanda, and the Population Health Research Institute at the McMaster University for funding my doctoral training and the research contained in this thesis.

Gerard Urimubenshi

Author’s declaration

I declare that this thesis was written by myself, that the work contained herein is my own except where explicitly stated otherwise in the text, and that this work has not been submitted for any other degree or processional qualification except as specified.

List of abbreviations

ADLs	Activities of Daily Living
AF	Atrial Fibrillation
AJOL	African Journals Online
CCI	Charlson Comorbidity Index
CFR	Case Fatality Rate
CHUB	"Centre Hospitalier Universitaire de Butare"
CHUK	"Centre Hospitalier Universitaire de Kigali"
CI	Confidence Interval
CNS	Canadian Neurological Scale
CT	Computerized Tomography
DALY	Disability-Adjusted Life-Year
DVT	Deep Vein Thrombosis
ESO	European Stroke Organization
FIM	Functional Independence Measure
GBD	Global Burden of Disease
GCS	Glasgow Coma Scale
HIC	High-Income Country
HR	Hazard Ratio
HRQOLISP	Health Related Quality of Life in Stroke Patients
ICH	Intracerebral Hemorrhage
IS	Ischemic Stroke
KPI	Key Performance Indicator
LMICs	Low and Middle-Income Countries
LoS	Length of hospital Stay
MDT	Multi-Disciplinary Team
MRI	Magnetic Resonance Imaging
mRS	modified Rankin Scale
NCDs	Non-Communicable Diseases
NEWSQOL	Newcastle Stroke-specific Quality of Life Measure
NIHSS	National Institutes for Health Stroke Scale
OCSP	Oxfordshire Community Stroke Project

OR	Odds Ratio
OSCAIL	Organized Stroke Care Across Income Levels
OT	Occupational Therapy
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PT	Physical Therapy
Q1	First quartile
Q3	Third quartile
QoL	Quality of Life
RCT	Randomized Controlled Trial
RR	Rate Ratio
SAH	Sub-Arachnoid Haemorrhage
SD	Standard Deviation
SSS	Scandinavian Stroke Scale
SSV	Six Simple Variables
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
USD	United States Dollar
WHO	World Health Organization
WSO	World Stroke Organization

0. General introduction

Stroke is the second most common cause of death (Lozano et al., 2010), and the third most common cause of disability-adjusted life-years (DALYs) lost worldwide (Murray et al., 2012). In contrast to high income countries (HICs) where stroke mortality rates have declined, the burden of stroke in developing countries has risen in recent years and is expected to accelerate (Feigin et al., 2014). Eighty-six percent of all stroke deaths around the world take place in African and other low and middle-income countries (LMICs) (Feigin, 2005). Further, African and other LMICs account for over 87% DALYs lost from stroke, which is about seven times the DALYs lost in HICs (Johnston et al., 2009). In the absence of significant international public health responses, projections based on the current trends, incidence velocity, risk factor prevalence, population-attributable risks, and relative risk for risk factors, indicate that by 2030, stroke will be the first leading cause of death in middle-income countries and the third in low-income countries, especially in Africa (Owalabi et al., 2015).

Many African countries are undergoing progression of the epidemiological transition driven by socio-demographic and lifestyle changes, related to unchecked industrialisation, and a rise in many modifiable, lifestyle-related vascular disease risk factors (Kabudula et al., 2017). These include smoking, harmful use of alcohol, physical inactivity and unhealthy diets resulting in an increased prevalence of obesity and hypertension, precursors for heart disease, diabetes and stroke (Connor et al., 2007; Owolabi et al. 2014). Consequently, the burden of non-communicable diseases (NCDs) in Africa is growing (Owolabi et al. 2014). A systematic review (Owolabi et al., 2015) of community-based studies revealed an age-standardised annual stroke incidence rate of up to 316 per 100,000 population, and age-standardised prevalence rates of up to 981 per 100,000 in Africa.

Despite the available evidence regarding the burden of stroke in Africa, health systems in many African countries are characterised by geographical and financial inaccessibility, rapid turnover of people in key positions, lack of continuity in policy, lack of resources, poor management of available resources and poor implementation (Sambo, 2012). Specifically, the lack of functional stroke units, neurologists, health workers, cranial computed tomography (CT) scans, magnetic resonance imaging (MRI) and echo-doppler machines, among many others, has negatively affected stroke outcomes (Chin, 2012). Additionally, the high cost of medical care in a relatively low-income African society without universal health care coverage

could have contributed to high stroke fatalities (Johnston et al., 2009). Moreover, some patients with stroke in Africa prefer to patronise traditional healers because they still believe that stroke is related to bad spiritual forces (Mapoure et al., 2014).

It is recommended that appropriate systems of stroke care be established in Africa and other LMIC regions to control the increasing death and disability associated with stroke (Feigin et al., 2009; Langhorne et al., 2012). Stroke units can provide one of the most effective and generally applicable interventions to reduce the risk of death and disability for patients admitted to hospital after stroke. A stroke unit is a complex intervention that entails a combination of medical and rehabilitation interventions that are delivered by a multidisciplinary team of stroke specialists who work in a focussed and coordinated way to provide care for patients with stroke in hospital (Stroke Unit Trialists' Collaboration; 2013).

Stroke units have become established as the central component of a modern stroke service (Langhorne and Rudd, 2009). However, since stroke unit implementation requires a range of health professional resources, co-location of beds and clinical leadership, most service developments have taken place in high income countries (Langhorne et al., 2012). This raises the question of whether stroke unit care is feasible and applicable to LMIC settings like Rwanda. My thesis aimed to establish, for countries like Rwanda, how much stroke is a major problem (chapter 1), if services are well prepared (chapter 2), what are the key indicators of successful implementation of stroke unit care (chapters 3-4), and then how to develop and implement a relevant service improvement (chapter 5). The findings and future implications of my thesis are summerized in chapter 6.

Chapter 1: Epidemiology and impact of stroke in Africa: a systematic review of the literature

1.1 Introduction

Globally, about 16 million new cases of stroke and 62 million stroke survivors were estimated in 2005, with deaths from stroke accounting for 9.7% of all global deaths. In the absence of significant international public health responses, this is expected to increase to over 23 million new stroke cases and 7.8 million stroke deaths by 2030 (World Health Organization [WHO], 2004; Strong et al., 2007).

Within HICs, adequate health services and strategies for stroke prevention and care such as smoking cessation, control of hypertension, and acute stroke units appear to have contributed to the decline in stroke incidence, mortality, mortality-to-incidence ratios, and DALYs since 1940 (Whisnant, 1984; Feigin et al., 2014). A systematic review of population-based studies of stroke incidence (Feigin et al., 2009) showed that while there was 42% decrease in incidence in HICs in the previous four decades. However, in African and other LMIC countries, the incidence of stroke is increasing (Feigin et al., 2009).

Between 2002 and 2004, estimates revealed an increasing incidence and prevalence with 8% of new stroke cases and 5% of stroke survivors occurring in Africa (Truelsen, 2010). The Global Burden of Disease (GBD) 2010 data also revealed an increase in age-standardised ischaemic stroke incidence from 1990 to 2010 which ranged between 5.2% (South Africa) and 27.8% (Democratic Republic of Congo) (Owolabi et al., 2015). Overall, in Africa, there was significant mean increase in age-standardised ischaemic stroke incidence of 14.8% between 1990 and 2010. Similarly, the increase in age-standardised haemorrhagic stroke incidence from 1990 to 2010 ranged between 13.0% (Gambia) and 45.7% (Burundi). Overall, in Africa, there was significant mean increase in age-standardised haemorrhagic stroke incidence of 28.7% between 1990 and 2010.

Accurate, up-to-date information on stroke burden is necessary for the development and evaluation of effective and efficient preventative, acute care, and rehabilitation programmes for stroke patients (Owolabi et al., 2015). Information on the current burden of stroke in Africa is however limited. In an attempt to fill the gap of lack of data on stroke burden in developing countries, there have been global reviews of stroke with a few studies of African populations

included (Aho et al., 1980; Feigin et al., 2003; Feigin et al., 2009). For example, a systematic review (Feigin et al., 2003) which was confined to stroke epidemiology included population-based studies only. This criterion refers to the most vigorous design but is challenging for most African countries. Also, only the Medline database was consulted, and papers in English only were considered, and there was no single study from Africa that was eligible for inclusion.

In a subsequent systematic review of 56 population-based studies globally (Feigin et al., 2009), only one African site (Ibadan, Nigeria) was included. The result from this survey may not necessarily reflect the overall burden of stroke in Africa (Adeloye, 2014). The Global GBD collaborators (Krishnamurthi et al., 2013; Feigin et al., 2014), using multi-state models, published data on the burden of stroke and stroke subtype in various countries across the globe but without specific focus on Africa (Owolabi et al., 2015).

Some systematic reviews have been published on the burden of stroke in Africa, but I believe their literature searching methodology may have resulted in them missing some relevant information on stroke in Africa. For example, a meta-analysis by Adeloye (2014) was limited to the prevalence and incidence of stroke in Africa, though with pooled data of uneven quality (Owolabi et al., 2015). Furthermore, this meta-analysis (Adeloye, 2014) searched three databases only (Medline, Embase and Global Health), and I believe that not considering the African Journals Online (AJOL) database could have resulted in missing some important information on stroke in Africa. A systematic review by Owolabi et al. (2015) aimed to examine the burden and epidemiological trends of stroke in Africa but was limited to searching publications indexed in PubMed and AJOL databases only. Additionally, this review was confined to studies published in English while some of the African researchers are more likely to publish in French. A recent meta-analysis (Ezejimofor et al., 2016) on stroke in LMICs in different continents including Africa provided estimates on the prevalence of stroke survivors and secular trends only. This analysis pooled data from uneven quality studies, while data on stroke incidence and stroke-related mortality, disability, quality of life and cost were not included. These are also important for health care planning. This review also divided Africa in two regions including North Africa and Sub-Saharan Africa and combined data from North Africa with those from Middle East.

With this background, and evidence of changing stroke epidemiology and impact (Feigin et al., 2003, Ezejimofor et al., 2016), I aimed to conduct an updated systematic literature review on the epidemiology (incidence, prevalence, mortality, one month-case-fatality) and impact (disability, quality of life, and cost) of stroke in Africa. I hope this review will increase our current knowledge of epidemiology and impact of stroke and inform policy makers and health care professionals about appropriate responses and health system interventions across many African countries.

1.2 Methods

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2015), and I used the following methods:

1.2.1 Search strategy

Studies for this review were identified by searches of Medline, Embase, PubMed, and AJOL databases. There was no language restriction, but the search was limited to full-text manuscripts published from January 1st, 1980 to June 8th, 2017.

I used Medical Subject Headings (MeSH) and all subheading terms including "stroke", "cerebrovascular accident", "cerebrovascular disease", "cerebrovascular disorders", "epidemiology", "burden", "incidence", "mortality", "case fatality", "prevalence", "impact", "disability", "quality of life", "cost", and "Africa". Additional searching was conducted on reference lists of relevant studies to identify publications that could have been omitted in the database searches. For further details of the search strategy, see the Appendix 1.1.

1.2.2 Inclusion criteria

The inclusion criteria were of studies that:

- Were conducted in an African country
- Described the epidemiology or impact of stroke
- Used a prospective quantitative study design
- Had full text available for review
- Used stroke case ascertainment by the WHO clinical criteria (WHO MONICA Project Principal Investigators, 1988) and/or CT or MRI scan
- For stroke case fatality, only those reporting a one-month case fatality were considered

- Followed the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (von Elm et al., 2007) for the items below:
    a. Providing an informative and balanced summary of what was done and what was found (STROBE criterion 1b)
    b. Describing the study setting, locations and relevant dates (STROBE criterion 5)
    c. Giving the eligibility criteria for the participants (STROBE criterion 6)
    d. Giving stroke diagnostic criteria (STROBE criterion 7).
    e. Giving details of methods of assessment (measurement) (STROBE criterion 8).
    f. Describing any efforts to address potential sources of bias (item number 9)
    g. Explaining how the study size was arrived at (STROBE criterion 10)
    h. Providing information on the follow-up time (item number 14c)

1.2.3 Exclusion criteria

Exclusion criteria included:

- Review articles
- Duplicate publications

1.2.4 Screening and quality assessment

The study selection involved three consecutive stages. In stage 1, I screened the retrieved publications for potential eligibility based on their titles and abstracts. In stage 2, I determined eligibility for further assessment based on the availability of full text. Stage 3 consisted of further assessment of eligibility and involved a full review of the publications using the inclusion criteria. After the initial screening process, the eligibility for 20 articles was unclear, and my primary supervisor and I independently performed a full review to determine if those 20 articles met the inclusion criteria. We then discussed them and reached a consensus about their eligibility. However, the quality appraisal for the studies included in the review was not undertaken.

1.2.5 Data extraction

After screening the articles identified and assessing them for quality, those which qualified for the review were categorized into seven themes: incidence, prevalence, mortality, case fatality, disability, quality of life and cost of stroke as shown in tables 1.1-1.7.

A data extraction form for each of the seven variables for the review was drafted and tested with extraction of data from two studies for further refinement. Thereafter, I systematically extracted data from each study in discussion with my primary supervirsor and recorded the data on the corresponding final extraction form as indicated in tables 1.1-1.7.

1.2.6 Data analysis

For the studies on incidence, prevalence or mortality rates of stroke in Africa, data were presented either per 1,000 or per 100,000 population. During the analysis, all the data were presented per 100,000 population.

For case fatality, all studies which reported stroke case fatality for 28 days (four weeks) or 30 days were all considered for one-month stroke case fatality outcomes.

Disability post stroke was anticipated to use outcome measures such as the modified Rankin Scale (mRS) and the Glasgow Outcome Scale (GOS). For easy interpretation and comparison, I planned to present findings on disability of stroke survivors under three categories. These include mild disability (mRS=0-2 and GOS=5), moderate disability (mRS=3 and GOS=4), and severe disability (mRS=4-5 and GOS=2-3).

For the data on cost of stroke care, an average for ischemic and hemorrhagic stroke costs in the Cameroonian study (Mapoure et al., 2014) was calculated and used for further interpretation. Because the reviewed studies were conducted in different years and in different currencies, the data on cost of stroke care was converted to 2016 United States Dollar (USD) currency values using a web-based tool (CCEMG-EPPI-centre cost converter) and using the International Monetary Fund (IMF) for the purchasing power parity (PPP) values.

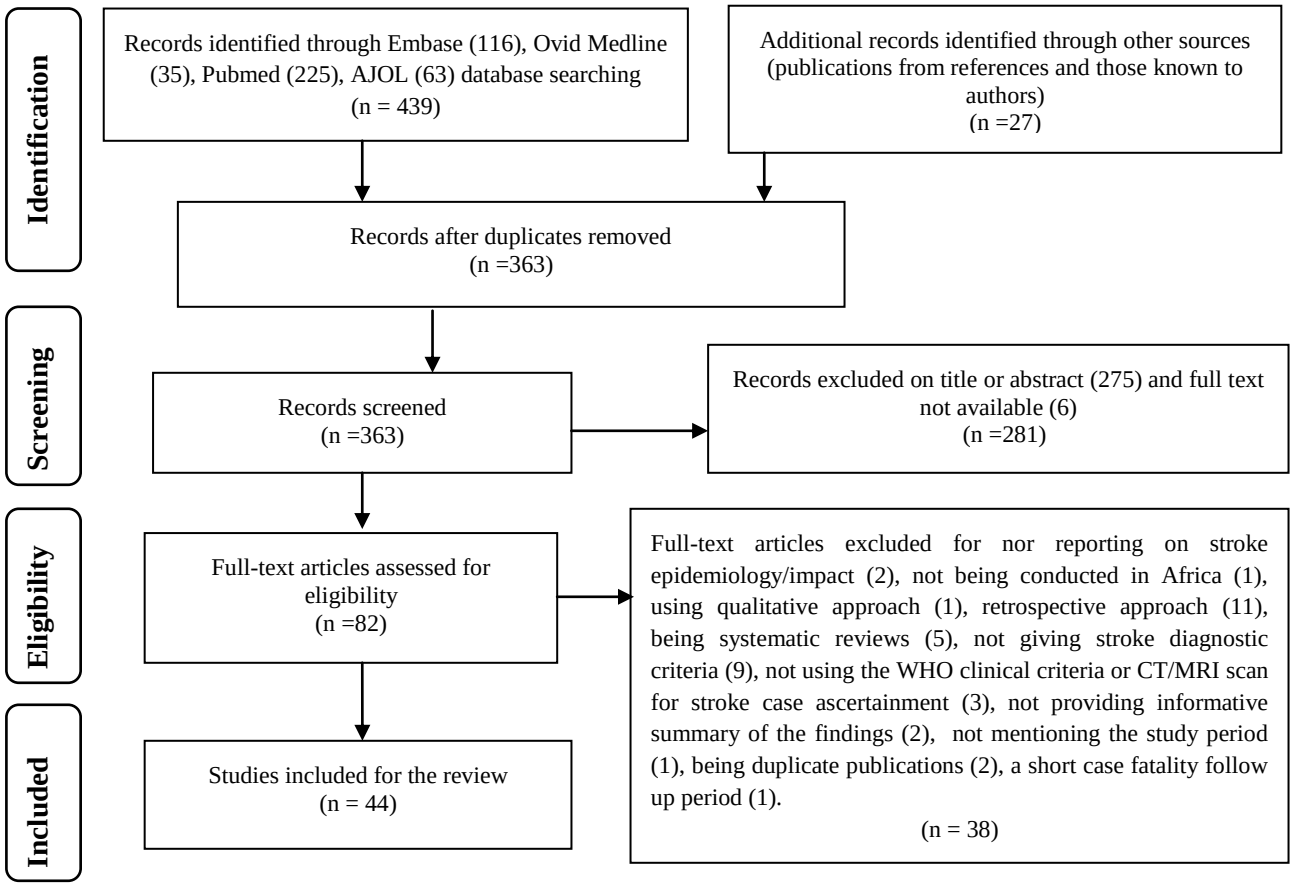
A Tanzanian study (Walker et al., 2000) provided separate data for males and females regarding both crude and age-adjusted stroke mortality rate. For these data, averages were calculated for easy further analysis and interpretation.

To determine the overall estimates of stroke epidemiology and impact variables in Africa, the overall means with standard deviation (SD) were calculated.

1.3 Results

The search results and review profile are shown in Figure 1.1. I identified a total of 466 references from which 44 studies were eligible for my review.

Figure 1. 1: Review profile showing selection of studies reporting on epidemiology or impact of stroke in Africa



Characteristics of the included studies

Tables 1.1-1.7 show the studies considered for my systematic literature review. Forty-two studies were published in English and the remaining two (Adoukonou et al., 2013; Mapoure et al., 2014) were in French. The included studies were conducted across the main regions of Africa (east, west, central, north, and south), and were conducted in 15 countries including Nigeria (15), Egypt (6), South Africa (4), Benin (3), Tanzania (3), Gambia (2), Malawi (2), Uganda (2), Cameroon (1), Democratic Republic of Congo (DRC) (1), Ghana (1), Libya (1), Morocco (1), Mozambique (1), and Zimbabwe (1).

Among the 44 studies, 21 were hospital based and 23 were community based. The majority (30/44) of the studies were conducted in urban settings.

Table 1. 1: Studies reporting the incidence of stroke in Africa

Study Reference	Country	Location	Rural/ Urban	Data collection Period	Sample size	Age group	First ever or Recurrent	N. of cases	Crude incidence /100,000	Age-adjusted incidence /100,000
Hospital-based studies										
Ashok et al., 1986	Libya	Benghazi	Urban	Nov 1983-Oct 1984	518,745	All	First ever	329	63	
Rosman, 1986	SA	Pretoria	Urban	May 1984-Apr 1985	114,931	≥ 20	All	116	101	
Matenga, 1997	Zimbabwe	Harare	Urban	Jan-Dec 1991	887,768	All	First ever	273	30.7	68
Damasceno et al., 2010	Mozambique	Maputo	Urban	Aug 2005-Jul 2006	2007 Census*	≥ 25	All	651	148.7	260.1
Community-based studies										
Kandil et al., 2006	Egypt	Sohag	Mixed	1992	20,900	All	All	39	186.6	
Walker et al., 2010	Tanzania	Hai	Rural	Jun 2003-Jun 2006	159,814	All	All	453	94.5	108.6
		D-e-S	Urban		56,517			183	107.9	315.9
Farghaly et al., 2013	Egypt	Al Kharga	Mixed	Jan-Dec 2007	62,583	All	All	156	250	
El Tallawy et al., 2013	Egypt	Al Quseir	Urban	Jul 2009 – Jan 2012	19,848	≥ 20	All	36	181	
Okon et al., 2015	Nigeria	Akure	Urban	Nov 2010-Oct2011	491,033	All	First ever	298	60.69	60.67

Abbreviations: D-e-S, Dar-es-Salaam; N., Number; SA, South Africa

There were four hospital-based and five community-based studies on incidence of stroke in Africa. The hospital-based studies provided a crude incidence mean of 85.9 (SD: 50.8)/100,000 population. The age-adjusted stroke incidence mean from two hospital based studies was 164.1 (SD: 135.8)/100,000 population. Regarding the community-based studies, the crude stroke incidence mean was 146.8 (SD: 70.81)/100,000 population. The community-based age-adjusted stroke incidence mean from three African settings was 161.7 (SD: 135.7)/100,000 population. For all the studies on incidence in Africa, the crude incidence mean was 122.4 (SD: 68.1)/100,000 population while the age-adjusted incidence mean was 162. 7 (SD: 117.5) /100,000 population.

Table 1. 2: Studies reporting the prevalence of stroke in Africa

Study Reference	Country	Location	Rural/ Urban	Data collection period	Sample size	Age group	N. of cases	Crude prevalence /100,000	Age-adjusted prevalence /100,000
Osuntokun et al., 1987	Nigeria	Igbo-Ora	Urban	1982-1983	18954	All	11	58	
The SASPI Project Team, 2004	SA	Agincourt subdistrict	Rural	Aug-Nov 2001	42 378	≥15	103	243	330
Kandil et al., 2006	Egypt	Sohag	Mixed	Jan 1992-Apr 1993	25000	All	127	508	
Danesi et al., 2007	Nigeria	Lagos	Urban	Jun 2005-May 2006	13,127	All	15	114	114
Cossi et al., 2012a	Benin	Cotonou	Urban	Sept 2008- May 2009	15,155	≥ 15	70	460	870
El Tallawy et al., 2013	Egypt	Al Quseir	Urban	Jul 2009 – Jan 2012	19,848	≥20	130	655	
Farghaly et al., 2013	Egypt	Al Kharga	Mixed	Jun 2005-May 2008	62,583	All	351	560	
Khedr et al., 2013	Egypt	Assiut Governorate	Urban	Jan-Dec 2010	5920	≥15	57	963	980.9
Khedr et al., 2014	Egypt	Qena Governorate	Mainly Rural	Sept 2011-Aug 2013.	8027	All	74	922	1221.7
Engels et al., 2014	Morocco	Rabat-Casablanca	Mixed	Nov 2008-Apr 2009	44742	≥15	127	284	
Enwereji et al., 2014	Nigeria	Ukpo	Rural	2011	6,150	All	10	163	100
Onwuchekwa et al., 2014	Nigeria	Niger Delta	Rural	July 2008	1057	≥18	9	851	1230
El Tallawy et al., 2015	Egypt	Upper Egypt	Mixed	Jan 2006-Jan 2012	55,664	≥20	470	844	
Sanya et al., 2015	Nigeria	Kwara state	Semi-urban	Oct 2009- Aug 2010	12,992	≥18	17	131	
Ezejimofor et al., 2017	Nigeria	Niger Delta	Rural	June-Sept 2014	2028	≥18	27	1331	1460

Abbreviations: N., Number; SA, South Africa, SASPI: Southern Africa Stroke Prevention Initiative

Fifteen studies in total reported on the prevalence of stroke in Africa, and they were all community-based. One study in Egypt (El Tallawy et al., 2015) included seven transient ischemic attack (TIA) cases. These were removed and a total of 470 stroke cases only were considered in the current review. The highest crude prevalence was reported in Nigeria (1331/100,000 population) and the lowest was reported in Nigeria (58/100,000 population). The crude prevalence mean is 539.1 (SD: 381.5)/100,000 population.

Some studies determined the age-adjusted prevalence of stroke which ranges between 100 (Ukpo, Nigeria) and 1460 (Niger Delta, Nigeria) /100,000 population, an age-adjusted prevalence mean of 788.3 (SD: 536.7)/100,000 population.

Table 1. 3: Studies reporting the mortality of stroke in Africa

Study Reference	Study	Location	Rural/ Urban	Data collection period	Sample size	Age group	N. of deaths due to stroke	Crude Rate/ 100,000	Age-standardized rate /100,000
Osuntokun et al., 1987	Nigeria	Igbo-Ora	Urban	Jan1982-Jun 1983	18,954	All	-	70	
Kahn and Tollman, 1999	SA	Agincourt District	Rural	1992 -1995	-	≥35	55	127	
Walker et al., 2000	Tanzania	Dar-es-Salaam	Urban	Jun 1992-May 1995	65,826	≥15	104	79.5*	368.5*
		Hai	Rural		142,414		235	99.5*	134.5*
		Morogoro	Rural		99,672		82	47.5*	75*

Abbreviations: N**.,** Number; SA, South Africa

* Numbers are averages from original separate data for females and males

There were three community-based studies that repored on stroke mortality in Africa. With regard to crude mortality, the highest rate was found in South Africa (127/100,000 population) and the lowest was reported in Morogoro District of Tanzania (47.5/100,000). The overall crude mortality mean rate was 84.7 (SD: 30.15)/100,000 population.

The study in Tanzania (Walker et al., 2000) determined the age-standardized mortality rate ranging between 75/100,000 population in the rural setting of Morogoro District and 368.5/100,000 population in the urban setting (Dar-Es-Salaam). The age-adjusted mortality mean rate was 192.7(SD: 155.2)/100,000 population.

Table 1. 4: Studies reporting one-month stroke case fatality rate in Africa

Study Reference	Country	Location	Rural/ Urban	Data collection period	N. of stroke cases	First ever/ Recurrent	Age group	N. of stroke deaths	CF rate (%)
Hospital-based studies									
Ashok et al., 1986	Libya	Benghazi	Urban	Nov 1983-Oct 1984	329	First ever	All	57	17.3
Rosman, 1986	South Africa	Pretoria	Urban	May 1984-Apr 1985	116	All	≥ 20	-	33.6
Walker et al., 2003	Gambia	Banjul	Urban	1990-1991	106	All	All	29	27
Garbusinski et al., 2005	Gambia	Banjul	Urban	Feb 2000-Feb 2001	148	All	≥15	-	46
Komolafe et al., 2008	Nigeria	Ile-Ife	Urban	2000-2005	135	All	All	21	15.6
Longo-Mbenza et al., 2008	DRC	Kinshasa	Urban	1989-1992	212	All	All	94	44
Damasceno et al., 2010	Mozambique	Maputo	Urban	Aug 2005-Jul 2006	651	All	≥ 25	-	49.6
Musa et al., 2012	Nigeria	Maiduguri	Urban	2005-2009	91	First ever	All	18	19.78
Alkali et al., 2013	Nigeria	Abuja	Urban	Jan 2010 –Jun 2012	272	All	≥25	51	18.8
Owolabi and Nagoda, 2013	Nigeria	Kano	Urban	Jun 2007-Jun 2010	273	All	All	102	37
Kwarisiima et al., 2014	Uganda	Mulago	Urban	Jul 2010-Jan 2011.	128	All	≥18	56	43.8
Ekeh et al., 2015	Nigeria	Jos	Urban	Jan-Dec 2006	120	All	≥16	40	33.3
Nakibuuka et al., 2015	Uganda	Kampala	Urban	Feb-July 2014	127	All	All	34	26.8
Community-based studies									
Walker et al., 2011	Tanzania	Hai District	Rural	Jun 2006- Jun 2009	353	All	All	95	26.9
Danesi et al., 2013	Nigeria	Lagos	Urban	Jan-Dec 2007	160	First ever	All	26	16.2

Abbreviations: CF, case fatality; N., Number; %, percentage

Almost all the studies on one-month stroke case fatality in Africa (86.7%) were hospital based and showed that stroke case fatality in Africa for one month varies between 15.6% and 49.6%. The case fatality mean rate in one-month post stroke as reported by hospital-based studies in Africa was 31.7% (SD: 11.8%). The community-based studies found that one-month fatality rate was 16.2% in Nigeria and 26.9% in Tanzania, with a mean equal to 21.6% (SD: 7.6%). Overall, the one-month case fatality mean rate for stroke in African studies was 30.4% (SD: 11.7%).

Table 1. 5: Studies reporting the disability of stroke survivors in Africa

Study Reference	Country	Location	Rural/ Urban	Data collection period	Sample size	Age group	Assessment Tool	Period post stroke	Disability categories (%)		
									Mild	Moderate	Severe
Komolafe et al., 2008	Nigeria	Ile-Ife	Urban	2000-2005	111	All	GOS	30 days	7.2	66.7	26.1
Damasceno et al., 2010	Mozambique	Maputo	Urban	Aug 2005-July 2006	370	≥25	mRS	28 days	35.6	27.8	36.6
de Villiers et al., 2011	South Africa	Cape Town	Urban	Aug 2004- Jan 2006	117	All	mRS	6 months	52	26	22
Heikinheimo et al., 2012	Malawi	Blantyre	Urban	Feb 2008 -Apr 2009	96	≥18	mRS	6 weeks	33.3	31.3	35.4
					81			6 months	59.3	24.7	16.0
					72			1 year	69.4	15.3	15.3
Owolabi and Nagoda, 2012	Nigeria	Kano	Urban	Jun 2008-Jun 2010	106	All	mRS	6 months	66	11	23

Abbreviations: GOS, Glasgow Outcome Scale; mRS, modified Rankin Scale; %, percentage

Most of the studies conducted on disability in Africa included in the review used the modified Rankin Scale. As shown in table 1.5, it was found that at one-month post stroke, 64.4% (Mozambique) and 92.8% (Nigeria) of stroke survivors have moderate or severe disability.

At 6-month post stroke, many stroke survivors (34% in Nigeria, 40.7% in Malawi, and 48 % in South Africa) have moderate or severe disability.

At one-year post stroke, 30.6% of stroke survivors have moderate or severe disability.

Table 1. 6: Studies reporting the quality of life among stroke survivors in Africa

Study Reference	Country	Location	Rural/ Urban	Data collection period	Sample size	Age group	Tool	Post-stroke duration	Mean score
Owolabi and Ogunniyi, 2009	Nigeria	Ibadan	Urban	2002-2004	100		HRQOLISP	28.5 months	73.5%
Donkor et al., 2014a	Ghana	Accra and Tema	Urban	Jan 2012-Sept 2013	156	All	HRQOLISP	29 months (Mean)	69%
Heikinheimo and Chimbayo, 2015	Malawi	Blantyre	Urban	Aug 2008-Apr 2010	25	≥18	NEWSQOL	6 months [a]	78% [b]

Abbreviations: NEWSQOL, Newcastle Stroke-specific Quality of Life Measure**;** HRQOLISP; Health Related Quality of Life in Stroke Patients

[a]: Seven interviews were conducted at 12 months post stroke.

[b]: The mean was calculated using the reported mean scores for all NEWSQOL domains

Three studies only were included in my review, and they were all community-based. One study measured the level of quality of life of 25 participants at six or 12 months post stroke using the NEWSQOL and showed that the score across the QoL domains was ranging between 70%-88%, with a mean of 78%, meaning good QoL. The other ones in Ghana (Donkor et al., 2014a) and Nigeria (Owolabi and Ogunniyi, 2009) assessed the quality of life post stroke at an average of 29 months post stroke using the HRQOLISP and revealed that the participants had neither poor nor good QoL (69% and 73.5%, mean=71%).

Table 1. 7: Studies reporting the cost of stroke in Africa

Study Reference	Country	Location	Rural/ Urban	Data collection period	Sample size	Age group	Estimation procedure	Length of care	Currency	Mean	Mean* in USD-2016
Adoukonou et al., 2013	Benin	Parakou	Urban	Jun 210-May 2011	78	All	Bottom up	14.4 days	CFA-2011	316,810.3	1588.21
Gnonlonfoun et al., 2013	Benin	Cotonou	Urban	Feb-Sept 2001	122	≥20	Bottom up	-	USD-2011	1030	1105.17
Mapoure et al., 2014	Cameroon	Douala	Urban	Apr 2012-Apr 2013	71	>15	Bottom up				
								In hospital care cost			
								10 days	CFA 2013	718,970	3220.47
								After discharge care cost			
								9 months	CFA 2013	1,031,888	4622.12

Abbreviations: CFA, Communauté financière d'Afrique (Financial Community of Africa) franc

* The cost data were converted to 2016 USD currency values using a web-based tool (CCEMG-EPPI-centre cost converter)

Three studies were considered for review about the cost of stroke care in Africa. All the included studies focused on the direct cost, being medical or non-medical. Considering the in-hospital care cost, the mean of the estimates as reported in the three studies was 1971 (SD: 1108) USD. A single study conducted in Cameroon (Mapoure et al., 2014) showed a higher cost for the post-discharge period (4622.12 USD).

1.4 Discussion

1.4.1 Incidence of stroke in Africa

In total, nine studies on the incidence of stroke in Africa were identified. Eight of the nine studies were conducted over a period of one year, and the remaining study (Walker et al., 2010) was conducted for a period of three years. Four out of the nine studies were hospital-based, and most of them were conducted between 1983 and 1991. The hospital-based studies are subject to several limitations and their results must be interpreted with caution. First, hospital-based data cannot provide reliable incidence estimates because the population at risk (i.e. the denominator) is not well known (Owolabi et al. 2015). Second, hospital-based studies underestimate stroke incidence as a result of exclusion of fatal or mild cases who do not present to hospital. For instance, transport problems and large distances to hospital from some patients' homes in Africa mean that a significant number of patients with stroke die before reaching the hospital. Third, hospital-based studies do not capture patients who patronise traditional healers or those who don't go to hospital at all because of financial problems. Five studies reporting on stroke incidence in Africa were community or population-based and most of them were conducted between 2003 and 2011, indicating that in Africa there has been a progressive shift from hospital-based to community or population-based studies on stroke incidence.

The case ascertainment was achieved by a clinical examination mainly based on WHO clinical criteria (WHO, 1988) and confirmed by CT or MRI scan, except for one study (Matenga, 1997) where the diagnosis was determined based on the WHO clinical criteria alone. However, case ascertainment for stroke in Africa is very difficult due to several challenges such as difficulties resulting from the very large study populations with limited resources, and because of non-inclusion of those who patronise traditional healers (Osuntokun et al., 1979; Owolabi et al., 2015).

The hospital-based studies on incidence of stroke in Africa provided a crude incidence mean of 86/100,000, and an age-adjusted stroke incidence mean from two studies (Matenga, 1997; Damasceno et al., 2010) of 164/100,000 population. There was a wide range of results from the hospital-based studies of crude stroke incidence: 30.7 per 100,000 population in Zimbabwe, 63 in Libya, 101 in South Africa, and 148.7 in Mozambique. Although not all the studies provided the age-adjusted stroke incidence to allow easy comparison, the variation in

the results may be partly explained by the methodological differences across the four hospital-based studies. For instance, studies with higher crude stroke incidence (Rosman, 1986; Damasceno et al., 2010) not only included both first ever and recurrent incidences, but also they recruited participants aged 25 years and above in Mozambique (Damasceno et al., 2010), 20 years and above in South Africa (Rosman, 1986), while other studies (Ashok et al., 1986; Matenga, 1997) considered first ever stroke incidents only and included all age groups. Different studies have shown that the risk of stroke increases with age (Feigin et al., 2003; Connor et al., 2007).

The current crude stroke incidence mean is higher than the pooled estimate (77.4/100,000 population) found in a meta-analysis of hospital-based studies (Adeloye, 2014), the observed difference may be because the meta-analysis included a study with a low rate of 48.0/100,000 population which did not meet my inclusion criteria because its full text was not available for my current review. Community-based studies yielded higher crude incidence mean rate (147/100,000 population). It has been noted that hospital-based studies underestimate the incidence rates because they are affected by referral bias as patients who die quickly from stroke or those with mild stroke do not present in hospitals (Owolabi, 2011). Furthermore, in African cultures, stroke can be attributed to a supernatural force requiring intervention by a traditional healer (Mshana et al., 2008), and some people with stroke symptoms may not present to hospitals, leading to the underestimation of stroke incidence.

However, the community-based age-adjusted incidence mean rate (162) was slightly lower than the hospital-based one (164/100,000 population). In fact, one (Damasceno et al., 2010) of the two hospital-based studies that reported the adjusted incidence rates included only participants of 25 years old and above while the community-based studies (Walker et al., 2010, Okon et al., 2015) included all age groups. This could have resulted in higher hospital-based rates since we know that the risk for stroke increases with age (Feigin et al., 2003; Connor et al., 2007).

The current community or population-based studies review results are higher than the results from previous similar reviews which revealed the population-based crude incidence of 73-165 (Feigin et al., 2009) and 112.94 (Adeloye, 2014) per 100,000 population. Some factors may have contributed to the lower rates reported by these reviews: two studies with low incidence rates (25.2 and 26.0/100,000 population) were considered in the review by Adeloye (2014) but

which were not included in my review on community-based stroke incidence. One of the two studies was published in 1979 while the other one did not include persons who died from stroke before presenting to hospital. The rate reported by Feigin et al. (2009) is for LMICs among which only one African country (Nigeria) was included. In addition, the rate as reported by Feigin et al. (2009) is for the period from 2000 to 2008. After the year 2008, there may have been increasing incidence.

The results from the community-based Tanzanian study (Walker et al., 2010) showed that the age-adjusted stroke incidence in Dar-es-Salaam (316) is higher than the rates for HICs (246.32; 221.19; and 217.26 in 1990; 2005; and 2010 respectively) and the rates for all LMICs in general (251.93; 277.48; 281.12 in 1990; 2005; and 2010 respectively) (Feigin et al., 2014). The recent GBD 2016 estimates indicate that while the age-standardised incidence declined from 1990 to 2016 globally (–8.1% [–10.7 to –5.5]), it increased for 1.9% (–0.5 to 4.7) in southern sub-Saharan Africa (GBD 2016 Stroke Collaborators, 2019). Urbanisation, growing industrialisation, and other socio-demographic and lifestyle changes in Africa, are increasing rapidly and, in the absence of effective preventive measures, this is likely to lead to further substantial increases in stroke incidence.

1.4.2 Prevalence of stroke in Africa

All 15 studies on stroke prevalence in Africa included in this review were community or population-based. Community or population-based studies constitute the best way to determine the true prevalence of stroke, although they are very rare in Africa due to lack of the required resources (Owolabi et al., 2015). The observed crude prevalence rates of stroke survivors varied between 58 (in Igbo-Ora, Nigeria) and 1331 (in Niger Delta, Nigeria) with a mean rate of 539 per 100, 000 population.

The low prevalence rate that was recorded in Nigeria in 1982-1983 (Osuntokun et al., 1987) may be attributed to various factors. It may be due the high case fatality rates from stroke, which has generally been reported in many parts of Africa (Bonita and Truelsen, 2003). The result is also likely an underestimate because the study was a broad door-to-door survey of neurological disorders in the community, which could imply that active case recognition of specific stroke cases may be less rigorous. Furthermore, the reported prevalence rate is a point prevalence as the new stroke cases which occurred after the reference date (15 February 1982) were not included (Osuntokun et al., 1987). The study period could be another factor. The

survey was done in 1980's, and after that period the stroke incidence and prevalence could have increased as suggested by the literature (Feigin et al., 2003; Ezejimofor et al., 2016). Finally, because of Nigerian cultural attitudes, some stroke survivors may have been hidden and not made available to interviewers during the survey (Osuntokun et al., 1987). In fact, some interviewers were strangers in their data collection areas, and subjects tend to be unwilling to offer information to unfamiliar faces about their relatives suffering from stroke which is sometimes regarded as a social stigma in Africa (Osuntokun et al., 1987)

The crude prevalence mean rate of 539/100,000 population is higher than the previous pooled prevalence rate of 388/100,000 population from a meta-analysis (Adeloye, 2014) which included two studies from Ethiopia (Tekle-Haimanotet al., 1990) and Tunisia (Romdhane et al., 1993) reporting low prevalence rates (15 and 42/100,000 population respectively), but did not meet the inclusion criteria for my review as their full texts were not available.

The age-adjusted mean prevalence of 788 found in this current review was higher than the rates of 546; 676 and 715 for HICs in 1990; 2005 and 2010 respectively, and higher than the rates for all LMICs in general (360; 387; and 393 in 1990, 2005 and 2010 respectively) (Feigin et al., 2014). The high age-adjusted prevalence of stroke as revealed by the current review may reflect the increased exposure to risk factors for stroke in Africa due to ongoing epidemiological and demographic transitions (Owolabi et al., 2015).

1.4.3 Mortality rate of stroke in Africa

It is very difficult to estimate the mortality burden of stroke in Africa as the relevant studies are rare. Three studies only (Nigeria, Tanzania and South Africa) which were community-based have been included in my review. The highest crude mortality rate was found in South Africa (127/100,000 population) and the lowest was reported in Morogoro District of Tanzania (47.5/100,000). The crude mortality rate mean is 85/100,000 population. The high mortality rate in South Africa was likely influenced by considering a population of at least 35 while the study in Nigeria included all age groups and the study in Tanzania included the population of 15 years and above. The low rate reported in Morogoro, a rural area of Tanzania is probably due to lower exposure to stroke risk factors, and consequently lower stroke incidence.

It is a challenge to compare the results on stroke mortality rate in Africa as only one study conducted in three different areas of Tanzania including Dar-es-Salaam (urban), Hai (prosperous rural) and Morogoro (impoverished rural) provided the age-adjusted mortality rate ranging between 369/100,000 population in the urban setting (Dar-Es-Salaam) and 75/100,000 population in the rural setting of Morogoro District, with an overall mean rate 193/100,000 population. This age-adjusted mortality rate is higher than the rates in HICs (96; 72; and 61 per 100,000 person years in 1990, 2005 and 2010 respectively) (Feigin et al., 2014). The higher stroke mortality in Africa may be attributed to the high stroke incidence rate associated with poor health care services. As the African population is undergoing epidemiological and demographic transitions leading to risk factors for stroke, mortality rate for stroke is expected to increase in the absence of relevant preventive, curative and rehabilitative interventions to mitigate the burden.

1.4.4 One-month case fatality rate of stroke in Africa

Thirteen out of 15 studies (87%) reporting one-month stroke case fatality rate (CFR) in Africa were hospital-based, and provided rates ranging from 16% and 50% with a mean rate of 32%. The results are however biased towards urban settings (with reasonably better resourced health-care systems) than rural settings. This hospital-based CFR mean observed in my review is higher than the one-month CFR of 22% in the African countries as shown by the hospital-based INTERSTROKE study (O'Donnell et al., 2010). The lower rate reported by the INTERSTROKE study might be due to having involved five African countries only and selected patients for inclusion in the study.

The variations in CFR across African countries can be attributed to both study methodologies and differences in quality of stroke care. Most of the studies with lower case fatality did not include patients with high risk of death. For instance, in the study in Maiduguri, Nigeria with a CFR of 19.8%, patients with diagnosis of subarachnoid hemorrhage, subdural hematoma, those with a past history of stroke, and those who died within 24 hours of admission were excluded. The CFR found in Ile-Ife, Nigeria (15.6%) was lower than the rate of 17% identified from the Oxfordshire community stroke study in UK. The Nigerian study was hospital-based and showed that some patients presented to the hospital very late, up to two weeks after the onset. It is most likely that patients with severe stroke died before reaching the hospital, thus a low in-hospital CFR.

The observed high CFRs in Maputo, Mozambique (50%) and Banjul, Gambia (46%) have been attributed to the scarce human, technical, and pharmacological resources; patients are cared for in a general medical ward and not in stroke units, thrombolysis is not available for acute management of stroke, and there is poor access to secondary and tertiary prevention (Damasceno et al., 2010). The study in Gambia also showed that the high CFR for stroke is associated with poor accessibility to hospital care, swallowing difficulties, lung infection, fever, bed sores, and absence of aspirin treatment (Garbusinski et al., 2005).

By contrast, lower CFRs were reported in settings with better health care systems. For example, in Benghazi (Libya) with a rate of 17% (Ashok et al., 1986), the medical organisation was reported to be efficient and comprehensive. Patients were referred from the walk-in polyclinics to the four university hospitals and to a rehabilitation centre for persons with disabilities. The health care was public and free, patients with neurological problems were referred from the medical clinics and university hospitals to the neurology outpatient clinics. In addition, there was a Neurology Unit in Benghazi with three qualified neurologists, and neuro-radiological investigations were facilitated by the availability of two computed tomography scanners in Benghazi. All the stroke cases were personally examined by one of the neurologists (Ashok et al., 1986).

Post-stroke CFRs should ideally be calculated using community-based studies because of the likelihood that many patients are not admitted to hospital (Connor et al., 2007). This review identified two community-based studies which provided a one-month CFR of 16% and 27% in Nigeria and Tanzania respectively, with a mean equal to 22%. The mean community-based CFR found in the current review falls within the rate range of 18-35% for all LMICs reported previously (Feigin et al., 2009), but is lower than the median hospital-based rate found. Case fatality rates may be higher in hospital-based than community-based studies (as was found in the current review) because the hospital-based studies may be affected by referral bias. In fact, often only those with moderate to severe stroke, consequently with higher risk for death, tend to present to hospital. However, I believe the findings from the two community-based studies provided an underestimated CFR. The study in Nigeria (Danesi et al., 2013) determined the CFR based on hospitalized patients only, and the limitations of such a data collection approach were discussed earlier. The findings from the study in Tanzania (Walker et al., 2011) are also likely to be underestimates because data was collected by verbal autopsy (VA) and the

information being gathered retrospectively, relies heavily on the recall of those interviewed for the VA and, therefore, may be inaccurate (Walker et al., 2011).

Despite the limitations I discussed above for the underestimation of CFRs, the overall one-month mean CFR for stroke in Africa from both hospital and community-based studies of 30% is higher than the CFR in High Income Countries (HICs) (21.5%, 22.2% and 19.8% in 1980–89, 1990–99, and 2000–2008, respectively) (Feigin et al., 2009). This difference could be due to variations in stroke severity or co-morbidities but it seems more likely that it can be explained by poorer management of stroke in Africa compared with the management in HICs (Ingall et al., 2000).

1.4.5 Disability post stroke in Africa

Five studies were included in this review for disability among stroke survivors in Africa, but none of them assessed DALYs due to stroke. Rather, they assessed levels of activity limitations and participation restrictions using the mRS (Damasceno et al., 2010; de Villiers et al., 2011; Heikinheimo et al., 2012; Owolabi and Nagoda, 2012) and Glasgow outcome scale (GOS) (Komolafe et al., 2008).

At one-month post stroke, 64% and 93% of stroke survivors in Mozambique (Damasceno et al., 2010) and Nigeria (Komolafe et al., 2008), respectively, were reported to have moderate or severe disability. The percentage in Nigeria may be high because the study used a different outcome measure (GOS), and patients corresponding to score 1 (No significant disability despite symptoms) and score 2 (Slight disability) of the mRS could have been classified as having moderate disability. Therefore, results from the two studies should be compared with caution.

At six-month post stroke, the proportion of stroke survivors left with moderate or severe disability in Nigeria, Malawi and South Africa, ranged from 34 to 48%. The differences in proportion of patients with moderate or severe disability at six months could be due to the quality of care and rehabilitation post discharge. The management of stroke patients in the rehabilitation centers in Nigeria was in accordance with Aminu Kano Teaching Hospital guideline on stroke management which is a modification of American Heart Association/American stroke association (AHA/ASA) guidelines (Owolabi and Nagoda, 2012). In Malawi, some patients were transferred to a residential rehabilitation unit and others continued getting outpatient physiotherapy, but no information was provided about the

structure and process of the rehabilitation post discharge (Heikinheimo et al., 2012). The study in South Africa however, was conducted in a socio-economically disadvantaged community where poor housing was found to be an independent predictor of poor functional outcome, and there were limited rehabilitation resources (de Villiers et al., 2011).

The study in Malawi (Heikinheimo et al., 2012) indicated that at one-year post stroke, 31% of stroke survivors have moderate or severe disability. The decrease in percentages of stroke survivors with moderate to severe disability from one month to six and 12 months post stroke may reflect improvement from rehabilitation services and secondary prevention of stroke (Owolabi and Nagoda, 2012). However, some of the patients lost to follow-up across the studies included in this review could be as a result of unreported death at home as disability was found to be an independent predictor of death post stroke. In addition, some stroke survivors with severe disability may have been hidden by family members and not made available for assessment due to the stigma attached to disability.

Stroke is estimated to be the seventh leading cause of DALYs (Feigin et al., 2009). Estimates indicated there were 102.2 million DALYs in 2010 with 78% of them attributed to LMICs only (Feigin et al., 2014). Direct studies of DALYs due to stroke are very rare in Africa. The burden of disease due to stroke in South Africa (2008) was 564 000 DALYs, and of this, 17% was contributed by years lived with disability (Bertram et al., 2013). The estimated proportion of DALYs due to stroke was in 2002 (Johnston et al., 2009) 1,230 per 100,000 in Angola (Africa), compared to 200 per 100,000 in Switzerland (Europe).

It was not possible to compare the current results on disability in Africa with the results from international studies which used the common DALYs approach. Future researchers on disability post stroke in Africa are therefore encouraged to adopt the common international approaches. Despite the limitations, the studies included in this review indicate that disability post stroke is common in Africa. Disability, as manifested by limitations in activities of daily living and restrictions in involvement in social life, is a burden not only to the survivor but also to his or her family and society in general. There is therefore a need for appropriate strategies for the prevention and rehabilitation of post-stroke disability.

1.4.6 Quality of life among stroke survivors in Africa

Assessment of QoL could help both in understanding the areas in which a patient is most affected by a disease and in planning effective therapeutic and rehabilitative interventions (Owolabi and Platz, 2008). Studies on QoL post stroke in Africa are however very rare. Only three studies were available and met inclusion criteria for my review. Referring to the guide for score interpretation provided by Ali et al. (2013), one study (Heikinheimo and Chimbayo, 2015) reported that stroke survivors had good quality of life (the mean score was >75%) at 6 to 12 months post stroke while the remaining two studies (Owolabi and Ogunniyi, 2009; Donkor et al., 2014a) reported moderate quality of life (the mean score was 71%) at 29 months post stroke.

Although those three studies used standardized instruments with good validity and reliability (Buck et al., 2004; Owolabi and Ogunniyi, 2009), they have some limitations that raise concerns about the external validity of the results. Firstly, the study samples were not representative because stroke survivors with very poor quality of life do not participate in study interviews. For instance, out of 81 stroke survivors at six months (Heikinheimo and Chimbayo, 2015), 23 of them with severe expressive or receptive dysphasia and four who were severely ill or bed-ridden did not participate to the NEWSQOL interview. The study in Ghana (Donkor et al., 2014a) recruited participants attending two major urban hospitals for rehabilitation only, and who developed stroke at least one month before the time of interview in order to exclude acute cases of stroke. Secondly, the majority of the stroke survivors in the study in Ghana (52.6%) had experienced mild stroke. Finally, responses for some stroke survivors with communication problems were provided by their caregivers (Donkor et al., 2014a), and I believe that the information provided by a caregiver may not represent the real life experiences of the stroke survivor.

1.4.7 Cost of stroke in Africa

The cost of the disease comprises both direct and indirect cost. Direct cost encompasses medical treatment and various mobilized resources in order to improve and stabilize the disease (hospitalization cost in acute stage, rehabilitation care, ambulatory care, care from relatives and next of kin) (Mamoli et al., 1999). Estimating indirect cost is pretty complex as it globally comprises the socio-professional effects on the disease (loss of productivity,

absenteeism, work or activity cessation, social aid, adjustment to social life, incentives in compensation to the disability etc.) (Claesson et al., 2000).

Measuring cost of stroke in Africa is very difficult. Due to limited resources, estimating the lifetime costs of a stroke from its onset to its termination, especially the follow-up after discharge from hospital, is a major challenge, and the available relevant studies provide only a snapshot of costs at a particular point in time. Aditionally, some patients in Africa spend more money by consulting traditional healers because they still believe that stroke is related to bad spiritual forces (Mapoure et al., 2014), and capturing such costs is a big challenge. Poor documentation in Africa is another problem. For instance, a pilot study (Kabadi et al., 2013) that was conducted in Tanzania did not include the costs of physiotherapy services for one of the study settings because they were not available. Regarding the indirect cost of stroke, the productivity losses are likely to be undervalued in the estimation process for patients without formal employment from which actual monetary losses can be precisely estimated. Furthemore, actual productivity losses can be underestimated due to recall bias and/or the difficulty in documenting and valuing all gainful activities patients were involved in before stroke (Kabadi et al., 2013).

Three studies (Adoukonou et al., 2013; Gnonlonfoun et al., 2013; Mapoure et al., 2014) were considered for review about the cost of stroke in Africa. All the included studies focused on the direct cost. The in-hospital care mean cost per patient was found to be 1,971 USD. It was also reported that length of hospitalization, hemorrhagic stroke, and stroke initial severity (Adoukonou et al., 2013; Gnonlonfoun et al., 2013) are the most powerful factors influencing the cost of stroke.

The cost variations are not surprising if we consider the differences in research methodologies, hospital levels and the management systems across and within countries. The Benin study (Gnonlonfoun et al., 2013) conducted in Cotonou (cost mean: 1,105 USD) aimed to determine factors associated with direct cost of stroke hospitalization while the other Benin study (Adoukonou et al., 2013) in Parakou (cost mean: 1,588 USD) aimed at determining the direct cost of in-hospital stroke care, which could imply that recording the cost for stroke patients may be more rigorous.

The highest cost in Cameroon of USD 3,220 per person could be due to several reasons. First, the study in Cameroon was conducted in a specialized hospital that has neurologists, physiotherapists, speech therapists and occupational therapists, and various diagnostic

procedures like CT scanning, electrocardiogram, trans-thoracic echocardiogram, and the supra-aortic duplex ultrasound among others, and those resources are not or are rarely found in other settings. Secondly, the Cameroonian setting was a specialized hospital in Douala, the richest city in the whole Economic and Monetary Community of Central Africa (CEMAC) region, and the prices of goods and services are likely to be high. Additionally, it was reported that since 2008 in Cameroon, there was an increase of salaries for the employees including the health care professionals (Mapoure et al., 2014). Finally, the aim of the study was to find the data to serve as an evidence to advocate for the financial support from the Government of Cameroon for the management of stroke patients (Mapoure et al., 2014). Consequently, the recording of stroke costs may have been more rigorous than in other studies.

It appears that stroke patients in Africa have less spent on them than patients in HICs do for example 70,330 USD per patient in Sweden (Jorgensen et al., 1997), £15,306 per patient in UK (Beech et al., 1999), and €17,799 per patient in France (Launois et al., 2004). In reality however, they spend a greater proportion of income than patients from HICs if we consider their low purchasing power. For instance, the ratio cost/gross domestic product (GDP) per inhabitant in Benin (Gnonlonfoun et al., 2013) shows that the direct cost per patient represents in Benin 1.3 times the GDP per inhabitant. Accordingly, most people from Benin cannot access specialized neurology care for a stroke.

To sum up, the cost of stroke constitutes a high economic burden in Africa, but the available data appears to underestimate the real total cost. In fact, most of the studies did not include the cost of care post discharge, and all the studies did not include the indirect cost associated with changes in productivity resulting from stroke, including productivity gains or resulting from patient time spent in treatment or healthcare facilities.

Strengths and weaknesses

Several systematic reviews on stroke in Africa have been published previously but, to the best of my knowledge, this review on the epidemiology and impact of stroke in Africa seems to be more up-to-date and comprehensive. My review was systematic, and I searched many relevant databases including Medline, Embase, PubMed, and AJOL, with no language restriction. In addition, the STROBE guidelines were used to assess the identified publications while the PRISMA ones were used to write the review report. However, my review may well be subject to publication bias as only the electronic databases and references were considered.

Furthermore, the investigators of the identified studies were not contacted to confirm data, and two persons (GU and PL) only were involved in screening and quality assessment of the identified studies. The studies included for the review had various limitations and the results need to be interpreted with caution. Last but not least, most of the studies reviewed were conducted in urban settings and therefore might not show the situation in rural areas.

1.5 Conclusion

This systematic review showed that stroke is common and important in Africa. It also showed that robust high-quality studies are needed to help policy makers and health care professionals to control the stroke burden in Africa. More attention should be put on community or population-based studies with large sample size, in both urban and rural settings. Appropriate preventive and therapeutic measures should be promoted to decrease the incidence of stroke, improve the outcomes, and maintain the survivors' quality of life in Africa.

Chapter 2: Stroke care in Africa: a systematic review of the literature

2.1 Introduction

The previous chapter raised a question on the availability, accessibility and quality of stroke services in Africa. In contrast to high income countries (HICs) where stroke mortality rates have declined, the burden of stroke in developing countries has risen in recent years and is expected to accelerate (Feigin et al., 2014). Eighty-six percent of all stroke deaths around the world take place in LMICs (Feigin, 2005). Further, LMICs account for over 87% DALYs from stroke, which is about seven times the DALYs in HICs (Johnston et al., 2009).

African countries are undergoing an epidemiological transition driven by socio-demographic and lifestyle changes related to unchecked industrialization and a rise in many modifiable vascular disease risk factors. These include smoking, harmful use of alcohol, physical inactivity and unhealthy diets resulting in an increased prevalence of hypertension, diabetes and obesity (Owolabi et al., 2014). Consequently, the burden of NCDs including stroke is growing (Owolabi et al., 2014). A systematic review (Owolabi et al., 2015) of community-based studies revealed an age-standardised annual stroke incidence rate of up to 316 per 100,000 population, and age-standardised prevalence rates of up to 981 per 100,000 in Africa. However, health systems in many African countries are characterised by geographical and financial inaccessibility, rapid turnover of people in key positions, lack of continuity in policy, lack of resources, poor management of available resources and poor implementation (Sambo, 2012).

It is recommended that appropriate systems of stroke care be established in Africa and other LMIC regions to control the increasing death and disability associated with stroke (Feigin et al., 2009; Langhorne et al., 2012). However, we need information about the existing resources and current practices for stroke care in Africa. There have been some international reviews and surveys (not offered in languages other than English) on stroke care, but few studies included Africa. Several have relied on self-reported information which may be biased or had a very narrow focus (Brainin et al., 2007; Langhorne et al., 2012; Giruparajah et al., 2015; Wintermark et al., 2015). This motivated me to conduct a systematic literature review on systems of stroke care in Africa to inform policy makers and health care professionals about areas for improvement across the whole stroke care pathway.

2.2 Methods

This review was performed according to the PRISMA guidelines (Moher et al., 2015).

2.2.1 Search strategy

Studies for this review were identified by searches of Ovid Medline, Embase, Amed, CINAHL, PubMed, and AJOL databases. There was no language restriction, but the search was limited to contemporary full-text publications (from January 1st, 2006 to June 20th, 2017). I used Medical Subject Headings (MeSH) and all subheading terms including "awareness", "health care delivery", "health care", "health care system", "health care facility", "health service", "health care access", "rehabilitation", "therapy", "stroke unit", "patient referral", diagnosis, "secondary prevention", and "Africa".

Additional searching was conducted on reference lists of relevant studies to identify publications that could have been omitted in the database searches. The search strategies through different databases as detailed in Appendix 2.1 were developed in consultation with a medical literature search specialist.

2.2.2 Inclusion criteria

The inclusion criteria were of studies that:

- Were conducted in an African country
- Reported on any of the six phases of the continuum of stroke care as conceptualized in the WSO Stroke Services Framework (Lindsay et al., 2014): systems for stroke recognition and response, hyperacute stroke care, acute inpatient care, stroke rehabilitation, secondary stroke prevention, and longer-term stroke recovery.
- Due to the paucity of data, any study design was allowed.

2.2.3 Exclusion criteria

Exclusion criteria included:

- Publications reviewing other studies
- Clinical trial publications

2.2.4 Screening and quality assessment

I screened the titles and abstracts of all the retrieved articles and assessed them for eligibility for narrative analysis using the inclusion criteria. However, the eligibility for 13 articles based on the title or abstract was unclear, and I screened them in discussion with my primary supervisor. Five of the 13 articles remained uncertain, and we independently performed a full review to determine if they met the inclusion criteria. In cases of disagreement, final determination was by discussion and consensus. The quality assessment for the studies included in the review was not undertaken.

2.2.5 Data extraction

Data were extracted using the World Stroke Organisation (WSO) Stroke Services Framework (Lindsay et al., 2014) which consists of six phases of the continuum of stroke care: systems for stroke recognition and response, hyperacute stroke care, acute inpatient care, stroke rehabilitation, secondary stroke prevention, and longer-term stroke recovery.

The draft form was pilot tested on five studies for further refinement. The final version (Appendix 2.2) allowed extracting data regarding the country, study setting, sample, key element(s) investigated, and the main results.

Before extracting the data, I read each publication included for the review three times, but there was more reading for any paper which was not easily understood. Thereafter, using the data extraction form, I systematically retrieved the data from each publication considered for the review. I extracted data about the author(s), publication year, study setting, type of setting (rural or urban), study design, sample size, participants, and main findings. Thereafter, I reviewed the main findings to identify the stroke care key elements and phase(s) reported. This process was done with reference to the stroke care key elements and the six phases of the continuum of stroke care as consptualized in the WSO Stroke Services Framework (Lindsay et al., 2014). The reported stroke care elements were unclear for 10 of the 38 reviewed publications. My primary supervisor reviewed those 10 papers, and we reached a consensus by discussion. To ensure accuracy and consistency, I carried out the data extraction processes twice.

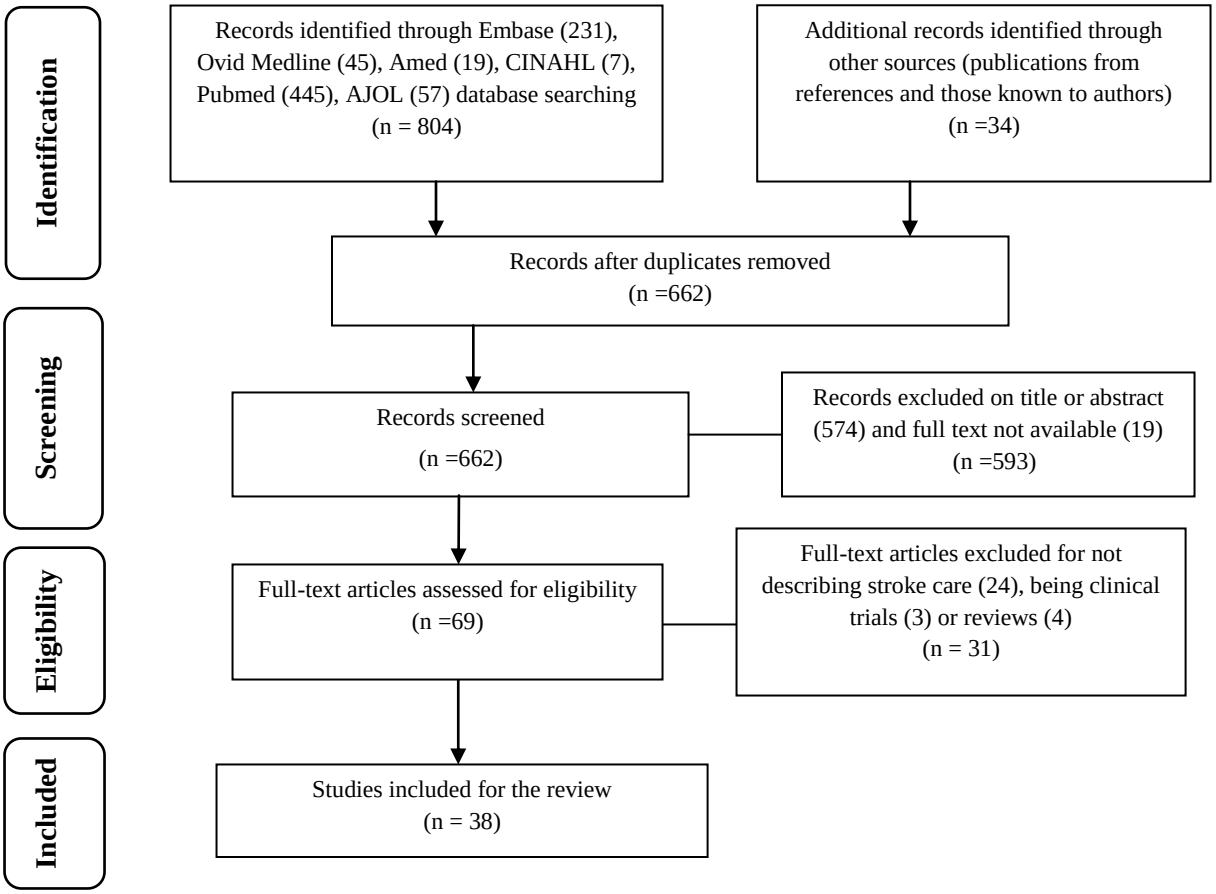
2.2.6 Data analysis

I anticipated that there would be limited, and heterogeneous data identified. Therefore, I planned to use a narrative synthesis to summarise the information from the included studies. Information was reported according to the phase of patient journey as conceptualized by the WSO framework (Lindsay et al., 2014).

2.3 Results

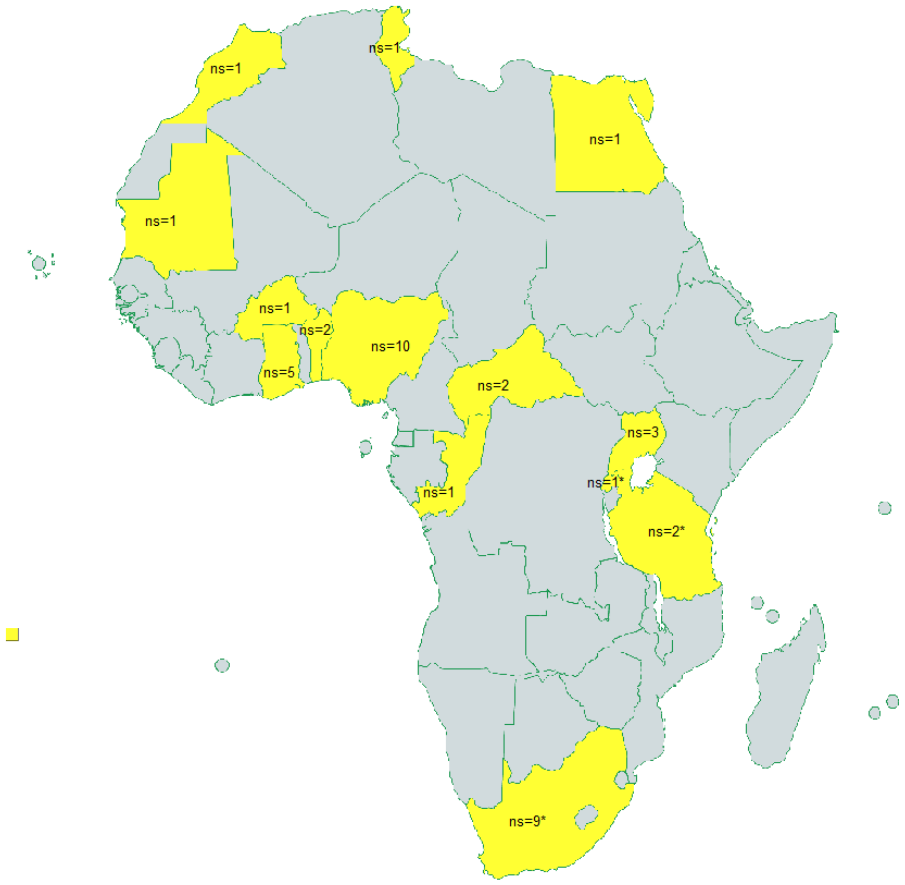
The review profile is shown in Figure 2.1. I identified 838 references from which 38 publications (16-53) were eligible for my review following de-duplication and screening.

Figure 2. 1: Review profile showing selection of studies reporting on stroke care in Africa



The included publications represent 14/54 African countries from all the main regions (east, west, central, north, and south) (Figure 2.2).

Figure 2. 2: African map showing countries (in yellow) with included publications on stroke care in Africa



Abbreviation: ns, number of studies.

*One study (Rhoda et al., 2015) was conducted in three countries including Rwanda, South Africa and Tanzania.

The data ranged from 2008 to 2017, with most (24/38) published between 2013 and 2017. The publications included single and multi-site studies with varying numbers of participants (from 1 (Ellenga-Mbolla et al., 2013) to 15,155 participants (Cossi et al., 2012b)). Nigeria and South Africa provided 10 (27.8%) and 9 (25.0%) of the selected publications, respectively. The majority (30/38) of the studies were conducted in urban hospitals or urban communities. Two publications (Diagana et al., 2008; Jemaa et al., 2008) were written in French and the remainder were in English. The studies included for the review used different study designs including cross-sectional survey (n=14), prospective follow up (n=13), retrospective approach (n=8), case reports (n=2) and qualitative interviews (n=1). Table 2.1 provides a list of the number of publications with information on each stroke care phase from 2008 to 2017.

Table 2. 1: Availability of information reported by stroke care phase from the publications by year

WSO Template	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Systems for stroke recognition and response	2	2	0	1	3	0	2	3	2	1	16
Hyperacute stroke care	1	1	0	0	1	2	1	2	2	1	11
Acute inpatient care	2	2	0	0	1	0	0	1	1	0	7
Stroke rehabilitation	0	1	0	0	1	2	0	1	0	2	7
Secondary stroke prevention	0	1	0	0	0	0	0	0	1	2	4
Longer-term stroke recovery	0	1	0	0	0	0	0	0	0	0	1

Some publications (Jemaa et al., 2008; Wasserman et al., 2009; Adoukonou et al., 2012; Rhoda et al., 2015; Ossou-Nguiet et al., 2016) provided information on more than one stroke care phase. Only the first and second phases of stroke care were reported in at least a quarter of the included publications. Secondary stroke prevention and longer-term stroke recovery were rarely reported. The reported core elements related to the stroke care phases are summarized in Table 2.2.

Table 2. 2: Stroke care in Africa

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
			Systems for stroke recognition and response		
Mshana et al., 2008	Tanzania	Rural and urban community	80 people	Perception of adequate response to stroke signs and symptoms	In rural area (Hai) where stroke was believed to come from natural causes, hospital treatment was the first option while in urban area (Dar-es-Salaam) where stroke was widely believed to emanate from supernatural causes the first option was traditional healers.
Wahab et al., 2008	Nigeria	Urban hospital	225 patients with hypertension or diabetes	Knowledge of stroke signs and symptoms	The commonest sign identified was sudden unilateral limb weakness (24.4%), and 136 (60.4%) of the participants had no knowledge of any warning sign. Male sex and higher education were independently associated with better knowledge
Akinyemi et al., 2009	Nigeria	Urban hospital	370 hospital workers	Knowledge of stroke signs and symptoms and perception of adequate response	Weakness on one side (61.9%) was the most commonly identified warning symptom, and 8.6% of the participants could not identify a single warning symptom. Hospital treatment (61.1%) was the most preferred option while 13% of the participants preferred spiritual healing. Higher level of education was significantly associated with better stroke knowledge and perception.
Wasserman et al., 2009	SA	Rural hospital	1 hospital	Availability and accessibility of stroke care resources	In 2007, at Mosvold Hospital (rural), there were 13 doctors and 59 professional nurses, 4 PTs, 1 OT, 1 ST, 1 dietician and 2 social workers only for a municipality with a population of 184 049. These staff were responsible for managing 49 000 outpatients annually, and admitting 9400 patients per year, whose average stay was 7 days. Basic radiography and ultrasound were available, but no CT scanner. The nearest referral facility with a CT scanner was 3 hours' drive away.
Gould et al., 2011	Ghana	Urban hospital	2 hospitals	Initiative to support stroke unit establishment	There was no stroke unit in Ghana, but a collaborative partnership between staff from England and Ghana was initiated to review and plan local services and provide multidisciplinary education and training with a goal of establishing the Ghana's first stroke unit.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
			Systems for stroke recognition and response		
Adoukonou et al., 2012	Benin	Urban hospitals (n=2)	2 hospitals	Availability and accessibility of stroke care services	There were 2 neurologic departments only in Benin (one in Cotonou and the other in Parakou) for a population of 9 million. There were 3 CT scanners only, and none of 2 existing neurologic departments could conduct vascular sequences. In Parakou as example, there was also shortage of staff in all healthcare domains, and the costs for diagnostic exams such as CT scan ($100 USD) was high, and awareness of early stroke symptoms was very poor. For improvement, evidence-based accessible multidisciplinary care pathways for stroke management were set up, and there were public campaigns related to stroke awareness.
Chin, 2012	Uganda	Urban hospital	1 hospital	Availability and accessibility of stroke care services	Patients were brought to the emergency room by family members. Many patients presented to hospital several days or more after stroke onset and travelled long distances by public transportation. There was only one government health facility in the whole country that had a CT scanner, but there was no MRI unit or equipment for contrast angiography. The cost for a brain CT was approximately $60 USD. For those who could afford a CT scan, additional diagnostic tests (EKG, carotid ultrasound, and echocardiogram) were usually not affordable. Thrombolytics and IV heparin were not available. Neurosurgical consultation was available for emergency decompression of large intracerebral hemorrhages. Inpatient physical therapy services were very limited and basic equipment (quad canes, walkers, wheelchairs) were obtained privately by the patient. Long-term rehabilitation facilities did not exist.
Cossi et al., 2012b	Benin	Urban community	15155 people aged ≥15 years	Knowledge of stroke signs and symptoms and perception of adequate response	The most often cited warning signs were paralysis and hemiplegia (34.4%). A proportion of 27.2% were unable to cite any stroke symptom. A proportion of 94.1% of subjects reported that they would go to a hospital if one of their relatives experienced stroke symptoms while 3.5% said they would wait and let the patient rest. Older age (>40 years), family history of stroke, higher education level, having hypertension, overweight or obesity were independently associated with better knowledge and better reaction to stroke symptoms.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
			Systems for stroke recognition and response		
Donkor et al., 2014b	Ghana	Urban Community	693 people between 18 and 60 years	Knowledge of stroke signs and perception of adequate response	Numbness on one side (44%) was the commonest warning sign cited, and 22% of the participants had no knowledge of any warning sign. The majority (77%) of the participants believed that stroke requires emergency treatment.
Obembe et al., 2014	Nigeria	Urban university	994 (500 students and 494 staff)	Knowledge of stroke signs and symptoms and perception of adequate response	Weakness (66.2%) was the most commonly identified warning sign, and 12.2% of the participants had no knowledge of any warning sign. Predictors for adequate awareness were being female, younger age (< 40 years), and higher education level. Four hundred ninety-three (49.6%) participants indicated that they would take the person to the hospital while 3.2% would seek spiritual attention if a stroke happens near them.
Kaddumukasa et al., 2015	Uganda	Rural and urban community	377 adult people	Knowledge of stroke signs and symptoms	Paralysis (18.3%) was the most commonly identified warning sign of stroke, and 215 (57%) had no knowledge of any warning sign. Urban residence and knowing that stroke is preventable were independently associated with better awareness of stroke warning signs.
Komolafe et al., 2015	Nigeria	Urban secondary schools (n=4)	703 (589 students and 114 teachers)	Knowledge of stroke signs and symptoms and perception of adequate response	Weakness (51.9%) was the most commonly identified warning sign of stroke, but 23.7% of the teachers had no knowledge of any warning sign. Better awareness of warning signs was associated with having had stroke in the family and being hypertensive. Four hundred ninety-three (41.4%) participants indicated that they would take the person to the hospital while 20 (2.8%) participants indicated that they would seek spiritual attention if a stroke happens near them.
Nel and Stassen, 2015	SA	Four urban emergency stations	40 Ambulance personnel	Ability to recognize stroke signs and symptoms and identify stroke	The combined sensitivity and specificity were 91.5% and 92.0% respectively.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
			Systems for stroke recognition and response		
Burton, 2016	SA	Nationwide	-	Initiative to support stroke unit establishment	Stroke experts from different countries spoke at the meeting sessions organized by South African team during October 2014-October 2015, and neurologists and neurology registrars with much experience in European stroke units led the scheduled training sessions. By December 2015, 17 new stroke units were initiated, and many more were expected to join later. There was a challenge whereby the Ministry of Health was unwilling to support a project to start stroke units, focusing on a single non-communicable disease. Starting up a stroke unit focused on formation of stroke teams, distributing post stroke care protocol templates, and trainings on stroke care by led by international experts. There was also selection of site champions. These were staff enthusiastic about improving care, and who could help organise meetings and training sessions.
Shehata et al., 2016	Egypt	Urban Cairo University Hospitals	111 hospital workers	Knowledge of stroke signs and symptoms and perception of adequate response	The most common identified stroke symptoms were slurring of speech (38.5%) and elevated blood pressure (38.5%), but 12% of the participants did not know any symptom. The most frequent response to an attack of stroke was transferring the patients to a hospital (59.8%) while 1.1% preferred calling a religious person. Clinical workers were more likely to identify the stroke symptoms compared with nonclinical workers.
Baatiema et al., 2017	Ghana	Hospital	11 major referral hospitals	Availability of stroke care services and Health policies for stroke care	One hospital had a stroke unit, but thrombolytic therapy using rtpA for ischemic stroke (IS) care was not available in any of the study hospitals. Although eight study sites reported having a brain CT scan, only 7 (63.6%) were functional at the time of the study. MRI scan services were also limited to only 4 (36.4%) hospitals (only functional in three). Acute stroke care by specialists, especially neurologists, was found in 36.4% (4) of the study hospitals whilst none of the study hospitals had an OT or a ST. There was no direct health policy support from the state or national level for stroke care, or a national stroke policy framework, or national stroke clinical guideline existed. There were some broad policies on health care improvement, non-communicable diseases and staff professional development, but these were not being implemented due to lack of funds.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
				Hyperacute stroke care	
Jemaa et al., 2008	Tunisia	Urban hospital	203 patients	Time from stroke onset to hospital arrival and time from stroke onset to CT Scan	Only 17.3% used medical ambulance transport. Arrival to emergency time mean was 16h (median=4h), and arrival to emergency within 3h rate was 42.9%. Early arrival to emergency was associated with urban residence and having motor deficit or higher NIHSS score. Stroke onset-access to CT interval mean was 19h07' (median= 8h45'), and access to CT within 3h and 24 h rate was 13.3% and 77.8% respectively. The waiting time mean for CT scan access was 3h. Early access to CT was associated with subarachnoid hemorrhage.
Wasserman et al., 2009	SA	Rural hospital	30 patients	Time from stroke onset to hospital arrival and access to CT scan	Mean delay of almost 2 days from symptoms onset to presentation at hospital; only 4 (13.3%) had CT brain scans.
Owolabi and Nagoda, 2012	Nigeria	Urban hospitals (n=2)	273 patients	Time from stroke onset to hospital arrival and access to CT/MRI Scan	Only 20.1% and 28.9% of the participants presented before 3h and within 6h of stroke onset respectively. The main reasons for delay included delay referral from private hospital (49.1%), transportation problem (32.2%), prior visit to traditional homes (10.6%) and treatment at home (7%). Only 36.3% and 2.2% had CT and MRI scans respectively, and of these, only 32.3% had imaging within 24 hours.
Ellenga-Mbolla et al., 2013	Congo Brazzaville	Urban hospital	1 patient	The first ever thrombolysis	The first ever thrombolysis with tenecteplase in Congo Brazzaville was indicated and performed by a neurologist and the CT scan performed at 24 hours did not show bleeding.
Ossou-Nguiet et al., 2013	CAR	Urban hospital	1680 patients	Access to CT scan and its impact	Between 2006 and 2011, there was a significant increase in CT scan completion rate which was 5.81% in 2006 versus 93.68% in 2011 (OR: 15.4, CI: 8.2-29.4), a significant increase in cases of cerebral hemorrhage between 2006 and 2011 (OR: 5.21, CI: 2.6-17.3), and a decrease in mortality (OR: 2.41, CI: 1.4-8.2).
Ekeh and Isamade, 2014	Nigeria	Urban hospital	128 patients	Time from stroke onset to hospital arrival	Only 10.2% presented in 3h; 17.2% presented more than one week after stroke onset.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
				Hyperacute stroke care	
Ogbole et al., 2015	Nigeria	Urban hospital	83 patients	Time from stroke onset to CT Scan	Mean presentation time for CT scan was 70 h with a median time of 24 hours. None presented for CT scan within 3 hours, and only 31.3 % and 54% presented within 12h and 24h respectively after stroke onset. IS was associated with higher presentation delay.
Philip-Ephraim et al., 2015	Nigeria	Urban hospital	81 patients	Time from stroke onset to hospital arrival	Only 17 (21%) of the patients arrived at the hospital within three-hours of stroke onset, while 53 (65.4%) patients arrived >24 h after symptom onset. None of the patients were brought by ambulance service. Only lack of awareness of the symptoms of stroke was independently associated with delayed presentation.
Chtaou et al., 2016	Morocco	Urban hospital	52 patients	Stroke onset/door-to-needle time for thrombolysis	Seventeen of 52 patients were treated within a 3 hours window of stroke onset and 35 of 52 patients were treated within 3-4.5 h. The mean door-to-needle time was 1h15 minutes while the mean onset-to treatment time was 3h32 minutes.
Ossou-Nguiet et al., 2016	CAR	Urban hospital	737 patients	Proportion of IS patients treated with thrombolysis	Twenty six of 464 patients with IS were eligible for IV rt-PA, but none was thrombolysed because of the high cost of rt-PA, and Congolese patients had to pay themselves before all treatment.
Napon et al., 2017	Burkinafaso	Urban hospital	227 patients	Route and time from stroke onset to hospital arrival, time from stroke onset to CT Scan, and access to thrombolysis	The time between the stroke onset and the first contact with the first health facility ranged between 30 min and 24 h with an average of 6 h and 56 min and the one between first health facility and medical emergency ranged between 15 min and two weeks. Patients spent on average 2 days (41 h 48 min) in the first health facilities, with no CT scans or neurologist there. After their arrival in medical emergency, patients spent on average 21 h and 18 min to achieve the cerebral CT scan. Thrombolysis was not available yet while 19% of patients were eligible according to the 4h30mn period.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
				Acute inpatient care	
Diagana et al., 2008	Mauritania	Urban hospital	82 patients (42 for neurology unit and 40 for internal medicine and cardiology unit)	Impact of acute admission unit	Stroke onset-CT scan interval: 3.12 for neurology unit versus 3.73 days for internal medicine and cardiology unit; stroke onset-hospitalization interval: 2.05 for neurology unit versus 1.36 days for internal medicine and cardiology unit; stroke onset-rehabilitation start interval: 9.11 for neurology unit versus 19.53 days for internal medicine and cardiology unit (p=0.0002); there was more 3-month functional independence improvement for the neurology unit admission (59.52%) than the internal medicine and cardiology unit admission (25%) (p=0.001).
Jemaa et al., 2008	Tunisia	Urban hospital	203 patients	Time from stroke onset to admission	Time onset-admission mean was 29h23' (median= 15h), and only 1% of patients were admitted within 3 h from stroke onset.
de Villiers et al., 2009	SA	Urban hospital	195 patients	Impact of stroke unit admission (n=101) compared to general ward admission (n=94)	Inpatient mortality decreased from 33% to 16% (P=0.005); LoS increased from a mean of 5.1 days to 6.8 days (P=0.01), referral at discharge to inpatient rehabilitation increased from 5% to19% (P=0.04). Number of CT scans performed (13% GW versus 16% SU) and the number of referrals to the tertiary academic hospital (7% GW versus 4% SU) did not increase significantly.
Wasserman et al., 2009	SA	Rural hospital	30 patients	Acute admission, family education, and discharge planning	Mean duration of hospital stay was 6 days. Two-thirds of all families received no stroke education before discharge. All the patients were discharged into family care as there was no stroke rehabilitation facility available to the community.
Adoukonou et al., 2012	Benin	Urban hospitals (n=2)	122 patients	Time from stroke onset to admission	In 2011, only 17.2% of 122 patients were admitted within 3 hours of stroke onset.
Rhoda et al., 2015	Rwanda, SA and Tanzania	Hospitals (n=3)	452 patients	Time from stroke onset to admission	Time onset-admission interval was 6.8, 0.3 and 1.2 days and the length of hospital stay (LoS) was 8.2, 7.38 and 12.16 days for Rwanda, SA and Tanzania respectively.
Ossou-Nguiet et al., 2016	CAR	Urban hospital	737 patients	Impact of stroke unit admission	During the first year (2004) of stroke unit admission, there was 30% mortality rate decrease compared to the previous year.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
				Stroke rehabilitation	
Rhoda et al., 2009	SA	Urban Community Health Centres (n=20)	100 patients	Rehabilitation services received	At two months post stroke, most participants were treated by PT (98.8%) and medical doctor (62.5%), and only 25% were treated by OT. At six months also, many participants were treated by PT (57.9%) and medical doctor (82.9%), and only 21.1% were treated by OT. Surprisingly, at both two and six months, less than 10% of the participants were treated by any of other rehabilitation team members including ST, home-based carer, nurse, social worker, dietitian, rehabilitation worker, and other rehabilitation specialists. By six months post stroke, the majority (68%) of the participants received between one and 5 physiotherapy sessions. Almost half (49%) of the participants received between one and four hours of physiotherapy.
Ntsiea et al., 2012	SA	Rehabilitation facilities	36 facilities	Practice in return to work (RTW) intervention programmes	Seventeen clinical settings referred patients to facilities offering RTW services, and seven facilities offered RTW services. Of the seven facilities that rendered post stroke RTW services, five communicated with the employer to discuss reasonable accommodation and four did assessments for potential to RTW. The most common reasons given by the 29 facilities for not offering RTW services were that they referred patients to other therapists who offered these services, staff shortage, and the unemployed status of the patient at the time of having stroke.
Joseph and Rhoda, 2013	SA	Urban rehabilitation centre	67 patients	Rehabilitation services received and outcomes	LOS was 52 days. Health professionals seen by patients were nurse (100%), doctor (98.48%), PT (98.48%), social worker (96.96%), OT (95.45%), ST (54.54%), dietitian (16.66%), psychologist (10.60%). Discharge destination was mainly home (82.08%). The mean Barthel Index scores on admission and discharge were 58.85 and 81.59 respectively ($p<0.01$).
Ntamo et al., 2013	SA	Rural hospital	103 patients	Rate of attendance to outpatient physiotherapy services	The majority (86%) of patients did not attend out-patient physiotherapy. The major reasons for poor attendance were lack of finances (95%), migration to other areas (36%), and living a long distance from the hospital (38%).
Rhoda et al., 2015	Rwanda, SA and Tanzania	Hospitals (n=3)	452 patients	Inpatient PT rehabilitation	A proportion of 40%, 68% and 98% of stroke patients in Rwanda, Tanzania and SA respectively received PT rehabilitation during acute hospital stay.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
			Stroke rehabilitation		
Olaleye et al., 2017	Nigeria	Urban hospitals (n=3)	60 patients	Satisfaction with outpatient physiotherapy services	Nearly all the participants (98.3%) indicated one of good, very good, and excellent improvement in their clinical conditions with physiotherapy. Majority expressed satisfaction with their physiotherapy care, the modal response being very good (59.3%). However, lack of continuity (being treated by different physiotherapists) and cost of care were sources of dissatisfaction.
Olaleye and Lawal, 2017	Nigeria	Urban hospital	783 patients	Inpatient PT rehabilitation	The mean LoS was 16.2 days. Referral rate for PT was high (75.8%) and the mean time from admission to referral for PT was three days. The majority (63.4%) of patients referred utilised PT and the mean number of PT sessions received during in-patient care was 8.7. Utilisation of in-patient PT was significantly associated with reduced LoS.

Table 2. 2: Stroke care in Africa ***Continued***

Study reference	Country	Study setting type	Sample	Key element(s) investigated	Main results
				Secondary stroke prevention	
Wasserman et al., 2009	SA	Rural hospital	30 patients	Rate of adherence to secondary prevention	At three months after discharge follow up, all patients claimed to be taking their antihypertensive medication but 11 (55%) of those who had been prescribed aspirin admitted to defaulting.
Mugwano et al., 2016	Uganda	Urban hospitals (n=2)	112 patients	Rate of adherence to secondary prevention	Only 17% were highly compliant with anti-hypertensive medications. The main reasons for poor drug adherence were lack of knowledge of the chronicity of hypertension (73%), cost of the drugs (63%) and access to health care provision (15%). However, 19% of the study participants were not able to provide a reason for the poor drug adherence.
Sarfo et al., 2017a	Ghana	Urban clinic	418 patients	Rates and determinants of persistent utilization of secondary prevention therapies	At one-year post stroke, 92.1% of subjects were persistent on secondary prevention medications initiated at enrollment with medication class specific rates of 97.5% for antihypertensive, 94.8% for anti-platelets, 94.1% for statins, 85.7% for anti-diabetic and 50% for anticoagulants. Abuse of alcohol was significantly associated with non-persistence, adjusted OR (95% CI) of 3.08 (1.13–8.38).
Sarfo et al., 2017b	Ghana	Urban clinic	602 patients	Rates and determinants of uncontrolled systolic blood pressure (SBP)	At one-year post stroke, up to 35% of subjects had SBP above 140 mmHg during follow-up clinic visits. Predictors of uncontrolled SBP were SBP at enrollment into clinic, with an adjusted odds ratio (OR [95% confidence interval (CI)]) of 1.31 (1.17-1.47)/10 mmHg increase, and average number of antihypertensive medications prescribed, with an adjusted OR (95% CI) of 1.30 (1.06-1.60).
				Longer-term stroke recovery	
Wasserman et al., 2009	SA[28]	Rural hospital	30 patients	Training of home-based carers (HBCs)' and patients' follow-up in community	The HBCs received no specific stroke care training. Each carer travelled about 7 km each day on foot or bicycle to conduct home visits. In three months after discharge, only 13 of 20 (65%) surviving patients were visited by home-based carers, nine patients were visited by a physiotherapist, and 2 could consult a social worker during this period.

Abbreviations: CAR, Central African Republic; CT, computerized tomography; EKG, electrocardiogram; IV, intravenous; LOS, length of hospital stay; MRI, magnetic resonance imaging; OT, occupational therapy(ist); PT, physiotherapy(ist); rtpA, recombinant tissue plasminogen activator; SA, South Africa; ST, speech therapist.

2.3.1 Systems for stroke recognition and response

The main core elements related to systems for stroke recognition and response were knowledge of stroke signs and symptoms, perception of adequate response to stroke signs and symptoms, availability and accessibility of stroke care policies and services.

Regarding the awareness about stroke signs and symptoms, the greatest proportion of participants who knew any of the established stroke signs and symptoms ranged between 18% for paralysis in Uganda (Kaddumukasa et al., 2015) and 66% for weakness in Nigeria (Obembe et al., 2014). The most preferred response to stroke signs and symptoms (range: 41%-94%) was bringing the patient to the hospital (Akinyemi et al., 2009; Obembe et al., 2014; Donkor et al., 2014b; Komolafe et al., 2015; Shehata et al., 2016), but some participants, between 1-13%, identified seeking spiritual intervention as the first option (Akinyemi et al., 2009; Cossi et al., 2012b; Obembe et al., 2014; Komolafe et al., 2015; Shehata et al., 2016). In several studies, higher education level was significantly associated with better knowledge (Wahab et al., 2008; Akinyemi et al., 2009; Cossi et al., 2012b; Obembe et al., 2014) of, and better response (Akinyemi et al., 2009; Cossi et al., 2012b) to, stroke signs and symptoms.

Gaps were reported in the availability of stroke care services with variations across countries and settings. The areas in which shortage was commonly reported included medical transportation (Jemaa et al., 2008; Chin, 2012; Owolabi and Nagoda, 2012; Philip-Ephraim et al., 2015), CT and MRI scanning machines (Wasserman et al., 2009; Adoukonou et al., 2012, Chin, 2012; Baatiema et al., 2017), stroke units (Gould et al., 2011; Baatiema et al., 2017), thrombolysis (Chin, 2012; Baatiema et al., 2017; Napon et al., 2017), inpatient and long-term rehabilitation services (Chin, 2012), and healthcare personnel in overall number and specialties (Wasserman et al., 2009; Adoukonou et al., 2012; Baatiema et al., 2017; Napon et al., 2017).

The high cost of infrastructure resources where they exist such as CT scanners (Adoukonou et al., 2012, Chin, 2012; Ossou-Nguiet et al., 2013), medications such as thrombolysis (Ossou-Nguiet et al., 2016), and outpatient physiotherapy rehabilitation services (Olaleye et al., 2017) were reported as major barriers for stroke care in Africa. In addition, a study from Ghana (Baatiema et al., 2017) identified the lack of direct regional or national health policy to support

stroke care, including a lack of a national stroke policy framework and national stroke clinical guidelines.

2.3.2 Hyperacute stroke care

The most common elements related to hyperacute stroke care reported included time from stroke onset to hospital arrival and patient access to CT/MRI brain imaging (Jemaa et al., 2008; Wasserman et al., 2009; Owolabi and Nagoda, 2012; Ellenga-Mbolla et al., 2013; Ossou-Nguiet et al., 2013; Ekeh and Isamade, 2014; Philip-Ephraim et al., 2015; Ogbole et al., 2015; Chtaou et al., 2016; Ossou-Nguietet al., 2016; Napon et al., 2017).

Several publications consistently identified that patients with stroke in Africa were late in arriving to hospital. The highest reported proportion of stroke patients who arrived at hospital within three hours from stroke onset was 43% in Tunisia (Jemaa et al., 2008) while the lowest proportion (10%) was reported in Nigeria (Ekeh and Isamade, 2015). The reported proportions of stroke patients who received CT brain imaging within three hours of stroke onset varied between 0% (35) and 13% (Jemaa et al., 2008), and where operational CT/MRI scan machines existed, the reported proportion of patients who received CT/MRI brain imaging varied between 13% (Wasserman et al., 2009) and 36% (Owolabi and Nagoda, 2012).

2.3.3 Acute inpatient care

The main core elements related to acute inpatient care for stroke patients that were reported included the time from stroke onset to hospital admission, and access to stroke units (Diagana et al., 2008; Jemaa et al., 2008; de Villiers et al., 2009; Wasserman et al., 2009; Adoukonou et al., 2012; Rhoda et al., 2015; Ossou-Nguiet et al., 2016).

The interval between time of stroke onset and hospital admission varied between 7.2 hours and 6.8 days (Diagana et al., 2008; Rhoda et al., 2015), with a median of 1.3 day. Few patients, 1% in Tunisia (Jemaa et al., 2008) and 17% in Benin (Adoukonou et al., 2012), were reported to have been admitted within three hours of stroke onset. Regarding access to stroke units, South Africa was reported to have 21 stroke units (Burton et al., 2016), and the only other countries reported to have a stroke unit were Ghana (Baatiema et al., 2017) and the Central African Republic (Ossou-Nguiet et al., 2016). Two studies (de Villiers et al., 2009; Ossou-Nguiet et al., 2016) included in my review reported that stroke unit admission was associated with a decrease in inpatient mortality rate of 17-30%.

2.3.4 Stroke rehabilitation

The proportion of patients reported to receive inpatient physiotherapy rehabilitation was greatest in South Africa (98%) and smallest in Rwanda (40%) (Rhoda et al., 2015). A South African publication describing access to outpatient physiotherapy rehabilitation (Ntamo et al., 2013) identified low attendance rates (14%) as being associated with lack of finances (95%), patient migration to other areas (36%), and living a long distance from the hospital (38%) (Ntamo et al., 2013). In a study from Nigeria (Olaleye et al., 2017) the majority (59%) of patients were highly satisfied with outpatient physiotherapy services, however the high cost of these services and lack of continuity of care were sources of dissatisfaction.

Three South African studies (Rhoda et al., 2009; Ntsiea et al., 2012; Joseph and Rhoda, 2013) reported information on rehabilitation after discharge from the acute inpatient settings. It appeared that patients treated in a specialized rehabilitation facility received a variety of rehabilitation services from medical doctors, nurses, physiotherapists, social workers, occupational therapists, and speech therapists, although few of them received dietetics (17%) or psychology (11%) services (Joseph and Rhoda, 2013). In contrast, services offered in community health centres were mostly limited to physiotherapy and medical rehabilitation services (Rhoda et al., 2009).

2.3.5 Secondary stroke prevention

A retrospective observational study (Sarfo et al., 2017a) involving 418 stroke survivors enrolled into a neurology clinic in Ghana showed that, at one-year post stroke, 92% of subjects were persisting with secondary prevention medications. However, in two publications (Wasserman et al., 2009; Mugwano et al., 2016) included in my review, evidence of poor compliance with secondary prevention medications was reported. In one study (Wasserman et al., 2009) of stroke survivors living in a rural South African community who were prescribed aspirin for secondary prevention, 9/20 (45%) reported taking this medication at three months post stroke. In a similar study conducted in Uganda (Mugwano et al., 2016) which involved 112 participants, only 17% were adhering to anti-hypertensive medications as prescribed. The main reasons for poor drug adherence were lack of knowledge of the chronicity of hypertension (73%) and cost of the drugs (63%). Other factors that were reported to be associated with poor compliance with secondary prevention medications were alcohol abuse

Sarfo et al., 2017a) and average number of antihypertensive medications prescribed (Sarfo et al., 2017b).

2.3.6 Longer-term stroke recovery

Regarding longer-term stroke recovery, many challenges were identified in a South African study (Wasserman et al., 2009). Three months post stroke, 20 survivors living in a rural community had no access to a rehabilitation facility and did not get support from government or local authorities, leaving the responsibility to some local non-governmental organizations which also had limited resources to provide stroke survivors support.

2.4 Discussion

Overall, very few studies on stroke care have been published about the vast continent of Africa, and only one study (Wasserman et al., 2009) included information on longer-term stroke recovery. From the available data, I identified only a small proportion of patients with stroke that arrived at a hospital within three hours from symptom onset (Jemaa et al., 2008; Ekeh and Isamade, 2014) and, consequently, less than 20% (Jemaa et al., 2008; Adoukonou et al., 2012) of patients were admitted within three hours of stroke onset. Studies from other non-African LMICs showed a similar delay (Nandigam et al., 2003; Ghandehari et al., 2009). Late presentation to hospital has been reported to be associated with poor awareness of stroke signs and symptoms, late referral from private hospitals, transportation problems, visit to traditional healers before coming to hospital, and treatment at home (Owolabi and Nagoda, 2012; Philip-Ephraim et al., 2015). These were also identified in my review. Delays in presentation to hospital prevent patients from benefiting from emergency interventions such as brain imaging and thrombolysis for IS among others. Also, although diagnostic CT or MRI scan imaging is important when antithrombotic treatments are being considered, my review showed that the CT/MRI brain imaging services were rare or too expensive for many patients in Africa (Wasserman et al., 2009; Owolabi and Nagoda, 2012). My review showed that no patients in a Nigerian hospital (Ogbole et al., 2015) and only 13% of stroke patients in Tunisia (Jemaa et al., 2008) received a CT scan within three hours of stroke onset. This is a major barrier to meet the recommended standard of thrombolysis for IS within four and half hours of stroke onset (Lindsay et al., 2014).

Despite the evidence that thrombolysis can improve outcome in ischaemic stroke (The IST-3 collaborative group, 2013), my review indicates that intravenous thrombolysis remains 'a desirable dream' in many African countries (Ossou-Nguiet et al., 2016; Napon et al., 2017). This finding was consistent with the results of a survey (Wintermark et al., 2015) whereby none of the African centres surveyed in 2012 administered acute revascularization therapy to patients with acute stroke. In another systematic review (Berkowitz et al., 2014) only 3% of low-income countries were found to use thrombolysis for acute IS. The most important barrier of thrombolysis therapy in Africa, as in other low-income countries, is reported to be cost (Owolabi and Nagoda, 2012; Ossou-Nguiet et al., 2016). This emphasizes the need for governments and health systems of developing countries to develop strategies to enhance accessibility to thrombolysis.

Despite the available evidence for the benefits associated with stroke unit admission, the stroke unit model for stroke care appeared to be rare in Africa. In fact, collectively I identified that there were only 23 stroke units from the available publications I reviewed. Fortunately, there is the intention for the establishment of more stroke units in Africa in the next few years (Gould et al., 2011; Burton et al., 2016).

The WSO recommended early adequate rehabilitation to reduce the social and economic costs related to long-term care (Lindsay et al., 2014). However, it appeared that only medical and physiotherapy rehabilitation services are common in Africa (Joseph and Rhoda, 2013; Rhoda et al., 2015; Baatiema et al., 2017), and that the physiotherapy services are accessible to a limited number of patients. We need to address the identified barriers for inpatient and outpatient physiotherapy rehabilitation including high cost, geographical inaccessibility and lack of continuity of care.

While aspirin and antihypertensive drugs were found to be associated with lower risk for stroke recurrence (PROGRESS Collaborative Group, 2001; van Gijn and Algra, 2003), my review findings indicated poor compliance with secondary prevention anti-hypertensive medications in Uganda (Mugwano et al., 2016) and aspirin in South Africa (Wasserman et al., 2009) most likely because of cost and lack of knowledge about the risk of stroke recurrence. This challenge should be addressed in education sessions for stroke patients and their caregivers.

Other important challenges that were raised were shortage or high cost of medical transportation, brain imaging infrastructure, stroke units, and healthcare personnel (Jemaa et al., 2008; Wasserman et al., 2009; Adoukonou et al., 2012; Chin; Owolabi and Nagoda, 2012; Ossou-Nguiet et al., 2013; Philip-Ephraim et al., 2015; Baatiema et al., 2017; Napon et al., 2017). To address this gap, politicians in most African countries need to invest in stroke care by developing and implementing direct health policies for stroke, training and staffing key rehabilitation professionals, making available and accessible the appropriate infrastructure, equipment and medications for quality stroke care, building national insurance systems to reduce the cost for care (Mills, 2014), and establishing partnerships with international experts to improve stroke care in African countries as they appeared to be effective in South Africa (Burton, 2016).

Strengths and weaknesses

To the best of my knowledge, this is the first review on delivery of stroke care with focus on Africa. It provides a systematic, up-to-date overview of the available data on this topic. I searched a range of relevant databases, with no language restriction. Additionally, data from eligible publications were extracted and analysed based on the WSO Stroke services Framework (Lindsay et al., 2014) while the review report is based on the PRISMA guidelines. However, my review may well be subject to publication bias as only the electronic databases and references were considered. Furthermore, the investigators of the identified studies were not contacted to confirm data. Among the studies that were considered for my review, nine were retrospective and the shortcomings of this study design needs to be considered when interpreting the results. Furthermore, most of the publications were conducted in cities, and some of them were single studies and generalisability to rural settings or whole countries is limited. Therefore, national or regional prospective observational studies on the provision of stroke care in African countries are needed. The lack of data from many African countries is also a limitation and highlights the urgent need to establish systems of routine and reliable data monitoring across this continent. Finally, there were limited data on important phases of stroke care including secondary prevention and longer-term recovery. More studies about these two phases are required.

2.5 Conclusion

Overall, the reported provision of stroke care in Africa is below the recommended standards with variations across countries and settings. Combined efforts from policy makers and health care professionals in Africa are needed to ensure greater access to essential infrastructure such as stroke units. More high-quality studies are needed to inform how to establish infrastructure in African settings where there are limited resources and diverse socio-cultural contexts. Mechanisms to routinely monitor usual care (i.e. registries or audits) would be invaluable to inform policy and practice.

Chapter 3: Key performance indicators of quality stroke care and their association with patient outcomes: a systematic review of the literature and meta-analysis

3.1 Introduction

The previous two chapters have outlined the increasing burden of stroke in Africa and the need to develop services to respond to this burden of disease. There are major challenges to design and deliver service initiatives and also to measure and monitor their progress in improving the quality of care. In recent years there have been concerted efforts to develop and implement clinical practice guidelines for the management of patients with acute stroke (Adams et al., 2003). Clinical guidelines are written to promote diagnostic or therapeutic interventions applicable to the majority of patients in most circumstances. However, the use of guideline recommendations for individual patients has traditionally been left to the discretion of individual clinicians (American Heart Association, 2000). A recognised approach to assist the translation of research evidence into clinical practice is to monitor the quality of care using standardized performance indicators (Grol and Grimshaw, 2003) also called quality indicators, process of care measures or key performance indicators (KPIs). Performance indicators are standards of care that imply that health care professionals are providing inadequate care if eligible patients do not receive that standard of care. Performance indicators can be used to monitor the adherence to current guidelines and support the transfer of new evidence into everyday clinical practice (Grube et al., 2012).

There are now numerous stroke interventions that have been shown to improve patient outcomes in research trials; admission to specialized stroke units, use of intravenous thrombolysis, mechanical thrombectomy, antiplatelet drugs, anticoagulants, and management of fever, hyperglycaemia, and swallowing dysfunction for selected patient groups (Sandercock et a., 2003; Kwan and Sandercock, 2004; Saxena and Koudstaal, 2004; Middleton et al., 2011; Goyal et al., 2016). However, application into routine practice is challenging and regular monitoring is important (Cadilhac et al., 2016). Ideally, implementation of clinical evidence can be demonstrated using a range of stroke KPIs, which offer proxy measures for ideal care being delivered. In turn this would lead to evidence of better patient outcomes (Quality of Care and Outcomes Research in CVD and Stroke Working Groups, 2000).

In a previous systematic review of the association between stroke quality (performance) indicators and patient-centered outcomes, out of 14 studies that met the eligibility criteria; nine had mostly positive associations, whereas five reported little or no association with a lower risk for mortality, disability, medical complications, stroke recurrence, or patient dissatisfaction (Parker et al., 2012). A limitation of that review was the exclusion of stroke unit care as a performance indicator. With the ongoing developments in clinical guidelines and quality indicators for monitoring the application of these guidelines (Reeves et al., 2010; Cadilhac et al., 2016), I believe that there is a need for up-to date comprehensive information on KPIs for stroke care.

I aimed to conduct a systematic literature review to identify the KPIs that have been described in stroke care and to summarise their association with patient outcomes. I intend that information gathered from this review will provide decision makers and health care professionals with information on reliable and meaningful KPIs that can be implemented to improve outcomes post stroke.

3.2 Methods

This review was performed according to the PRISMA guidelines (Moher et al., 2015). This review was registered in Prospero Database (CRD42016050798).

3.2.1 Search strategy

Searching sources were Ovid Medline, Embase and PubMed databases, and relevant references from screening the bibliographies of the initial articles included in the search.
I used Medical Subject Headings (MeSH) and all subheading terms including "stroke", "cerebrovascular accident", "cerebrovascular disease", "cerebrovascular disorders", "brain hemorrhage", "intracranial hemorrhages", "brain infarction", "subarachnoid hemorrhage", "health care quality", "quality of health care" "quality indicators, health care", "quality assurance, health care", "quality control", "quality indicator", "performance indicator", "register", "registries", "clinical audit", "treatment outcome" , "case fatality rate", "mortality", "survival", "disability", "functional status"," hospitalization", "cost", "quality of life", "complication", "hospital discharge" and "stroke recurrence". My search was restricted to full-text manuscripts published in English from January 1st, 2000 to May 24th, 2017.
The search strategies for different databases are detailed in Appendix 3.1.

3.2.2 Inclusion criteria

I included national or regional registers that recorded the independent association (after adjusting for at least age and a measure of stroke severity) between the KPIs and stroke patient outcomes, I anticipated that there could be a wide range of eligible studies, so I limited my review to only those studies that recruited patients from three or more hospitals and thus having an increased external valididy of the results. Due to various inclusion criteria across the eligible studies, I did not limit my literature search to any patient characteristics such as stroke types or age groups. Additionally, based on the aim of my review, there was no restriction to any stroke KPIs or patient outcomes.

3.2.3 Exclusion criteria

I excluded reports that were reviews or did not provide odds ratio (OR), hazard ratio (HR) or rate ratio (RR) data.

3.2.4 Screening and quality assessment

I reviewed each title and excluded obviously irrelevant studies. My primary supervisor and I performed a full review of articles identified as potentially relevant to determine if they met the inclusion criteria. In cases of disagreement, final determination was by discussion and consensus. In the synthesis of the papers, we assessed whether the publications recorded the independent association (after adjusting for at least age and stroke severity) between the KPIs and patient outcomes. However, the quality assessment was not undertaken.

3.2.5 Data extraction

I used a standardized form to record information on country, main inclusion or exclusion criteria for the recruitment of participants, sample size, stroke severity measure, KPIs and outcome(s) reported, and reported results (and 95% CI).

3.2.6 Data analysis

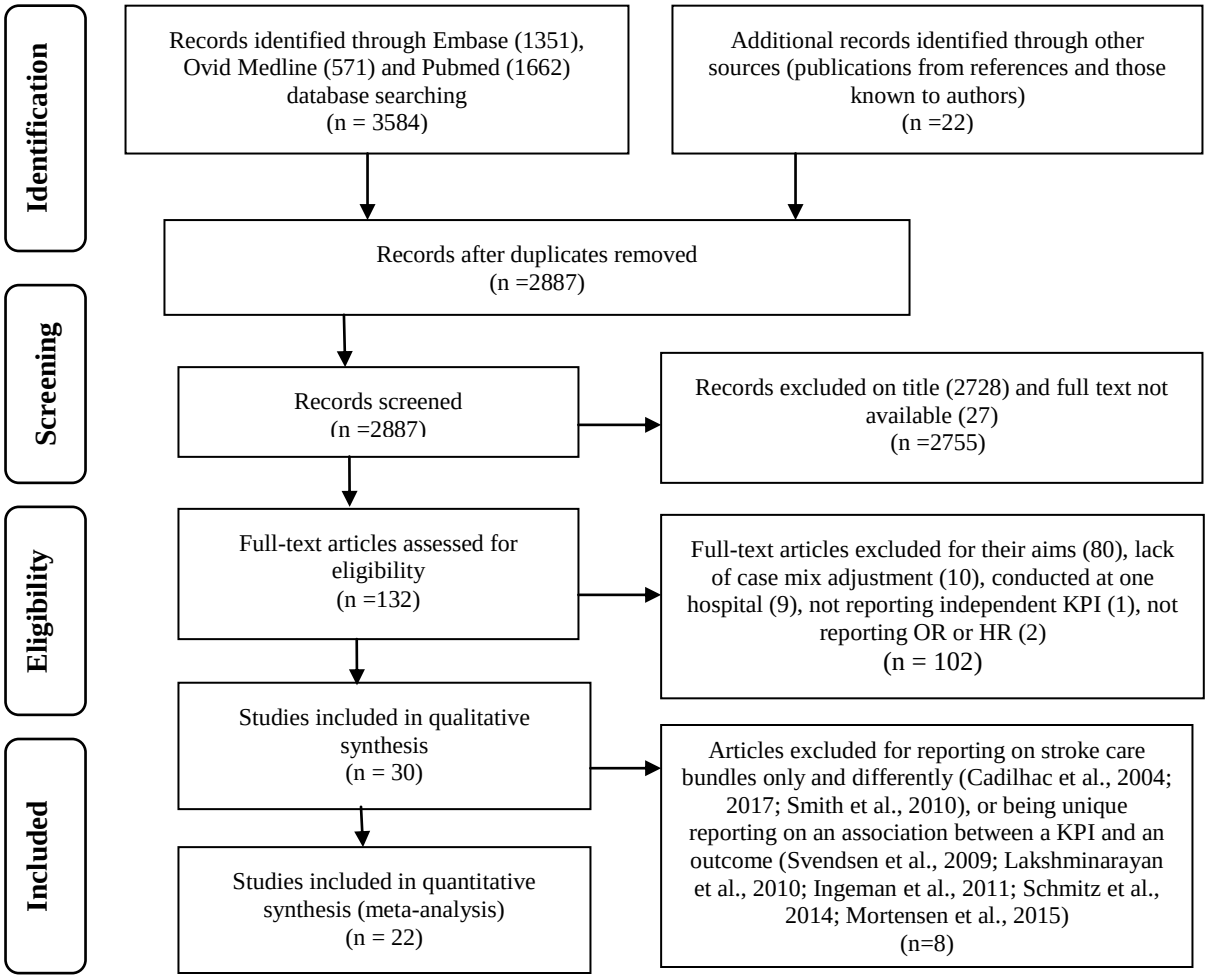
Initially, the identified KPIs and their association with the patient outcomes were categorized on whether the authors reported a significant association between the KPI and patient outcome. There was then a further quantitative analysis (meta-analysis) of the relationship (adjusted for at least age and stroke severity) between the KPIs identified and patient outcomes. Some checking of the consistency of KPIs and outcomes was required with grouping of similar KPIs. For the meta-analysis, I sought information on case fatality and poor outcome (death and disability or requiring support) after stroke.

The meta-analysis was done using the Review Manager (version 5.3) software. Log ORs were combined using an inverse variance analysis (random effects model). First, I assumed that HRs and RRs approximate to ORs and performed the primary meta-analysis including all studies reporting on association of KPIs with case fatality and poor outcome. Second, I performed sensitivity meta-analysis by excluding studies that used HR or RR as measures of association.

3.3 Results

The review profile is shown in Figure 3.1. I identified 3606 references from which 30 studies were eligible for the qualitative review. Among these, only 22 were eligible for the meta-analysis.

Figure 3. 1: Review profile showing selection of studies reporting on stroke KPIs



Abbreviations: HR, hazard ratio; KPI, key performance indicator; OR, odds ratio.

3.3.1 Included studies

Table 3.1 shows the studies considered for my systematic literature review. Most of the included studies (n=15) were conducted in Europe: One European study (Bhalla et al., 2004) was multinational (across ten countries), the rest were conducted in Denmark (n=6), Sweden (n=2), United Kingdom (n=3) (one in England and two in Scotland), Italy (n=1), Spain (n=1), and Greece (n=1). The non-European studies were conducted in the USA, Canada, Chile, Australia, New Zealand, China, Thailand and Taiwan.

Two reports from Denmark (Ingeman et al., 2008; Svendsen et al., 2009) and two from Scotland (Turner et al., 2015a; Turner et al., 2015b) were based on the same datasets but since they provided associations with different outcomes, they were all included in this systematic review.

Table 3. 1: Studies eligible for the systematic literature review

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Glader et al., 2001	Sweden	SAH excluded	Level of consciousness	8194 (All hospitals in Sweden)	Stroke unit (Independent before stroke)	2-year case fatality	0.81	0.72-0.92
						2-year dependency	0.79	0.66-0.94
McNaughton et al., 2003	New Zealand	All stroke types	Age, initial FIM, pre-stroke FIM, and being European	181 (3 hospitals)	Swallowing assessment	1-year Poor outcome (death or moved from home) for swallowing recorded "no"	3.2	0.97-10.7
Bhalla et al., 2004	Europe	SAH excluded	Level of consciousness, incontinence, dysphagia dysphasia and paralysis	1847 (10 countries)	Brain imaging	3-month case fatality	0.7	0.4-1.3
						3-month disability (BI≤18)	1.45	0.39–7.4
					Organized stroke care[a]	3-month case fatality	0.5	0.3-0.8
						3-month disability (BI≤18)	1.3	0.6–1.76
Cadilhac et al., 2004	Australia	SAH excluded	GCS, ability to lift both arms, ability to walk, and urinary incontinence	468 (8 hospitals)	Thorough (n-l≤1) [b] adherence to 15 processes of stroke care [c]	Independent at 28 weeks	1.78	0.93–3.38
						Being at home at 28 weeks	1.69	0.86–3.32
						Alive at 28 weeks	2.10	0.92–4.82
Andersen and Olsen, 2007	Denmark	IS	SSS Scale (SSS)	22179(All Danish hospitals)	Anticoagulants for IS with AF	4-year survival	1.91	1.44-2.52
Candelise et al., 2007	Italy	All stroke types Level of consciousness		11572 (424 stroke units and 260 hospitals)	Stroke Unit	2-year case fatality	0.79	0.68–0.91
						2-year death or disability (mRS>2)	0.81	0.72–0.91
						2-year not living at home	0.85	0.74–0.97

Table 3. 1: Studies eligible for the systematic literature review *Continued*

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Ingeman et al., 2008		SAH excluded	SSS	29573 (40 hospitals)	Specialized stroke unit by 2nd day	90 –day case fatality	0.76	0.69–0.83
					Antiplatelet therapy by 2nd day		0.71	0.62–0.81
					Anticoagulants for IS with AF by 14th day		0.41	0.31–0.52
					CT/MRI scan by first day		1.35	1.24–1.46
					Assessment by a PT by 2nd day		0.81	0.73–0.88
					Assessment by an OT by 2nd day		0.83	0.75–0.91
					Nutritional risk assessment by 2nd d.		0.69	0.61–0.76
					Number of criteria fulfilled			
					1 vs 0		0.94	0.65-1.49
					2 vs 0		0.78	0.54–1.02
					3 vs 0		0.60	0.42–0.78
					4 vs 0		0.61	0.42–0.79
					5 vs 0		0.45	0.31–0.60
					6 vs 0		0.48	0.31–0.65
Saposnik et al., 2008	Canada	IS	CNS	3631 (11 hospitals)	OCI[d] 1 vs 0	1-year case fatality	0.69	0.44–1.09
					OCI 2 vs 0		0.39	0.25–0.62
					OCI 3 vs 0		0.40	0.25–0.64
					Antithrombotic therapy		0.33	0.22-0.50
Ding et al., 2009	China	IS	NIHSS	1951 (23 hospitals in 11 major cities of China)	Antiplatelet therapy for IS	1-year case fatality	0.42	0.21–0.86
						Recurrent cerebrovascular event	0.58	0.36–0.92
						Functional improvement	1.25	1.02–1.52
Milionis et al., 2009	Greece	First-ever acute IS	SSS	794 (Different Athenian hospitals)	Statin at discharge	10 year-Case fatality	0.43	0.29-0.61
						10-year stroke recurrence	0.65	0.39-0.97

Table 3. 1: Studies eligible for the systematic literature review ***Continued***

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Svendsen et al., 2009	Denmark	SAH excluded	SSS	2636 (7 stroke units)	Stroke unit (2nd day)	Prolonged LoS	0.71	0.65–0.77
					Antiplatelet for IS (2nd day)		0.80	0.73–0.87
					Anticoagulant for IS with AF (14th day)		0.78	0.62–0.98
					CT/MRI scan (2nd day)		0.82	0.74–0.91
					PT assessment (2nd day)		0.87	0.81–0.93
					OT assessment (2nd day)		0.85	0.80–0.91
					Nutritional risk assessment (2nd day)		0.83	0.77–0.90
					Swallowing assessment (2nd day)		0.78	0.69–0.87
					Constipation risk assessment (2nd day)		0.70	0.63–0.78
					Mobilization (2nd day)		0.67	0.61–0.73
					Intermittent catheterisation (2nd day)		0.77	0.64–0.92
					DVT prophylaxis (2nd day)		0.82	0.71–0.95
					Percentage of criteria fulfilled			
					25%–49% vs 0%–24%		0.77	0.69–0.86
					50%–74% vs 0%–24%		0.67	0.60–0.75
					75%–100% vs 0%–24%		0.53	0.48–0.59
Åsberg et al., 2010	Sweden	First ever IS cases	ADLs Function	14 529 (All hospitals in Sweden)	Antiplatelet therapy for IS	3-month case fatality	0.83	0.68-1.01
					ACE inhibitors therapy		1.00	0.87–1.14
					Statins Therapy		0.78	0.67–0.91
					Anticoagulants therapy for IS with AF		0.58	0.44–0.76
Bravata et al., 2010	USA	IS	NIHSS	1363 (5 hospitals)	Neurology assessment	In-hospital mortality, discharge to hospice, or discharge to a skilled nursing facility	1.13	0.59-2.17
					Swallowing evaluation		0.64	0.43-0.94
					DVT prophylaxis		0.60	0.37-0.96
					Early mobilization		0.69	0.42-1.14
					Blood pressure management		1.00	0.67-1.50
					Fever management		0.71	0.35-1.41
					Hypoxia management		0.26	0.09-0.73

Table 3. 1: Studies eligible for the systematic literature review *Continued*

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Hsieh et al., 2010	Taiwan	All stroke types	NIHSS	30599 (39 hospitals)	IV tPA for 2 hours	6-momth functional dependency (mRS≥2)	0.52	0.35-0.76
					Antithrombotics at discharge	6-momth risk of cardiovascular events and death	0.41	0.35-0.47
					Anticoagulation for IS with AF at discharge		0.59	0.44-0.80
					Lipid-lowering agents at discharge		0.94	0.78-1.13
Lakshminarayan et al., 2010	USA	All stroke types	Weakness and altered level of consciousness	18017(222 hospitals from 6 States)	Dysphagia screening	Higher risk of pneumonia for no screening	2.15	1.74-2.66
Smith et al., 2010	Canada	IS	CNS	6223 (12 Centres)	OCI[d] 2–3 vs 0–1	30-day case fatality	0.23	0.19-0.28
Ingeman et al., 2011	Denmark	All stroke types	SSS	11757 (10 stroke units in 2 counties)	Early admission to a stroke unit	Any medical complication[e] during admission (LoS=13 days)	0.79	0.68–0.92
					Antiplatelet therapy for IS		0.95	0.79–1.15
					Anticoagulant therapy for IS with AF		0.59	0.45–0.76
					CT/MRI scan		1.52	1.35–1.72
					Assessment by a PT		1.10	0.94-1.28
					Assessment by an OT		1.10	0.94–1.27
					Assessment of Nutritional risk		0.87	0.70–1.07
					Swallowing assessment		0.97	0.84–1.11
					Early mobilization		0.43	0.35–0.53
					Percentage of criteria fulfilled			
					25%–49% vs 0%–24%		0.77	0.67–0.88
					50%–74% vs 0%–24%		0.57	0.46–0.70
					75%–100% vs 0%–24%		0.50	0.36–0.68

Table 3. 1: Studies eligible for the systematic literature review *Continued*

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Abilleira et al., 2012	Spain	SAH excluded	NIHSS	1767 (47 hospitals)	Brain imaging < 24 hours	1-year case fatality risk for noncompliance	1.4	0.71–2.76
					Screening of dysphagia		1.23	0.88–1.71
					Antiplatelets < 48 h for IS		1.3	0.84–2.02
					Early mobilization		1.54	1.05–2.24
					Assessment of rehabilitation needs		1.48	1.06–2.07
					DVT prevention		0.98	0.60–1.60
					Management of hyperthermia		0.67	0.25–1.79
					Management of hypertension		1.87	1.22–2.86
					Management of dyslipidemia		1.29	0.86–1.93
					Anticoagulants for IS with AF		1.70	0.95–3.05
					Antithrombotics at discharge (IS)		2.79	1.41–5.54
Dowlatshahi et al., 2012	Canada	Intracerebral Haemorrhage Stroke	CNS	2466 (11 hospitals)	Statin use in hospital	6 months case fatality	0.2	0.1–0.3
						Poor outcome (mRS=4–6) at discharge	0.6	0.4–0.9
Hubbard et al., 2012	Australia	All stroke types	FIM	2119 (108 Rehabilitations units)	ADLs rehabilitation	Discharged home (Median LoS= 26 days)	1.01	0.33–3.13
					DVT prevention		0.58	0.41–0.81
					Home assessment		6.15	3.70–10.22
					Balance rehabilitation		0.54	0.35–0.83
					Secondary prevention on discharge [f]		1.99	1.12–3.53
					Education to patients [g]		2.37	1.30–4.29
					Discussing post-discharge needs with patients		1.27	0.66–2.43

Table 3. 1: Studies eligible for the systematic literature review ***Continued***

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Bray et al., 2013	UK (England)	Ischaemic stroke	Level of consciousness and neurological deficit	36197 (106 hospitals)	Seen by a stroke consultant or associate specialist within 24 h hours	30-day case fatality	0.88	0.80-0.97
					Brain scan within 24 hours		0.96	0.86-1.07
					Bundle 1: seen by nurse and one therapist within 24 hours and all relevant therapists within 72 hours		0.90	0.82-0.99
					Bundle 2: nutrition screening and formal swallow assessment within 72 hours where appropriate		0.76	0.67-0.87
					Bundle 3: patient's first ward of admission was stroke unit and they arrived there within four hours of hospital admission		0.99	0.90-1.08
					Bundle 4: patient given antiplatelet therapy where appropriate and had adequate fluid and nutrition for first 72h		0.46	0.42-0.50
					Quality score 5 or 6 *v* 0-4		0.74	0.66-0.83
Hoffmeister et al., 2013	Chile	IS	Aphasia, hemiplegia, reduced level of consciousness, and speech disturbance	677 (7 hospitals)	Neurological evaluation on admission	30-day case fatality	2.02	0.77-5.30
						In-hospital pneumonia	1.07	0.79-1.44
					Dysphagia screening within 48hours	30-day case fatality	0.52	0.26-1.04
						In-hospital pneumonia	1.58	0.60- 4.15
					Complete (n-l≤0) adherence to 15 processes of stroke care	Independent at 28 weeks	2.61	0.96–7.10
						Being at home at 28 weeks	3.09	0.96–9.87
						Alive at 28 weeks	3.22	0.66-15.86
Nilanont et al., 2014	Thailand	IS	NIHSS	1222 (76 hospitals)	Stroke unit admission	Poor outcome (mRS 5-6 at discharge) (LoS=4 days)	0.54	0.33-0.87
					Thrombolysis		0.09	0.03-0.23
					Aspirin within 48 hours		1.25	0.73-2.15

Table 3. 1: Studies eligible for the systematic literature review ***Continued***

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Pan et al., 2014	China	ICH stroke	NIHSS	3218 (132 hospitals)	Stain use during hospitalization	1-year Case fatality	0.49	0.27–0.86
						1-year Good functional outcome	2.04	1.37–3.06
Schmitz et al, 2014	Denmark	All IS cases	SSS	4292 (All Danish hospitals)	Thrombolysis	1.4 year-mortality	0.66	0.49–0.88
						1.4 year-recurrent stroke	1.05	0.68–1.64
						1.4 years major bleeding	0.59	0.24–1.47
Song et al., 2014	China	First ever IS	NIHSS	7455 (132 hospitals)	Stain use during hospitalization	3-month Case fatality	0.51	0.38–0.67
						3-months dependency	0.95	0.81–1.11
Mortensen et al., 2015	Denmark	First ever IS cases	SSS	5070 (Aarhus County)	Antidepressants during hospitalization	30-day case fatality	0.28	0.18–0.43
Turner et al., 2015a	UK (Scotland)	All stroke types	SSV	41692 (36 hospitals)	Admission to stroke unit	1-year survival	1.43	1.34-1.54
						6-month discharged home	1.19	1.11-1.28
Turner et al., 2015b	UK (Scotland)	All stroke types	SSV	36055 (36 hospitals)	Stroke unit on day 0 or 1	6-month case fatality	0.79	0.74–0.85
					Swallow screen on day 0		0.95	0.86–1.04
					Brain scan on day 0		0.95	0.88–1.03
					Aspirin on day 0 or 1		0.54	0.49–0.58
					Number of criteria fulfilled	6-month case fatality		
					0 vs 4		2.26	1.60–3.21
					1 vs 4		1.67	1.45–1.93
					2 vs 4		1.44	1.31–1.59
					3 vs 4		1.17	1.08–1.27
					Number of criteria fulfilled	Discharge to home/usual residence at 6 months		
					0 vs 4		0.70	0.50–0.98
					1 vs 4		0.74	0.65–0.84
					2 vs 4		0.84	0.76–0.91
					3 vs 4		0.91	0.85-0.98

Table 3. 1: Studies eligible for the systematic literature review ***Continued***

Study reference	Country	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/RR	95% CI
Cadilhac et al., 2017	Australia	All stroke types	Ability to walk on Admission	16665 (42 Hospitals)	1 process received vs 0	180-days Case fatality	0.63	0.41-0.97
					2 processes received vs 0		0.46	0.31-0.68
					3 processes received vs 0		0.30	0.18-0.47
					1 process received vs 0	90-180-days QoL	12.53*	−2.22-27.28
					2 processes received vs 0		16.67*	0.30-33.05
					3 processes received vs 0		18.70*	1.86-35.55

Abbreviations: ACE, angiotensin-converting enzyme; ADLs, Activities of Daily Living; AF, atrial fibrillation; BI, Barthel Index; CNS, Canadian neurological scale; CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; FIM, functional independence measure; GCS, Glasgow coma scale;
HR, hazard ratio; IS, ischemic stroke; LoS, length of hospital stay; mRS, modified Rankin Scale; NIHSS, national institute of health stroke scale; PT, physiotherapy; OR, odds ratio; OT, occupational therapy; RR, rate ratio; SAH, subarachnoid hemorrhage; SSS, Scandinavian stroke scale; SSV, six simple variable.

* Visual analogue scale score (the health-related quality of life was measured with EQ-5D-3L16 visual analogue scale with deaths coded as zero).

[a] Organized stroke care included wards which encompassed multidisciplinary team-working, a physician with an interest in stroke, as well as taking into account the proportion of time spent (>50% of their length of stay) in such an environment. The wards that encompassed organized stroke care included neurology, elderly care, stroke specific unit and intensive care unit.

[b] n indicates number of applicable processes of care (PoC); i, number of PoC adhered to.

[c] The 15 processes of care consisted of CT scan < 24 h since admission, swallow < 24 h since admission, allied health < 24 h since admission, incontinence addressed, discharged on antiplatelet

[d] Organized care index (OCI) is a summary score based on the presence of occupational therapy or physiotherapy, stroke team assessment, and admission to a stroke unit. A score of zero indicates that stroke patients received none of these services, and higher scores indicate access to more services. The "organized care" index was classified as having received 0, 1, 2, or 3 services.
agent, fever > 38.5 managed, documented premorbid function, documented discharge needs, regular neurology observations for the first 24 h of admission, physiotherapist within 24 h, occupational therapist within 24 h, speech pathologist within 24 h, enteric feeding if nil by mouth > 48 h, aspiration avoidance, and DVT prophylaxis if not ambulant.

[e] The complications that were considered in the analysis included pneumonia, urinary tract infection, pressure ulcer, falls, venous thromboembolism, and constipation.

[f] Secondary prevention included deep vein thrombosis prophylaxis, discharged on lipid-lowering medication, discharged on blood-pressure–lowering medication, and discharged on antithrombotics.

[g] Education to patients consisted of lifestyle advice, information on sexuality poststroke, information about peer support, information on self-management programs, carer training, and providing contact to patient.

The majority (23/30) of the included studies used prospective recruitment while the rest (Milionis et al., 2009; Bravata et al., 2010; Abilleira et al., 2012; Hubbard et al., 2012; Hoffmeister et al., 2013; Turner et al., 2015a; Turner et al., 2015b) consisted of retrospective audits. Thirteen (Andersen and Olsen, 2007; Saposnik et al., 2008; Ding et al., 2009; Milionis et al., 2009; Åsberg et al., 2010; Bravata et al., 2010; Smith et al., 2010; Bray et al., 2013; Hoffmeister et al., 2013; Nilanont et al., 2014; Schmitz et al., 2014; Song et al., 2014; Mortensen et al., 2015) included only patients with IS, and two (Dowlatshahi et al., 2012; Pan et al., 2014) included only patients with intracerebral haemorrhage. The remainder included both ischemic and haemorrhagic stroke. Among those studies that included both types of stroke, six (Glader et al., 2001; Bhalla et al., 2004; Cadilhac et al., 2004; Ingeman et al., 2008; Svendsen et al., 2009; Abilleira et al., 2012) excluded patients with subarachnoid haemorrhage.

For the association between KPIs and patient outcomes, the majority (n=22) of the included studies used OR, six studies (Andersen and Olsen, 2007; Ding et al., 2009; Milionis et al., 2009; Åsberg et al., 2010; Schmitz et al., 2014; Cadilhac et al., 2017) used HR while the remaining two (Ingeman et al., 2008; Svendsen et al., 2009) used rate RR. The included studies also used different measures for stroke severity as a case mix variable for adjustment to estimate the independent association between a KPI and a patient outcome. Twenty of the included studies used validated tools including National Institute of Health Stroke Scale (Ding et al., 2009; Bravata et al., 2010; Hsieh et al., 2010; Abilleira et al., 2012; Nilanont et al., 2014; Pan et al., 2014; Song et al., 2014), Scandinavian Stroke Scale (Andersen and Olsen, 2007; Ingeman et al., 2008; Milionis et al., 2009; Svendsen et al., 2009; Ingeman et al., 2011; Schmitz et al., 2014; Mortensen et al., 2015), Canadian Neurological Scale (Saposnik et al., 2008; Smith et al., 2010; Dowlatshahi et al., 2012), Six Simple Variables (Turner et al., 2015a; Turner et al., 2015b), and Glasgow Coma Scale (Cadilhac et al., 2004), while the remainder used stroke severity proxies such as level of consciousness, incontinence, dysphagia, dysphasia, paralysis, and disability.

3.3.2 Reporting of published KPIs

As there were some variations in data definitions and analysis methods, several assumptions were made to allow easy comparison between the studies:

Swallow/nutritional assessment – This single KPI comprised an assessment of swallowing, dysphagia, and/or nutritional risk. If separate data for both swallow and nutritional risk assessment (Svendsen et al., 2009; Ingeman et al., 2011) were reported, I preferentially included data for swallow assessment.

Antiplatelet drugs for IS – Aspirin administration reported in two studies (Nilanont et al., 2014; Turner et al., 2015b) was combined with a KPI for antiplatelet drugs for IS reported in seven studies (Ingeman et al., 2008; Ding et al., 2009; Svendsen et al., 2009; Åsberg et al., 2010; Ingeman et al., 2011; Abilleira et al., 2012; Bray et al., 2013).

Early nurse/rehabilitation assessment – This combined indicator of early assessment by a nurse (Bray et al., 2013) and early assessment of rehabilitation needs (Abilleira et al., 2012).

Early physiotherapy/mobilization – This combined four reports of early mobilization (Svendsen et al., 2009; Bravata et al., 2010; Ingeman et al., 2011; Abilleira et al., 2012) with one (Ingeman et al., 2008) about early physiotherapy assessment.

3.3.3 Selection of outcome measures

As there were minor variations in the approach to outcome analysis adjustments were made to the reported OR, HR, RR and CI to allow comparisons between the studies. Table 3.2 provides a summary of the adjustments made.

Table 3. 2: Adjustment of reported odds ratios/hazard ratios/rate ratios and confidence intervals (CIs) to allow comparisons between the studies

Study	Reported data	Adjusted data
Andersen and Olsen, 2007	Association between anticoagulants for IS with atrial fibrillation (AF) and **survival rate** (HR: 1.91, 95% CI: 1.44-2.52).	Association between anticoagulants for IS with AF and **case fatality rate** by calculating the inverse (1/x) of the reported data (HR: 0.52, 95% CI: 0.40-0.69).
Turner et al., 2015b	Association between the number of quality stroke care criteria fulfilled and **being discharged** home or to usual care:	Association between the number of quality stroke care criteria fulfilled and **not being discharged** home or to usual care:
Turner et al., 2015a	Association between stroke unit admission and **survival rate** (OR: 1.43, 95% CI: 2.71-3.56) and **being discharged home** (OR: 1.19, 95% CI: 1.11-1.28).	Association between stroke unit admission and **case fatality** (OR: 0.70, 95% CI:0.65-0.75), and **not being discharged home** (OR: 0.84, 95% CI: 0.78-0.90)
Abilleira et al., 2012	Association between **noncompliance** to 11 KPIs and case fatality risk at one-year post stroke	Association between **compliance** to 11 KPIs and case fatality risk at one-year post stroke
Lakshminarayan et al., 2010	Association between **lack of dysphagia screening** and higher risk of pneumonia (OR: 2.15, 95% CI: 1.74-2.66)	Association between **dysphagia screening** and higher risk of pneumonia (OR: 0.47, 95% CI: 0.38-0.57)
Cadilhac et al., 2004	Association between thorough (n-l≤1)[c] adherence to 15 processes of stroke care and **being at home** at 28 weeks (OR: 1.69, 95% CI: 0.86–3.32) and **being alive** at 28 weeks (OR: 2.10, 95% CI: 0.92–4.82).	Association between thorough (n-l≤1)[c] adherence to 15 processes of stroke care and **not being at home** at 28 weeks (OR: 0.59, 95% CI: 0.30-1.16) and **case fatality** at 28 weeks (OR: 0.48, 95% CI: 0.21-1.09).
	Association between Complete (n-l≤0) adherence to 15 processes of stroke care and being at home at 28 weeks (OR: 3.09, 95% CI: 0.96–9.87) and **being alive** at 28 weeks (OR: 3.22, 95% CI: 0.66-15.86).	Association between Complete (n-l≤0) adherence to 15 processes of stroke care and **not** being at home at 28 weeks (OR: 0.32, 95% CI: 0.10-1.04) and **case fatality** at 28 weeks (OR: 0.31, 95% CI: 0.06-1.52).
Hubbard et al., 2012	Association between adherence to seven KPIs and **being discharged home**.	Association between adherence to a KPI and **not being discharged home**.
McNaughton et al., 2003	Relationship between **"no" swallowing recorded** and poor discharge outcome (OR: 3.2, 95% CI: 0.97 -10.7).	Relationship between **swallowing recorded** and poor discharge outcome (OR: 0.31, 95% CI: 0.09-1.03).
Ding et al., 2009	Association of antiplatelets for IS with **improvement in daily life activities** (HR: 1.25, 95% CI: 1.02–1.52).	Association of antiplatelets for IS with **deteriorations in daily life activities** (HR: 0.80, 95% CI: 0.66-0.98).
Pan et al., 2014	Association of statin use with **good functional outcome** (OR: 2.04, 95% CI: 1.37–3.06).	Association of statin use with **poor functional outcome** (OR: 0.49, 95% CI: 0.33-0.73).

Data reported in terms of poor outcome (McNaughton et al., 2003; Dowlatshahi et al., 2012; Nilanont et al., 2014), disability (Glader et al., 2001; Bhalla et al., 2004; Hsieh et al., 2010; Song et al., 2014), death or disability (Ingeman et al., 2008; Bravata Bravata et al., 2010), or not returning home (Candelise et al., 2007) post stroke were all combined as a "poor outcome" post stroke. Finally, the results on the association between KPIs and stroke case fatality were categorized at the end of scheduled follow up although the timing of follow up was included in sensitivity analyses.

3.3.4 Key performance indicators

There were 25 reported KPIs in total. The KPIs that were reported by at least a quarter of the eligible studies were swallow/nutritional assessment, stroke unit admission, and antiplatelets for IS.

Stroke unit admission was variably defined across the related studies (Glader et al., 2001; Bhalla et al., 2004; Candelise et al., 2007; Ingeman et al., 2008; Svendsen et al., 2009; Ingeman et al., 2011; Bray et al., 2013; Nilanont et al., 2014; Turner et al., 2015a; Turner et al., 2015b). Two Danish studies (Ingeman et al., 2008; Svendsen et al., 2009) defined a "stroke unit" as a hospital department/unit that exclusively or primarily is dedicated to patients with stroke and which is characterized by multidisciplinary teams, a staff with a specific interest in stroke, involvement of relatives, and continuous education of the staff. In the Italian study (Candelise et al., 2007), stroke unit was defined as a hospital ward with dedicated beds (at least 80% stroke admission) and with a dedicated stroke staff (at least one physician and one nurse) who work exclusively in the care of stroke patients.

Table 3.3 provides a list of reported KPIs and their frequencies out of the 30 studies.

Table 3. 3: Reported individual KPIs across the eligible studies

Reported individual KPI	Number of reporting studies/30
Swallow/nutritional assessment	11
Stroke unit admission	10
Antiplatelets for IS	9
CT/MRI brain imaging	7
Anticoagulants for IS with AF	7
Lipid management	7
DVT Prophylaxis	6
Early physiotherapy/mobilization	5
Blood pressure lowering therapy	3
Occupational therapy assessment	3
Thrombolysis	3
Neurological Assessment	2
Early nurse/rehabilitation assessment	2
Hyperthermia management	2
Hypoxia management	1
Early medical assessment	1
Antidepressant therapy	1
ADLs rehabilitation	1
Home assessment	1
Balance rehabilitation	1
Secondary prevention on discharge	1
Education to patients	1
Discussing post-discharge needs with patients	1
Intermittent catheterization	1
Constipation risk assessment	1

Table 3.4 indicates the reported KPIs and their association with patient outcomes.

Table 3. 4: Reported KPIs and their association with patient outcomes

1. Reported KPIs and their association with case fatality					
KPI	**Study**	**Treatment Time**	**End FU period**	**OR/HR/ RR**	**95% CI**
CT/MRI brain imaging	Bhalla et al., 2004		3 months	0.70	0.40-1.30
	Ingeman et al., 2008	1st day of LoS	3 months	1.35	1.24–1.46
	Abilleira et al., 2012	<24h	1 year	0.71	0.36-1.41
	Bray et al., 2013	≤24h	1 month	0.96	0.86-1.07
	Turner et al., 2015b	day 0	6 months	0.95	0.88–1.03
Neurological Assessment	Hoffmeister et al., 2013	On admission	1 month	2.02	0.77-5.30
Thrombolysis	Schmitz et al., 2014		1.4 year	0.66	0.49–0.88
Stroke unit admission	Glader et al., 2001		2 years	0.81	0.72-0.92
	Bhalla et al., 2004		3 months	0.50	0.30-0.80
	Candelise et al., 2007		2 years	0.79	0.68–0.91
	Ingeman et al., 2008	2nd day of LoS	3 months	0.76	0.69–0.83
	Bray et al., 2013	≤4h	1 month	0.99	0.90-1.08
	Turner et al., 2015a		1 year	0.70	0.65-0.75
	Turner et al., 2015b	day 0 or 1	6 months	0.79	0.74–0.85
Swallow/nutritional assessment	Ingeman et al., 2008	2nd day of LoS	3 months	0.69	0.61–0.76
	Abilleira et al., 2012		1 year	0.81	0.58-1.14
	Bray et al., 2013	≤72h	1 month	0.76	0.67- 0.87
	Hoffmeister et al., 2013	≤48h	1 month	0.52	0.26-1.04
	Turner et al., 2015b	day 0	6 months	0.95	0.86–1.04
Antiplatelets for IS	Ingeman et al., 2008	2nd day of LoS	3 months	0.71	0.62–0.81
	Ding et al., 2009	LoS	1 year	0.42	0.21–0.86
	Åsberg et al., 2010	-	3 months	0.83	0.68-1.01
	Abilleira et al., 2012	< 48 hours	1 year	0.77	0.50-1.19
	Bray et al., 2013	≤72h	1 month	0.46	0.42-0.50
	Turner et al., 2015b	day 0 or 1	6 months	0.54	0.49–0.58
Anticoagulants for IS with AF	Andersen and Olsen,2007	Acute LoS	4 years	0.52	0.40-0.69
	Ingeman et al., 2008	By 14th day	3 months	0.41	0.31–0.52
	Åsberg et al., 2010	-	3 months	0.58	0.44–0.76
	Abilleira et al., 2012		1 year	0.59	0.33-1.05
Blood pressure lowering therapy	Åsberg et al., 2010	-	3 months	1.00	0.87–1.14
	Abilleira et al., 2012		1 year	0.53	0.35-0.82
Hyperthermia management	Abilleira et al., 2012		1 year	1.50	0.56-4.00
Lipid management	Milionis et al., 2009	At discharge	10 years	0.43	0.29-0.61
	Åsberg et al., 2010	-	3 months	0.78	0.67–0.91
	Abilleira et al., 2012		1 year	0.78	0.52-1.16
	Dowlatshahi et al., 2012	Acute LoS	6 months	0.2	0.1–0.3
	Pan et al., 2014	Acute LoS	1 year	0.49	0.27–0.86
	Song et al., 2014	LoS	3months	0.51	0.38–0.67
DVT Prophylaxis	Saposnik et al., 2008	Acute LoS	1 year	0.33	0.22–0.50
	Abilleira et al., 2012		1 year	1.02	0.63-1.67
Early medical assessment	Bray et al., 2013	≤24h	1 month	0.88	0.80- 0.97
Early nurse/rehabilitation assessment	Abilleira et al., 2012		1 year	0.68	0.48-0.94
	Bray et al., 2013	≤24h	1 month	0.90	0.82-0.99
Early physiotherapy/ mobilization	Ingeman et al., 2008	2nd day of LoS	3 months	0.81	0.73–0.88
	Abilleira et al., 2012		1 year	0.65	0.45-0.95
Occupational therapy assessment	Ingeman et al., 2008	2nd day of LoS	3 months	0.83	0.75–0.91
Antidepressant therapy	Mortensen et al., 2015	LoS	1 month	0.28	0.18–0.43

Table 3.4: Reported KPIs and their association with patient outcomes *Continued*

2. Reported KPIs and their association with poor outcome					
KPI	**Study**	**Treatment time**	**End FU period**	**OR/HR/RR**	**95% CI**
CT/MRI brain imaging	Bhalla et al., 2004		3 months	1.45	0.39–7.4
Thrombolysis	Hsieh et al, 2010	3h of onset	6 months	0.52	0.35-0.76
	Nilanont et al., 2014		LoS=4 days	0.09	0.03-0.23
Neurological Assessment	Bravata et al, 2010		LoS	1.13	0.59-2.17
Stroke unit admission	Glader et al., 2001		2 years	0.79	0.66-0.94
	Bhalla et al., 2004		3 months	1.3	0.6–1.76
	Candelise et al., 2007		2 years	0.85	0.74–0.97
	Nilanont et al., 2014		LoS=4 days	0.54	0.33-0.87
	Turner et al., 2015a		6 months	0.84	0.78-0.90
Swallow/nutritional assessment	McNaughton et al., 2003		1 year	0.31	0.09-1.03
	Bravata et al, 2010		LoS	0.64	0.43-0.94
	Nilanont et al., 2014		LoS=4 days	0.54	0.33-0.87
Antiplatelets for IS	Ding et al., 2009	LoS	1 year	0.80	0.66-0.98
	Nilanont et al., 2014	48h	LoS=4 days	1.25	0.73-2.15
Blood pressure lowering therapy	Bravata et al, 2010		LoS	1.00	0.67-1.50
Hyperthermia management	Bravata et al, 2010	All episodes	LoS	0.71	0.35-1.41
Hypoxia management	Bravata et al, 2010	All episodes	LoS	0.26	0.09-0.73
DVT Prophylaxis	Bravata et al, 2010		LoS	0.60	0.37-0.96
	Hubbard et al., 2012		26 days	1.72	1.23-2.44
Early physiotherapy/mobilization	Bravata et al, 2010		LoS	0.69	0.42-1.14
ADLs rehabilitation	Hubbard et al., 2012		26 days	0.99	0.32-3.03
Home assessment	Hubbard et al., 2012		26 days	0.16	0.10-0.27
Balance rehabilitation	Hubbard et al., 2012		26 days	1.85	1.20-2.86
Secondary prevention on discharge	Hubbard et al., 2012		26 days	0.50	0.28-0.89
Education to patients	Hubbard et al., 2012		26 days	0.42	0.23-0.77
Discussing post-discharge needs with patients	Hubbard et al., 2012		26 days	0.79	0.41-1.52
Lipid management	Dowlatshahi et al., 2012	Acute LoS	At discharge	0.6	0.4–0.9
	Pan et al., 2014	Acute LoS	1 year	0.49	0.33-0.73
	Song et al., 2014	Acute LoS	3 months	0.95	0.81–1.11
3. Reported KPIs and their association with prolonged LoS					
Stroke unit admission	Svendsen et al., 2009	2nd day		0.71	0.65–0.77
Antiplatelets for IS	Svendsen et al., 2009	2nd day		0.80	0.73–0.87
Anticoagulants for IS with AF	Svendsen et al., 2009	14th day		0.78	0.62–0.98
CT/MRI brain imaging	Svendsen et al., 2009	2nd day		0.82	0.74–0.91
Swallow/nutritional assessment	Svendsen et al., 2009	2nd day		0.78	0.69–0.87
Constipation risk assessment	Svendsen et al., 2009	2nd day		0.70	0.63-0.78
Early physiotherapy/mobilization	Svendsen et al., 2009	2nd day		0.67	0.61–0.73
Occupational therapy assessment	Svendsen et al., 2009	2nd day		0.85	0.80–0.91
Intermittent catheterization	Svendsen et al., 2009	2nd day		0.77	0.64–0.92
DVT Prophylaxis	Svendsen et al., 2009	2nd day		0.82	0.71–0.95

Table 3.4: Reported KPIs and their association with patient outcomes ***Continued***

4. Reported KPIs and their association with medical complications					
KPI	**Study**	**Treatment time**	**End FU period**	**OR/HR/RR**	**95% CI**
CT/MRI brain imaging	Ingeman et al., 2011		LoS=13days	1.52	1.35–1.72
Neurological Assessment	Hoffmeister et al., 2013	On admission	30 days	1.07	0.79-1.44
Stroke unit admission	Ingeman et al., 2011		LoS=13days	0.79	0.68–0.92
Swallow/nutritional assessment	Lakshminarayan et al., 2010		LoS=5days	0.47	0.38-0.57
	Ingeman et al., 2011		LoS=13days	0.97	0.84–1.11
	Hoffmeister et al., 2013	≤48h	30 days	1.58	0.60- 4.15
Antiplatelets for IS	Ingeman et al., 2011		LoS=13days	0.95	0.79–1.15
Anticoagulants for IS with AF	Ingeman et al., 2011		LoS=13days	0.59	0.45–0.76
Early physiotherapy/mobilization	Ingeman et al., 2011		LoS=13days	0.43	0.35–0.53
Occupational therapy assessment	Ingeman et al., 2011		LoS=13days	1.10	0.94–1.27
Thrombolysis	Schmitz et al., 2014		1.4 year	0.59	0.24–1.47
5. Reported KPIs and their association with stroke recurrence					
Antiplatelets for IS	Ding et al., 2009	LoS	12 months	0.58	0.36–0.92
Anticoagulants for IS with AF	Hsieh et al., 2010	At discharge	6 months	0.59	0.44-0.80
Lipid management	Milionis et al., 2009	At discharge	10 years	0.65	0.39- 0.97
	Hsieh et al., 2010	At discharge	6 months	0.94	0.78-1.13
DVT Prophylaxis	Hsieh et al., 2010	At discharge	6 months	0.41	0.35-0.47
Thrombolysis	Schmitz et al., 2014		1.4 year	1.05	0.68–1.64

Abbreviations: ADLs, activities of daily living; AF, atrial fibrillation; CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; FU, follow up; HR, hazard ratio; IS, ischemic stroke; KPI, key performance indicator; LoS, length of hospital stay; OR, odds ratio; RR, rate ratio.

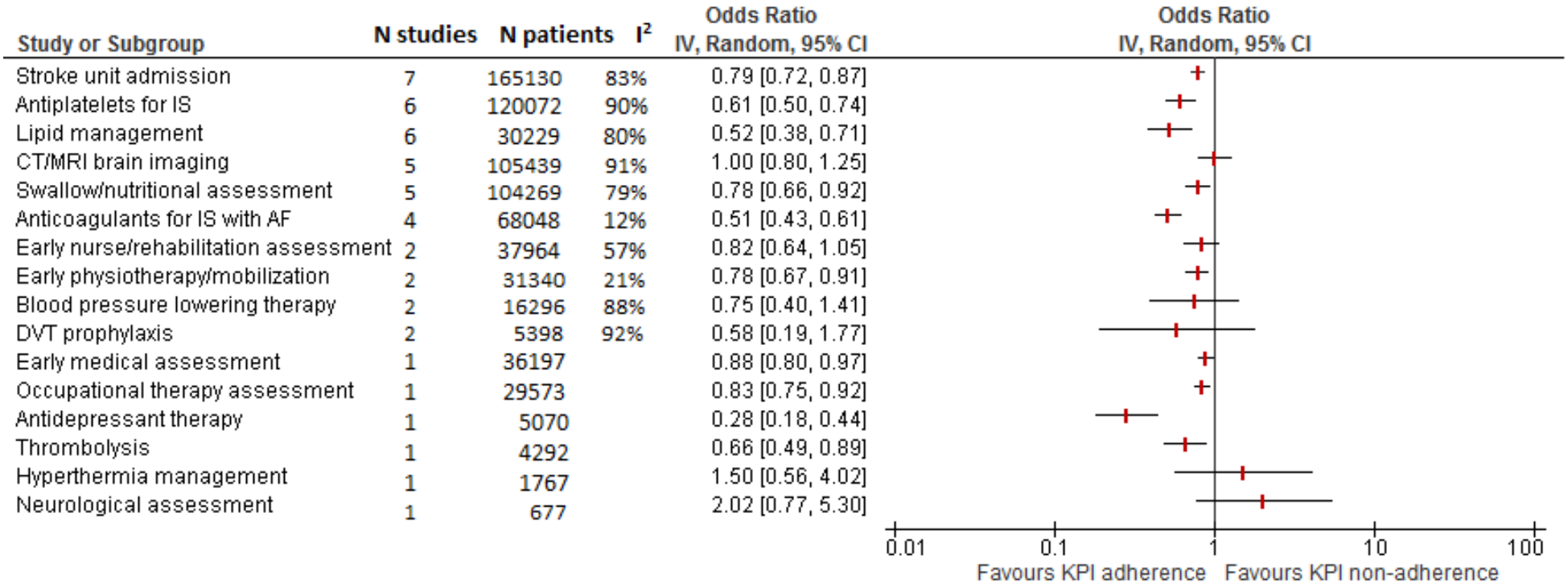
3.3.5 Association between individual KPIs and case fatality at the end of scheduled follow up

The median time of scheduled follow up for the studies reporting on the association between individual KPIs and case fatality was one year; range from one month to 10 years. Significant reductions in case fatality were observed across multiple studies for stroke unit admission (Glader et al., 2001; Bhalla et al, 2004; Candelise et al., 2007; Ingeman et al., 2008; Turner et al., 2015a; Turner et al., 2015b), swallow/nutritional assessment (Ingeman et al., 2008; Bray et al., 2013), antiplatelets for IS (Ingeman et al., 2008; Ding et al, 2009; Bray et al., 2013; Turner et al., 2015b), anticoagulants for IS with AF (Andersen and Olsen, 2007; Ingeman et al., 2008; Åsberg et al., 2010), lipid management (Milionis et al., 2009; Åsberg et al., 2010; Dowlatshahi et al., 2012; Pan et al., 2014; Song et al., 2014), early nurse/rehabilitation assessment (Abilleira et al., 2012; Bray et al., 2013), early physiotherapy/mobilization (Ingeman et al., 2008; Abilleira et al., 2012). In addition, significant associations within single studies were observed for deep vein thrombosis (DVT) prophylaxis (Saposnik et al., 2008) and blood pressure lowering therapy (Abilleira et al., 2012).

In contrast, several studies reported wide CIs and no statistically significant association between the reported KPIs and stroke case fatality; stroke unit admission (Bray et al., 2013), swallow/nutritional assessment (Abilleira et al., 2012; Hoffmeister et al., 2013; Turner et al., 2015b), antiplatelets for IS (Åsberg et al., 2010; Abilleira et al., 2012), anticoagulants for IS with AF, lipid management (Abilleira et al., 2012), DVT prophylaxis (Abilleira et al., 2012) and blood pressure lowering therapy (Åsberg et al., 2010). In one study (Ingeman et al., 2008) the CT/MRI brain imaging was associated with increased risk of early case fatality (RR: 1.35, 95% CI: 1.24-1.46), while in other studies (Bhalla et al., 2004; Abilleira et al., 2012; Bray et al., 2013; Turner et al., 2015b) no evidence for an association of CT/MRI brain imaging and stroke case fatality was found.

Figure 3.2 summarises the primary meta-analysis results regarding the associations between individual KPIs and stroke case fatality at the end of follow up. The KPIs that were associated with lower risk for case fatality include stroke unit admission (OR: 0.79, 95% CI: 0.72-0.87), swallow/nutritional assessment (OR: 0.78, 95% CI: 0.66-0.92), antiplatelets for IS (OR: 0.61, 95% CI: 0.50-0.74), anticoagulants for IS with AF (OR: 0.51, 95% CI: 0.43-0.61), lipid management (OR: 0.52, 95% CI: 0.38-0.71), and early physiotherapy/mobilization (OR: 0.78, 95% CI: 0.67-0.91). However, the significant associations of stroke unit admission, swallow/nutritional assessment, antiplatelets for IS and lipid management were complicated by substantial heterogeneity (I^2>50%). When analyzed at a fixed time point, swallow/nutritional assessment (OR: 0.72, 95% CI: 0.66-0.79), antiplatelets for IS (OR: 0.64, 95% CI: 0.44-0.93) and lipid management (OR: 0.64, 95% CI: 0.42-0.97) were associated with a lower risk for early case fatality (up to three months post stroke), but the heterogeneity was reduced for swallow/nutritional assessment (I^2=1%) only. Stroke unit admission (OR: 0.77, 95% CI: 0.71-0.82), antiplatelets for IS (OR: 0.57, 95% CI: 0.45-0.72) and lipid management (OR: 0.45, 95% CI: 0.27-0.74) were associated with lower risk for late case fatality (beyond three months post stroke), but the heterogeneity was reduced for antiplatelets for IS (I^2=34%) only.

Figure 3. 2: Association between individual KPIs and case fatality



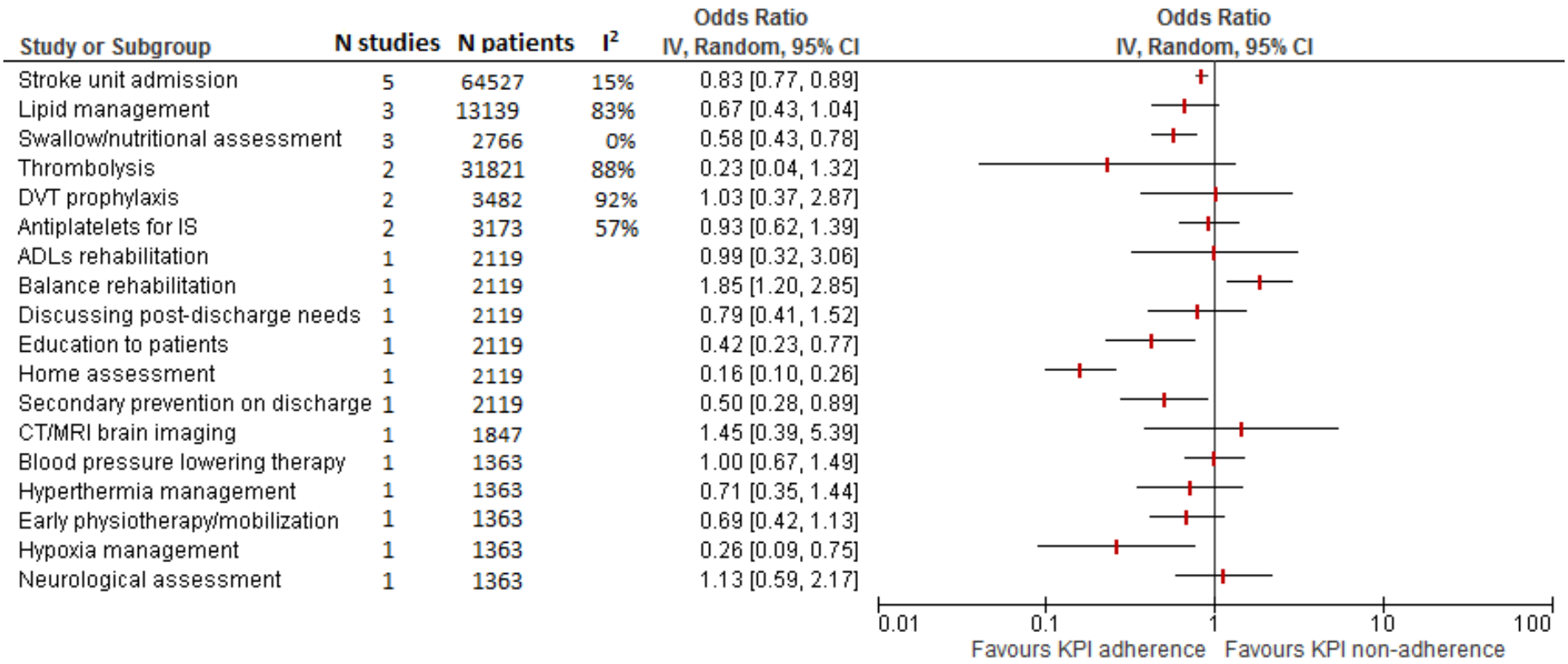
Abbreviations: AF, atrial fibrillation; CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; I^2, heterogeneity; IS, ischemic stroke; IV, inverse variance; KPI, key performance indicator; N, number of.

The meta-analysis showed no evidence for the association between the stroke case fatality and DVT prophylaxis, blood pressure lowering therapy, early nurse/rehabilitation assessment, and CT/MRI brain imaging. The sensitivity analysis excluding those that used HR or RR produced results that were similar to those in Figure 3.2 (data not shown): stroke unit admission (OR: 0.79, 95% CI: 0.71-0.89), swallow/nutritional assessment (OR: 0.82, 95% CI: 0.69-0.98), antiplatelets for IS (OR: 0.53, 95% CI: 0.44-0.63), and lipid management (OR: 0.47, 95% CI: 0.30-0.74) remained associated with lower risk for case fatality, and there was no evidence for the association between the stroke case fatality and DVT prophylaxis, early nurse/rehabilitation assessment, and CT/MRI brain imaging. Significant associations within single studies were observed for thrombolysis (Schmitz et al., 2014), early medical assessment (Bray et al., 2013), OT assessment (Ingeman et al., 2008), and antidepressant therapy (Mortensen et al., 2015), but there was no evidence for the association between stroke case fatality and hyperthermia management (Abilleira et al., 2012), and neurological assessment (Hoffmeister et al., 2013).

3.3.6 Association between individual KPIs and poor outcome

For studies reporting on the association between individual KPIs and poor outcome the available follow up periods were between four days and two years, with a mean of 282 days. KPIs that were reported to be associated with the lower risk for poor outcome included thrombolysis (Hsieh et al., 2010; Nilanont et al., 2014), stroke unit admission (Glader et al., 2001; Candelise et al., 2007; Nilanont et al., 2014; Turner et al., 2015a), swallowing/nutritional assessment (Bravata et al., 2010; Nilanont et al., 2014), antiplatelets for IS (Ding et al., 2009), DVT prophylaxis (Bravata et al., 2010), and lipid management (Dowlatshahi et al., 2012; Pan et al., 2014). However, some studies found no evidence of an association with poor outcome and stroke unit admission (Bhalla et al., 2004); swallowing/nutritional assessment (McNaughton et al., 2003), antiplatelets for IS (Nilanont et al., 2014), DVT prophylaxis (Hubbard et al., 2012) and lipid management (Song et al., 2014). As summarized in Figure 3.3, the meta-analysis showed that the KPIs associated with the lower risk for poor outcome were stroke unit admission (OR: 0.83, 95% CI: 0.77-0.89) and swallowing/nutritional assessment (OR: 0.58, 95% CI: 0.43-0.78) while there was no evidence for a significant association with poor outcome for thrombolysis, antiplatelets for ischaemic stroke, DVT prophylaxis, and lipid management.

Figure 3. 3: Association between individual KPIs and poor outcome



Abbreviations: ADLs, activities of daily living; CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; I^2, heterogeneity; IS, ischemic stroke; IV, inverse variance; KPI, key performance indicator; N, number of.

Several individual studies reported significant associations between lower risk for poor outcome and hypoxia management (Bravata et al., 2010); home assessment, secondary prevention on discharge, and education to patients (Hubbard et al., 2012). No association with poor outcome was found for CT/MRI brain imaging (Bhalla et al., 2004); neurological assessment, blood pressure lowering therapy, hyperthermia management and early physiotherapy/mobilization (Bravata et al., 2010); ADLs rehabilitation, balance rehabilitation and discussing post-discharge needs with patients (Hubbard et al., 2012).

All the studies included for the primary meta-analysis about the association of KPIs with poor outcome used ORs, except one Chinese study (Ding et al., 2009). After excluding that study, antiplatelets for IS remained with a single study (Nilanont et al., 2014) which showed no association with poor outcome (OR: 1.25, 95% CI: 0.73-2.14).

3.3.7 Association between individual KPIs and relative LoS

A single Danish study (Svendsen et al., 2009), reported that a shorter relative LoS was associated with stroke unit admission, antiplatelets and anticoagulants for IS with AF, CT/MRI brain imaging, early physiotherapy/mobilization, occupational therapy assessment, swallowing/nutritional assessment, and DVT prophylaxis, with rate ratio ranging from 0.67 (0.61–0.73) for early physiotherapy/mobilization to 0.85 (0.80–0.91) for occupational therapy assessment.

3.3.8 Association between individual KPIs and the risk for medical complications and stroke recurrence

Stroke unit admission, anticoagulants for IS with AF, and early physiotherapy/mobilization (Ingeman et al., 2011), as well as swallow/nutritional assessment (Lakshminarayan et al., 2010) were found to be associated with lower risk for medical complications (OR: 0.79; 0.68–0.92; 0.59, 0.45–0.76 and 0.43, 0.35–0.53; 0.47, 0.38-0.57 respectively). By contrast, CT/MRI brain imaging was associated with a greater risk for medical complications (OR: 1.52, 1.35–1.72 (Ingeman et al., 2011). Other studies with wide CIs did not show evidence for the association between the occurrence of medical complications and neurological assessment (Hoffmeister et al., 2013); swallow/nutritional assessment (Ingeman et al., 2011; Hoffmeister et al., 2013); antiplatelets for IS, occupational therapy assessment (Ingeman et al., 2011); and thrombolysis (Schmitz et al., 2014).

KPIs that were reported to be associated with lower recurrence rate for stroke included antiplatelets for IS Ding et al., 2009), anticoagulants for IS with AF and DVT prophylaxis (Hsieh et al., 2010), and lipid management (Milionis et al., 2009). However, in one study (Ingeman et al., 2011) evidence for the association between lipid management and stroke recurrence was not found (Hsieh et al., 2010), and there was no evidence of an association with thrombolysis (Schmitz et al., 2014).

3.3.9 Association between adherence to groups of KPIs and the risk for case fatality

Seven studies (Cadilhac et al., 2004; Ingeman et al., 2008; Saposnik et al., 2008; Smith et al., 2010; Bray et al., 2013; Turner et al., 2015b; Cadilhac et al., 2017) had consistent findings whereby adherence to a combination of several KPIs ("bundle") was associated with a greater decrease in stroke mortality. A lower risk for poor outcome was also reported when full stroke care bundle was achieved (Cadilhac et al., 2004; Turner et al., 2015b). An Australian study (Cadilhac et al., 2017) also showed that achieving full care bundle was associated with better quality of life at three to six months post stroke. Increased adherence to stroke care KPIs (Svendsen et al., 2009) was associated with shorter LoS (data are not shown in Table 3.5).

Table 3. 5: Association between the number of KPIs achieved and patient outcomes

	Case Fatality				Poor Outcome				Quality of Life			
Study	**FU Period**	**Number of processes**	**HR**	**95%CI**	**FU Period**	**Number of processes**	**OR/ HR/ RR**	**95%CI**	**FU Period**	**Number of processes**	**OR/ HR/ RR**	**95%CI**
Cadilhac et al., 2004	6 months	All or n-1	0.48	0.21-1.09	6 months	All or n-1	0.59	0.30-1.16				
		All	0.31	0.06-1.52		All	0.32	0.10-1.04				
Ingeman et al., 2008	3 months	1 vs 0	0.94	0.65-1.49								
		2 vs 0	0.78	0.54–1.02								
		3 vs 0	0.60	0.42–0.78								
		4 vs 0	0.61	0.42–0.79								
		5 vs 0	0.45	0.31–0.60								
		6 vs 0	0.48	0.31–0.65								
Saposnik et al., 2008	12 months	OCI 1 vs 0	0.69	0.44–1.09								
		OCI 2 vs 0	0.39	0.25–0.62								
		OCI 3 vs 0	0.40	0.25–0.64								
Smith et al., 2010	1 month	2-3 vs 0-1	0.23	0.19-0.28								
Bray et al., 2013	1 month	5-6 vs 0-4	0.74	0.66- 0.83								
Turner et al., 2015b	6 months	0 vs 4	2.26	1.60–3.21	6 months	0 vs 4	1.43	1.02-2.00				
		1 vs 4	1.67	1.45–1.93		1 vs 4	1.35	1.19-1.54				
		2 vs 4	1.44	1.31–1.59		2 vs 4	1.19	1.10-1.32				
		3 vs 4	1.17	1.08-1.27		3 vs 4	1.10	1.02-1.18				
Cadilhac et al., 2017	6 months	1 vs 0	0.63	0.41-0.97					3-6 months	1 vs 0	12.53*	−2.22-27.28
		2 vs 0	0.46	0.31-0.68						2 vs 0	16.67*	0.30-33.05
		3 vs 0	0.30	0.18-0.47						3 vs 0	18.70*	1.86-35.55

Abbreviations: CI, confidence interval; FU, Follow up; HR, hazard ratio; n, number of applicable processes of care; OCI, Organized care index; OR, odds ratio; RR, rate ratio.
* Visual analogue scale score (the health-related quality of life was measured with EQ-5D-3L16 visual analogue scale with deaths coded as zero).

Overall (see Table 3.6), only stroke unit admission, swallow/nutritional assessment, antiplatelets for IS, anticoagulants for IS with AF, lipid management and early physiotherapy/mobilization were found to be significantly associated with improved outcomes after a meta-analysis of two or more studies. Thrombolysis results were associated with reduced poor outcome in two studies, but the combined analysis was not significant due to substantial heterogeneity. Data were very limited for the outcomes of length of stay, stroke recurrence or medical complications.

Table 3. 6: Summary of results related to individual KPIs and outcomes

KPI	Case fatality	Poor outcome	Relative length of stay	Medical complications	Stroke recurrence
Swallow/nutritional assessment	5 studies, 0.78[a] (0.66-0.92) [b]	3 studies, 0.58 (0.43-0.78)	1 study, 0.78 (0.69-0.87)	3 studies: 2 studies, NS; 1 study, 0.47 (0.38-0.57)	
Stroke unit admission	7 studies, 0.79 (0.72-0.87)	5 studies, 0.83 (0.77-0.89)	1 study, 0.71 (0.65-0.77)	1 study, 0.79 (0.68-0.92)	
Antiplatelets for IS	6 studies, 0.61 (0.50-0.74)	2 studies, NS	1 study. 0.80 (0.73-0.87)	1 study, NS	1 study, 0.58 (0.36-0.92)
CT/MRI brain imaging	5 studies, NS	1 study, NS	1 study, 0.82 (0.74-0.91)	1 study, 1.52 (1.35-1.72)	
Anticoagulants for IS with AF	4 studies, 0.51 (0.43-0.61)		1 study, 0.78 (0.62-0.98)	1 study, 0.59 (0.45-0.76)	1 study, 0.59 (0.44-0.80)
Lipid management	6 studies, 0.52 (0.38-0.71)	3 studies, NS			2 studies: 1 study, NS; 1 study, 0.65 (0.39-0.97)
DVT Prophylaxis	2 studies, NS	2 studies, NS	1 study, 0.82 (0.71-.095)		1 study, 0.41 (0.35-0.47)
Early physiotherapy/mobilization	2 studies, 0.78 (0.67-0.91)	1 study, NS	1 study, 0.67 (0.61-0.73)	1 study, 0.43 (0.35-0.53)	
Blood pressure lowering therapy	2 studies, NS	1 study, NS			
Occupational therapy assessment	1 study, 0.83 (0.75-0.92)		1 study, 0.85 (0.80-0.91)	1 study, NS	
Thrombolysis	1 study, 0.66 (0.49-0.89)	2 studies, NS		1 study, NS	1 study, NS
Neurological Assessment	1 study, NS	1 study, NS		1 study, NS	
Early nurse/rehabilitation assessment	2 studies, NS				
Hyperthermia management	1 study, NS	1 study, NS			
Hypoxia management		1 study, 0.26 (0.09-0.75)			
Early medical assessment	1 study, 0.88 (0.80-0.97)				
Antidepressant therapy	1 study, 0.28 (0.18-0.44)				
ADLs rehabilitation		1 study, NS			
Home assessment		1 study, 0.16 (0.10-0.26)			
Balance rehabilitation		1 study, NS			
Secondary prevention on discharge		1 study, 0.50 (0.28-0.89)			
Education to patients		1 study, 0.42 (0.23-0.77)			
Discussing post-discharge needs with patients		1 study, NS			
Intermittent catheterization			1 study, 0.77 (0.64-0.92)		
Constipation risk assessment			1 study, 0.70 (0.63-0.78)		

Abbreviations: ADLs, activities of daily living; AF, atrial fibrillation; CT/MRI, computerized tomography/magnetic resonance imaging; DVT, deep vein thrombosis; IS, ischemic stroke; KPI, key performance indicator; NS, no statistically significant association.

[a] Overall odds ratio; [b] 95% confidence interval.

3.4 Discussion

The publications I have reviewed provide a large and diverse body of evidence on whether quality of care, as measured by adherence to a KPI, is associated with improved clinical outcomes in patients hospitalized with stroke. My primary meta-analysis indicated that several KPIs including stroke unit admission, swallowing/nutritional risk assessment, antiplatelets for IS, anticoagulants for IS with AF, lipid management and early physiotherapy/mobilization were associated with a reduction in case fatality or poor outcome. However, although my meta-analysis showed significant associations between lower risk for case fatality and several individual KPs at the end of scheduled follow up, there was substantial heterogeneity (I^2>50%) for stroke unit admission, swallowing/nutritional risk assessment, antiplatelets for IS and lipid management. Therefore, my meta-analysis results need to be interpreted with caution.

The strong association of stroke unit care with improved outcomes could be anticipated from a substantial number of RCTs (Stroke Unit Trialists' Collaboration, 2013). My review confirms this across a range of studies in routine care. Given the evidence for specialized multidisciplinary stroke unit care in stroke (Stroke Unit Trialists' Collaboration, 2013), one might also expect to see benefits associated with early nurse or rehabilitation assessment and early medical assessment (Bray et al., 2013), as well as occupational therapy assessment (Ingeman et al., 2008). These indicators lack direct evidence from randomized trials but may possibly be markers for admission to a stroke unit and multidisciplinary stroke care. However, there were no comparable data from many studies about early medical assessment, early nurse or rehabilitation assessment or early occupational therapy assessment for my review.
My finding of a reduced risk of case fatality after early physiotherapy/mobilization was in accordance with the literature about stroke unit care (Stroke Unit Trialists' Collaboration, 2013), and some small RCTs (Langhorne and Pollock, 2002) but not consistent with recent RCTs of very early mobilisation (The AVERT Trial Collaboration group, 2015). However, the recent AVERT trial tested mobilisation at an earlier stage than in routine care so the optimal timing of mobilization remains unclear, and very early intensive mobilization within 24 hours may carry some hazard (The AVERT Trial Collaboration group, 2015).

My meta-analysis showed that swallow or nutritional assessment was associated with lower risk for both mortality and disability post stroke. This finding was consistent with a

randomized controlled trial (RCT) (Middleton et al., 2011) which found that reinforcement of multidisciplinary management of swallowing dysfunction was significantly associated with lower risk for death or dependency. Thus, swallowing or nutritional assessment may be of paramount importance. The current meta-analysis also showed that early antiplatelet use for IS was associated with reduction in case fatality, and this was consistent with the results from a previous systematic review (Sandercock et al., 2014) of eight RCTs. It showed that early antiplatelet therapy was associated with mortality reduction at a final follow-up between one and six months. However, my review showed greater apparent benefit than the 8% reduction in case fatality that was reported in the review of RCTs (Sandercock et al., 2014). However, a recent individual patient data meta-analysis of aspirin trials (Rothwell et al., 2016) confirms an important short-term benefit of aspirin therapy in preventing recurrent cerebral ischemia and that benefits may be greater than previously estimated. My meta-analysis finding of a reduced risk of stroke case fatality associated with lipid management was consistent with the results from a meta-analysis (O'Regan et al., 2008) of 42 RCTs.

One major disagreement with the RCTs is that my meta-analysis also showed that early anticoagulant use for IS with AF was associated with a reduction in early and late case fatality. However, this finding was not supported by a review (Sandercock et al., 2015) of 24 RCTs. This disagreement may be explained by the participants' inclusion criteria. In fact, while the RCTs included in the review (Sandercock et al., 2015) recruited patients with presumed or confirmed ischaemic stroke, the studies included in my review considered only patients with IS and AF. Additionally, as the studies included in my review were neither randomized nor blinded, the apparent effects of antiplatelets and anticoagulants for IS may have been overestimated due to selection bias and incomplete adjustment for confounders. Alternatively, KPIs may also reflect other important and unmeasured aspects of care which would not be tested in a well-designed RCT. Additionally, the duration of follow-up for the studies included in my meta-analysis varied between three and 48 months (mean: 16.5 ±21.4 months) while the duration of follow-up in the trials was generally shorter. This short-term follow-up may lead to missing a significant proportion of deaths that occur after one month, and disability is best assessed between three to six months when most of the recovery has taken place (Sandercock et al., 2015).

My review has also identified some areas with inconsistent evidence of the association of KPIs with outcome. DVT prophylaxis was found to be associated with significant benefits in studies

in Canada (Saposnik et al., 2008) and the USA (Bravata et al., 2010) but not in Spain (Abilleira et al., 2012). However, a meta-analysis of RCTs has failed to show improvements in survival or independence (Sandercock et al., 2015).

Regarding thrombolysis, in two studies included for my review (Hsieh et al., 2010; Nilanont et al., 2014) thrombolysis was associated with a lower risk for poor functional outcome, and this was consistent with the systematic review of the RCTs (Wardlaw et al., 2014). However, because of high heterogeneity (I^2=88%) between the two studies reviewed, the summary effect was not statistically significant.

My review showed that CT/MRI brain imaging and neurological assessment were not associated with any reported patient outcomes. This may be due to several reasons. First, the assessment itself, if not combined with adequate care, is unlikely to show any difference in outcome. For instance, once IS is diagnosed with brain imaging, further management by intravenous tissue plasminogen activator was found to be effective. It was however recently reported that only 3% of low-income, 19% of lower-middle-income, 33% of upper-middle-income, and 50% of high-income-countries use it (Berkowitz et al., 2014). Second, the increased risk of early case fatality (Ingeman et al., 2008) and medical complications (Ingeman et al., 2011) that were reported after early CT/MRI brain imaging in two Danish studies, was most likely due to reverse causality; patients who deteriorated during the first hours after hospitalization were more likely to receive an early CT/MRI brain imaging, and also had a greater risk of death or medical complications (Ingeman et al., 2011). Third, some of the analyses of data may have been hampered by small sample sizes, and lack of statistical power to show the differential benefit.

Adherence to an individual measure in isolation may not have a clinically detectable impact on outcomes, making determination of an effect more difficult (Katzan, 2011). However, adherence to several KPIs was always associated with improved outcomes.

Strengths and weaknesses

My systematic review has several strengths including searching a wide range of databases using standardised methodology. Furthermore, the review report was based on the PRISMA guidelines. The studies that were included in my review involved large sample sizes in general, allowing sufficient statistical power and enhancing the external validity of the results.

One study (Bhalla et al., 2004) was multinational, and 12 studies (Glader et al., 2001; Andersen and Olsen, 2007; Candelise et al., 2007; Ingeman et al., 2008; Åsberg et al., 2010; Hsieh et al., 2010; Hubbard et al., 2012; Nilanont et al., 2014; Pan et al., 2014; Schmitz et al., 2014; Song et al., 2014; Cadilhac et al., 2017) involved nationwide datasets. The remaining studies were conducted regionally with the recruitment of participants from between three (McNaughton et al., 2003) to 222 hospitals (Lakshminarayan et al., 2010). Additionally, I only conducted analyses using data from studies that corrected for patient casemix (age and stroke severity). My approach to meta-analysis has used a conservative random-effects approach to acknowledge the diversity of studies identified. Finally, I performed a sensitivity analysis to evaluate the robustness of my findings.

I must acknowledge some weaknesses. I did not use any scoring system to assess risk of bias in included studies, but simply included large register studies reporting independent association of KPIs with patient outcomes after adjusting at least two variables including age and stroke severity. Second, the review was based on data from observational studies with different follow-up time periods and designs. Third, although I have only included data that used a multivariable analysis to correct for patient casemix, there remains the possibility that the patient outcomes were influenced by unmeasured or residual confounding factors such as indication bias or factors related to the nonrandomized study design rather than the reported KPIs themselves. Fourthly, my review could be subject to publication bias because my search strategy was limited to electronic databases and references known to the authors, and manuscripts published in English only. Fifth, there is a potential concern about combining results from studies from different settings and using different research methodologies. For instance, there were different measures for stroke severity for case mix adjustment, different models of stroke unit, and different models of implementing or measuring the KPIs. Finally, I was limited to a few studies reporting data on important outcomes such as the LoS and QoL, and none of the studies considered the cost of care which is clearly important in a disabling condition such as stroke.

3.5 Conclusion

My review showed that the most frequently reported KPIs for stroke care were swallow/nutritional assessment, stroke unit admission, antiplatelets for IS, CT/MRI brain imaging, anticoagulants for IS with AF, lipid management, DVT prophylaxis, and early physiotherapy/mobilization. Stroke unit admission and early interventions including swallowing/nutritional risk assessment, antiplatelets for IS, anticoagulants for IS with AF, lipid management and physiotherapy/mobilization were all associated with better patient outcomes. Achieving a combination of several KPIs was always associated with a better outcome. Both policy makers and health care professionals should be encouraged to implement the KPIs for stroke management that are reliable and meaningful for regularly monitoring the quality of stroke care. Future research could focus on stroke care quality indicators that are never or rarely reported, particularly in the post-acute period. Such quality indicators could include for instance access to early supported discharge and ADLs rehabilitation.

Chapter 4: Stroke services in African and other low and middle-income countries in an international study

4.1 Introduction

In my systematic literature review on the epidemiology and impact of stroke in Africa I found that stroke is common and important in Africa. By contrast, in my second review, I found that the provision of stroke care in Africa was below the recommended standards with variations across countries and settings. There is therefore a need for appropriate measures to improve stroke care in African countries, and hence reduce mortality and disability after stroke. The third thesis chapter explored the role of key performance indicators of quality stroke care and their association with patient outcomes. However, the publications I reviewed were mainly from high-income countries (HICs). This raises a question of whether the key performance indicators in HICs are applicable to LMICs. I am convinced that initiatives to improve stroke care in Africa should focus on those stroke care elements that are relevant to the local context in terms of feasibility and effectiveness. I therefore aimed to explore the examples of key stroke care elements outside high-income healthcare settings. First, I aimed to identify those stroke care elements that have been established in low and middle-income world settings, generally and African settings in particular. Second, I aimed to assess the association of the existing stroke care services with patient outcomes in those countries with limited resources.

4.2 Methods

I used the INTERSTROKE study data to identify the availability and delivery of stroke care services and their association with patient outcomes in LMICs generally and African countries in particular.

4.2.1 INTERSTROKE study

The INTERSTROKE study is an international, multicentre, case-control study, designed to establish the association of traditional and emerging risk factors with stroke (and primary stroke subtypes) in countries of high, middle, and low income. I explored data from the second phase of the INTERSTROKE study which was conducted between Jan 11, 2007, and Aug 8, 2015. This second phase of the INTERSTROKE study involved 13447 stroke cases and 13472 controls. The 13447 stroke patients were enrolled from 142 hospitals in 32 countries in Asia, Africa, Europe, the Middle East, North America, South America, and Australia. The African

countries were five in total including South Africa, Mozambique, Uganda, Sudan and Nigeria. Recruitment, inclusion and exclusion criteria for the study participants as well as the data collection process have been described elsewhere (O'Donnell et al., 2016).

INTERSTROKE data collection was at two levels:

i) Individual stroke patient data included the following; demographic features (age, sex, level of education, marital status, main occupation before stroke, mother's and father's level of education), risk factors, pre-stroke disability (using the modified Rankin Score), comorbidity (based on the Charleston Comorbidity Index), stroke characteristics (including haemorrhage or infarct classified with the Oxfordshire Community Stroke Project (OCSP) classification), modified Rankin Score at baseline, level of consciousness at baseline) and acute management received (brain imaging, antiplatelet therapy, thrombolysis, lipid lowering therapy and blood pressure lowering therapy).

ii) Service-level data; Using a short questionnaire, information was collected on health-care and stroke service facilities at each participating hospital: a) local and national healthcare system characteristics b) hospital characteristics and resources (e.g. tertiary or secondary level hospital, departments and beds available), c) stroke service characteristics (presence of stroke unit, stroke unit characteristics and resources), d) additional features (other aspects of patient care such as post-discharge rehabilitation).

After combining all the data, there was complete information for 12343 (92%) of 13447 INTERSTROKE patients, from 108 hospitals in 28 countries; 2577 from 38 hospitals in ten HICs and 9766 from 70 hospitals in 18 LMICs.

The list of the involved countries, grouped according to their 2015 World Bank classification by income, with the number of the centres and participants are provided in table 4.1.

Table 4. 1: Countries involved in the INTERSTROKE study

African low-income and middle-income countries		
Country	**Total number of hospitals**	**N**
South Africa	3	100
Mozambique	1	281
Uganda	2	265
Sudan	1	308
Nigeria	1	29
Sub-total 1	8	983
Other low-income and middle-income countries		
Russia	1	204
China	12	3456
India	11	2162
Pakistan	1	291
Argentina	6	129
Brazil	15	384
Chile	1	101
Colombia	3	181
Ecuador	2	600
Peru	1	143
Turkey	5	297
Philippines	3	571
Malaysia	1	264
Sub-total 2	62	8783
High-income countries		
Canada	3	259
Australia	4	120
Germany	3	293
Denmark	1	36
Sweden	2	166
UK	19	1002
Ireland	1	25
Poland	2	409
Croatia	1	61
UAE	2	206
Sub-total 3	38	2577
Total	**108**	**12343**

Abbreviations: UAE, United Arab Emirates; UK, United Kingdom

I was interested in exploring the results from the INTERSTROKE study because it was the novel study that describes the pattern of stroke care on a large scale covering many low-income and middle-income countries.

Seventy-one percent of the centers and 80% of the participants for the INTERSTROKE study were in LMICs.

Permission to use the INTERSTROKE data

Permission to use the INTERSTROKE data was provided by Professor Martin J O'Donnell on behalf of the INTERSTROKE investigators.

4.2.2 INTERSTROKE data included in my analysis

I analyzed the data about the participants with stroke because my objective was to identify the services that were available or offered to patients with stroke. I analyzed data for 12343 INTERSTROKE participants with stroke for whom there were complete data. The data included in my analysis consisted of demographic and clinical characteristics of the participants, and stroke care services available for or offered to patients with stroke.

Patient demographic variables included in my analyses were age, sex, and level of education and the clinical ones were Charlson Comorbidity Index (CCI), baseline mRS score, baseline level of consciousness, stroke type, the OCSP classification of stroke, and 30-day patient outcomes.

Regarding the stroke care services, I analyzed data about healthcare service funding and availability of special services for stroke care. I also analyzed data about the capacity of the available stroke services plus the education of patient families about rehabilitation and availability of post-discharge rehabilitation services.
Finally, I explored the data about the provision of stroke care interventions at hospital such as brain imaging, thrombolysis, carotid surgery or stenting for revascularization, and medications given.

4.2.3 Statistical analysis

I analyzed the data using the Statistical Package for the Social Sciences (SPSS) software, version 24. I aimed to compare African countries to all LMICs in general for all the analyses. I computed both descriptive and inferential statistics. First, I computed the descriptive statistics including the frequencies and percentages for categorical variables and means/ranges for continuous variables to describe the characteristics of the participants and the availability or delivery of stroke care services. Regarding the stroke care services, I computed the frequency and percentage of the participants who had the services available for them to use, and the participants who received each of the interventions included in my analysis. The availability of stroke care services was determined as proportions of participants that the local investigator estimated had the services available for them. This was cross-validated using the number of beds available relative to the number of patients admitted. The implementation of each of the stroke care interventions was measured as the number of participants who received an intervention in relation to the total number of the participants. Both the available stroke care services and the interventions received by the participants were all grouped as “stroke care variables”.

Second, I performed univariate and multivariate logistic regression analyses to generate odds ratios (ORs) with 95% CI and chi-squared (χ^2) test p-values for determining the association between patient outcomes and individual selected stroke care services, comparing African countries to all LMICs and all study countries. The patient outcomes that were considered in my analysis included 30-day case fatality and 30-day death or severe disability (inability to walk independently) (mRS=4-6) (Langhorne et al., 2018). The stroke care variables that were considered in my analysis for association with patient outcomes included brain imaging with CT scan on the day of admission, availability of a stroke unit for at least (≥) 50% of stroke patients, availability of a stroke specialist for at least (≥) 50% of stroke patients, lipid therapy, antihypertensive therapy, antiplatelet therapy for IS, availability of continuing rehabilitation in hospital, and the availability of post-discharge rehabilitation. The patient characteristics that were considered for the case mix adjustment for the multivariate logistic regression analysis included age, baseline level of consciousness, OCSP classification of stroke and baseline stroke severity. These variables were selected because a logistic regression analysis showed that only them were significantly ($p<0.0001$) associated with patient outcomes. A regression analysis for collinearity diagnosis showed that there was no significant collinearity (variance inflation factors (VIF (j)) <2.2) between the covariates.

While performing the logistic regression analysis for each variable, I followed the "rule of thumb" according to which there should be no fewer than 10 outcomes for each binary category (e.g., alive / dead) in both intervention and control groups (Stoltzfus, 2011). As I had eight independent variables for my regression analysis, I used the Bonferroni correction method to control the familywise error rate (false predictors). For this, I determined the critical p-value (alpha) by dividing p=0.05 by 8 and I got Bonferroni critical value p= 0.006 as the level of significance for all the regression analyses.

Third, I aimed to assess the association between patient outcomes and the level of adherence to a stroke care bundle consisting of five variables including brain CT scan on the day of admission, availability of stroke unit for at least (≥) 50% of stroke patients, availability of stroke specialist for at least (≥) 50% of stroke patients, antiplatelet therapy in hospital, and the availability of post-discharge rehabilitation. "Antiplatelet therapy" was defined as giving antiplatelet drugs for IS or not giving them in case of hemorrhagic stroke. This sub-analysis was only possible to do among participants who were assumed to be eligible for all the stroke care bundle components. Consequently, lipid therapy and

antihypertensive therapy in hospital were not included in the bundle because I could not determine who was eligible for those interventions.
Availability of continuing rehabilitation in hospital variable was also not included in the stroke care bundle because of insufficient data (it was generating a logistic regression model with a category of participants who did not achieve any component (score 0) for which there was no any single death case).

Stroke care bundle score "0", "1", "2", "3", "4", "5" corresponded respectively to having achieved none, one, two, three, four, five stroke care bundle components. Participants who achieved the full bundle were used as the reference group. The level of significance for this analysis was the same (p=0.006) as for the analyses for the association between patient outcomes and individual stroke care variables.

4.3 Results

Table 4.2 shows the demographic and clinical characteristics of the 12343 INTERSTROKE study participants included in my analysis. However, as they were missing data with variations across the variables investigated, the sample size varied across the analyses.

African participants were younger (mean age was 58.8 years) than the participants from LMICs in general (mean age was 61.4 years) and all the study countries (mean age was 62.3 years). The majority (66%) of African participants compared to 62% for all LMICs and 53% for all countries did not have more than eight years of education. Regarding the CCI, I found that 87% of the African participants compared to only 66% for all LMICs and 67% for all countries had CCI score of 1 and above. The study results also indicated that a large majority (87.3%) of African participants compared to 68.5% of all LMICs participants and 62% of all study participants had moderate to severe disability (mRS 3-6) at baseline. African participants were more likely to have a reduced level of consciousness at baseline. The proportion of hemorrhagic type of stroke was higher in African countries (30.3%) and all LMICs in general (29.5%) than the percentage for all the countries (25.0%).

Table 4. 2: Demographic and clinical characteristics of the participants

	Overall, N=12343	LMICs, n=9766	African countries, n=983
Age, years			
Mean	62.3	61.4	58.8
Range	17-99	17-99	18-97
Sex, male	7233 (58.6%)	5690 (58.3%)	498 (50.7%)
Education			
None	1918 (15.5%)	1855 (19.0%)	253 (25.7%)
1-8 years	4598 (37.3%)	4212 (43.1%)	398 (40.5%)
9-12 years	3346 (27.1%)	2198 (22.5%)	194 (19.7%)
Trade school	1036 (8.4%)	675 (6.9%)	44 (4.5%)
College/University	1444 (11.7%)	825 (8.4%)	94 (9.6%)
Charlson Comorbidity Index (CCI)			
0	4046 (32.8%)	3316 (34.0%)	117 (11.9%)
1	8048 (65.2%)	6253 (64.0%)	809 (82.3%)
2	206 (1.7%)	157 (1.6%)	20 (2.0%)
3	40 (0.3%)	39 (0.4%)	37 (3.8%)
Baseline mRS score			
mRS = 0-2	4679 (37.9%)	3074 (31.5%)	125 (12.7%)
mRS = 3	3102 (25.1%)	2630 (26.9%)	326 (33.2%)
mRS = 4	2840 (23.0%)	2467 (25.3%)	338 (34.4%)
mRS = 5	1719 (13.9%)	1593 (16.3%)	194 (19.7%)
Baseline level of consciousness			
Alert	8387 (68.0%)	6005 (61.5%)	529 (53.8%)
Reduced	3945 (32.0%)	3756 (38.5%)	454 (46.2%)
Stroke type			
Infarct	9251 (75.0%)	6881 (70.5%)	684 (69.7%)
Hemorrhage	3088 (25.0%)	2882 (29.5%)	297 (30.3%)
OCSP stroke classification			
Hemorrhage	3199 (25.9%)	2941 (30.1%)	308 (31.3%)
Total anterior circulation infarct	599 (4.9%)	488 (5.0%)	87 (8.9%)
Partial anterior circulation infarct	4268 (34.6%)	3246 (33.2%)	398 (40.5%)
Posterior circulation infarct	1266 (10.3%)	860 (8.8%)	54 (5.5%)
Lacunar infarction	2429 (19.7%)	1723 (17.6%)	89 (9.1%)
Other/Undetermined	577 (4.7%)	407 (5.2%)	47 (4.8%)
Patient outcomes, yes, n (%)			
Death at 30 days	1190 (9.7%)	1136 (11.7%)	203 (21.0%)
Death or severe disability (mRS 4-6) at 30 days	2427 (19.8%)	2180 (22.4%)	333 (34.5%)

Abbreviations: LMICs, low and middle-income countries; mRS, modified Rankin scale; OCSP, Oxfordshire Community Stroke Project.

For the patient outcomes, the results showed that the rates for both 30-day case fatality (21.0%) and inability to walk independently (34.5%) in African countries were higher than the rates found in all LMICs (11.7% for case fatality and 22.4% for inability to walk independently) and all the study countries (9.7% for case fatality and 19.8% for inability to walk independently).

Table 4.3 shows the levels of availability and delivery of stroke care services in African countries compared with LMICs

Table 4. 3: Stroke care services in African countries compared with LMICs

	Overall	LMICs	African countries
Healthcare service funding, n (%)			
Government funding	3781 (30.6%)	2068 (21.2%)	439 (44.7%)
Health insurance funding	1307 (10.6%)	214 (2.2%)	0 (0%)
Private funding	2542 (20.6%)	2542 (26.0%)	29 (0.3%)
Mixed funding	5847 (47.4%)	574 (58.8%)	515 (52.4%)
Availability of specialties for stroke care, n (%)			
Neurology	8638 (70.0%)	7462 (76.4%)	658 (66.9%)
General (internal) medicine	8872 (71.9%)	7554 (77.3%)	983 (100%)
Geriatric medicine	2255 (18.3%)	1036 (10.6%)	0 (0%)
Rehabilitation medicine	4976 (40.6%)	4150 (42.5%)	368 (37.4%)
Stroke medicine	4632 (37.5%)	2975 (30.5%)	0 (0%)
Family medicine	1701 (13.8%)	1587 (16.3%)	0 (0%)
Availability of stroke specialist, yes, n (%)			
SS available	9962 (81.2%)	7565 (77.5%)	615 (62.6%)
SS available to ≥50% of stroke patients	8576 (69.9%)	6317 (64.7%)	387 (39.4%)
Availability and capacity of stroke units, yes, n (%)			
SU available	6055 (49.1%)	3685 (37.7%)	373 (37.9%)
SU available to ≥50% of stroke patients	4867 (39.7%)	2631 (26.9%)	44 (4.5%)
Number of beds in stroke unit			
Mean	6.8	3.8	1.7
Range	0-59	0-34	0-6
Estimated proportion (%) of patients admitted to SU per month			
% Mean	34.2%	21.8%	6.5%
Range	0-100%	0-100%	0-70%
Staff workload for stroke patients in a 10-bed stroke unit, yes, n (%)			
Doctors at least 0.1 WTE	5752 (96.3%)	3604 (98.1%)	308 (82.6%)
Nurses at least 1.0 WTE	1651 (27.7%)	1131 (30.8%)	308 (82.6)
PT at least 1.0 WTE	5227 (87.5%)	3400 (92.5%)	308 (82.6)
OT at least 1.0 WTE	2136 (35.8%)	1349 (36.7%)	0 (0%)
SLP at least 0.04 WTE	4175 (69.9%)	2650 (72.1%)	21 (5.6%)
MDT meetings at least once per week yes, n (%)	4764 (40.0%)	2667 (28.5%)	100 (14.2%)
Availability of continuing rehabilitation in hospital, yes, n (%)	10733 (87.0%)	8170 (83.7%)	675 (68.7%)
Availability of post-discharge rehabilitation, yes, n (%)	5741 (46.5%)	3384 (34.7%)	100 (10.2%)
Availability of education to family members about rehabilitation, yes, n (%)	9096 (73.7%)	6927 (70.9%)	286 (29.1%)
Delivery of stroke care interventions in hospital, yes, n (%)			
Brain CT Scan by day 1	11482 (93.2%)	9022 (92.6%)	655 (66.8%)
Antihypertensive therapy	8671 (70.3%)	6853 (70.2%)	640 (65.2%)
Lipid therapy	8674 (70.3%)	7856 (70.2%)	641 (65.2%)
Aspirin for IS	6951 (75.1%)	5083 (73.9%)	440 (64.3%)
Antiplatelet for IS	7693(83.2%)	5555 (80.7%)	451 (65.9%)
Oral anticoagulants for IS	475 (5.1%)	265 (3.9%)	34 (5.0%)
Thrombolysis for IS	704 (7.6%)	241(3.5%)	4 (0.6%)
Carotid surgery or stent for IS	97/ (1.1%)	18 (0.3%)	0 (0.0%)

Abbreviations: CT Scan, Computerized Tomography Scanning; IS, ischemic stroke; LMICs, low and middle-income countries; OT, occupational therapist; PT, physiotherapist, SLP, speech and language pathologist; SS, stroke specialist; SU, stroke unit; WTE, Whole Time Equivalent.

Government-funded healthcare systems were reported to be more available for African participants (44.7%) than all LMICs participants (21.2%). Health insurance funding was reported to be non-existent for the African participants (0%) and rare for LMICs in general

(2.2%) compared to 10.6% for all study countries. Mixed funding was the most common funding system in all LMICs (58.8%), African countries (52.4%), and all countries (47.4%). The most available specialties to African participants were internal or general medicine (100%) and neurology (66.9%), and this was the same for all LMICs (77.3% for internal or general medicine and 76.4% for neurology). However, in all African study centers, there were neither geriatric, stroke nor family medicine although they were reported in other LMICs.

Stroke units were equally rare in African countries (37.9%) and in all LMICs in general (37.7%) compared to the availability rate (49.1%) for all the study countries. The study also showed that the stroke units that could manage at least 50% of stroke patients that present to hospital were available for only 4.5% of the African participants compared to 26.9% and 39.7% of LMICs and all the study participants in general respectively.

Regarding the capacity and admission rate, the average of beds per stroke unit in Africa (1.7) was lower than the ones found in all LMICs in general (3.8) and in all the study countries (6.8), and the stroke unit admission rate in Africa (6.5%) was also lower than the rates reported in all LMICs in general (21.8%) and in all the study countries (34.2%).
There were also stroke unit staffing variations across the countries especially for the occupational therapists (OTs) and speech and language pathologists (SLPs). For instance, it was found that the percentage of OTs who could spend at least 10% of their time in a 10-bed stroke unit was 0 in African countries compared to 36.7 for all LMICs in general. The percentage of speech and language pathologists who could spend at least 4% of their time in a 10-bed stroke unit was 5.6 in African countries compared to 72.1 for all LMICs in general.

Concerning rehabilitation, the results indicated that both in-hospital and post-discharge stroke rehabilitation services were available to only 68.7% and 10.2% respectively in African countries compared to the rates of 83.7% and 34.7% for all LMICs in general, 87.0% and 46.5% for all the study countries.

Table 4.3 also illustrates that the provision of any of the stroke care interventions that were investigated was lower in African countries than in all LMICs in general. The proportion of African participants who received any of the interventions including brain CT scan on the day of admission, antihypertensive therapy in hospital, lipid therapy in hospital and antiplatelet for IS in hospital was lower than 67%. Carotid surgery was not performed for any African participant, and oral anticoagulants for IS (5%) as well as thrombolysis

(0.6%) were rarely received during the hospital stay. This finding was common to all LMICs: 0.3% for carotid surgery, 3.9% for oral anticoagulants and 3.5% for thrombolysis.

In summary, neurology and general (internal) medicine specialties, continuing rehabilitation in hospital services were available, and brain CT scan on the day of admission, antihypertensive and lipid therapy as well antiplatelet for IS services were delivered to more than a half of the participants from African countries. In all LMICs combined, in addition to those services commonly found in African countries, stroke specialist to at least 50% of stroke patients and education to family members about rehabilitation services were available to more than a half of the participants.

Table 4.4 presents the odds ratios for 30-day case fatality and death or severe disability (mRS=4-6) for the stroke care variables comparing African countries with LMICs, and all countries in general.

Table 4. 4: Association between stroke care variables and 30-day patient outcomes

	Crude ORs (95%CI)			Adjusted* ORs (95%CI)		
Stroke care variable	**All countries**	**LMICs**	**African countries**	**All countries**	**LMICs**	**African countries**
			30-day case fatality			
Brain CT scan by day 1	0.77(0.62-0.96), p=0.018	0.83(0.66-1.03), p=0.090	1.26(0.90-1.76), p=0.186	0.82(0.64-1.05), p=0.121	0.85(0.66-1.10), p=0.211	1.08(0.73-1.60), p=0.705
Availability of stroke unit ≥ 50%	0.66(0.58-0.75), p<0.0001	1.08(0.94-1.24), p=0.260	Insufficient data	**0.67(0.58-0.78), p<0.0001**	**0.71(0.60-0.83), p<0.0001**	Insufficient data
Availability of stroke specialist ≥ 50%	0.41(0.36-0.46), p<0.0001	0.48(0.43-0.55), p<0.0001	1.21(0.89-1.66), p=0.226	**0.72(0.62-0.83), p<0.0001**	**0.74(0.64-0.85). p<0.0001**	1.41(0.96-2.05), p=0.077
Lipid therapy in hospital	1.19(1.04-1.37), p=0.011	1.18(1.02-1.35), p=0.021	0.87(0.63-1.21), p=0.411	0.87(0.74-1.02), p=0.080	0.87(0.74-1.03), p=0.095	0.73(0.50-1.06), p=0.099
Antihypertensive therapy in hospital	1.19(1.04-1.37), p=0.011	1.18(1.03-1.35), p=0.021	0.87(0.63-1.21), p=0.418	0.87(0.74-1.02), p=0.081	0.87(0.74-1.03), p=0.096	0.73(0.50-1.07), p=0.102
Antiplatelet therapy for IS	0.41(0.34-0.48), p<0.0001	0.46(0.38-0.55), p<0.0001	0.93(0.62-1.39), p=0.724	**0.65(0.53-0.80), p<0.0001**	**0.69(0.56-0.85), p=0.001**	1.08(0.68-1.73), p=0.748
Availability of continuing rehabilitation in hospital	0.99(0.83-1.19), p=0.940	1.26(1.05-1.50), p=0.012	0.59(0.43-0.81), p=0.001	**0.66(0.53-0.82), p<0.0001**	**0.70(0.57-0.87), p=0.001**	0.59(0.40-0.88), p=0.009
Availability of post-discharge rehabilitation	0.30(0.26-0.35), p<0.0001	0.41(0.35-0.48), p<0.0001	Insufficient data	**0.41(0.35-0.48), p<0.0001**	**0.41(0.34-0.48), p<0.0001**	Insufficient data

Table 4.4: Association between stroke care variables and 30-day patient outcomes ***Continued***

	Crude ORs (95%CI)			Adjusted* ORs (95%CI)		
Stroke care variable	**All countries**	**LMICs**	**African countries**	**All countries**	**LMICs**	**African countries**
			30-day death or severe disability			
Brain CT scan by day 1	0.72 (0.61-0.85), p<0.0001	0.72(0.61-0.85), p<0.0001	1.12(0.85-1.49), p=0.423	**0.75(0.61-0.92), p=0.005**	**0.71(0.58-0.88), p=0.001**	1.04(0.74-1.47), p=0.833
Availability of stroke unit ≥ 50%	0.80(0.73-0.88), p<0.0001	1.17(1.05-1.30), p=0.003	1.47(0.80-2.71), p=0.215	**0.68 (0.61-0.77), p<0.0001**	**0.62(0.55-0.71), p<0.0001**	Insufficient data
Availability of stroke specialist ≥ 50%	0.60 (0.54-0.65), p<0.0001	0.65(0.59-0.72), p<0.0001	1.03(0.79-1.35), p=0.829	1.21(1.07-1.36), p=0.002	1.17(1.04-1.32), p=0.010	1.13(0.80-1.58), p=0.490
Lipid therapy in hospital	1.20(1.08-1.32), p<0.0001	1.16(1.04-1.29), p=0.006	1.11(0.84-1.46), p=0.484	0.92(0.81-1.04), p=0.194	0.89(0.78-1.02), p=0.099	1.07(0.76-1.50), p=0.712
Antihypertensive therapy in hospital	1.20(1.08-1.32), p<0.0001	1.16(1.04-1.29), p=0.006	1.11(0.84-1.47), p=0.474	0.92(0.81-1.04), p=0.197	0.90(0.78-1.02), p=0.100	1.07(0.76-1.51), p=0.701
Antiplatelet therapy for IS	0.55(0.48-0.62), p<0.0001	0.56(0.49-0.65), p<0.0001	1.22(0.86-1.73), p=0.258	0.84(0.71-0.99), p=0.048	0.81(0.68-0.97), p=0.022	1.58(1.04-2.40), p=0.033
Availability of continuing rehabilitation in hospital	1.29(1.12-1.48), p<0.0001	1.55(1.34-1.78), p<0.0001	0.87(0.65-1.15), p=0.318	0.96(0.81-1.15), p=0.663	0.97(0.82-1.16), p=0.737	0.90(0.63-1.30), p=0.576
Availability of post-discharge rehabilitation	0.64(0.59-0.71), p<0.0001	0.83(0.75-0.92), p<0.0001	0.68(0.43-1.07), p=0.095	0.90(0.80-1.00), p=0.059	0.87(0.77-0.98), p=0.024	Insufficient data

Abbreviations: CI, confidence interval; CT Scan, Computerized Tomography Scanning; LMICs, low and middle-income countries, OR, odds ratio; p, p-value for the χ^2 test

*Adjusted for age, baseline stroke severity, baseline level of consciousness, and Oxfordshire Community Stroke Project (OCSP) classification of stroke.

The analysis before case mix adjustment suggested that in Africa only the availability of continuing rehabilitation in hospital was associated with lower risk for 30-day case fatality (crude OR: 0.59, 0.43-0.81; p=0.001). In all study countries and LMICs in general, stroke care variables that were found to be associated with lower risk for 30-day case fatality (p<0.006) included availability of a stroke specialist for the majority of stroke patients, antiplatelet therapy for IS and availability of post-discharge rehabilitation. Availability of a stroke unit for the majority of stroke patients (crude OR: 0.66, 0.58-0.75; p<0.0001) was associated with lower risk for 30-day case fatality only in all the study countries combined. After adjustment, I found that the availability of a stroke unit and stroke specialist for the majority of stroke patients, ongoing in-hospital and post-discharge rehabilitation, and delivery of antiplatelet therapy for IS during the hospital stay were all independent predictors of lower risk for 30-day case fatality (p<0.006) in all countries and in LMICs, but not in African countries.

Regarding the relationship with 30-day death or severe disability (mRS=4-6), the univariate analysis showed that brain CT scan on the day of admission, availability of a stroke specialist for the majority of stroke patients, antiplatelet therapy for IS and availability of post-discharge rehabilitation were all associated with lower risk for 30-day death or severe disability (p<0.006), not only in all countries together, but also in LMICs in particular, and not in the African group considered apart. In all countries combined, the availability of a stroke unit for the majority of stroke patients also was found to be associated with lower risk (crude OR: 0.80, 0.73-0.88; p<0.0001) for death or severe disability. After adjustment however, I only found that brain CT scan on the day of admission and availability of a stroke unit for the majority of stroke patients were associated with lower risk for 30-day death or severe disability not only in all countries (adjusted OR: 0.75, 0.61-0.92; p=0.005 and 0.68, 0.61-0.77; p<0.0001 respectively), but also in LMICs considered apart (adjusted OR: 0.71; 0.58-0.88, p=0.001 and 0.62, 0.55-0.71; p<0.0001 respectively). By contrast, the availability of a stroke specialist appeared to be independently associated with higher risk for 30-day death or severe disability in all countries combined (adjusted OR: 1.21, 1.07-1.36; p=0.002). Table 4.5 illustrates the frequency of participants per number of stroke care components achieved, and the proportions for patient outcomes for each stroke care bundle score.

Table 4. 5: Proportions of stroke care bundle scores and patient outcomes

Stroke care bundle score	All countries n (%)	30-day CF rate	30-day mRS=4-6 rate	LMICs n (%)	30-day CF rate	30-day mRS=4-6 rate	African countries n (%)	30-day CF rate	30-day mRS=4-6 rate
0	115 (0.9%)	18(15.7%)	29(25.2%)	115(1.2%)	18(15.7%)	29(25.2%)	106(10.8%)	15(14.2%)	26(24.5%)
1	576 (4.7%)	93(16.4%)	158(27.8%)	568(5.8%)	93(16.6%)	158(28.2%)	243(24.8%)	54(22.5%)	85(35.4%)
2	2491(20.4%)	355(14.4%)	582(23.6%)	2293(23.5%)	352(15.5%)	568(25.1%)	308(31.4%)	70(23.3%)	118(39.3%)
3	3851 (31.5%)	484(12.6%)	827(21.5%)	3819(39.2%)	483(12.7%)	825(21.7%)	250(25.5%)	58(23.8%)	81(33.2%)
4	2168 (17.7%)	130(6.0%)	431(19.9%)	1787(18.3%)	118(6.6%)	397(22.2%)	63(6.4%)	3(4.8%)	14(22.2%)
5	3037(24.8%)	102(3.4%)	384(12.7%)	1157(11.9%)	66(5.7%)	194(16.8%)	10(1.0%)	2 (20.0%)	8(80.0%)

Abbreviations: CF, case fatality; mRS, modified Rankin Scale score

The analysis regarding the association between the number of stroke care variables met and patient outcomes consisted of 12238 participants in total. Only 32.9% of the African participants compared to 69.4% in LMICs in general and 74% for all countries had achieved from three to five stroke care bundle components. Additionally, among 115 participants in total who did not achieve any component, almost all of them (92.2%) were from African countries, and among 3037 participants who achieved all five stroke care bundle components, only 10 of them were from Africa.

The highest mortality rates were observed among the participants who achieved a smaller number of stroke care bundle components: 30-day case fatality rate was 15.7% for the participants who did not achieve any component and it was 16.4% for the participants who achieved one component only for all the countries together. For LMICs alone, the 30-day case fatality rate was also 15.7% for the participants who did not achieve any component and it was 16.6% for the participants who achieved one component only
In African countries, the highest case fatality rates were found among the participants who achieved three (30-day case fatality was 23.8%) or two components (30-day case fatality was 23.3%).

The findings about 30-day death or severe disability were consistent with those for the 30-day case fatality. The highest 30-day death or severe disability rates were found among the participants with the lowest stroke care bundle scores in all countries together (25.2%) for the participants who did not achieve any component and 27.8% for those who achieved one component only) and in LMICs (25.2% for the participants who did not achieve any component and 28.2% for those who achieved one component only). By contrast, in African countries the highest 30-day death or severe disability rates were found among the participants who achieved all components (eight out of ten participants) and those who achieved two components (39.3%).

Table 4.6 shows crude and adjusted 30-day case fatality and 30-day death or severe disability rates by number of stroke care components achieved among patients who were eligible for all the stroke care bundle components.

Table 4. 6: Association between stroke care bundle scores and 30-day patient outcomes

Stroke care bundle score	Crude ORs (95%CI)			Adjusted* ORs (95%CI)		
	All countries	LMICs	African countries	All countries	LMICs	African countries
			30-day case fatality			
5 (Ref.)	1	1	1	1	1	1
4	1.83(1.40-2.38); P<0.0001	1.17(0.86-1.60), p=0.325	0.20(0.03-1.39); P=0.103	1.05(0.79-1.41); P=0.722	1.00(0.72-1.39), p=0.986	0.46(0.06-3.62); P=0.461
3	4.12(3.31-5.13); P<0.0001	2.40(1.84-3.13), P<0.0001	1.25(0.26-6.04); P=0.784	2.50(1.96-3.18); P<0.0001	2.44(1.83-3.25), P<0.0001	1.54(0.27-8.74); P=0.624
2	4.81(3.84-6.04); P<0.0001	3.04(2.31-3.99); P<0.0001	1.22(0.25-5.87); P=0.806	2.60(2.02-3.35); P<0.0001	2.64(1.96-3.55), P<0.0001	1.35(0.24-7.56); P=0.731
1	5.60(4.16-7.53); P<0.0001	3.29(2.36-4.60); P<0.0001	1.16(0.24-5.63); P=0.853	3.02(2.16-4.24); P<0.0001	2.96(2.04-4.29), P<0.0001	1.49(0.26-8.35); P=0.653
0	5.30(3.09-9.10); P<0.0001	3.07(1.75-5.37); P<0.0001	0.66(0.13-3.41); P=0.619	4.10(2.22-7.57); P<0.0001	3.95(2.10-7.43), P<0.0001	1.16(0.19-6.97); P=0.870
			30-day death or severe disability			
5 (Ref.)	1	1	1	1	1	1
4	1.71(1.47-1.98); P<0.0001	1.42(1.17-1.72), P<0.0001	0.07(0.01-0.38); P=0.002	1.17(0.98-1.40); P=0.087	1.46(1.17-1.82), P<0.0001	0.13(0.02-0.70); P=0.018
3	1.88(1.65-2.15); P<0.0001	1.37(1.15-1.63), P<0.0001	0.12(0.03-0.60); P=0.009	1.24(1.05-1.45); P=0.010	1.50(1.23-1.84), P<0.0001	0.16(0.03-0.83); P=0.029
2	2.12(1.84-2.45); P<0.0001	1.66(1.39-1.99), P<0.0001	0.16(0.03-0.78); P=0.023	1.27(1.07-1.51); P=0.007	1.58(1.28-1.96), P<0.0001	0.20(0.04-1.06); P=0.058
1	2.64(2.14-3.27); P<0.0001	1.95(1.53-2.48), P<0.0001	0.14(0.03-0.66); P=0.013	1.66(1.28-2.17); P<0.0001	2.03(1.52-2.70), P<0.0001	0.19(0.04-0.99); P=0.048
0	2.31(1.50-3.57); P<0.0001	1.67(1.07-2.62), P<0.0001	0.08(0.02-0.41), p=0.002	1.68(1.02-2.78); P=0.043	2.01(1.20-3.35), P<0.0001	0.13(0.02-0.72); P=0.019

Abbreviations: CI, confidence interval; LMICs, low and middle-income countries; OR, odds ratio

*Adjusted for age, baseline stroke severity, baseline level of consciousness, and Oxfordshire Community Stroke Project (OCSP) classification of stroke.

I found an indication of an inverse dose-response relationship between the number of stroke care components achieved and mortality as well as mortality or severe disability. In other words, lower level of care was associated with higher stroke mortality or severe disability. The highest 30-day case fatality, death or severe disability rates were found among patients for whom none or only one of stroke care bundle components was achieved, not only in all study countries in general, but also in LMICs alone. Only relatively small differences were seen between the univariate and multivariable-adjusted ORs.

Overall, for the participants who did not meet any component, the adjusted OR was 4.10, 2.22-7.57; P<0.0001 for 30-day case fatality and was 1.68, 1.02-2.78; P=0.043 (although not statistically significant) for 30-day death or severe disability, compared to those who met all the stroke care components. This pattern was the same for LMICs alone: the adjusted OR was 3.95, 2.10-7.43; P<0.0001 for 30-day case fatality and was 2.01, 1.20-3.35; P<0.0001 for 30-day death or severe disability for the participants who did not meet any component compared to those who met all the stroke care components. For the African countries alone, I did not find evidence of an association between the number of stroke care components met and 30-day patient outcomes.

To further examine the impact of each of the individual stroke care components within the logistic regression model, I performed a sensitivity analysis excluding the five stroke care bundle components one by one and I found that removing any of the components did not change the pattern of the results. Appendix 4.1 provides the sensitivity analysis results.

In summary, in LMICs, availability of a stroke unit (adjusted OR: 0.71, 0.60-0.83; p<0.0001) and stroke specialist (adjusted OR: 0.74, 0.64-0.85; p<0.0001) for the majority of stroke patients, antiplatelet therapy for IS (adjusted OR: 0.69, 0.56-0.85; p=0.001), availability of continuing in-hospital (adjusted OR: 0.70, 0.57-0.87; p=0.001) and post-discharge (adjusted OR: 0.41, 0.34-0.48; p<0.0001) rehabilitation all appeared to be associated with lower risk for 30-day case fatality. In the same LMICs, brain CT scan on the day of admission (adjusted OR: 0.71, 0.58-0.88; p=0.001) and availability of a stroke unit for the majority of stroke patients (adjusted OR: 0.62, 0.55-0.71; p<0.0001) both appeared to be associated with lower risk for 30-day death or severe disability (mRS=4-6). There was an inverse dose-response relationship between the number of stroke care components achieved and mortality as well as mortality or severe disability. For instance, the adjusted OR for 30-day case fatality was 3.95, 2.10-7.43; P<0.0001 and for 30-day

death or severe disability it was 2.01, 1.20-3.35; P<0.0001 for the participants who did not meet any component compared to those who met all the stroke care components.

However, for the African countries alone, I had not enough evidence to show an association between any of the stroke care variables investigated and patient outcomes.

4.4 Discussion

My analysis indicated that several KPIs including the availability of stroke unit and stroke specialist for the majority of stroke patients, in-hospital and post-discharge rehabilitation, as well as antiplatelet therapy for IS, and brain CT scan on the day of admission in LMICs were independently associated with lower risk for 30-day mortality or poor outcome (death or severe disability). These findings were generally consistent with the ones from various clinical trials and our recent review and meta-analysis (Urimubenshi et al., 2017) of national or regional registers mostly from HICs.

Given the evidence for the association between stroke unit admission and specialized multidisciplinary stroke unit care with better patient outcomes (Langhorne and Pollock, 2002; Stroke Unit Trialists' Collaboration, 2013; Urimubenshi et al., 2017), one might also expect to see benefits associated with the availability of stroke unit and stroke specialist for the majority of stroke patients, as well as in-hospital and post-discharge rehabilitation. However, while several small clinical trials (Chieu and Man, 2004; McClellan and Ada, 2004; Sackley et al., 2006; Chaiyawat and Kulkantrakorn, 2012; Chumbler et al., 2012), showed that post-discharge rehabilitation was associated with better functional outcome, I did not find enough evidence for the association between the availability of post-discharge rehabilitation and lower risk for death or severe disability. This disagreement can be attributed to several reasons. For instance, the availability of post-discharge rehabilitation services does not necessarily imply that they were received by every patient for instance due to geographical or financial inaccessibility. Second, the duration of follow-up for my analysis was shorter (30 days) than the follow-up duration (3 months at least) for the clinical trials. This short-term follow-up may lead to missing a significant proportion of outcome changes after one month, and disability is best assessed between three to six months when most of the recovery has taken place (Sandercock et al., 2015). However, if I had considered p=0.05 as the significance value, I would also conclude that the availability of post-discharge rehabilitation was associated with lower risk for poor outcome in LMICs (adjusted OR: 0.87, 95% CI: 0.77-0.98; p=0.024).

The finding that the availability of a stroke specialist was associated with higher risk for 30-day death or severe disability in all countries combined (adjusted OR: 1.21, 1.07-1.36; p=0.002) may be explained by an indication bias. In fact, stroke specialists in all countries in general may have been often involved in the management of more severe stroke patients, and stroke severity is a strong independent predictor for poor outcome (Govan et al., 2009).

The findings also showed that antiplatelet use for IS in LMICs was associated with reduction in case fatality and this was consistent with the results from previous systematic reviews of observation studies (Urimubenshi et al., 2017) and RCTs that were mainly from HICs. However, my INTERSTROKE data analysis showed greater apparent benefit than the 8% reduction in case fatality that was reported in the review of RCTs (Sandercock et al., 2014). Perhaps, as the INTERSTROKE study was observational, the apparent effects of antiplatelets for IS may have been overestimated due to selection bias and incomplete adjustment for confounders. Alternatively, KPIs may also reflect other important and unmeasured aspects of care which would not be tested in a well-designed RCT (Urimubenshi et al., 2017).

Early brain CT scan was independently associated with a reduced risk for death or severe disability in LMICs. Although there are no comparable data from clinical trials or similar studies, the benefits from early brain CT scan may be linked to subsequent early interventions such as antiplatelet therapy for instance that was found to be associated with better patient outcomes. I also found that in LMICs there was a dose dependent relationship of number of KPIs with a better outcome, and this finding was consistent with results from HICs (Urimubenshi et al., 2017).

However, for the African countries alone, I had not enough evidence to show an association between any of the stroke care variables investigated and patient outcomes possibly due to two main reasons. First, some of the analyses may have been hampered by small sample sizes, and lack of statistical power to show the differential benefit. Second, perhaps the stroke services were poorer in African countries than in LMICs in general and were consequently unable to demonstrate a difference in terms of patient outcomes.

Despite the available evidence, my INTERSTROKE data analysis indicated that in LMICs, stroke units with adequate capacity (26.9%) and post-stroke rehabilitation (34.7%) were available to less than a half of the participants from LMICs. In the same LMICs, stroke specialist for the majority of stroke patients and ongoing in-hospital rehabilitation were available to only 64.7% and 83.7% of the participants respectively. Additionally, only

80.7% of the participants with IS were given antiplatelet therapy. Furthermore, I found that several other KPIs (not included in my regression analysis) such as carotid surgery (0.3%), oral anticoagulants (3.9%) as well as thrombolysis (3.5%) for IS were rarely received by the participants from LMICs during their hospital stay.

The situation was particularly limited in the African countries; only 4.5% had access to an adequate stroke unit and 39.4% to a stroke specialist as well as 68.7% and 10.2% respectively for in-hospital and post-discharge rehabilitation availability, and 0% for carotid surgery, 5% for oral anticoagulants, 65.9% for antiplatelet and 0.6% for thrombolysis for IS. These findings on service availability or delivery may partly explain the ones that participants enrolled from African countries had poorer clinical outcomes than those enrolled from all LMICs in general (case fatality 21% *vs* 12%; death or severe disability 35% *vs* 22%). However, the differences in patient outcomes can also be partly explained by the differences in stroke severity: African participants had higher proportions of severe baseline mRS score (mRS=4-6), reduced level of consciousness at baseline and hemorrhagic stroke type than LMIC participants in general. That was the reason for adjustment during the analysis for the association between stroke care variables and patient outcomes. Strategies to improve the availability and delivery of stroke care services in all LMICs are suggested.

Strengths and weaknesses

Several studies on stroke KPIs and their association with patient outcomes have been published previously but, to the best of my knowledge, this is the first analysis on the same topic focusing on LMICs. I analysed data from the INTERSTROKE study that was the novel study that described the pattern of stroke care on a large scale covering many low-income and middle-income countries. On this note, the INTERSTROKE study included 9766 participants from 70 hospitals in 18 low and middle-income countries. Second, I followed the "rule of thumb" and only performed the logistic regression analyses with sufficient sample sizes.

Third, I performed a sensitivity analysis to confirm my results regarding the association between the number of stroke care variables met and patient outcomes.

However, my analysis may well be subject to some weaknesses. First, the current results may not indicate the real picture about stroke KPIs in LMICs. In fact, only five of 32 countries included in the study were African and of 70 hospitals from LMICs assessed for

the INTERSTROKE study, only three were from low-income countries (Mozambique and Uganda). Additionally, many of the participants may have been recruited from urban settings with better resources and services. Second, only those patients with stroke in whom CT or MRI brain imaging could be completed within 1 week of presentation were included in the study while the study did not cover the brain imaging costs. This implies that patients who could not afford brain imaging costs and as early as possible, this being the common scenario in Africa, were automatically excluded from the study. Consequently, the current results cannot be generalized within or across all LMICs. Third, during service-level data collection, a reporting bias by drawing a too positive picture cannot be excluded especially when study investigators or health-care providers describe their own institutions (Brainin, 2018). Fourth, various KPIs were assessed for availability at hospital level and I cannot be certain which specific patients received any of those KPIs. It was for this reason that I chose availability of a stroke unit or stroke specialist for at least 50% of stroke patients to ensure a higher probability of receiving the KPI. Fifth, the INTERSTROKE study assessed the patient outcomes at only one month of follow-up. This short-term follow-up may lead to missing a significant proportion of deaths that occur after one month, and disability is best assessed between three to six months when most of the recovery has taken place (Sandercock et al., 2015). Sixth, the data I analysed were from an observational study and having performed a multivariate analysis to correct for patient case mix does not exclude the possibility that the patient outcomes were influenced by unmeasured or residual confounding factors. However, to control the possibility of chance findings, I used the Bonferroni correction method and considered 0.006 as the p-value of significance.

4.5 Conclusion

My INTERSTROKE data analysis showed that many stroke patients in LMICs, particularly in Africa, do not have access to commonly well-established stroke KPIs. My findings also suggest that the commonly reported KPIs including early brain CT scan, stroke unit, stroke specialist, antiplatelet therapy for IS, in-hospital and post-discharge rehabilitation, may have similar utility in LMICs as has been noted in HICs. Initiatives to promote the implementation of common stroke KPIs in all LMIC settings for improving the quality of care and stroke outcomes are suggested.

Chapter 5: Implementing stroke unit care in Rwanda: a two-hospital before and after implementation trial

5.1 Introduction

The first chapter of the thesis demonstrated that stroke is common and important in Africa. In contrast, the second and fourth chapters revealed that the provision of stroke care in Africa appears to be below the recommended standards using the measures summarised in chapter three. There were also considerable variations across countries and settings. In Rwanda, stroke is estimated to be the third cause of mortality, accounting for 6.4% of all deaths (WHO, 2015). As the Rwandan economy grows, the burden of stroke is expected to increase even more. The Ministry of Health of Rwanda reported that NCDs and their risk factors are a significant public health problem and called for more relevant research to generate evidence for the policy makers to respond efficiently to the scourge (Ministry of Health, 2014a). In 2012, the Ministry of Health of Rwanda published the clinical treatment guidelines for various conditions including stroke, although not comprehensive. Later in 2016, the same ministry published emergency medicine clinical guidelines. However, translating research evidence into clinical practice is very difficult. Healthcare professionals sometimes fail to provide the level of care to which they aspire and, consequently, patients don't benefit optimally from advances in healthcare resulting in poorer quality of life and loss of productivity both personally and at the societal level (Grimshaw et al., 2012).

Organised in-patient (stroke unit) care has become established as the central component of a modern stroke service to reduce the risk of death and disability for patients admitted to hospital after stroke (Langhorne and Rudd, 2009). A stroke unit is a complex intervention that entails a combination of medical and rehabilitation interventions that are delivered by a multidisciplinary team of stroke specialists who work in a focussed and coordinated way to provide care for patients with stroke in hospital (Stroke Unit Trialists' Collaboration, 2013).

A systematic review to identify the effectiveness of a stroke unit compared with a general medical ward on system- and patient-level outcomes for the management of stroke showed that, compared to persons admitted to a general medical ward, those admitted to a stroke unit had a 19% odds reduction in death, a 20% odds reduction in death or institutionalization, and a 21% odds reduction in institutionalization. In addition, the trials showed that there was a 13% odds reduction in death or dependency, and a possible

reduction in the LoS in persons admitted to a stroke unit (Health Quality Ontario, 2014). However, since stroke unit implementation requires a range of health professional resources, co-location of beds and clinical leadership, most service developments have taken place in HICs in which most of the health service is publicly funded.

A review by Langhorne et al. (2012) to explore the applicability of stroke-unit care to low income settings revealed lower death rates in patients admitted to a stroke unit than in alternative services, and the difference was statistically significant for many of the studies. The authors noted that the interpretation of this information is difficult because many settings in low-income countries are likely to be characterized as much by diversity (inequity) of resources as by universally low resources. Most of the studies identified were done in large cities and therefore might not show the situation in rural areas. This raises the question of whether stroke unit care is feasible and applicable to low income and middle-income country settings (Langhorne et al., 2012) like Rwanda. I aimed to explore the feasibility and effectiveness of implementing stroke unit care in selected hospitals in Rwanda with the aim of developing a transferable model for wider implementation.

5.2 Methods

My study was part of an international initiative "Organized Stroke Care Across Income Levels (OSCAIL)". This study aimed to investigate whether stroke services and patient outcomes can be improved through providing tailored support in LMIC settings and was being conducted in four LMICs including South Africa, India, Uganda and Rwanda.

5.2.1 Study design

A before and after implementation trial design was used for the purpose of my study. A similar study (Middleton et al., 2011) showed the possibility of improving aspects of acute stroke care using an implementation trial design. However, while the study by Middleton et al. (2011) used a controlled trial, I was unable to conduct my study on the process of implementing a stroke unit care in Rwanda using a controlled trial design because of practical and logistical reasons. First, although controlled before and after studies can protect against secular trends and sudden changes in guideline implementation performance, it is often difficult to identify a comparable control group (Grimshaw et al., 2000). However, even in apparently well-matched control and intervention groups, performance at baseline is often observed to differ (Grimshaw et al., 2000). Second, there was a danger of contamination if the clinical staff at the study hospitals were allocated in

either control or intervention groups. Furthermore, randomizing the staff into control and intervention groups was not practical because of the existing staff shortage and the randomization could conflict with the staff rotation plans in place. I could not use cluster randomization to compare hospitals implementing the intervention to those not implementing the intervention because this was very difficult and expensive to undertake (Goodacre, 2015). Moreover, I was unable to use interrupted time series analysis because this also would have taken more time and funds (Goodacre, 2015) while I had limited resources. I therefore used an uncontrolled before and after implementation trial approach. The trial was designed according to the Standards for Reporting Implementation Studies (StaRI) (Pinnock et al., 2017).

5.2.2 Study context

Rwanda is a small, hilly, landlocked sub-Saharan country with 26,338 Km^2 only and a densely packed population of about 12,374,397 (National Institute of Statistics, 2019a). About 85% of the Rwandan population lives in rural areas. 76% of the population is aged 34 years or younger, with people aged 65 years and above making up 3% of the population (National Institute of Statistics, 2017). Rwanda borders the Democratic Republic of Congo to the west, Tanzania to the east, Uganda to the north, and Burundi to the south. Figure 5.1 shows the location of Rwanda on the African map.

Figure 5. 1: Location of Rwanda on the African map

Socio-economic context

Rwanda is a low-income country and its economy is agriculture-based (World Bank, 2017). Rwanda's development goals seek to transform the country from an agriculture-based to a knowledge and service-oriented economy. In 2018, Gross Domestic Product (GDP) at market prices was estimated to be Rwandan francs 8,189 billion, up from Rwandan francs 7,600 billion in 2017. Services sector contributed 48 percent of GDP, agriculture sector contributed 29 percent of the GDP, and industry sector contributed 16 percent of GDP while 7 percent was attributed to adjustment for taxes less subsidies on products. In 2018, GDP per head in USD was estimated at 787 up from 774 in the previous year of 2017 (National Institute of Statistics, 2018). The strong economic growth was accompanied by substantial improvements in living standards, with a two-thirds drop in child mortality and near-universal primary school enrolment (World Bank, 2017). A strong focus on homegrown policies and initiatives has contributed to significant improvement in access to services and human development indicators. For instance, the life expectancy at birth has reached to 67 years in 2018 (National Institute of Statistics, 2019b). The poverty rate dropped from 44% in 2011 to 39% in 2014, while inequality measured by the Gini coefficient fell from 0.49 to 0.45 (World Bank, 2017).

Health context

For over a century, Rwanda experienced governance problems which culminated in the Genocide against Tutsi in 1994. The Post-Genocide Government inherited a country with a situation characterized by poor resources and systems in all areas, health sector included. Fortunately, after the genocide, Rwanda has seen great improvements in several key health indicators. For instance, estimates by several United Nations agencies and the World Bank categorised Rwanda among 11 countries that are 'on track' to achieve target 5A of the Millennium Development Goals, which involves a decline of the maternal mortality rate by at least 75 % between 1990 and 2013 (WHO, 2016). Rwanda has also made relatively good progress in improving access to health care services; the average time to walk to a nearby health facility was 57 minutes (Ministry of Health, 2018). Additionally, the national health insurance programme, "Mutuelle de Santé", has increased the utilisation of health care services, and decreased the percentage of households facing catastrophic health expenditure by more than 1.5 percent between 2005 and 2010 (Ministry of Health, 2015a).

Despite substantial efforts by the Government of Rwanda (GOR) to provide quality health care services, various problems remain regarding the achievement of universal access to

affordable quality health care services. The main challenge to the health care system is the shortage of qualified healthcare staff. In 2016, qualified healthcare staff per population ratio was 1/10,055 for doctor (general practitioners and specialists as well), 1/1,094 for nurse, 1/4,064 for midwife (women aged from 15-49), 1/16,871 for pharmacist, and 1/10,500 for laboratory technician (Ministry of Health, 2018). A related challenge is the skewed distribution of health care providers (Ministry of Health, 2014b). Most specialised care providers are in urban areas, particularly Kigali City, leaving the rural districts, where the majority of Rwandans live, with limited access to specialised care. Another important challenge is the lack of diagnostic medical equipment and maintenance technicians. There is also a very high import dependency and a heavy dependency on foreign donor support (National Institute of Statistics, 2017).

Non-communicable diseases (NCDs) in Rwanda

As in many other low-income countries, non-communicable diseases (NCDs) are an emerging problem in Rwanda. NCDs include cancers, cardiovascular diseases, chronic respiratory diseases, diabetes, and kidney diseases. The main risk factors for NCDs include tobacco use, unhealthy diet, harmful alcohol consumption, injury, physical inactivity and obesity (Ministry of Health, 2015a). According to Rwanda's Health Management Information Systems (HMIS) data in 2013, NCDs accounted for at least 51.9 percent of all district hospital outpatients' consultation and 22.3 percent of district hospital inpatients (Ministry of Health, 2015a). The WHO Global Health observatory showed that Rwanda had an NCD death rate of 607 deaths per 100,000 people in 2015 (WHO, 2017). Health services and personnel are however not well trained and equipped to diagnose and treat NCDs at early stages, coupled with inadequate information to the population on prevention and management of NCDs (National Institute of Statistics, 2017). Additionally, most of the population is ensured by community-based health insurance "Mutuelle de Santé" and does not yet have access to private and some high level NCDs services (Ministry of Health, 2015b).

5.2.3 Study sites

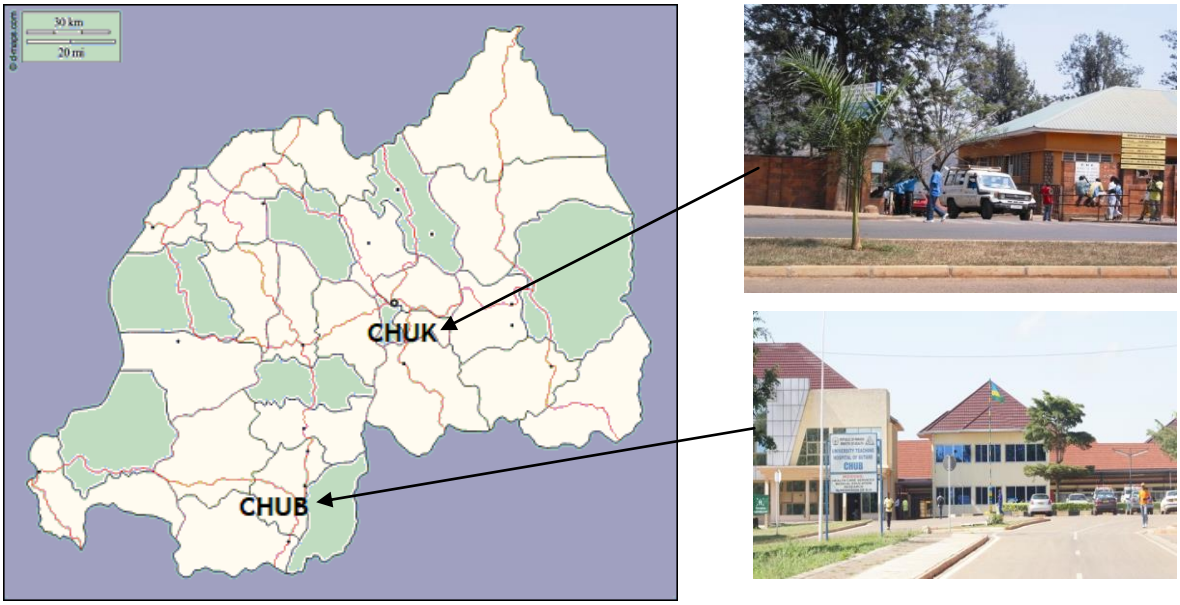
I conducted my study at two public referral hospitals in Rwanda including "Centre Hospitalier Universitaire de Kigali" (CHUK) and "Centre Hospitalier Universitaire de Butare" (CHUB). To select the two hospitals, two criteria were considered:

1) No stroke unit or plans for implementing a stroke unit in the following year;

2) Sites that are similar to each other in terms of resources, bed size, funding structure and interventions.

To identify the suitable study sites, I sent a survey questionnaire to four referral hospitals in Rwanda to assess the existing services and resources, and readiness to take part in my implementation study. The questionnaire consisted of several items including the stroke admission areas and specialties of staff who look after stroke patients. The last question was about whether the hospital was willing to participate in the study. Based on the answers provided, I selected two most suitable hospitals as my study settings.
The locations of the study hospitals on the Rwandan map are indicated on figure 5.2.

Figure 5. 2: Locations of the study sites on Rwandan map



Centre Hospitalier Universitaire de Kigali (CHUK)

CHUK is a referral hospital located in District of Nyarugenge at KN 4 Ave, Kigali City. It is also the biggest hospital of the country with a capacity of 519 beds with a turnover of 1,000 patients per day.
The hospital has around 800 staff including 100 doctors, 400 nurses and midwives, 200 paramedicals, and 100 other (administrative and support) staff.

CHUK has a mandate to provide quality healthcare to the population, training, clinical research and technical support to district hospitals. Its current clinical services include emergency, intensive care unit, high dependency unit, neurosurgery, anaesthesiology and critical care medicine, out-patient department, internal medicine, surgery, gynaecology and

obstetrics, paediatrics, ear-nose-throat (ENT), ophthalmology, dermatology, mental health, medical laboratory, imaging services including CT-scan, pharmacy, physiotherapy, prosthetics and orthotics, nutrition and dietetics, social work, community health supervision, and quality assurance and accreditation.

Stroke patients at CHUK are first received at the emergency department and then, after the triage process, admitted in high dependency unit (HDU) or intensive care unit (ICU) or neurosurgery or internal medicine ward. However, the facility has no specific protocol for stroke patients' hospitalisation. Once admitted, stroke patients are mainly looked after by internist doctors, nurses and physiotherapists, but none of them received specialist stroke care training, and none is dedicated to caring for stroke patients only.

Centre Hospitalier Universitaire de Butare (CHUB)

CHUB is referral hospital located at Mamba, Butare Cell, Huye District in the Southern Province of Rwanda. The hospital has a capacity of 500 beds, with 540 staff members among whom only 40 are specialists, but no cardiologist, no neurosurgeon (only three in the whole country), no nephrologist, no neurologist. CHUB serves the Southern Province's populations and others from some districts of the Western Province. Its catchment area consists of 15 district hospitals and, according to the last 2012 national census, the total population to be served by CHUB is more than 3,772,230 people.

The hospital has various clinical services including internal medicine, surgery, gynecology and obstetrics, accident and emergency, pediatrics, ear-nose-throat (ENT), ophthalmology, anesthesiology and critical care medicine, dialysis, dermatology, mental health, pathology services, imaging services including CT-scan, pharmacy, physiotherapy and functional rehabilitation, nutrition and dietetics, social work, community health supervision, and quality assurance and accreditation.

Stroke patients at CHUB are first received at the emergency department and later, after the triage process, are admitted in intensive care unit (ICU), or a general ward. Like CHUK, CHUB has no specific protocol for stroke patients' hospitalisation. Stroke patients are mainly looked after by internist doctors, nurses and physiotherapists, but none of them received specialist stroke care training, and none is dedicated to caring for stroke patients only.

Although both study sites are university teaching hospitals, there are some relevant differences between them that should be noted. First, while CHUB is located in a

secondary city of Rwanda, CHUK is in the capital city of the country, Kigali, and has better resources. For instance, there were a neurologist, a neurosurgeon and a high dependency unit (HDU) at CHUK but not at CHUB. Second, in case the CT-scan is not functioning, patients at CHUK can get brain imaging from nearby hospitals in Kigali while the patients at CHUB would travel to Kigali for a distance of 135 km. Third, while CHUB serves only about a quarter of the national population, CHUK receives patients from all parts of the country. Therefore, the patient recruitment rate would likey be higher at CHUK than CHUB.

5.2.4 Population, inclusion criteria and sample size

Population and inclusion criteria

The study population consisted of all stroke patients hospitalized at CHUK and CHUB. Only patients diagnosed for stroke with brain imaging or satisfying the WHO clinical criteria for stroke were recruited as study participants "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin" (WHO MONICA Project Investigators, 1988).

Sample size

Before the implementation of the intervention, I recruited a pre-intervention patient cohort to provide baseline data. After the intervention, I recruited a second cohort to evaluate changes in stroke services and patient outcomes. The INTERSTROKE study showed that the delivery of eight stroke care interventions in African hospitals varied between 0% for carotid surgery or stenting for IS and 66.8% early brain CT scan (Chapter 4), giving an average implementation rate of approximately 40% in Africa. I estimated that I needed 62 patients per each site and phase to have 80% power at 5% two-sided significance level to show 25% improvement (Campbell et al., 1995) in adherence to stroke key performance indicators (KPIs). However, previous similar studies recorded a 3-month loss to follow-up which varied between 5% (Bhalla et al., 2004) and 12% (Åsberg et al., 2010). I therefore aimed to recruit 70 stroke patients at each hospital, and for each phase of the study.

5.2.5 Description of the clinical intervention

My clinical intervention was the "stroke unit care". This is more than a hospital geographic physical area. It consists of a discrete area of a hospital that takes care of stroke patients, a specialist multidisciplinary stroke team, coordination through regular meetings to plan patient care, and existence of protocols of care to cover common problems (ESO Executive Committee and Writing Committee, 2008). To determine the stroke KPIs to include in my clinical intervention, I considered the results from the pre-intervention audit and my systematic review of the literature on stroke KPIs (chapter 3) and analysis of INTERSTROKE study (chapter 4), the recommendations from the WSO stroke services framework (Lindsay et al., 2014) plus the Rwandan context and clinical guidelines (however these were too broad to highlight the necessary key elements of quality stroke care). Therefore, my intervention consisted of 11 key stroke unit care elements including acute stroke diagnosis (recognition of strokes and brain imaging), use of stroke severity assessment tools, admission to a geographic stroke unit, swallowing assessment, antithrombotic therapy (such as aspirin, enoxaparin/lovenox) for IS, management of intracerebral hemorrhage (ICH), early mobilization, blood sugar and pressure monitoring and treatment, secondary prevention, and multidisciplinary team meetings.

5.2.6 Description of the implementation intervention

The Cochrane Effective Practice and Organization of Care (EPOC) Review Group (2002) classified the implementation interventions or strategies that are often used to change practice in the categories of professional, financial, organizational and regulatory. Others have identified three main categories of the practice change interventions: persuasive; educational and informational; and action and monitoring (Johnson and May, 2015). Powell et al. (2015) identified 73 potential implementation techniques from which relevant components may be selected. A systematic overview (Johnson and May, 2015) of systematic reviews on the effectiveness of behavior change interventions revealed that using the interventions focusing on action or education including audit and feedback, reminders and educational outreach appeared to be associated with better improvements in professional practice and/or patient outcomes. The same review also showed that bundles of interventions packaged together seem more effective than single interventions.

Based on the available evidence on the effectiveness of various implementation interventions (Johnson and May, 2015) and the local context, I targeted clinical staff involved in stroke care and hospital directors and used a combination of four main

interacting interventions. These included identification and preparation of site champions, provision of educational materials (soft and printed copies), face-to-face educational seminar including feedback on usual care audit results, training on stroke KPIs and local consensus discussions), and discussions with the study hospital directors.

Identification and preparation of site champions

Based on their important roles in daily stroke care, their willingness and readiness to facilitate the implementation of my clinical intervention, two site champions (one at each study hospital) were identified first. Thereafter, I informed them about the study aim and process, discussed and agreed with them on what was expected from them:

- Completing the survey questionnaires to assess if their working hospitals were eligible to participate in the OSCAIL study;
- Contacting the hospital administration about the maximum number of staff who could be released from work to attend the educational seminar;
- Participating in planning the intervention by identifying the most suitable staff to invite to the educational seminar and those who can facilitate some topics);
- Facilitating some intervention training modules;
- After the training, monitoring whether the key stroke care elements were getting implemented and, if gaps were noticed, encouraging their colleagues to improve their services;
- Conducting additional training sessions for local staff as needs arise.

We provided the site champions with reasonable communication fees during intervention and post intervention data collection periods.

Provision of educational materials

A week prior to the face-to-face educational seminar, recommended and optional documents to read were sent to the educational seminar participants through the site champions' emails with an intention to provide them with basic knowledge as a pre-requisite to easily follow the presentations and discussions. After the seminar, the participants were informed that they could get soft and hard copies from the site champions.

The recommended reading documents included the Rwandan internal medicine clinical treatment guidelines (Ministry of Health, 2012) and emergency medicine clinical guidelines (Ministry of Health, 2016), the world stroke organization global stroke services

guidelines and action plan (Lindsay et al., 2014), and the applicability of stroke unit care to LMICs (Langhorne et al., 2012).

The optional reading documents were the road map for quality stroke care (Lindsay et al., 2014), the impact of multidisciplinary stroke care in a secondary-level hospital in South Africa (de Villiers et al., 2009), the development of stroke care in Ghana (Gould et al., 2011), the collaboration works to improve stroke outcomes in Ghana (Morris, 2011), the best practice guidelines for stroke in Cameroon (Cockburn et al., 2014), the United Kingdom clinical guideline for stroke (Royal College of Physicians, 2016), the clinical guideline for stroke in childhood (Royal College of Paediatrics and Child Health, 2017), the lessons from the Wessex-Ghana stroke partnership (Johnsona, 2017), strategies to improve stroke care services in LMICs (Pandian et al., 2017), and the key performance indicators of stroke care quality and their association with patient outcomes (Urimubenshi et al., 2017).

Face-to-face educational seminar

The face-to-face education seminar covered three interventions including feedback on usual care audit results, training on stroke KPIs and local consensus discussions. It was a two-day seminar that took place at CHUK on 17-18 April 2018. The seminar aimed to promote the implementation of the KPIs of quality stroke care. For this purpose, I aimed to invite the hospital staff members including medical doctors, nurses, and physiotherapists mainly that were known to be involved in stroke care in their daily practice. After consideration of the needs of the study, I aimed to cover 11 KPIs as described under clinical intervention. However, my training was broad for covering all the OSCAIL study objectives, and consisted of 20 modules that I developed in collaboration with the OSCAIL study team:

Module 1: Holistic case management approach (Introduction to the International Classification of Functioning, Disability and Health (ICF) framework);

Module 2: General approach to organised stroke care;

Module 3: Importance of stroke units;

Module 4: Preliminary OSCAIL baseline findings and opportunities for improvement;

Module 5: Recognition of strokes, Radiology, Acute stroke diagnosis;

Module 6: Thrombolysis;

Module 7: Intra-arterial interventions and management of intra-cerebral haemorrhage (ICH);

Module 8: Fever monitoring and treatment;

Module 9: Blood sugar monitoring and treatment;
Module 10: Geographic stroke unit;
Module 11: Multidisciplinary teams;
Module 12: Stroke severity scales;
Module 13: Swallowing;
Module 14: Bowels, bladder and pressure care;
Module 15: Early Mobility;
Module 16: Prevention of secondary strokes;
Module 17: Psychological aspects of stroke care;
Module18: Discharge planning;
Module 19: Self-management;
Module 20: Stroke support group.

All the training presentations were structured to include evidence summaries, guidelines' recommendations, and the presentation of the pre-intervention usual care audit results followed by further discussion on exiting gaps and recommendations for improvement.

I used several strategies to optimize the training attendance rate and the adoption of the training content by the training participants:

a) The educational seminar was accredited by Rwanda Allied Health Professions Council (Accreditation number: 0023/RAHPC/17) for continuing professional development (CPD) for a maximum of 12 credits for participants (1 credit=1 hour-attendance) and 24 credits for facilitators (2 credits=1 hour-facilitation);
b) Lunch, transport fees to and from the training venue for all participants, and one-night accommodation fees for participants from CHUB were provided;
c) I involved the principal of the College of Medicine and Health Sciences (CMHS) at the University of Rwanda (UR) in two ways. First, the training participants were officially invited by the Principal of the CMHS at the UR through the director generals of the two study hospitals. In fact, the study sites, being the university teaching hospitals, have close collaboration with the CMHS at the UR, and the principal of CMHS was as a key person who could influence the adoption of my intervention by the hospital staff. Second, the Principal of CMHS-UR introduced the training facilitators and presented on an introductory topic about the comprehensive patient management;
d) The seminar was officially opened and closed by the head of clinical services division at CHUK;

e) I involved two OSCAIL investigators as experts in stroke care and research including Peter Langhorne and Jackie Bosch.

Peter Langhorne is Professor of Stroke Care at the University of Glasgow, United Kingdom. His research work has focused on the effectiveness of different treatment strategies for stroke patients, including service delivery (e.g. stroke units and early supported discharge) and stroke rehabilitation (e.g. early rehabilitation). He is also the coordinating editor of the Cochrane Stroke Group.

Jackie Bosch is Associate Professor at McMaster University, School of Rehabilitation Science and Population Health Research Institute, Hamilton, Ontario, Canada. Her clinical interests are in adult neurological rehabilitation and functional recovery post-stroke particularly. She has conducted many large trials in cardiovascular disease prevention as well as studies on stroke rehabilitation. She is interested in understanding the causes of functional declines and interventions to address these problems. She is a full time faculty member in the School of Rehabilitation Science and an Investigator at the Population Health Research Institute, McMaster University.

Discussions with the study hospital directors

Two OSCAIL investigators (PL and JB) and I as the OSCAIL national champion for Rwanda met with the head of clinical services division (also deputy director) at CHUK on different occasions on 17th and 18th April 2018. A similar meeting was held with the Director General of CHUB on 19th April 2018 in the director's office. The aim of the meetings was to discuss on the way forward to translate the knowledge gained from the seminar and the participants' recommendations into practice.

5.2.7 Implementation intervention outcomes

The primary outcome of the implementation intervention was an increase in the proportion of participants who received the selected stroke KPIs. The secondary outcome was an increase in the proportion of participants with better outcomes including in-hospital and 3-month post stroke survival, 3-month independent survival (mRS=0-2), shorter LoS, and 3-month post stroke good quality of life (quality of life score ≥ 75%).

5.2.8 Data collection

We collected data before and after the implementation intervention.

Pre-intervention audit of usual stroke care

The pre-intervention audit consisted of collecting data about the participant demographic and clinical characteristics, the implementation of selected stroke KPIs, and the patient outcomes. To select the KPIs that I considered for the audit, I used the results from my systematic review of the literature on stroke KPIs (chapter 3) and analysis of INTERSTROKE study (chapter 4), and the recommendations from the WSO stroke services framework (Lindsay et al., 2014). Table 5.1 summarizes the definitions of the stroke KPIs considered in my data collection.

Table 5. 1: Definitions of the selected stroke KPIs for audit

KPI	Definition
Brain imaging	Participant having been examined with CT scan or MRI. I did not consider "early brain imaging" because the date and/or time of the examination were missing for many participants
Use of standardized (stroke) assessment measure	Participant having been assessed with any of the standardized (stroke) assessment tools including mRS, National Institutes for Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS), Functional Independence Measure (FIM) or any other tool at arrival or during admission
Admission to a geographic stroke unit	Participant having been admitted in a hospital area dedicated to stroke patients
Swallowing assessment	Participant having been assessed for swallowing function during hospital stay before being offered food, drink, or oral medications
Antithrombotic therapy for IS	Participant with IS having received any antithrombotic drugs (such as aspirin, enoxaparin/lovenox)
Surgery for ICH	Participant with ICH having received surgical intervention
Blood sugar lowering therapy	Participant with elevated blood sugar (Fasting: >6.0 mmol/L (108 mg/dL); Non-fasting: >11.1 mmol/L (>200 mg/dL); 2 Hour Glucose Tolerance Test (GTT): >7.8 mmol/L (140 mg/dL)) having received any blood sugar lowering drugs
Blood pressure lowering therapy	Participant with systolic blood pressure equal to or greater than 130 mmHg or diastolic blood pressure equal to or greater than 80 mmHg having received any hypertensive drugs
Mobilization	Participant having been mobilized during the hospital stay. Mobilization included different aspects such as passive movements and proper positioning in bed, rolling and moving in bed and up to chair, and walking retraining. The date for the first mobilization session was also captured if documented.
Multidisciplinary team meeting	At least one documented meeting of health-care professionals in hospital to coordinate the patient care

The patient outcomes investigated included in-hospital case fatality, LoS, mRS and quality of life scores at three months post stroke.

Data were collected by a trained staff at each hospital using the case report form (CRF) that I developed in collaboration with the OSCAIL study team. The first CRF draft was pilot tested with four medical files, and necessary modifications were made.

The final CRF version included three parts: admission CRF, Discharge CRF, and 3-month follow-up CRF. These CRFs, in addition to variables relevant to my thesis, comprised other several variables for the OSCAIL study.

Admission CRF. This consisted of data about patient characteristics and clinical information (see appendix 5.1).
Discharge CRF. This consisted of data about discharge or death, past medical history, medications, standardized patient outcome scores and details of care (see appendix 5.2).
Three-month follow-up CRF. This consisted of data about patient status at 3-months post stroke, visit completion details, participant details, participant income status, and health related quality of life (see appendix 5.3).

Admission and discharge data were collected from patient medical files while the 3-month post-stroke onset data were collected using telephone interviews.

Before starting data collection, the data collectors were trained on participant recruitment, admission, discharge and 3-month follow-up CRFs, and the process for data collection. There was an initial one-hour online Skype training, a four-hour face-to face training, and regular reminders through email, WhatsApp and face-to-face contacts.

For quality assurance purposes, I reviewed the first 10 audited medical files at each site in collaboration with the data collector with agreement occurring 98% of the time, and disagreement was managed by discussion and consensus.
Additionally, data quality reports were generated and sent to data collectors weekly to review the missing and misreported data and do corrections.

Post-intervention data collection

After delivering the implementation interventions, we had a 2-week bedding down period to allow the stroke KPIs to become embedded into usual care before recruitment of the post-intervention cohort. The post-intervention data were collected using identical tools and methods to those used to collect the pre-intervention data.

5.2.9 Data analysis

While the OSCAIL study considered several variables, I only analyzed the data for the variables that were relevant to my thesis. I used the Statistical Package for the Social Sciences (IBM Corp., USA) version 25, Minitab version 18 and Excel version 2010 programs to analyse the data, comparing the before and after intervention phases.

First, I summarised continuous and categorical data using conventional descriptive statistics including median with lower and upper quartiles (data were not normally distributed), frequency distribution and percentage. Regarding the implementation of stroke KPIs, as the guidelines and good clinical practice specify that the steps in the management of patients with stroke should be well documented, where there was no documentation to suggest that the stipulated standard of care (brain imaging, swallowing assessment, use of standardized outcome tool, elevated blood sugar or pressure lowering therapy, antithrombotic therapy for IS, surgical intervention for ICH, mobilization and multidisciplinary team meeting) had been met, the cases were analyzed as if the KPIs had not been implemented (Faluyi et al., 2008). Using the available data, I generated two variables including antithrombotic therapy and early mobilization. Antithrombotic therapy was defined as "giving any antithrombotic drugs (such as aspirin, enoxaparin/lovenox) for IS or not giving them in case of hemorrhagic stroke" while early mobilization was defined as "starting mobilization within the first two days of admission".

Before and after intervention continuous variables were compared using the Mann-Whitney test (the variables' values were not normally distributed) and categorical variables were compared using the unpaired $\chi 2$ test. As I could not specify with certainty the direction of any difference in stroke services and patient outcomes between the two study phases before collecting data, I calculated two-sided p-values and one of 0.05 or less was considered significant. The data were presented in the forms of normal tables.

Second, I performed univariate and multivariate logistic regression analyses to generate unadjusted and adjusted odds ratios (ORs) with 95% CI and $\chi 2$ test p-values for determining the association between the after-intervention phase and receiving a KPI and the association between the after-intervention phase and better patient outcomes.

The baseline variables that were considered for the case mix adjustment for the multivariate logistic regression analysis included the six simple variables (age, living alone before stroke, being independent in everyday activities before stroke, being able to talk, being able to lift both arms to horizontal and being able to walk independently), stroke type and stroke onset-hospital arrival interval. The stroke KPIs that were never or were rarely

implemented including admission to a geographic stroke unit, surgery for ICH and blood sugar lowering therapy were not included in the logistic regression analyses.

5.2.10 Ethical considerations

My study was approved by the Ethics Committee of the College of Medical, Veterinary and Life Sciences (MVLS) at University of Glasgow (Appendix 5.4), the Institutional Review Board of the College of Medicine and Health Sciences (IRB-CMHS) at the University of Rwanda (Appendix 5.5), CHUK (Appendix 5.6) and CHUB (Appendix 5.7).

Before collecting the data, potential participants who met inclusion criteria and their guardians were informed about the study using the participant information sheet (Appendix 5.8). They were assured about confidentiality and anonymity, as well as the right to withdraw from the study at any time and without giving a reason. Potential participants were given time to ask questions about the study and their participation. Twenty-four hours at least after informing the patients and guardians, written informed consent or assent (Appendix 5.9 and Appendix 5.10) was requested from all patients or their guardians where the participants were less than 18 years-old, or not able to provide consent due to communication or cognitive limitation. In this case however, when the participants' condition improved, we requested their consent to continue in the study (Appendix 5.11). The participant information sheet, the written informed consent and assent forms were translated in Kinyarwanda (Appendix 5.12, 5.13, 5.14, 5.15), the language commonly used by the potential participants.

The administration of the study hospitals will get a copy of the study results not later than February 2020.

5.2.11 Funding

My study was conducted in Rwanda as part of the international OSCAIL study as mentioned earlier and was funded by a grant from the Population Health Research Institute (PHRI) at McMaster University in Canada. There was no financial or other conflict of interest for the study.

5.3 Results

5.3.1 Educational seminar achievements

The educational seminar was well attended, multidisciplinary, and covered the common stroke KPIs.

Excellent attendance rate

Thirty-nine out of 40 invited participants attended to the training, giving an excellent attendance rate (97.5%). There were 20 and 19 participants from CHUK and CHUB respectively. Figure 5.3 shows the seminar participants and the facilitators.

Figure 5. 3: Educational seminar participants and facilitators

Multidisciplinary seminar

The participants from CHUK included the head of clinical services division, the head of emergency department, the director of quality assurance, a neurosurgeon, four internal medicine physicians, six nurses, two physiotherapists, one psychiatrist, one clinical psychologist, one anaesthetist and one nutritionist.

The participants from CHUB included six internal medicine physicians, 11 nurses and two physiotherapists.

Comprehensive seminar

We covered all the modules on 11 stroke KPIs including multidisciplinary teams, acute stroke diagnosis (recognition of strokes and brain imaging), use of stroke severity assessment tools, swallowing assessment, blood sugar and pressure monitoring and treatment, early mobilization, geographic stroke unit, antithrombotic (oral drugs and thrombolysis) therapy for IS, management of intra-cerebral haemorrhage (ICH) and the prevention of secondary strokes.

The participants were asked to rate several aspects of the seminar using a 1 (strongly disagree) to 5 (strongly agree) scale. The mean scores indicated that the seminar was highly appreciated by the participants from both study hospitals as showed in table 5.2.

Table 5. 2: Educational seminar evaluation results

Seminar aspect, Median score [a] (Q1-Q3)	All	CHUK	CHUB
Overall	5 (4-5)	5 (4-5)	4 (4-5)
Expectations met	5 (4-5)	5 (4-5)	5 (4-5)
Content appropriate/relevant	5 (4-5)	5 (4-5)	5 (4-5)
Time allocation for modules	4 (4-5)	5 (4-5)	4 (3-4)
Sessions flow	4 (4-4)	4 (4-4.5)	4 (4-4)
Time for asking questions	5 (4-5)	5 (4-5)	5 (4-5)
Own opinions respected	5 (4-5)	5 (4-5)	5 (4-5)
Workshop was collaborative	5 (5-5)	5 (5-5)	5 (5-5)
Readings [b] were relative to work	5 (4-5)	4.5 (4-5)	5 (4-5)

[a] A scale of 1-5 was used (1= strongly disagree; 2= disagree; 3= neutral; 4= agree; 5= strongly agree).

[b] Educational documents were sent to participants a week before the seminar.

Consensus on stroke service improvement

At the end of the two-day educational seminar, the participants discussed on KPIs that they could improve and agreed on six recommendations:

a. CHUK and CHUB should plan to establish geographic stroke units as soon as possible. Meanwhile, stroke patients within a general ward should be admitted in the same area/corner;
b. All stroke patients should receive mobility assessment and treatment if there is no contraindication with 24-48 hours of admission;
c. Stroke care team should meet at least once a week;

d. Every activity should be accurately documented, and using standardized forms if these are available;
e. Stroke care members are encouraged to use standardized outcome measures while assessing stroke severity and disability;
f. The training participants should transfer their knowledge to their workmates who did not attend the training

Furthermore, the participants were individually asked to indicate the KPIs that could be improved immediately after the seminar. Table 5.3 shows the number (percentage) of participants who indicated that KPIs could be better implemented at their work hospitals.

Table 5. 3: Number (percentage) of participants who indicated that KPIs could be better implemented at their work hospitals

KPI, n (%)	All n=38	CHUB n=19	CHUK n=19
Early Mobilization	22 (57.9)	10 (52.6)	12 (63.2)
Swallowing Assessment	20 (52.6)	8 (42.1)	12 (63.2)
Multidisciplinary teams	17 (44.7)	9 (47.4)	8 (42.1)
Blood sugar monitoring and treatment	9 (23.9)	5 (26.3)	4 (21.1)
Prevention of secondary strokes	9 (23.9)	4 (21.1)	5 (26.3)
Acute stroke diagnosis	6 (15.8)	5 (26.3)	1 (5.3)
Geographic stroke unit	1 (2.6)	0	1 (5.3)
None	2 (5.3)	1 (5.3)	1 (5.3)

In general, more than 20% of the seminar participants indicated that early mobilization (58%), swallowing assessment (53%), multidisciplinary meetings (45%), blood sugar lowering therapy (24%) and secondary stroke prevention (24%) could be improved. Two seminar participants (one from each hospital) however responded that none of the KPIs could be improved. Regarding the geographic stroke unit, only one participant from CHUK thought that the geographic stroke unit could be established.

5.3.2 Participants recruitment

Overall, we recruited 106 participants for each of the two study phases. For CHUK, we recruited 71 and 70 participants during the pre and post-intervention phases respectively. The recruitment rate was therefore 100%. During the pre-intervention phase, 74 patients admitted for stroke at CHUK from 12th July 2017 to 12th January 2018 were contacted to participate in the study. Seventy-one patients or their proxies agreed to participate in the

study. One of the 71 participants was found to have a different diagnosis (brain atrophy) at discharge but was considered for intention to treat analysis. During the post-intervention phase from 16th May 2018 to 31st August 2018, we contacted 71 patients admitted for stroke. One patient was unable to communicate and there was no a competent person to provide consent and only 70 patients were recruited.

For CHUB, although the recruitment lasted longer compared to CHUK, we did not reach the desired sample size. During the pre-intervention phase, we contacted 37 patients admitted for stroke at CHUB from 15th July 2017 to 30th April 2018 to participate in the study. Thirty-five patients or their proxies agreed to participate in the study. Three of the 35 patients had different diagnoses (right parietal glioblastoma, brain tumor, and suspected spaceoccupying lesion or meningitis or brain abscess) at discharge but were considered for intention to treat analysis. For the post-intervention phase, 36 patients were recruited from 18th May 2018 to 1st January 2019.

However, as there were missing data for both hospitals with variations across the variables investigated, the sample size varied across the analyses. Table 5.4 shows the demographic and clinical characteristics of participants according to phase of study.

Table 5. 4: Baseline characteristics of participants according to phase of study

Variable	All			CHUB			CHUK		
	Pre-intervention n=106	**Post-intervention n=106**	**P-value**	**Pre-intervention n=35**	**Post-intervention n=36**	**P-value**	**Pre-intervention n=71**	**Post-intervention n=70**	**P-value**
Age, years, median (Q1-Q3)	61 (45-70.25)	62 (50-73.25)	0.265	63 (50-74)	65 (51.25-73.75)	0.683	60 (40-68)	61.5 (49.5-73.25)	0.283
Male sex	55 (51.9)	53 (50.0)	0.783	13 (37.1)	21 (58.3)	0.074	42 (59.2)	32 (45.7)	0.110
Living alone, Yes, n (%)	52 (49.1)	26 (24.5)	**<0.0001**	17 (48.6)	18 (50.0)	0.904	35 (49.3)	8 (11.4)	**<0.0001**
Independent before stroke, Yes, n (%)	96 (90.6)	104 (98.1)	**0.017**	35 (100)	35 (97.2)	0.321	61 (85.9)	69 (98.6)	**0.005**
Can talk, Yes, n (%)	58 (54.7)	16 (15.1)	**<0.0001**	10 (28.6)	11 (30.6)	0.855	48 (67.6)	5 (7.1)	**<0.0001**
Can lift both arms, Yes, n (%)	17 (16.0)	7 (6.6)	**0.030**	3 (8.6)	3 (8.3)	0.971	14 (19.7)	4 (5.7)	**0.013**
Can walk, Yes, n (%)	12 (11.3)	3 (2.8)	**0.016**	1 (2.9)	0	0.307	11 (15.5)	3 (4.3)	**0.026**
Stroke type									
Ischemic	57 (53.8)	37 (34.9)	**0.021**	16 (45.7)	12 (33.3)	0.518	41 (57.7)	25 (35.7)	**0.016**
Haemorrhagic	34 (32.1)	50 (47.2)		5 (14.3)	5 (13.9)		29 (40.8)	45 (64.3)	
Unknown	15 (14.2)	19 (17.9)					1 (1.4)	0	
Onset-hospital arrival interval, days, median (Q1-Q3)	4 (1-12)	2 (1-4.5)	**0.012**	7 (2.5-13)	3 (1-10)	0.107	3 (1-12)	1 (1-4)	**0.040**
Early arrival to study hospital [a, b], Yes, n (%)	32 (31.1)	49 (46.7)	**0.021**	7 (21.9)	9 (25.7)	0.713	25 (35.2)	40 (57.1)	**0.009**
Referred from a different hospital, Yes, n (%)	53 (50.0)	72 (67.9)	**0.013**	30 (85.7)	34 (94.4)	0.386	23 (32.4)	38 (54.3)	**0.008**
Onset-3-month interview interval, days, Median (Q1-Q3)	96.50 (92-104.75)	95 (92.25-102.75)	0.918	98 (91-123)	93 (91-102)	0.425	96 (92-103)	96 (93-104)	0.535

[a] Early arrival to study hospital was defined as arriving to the study hospital in not later than one day from the stroke onset date

[b] The denominator consisted of participants with documented stroke onset and hospital arrival dates.

Table 5.4: Baseline characteristics of participants according to phase of study ***Continued***

Variable	All			CHUB			CHUK		
	Pre-intervention n=106	**Post-intervention n=106**	**P-value**	**Pre-intervention n=35**	**Post-intervention n=36**	**P-value**	**Pre-intervention n=71**	**Post-intervention n=70**	**P-value**
Formal education [c]									
None	20 (30.3)	29 (32.6)	0.558	5 (26.3)	3 (11.5)	0.325	15 (31.9)	26 (41.3)	0.096
1-8 years	26 (39.4)	27 (30.3)		11 (57.9)	18 (69.2)		15 (31.9)	9 (14.3)	
9-12 years	12 (18.2)	14 (15.7)		2 (10.5)	5 (19.2)		10 (21.3)	9 (14.3)	
Vocation Training	3 (4.5)	8 (9.0)		0	0		3 (6.4)	8 (12.7)	
College/University	5 (7.6)	11 (12.4)		1 (5.3)	0		4 (8.5)	11 (17.5)	
Ubudehe category [C, d]									
1	16 (24.2)	15 (17.2)	0.461	9 (47.4)	9 (37.5)	0.075	7 (14.9)	6 (9.5)	0.575
2	10 (15.2)	18 (20.7)		1 (5.3)	8 (33.3)		9 (19.1)	10 (15.9)	
3	40 (60.6)	54 (62.1)		9 (47.4)	7 (29.2)		31 (66.0)	47 (74.6)	
4	0	0		0	0		0	0	

[c] The sample size included the participants who did not die in hospital and for whom the information was available during the follow-up interviews.

[d] Category 1: Families who do not own a house and can hardly afford basic needs; Category 2: Those who have a dwelling of their own or are able to rent one but rarely get full time jobs; Category 3: Those who have a job and farmers who go beyond subsistence farming to produce a surplus which can be sold. The latter also includes those with small and medium enterprises who can provide employment to dozens of people; Category 4: Those who own large-scale businesses, individuals working with international organizations and industries as well as public servants.

Participants in both study phases were similar for the demographic characteristics including age, sex, education and socio-economic status distributions, but it appeared that the post-intervention participants had more severe strokes than the pre-intervention participants. In fact, the proportion of hemorrhagic stroke (p=0.021), and participants who could not talk (p<0.0001), lift both arms (p=0.030) or walk (p=0.016) at their admission was higher in post than pre-intervention phase. I found that the proportion of the participants who were referred by other health care facilities (p=0.013) and also those who presented to hospital early (p=0.021) was higher in post than pre-intervention phase. For the study sites individually, the significant differences mentioned were remarkable at CHUK, but not at CHUB. There was no single participant with the highest socio-economic status at any of the two hospitals.

5.3.3 Implementation of stroke KPIs

Table 5.5 shows the proportion of participants who received the selected stroke KPIs according to phase of study. In general, there was a significant increase in participants who were assessed with a standardized tool (absolute increase of 22%, p=0.001) and those who received swallowing assessment (absolute increase of 31%, p<0.0001), mobilization (absolute increase of 14%, p=0.035), and multidisciplinary team meeting to plan care (absolute increase of 28%, p<0.0001).

At CHUK, I found significant increase in patients who received assessment with a standardized tool (absolute increase of 26%, p<0.0001), swallowing assessment (absolute increase of 42%, p<0.0001), mobilization (absolute increase of 26%, p=0.002) and multidisciplinary team meeting to plan care (absolute increase of 43%, p<0.0001). At CHUB, there was a significant increase only in participants who received early mobilization (absolute increase of 24%; p=0.049). No participant was admitted in a geographic stroke unit during either study phase.

Table 5. 5: Number (Percentage) of participants who received KPIs according to phase of study

KPI	All			CHUB			CHUK		
	Pre-intervention	**Post-intervention**	**P-value**	**Pre-intervention**	**Post-intervention**	**P-value**	**Pre-intervention**	**Post-intervention**	**P-value**
Brain Imaging	91 (85.8)	90 (84.9)	0.846	23 (65.7)	21 (58.3)	0.522	68 (95.8)	69 (98.6)	0.317
Use of standardized assessment tool [a]	33 (31.1)	56 (52.8)	**0.001**	30 (85.7)	35 (97.2)	0.081	3 (4.2)	21 (30.0)	**<0.0001**
Admission in a geographic stroke unit	0	0		0	0		0	0	
Swallowing assessment	6 (5.7)	39 (36.8)	**<0.0001**	5 (14.3)	9 (25.0)	0.257	1 (1.4)	30 (42.9)	**<0.0001**
Antithrombotic therapy for IS	51 (89.5)	34 (91.9)	0.697	14 (87.5)	9 (75.0)	0.393	37 (90.2)	25 (100)	0.107
Antithrombotic therapy [b]	82 (90.1%)	80 (92.0)	0.667	17 (81.0)	14 (82.4)	0.912	65 (92.9)	66 (94.3)	0.730
Surgery for ICH	3 (8.8)	7 (14.0)	0.472	0	0		3 (10.3)	7 (15.6)	0.522
Sugar lowering therapy	9 (64.3)	13 (56.5)	0.641	2 (66.7)	3 (60.0)	0.850	7 (63.6)	10 (55.6)	0.668
Blood pressure lowering therapy	42 (71.2)	61 (78.2)	0.346	10 (62.5)	15 (68.2)	0.715	32 (74.4)	46 (82.1)	0.351
Mobilization	57 (53.8)	72 (67.9)	**0.035**	25 (71.4)	22 (61.1)	0.358	32 (45.1)	50 (71.4)	**0.002**
Early mobilization [C]	15 (29.4)	20 (33.3)	0.658	3 (12.8)	8 (36.4)	**0.049**	12 (46.2)	12 (31.6)	0.237
MDT Meeting	5 (4.7)	35 (33.0)	**<0.0001**	3 (8.6)	3 (8.3)	0.971	2 (2.8)	32 (45.7)	**<0.0001**

Abbreviations: IS, ischemic stroke; KPI, stroke key performance indicator; MDT, multidisciplinary team

[a] Use of any of the following tools: modified Rankin Scale (mRS], National Institutes for Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS) and Functional Independence Measure (FIM)

[b] Giving any antithrombotic drugs (such as aspirin, enoxaparin/lovenox) for IS or not giving them in case of hemorrhagic stroke

[C] Starting mobilization within the first two days of admission

Table 5.6 presents the odds ratios for receiving a KPI after implementation of the intervention.

Table 5. 6: Odds ratios for receiving a KPI after implementation of the intervention

KPI	All			CHUB			CHUK		
	OR [c]	95% CI	p-value	OR [c]	95% CI	p-value	OR [c]	95% CI	p-value
				Unadjusted ORs					
Brain Imaging	0.93	0.43-1.99	0.846	0.73	0.28-1.91	0.522	3.04	0.31-30.00	0.340
Use of standardized assessment tool [a]	2.48	1.41-4.34	**0.002**	5.83	0.65-52.74	0.116	9.71	2.74-34.39	**<0.0001**
Swallowing assessment	9.70	3.89-24.19	**<0.0001**	2.00	0.60-6.71	0.262	52.50	6.90-399.69	**<0.0001**
Antithrombotic Therapy	1.25	0.45-3.53	0.668	1.10	0.21-5.75	0.912	1.27	0.33-4.94	0.731
Blood pressure lowering therapy	1.45	0.67-3.16	0.348	1.29	0.33-4.97	0.716	1.58	0.60-4.16	0.353
Mobilization	1.82	1.04-3.18	**0.036**	0.63	0.23-1.70	0.360	3.05	1.52-6.12	**0.002**
Early mobilization	1.20	0.54-2.69	0.658	4.19	0.95-18.53	0.059	0.54	0.19-1.51	0.239
MDT Meeting [b]	9.96	3.72-26.66	**<0.0001**	0.97	0.18-5.16	0.971	29.05	6.60-127.94	**<0.0001**
				Adjusted for SSV					
Brain Imaging	1.02	0.43-2.45	0.964	0.67	0.25-1.82	0.436	1.66	0.09-31.61	0.737
Use of standardized assessment tool [a]	2.18	1.14-4.17	**0.019**	2.92	0.24-34.78	0.397	12.66	1.76-91.30	**0.012**
Swallowing assessment	5.41	2.01-14.58	**0.001**	3.19	0.78-13.11	0.107	47.33	3.08-728.37	**0.006**
Antithrombotic Therapy	0.93	0.27-3.23	0.906	1.80	0.27-12.07	0.547	0.45	0.05-4.08	0.479
Blood pressure lowering therapy	1.79	0.71-4.47	0.215	1.20	0.29-4.93	0.797	3.93	0.98-15.75	0.053
Mobilization	1.92	1.01-3.64	**0.047**	0.69	0.22-2.15	0.527	4.88	1.72-13.84	**0.003**
Early mobilization	1.82	0.70-4.74	0.219	5.34	0.82-34.57	0.079	0.49	0.11-2.19	0.353
MDT Meeting [b]	9.28	2.80-30.76	**<0.0001**	1.17	0.19-7.29	0.869	36.58	3.60-372.10	0.002

Table 5.6: Odds ratios for receiving a KPI after implementation of the intervention ***Continued***

KPI	All			CHUB			CHUK		
	OR [c]	**95% CI**	**p-value**	**OR [c]**	**95% CI**	**p-value**	**OR [c]**	**95% CI**	**p-value**
				Adjusted for SSV and stroke type					
Brain Imaging	2.06	0.54-7.90	0.292	1.90	0.24-15.35	0.547	1.87	0.11-32.95	0.668
Use of standardized assessment tool [a]	2.03	1.04-3.96	**0.038**	3.03	0.25-37.02	0.386	12.63	1.75-91.11	**0.012**
Swallowing assessment	6.17	2.23-17.07	**<0.0001**	3.75	0.86-16.36	0.079	54.80	3.52-854.37	**0.004**
Antithrombotic Therapy	0.94	0.27-3.28	0.918	1.79	0.27-12.09	0.549	0.48	0.06-4.13	0.501
Blood pressure lowering therapy	1.80	0.71-4.57	0.216	1.28	0.29-5.61	0.745	4.57	1.08-19.31	**0.039**
Mobilization	2.05	1.07-3.92	**0.031**	0.77	0.24-2.46	0.660	5.41	1.85-15.80	**0.002**
Early mobilization	1.47	0.54-4.00	0.449	5.28	0.76-36.77	0.093	0.34	0.07-1.68	0.187
MDT Meeting [b]	9.66	2.92-32.01	**<0.0001**	1.25	0.19-8.14	0.815	36.57	3.59-372.25	**0.002**
				Adjusted for SSV, stroke type and stroke onset-hospital arrival interval					
Brain Imaging	1.69	0.41-7.05	0.469	1.67	0.13-22.24	0.699	0.51	0.01-22.78	0.730
Use of standardized assessment tool [a]	2.98	1.36-6.51	**0.006**	3.72	0.25-54.45	0.338	19.38	2.15-174.42	**0.008**
Swallowing assessment	5.73	2.08-15.74	**0.001**	4.50	0.81-25.03	0.086	33.01	3.62-301.19	**0.002**
Antithrombotic Therapy	1.20	0.33-4.41	0.787	5.79	0.39-86.79	0.203	0.26	0.02-2.97	0.278
Blood pressure lowering therapy	2.21	0.83-5.92	0.114	1.64	0.32-8.37	0.552	5.04	1.15-22.18	**0.032**
Mobilization	2.30	1.16-4.56	**0.017**	0.88	0.24-3.19	0.843	5.29	1.80-15.67	**0.002**
Early mobilization	1.73	0.58-5.18	0.327	14.38	0.92-225.93	0.058	0.34	0.07-1.68	0.186
MDT Meeting [b]	9.04	2.74-29.86	**<0.0001**	1.66	0.22-12.81	0.626	18.62	3.19-108.87	**0.001**

Abbreviations: CI, confidence interval; KPI, stroke key performance indicator; MDT, multidisciplinary team; OR, odds ratio; SSV, six simple variables: (age, living alone before stroke, being independent in everyday activities before stroke, being able to talk, being able to lift both arms to horizontal and being able to walk independently)

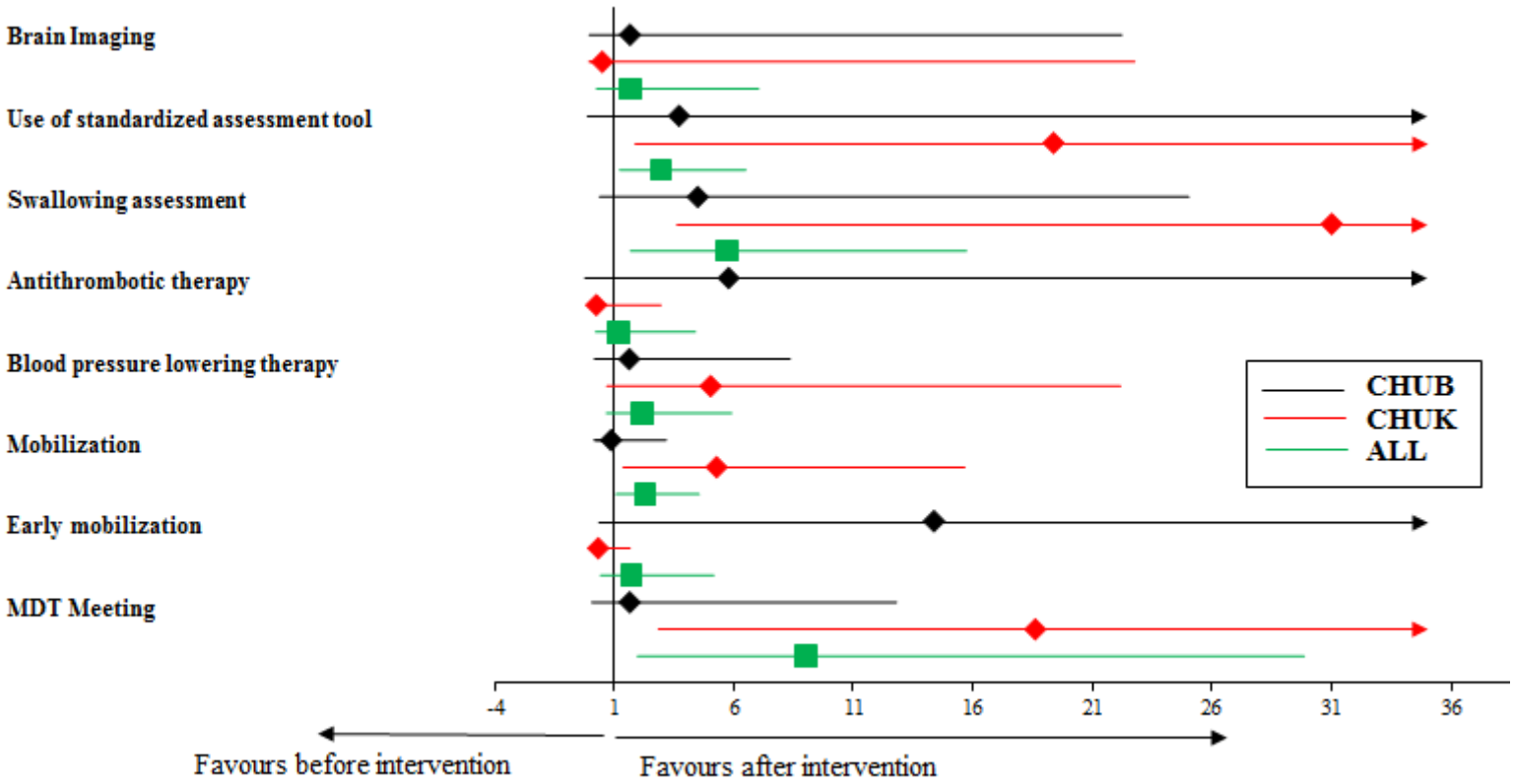
[a] Use of any of the following tools: modified Rankin Scale (mRS), National Institutes for Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS) and Functional Independence Measure (FIM)

[b] Starting mobilization within the first two days of admission

[C] Reference is the pre-intervention phase

As summarized in Figure 5.4, after case mix adjustment for six simple variables, stroke type and stroke onset-hospital arrival interval, I found a consistent trend of associations between the intervention and an increase in participants who received the KPIs investigated, although the associations were generally complicated by very wide CIs, and were significant for the use of standardized assessment tool, swallowing assessment, mobilization and multidisciplinary team meetings in general and at CHUK considered alone only. There was also a significant association between the intervention and the delivery of blood pressure lowering therapy (adjusted OR: 5.04; 1.15-22.18, p=0.032) at CHUK. I did not find evidence for improved KPI delivery at CHUB.

Figure 5. 4: Adjusted odds ratios for receiving KPIs after implementation of the intervention



5.3.4 Patient outcomes

Table 5.7 shows the number of participants with better outcomes according to phase of study

Table 5. 7: Number (Percentage) of participants with better outcomes according to phase of study

Variable, n (%)	All			CHUB			CHUK		
	Pre-intervention	**Post-intervention**	**P-value**	**Pre-intervention**	**Post-intervention**	**P-value**	**Pre-intervention**	**Post-intervention**	**P-value**
Survival in hospital	82 (77.4)	90 (84.9)	0.160	28 (80.0)	29 (80.6)	0.953	54 (76.1)	61 (87.1)	0.090
Survival at 3 months post stroke onset	68 (64.8)	76 (71.7)	0.279	20 (58.8)	22 (61.1)	0.845	48 (67.6)	54 (77.1)	0.206
Independent survival (mRS=0-2) at 3 months post stroke onset	20 (26.0)	36 (40.4)	**0.049**	4 (16.7)	6 (23.1)	0.571	16 (30.2)	30 (47.6)	0.056
Shorter LoS (<10 days)	50 (47.6)	52 (50.0)	0.731	10 (29.4)	18 (50.0)	0.079	40 (56.3)	34 (50.0)	0.454
Good quality of life [a] at 3 months post stroke onset	11 (16.4)	29 (34.9)	**0.011**	1 (5.0)	4 (15.4)	0.262	10 (21.3)	25 (43.9)	**0.015**

Abbreviations: LoS, length of hospital stay; mRS, modified Rankin Scale

[a] Good quality of life was defined as quality of life score ≥ 75%

I found a trend of improved patient outcomes in general and at both hospitals individually, although the improvements were significant for the survival with independence (mRS=0-2) (absolute increase of 14%, p=0.049) and the survival with good quality of life (absolute increase of 19%, p=0.011) both sites combined. For individual sites, there was significant improvement for good quality of life at CHUK (absolute increase of 23%, p=0.015) only. I did not find evidence for improved patient outcomes at CHUB.

Table 5.8 presents the odds ratios for receiving a KPI after implementation of the intervention.

Table 5. 8: Odds ratios for better outcomes after implementation of the intervention

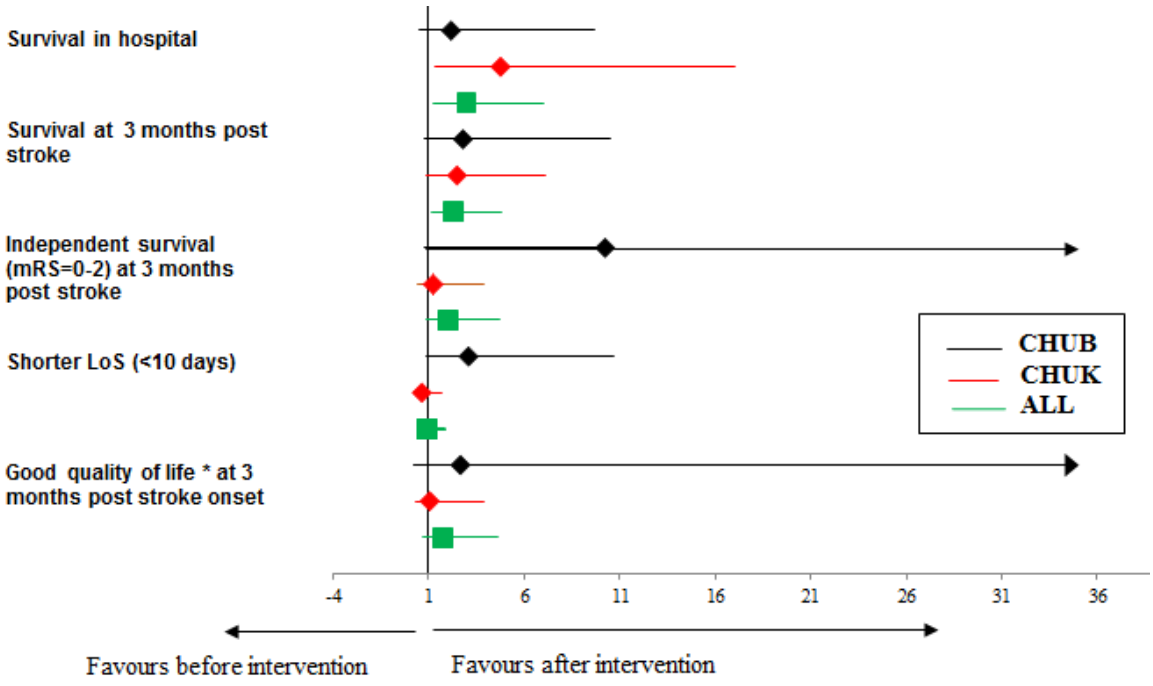
Variable	All			CHUB			CHUK		
	OR [b]	95% CI	p-value	OR*	95% CI	p-value	OR*	95% CI	p-value
Unadjusted ORs									
Survival in hospital	1.65	0.82-3.32	0.163	1.04	0.32-3.34	0.953	2.13	0.88-5.18	0.094
Survival at 3 months post stroke onset	1.38	0.77-2.47	0.280	1.10	0.42-2.86	0.845	1.62	0.77-3.41	0.207
Independent survival (mRS=0-2) at 3 months post stroke	1.94	1.00-3.74	**0.050**	1.50	0.37-6.14	0.573	2.10	0.98-4.53	0.058
Shorter LoS (<10 days)	1.10	0.64-1.89	0.731	2.40	0.90-6.43	0.082	0.76	0.40-1.51	0.454
Good quality of life [a] at 3 months post stroke onset	2.73	1.24-6.01	**0.012**	3.46	0.36-33.63	0.286	2.89	1.21-6.92	**0.017**
ORs adjusted for SSV									
Survival in hospital	2.32	1.02-5.28	**0.045**	1.25	0.35-4.40	0.733	4.65	1.32-16.47	**0.017**
Survival at 3 months post stroke onset	1.87	0.94-3.72	0.076	1.62	0.53-4.93	0.395	2.35	0.83-6.62	0.107
Independent survival (mRS=0-2) at 3 months post stroke	1.55	0.71-3.37	0.273	3.18	0.51-19.99	0.218	1.19	0.38-3.70	0.761
Shorter LoS (<10 days)	1.09	0.58-2.02	0.796	2.74	0.95-7.93	0.062	0.67	0.26-1.72	0.409
Good quality of life [a] at 3 months post stroke onset	1.95	0.77-4.99	0.162	4.17	0.36-48.69	0.255	1.11	0.31-3.95	0.874
ORs adjusted for SSV and stroke type									
Survival in hospital	2.59	1.12-5.98	**0.026**	1.61	0.40-6.43	0.501	4.64	1.31-16.48	**0.018**
Survival at 3 months post stroke onset	1.99	0.98-4.04	0.056	1.97	0.59-6.63	0.273	2.34	0.82-6.62	0.111
Independent survival (mRS=0-2) at 3 months post stroke	1.60	0.72-3.57	0.250	3.11	0.48-20.07	0.233	1.22	0.39-3.79	0.737
Shorter LoS (<10 days)	0.99	0.52-1.86	0.967	2.85	0.96-8.45	0.059	0.64	0.24-1.68	0.364
Good quality of life [a] at 3 months post stroke onset	1.84	0.70-4.84	0.217	3.61	0.28-45.99	0.323	1.09	0.30-3.93	0.896
ORs adjusted for SSV, stroke type and stroke onset-hospital arrival interval									
Survival in hospital	2.97	1.25-7.05	**0.014**	2.17	0.48-9.72	0.312	4.76	1.33-17.03	**0.016**
Survival at 3 months post stroke onset	2.30	1.10-4.78	**0.026**	2.79	0.74-10.50	0.130	2.48	0.87-7.09	0.091
Independent survival (mRS=0-2) at 3 months post stroke	2.05	0.87-4.82	0.100	10.23	0.78-134.41	0.077	1.20	0.37-3.87	0.756
Shorter LoS (<10 days)	0.93	0.48-1.80	0.825	3.08	0.89-10.67	0.076	0.64	0.24-1.72	0.378
Good quality of life [a] at 3 months post stroke onset	1.73	0.65-4.62	0.275	2.66	0.19-37.57	0.469	1.05	0.28-3.91	0.940

Abbreviations: CI, confidence interval; LoS, length of hospital stay; mRS, modified Rankin Scale; OR, odds ratio; SSV, six simple variables: (age, living alone before stroke, being independent in everyday activities before stroke, being able to talk, being able to lift both arms to horizontal and being able to walk independently)

[a] Good quality of life was defined as quality of life score ≥ 75%; [b] Reference is the pre-intervention phase

As summarized in Figure 5.5, after case mix adjustment for six simple variables, stroke type and stroke onset-hospital arrival interval, all the results, except for the LoS, consistently suggested improved patient outcomes. However, the results were significant for the survival in hospital for CHUK (adjusted OR: 4.76; 1.33-17.03, p=0.016) and both sites combined (adjusted OR: 2.97; 1.25-7.05, p=0.014), and the survival at three months post stroke onset both sites combined (adjusted OR: 2.30; 1.10-4.78, p=0.026) only.

Figure 5. 5: Adjusted odds ratios for better outcomes after implementation of the intervention



Abbreviations: LoS, length of hospital stay; mRS, modified Rankin Scale

[a] Good quality of life was defined as quality of life score ≥ 75%

5.4 Facilitators and barriers to stroke unit care implementation

5.4.1 Facilitators

The hospital directors were aware of the need for stroke service improvement and pledged their support to the success of the study. For instance, the two directors said that it was important to improve stroke care in their hospitals and nationally because NCDs were rising and were recognized as important causes of death and disability in Rwanda. They also mentioned that my study was in line with the hospitals' vision to provide evidence-based quality services to their clients and commended their staff to translate the knowledge gained during the educational seminar into practice.

5.4.2 Barriers

Although there was a consensus to implement all stroke care elements that were presented during the training, there were several barriers to stroke unit care implementation in the study hospitals and in Rwanda in general.

First, there were challenges to deliver thrombolysis, intra-arterial interventions and ICH management services including lack or shortage of infrastructure and competent personnel, and patient transfer delays. My audit results also showed the delays in arriving to hospital, and they were barriers to deliver the KPIs as early as recommended. Second, the hospital directors and the seminar participants said that there were no resources to establish geographic stroke units. Meanwhile, they agreed on the possibility of organizing stroke patients' beds in the same ward areas. Third, during the post-intervention patient recruitment period, the CT scan machine at CHUB was not functioning, and patients were referred to other hospitals for brain imaging.

5.5 Discussion

The key finding of this study was that, after adjusting for casemix and hospital arrival delay, the intervention was significantly associated with improved delivery of almost all the KPIs investigated including; the use of standardized assessment tool (adjusted OR: 2.98; 1.36-6.51, p=0.006), swallowing assessment (adjusted OR: 5.73; 2.08-15.74, p=0.001), mobilization (adjusted OR: 2.30; 1.16-4.56, p=0.017) and multidisciplinary team meetings (adjusted OR: 9.04; 2.74-29.86, p<0.0001). Secondly, I found that, after adjusting for casemix and hospital arrival delay, the intervention was significantly associated with

improved survival in hospital (adjusted OR: 2.97; 1.25-7.05, p=0.014) and survival at three months post stroke (adjusted OR 2.30; 1.10-4.78, p=0.026).

Overall, I found that my implementation intervention resulted in an absolute increase in the percentage of participants who received any of the KPIs investigated, except for brain imaging and availability of a geographic stroke unit. However, the improvements were statistically significant only for the use of standardized assessment tools, swallowing assessment, mobilization, and multidisciplinary team meetings. These results were in agreement with the views from the educational seminar participants who indicated that early mobilisation, swallowing assessment and multidisciplinary teams were the top three KPIs that could be improved. Regarding swallowing assessment, a similar Australian study (Middleton et al., 2011) showed an absolute increase of 39%, which was similar to what I found (absolute increase of 31%). Any difference might be due imprecision or a lower compliance to the intervention by the study hospitals staff.

Despite the available evidence for the substantial benefits from a stroke unit admission (Health Quality Ontario, 2014), geographic stroke units were not yet established at either study hospital. During the consensus discussions, only one of 38 participants thought that a geographic stroke unit could be established at the work place. As access to a geographic stroke unit is associated with improved use of investigations and treatments, access to other rehabilitation services, and consequently improved patient outcomes (de Villiers et al., 2009; Langhorne et al., 2018), lack of geographic stroke unit and multidisciplinary teams dedicated to stroke patients' management at the study settings was a major barrier for stroke service improvement. Surgical intervention for ICH was also rarely performed despite the high proportion of hemorrhagic strokes (32% and 47% during the pre and post-intervention phase respectively) and some promising evidence for its benefits (Dey et al., 2014). Lack of positive change for brain imaging could be attributed to the fact that the CT-scan machine at one hospital was not functioning during the post-intervention patient recruitment period, and patients could only get the imaging services in other hospitals by travelling a distance of 135 km.

Despite the significant improvements in the delivery of several KPIs, the absolute performance rates were low when compared to the quality standards according to which stroke patients should receive every KPI if they are eligible (Lindsay et al., 2014). I conducted my study in hospitals with support from the directors, and the educational seminar participants were convinced to improve their practice. Despite this common

willingness, there were challenges in terms of technical, material, financial and human resources that need to be addressed for implementing all key stroke unit care components.

Given the results of improvements in stroke KPIs delivery and the evidence for the association of swallowing assessment and mobilisation with improved patient outcomes (Urimubenshi et al., 2017), one might also expect better outcomes from my intervention. I found a trend of improved patient outcomes in general and at both hospitals individually, although the improvements were only statistically significant for the survival with independence (mRS=0-2) and better quality of life. My results were consistent with the ones from a previous similar study (Middleton et al., 2011) which showed that a multidisciplinary intervention to support proactive evidence-based management of fever, hyper glycaemia, and swallowing was associated with 10% absolute increase in survival with independence at three months post stroke onset. The higher absolute increase of 14% found in my study could be due to having had a clinical intervention of 11 KPIs compared to three KPIs only in the other study while there is evidence of an association between achieving a greater number of KPIs and better patient outcomes (Urimubenshi et al., 2017). Additionally, the differences might be due to different baseline services (stroke units versus general medical wards).

When looking at both sites combined, I found that my intervention was independently associated with improved survival in hospital (adjusted OR: 2.97; 1.25-7.05, p=0.014) and survival at three months post stroke (adjusted OR 2.30; 1.10-4.78, p=0.026). Patient outcomes for CHUB were not statistically significant probably due to a very small sample size, but I found a clear association between my intervention and the survival in hospital for CHUK (adjusted OR: 4.76; 1.33-17.03, p=0.016). The clinical significance of these results is more remarkable when compared against other established clinical interventions, namely swallowing assessment and mobilisation (Urimubenshi et al., 2017). Although not shown to be statistically significant, the promise of an increase in stroke survivors with independence (mRS=0-2) and also in those with better quality of life at three months post stroke could represent substantial benefits for patients.

I did not find evidence for the association between my intervention and reduced LoS for each hospital individually and in general. However, previous similar studies also provided inconsistent results. A South African study (de Villiers et al., 2009) has shown that implementing multidisciplinary stroke care was significantly associated with an increase in LoS. By contrast, a Danish study (Svendsen et al., 2009) reported that any of several KPIs

including stroke unit admission, antiplatelets and anticoagulants for IS with AF, brain imaging, early mobilization, occupational therapy assessment, swallowing assessment or deep vein thrombosis prophylaxis was significantly associated with a decrease in LoS.

Strengths and weaknesses

To the best of my knowledge, this is the first study to provide evidence on the feasibility of implementing aspects of stroke unit care in two selected hospitals in Rwanda, a low-income country with limited resources. The data suggest that using site champions, feedback on usual care and on-site training on stroke KPIs may facilitate stroke service delivery and better patient outcomes. The study, however, has several limitations. First, as I conducted the study in referral university teaching hospitals with better resources and services, my findings are not necessarily generalizable to all hospitals in Rwanda. Second, I achieved the desired sample size at CHUK, but not at CHUB because the recruitment was very slow while I had a time limit for the research project. This could have resulted to lack of power to provide evidence on the potential benefits associated with implementing stroke unit care KPIs at CHUB. Third, in-hospital data were obtained from patient medical files and there were considerable missing data. Specifically, as in my analysis I considered the undocumented KPIs as if they had not been implemented, there remains the possibility that my results do not reflect the real picture of stroke service delivery, and the intervention outcomes may have been influenced by improvements in documentation by the hospital staff. Fourth, I did not capture if the KPIs were delivered in accordance with the recommended quality standards. I hope future interventions to change practice could still further look at the quality of care received by the stroke patients. Fifth, my study was limited in that patients with severe strokes were relatively underrepresented. Although, I considered the six simple variables and stroke type for the casemix adjustment, my pre and post-intervention cohorts consisted of patients who survived for the first four and two days respectively. My results may therefore not represent the intervention benefits for patients with more severe strokes.

5.6 Conclusion

My study indicated that several common KPIs for a stroke unit care can be implemented in two selected hospitals in Rwanda although there were limited resources, and some important KPIs such as geographic stroke unit and thrombolysis were not yet implemented. The data suggested that there may be improved patient outcomes in hospital and at three months post stroke. Policy makers and health care professionals should consider implementing the stroke unit care KPIs including those that are not yet initiated like a geographic stroke unit. Future similar studies should consider assessing the quality of the delivery of the KPIs.

Chapter 6: Final discussion

6.1 A summary of my research

The aim of my thesis was to establish, for countries like Rwanda, how much stroke is a major problem (chapter 1), if services are well prepared (chapter 2) and then how to develop and implement a relevant service improvement (chapter 3-5).

Epidemiology and impact of stroke in Africa

An initial concern at the beginning was the relevance of the project and I aimed to explore to which extent stroke was a problem in Africa. As discussed in chapter 1, before my thesis there were several systematic reviews on the same topic. However, the literature searching methodologies of those previous systematic reviews may have resulted in them missing some relevant information on stroke in Africa. For example, the reviews were confined to studies published in English while some of the African researchers are more likely to publish in French. Additionally, the reviews included studies conducted in a small number of African countries. I therefore performed a systematic review of the literature on the epidemiology (incidence, prevalence, mortality, one month-case-fatality) and impact (disability, quality of life, and cost) of stroke in Africa. I searched many relevant databases including Medline, Embase, PubMed, and AJOL, with no language restriction. The review provided up-to-date and comprehensive results showing that stroke was common and important in Africa. I could not have achieved this by doing a simple narrative review. Since it is reported that adequate health services and strategies for stroke prevention in HICs have contributed to the decline in stroke mortality and disability rates, my findings raised a question on the availability, accessibility and quality of stroke services in Africa.

Stroke care in Africa

To develop and implement a relevant service improvement in countries like Rwanda, I had to gain a clearer understanding of the systems of stroke care in Africa and the areas for improvement. As shown in chapter 2, I performed a systematic review of the literature by searches of Ovid Medline, Embase, Amed, CINAHL, PubMed, and AJOL databases. There was no language restriction, but the search was limited to contemporary full-text publications (from January 1st, 2006 to June 20th, 2017). Previous similar reviews were confined to studies published in English while some of the African researchers are more likely to publish in French, and none of them focused of the delivery of stroke care in

Africa. Data from eligible publications were extracted and analysed based on the WSO Stroke services Framework (Lindsay et al., 2014). The findings showed that in the published reports the provision of stroke care in Africa was below the recommended standards with variations across and within counties, and they informed me about what I would include in the content of my stroke unit care intervention.

First, I learned much from previous initiatives to start-up stroke units in African countries**.** Collectively, 23 stroke units were reported; 21 in South Africa, one in Ghana and the remaining one in Central African Republic. There were three main lessons from South Africa (Burton et al. 2016):

i) Some stakeholders may not understand and support the idea immediately. For instance, the Ministry of Health in South Africa was unwilling to support a project to start stroke units, focusing on a single non-communicable disease;
ii) Starting up a stroke unit does not necessarily make it compliant with accepted international standards. In South Africa, they started with the formation of stroke teams, distributing post stroke care protocol templates, and trainings on stroke care by led by international experts.
iii) Finding champions for the cause, people enthusiastic about improving care who could help organise meetings and training sessions, was a key factor for the achievements made.

With the experience in South Africa, it became clear that I would have to communicate with the study hospitals' directors with enough information about the evidence on potential benefits of a stroke unit care. It also became clear that I had to consider the local context in developing the stroke unit care intervention, and use local champions as one of the implementation strategies.

Regarding the reports from Ghana (Baatiema et al., 2017) and the Central African Republic (Ossou-Nguiet et al., 2016), beyond being a geographic hospital area dedicated to stroke patients, there was no clear information on the characteristics of the stroke unit care. This finding indicated the need for a model of stroke unit care KPIs applicable in LMIC settings.

Second, the findings from several African countries suggested that implementing some interventions such as thrombolysis, intra-arterial interventions and ICH management in Rwanda may not be possible because of delays in arriving to hospital and the shortage of the resources required.

Third, the review showed that only a small proportion of patients with stroke arrived at a hospital within three hours from symptom onset and, consequently, less than 20% of patients were admitted within three hours of stroke onset. Such delays in presentation to hospital prevent patients from benefiting from some emergency interventions such as brain imaging and thrombolysis for IS among others. This finding implied a need for interventions in community and primary health care facilities to raise awareness of stroke signs and symptoms, and prompt referrals to hospitals. This issue was not addressed in this thesis because of limited time and financial resources. In my future plans I will consider this gap.

Key performance indicators of quality stroke care and their association with patient outcomes

I am convinced that initiatives to improve stroke care in any setting should focus on those stroke care elements that are relevant to the local context in terms of feasibility and effectiveness. As discussed in chapter 2, there is a need for determining the applicable key components to start up a stroke unit care in a given setting. I therefore aimed to identify the key elements of quality stroke care to inform the content of my stroke unit care intervention. As shown in chapter 3, I conducted a systematic literature review to identify the KPIs that have been described in stroke care and to summarise their association with patient outcomes. Searching sources were Ovid Medline, Embase and PubMed databases, and relevant references from screening the bibliographies of the initial articles included in the search. I included national or regional registers that recorded the independent association (after adjusting for at least age and a measure of stroke severity) between the KPIs and stroke patient outcomes.

I found that the most frequently reported KPIs for stroke care were swallowing assessment, stroke unit admission, antiplatelets for IS, brain imaging, anticoagulants for IS with AF, lipid management, deep vein thrombosis prophylaxis, and early mobilization. Stroke unit admission and early interventions including swallowing assessment, antiplatelets for IS, anticoagulants for IS with AF, lipid management and mobilization were all associated with better patient outcomes. Achieving a combination of several KPIs was always associated with a better outcome.

The studies that were included in my review involved large sample sizes in general, allowing sufficient statistical power and enhancing the external validity of the results.

However, the publications I reviewed were mainly from HICs. This raises a question of whether the KPIs in HICs are applicable to LMICs. As shown in chapter 4, I aimed to explore the examples of key stroke care elements outside high-income healthcare settings. I used the INTERSTROKE study data to identify the availability and delivery of stroke care services and their association with patient outcomes in LMICs generally and African countries in particular. I found that the commonly reported KPIs including early brain CT scan, access to a stroke unit or stroke specialist, antiplatelet therapy for IS, in-hospital and post-discharge rehabilitation, may have similar utility in LMICs as has been noted in HICs. Information on stroke KPIs in countries with different income levels was crucial in ensuring that the eventual intervention to implement stroke unit care in centres in Rwanda was going to be relevant and applicable in similar settings.

Developing a stroke unit care intervention relevant to Rwandan and other LMIC settings

The information that in Africa stroke was common and important (chapter 1), and that stroke services were below the recommended standards (chapter 2) suggested that interventions to improve stroke services and patient outcomes in Africa are necessary.
My contribution to this objective was to develop a model of stroke unit care relevant to Rwandan and other LMIC settings. Stroke unit care has become established as the central component of a modern stroke service to reduce the risk of death and disability after stroke. A "stroke unit" is defined as is a complex intervention that entails a combination of medical and rehabilitation interventions that are delivered by a multidisciplinary team of stroke specialists who work in a focussed and coordinated way to provide care for patients with stroke in hospital (Stroke Unit Trialists' Collaboration, 2013). In order to achieve my envisioned aim, I had to select the KPIs to include in my stroke unit care intervention. For this purpose, I used the results from my systematic review of the literature on stroke KPIs and analysis of INTERSTROKE study, the recommendations from the WSO stroke services framework (Lindsay et al., 2014) plus the Rwandan clinical guidelines (Ministry of Health, 2012; 2016). The Rwandan clinical guidelines included the clinical treatment guidelines for various conditions. However, the guidelines for stroke were limited to some aspects of investigations and management. Regarding the investigations, the guidelines included only blood tests, brain imaging, and investigations for the heart and carotid artery. For the management, the guidelines were limited to oxygen therapy, fever management, hydration and nutrition, antihypertensive therapy, pressure care, early mobilisation, drug

therapy for ischemic stroke, prevention of complications and secondary stroke, as well as counseling for patient and family. Several important aspects of stroke care such as swallowing assessment, speech and language therapy, and occupational therapy among others (Lindsay et al., 2014) were not included in the Rwandan guidelines. At present, no training in speech and language therapy is provided in Rwanda, and the 4-year training in OT started recently in 2015. Approximately, only five occupational therapists are employed in Rwanda, and none of them is at any of the two study hospitals.

Considering several sources of evidence enabled me to design a stroke unit care intervention that is meaningful, likely to be feasible and fit for wider implementation. My intervention consisted of 11 key elements including acute stroke diagnosis (recognition of strokes and brain imaging), use of stroke severity assessment tools, admission to a geographic stroke unit, swallowing assessment, antithrombotic therapy for IS, management of ICH, early mobilization, blood sugar and pressure monitoring and treatment, secondary prevention, and multidisciplinary team meetings.

Designing and testing a process of implementing stroke unit care in Rwanda

Despite the current evidence for its benefits, stroke unit implementation requires a range of health professional resources, co-location of beds and clinical leadership. Therefore, a project to implement stroke units in Rwanda, a low-income country appeared to be ambitious. I did not have funds to supplement the existing hospital resources, and my aim was to test the feasibility of a stroke unit care using available resources and thus ensuring potential sustainability. In the "WSO *Global Stroke Quality Action Plan"* (Lindsay et al., 2014, p. 2), it is stated that "even with the absolute minimal services available to you, at least something can be done for people with stroke that could make a difference to their recovery and outcomes".

Based on the available evidence on the effectiveness of various implementation interventions (Johnson and May, 2015) and the local context, I proposed to use a combination of several interventions including identification and preparation of site champions, provision of educational materials (soft and printed copies), face-to-face educational visit, feedback on usual care audit results, local consensus discussions, and discussions with the directors of the study hospitals. My supervisors have experience in conducting clinical trials. Their insights inspired me to consider several practical issues. For instance, it became clear to me that training the staff with different specialties together

was a good approach for each one to understand what others can do. This appeared as a strategy to enhance the multidisciplinary teamwork, and referrals between services. The site champions also advised me on a strategy to ensure that the educational seminar is attended from the beginning to the end. Lunch, transport fees to and from the training venue for all participants, and one-night accommodation fees for participants from CHUB were provided. The presence and contributions of two OSCAIL investigators during the educational seminar and meetings with the directors of the study hospitals was a strong support to show the importance of the study.

I am convinced that using such combined behavior change interventions was the best approach to optimize the compliance with the stroke unit care KPIs. After adjustment for case mix and stroke onset-hospital arrival interval, I found a consistent trend of associations between the implementation intervention and an increase in participants who received the KPIs investigated and a probable increase in better patient outcomes.

Limitations

My thesis is subject to three main limitations. First, my entire thesis project was subject to a limitation for generalisability. Findings from my systematic reviews on stroke epidemiology, impact and care in Africa were from studies that were conducted in urban settings and therefore might not show the situation in rural areas. Findings from the INTERSTROKE data analysis may not indicate the real picture about stroke KPIs in LMICs because of 70 hospitals from LMICs assessed for the INTERSTROKE study, only three were from low-income countries (Mozambique and Uganda). Additionally, many of the participants may have been recruited from urban settings with better resources and services. Consequently, the results cannot be generalized within or across all LMICs. Finally, I conducted the stroke unit care implementation trial in referral university teaching hospitals with better resources and services, and the findings are not necessarily generalizable to all hospitals in Rwanda. Further studies involving rural and primary health care facilities are recommended.

Second, my intervention did not result in the implementation of geographic stroke units despite the available evidence that they are associated with reduced risks of death and disability. The hospital directors and the educational seminar participants said that there were no resources to establish such units. Potential solutions to achieve this in future would be to have a collaboration partnership with the hospitals to further explore how

geographic stroke units can be established. This can be done in stages starting with at least a hospital area with dedicated beds and nursing staff as suggested by Langhorne et al. (2012).

Third, I cannot exclude the possibility that my intervention results were influenced by unmeasured factors. For instance, my trial was a before and after study and the associations between the implementation intervention and patient outcomes may have been influenced by residual confounding factors. Additionally, the in-hospital data for the trial were obtained from patient medical files and there were considerable missing data. Specifically, as in my analysis I considered the undocumented KPIs as if they had not been implemented, there remains the possibility that my results do not reflect the real picture of stroke service delivery, and the intervention outcomes may have been influenced by improvements in documentation by the hospital staff.

6.2 Future and wider implications for my thesis

Developing and testing a process of implementing stroke unit care in Rwanda was in line with the call from the Government of Rwanda for relevant studies to generate evidence for the policy makers to respond efficiently to the growing burden of NCDs including stroke (Ministry of Health, 2015c). My thesis provides the policy makers and healthcare professionals in Rwanda and other LMICs with a strategy to improve stroke care and outcomes. The implementation approach may also be relevant for other similar NCD conditions.

At present, it is not known if the study hospitals are maintaining the momentum for stroke service improvement. I am planning to have long-term collaborations with the two study hospitals and others in Rwanda for promoting quality stroke care. Specifically, in collaboration with the OSCAIL investigators, I have now developed a 3-year project entitled “Improving Stroke Care and Outcomes in Rwanda (ISCOR)”. The project is expected to start in January 2020 and will consist of four main activities:

(i) To understand the burden of stroke in the community and health facilities, the ISCOR team will collect data on stroke prevalence and incidence, mortality, morbidity and stroke care practices (e.g. amount of physiotherapy provided, use of secondary prevention treatments) in selected settings depending on the budget that will be available;

(ii) To collaborate with CHUK for establishing a geographic stroke unit;

(iii) To train multidisciplinary teams with expertise in stroke care. Physicians, nurses, physiotherapists, occupational therapists, speech therapists and community health care workers from Rwandan health care facilities (as many as possible) will be trained by local and international experts in stroke best practices, directly relevant to the needs of Rwandan stroke patients and with consideration of available resources. Specifically, as shown by the results in chapters 2 and 5, patients with stroke in Rwanda like in other African countries are late in arriving to hospital. Late presentation to hospital has been reported to be associated with poor awareness of stroke signs and symptoms, late referral from private hospitals, transportation problems, visit to traditional healers before coming to hospital, and treatment at home (Owolabi and Nagoda, 2012; Philip-Ephraim et al., 2015). Therefore, interventions to raise awareness about stroke in community and primary health care facilities will be considered;

(iv) To develop and test efficient and applicable stroke interventions, we will use the data on unmet stroke needs to determine intervention priorities. We will then determine current best practices and available evidence and assess applicability to the Rwandan setting.

We have already identified the key stakeholders and submitted the project to the Ministry of Health of Rwanda for approval.

Future well designed studies are recommended and should consider assessing the quality of the delivery of the KPIs.

6.3 A final note

The burden of stroke in LMICs has risen sharply in recent years and the rate of increase is set to accelerate. There is evidence that stroke unit care is associated with lower risks for death and disability, but it requires a range of health professional resources, co-location of beds and clinical leadership. My thesis addresses the strategies to implement stroke unit care in settings with limited resources. This thesis represents my first step in developing and implementing interventions to promote stroke unit care in hospitals in Rwanda and other under-resourced countries.

Appendices

Appendix 1. 1: Details for search strategies for epidemiology and impact of stroke in Africa

Medline

1. Stroke/
2. Cerebrovascular Disorders/
3. Epidemiology/
4. burden.mp.
5. Incidence/
6. Mortality/
7. Prevalence/
8. impact.mp.
9. disability.mp.
10. "Quality of Life"/
11. cost.mp.
12. Africa, Western/ or Africa, Northern/ or South Africa/ or Africa, Eastern/ or Africa.mp. or "Africa South of the Sahara"/ or Africa, Central/ or Africa/ or Africa, Southern/
13. 1 or 2
14. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
15. 12 and 13 and 14
16. limit 15 to (full text and yr="1980 - 2017")

Embase

1. stroke.mp.
2. cerebrovascular accident/
3. cerebrovascular disease/
4. epidemiology/
5. burden.mp.
6. incidence/
7. mortality/ or mortality rate/
8. case fatality.mp. or case fatality rate/
9. prevalence/
10. impact.mp.
11. disability/
12. "quality of life"/
13. "health care cost"/ or "cost"/ or "hospital cost"/ or "hospitalization cost"/
14. "Africa south of the Sahara"/ or South Africa/ or Africa/ or North Africa/ or Central Africa/ or Africa.mp.
15. 1 or 2 or 3

16. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

17. 14 and 15 and 16

18. limit 17 to (full text and yr="1980 - 2017")

Pubmed

(((((stroke[MeSH Terms]) OR cerebrovascular accident[MeSH Terms]) OR cerebrovascular disease[MeSH Terms])) AND ((((((((((epidemiology[MeSH Terms]) OR burden[MeSH Terms]) OR incidence[MeSH Terms]) OR mortality[MeSH Terms]) OR case fatality[MeSH Terms]) OR prevalence[MeSH Terms]) OR impact[MeSH Terms]) OR disability[MeSH Terms]) OR quality of life[MeSH Terms]) OR cost[MeSH Terms])) AND Africa[MeSH Terms] Filters: Full text, From 1980/01/01 to 2017/06/08

AJOL

Advanced search: stroke AND (epidemiology OR burden OR incidence OR mortality OR "case fatality" OR prevalence OR impact OR disability OR "quality of life" OR cost),
"cerebrovascular accident" AND (epidemiology OR burden OR incidence OR mortality OR "case fatality" OR prevalence OR impact OR disability OR "quality of life" OR cost),
"cerebrovascular disease" AND (epidemiology OR burden OR incidence OR mortality OR "case fatality" OR prevalence OR impact OR disability OR "quality of life" OR cost)
Advanced filters: Until June 8th, 2017

Appendix 2. 1: Details for search strategies for stroke care in Africa

Ovid Medline

1. exp Stroke/

2. exp Cerebrovascular Disorders/

3. exp Awareness/

4. exp "Delivery of Health Care"/

5. exp Health Services Accessibility/

6. exp Rehabilitation/

7. exp Therapeutics/

8. stroke unit.mp.

9. (referral and consultation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

10. exp Diagnosis/

11. exp Secondary Prevention/

12. exp Africa, Western/ or exp Africa, Central/ or exp "Africa South of the Sahara"/ or exp Africa/ or exp Africa, Northern/ or exp South Africa/ or exp Africa, Eastern/ or exp Africa, Southern/

13. 1 or 2

14. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11

15. 12 and 13 and 14

16. limit 15 to (full text and yr="2006 - 2017")

Embase

1. stroke.mp. or exp cerebrovascular accident/
2. exp cerebrovascular disease/
3. exp awareness/
4. exp health care delivery/
5. exp health care/
6. exp health care facility/
7. exp health care system/
8. exp health service/
9. exp health care access/
10. exp rehabilitation/
11. exp therapy/
12. exp stroke unit/
13. exp patient referral/
14. exp diagnosis/
15. exp secondary prevention/
16. exp "Africa south of the Sahara"/ or exp South Africa/ or exp Africa/ or exp North Africa/ or exp Central Africa/
17. 1 or 2
18. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
19. 16 and 17 and 18
20. limit 19 to (full text and yr="2006 - 2017")

Amed

1. exp stroke/
2. exp Cerebrovascular disorders/
3. exp Cerebrovascular accident/
4. exp Awareness/
5. exp "Delivery of health care"/
6. exp Health facilities/
7. exp Health services accessibility/
8. exp Rehabilitation/
9. exp therapeutics/
10. exp Therapy/
11. stroke unit.mp.
12. exp Diagnosis/
13. (referral and consultation).mp. [mp=abstract, heading words, title]
14. secondary prevention.mp.
15. exp Africa/
16. 1 or 2 or 3

17. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14

18. 15 and 16 and 17

19. limit 18 to yr="2006 - 2017"

CINAHL

http://search.ebscohost.com/login.aspx?direct=true&AuthType=athens,cookie,ip,url,uid&db=rzh&bquery=((MH+stroke)+OR+(MH+cerebrovascular+disorders))+AND+((MH+%26quot%3bAfrica%2b%26quot%3b)+OR+(MH+%26quot%3bAfrica+South+of+the+Sahara%2b%26quot%3b)+OR+(MH+%26quot%3bAfrica%2c+Western%2b%26quot%3b)+OR+(MH+%26quot%3bDemocratic+Nursing+Organisation+of+South+Africa%26quot%3b)+OR+(MH+%26quot%3bAfrica%2c+Southern%2b%26quot%3b)+OR+(MH+%26quot%3bAfrica%2c+Northern%2b%26quot%3b)+OR+(MH+%26quot%3bAfrica%2c+Eastern%2b%26quot%3b)+OR+(MH+%26quot%3bAfrica%2c+Central%2b%26quot%3b)+OR+(MH+%26quot%3bSouth+Africa%26quot%3b)+OR+(MH+%26quot%3bSouth+African+Nursing+Council%26quot%3b)+OR+(MH+%26quot%3bNamibia%26quot%3b))+AND+(((MH+awareness)+OR+(MH+health+care+delivery)+OR+(MH+health+care)+OR+(MH+health+care+system)+OR+(MH+health+care+facility)+OR+(MH+health+service)+OR+(MH+health+care+access)+OR+(MH+rehabilitation)+OR+(MH+therapy)+OR+(MH+stroke+units)+OR+(MH+patient+referral)+OR+(MH+diagnosis))+OR+(%26quot%3bsecondary+prevention%26quot%3b))&cli0=DT1&clv0=200601-201712&type=1&site=ehost-live

Pubmed

((("stroke"[MeSH Terms] OR "stroke"[MeSH Terms]) OR "cerebrovascular disorders"[MeSH Terms]) AND ((((((((((("awareness"[MeSH Terms] OR "delivery of health care"[MeSH Terms]) OR "delivery of health care"[MeSH Terms]) OR "delivery of health care"[MeSH Terms]) OR "health facilities"[MeSH Terms]) OR "health services"[MeSH Terms]) OR "health services accessibility"[MeSH Terms]) OR "rehabilitation"[MeSH Terms]) OR "therapeutics"[MeSH Terms]) OR "referral and consultation"[MeSH Terms]) OR "diagnosis"[MeSH Terms]) OR "secondary prevention"[MeSH Terms])) AND ("africa"[MeSH Terms] OR "africa"[All Fields]) AND ("loattrfull text"[sb] AND ("2006/01/01"[PDAT] : "2017/06/20"[PDAT]))

AJOL

(stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND awareness, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND health care, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND health service, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND diagnosis, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND treatment, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND management (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND rehabilitation, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND therapy , (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND stroke unit, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND referral, (stroke OR "cerebrovascular accident" OR "cerebrovascular disease") AND secondary prevention,

Appendix 2. 2: Form for extraction of data about stroke care in Africa

Author(s)		
Publication year		
Study setting		
Was the setting rural or urban?		
Study design		
Sample size		
Participants		
Main findings		
Key stroke care element(s) investigated		
The reported findings were about which of the six phases of the continuum of stroke care? Tick the box ☒ for Yes or No for each of the stroke care phases.		
Systems for stroke recognition and response	Yes ☐	No ☐
Hyperacute stroke care	Yes ☐	No ☐
Acute inpatient care	Yes ☐	No ☐
Stroke rehabilitation	Yes ☐	No ☐
Secondary stroke prevention	Yes ☐	No ☐
Longer-term stroke recovery	Yes ☐	No ☐

Appendix 3. 1: Details for search strategies for KPIs of quality stroke care and their association with patient outcomes

Ovid Medline

1. exp Stroke/
2. exp Cerebrovascular Disorders/
3. exp Intracranial Hemorrhages/
4. exp Brain Infarction/
5. exp Subarachnoid Hemorrhage/
6. exp "Quality of Health Care"/
7. exp Quality Indicators, Health Care/

8. exp Quality Assurance, Health Care/
9. exp Quality Control/
10. performance indicator.mp.
11. exp Registries/
12. exp Clinical Audit/
13. exp Treatment Outcome/
14. exp Mortality/
15. exp Survival/
16. disability.mp.
17. functional status.mp.
18. exp Hospitalization/
19. exp "Costs and Cost Analysis"/
20. exp "Quality of Life"/
21. complication.mp.
22. stroke recurrence.mp.
23. 1 or 2 or 3 or 4 or 5
24. 6 or 7 or 8 or 9 or 10
25. 11 or 12
26. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
27. 23 and 24 and 25 and 26
28. limit 27 to (english language and full text and yr="2000 -Current")

Embase

1. stroke.mp.
2. exp cerebrovascular accident/
3. exp cerebrovascular disease/
4. exp brain hemorrhage/
5. exp brain infarction/
6. exp subarachnoid hemorrhage/
7. exp health care quality/
8. exp quality control/
9. quality indicator.mp.
10. performance indicator.mp.
11. exp register/
12. exp clinical audit/
13. exp treatment outcome/
14. exp case fatality rate/
15. exp mortality/
16. exp survival/
17. exp disability/

18. exp functional status/
19. exp hospitalization/
20. exp "cost"/
21. exp "quality of life"/
22. exp complication/
23. exp hospital discharge/
24. stroke recurrence.mp.
25. 1 or 2 or 3 or 4 or 5 or 6
26. 7 or 8 or 9 or 10
27. 11 or 12
28. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
29. 25 and 26 and 27 and 28
30. 29 and 2000:2017.(sa_year).

Pubmed

(((((((((stroke[MeSH Terms]) OR cerebrovascular accident[MeSH Terms]) OR cerebrovascular disease[MeSH Terms]) OR brain hemorrhage[MeSH Terms]) OR brain infarction[MeSH Terms]) OR subarachnoid hemorrhage[MeSH Terms])) AND ((((health care quality[MeSH Terms]) OR quality indicators, health care[MeSH Terms]) OR quality control[MeSH Terms]) OR performance indicator[MeSH Terms])) AND ((registries[MeSH Terms]) OR clinical audit[MeSH Terms])) AND ((((((((((treatment outcome[MeSH Terms]) OR case fatality rate[MeSH Terms]) OR mortality[MeSH Terms]) OR survival[MeSH Terms]) OR disability[MeSH Terms]) OR functional status[MeSH Terms]) OR hospitalization[MeSH Terms]) OR cost[MeSH Terms]) OR quality of life[MeSH Terms]) OR complication[MeSH Terms]) OR hospital discharge[MeSH Terms]) OR stroke recurrence[MeSH Terms]) Filters: Full text, From 2000/01/01 to 2017/05/24, English

Appendix 4. 1: Details for the results from the logistic regression analysis for the association between stroke care bundle scores and 30-day patient outcomes

All countries						
	Analysis A	**Analysis B**	**Analysis C**	**Analysis D**	**Analysis E**	**Analysis F**
Bundle Score	**Crude ORs (95%CI) for 30-day case fatality**					
5	Reference					
4	1.83(1.40-2.38); P<0.0001	Reference	Reference	Reference	Reference	Reference
3	4.12(3.31-5.13); P<0.0001	3.44(2.77-4.26); P<0.0001	1.57(1.22-2.03); P<0.0001	2.59(2.09-3.20); P<0.0001	2.67(2.21-3.22); P<0.0001	1.86(1.43-2.43); P<0.0001
2	4.81(3.84-6.04); P<0.0001	4.44(3.55-5.55); P<0.0001	3.95(3.25-4.80); P<0.0001	3.18(2.62-3.85); P<0.0001	4.62(3.85-5.56); P<0.0001	4.22(3.41-5.23); P<0.0001
1	5.60(4.16-7.53); P<0.0001	5.47(4.08-7.34); P<0.0001	3.82(3.09-4.73); P<0.0001	4.12(3.25-5.22); P<0.0001	5.54(4.31-7.11); P<0.0001	5.36(4.30-6.68); P<0.0001
0	5.30(3.09-9.10); P<0.0001	5.26(3.07-9.03); P<0.0001	5.92(4.30-8.15); P<0.0001	5.47(3.50-8.55); P<0.0001	5.03(3.04-8.34); P<0.0001	4.05(2.85-5.75); P<0.0001
	Adjusted* ORs (95%CI) for 30-day case fatality					
5	Reference					
4	1.05(0.79-1.41); P=0.722	Reference	Reference	Reference	Reference	Reference
3	2.50(1.96-3.18); P<0.0001	1.94(1.53-2.45); P<0.0001	0.90(0.69-1.19); P=0.465	1.74(1.38-2.20); P<0.0001	2.24(1.82-2.75); P<0.0001	1.00(0.75-1.33); P=0.988
2	2.60(2.02-3.35); P<0.0001	2.44(1.90-3.12); P<0.0001	2.33(1.88-2.89); P<0.0001	2.70(2.18-3.35); P<0.0001	2.56(2.09-3.13); P<0.0001	2.50(1.97-3.16); P<0.0001
1	3.02(2.16-4.24); P<0.0001	2.95(2.12-4.12); P<0.0001	2.15(1.70-2.73); P<0.0001	3.01(2.30-3.93); P<0.0001	3.03(2.28-4.02); P<0.0001	2.80(2.20-3.59); P<0.0001
0	4.10(2.22-7.57); P<0.0001	4.02(2.18-7.43); P<0.0001	3.47(2.40-5.01); P<0.0001	4.09(2.43-6.87); P<0.0001	4.27(2.40-7.60); P<0.0001	2.66(1.79-3.96); P<0.0001

Appendix 4.1: Details for the results from the logistic regression analysis for the association between stroke care bundle scores and 30-day patient outcomes ***Continued***

All countries						
	Analysis A	**Analysis B**	**Analysis C**	**Analysis D**	**Analysis E**	**Analysis F**
Bundle Score	**Crude ORs (95%CI) for 30-day death or severe disability**					
5	Reference					
4	1.71(1.47-1.98); P<0.0001	Reference	Reference	Reference	Reference	Reference
3	1.88(1.65-2.15); P<0.0001	1.91(1.69-2.17); P<0.0001	1.63(1.41-1.89); P<0.0001	1.51(1.32-1.73); P<0.0001	1.50(1.34-1.69); P<0.0001	1.71(1.47-1.98); P<0.0001
2	2.12(1.84-2.45); P<0.0001	2.06(1.80-2.36); P<0.0001	1.97(1.74-2.23); P<0.0001	1.46(1.30-1.64); P<0.0001	1.96(1.74-2.20); P<0.0001	1.88(1.66-2.14); P<0.0001
1	2.64(2.14-3.27); P<0.0001	2.70(2.20-3.33); P<0.0001	1.84(1.59-2.11); P<0.0001	2.14(1.82-2.51); P<0.0001	2.41(2.00-2.90); P<0.0001	2.25(1.96-2.58); P<0.0001
0	2.31(1.50-3.57); P<0.0001	2.31(1.50-3.56); P<0.0001	2.96(2.31-3.80); P<0.0001	2.49(1.73-3.58); P<0.0001	2.10(1.38-3.19); P<0.0001	1.90(1.47-2.45); P<0.0001
	Adjusted* ORs (95%CI) for 30-day death or severe disability					
5	Reference					
4	1.17(0.98-1.40); P=0.087	Reference	Reference	Reference	Reference	Reference
3	1.24(1.05-1.45); P=0.010	1.22(1.04-1.41); P=0.012	1.15(0.96-1.37); P=0.135	1.03(0.88-1.21); P=0.707	1.32(1.15-1.52); P<0.0001	1.10(0.92-1.31); P=0.322
2	1.27(1.07-1.51); P=0.007	1.27(1.07-1.50); P=0.006	1.25(1.08-1.46); P=0.003	1.35(1.16-1.56); P<0.0001	1.02(0.88-1.18); P=0.835	1.21(1.03-1.41); P=0.019
1	1.66(1.28-2.17); P<0.0001	1.72(1.33-2.23); P<0.0001	1.18(0.99-1.41); P=0.062	1.75(1.43-2.14); P<0.0001	1.25(0.99-1.57); P=0.066	1.30(1.10-1.54); P=0.003
0	1.68(1.02-2.78); P=0.043	1.69(1.02-2.79); P=0.042	1.84(1.37-2.49); P<0.0001	1.79(1.15-2.79); P=0.010	1.53(0.94-2.49); P=0.089	1.40(1.02-1.91); P=0.035

Appendix 4.1: Details for the results from the logistic regression analysis for the association between stroke care bundle scores and 30-day patient outcomes ***Continued***

LMICs						
	Analysis A	**Analysis B**	**Analysis C**	**Analysis D**	**Analysis E**	**Analysis F**
Bundle Score	**Crude ORs (95%CI) for 30-day case fatality**					
5	Reference					
4	1.17(0.86-1.60), p=0.325	Reference	Reference	Reference	Reference	Reference
3	2.40(1.84-3.13), P<0.0001	2.15(1.65-2.79), P<0.0001	0.98(0.74-1.31), P<0.0001	1.63(1.28-2.07), P<0.0001	2.01(1.63-2.47), P<0.0001	1.20(0.89-1.64), P=0.235
2	3.04(2.31-3.99); P<0.0001	2.85(2.18-3.73), P<0.0001	2.31(1.83-2.93), P<0.0001	1.88(1.51-2.35), P<0.0001	3.53(2.88-4.33), P<0.0001	2.51(1.94-3.26), P<0.0001
1	3.29(2.36-4.60); P<0.0001	3.28(2.36-4.56), P<0.0001	2.47(1.92-3.17), P<0.0001	2.35(1.81-3.05), P<0.0001	3.96(3.04-5.16), P<0.0001	3.47(2.66-4.53), P<0.0001
0	3.07(1.75-5.37); P<0.0001	3.11(1.78-5.44), P<0.0001	3.50(2.48-4.94), P<0.0001	3.09(1.95-4.90), P<0.0001	3.55(2.12-5.92), P<0.0001	2.44(1.66-3.56), P<0.0001
	Adjusted* ORs (95%CI) for 30-day case fatality					
5	Reference					
4	1.00(0.72-1.39), p=0.986	Reference	Reference	Reference	Reference	Reference
3	2.44(1.83-3.25), P<0.0001	1.89(1.43-2.50), P<0.0001	0.88(0.65-1.20), p=0.415	1.74(1.34-2.26), P<0.0001	2.24(1.78-2.80), P<0.0001	0.97(0.70-1.35). P<0.0001
2	2.64(1.96-3.55), P<0.0001	2.44(1.83-3.27), P<0.0001	2.28(1.77-2.91), P<0.0001	2.75(2.15-3.51), P<0.0001	2.62(2.10-3.27), P<0.0001	2.47(1.87-3.27), P<0.0001
1	2.96(2.04-4.29), P<0.0001	2.87(1.99-4.14), P<0.0001	2.20(1.67-2.90), P<0.0001	2.99(2.23-4.00), P<0.0001	3.03(2.25-4.08), P<0.0001	2.89(2.16-3.85), P<0.0001
0	3.95(2.10-7.43), P<0.0001	3.84(2.05-7.22), P<0.0001	3.39(2.29-5.01), P<0.0001	4.04(2.38-6.86), P<0.0001	4.18(2.34-7.48, P<0.0001	2.64(1.73-4.03), P<0.0001

Appendix 4.1: Details for the results from the logistic regression analysis for the association between stroke care bundle scores and 30-day patient outcomes ***Continued***

LMICs						
	Analysis A	**Analysis B**	**Analysis C**	**Analysis D**	**Analysis E**	**Analysis F**
Bundle Score	**Crude ORs (95%CI) for 30-day death or severe disability**					
5	Reference					
4	1.42(1.17-1.72), P<0.0001	Reference	Reference	Reference	Reference	Reference
3	1.37(1.15-1.63), P<0.0001	1.50(1.27-1.77), P<0.0001	1.25(1.05-1.50), p=0.014	1.08(0.92-1.26), p=0.374	1.26(1.11-1.44), p=0.001	1.33(1.11-1.60), p=0.002
2	1.66(1.39-1.99), P<0.0001	1.65(1.38-1.97), P<0.0001	1.39(1.19-1.63), P<0.0001	0.97(0.84-1.13), p=0.717	1.65(1.44-1.89), P<0.0001	1.33(1.12-1.56), p=0.001
1	1.95(1.53-2.48), P<0.0001	2.05(1.62-2.59), P<0.0001	1.41(1.19-1.68), P<0.0001	1.39(1.16-1.66), P<0.0001	1.92(1.58-2.34), P<0.0001	1.71(1.44-2.03), P<0.0001
0	1.67(1.07-2.62), P<0.0001	1.72(1.10-2.69), P=0.017	2.11(1.62-2.76), P<0.0001	1.60(1.10-2.32), p=0.014	1.65(1.08-2.52), p=0.020	1.35(1.03-1.78), p=0.031
	Adjusted* ORs (95%CI) for 30-day death or severe disability					
5	Reference					
4	1.46(1.17-1.82), P<0.0001	Reference	Reference	Reference	Reference	Reference
3	1.50(1.23-1.84), P<0.0001	1.50(1.23-1.81), P<0.0001	1.37(1.11-1.68), P=0.003	1.19(0.98-1.43), P=0.074	1.45(1.24-1.70), P<0.0001	1.28(1.04-1.59), p=0.021
2	1.58(1.28-1.96), P<0.0001	1.58(1.29-1.94), P<0.0001	1.46(1.22-1.76), P<0.0001	1.54(1.29-1.84), P<0.0001	1.13(0.96-1.32), p=0.141	1.39(1.15-1.68), p=0.001
1	2.03(1.52-2.70), P<0.0001	2.10(1.58-2.78), P<0.0001	1.41(1.15-1.73), P=0.001	1.97(1.58-2.47), P<0.0001	1.37(1.08-1.74), p=0.010	1.53(1.25-1.88), P<0.0001
0	2.01(1.20-3.35), P<0.0001	2.01(1.21-3.36), P<0.0001	2.15(1.56-2.94), P<0.0001	2.02(1.29-3.16), P=0.002	1.63(1.00-2.65), p=0.050	1.60(1.15-2.22), P=0.005

Appendix 4.1: Details for the results from the logistic regression analysis for the association between stroke care bundle scores and 30-day patient outcomes ***Continued***

African countries						
	Analysis A	**Analysis B**	**Analysis C**	**Analysis D**	**Analysis E**	**Analysis F**
Bundle Score	**Crude ORs (95%CI) for 30-day case fatality**					
5	Reference					
4	0.20(0.03-1.39); P=0.103	Reference	Reference	Reference	Reference	Reference
3	1.25(0.26-6.04); P=0.784	1.07(0.22-5.18); P=0.932	0.21(0.03-1.44); P=0.112	0.21(0.03-1.34); P=0.098	3.68(1.10-12.32); P=0.035	0.25(0.03-2.35); P=0.225
2	1.22(0.25-5.87); P=0.806	1.14(0.24-5.49); P=0.870	1.53(0.32-7.22); P=0.594	1.21(0.25-5.79); P=0.810	3.91(1.17-13.02); P=0.027	2.84(0.97-8.71); P=0.057
1	1.16(0.24-5.63); P=0.853	1.15(0.24-5.57); P=0.863	1.25(0.26-5.90); P=0.783	1.23(0.26-5.93); P=0.796	3.77(1.12-12.69); P=0.032	2.79(0.97-8.02); P=0.056
0	0.66(0.13-3.41); P=0.619	0.65(0.13-3.37); P=0.610	1.09(0.23-5.17); P=0.919	0.77(0.15-3.95); P=0.758	2.14(0.59-7.82); P=0.244	1.72(0.57-5.24); P=0.337
	Adjusted* ORs (95%CI) for 30-day case fatality					
5	Reference					
4	0.46(0.06-3.62); P=0.461	Reference	Reference	Reference	Reference	Reference
3	1.54(0.27-8.74); P=0.624	1.35(0.24-7.73); P=0.734	0.48(0.06-3.68); P=0.478	0.41(0.06-2.97); P=0.380	2.17(0.59-7.97); P=0.244	0.50(0.05-4.93); P=0.554
2	1.35(0.24-7.56); P=0.731	1.19(0.21-6.74); P=0.843	1.83(0.33-10.07); P=0.490	1.42(0.26-7.90); P=0.686	2.08(0.55-7.37); P=0.289	2.30(0.71-7.45); P=0.165
1	1.49(0.26-8.35); P=0.653	1.38(0.24-7.88); P=0.717	1.31(0.24-7.19); P=0.757	1.58(0.28-8.76); P=0.602	2.25(0.61-8.28); P=0.224	2.17(0.69-6.83); P=0.184
0	1.16(0.19-6.97); P=0.870	1.11(0.18-6.76); P=0.913	1.49(0.27-8.20); P=0.645	1.32(0.22-7.78); P=0.761	1.78(0.45-7.10); P=0.416	1.75(0.53-5.82); P=0.359

Appendix 4.1: Details for the results from the logistic regression analysis for the association between stroke care bundle scores and 30-day patient outcomes ***Continued***

African countries

	Analysis A	Analysis B	Analysis C	Analysis D	Analysis E	Analysis F
Bundle Score	**Crude ORs (95%CI) for 30-day death or severe disability**					
5	Reference					
4	0.07(0.01-0.38); P=0.002	Reference	Reference	Reference	Reference	Reference
3	0.12(0.03-0.60); P=0.009	0.12(0.02-0.56); P=0.007	0.10(0.02-0.42); P=0.002	0.08(0.02-0.40), p=0.002	1.44(0.69-3.00); P=0.329	0.10(0.03-0.37); P=0.001
2	0.16(0.03-0.78); P=0.023	0.16(0.03-0.75); P=0.020	0.20(0.05-0.77); P=0.019	0.14(0.03-0.68), p=0.014	1.80(0.87-3.71); P=0.113	0.57(0.29-1.13); P=0.106
1	0.14(0.03-0.66); P=0.013	0.14(0.03-0.65); P=0.013	0.23(0.06-0.90); P=0.034	0.14(0.03-0.67), p=0.014	1.55(0.74-3.23); P=0.247	0.69(0.36-1.32); P=0.264
0	0.08(0.02-0.41), p=0.002	0.08(0.02-0.40), p=0.002	0.17(0.05-0.67); P=0.011	0.09(0.02-0.46), p=0.004	0.92(0.40-2.08), p=0.833	0.40(0.20-0.82); P=0.012
	Adjusted* ORs (95%CI) for 30-day death or severe disability					
5	Reference					
4	0.13(0.02-0.70); P=0.018	Reference	Reference	Reference	Reference	Reference
3	0.16(0.03-0.83); P=0.029	0.15(0.03-0.79); P=0.025	0.17(0.04-0.78); P=0.023	0.12(0.02-0.64), p=0.014	1.03(0.45-2.38); P=0.945	0.18(0.05-0.71); P=0.014
2	0.20(0.04-1.06); P=0.058	0.18(0.04-0.95); P=0.043	0.24(0.06-1.04); P=0.056	0.19(0.04-0.98), p=0.047	1.26(0.54-2.90); P=0.595	0.58(0.27-1.28); P=0.179
1	0.19(0.04-0.99); P=0.048	0.18(0.03-0.93); P=0.041	0.29(0.07-1.21); P=0.089	0.19(0.04-1.01), p=0.051	1.18(0.51-2.77); P=0.699	0.73(0.34-1.53); P=0.399
0	0.13(0.02-0.72); P=0.019	0.13(0.02-0.70); P=0.017	0.25(0.06-1.03); P=0.055	0.15(0.03-0.82), p=0.029	0.83(0.33-2.09), p=0.697	0.48(0.22-1.07); P=0.073

Abbreviations: LMICs, low and middle-income countries; OR, odds ratio

*Adjusted for age, baseline stroke severity, baseline level of consciousness, and Oxfordshire Community Stroke Project (OCSP) classification of stroke.

Analysis A: Logistic regression analysis for the association between patient outcomes and scores for the stroke care bundle of five components including brain CT scan by day 1, availability of stroke unit to at least (≥) 50% of stroke patients, availability of stroke specialist to at least (≥) 50% of stroke patients, antiplatelet therapy in hospital, and the availability of post-discharge rehabilitation
Analysis B: Analysis A after excluding availability of post-discharge rehabilitation from the stroke care bundle
Analysis C: Analysis A after excluding antiplatelet therapy in hospital from the stroke care bundle
Analysis D: Analysis A after excluding availability of stroke specialist to at least (≥) 50% of stroke patients from the stroke care bundle
Analysis E: Analysis A after excluding availability of stroke unit to at least (≥) 50% of stroke patients from the stroke care bundle
Analysis F: Analysis A after excluding brain CT scan by day 1 from the stroke care bundle

Appendix 5. 1: Admission Case Report Form (CRF)

OSCAIL ADMISSION CRF

SPECIFIC COMPLETION INSTRUCTIONS

B. CLINICAL INFORMATION

If participant has died, complete sections B with the details of the participant's time in hospital up to his/her death. Send the CRF to the Project Office as usual.

OSCAIL #138 Admission Pg 1 CRF 100 Visit 001

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Characteristics & Admission dates

A. PARTICIPANT CHARACTERISITCS

1. Date of birth: ☐☐☐☐☐☐☐☐ (year / month / day) 2. Sex: ☐ Female ☐ Male

3. Who did the participant live with before their stroke? (*select one*):

- ☐ Lives alone → ☐ Has professional caregivers / ☐ Does not have professional caregivers
- ☐ Living with family or friends → ☐ Has professional caregivers / ☐ Does not have professional caregivers
- ☐ Undocumented

B. CLINICAL INFORMATION

1. Blood Pressure at admission:

☐☐☐ (Systolic) ☐☐☐ (Diastolic) ☐ Undocumented

2. Date last seen normal (*stroke symptom onset*):

Date: ☐☐☐☐☐☐☐☐ (year / month / day) Time: ☐☐:☐☐ (00:00 - 23:59)

☐ Undocumented ☐ Undocumented

3. Arrival to current study hospital:

Date: ☐☐☐☐☐☐☐☐ (year / month / day) Time: ☐☐:☐☐ (00:00 - 23:59)

☐ Same date as 2 ☐ Undocumented

☐ Undocumented

4. Admission to current study hospital: ☐ Participant not admitted to study hospital (*skip to question #6*)

Date: ☐☐☐☐☐☐☐☐ (year / month / day) Time: ☐☐:☐☐ (00:00 - 23:59)

☐ Same date as 3 ☐ Undocumented

☐ Undocumented

5. Ward type participant was admitted to:

☐ Neurology ☐ Emergency Room ☐ General Medicine/Internal Medicine

☐ Intensive Care Unit ☐ High Dependency Unit ☐ Undocumented

☐ Other, *specify*:_____

SPECIFIC COMPLETION INSTRUCTIONS

B. CLINICAL INFORMATION (continued)

7. Did the participant die within 48 hours after admission?
Please indicate the cause of death using the two-digit coding provided.

01 - Stroke
02 - Complication of immobility (pneumonia, sepsis, pulmonary embolism, other)
03 - Cardiac arrest, MI, cardiac failure or other cardiac cause
04 - Malignancy, HIV/AIDS
05 - Other
06 - Unknown
07 - Undocumented

8. Six Simple Variables (SSV) at admission
Indicate undocumented, no or yes, for each question. If an answer to a question is not recorded, check ***undocumented***.

Glasgow Coma Scale Verbal Score on admission:

Behaviour	Response	Score
Best verbal response	Oriented to time, place, and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1

Medical Research Council (MRC) Scale of 3

Behaviour	Response	Score
Lifting both arms to horizontal	Complete paralysis	0
	Severe weakness (>50% loss of strength)	1
	Slight weakness (<50% loss of strength)	2
	Normal strength (against gravity)	3

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Transferred, Death & SSV

B. CLINICAL INFORMATION (continued)

6. Was the participant referred/transferred to this study hospital from a different healthcare centre?

☐ Undocumented

☐ No

☐ Yes → **a)** Date of arrival to previous hospital/healthcare centre: ☐☐☐☐☐☐☐☐ (year / month / day) ☐ Undocumented

b) Name of previous hospital/ healthcare centre:_____ ☐ Undocumented

7. Did the participant die within 48 hours after admission?

☐ No ☐ Yes → Date of death: ☐☐☐☐☐☐☐☐ (year / month / day)

→ Cause of death: ☐☐ (see instruction page for codes) If other, *specify*:_____

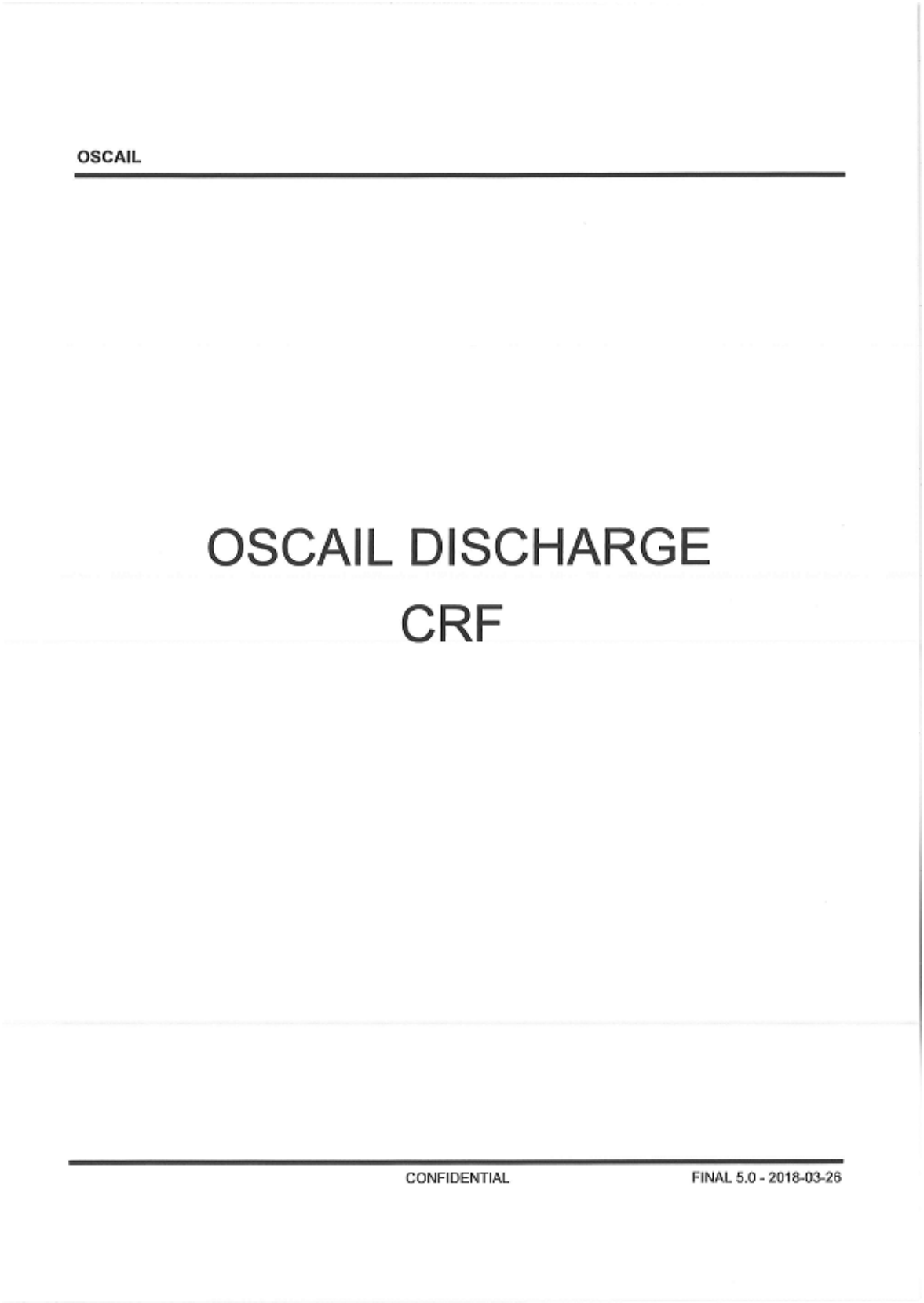
8. Six Simple Variables (SSV) at admission:

(Please check undocumented, no or yes for each question. See instruction page for Glasgow Coma Scale and MRC grade)

	Undocumented	No	Yes
c) Independent in everyday activities before stroke?:	☐	☐	☐
d) Glasgow Coma Scale - Verbal Score Normal?: (i.e. 5 - able to talk and not confused)	☐	☐	☐
e) Able to lift both arms to horizontal?: (i.e. at least an MRC grade of 3)	☐	☐	☐
f) Able to walk without the help of another person?: (although stick or frame allowed)	☐	☐	☐

Name of person completing form: _____ (Full name) Date completed: ☐☐☐☐☐☐☐☐ (year / month / day)

Appendix 5. 2: Discharge Case Report Form (CRF)



OSCAIL DISCHARGE CRF

SPECIFIC COMPLETION INSTRUCTIONS

A. DISCHARGE/DEATH

1. Participant status at discharge
If ***participant died in hospital***, record date of death and cause of death, complete CRFs with the details of the participant's time in hospital up to his/her death. Send the CRF to the Project Office as usual.

Please indicate the cause of death using the two-digit coding provided.

01 - Stroke
02 - Complication of immobility (pneumonia, sepsis, pulmonary embolism, other)
03 - Cardiac arrest, MI, cardiac failure or other cardiac cause
04 - Malignancy, HIV/AIDS
05 - Other
06 - Unknown
07 - Undocumented

Hospice is defined here as: an institution providing care for the terminally ill

4. Final stroke diagnosis at discharge (or at death or at 3-months if not discharged):
This is to confirm that the participant had a stroke.

Participant ID# ☐☐☐ ☐☐☐☐ *Site #* *Participant #*

Participant Initials ☐☐☐ *F M L*

Data collection date ☐☐☐☐☐☐ *year / month / day*

A. DISCHARGE/DEATH

Discharge

1. Participant status at discharge: *(select one)*

☐ Died in hospital → Date of death: ☐☐☐☐☐☐ *year / month / day* ☐ Undocumented

→ Cause of death: ☐☐ *(see instruction page for codes)* If other, *specify:*_____

☐ Discharged → Discharge destination:

☐ Home ☐ Relative's house ☐ Undocumented

☐ Hospital ☐ Rehabilitation facility

☐ Hospice ☐ Nursing home

☐ Prison ☐ Other, *specify:*_____

→ Date of discharge: ☐☐☐☐☐☐ *year / month / day* ☐ Undocumented

☐ Not discharged and 3-months since stroke symptom onset (date last seen normal)

2. Adverse events in hospital (before discharge, prior to death or at 3-months if not discharged):
*Check either **no** or **yes** for each question.*

	No	Yes	
a) Pneumonia	☐	☐ →	Aspiration pneumonia? ☐ No ☐ Yes ☐ Undocumented
b) Fall/broken bones	☐	☐	
c) Additional stroke	☐	☐	
d) Pressure Sores	☐	☐	
e) Bladder infection, UTI, Urosepsis	☐	☐ →	Was a catheter present? ☐ No ☐ Yes ☐ Undocumented

3. Blood pressure at discharge (or last blood pressure measurement before death or at 3-months)**:**

☐☐☐ *Systolic* ☐☐☐ *Diastolic* ☐ Undocumented

4. Final stroke diagnosis at discharge(or at death or at 3-months if not discharged):
(select one)

☐ Ischaemic stroke ☐ Haemorrhagic stroke ☐ Stroke (unknown subtype) ☐ Transient ischaemic attack (TIA)

☐ Not stroke or a TIA, *specify:*_____

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

History

B. PAST MEDICAL HISTORY (conditions participant had before the stroke)

*Please check either **no** or **yes** for **each question**.*

	No	Yes	
1. Prior stroke	☐	☐	→ ☐ Ischaemic; ☐ Haemorrhagic; ☐ Undocumented
2. Myocardial infarction	☐	☐	
3. Angina	☐	☐	
4. Hypertension	☐	☐	
5. High cholesterol	☐	☐	
6. Transient ischemic attack	☐	☐	
7. Diabetes mellitus	☐	☐	
8. Peripheral arterial disease	☐	☐	
9. Venous thromboembolism	☐	☐	
10. Rheumatic heart disease	☐	☐	
11. Atrial fibrillation/flutter	☐	☐	
12. Cancer	☐	☐	Primary site: → ☐ Lung ☐ Prostate ☐ Skin ☐ Colon ☐ Breast ☐ Undocumented ☐ Other, *specify:* _____
13. Renal dysfunction	☐	☐	
14. HIV/AIDS	☐	☐	
15. Tuberculosis (TB)	☐	☐	
16. Malaria	☐	☐	
17. Drinks alcohol	☐	☐	
18. Current smoker	☐	☐	

SPECIFIC COMPLETION INSTRUCTIONS

C. MEDICATIONS

Indicate whether the participant has been prescribed medications from each category for Pre-stroke and at discharge/death/3-months (post-stroke) (check all that apply). If a medication is not documented in the participant's records, please check ***no*** for that medication. No question can remain blank.
Refer to Appendix 1. Appendix 1 lists common generic and brand name drugs falling under each medication category.

Pre-stroke is defined as: Medications that the participant was taking up to 6-months prior to stroke (date last seen normal)
At Discharge/Death (post-stroke) is defined as: Medications that were prescribed at time of discharge or before death
(or at 3-months if participant has not been discharged from the hospital)

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

Medications

C. MEDICATIONS

*Please check either **no** or **yes** for **each question at pre-stroke and at discharge/death.***

	Pre-stroke		At Discharge/Death/3-months (post-stroke)	
1. Antithrombotics	**No**	**Yes**	**No**	**Yes**
a) Antiplatelets	☐	☐	☐	☐
b) Oral anticoagulants	☐	☐	☐	☐
2. Cholesterol-lowering	☐	☐	☐	☐
3. Antihypertensives	☐	☐	☐	☐
4. Other medications				
a) Antidepressant	☐	☐	☐	☐
b) Analgesic	☐	☐	☐	☐
c) NSAIDs	☐	☐	☐	☐
d) Antidiabetics	☐	☐	☐	☐

SPECIFIC COMPLETION INSTRUCTIONS

D. STANDARDIZED (STROKE) ASSESSMENT SCORES

1. Were any standardized (stroke) assessment measures used while the participant was in-hospital?
This question is concerned with any standardized assessment measures used (especially for stroke) at baseline and discharge. **Baseline** is the first time an assessment was done and **Discharge** is the assessment closest to discharge date (or death or 3 months if participant has not been discharged).

If there are no standardized assessment measures recorded, select ***no*** and move to Section E. If there was a standardized assessment measure used (e.g. NIHSS, m-RS, Glasgow Coma Scale, etc.) select ***yes*** and use the codes provided below to identify which standardized stroke assessment measure(s) was/were used.

Begin by completing 1.a). If there are more than one standardized stroke assessment measure used, record all of them using 1.b) -1.d).

If a documented score in the participant's records is discovered to be calculated incorrectly by the data collector, the corrected score should be recorded in the "Corrected Score" column. The reason for the corrected score should also be recorded using the coding found below.

Codes for Types of Standardized Assessment Measures:
01 - modified-Rankin Scale (m-RS)
02 - National Institutes of Health Stroke Scale (NIHSS)
03 - Glasgow Coma Scale
04 - Functional Independence Measure (FIM)
05 - Morse Fall Sore
06 - Pressure Risk Assessment Tool

Codes for Reason for Corrected Score
01 - Score miscalculated in the patient case notes

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Assessments

D. STANDARDIZED (STROKE) ASSESSMENT SCORES

1. Were any standardized (stroke) assessment measures used while the patient was in-hospital?:

☐ No

☐ Yes →

	Type:		Documented Score:	Date recorded:	Corrected Score:	Reason for Corrected Score
a)	☐☐	Baseline	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
		Discharge	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
b)	☐☐	Baseline	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
		Discharge	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
c)	☐☐	Baseline	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
		Discharge	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
d)	☐☐	Baseline	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
		Discharge	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
e)	Specify type: _____					
		Baseline	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐
		Discharge	☐☐☐	☐☐☐☐☐☐ year / month / day	☐☐☐	☐☐

SPECIFIC COMPLETION INSTRUCTIONS

E. DETAILS OF CARE

For each question, answer ***undocumented, no*** or ***yes***.

Please ensure you have thoroughly searched through all relevant patient records before answering ***undocumented*** to a question.

If ***yes***, follow the arrow, if ***no*** or ***undocumented***, move to the next numbered question (E.g. If no is checked for question 1, do not answer 1.a-e, advance to the question 2).

1.d) Was the scan administered more than 2 hours after arrival?
If the answer is yes, record the answer using the coding below.
01 - Long wait time
02 - Delayed admission to hospital/greater than 3 hours since last seen normal (stroke onset)
03 - Patient too unstable for assessment/treatment
04 - Unknown
05 - Contraindication
06 - Other
07 - Patient is uninsured/cannot afford health-care

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

Imaging

E. DETAILS OF CARE

1. Was brain imaging performed?

☐ **Undocumented**

☐ **No**

☐ **Yes** → **a) Date of imaging:** ☐☐☐☐☐☐☐☐ *year / month / day*

Time of imaging: ☐☐:☐☐ (00:00 - 23:59)

☐ Undocumented ☐ Undocumented

b) Brain imaging was performed at:

☐ Study hospital

☐ Other, *specify*: _____

c) Type of imaging:

☐ CT

☐ MRI

d) Was the scan administered more than 2 hours after arrival?

☐ Undocumented

☐ No

☐ Yes → Why? ☐☐ *(See instruction page for codes)* Other, *specify*: _____ *(code 06 selected)*

e) Was a new cerebral infarct or haemorrhage identified?

☐ No

☐ Yes → ☐ Ischaemic ☐ Haemorrhagic ☐ Undocumented

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Treatment

E. DETAILS OF CARE (continued)

2. Was a thrombectomy performed?

- ☐ Undocumented
- ☐ No
- ☐ Yes

3. Did participant receive antithrombotic therapy?

- ☐ Undocumented
- ☐ No
- ☐ Yes → **a) Date first administered:** ☐☐☐☐☐☐☐☐ (year / month / day) ☐ Undocumented

b) Type of therapy:

- ☐ Aspirin
- ☐ Alteplase
- ☐ Metalyse
- ☐ Enoxaparin/Lovenox
- ☐ Other, specify: _____

4. Was haemorrhagic stroke treatment administered?

- ☐ Undocumented
- ☐ No
- ☐ Yes → **a) Type of treament:**
  - ☐ Undocumented
  - ☐ Endovascular therapy
  - ☐ Surgery
  - ☐ Blood pressure management
  - ☐ Anti-convulsant medication
  - ☐ Other, *specify*: _____

b) Treatment administered at:

- ☐ Study hospital
- ☐ Other, *specify*: _____

5. Was atrial fibrillation detected?

- ☐ Undocumented
- ☐ No
- ☐ Yes

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Swallowing

E. DETAILS OF CARE (continued)

6. Was participant conscious at any time during hospital stay?

- ☐ **Undocumented**
- ☐ **No**
- ☐ **Yes** ⟶ **a) Did participant have a swallow srceen/assessment?**
  - ☐ Undocumented
  - ☐ No
  - ☐ Yes ⟶ **a) Date of assessment:**
    ☐☐☐☐☐☐☐☐ ☐ Undocumented
    year / month / day
    b) Type of screen/assessment: *(Select all that apply)*
    - ☐ Undocumented
    - ☐ Videofluoroscopy
    - ☐ Fiberoptic endoscopicevaluation (FEES)
    - ☐ Palpation
    - ☐ Assessment of facial/tongue/palatal asymmetries
    - ☐ Water Swallow Test ⟶ _____ mL ☐ Undocumented
    - ☐ Gag test
    - ☐ Other, *specify:* _____

7. Was participant NPO (nothing by mouth) during hospital stay?

- ☐ **Undocumented**
- ☐ **No**
- ☐ **Yes** ⟶ **a) NPO within the first 24 hours?:**
  - ☐ Undocumented
  - ☐ No
  - ☐ Yes

  b) Duration of NPO status:
  Number of days: ☐☐☐ ☐ Undocumented

  c) Was participant fed by a feeding tube?
  - ☐ Undocumented
  - ☐ No
  - ☐ Yes ⟶ Duration of tube feeding:
    Number of days: ☐☐☐ ☐ Undocumented

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Sugar

E. DETAILS OF CARE (continued)

8. Was an initial blood sugar assessment performed?

☐ **Undocumented**

☐ **No**

☐ **Yes** → **a) Date of assessment:** ☐☐☐☐☐☐☐☐ ☐ Undocumented
year / month / day

b) Was initial blood sugar/glucose elevated?

☐ Undocumented

☐ No

☐ Yes → **Measured blood glucose level:** *(Answer at least one of the following)*

☐ Undocumented

Fasting

☐ >6.0 mmol/L

☐ >108 mg/dL

Non-fasting

☐ >11.1 mmol/L

☐ >200 mg/dL

2 Hour GTT

☐ >7.8 mmol/L

☐ >140 mg/dL

→ **What treatment was provided for hyperglycaemia?:**

☐ Undocumented

☐ Dextrose/saline IV

☐ Insulin infusion or sliding scale

☐ Dextrose/saline IV and insulin infusion or sliding scale

☐ No treatment

☐ Other, *specify:*_____

c) Was blood sugar monitored?

☐ Undocumented

☐ No

☐ Yes → Frequency of monitoring: ☐☐ (test(s)) X ☐☐☐ (day(s)) ☐ Undocumented

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Temperature

E. DETAILS OF CARE (continued)

9. Was an initial temperature assessment performed?

- ☐ **Undocumented**
- ☐ **No**
- ☐ **Yes** → **a) Date of assessment:** ☐☐☐☐☐☐☐☐ ☐ Undocumented
  year / month / day
  - **b) Was initial temperature elevated (>38°C)?**
    - ☐ Undocumented
    - ☐ No
    - ☐ Yes → **What treatment was provided for fever?:**
      - ☐ Undocumented
      - ☐ No treatment
      - ☐ Aspirin
      - ☐ Paracetamol
      - ☐ Aspirin and Paracetamol
  - **c) Was temperature monitored?**
    - ☐ Undocumented
    - ☐ No
    - ☐ Yes → **Frequency of monitoring:** ☐☐ test(s) X ☐☐☐ day(s) ☐ Undocumented

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Mobility

E. DETAILS OF CARE (continued)

10. Was an initial mobility assessment done in hospital?

☐ **Undocumented**

☐ **No**

☐ **Yes** → **a) Who performed the mobility assessment?:** *(check all that apply)*

- ☐ Undocumented
- ☐ Nurse
- ☐ Physiotherapist
- ☐ Occupational therapist
- ☐ Physician

b) Date of mobility assessment:

☐☐☐☐☐☐☐☐ *year / month / day* ☐ Undocumented

c) What elements of mobility assessment were completed?: *(check all that apply)*

	Undocumented	No	Yes
a) Rolls in bed	☐	☐	☐
b) Sits up in bed	☐	☐	☐
c) Stands	☐	☐	☐
d) Walks	☐	☐	☐
e) Stairs	☐	☐	☐

11. Was mobility re-education training attempted?

☐ **Undocumented**

☐ **No**

☐ **Yes** → **a) Who performed the mobility re-education?:** *(check all that apply)*

- ☐ Undocumented
- ☐ Nurse
- ☐ Physiotherapist
- ☐ Occupational therapist
- ☐ Physician

b) Date mobility re-education started:

☐☐☐☐☐☐☐☐ *year / month / day* ☐ Undocumented

c) Frequency of mobility re-education training: ☐ **Prescribed** or ☐ **Actual**

- ☐ Once or twice ever
- ☐ Once a week
- ☐ Twice a week
- ☐ Three times a week
- ☐ Four times a week
- ☐ Five times a week
- ☐ Other, *specify:* _____

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Bowel, Bladder & Pressure

E. DETAILS OF CARE (continued)

12. At discharge was the participant able to use the toilet unassisted?(or just prior to death or at 3-months)

- ☐ **Undocumented**
- ☐ **Yes**
- ☐ **No** → **a) Please check all that apply**
  - ☐ Participant needed help of another person
  - ☐ Participant used a walker/cane
  - ☐ Participant used a bedpan/urinal
  - ☐ Paticipant used a nappy/diaper
  - ☐ Participant used a catheter → *type?* ☐ Indwelling ☐ Condom ☐ Unknown
  - ☐ Other, *specify:*_____

13. Did participant have evidence of pressure sores?

- ☐ **Undocumented**
- ☐ **No**
- ☐ **Yes** → **a) Were pressure sores resolved by discharge?**
  - ☐ Undocumented
  - ☐ No
  - ☐ Yes

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

2°Prevention

E. DETAILS OF CARE (continued)

14. Was secondary prevention prescribed/discussed?

- ☐ **Undocumented**
- ☐ **No**
- ☐ **Yes → What elements of secondary prevention were prescribed or discussed?**

	Undocumented	No	Yes
a) Antiplatelet therapy ?	☐	☐	☐ → ☐ Continued from pre-admission ☐ Started post-admission
b) Antihypertensive therapy ?	☐	☐	☐ → ☐ Continued from pre-admission ☐ Started post-admission
c) Anticoagulation therapy ?	☐	☐	☐ → ☐ Continued from pre-admission ☐ Started post-admission
d) Antibiotic therapy ?	☐	☐	☐ → ☐ Continued from pre-admission ☐ Started post-admission
e) Statin therapy ?	☐	☐	☐ → ☐ Continued from pre-admission ☐ Started post-admission
f) Does participant drink alcohol? (see question 17 on CRF 103)	☐	☐	☐ →Was advice to lower alcohol consumption given? ☐ Undocumented ☐ No ☐ Yes
g) Does the participant smoke? (see question 18 on CRF 103)	☐	☐	☐ →Was advice to decrease/quit smoking given? ☐ Undocumented ☐ No ☐ Yes
h) Was a dietary change required?	☐	☐	☐ →Was advice to improve diet given? ☐ Undocumented ☐ No ☐ Yes

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

Discharge Planning

E. DETAILS OF CARE (continued)

15. What elements of discharge planning were performed?

	Undocumented	No	Yes
a) Discharge location planned/assessed?	☐	☐	☐
b) Follow-up appointment scheduled?	☐	☐	☐
c) Referred to rehabilitation services?	☐	☐	☐
d) Diet and lifestyle recommendations?	☐	☐	☐
e) Did at least one health practitioner meet with a family member?	☐	☐	☐
f) Educated on stroke symptoms, expectations for recovery, and rehabilitation?	☐	☐	☐
g) Were all hospital care providers informed of the participant's discharge before the participant was discharged ?	☐	☐	☐
h) Was the family provided with training regarding care of participant post-discharge?	☐	☐	☐

↓

Type of training provided: *(select all that apply)*

	Written material provided? No	Yes
☐ Undocumented		
☐ Speech and language exercises →	☐	☐
☐ Pressure sore prevention →	☐	☐
☐ Mobility re-education →	☐	☐
☐ Dietary and lifestyle changes →	☐	☐
☐ Signs of recurrent stroke/ general stroke awareness →	☐	☐

SPECIFIC COMPLETION INSTRUCTIONS

E. DETAILS OF CARE (continued)

17. Was there evidence of meetings with multidisciplinary teams to coordinate patient care?

Answer ***yes*** if there is any indication (case notes, standardized form, ect.) that a multidisciplinary team (consisting of more than one type of health-care professional) had a meeting to coordinate the participant's care in-hospital and post-discharge. Please note that multidisciplinary team communication can include ward rounds.

Answer ***no*** if there is a note in the participant's records that a multidisciplinary team meeting did not take place to coordinate the participant's care in-hospital and post discharge.

Answer ***undocumented*** if there is no written indication in the participant's records of a multidisciplinary team meeting to coordinate the participant's care in-hospital and post-discharge.

Participant ID# ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Multidisciplinary

E. DETAILS OF CARE (continued)

16. Which team member(s) treated/cared for the participant?

- ☐ Physician
- ☐ Nurse
- ☐ Physiotherapist
- ☐ Occupational therapist
- ☐ Speech and language pathologist
- ☐ Dietician
- ☐ Social worker
- ☐ Undocumented
- ☐ Other, specify: _____

17. Was there evidence of meetings with multidisciplinary teams to coordinate participant care?

- ☐ **Undocumented**
- ☐ **No**
- ☐ **Yes → a) Who was present at the meeting(s)?**

	Undocumented	No	Yes
a) Physician	☐	☐	☐
b) Nurse	☐	☐	☐
c) Physiotherapist	☐	☐	☐
d) Occupational therapist	☐	☐	☐
e) Speech and language pathologist	☐	☐	☐
f) Dietician	☐	☐	☐
g) Social worker	☐	☐	☐
h) Participant's family member(s)	☐	☐	☐

Name of person completing form: _____ (Full name) Date completed: ☐☐☐☐☐☐☐☐ (year / month / day)

Appendix 5. 3: Three-month follow-up Case Report Form (CRF)

OSCAIL THREE-MONTH FOLLOW-UP CRF

SPECIFIC COMPLETION INSTRUCTIONS

The three-month follow-up visit is not required if the participant died in-hospital (not discharged from study hospital) or if the final diagnosis at discharge was not stroke/TIA.

If the participant died in-between hospital discharge and the three-month visit, please attempt to complete all three-month follow-up CRFs.

FAQs (Frequently asked questions)

1. Q. *If the final stroke diagnosis at discharge was a TIA (CRF 102) is the three-month follow-up visit required?*
   A. Yes. Please complete the three-month follow-up.
2. Q. *The participant is still in the hospital at the three-month follow-up date what do I do?*
   A. Please complete the three-month follow-up AND the Discharge CRFs at this time. Please select the option participant "not yet discharged from the study hospital" when available.
3. *The proxy does not know what the cause of death was.*
   A. Please select the code for "unknown" (06). This is a common response for the telephone interview.
4. *The participant/proxy does not feel comfortable answering the questions in Section D, Participant Income Status (CRF 121).*
   A. Please select "Decline to answer".

A. PARTICIPANT STATUS

1. At the 3-month follow-up date, the participant status is?

If the participant has died, please indicate the cause of death using the two-digit coding provided.

01 - Stroke
02 - Complication of immobility (pneumonia, sepsis, pulmonary embolism, other)
03 - Cardiac arrest, MI, cardiac failure or other cardiac cause
04 - Malignancy, HIV/AIDS
05 - Other
06 - Unknown
07 - Undocumented

If the date of death is unknown, please ask the proxy for their best estimate. If only the month is known, use the midpoint of the month (i.e. the 15th). Sometimes it can be helpful to ask the proxy of any events that may have taken place (e.g. birthdays or visits) that might aid to place the date.

B. VISIT COMPLETION DETAILS

1. Was this visit completed by the participant or proxy?

Proxy: a person that is capable of accurately answering questions on someone's behalf

Please indicate the proxy's relation to the participant using the two-digit coding provided.
01 - Son
02 - Daughter
03 - Partner/Common Law/Spouse
04 - Parent
05 - Sibling
06 - Friend/Neighbour
07 - Other

Abbreviations:
N/A= Not applicable

OSCAIL #138 3-Month F/U Pg 1 CRF 117 Visit 003

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

3-Month F/U interview date ☐☐☐☐☐☐ (year / month / day)

A. PARTICIPANT STATUS

Status Visit Completion

1. At the 3-month follow-up visit date, the participant's status is:

☐ Participant is alive

☐ Participant has died → Date of death: ☐☐☐☐☐☐ (year / month / day) *(provide an estimate if date unknown)*

→ Cause of death: ☐☐ *(see instruction page for codes)* If other, *specify*:_____

☐ Not yet discharged from the study hospital (complete this interview and discharge CRFs now)

B. VISIT COMPLETION DETAILS

1. Was this visit completed by the participant or proxy?:

☐ Yes → Who provided the visit information?

☐ Participant (the participant was capable of providing the information)

☐ Proxy: ☐☐ *(see instruction page for codes)* *why?* →

- ☐ Participant not capable to provide information
- ☐ Participant was capable, but not available
- ☐ Participant died

☐ No → Why was this visit not completed?

☐ Suitable proxy not available

☐ Participant/proxy refused *what?* →

	No	Yes
Further telephone contact?	☐	☐
Further in-person visits?	☐	☐
All third-party follow-up?	☐	☐

☐ Participant lost *Did data collector?* →

	No	Yes	N/A
Phone participant at home?	☐	☐	☐
Phone participant at work?	☐	☐	☐
Go to participant's house?	☐	☐	☐
Email participant?	☐	☐	☐
Phone contact person(s)	☐	☐	☐
Contact family physician?	☐	☐	☐

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Further stroke/rehab

C. PARTICIPANT DETAILS

1. Has the participant been readmitted to an acute care hospital since original hospitalization?:

☐ No

☐ Yes → a) Date of readmission: ☐☐☐☐☐☐☐☐ (year / month / day) ☐ unknown

b) Name of hospital:_____ ☐ unknown

2. Has the participant experienced another stroke?:

☐ No

☐ Yes → a) Date of recurrence: ☐☐☐☐☐☐☐☐ (year / month / day) ☐ unknown

b) Type of stroke: ☐ Ischaemic ☐ Haemorrhagic ☐ Unknown

3. Has the participant received further training/rehabilitation since leaving the hospital?

☐ No (or unknown)

☐ Yes → a) **Type:** *(Check all that apply)*

- ☐ Physiotherapy/Mobility Training
- ☐ Occupational Therapy
- ☐ Speech and Language Therapy
- ☐ General homecare
- ☐ Other, *specify:*_____

b) **Where does the participant receive this training?:** *(Check all that apply)*

- ☐ At home
- ☐ At the hospital, *specify which hospital:*_____
- ☐ At a rehabillitation facility, *specify:*_____
- ☐ Other, *specify:*_____

c) **Frequency of training:**

- ☐ 1-3 appointments since discharge
- ☐ Once per week
- ☐ Twice per week
- ☐ Daily (5 days/week)
- ☐ Other, *specify:*_____

SPECIFIC COMPLETION INSTRUCTIONS

C. PARTICIPANT DETAILS

4. Where does/did the participant live?
Please use the two-digit coding provided.
01 - Their house
02 - Their apartment
03 - Retirement home
04 - Relative's house/apartment
05 - Nursing home
06 - Rehabilitation Centre
07- Other

5. Who does/did the participant live with?
Please use the two-digit coding provided.
01 - Lives alone, has professional caregivers
02 - Lives alone, does not have professional care givers
03 - Living with family or friends, has professional caregivers
04 - Living with family or friends, does not have professional caregivers
05 - Unknown
06 - Other

6. Employment status
Please use the two-digit coding provided.
01 - General Labourer
02 - Clerical
03 - Professional
04 - Police/Military
05 - Business
06 - Skilled Labourer
07 - Housewife
08 - Farmer
09 - Disability/Social Security
10 - Retired
12 - Unknown

Participant ID # ☐☐☐ (Site #) ☐☐☐☐ (Participant #) Participant Initials ☐☐☐ (F M L)

Residence Employment Education

C. PARTICIPANT DETAILS (continued)

4. Where does the participant live (now or prior to death)?:

a) ☐☐ (see instruction page for codes) → **Is this the same as before their stroke?** ☐ Yes ☐ No → ☐☐ (see instruction page for codes)

5. Who does the participant live with (now or prior to death)?:

a) ☐☐ (see instruction page for codes) → **Is this the same as before their stroke?** ☐ Yes ☐ No → ☐☐ (see instruction page for codes)

6. What is the participant's employment status (now or prior to death)?:

a) ☐☐ (see instruction page for codes) → **Is this the same as before their stroke?** ☐ Yes ☐ No → ☐☐ (see instruction page for codes)

7. How many years of formal education has the participant completed?: *(Check highest level only)*

☐ None ☐ 1-8 ☐ 9-12 ☐ Vocational Training Centre ☐ College/university ☐ Unknown

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

Transport Bowel/bladder Care at Hospital

C. PARTICIPANT DETAILS (continued)

8. What is the participant's mode of transportation (now or prior to death)?: *(Check all that apply)*

☐ Unknown ☐ Driving ☐ Bicycle ☐ Public Transportation

☐ Driven by family member or friend ☐ Walking ☐ Other, *specify*: _____

9. What was the participant's mode of transportation prior to their stroke: *(Check all that apply)*

☐ Unknown ☐ Driving ☐ Bicycle ☐ Public Transportation

☐ Driven by family member or friend ☐ Walking ☐ Other, *specify*: _____

10. Is the participant able to use the toilet unassisted (now or prior to death)?:

☐ Yes

☐ No → a) Please check all that apply

- ☐ Participant needed help of another person
- ☐ Participant used a walker/cane
- ☐ Participant used a bedpan/urinal
- ☐ Paticipant used a nappy/diaper
- ☐ Participant used a catheter → *type?* ☐ Indwelling ☐ Condom ☐ Unknown
- ☐ Other, *specify*: _____

11. How satisfied were you with your care at the study hospital?: *(can be answered by the proxy or the participant)*

☐ Very satisfied

☐ Quite satisfied

☐ Neutral

☐ Quite dissatisfied → *why?* _____

☐ Very dissatisfied → *why?* _____

SPECIFIC COMPLETION INSTRUCTIONS

D. PARTICIPANT INCOME STATUS

1. Household Income

Household income is a measure of the combined incomes of all people sharing a particular household or place of residence. Please use these income range tables to select the income range which is appropriate for the participant's combined annual household income.

i) India (₹-Rupee)

Range 1	0-	19,999
Range 2	20,000-	39,999
Range 3	40,000-	59,999
Range 4	60,000-	79,999
Range 5	>80,000	

ii) Rwanda (FRw-Rwandan Francs)

Range 1	0-	329,999
Range 2	330,000-	659,999
Range 3	660,000-	989,999
Range 4	990,000-	1,319,999
Range 5	>1,320,000	

iii) South Africa (R-South African Rand)

Range 1	0-	19,200
Range 2	19,212	96,000
Range 3	96,012	204,000
Range 4	204,012	420,000
Range 5	>420,012	

iv) Uganda (USh-Ugandan Shillings)

Range 1	0-	
Range 2		
Range 3		
Range 4		
Range 5		

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

Income

D. PARTICIPANT INCOME STATUS

1. What range does/did the participant's total household income (including all others in the house contributing to household finances) fall within?:
(See instruction pages for range definitions)

☐ Range 1 ☐ Range 2 ☐ Range 3 ☐ Range 4 ☐ Range 5 ☐ Decline to answer ☐ Unknown

2. Did the participant's total household income change since having a stroke?:

☐ Decreased ☐ Increased ☐ Remained the same ☐ No income ☐ Decline to answer ☐ Unknown

3. How did the participant pay for medical services in hospital?:
(Check all that apply)

☐ Private health insurance ☐ Public health insurance ☐ Out-of-pocket (personal finances) ☐ Decline to answer ☐ Unknown

☐ Out-of-pocket (contributions by family/ friends) ☐ Could not afford health care (received limited services) ☐ Other, *specify*: _____

4. How does/did the participant pay for medical services after discharge (outside of the hospital)?:
(Check all that apply)

☐ Private health insurance ☐ Public health insurance ☐ Out-of-pocket (personal finances) ☐ Decline to answer ☐ Unknown

☐ Out-of-pocket (contributions by family/ friends) ☐ Could not afford health care (received limited services) ☐ Other, *specify*: _____

☐ Not required

SPECIFIC COMPLETION INSTRUCTIONS

EQ5D - EuroQol-5D Health Questionnaire - Telephone Interview Version

Participants should be instructed to answer all questions of the EuroQoL-5D *honestly* and *accurately* over the telephone and **without assistance**.

EQ5D - EuroQol-5D Health Questionnaire - Proxy Version

In the case that a patient is unable to complete the interview themselves, the EQ5D should be administered over the telephone to the proxy, and the proxy should be instructed to answer the questions as they think the patient him/herself would answer.

The questions should be read to the subject together with the response options allowing sufficient time for participants to respond. The telephone interviewer should avoid interpreting questions or answers for participants. If participants are unsure of which response to choose, they should choose the answer that comes closest to how they/the patient feels.

(If the participant has died, the proxy should be instructed to answer the questions as they think the patient him/herself would answer prior to death).

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

E. EQ5D - EuroQol-5D Health Questionnaire

By placing a check-mark in one box in each group below, please indicate which statements best describe your state of health today.

Mobility

I have no problems in walking about	☐
I have some problems in walking about	☐
I am confined to bed	☐

Self-Care

I have no problems with self-care	☐
I have some problems washing or dressing myself	☐
I am unable to wash or dress myself	☐

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities	☐
I have some problems with performing my usual activities	☐
I am unable to perform my usual activities	☐

Pain/Discomfort

I have no pain or discomfort	☐
I have moderate pain or discomfort	☐
I have extreme pain or discomfort	☐

Anxiety/Depression

I am not anxious or depressed	☐
I am moderately anxious or depressed	☐
I am extremely anxious or depressed	☐

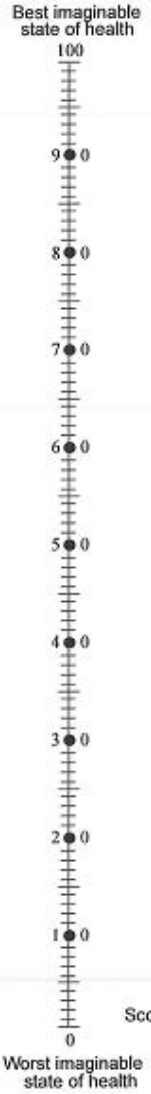
Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #)

Participant Initials ☐☐☐ (F M L)

To help people say how good or bad their state of health is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.

Your own state of health today



Score: ☐☐☐

SPECIFIC COMPLETION INSTRUCTIONS

F. STANDARDIZED (STROKE) ASSESMENT VARIABLES
1. m-RS Score

This score will be interpreted by the data collector conducting the phone interview, and verified by the Country Champion or the Project Officer before being integrated into the database. The m-RS Score will be able to be scored using the answers to the EuroQol-5D Questionnaire and Question 10 in Section C (Participant Details).

Below is the m-RS Score Chart. A score (from 00-06) should be recorded in the boxes provided before submitting this CRF to the Project Office.

m-RS Score Chart:

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

Participant ID # ☐☐☐ ☐☐☐☐ (Site # / Participant #) Participant Initials ☐☐☐ (F M L)

m-RS

F. STANDARDIZED (STROKE) ASSESSMENT VARIABLES

1. Modified-Rankin Score (m-RS) scored by Interviewer: ☐☐
(See instruction page)

m-RS Score Chart:

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

Name of person completing form: _____ (Full name)

Date completed: ☐☐☐☐☐☐☐☐ (year / month / day)

Appendix 5. 4: Ethics approval by the Committee of the College of Medical, Veterinary and Life Sciences (MVLS), University of Glasgow

University of Glasgow

05/12/2016

Dear Prof Langhorne,

MVLS College Ethics Committee

Project Title: Process of implementing stroke care units in selected hospitals in Rwanda
Project No: 200160048

The College Ethics Committee has reviewed your application and has agreed that there is no objection on ethical grounds to the proposed study. It is happy therefore to approve the project, subject to the following conditions:

- That local approvals from Rwanda are in place. Any substantial changes to the project following their review must be notified to this committee.
- Project end date: End January 2018
- The data should be held securely for a period of ten years after the completion of the research project, or for longer if specified by the research funder or sponsor, in accordance with the University's Code of Good Practice in Research: (http://www.gla.ac.uk/media/media_227599_en.pdf)
- The research should be carried out only on the sites, and/or with the groups defined in the application.
- Any proposed changes in the protocol should be submitted for reassessment, except when it is necessary to change the protocol to eliminate hazard to the subjects or where the change involves only the administrative aspects of the project. The Ethics Committee should be informed of any such changes.
- You should submit a short end of study report to the Ethics Committee within 3 months of completion.

Yours sincerely

Jesse Dawson

Chair MVLS Research Ethics Committee

Jesse Dawson
MD, FRCP, BSc (hons), MBChB (hons), FESO
Clinical Reader / Honorary Consultant

College of Medicine, Veterinary & Life Sciences
Institute of Cardiovascular and Medical Sciences
Western Infirmary
Glasgow
G11 6NT
jesse.dawson@glasgow.ac.uk
Tel – 0141 2116395 or page 4824

The University of Glasgow, charity number SC004401

Appendix 5. 5: Ethics approval by the Institutional Review Board of the College of Medicine and Health Sciences, the University of Rwanda

UNIVERSITY OF RWANDA — COLLEGE OF MEDICINE AND HEALTH SCIENCES

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 24/02/2017

URIMUBENSHI Gerard
College of Medicine and Health Sciences, UR

Approval Notice: No 166 /CMHS IRB/2017

Your Project Title:*" Feasibility Of Implementing Stroke Care Units In Selected Hospitals In Rwanda!"* has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS		X	
Dr Tumusiime K. David	UR-CMHS		X	
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS	X		
Prof Munyanshongore Cyprien	UR-CMHS		X	
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS		X	
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 23rd February 2017, **Approval letter has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months.**
You are responsible for fulfilling the following requirements:

EMAIL: researchcenter@ur.ac.rw P.O. Box: 3286, Kigali, Rwanda WEBSITE: http://cmhs.ur.ac.rw/

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 24th February 2017
Expiration date: The 24th February 2018

Professor Kato J. NJUNWA
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

UNIVERSITY OF RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 14/02/2018

URIMUBENSHI Gerard
College of Medicine and Health Sciences, UR

Notice of Renewal of Approval for Research Project: No 030 /CMHS IRB/2018

Your Project title ***"Feasibility Of Implementing Stroke Care Units In Selected Hospitals In Rwanda"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
		Yes	No (Reason)	
Name of Members	**Institute**		**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS	X		
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol, **Continuation of Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months.**
You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrollment of participants
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval.
5. Failure to submit a continuing review application will result in termination of the study.
6. Notify the Rwanda National Ethics committee once the study is finished.

Sincerely,

Date of Approval: February 14th, 2018
Expiration date: February 14th, 2019

Professor Kato J. NJUNWA
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

Appendix 5. 6: Ethics approval by CHUK ethics committee

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

March 31 st, 2017 Ref.: EC/CHUK/341/2017

Review Approval Notice

Dear Gerard Urimubenshi,

Your research project: "Feasibility of Implementing Stroke Care Units in selected Hospitals in Rwanda."

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 31/03/2017 to evaluate your protocol of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your protocol.

You are required to present the results of your study to CHUK Ethics Committee before publication.

PS: Please note that the present approval is valid for 12 months.
Yours sincerely,

ETHICS COMMITTEE
CHUK

John Nvirigira
The Secretary, Ethics Committee,
University Teaching Hospital of Kigali
<<University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations>>.

B.P. :655 Kigali- RWANDA www.chk.rw Tél. Fax : OO (250) 576638 E-mail :chu .hospital@chukigali.rw

CENTRE HOSPITALIER UNIVERSITAIRE UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

March 16th, 2018 Ref.: EC/CHUK/552/2018

Review Approval Notice

Dear Gerard Urimubenshi,

Your research project: "Feasibility of Implementing Stroke Care Units in selected Hospitals in Rwanda."

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that Was held on 16/03/2018 to evaluate your protocol of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your protocol.

You are required to present the results of your study to CHUK Ethics Committee before publication.
PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr. Rusingiza Emmanuel
The President, Ethics Committee,
University Teaching Hospital of Kigali

<<University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations

B.P.:655 Kigali- RWANDA www..chk.rw Tél. Fax : 00 (250) 576638
E-mail :chuk.hospital@chukigali.rw

Appendix 5. 7: Ethics approval by CHUB ethics committee

CENTRE HOSPITALIER UNIVERSEAIRE
UNIVERSITY TEACHING HOSPITAL

CENTRE HOSPITALIER UNIVERSITAIRE DE BUTARE (CHUB)
OFFICE OF DIRECTOR GENERAL

Huye, 06 APR 2017

N^{O} Ref: CHUB/DG/SA/04/642/2017

Gerard Urimubenshi
College of Medicine and Health Sciences
University of Rwanda
E-mail: ugerardus@gmail.com
Phone: +250788871371

Dear Urimubenshi,

Re: Your request for data collection

Reference made to your letter requesting for permission to collect the data within University Teaching Hospital of Butare, for your research proposal entitled "Feasibility of implementing Stroke care unity in selected Hospital in Rwanda", and based on approvals Notice: No 166/CMHS IRB/2017 from University of Rwanda and No RC/UTH/B/022/2017 from our research committee, we are pleased to inform you that your request was accepted. Please note that your final document will be submitted in our Research department.

Sincerely,

Dr. Augustin SENDEGEYA
Director General of CHUB

Cc:
- Medical Director
- Training and Research Manager

CHUB

Appendix 5. 8: Participant information sheet (English)

University of Glasgow | College of Medical, Veterinary & Life Sciences

PARTICIPANT INFORMATION SHEET

1. **Study title: Feasibility of implementing stroke care units in selected hospitals in Rwanda**
2. **Invitation paragraph**

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. **What is the purpose of the study?**

Stroke is the second most common cause of death worldwide and the seventh leading cause of disability. In Rwanda, stroke is estimated to be one of the major causes of illness. As the Rwandan economy grows, the burden of stroke will grow even more. Findings from clinical trials have shown that providing care in a stroke unit can increase the number of patients who survive, return home, and regain independence in daily activities. A stroke care unit is an organized in-hospital facility that is devoted to care for patients with stroke, and that is staffed by a multidisciplinary team with special knowledge in stroke care. However, since stroke units are complex and costly, most developments have taken place in high income countries where most of the health service is publicly funded. We aim to explore the feasibility of implementing stroke care units in selected hospitals in Rwanda with the aim of developing a model of care suitable for countries like Rwanda. The study will be conducted between April 2017 and January 2018.

4. **Why have I been chosen?**

All stroke patients attending two selected hospitals between April 2017 and January 2018 will be invited to take part in the study.

5. **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason.

6. **What will happen to me if I take part?**

If you agree to take part, some information from your medical file will be recorded, and 3 months after you got sick, you will be contacted on phone and be asked questions whether you got stroke again, whether you were readmitted to hospital, and your level of disability and quality of life.

7. **What do I have to do?**

This research is about collecting information about your care and outcome, and this does not recommend any restriction.

8. **What are the possible disadvantages and risks of taking part?**

No identifiable disadvantages or risks of taking part in this study.

9. **What are the possible benefits of taking part?**

You will not get any compensation as you will not have any extra financial expenses because of being research participants, and you will receive no direct benefit from taking part in this study. The information that is collected during this study will give us a better understanding of how to improve stroke care in Rwanda.

10. **Will my taking part in this study be kept confidential?**

All information which is collected about you, or responses that you provide, during the course of the research will be kept strictly confidential. You will be identified by an ID number, and any information about you will have your name and address removed so that you cannot be recognized from it.

11. **What will happen to the results of the research study?**

The results of the study will be used for my thesis, and some information will be published. You will be able to get copy of the results from January 2020 at your hospital, and the Department of Physiotherapy, University of Rwanda. You will never be identified in any report or publication.

12. **Who is organising and funding the research?**

The study is being organized by Gerard Urimubenshi, a PhD student at the University of Glasgow, under the supervision by researchers from the University of Glasgow, the University of Rwanda, the McMaster University, and South Africa and it is funded by a grant from McMaster University, Population Health Research Institute (PHRI).

13. **Who has reviewed the study?**

The study project has been reviewed by the Ethics Committee of the College of Medical, Veterinary and Life Sciences at the University of Glasgow, and Institutional Review Board of the College of Medicine and Health Sciences (CMHS) at the University of Rwanda.

14. **Contact for Further Information**

If you have any questions about the research study itself, please contact:
Gerard Urimubenshi, Cell phone number: 0788871371 in Rwanda or +447438930941 in United Kingdom (UK), E-mail: g.urimubenshi.1@research.gla.ac.uk. Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact the Vice Chairperson of the Institutional Review Board of the College of Medicine and Health Sciences (CMHS) at the University of Rwanda:
Prof. Jean Bosco Gahutu
College of Medicine and Health Sciences
University of Rwanda
Kigali, Rwanda
Phone: 0783340040, E-mail: jbgahutu@yahoo.com

15. **Thank you very much for taking part in this study!**

Appendix 5. 9: Consent form (English)

University of Glasgow | College of Medical, Veterinary & Life Sciences

Centre Number: **101/102**

Project Number: **200160048**

Subject Identification Number for this study:

CONSENT FORM

Title of Project: Feasibility of implementing stroke care units in selected hospitals in Rwanda

Name of Researcher(s): Gerard Urimubenshi

Please tick the box with "V"

I confirm that I have read the information sheet dated _____(version _____) for the above study, or it has been read to me, and understood it, and have had the opportunity to ask questions.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.	☐
I agree to take part in the above study.	☐

_____	_____	_____
Name of subject	Date	Signature/Thumb print
_____	_____	_____
Name of witness for accurate reading (in case the forms were read to the subject)	Date	Signature
_____	_____	_____
Name of person taking consent (if different from researcher)	Date	Signature
Gerard Urimubenshi _____	_____	_____
Researcher	Date	Signature

(1 copy for subject; 1 copy for researcher)

Appendix 5. 10: Assent form (English)

University of Glasgow | College of Medical, Veterinary & Life Sciences

Centre Number: **101/102**

Project Number: **200160048**

Subject Identification Number for this study:

ASSENT FORM

Title of Project: Feasibility of implementing stroke care units in selected hospitals in Rwanda

Name of Researcher(s): Gerard Urimubenshi

Please tick the box with "V"

I confirm that I have read the information sheet dated _____ (version _____) for the above study, or it has been read to me, and understood it, and have had the opportunity to ask questions. ☐

I understand that the participation of the patient whose I am the guardian is voluntary and that he/she is free to withdraw at any time, without giving any reason, without his/her legal rights being affected. ☐

I agree for him/her to take part in the above study. ☐

Name of guardian	Date	Signature/Thumb print
Name of witness for accurate reading (in case the forms were read to the guardian)	Date	Signature
Name of person taking assent (if different from researcher)	Date	Signature
Gerard Urimubenshi Researcher	Date	Signature

(1 copy for guardian; 1 copy for researcher)

Appendix 5. 11: Consent to continue form (English)

University of Glasgow | College of Medical, Veterinary & Life Sciences

Centre Number: **101/102**

Project Number: **200160048**

Subject Identification Number for this study:

CONSENT TO CONTINUE FORM

Title of Project: Feasibility of implementing stroke care units in selected hospitals in Rwanda

Name of Researcher(s): Gerard Urimubenshi

Please tick the box with "V"

I confirm that I have read the information sheet dated _____ (version _____) for the above study, or it has been read to me, and understood it, and have had the opportunity to ask questions. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐

I agree to continue to take part in the above study. ☐

Name of subject	Date	Signature/Thumb print
Name of witness for accurate reading (in case the forms were read to the subject)	Date	Signature
Name of person taking consent (if different from researcher)	Date	Signature
Gerard Urimubenshi Researcher	Date	Signature

(1 copy for subject; 1 copy for researcher)

Appendix 5. 12: Participant information sheet (Kinyarwanda)

University of Glasgow | College of Medical, Veterinary & Life Sciences

IBISOBANURO BIGENEWE USABWA KUGIRA URUHARE MU BUSHAKASHATSI

1. Izina ry'ubushakashatsi: Ishyirwa mu bikorwa ry'ubuvuzi bwihariye bwa sitoroke (paralizi iterwa no kuziba cyangwa guturika kw'imiyoboro y'amaraso mu bwonko) mu bitaro byo mu Rwanda

2. Ubusabe bwo kugira uruhare mu bushakashatsi

Turagusaba kugira uruhre mu bushakashatsi ku ishyirwa mu bikorwa ry'ubuvuzi bwihariye bwa sitoroke mu bitaro byo mu Rwanda. Ni ngombwa ko wumva impamvu ubu bushakashatsi bugiye gukorwa n'icyo uwemeye kubugiramo uruhare asabwa. Urasabwa rero gufata umwanya uhagije wo gusoma no kumva ibisobanuro bikurikira, ndetse ushobora no kubaza abandi uko ubyifuza mbere yo gufata umwanzuro wo kugira cyangwa kutagira uruhare muri ubu bushakashatsi. Wemerewe kutubaza ibyo udasobanukiwe neza cyangwa ibindi bisobanuro wakwifuza.

3. **Ubu bushakashatsi bugamije iki?**

Ku rwego rw'isi, sitoroke ni indwara iri ku mwanya wa kabiri mu gutera imfu nyinshi, ikaba ku mwanya wa karindwi mu mpamvu zitera ubumuga. No mu Rwanda, sitoroke ni mwe mu ndwara zikunda kwibasira abanyarwanda. Mu gihe u Rwanda rukataje mu iterambere, ibibazo biterwa na sitoroke byakomeza kwiyongera hadafashwe ingamba zo kubikumira. Ubushakashatsi bunyuranye bwagaragaje ko ubuvuzi bwihariye bwa sitoroke bugabanya umubare w'abapfa n'abagira ubumuga bitewe na sitoroke. Ubuvuzi bwihariye bwa sitoroke ni ubuvuzi bukorerwa ahantu hihariye hagenewe abarwayi b'iyo ndwara, kandi hakaba hari abakozi bo mu mashami anyuranye bazobereye mu buvuzi bwayo, kandi bagakora nk'ikipe. Nyamara ariko, kubera ubuvuzi bwihariye bw sitoroke busaba ibintu byinshi kandi buhenze, ubu buvuzi bukorwa cyane cyane mu bihugu byateye imbere, aho ibikorwa byinshi by'ubuvuzi byishyurwa na za Leta. Intego yacu ni ugutegura no gushyira mu bikorwa ubuvuzi bwihariye bwa sitoroke muri bimwe mu bitaro byo mu Rwanda, tugamije gutegura no kugerageza uburyo bwihariye bw'ubuvuzi bwa sitoroke bubereye ibihugu biri ku rwego rumwe nk'u Rwanda. Ubu bushakashatsi buzakorwa guhera muri Mata 2017 kugeza muri Mutarama 2018.

4. **Ese kuki nsabwa kugira uruhare muri ubu bushakashatsi?**

Abarwayi bose ba sitoroke bazivuriza mu bitaro byatoranyijwe hagati ya Mata 2017 kugeza muri Mutarama 2018 bazasabwa kugira uruhare muri ubu bushakashatsi.

5. **Ese ngomba kugira uruhare muri ubu bushakashatsi?**

Ni wowe ubwawe wifatira icyemezo niba wemeye kugira cyangwa kutagira uruhare muri ubu bushakashatsi. Niwemera kugira uruhare muri ubu bushakashatsi, uzahabwa iyi nyandiko uyigumane, hanyuma usabwe gusinya ku nyandiko yo kwemera kugira uruhare muri ubu bushakashatsi. Niba wemeye kugira uruhare muri ubu bushakashatsi, ufite uburenganzira bwo kwisubiraho ukivanamo igihe cyose ushakiye utagombye gutanga ibisobanuro.

6. **Ese bizangendekera gute ningira uruhare muri ubu bushakashatsi?**

Niwemera kugira uruhare muri ubu bushakashatsi, amwe mu makuru ari mu ifishi yawe yo kwa muganga azandukurwa, kandi nyuma yo gusezererwa mu bitaro, nyuma y'amezi atatu kuva urwaye sitoroke, tuzaguhamagara kuri telefoni tukubaze niba warongeye kurwara iyi ndwara bwa kabiri, niba warasubiye mu bitaro, tukubaze n'amakuru ajyanye n'ubumuga waba ufite ndetse n'ikigereranyo cy'uburyo uzaba ubayeho.

7. **Ese ndasabwa gukora iki?**

Ubu bushakashatsi bugamije gushaka amakuru yerekeye uko uzavurwa n'uburyo bizakugendekera nyuma yo kurwara no kuvurwa, kandi ntacyo usabwa kwigomwa cyangwa kwitondera kubera kugira uruhare muri ubu bushakashatsi.

8. **Ni izihe ngaruka zijyanye no kugira uruhare muri ubu bushakashatsi?**

Nta ngaruka tubona zaterwa no kugira uruhare muri ubu bushakashatsi.

9. **Ni izihe nyungu zijyanye no kugira uruhare muri ubu bushakashatsi?**

Nta nyungu cyangwa igihembo uzahabwa wowe ubwawe kubera kugira uruhare muri ubu bushakashatsi. Amakuru azava muri ubu bushakashatsi azadufasha kumva neza uburyo ubuvuzi bwa sitoroke mu Rwanda bwatezwa imbere.

10. **Ese kugira uruhare muri ubu bushakashatsi bizagirwa ibanga?**

Amakuru yose tuzafata akwerekeye cyangwa ibisubizo uzaduha muri ubu bushakashatsi azagirwa ibanga rikomeye. Uzahabwa nimero, naho amazina n'aho utuye ntibizagaragara muri raporo y'ubu bushakashatsi.

11. **Ese amakuru azava muri ubu bushakashatsi azakoreshwa iki?**

Amakuru azava muri ubu bushakashatsi azakoreshwa mu rwego rw'amasomo ndi kwiga, kandi amakuru amwe n'amwe azashyirwa ahagaragara binyuze mu binyamakuru by'ubumenyi. Uzashobora kubona kopi y'amakuru azava muri ubu bushakashatsi guhera muri Mutarama 2010 ku bitaro wivurijemo, n'agashami kigisha ubuvuzi bushingiye ku bugenge muri Kaminuza y'u Rwanda. Nta na rimwe uzigera umenyekana mu makuru azava muri ubu bushakashatsi.

12. **Ese ni nde uri gutegura ubu bushakashatsi? Use ni nde uzatera inkunga ubu bushakashatsi?**

Ubu busakashatsi buzakorwa na Gerard Urimubenshi, umunyeshuri muri Kaminuza ya "Glasgow" yo mu Bwongereza, akazaba ayobowe n'abashakashatsi banyuranye bo muri Kaminuza ya "Glasgow" yo mu Bwongereza, Kaminuza y'u Rwanda, Kaminuza ya "MacMaster"yo muri Kanada, na Afurika y'epfo. Ubu bushakashatsi buzaterwa inkunga n'ikigo cyo muri Kanada cyita ku bushakashatsi ku buzima bw'abaturage ibinyujije muri Kaminuza ya "MacMaster"yo muri Kanada.

13. **Ese ni nde wasesenguye ubu bushakashatsi?**

Ubu bushakashatsi bwasesenguwe na Komite ishinzwe ubushakashatsi muri Kaminuza ya "Glasgow" mu Bwongereza, ndetse n'urwego rushinzwe ubushakashatsi muri Koleji y'ubuvuzi n'ubuzima muri Kaminuza y'u Rwanda.

14. **Uwo wakwiyambaza ugize ikibazo**

Ugize ikibazo kuri ubu bushakashatsi, wakwiyambaza Gerard Urimubenshi kuri telefoni nimero 0788871371 mu Rwanda cyangwa +447438930941 mu Bwongereza, E-mail: g.urimubenshi.1@research.gla.ac.uk.

Uramutse ushatse kumenyekanisha ibibazo watewe no kugira uruhare muri ubu bushakashatsi, wakwiyambaza Porofeseri Jean Bosco Gahutu, umuyobozi wungirije w' urwego rushinzwe ubushakashatsi muri Koleji y'ubuvuzi n'ubuzima muri Kaminuza y'u Rwanda, kuri telefoni nimero 0783340040, E-mail: jbgahutu@yahoo.com

15. **Uzaba ukoze cyane kwemera kugira uruhare muri ubu bushakashatsi!**

Appendix 5. 13: Consent form (Kinyarwanda)

University of Glasgow | College of Medical, Veterinary & Life Sciences

Nimero y'ibitaro: **101/102**

Nimero y'ubushakashatsi: **200160048**

Nimero y'ugira uruhare mu bushakashatsi:

INYANDIKO YO KWEMERA KUGIRA URUHARE MU BUSHAKASHATSI

Izina ry'ubushakashatsi: Ishyirwa mu bikorwa ry'ubuvuzi bwihariye bwa sitoroke mu bitaro byo mu Rwanda

Izina ry'ukora ubushakashatsi: Gerard Urimubenshi

Shyira akamenyetso "V" mu gasanduku ku byo wemera

Ndemeza ko nasomye, cyangwa nasomewe kandi numvise ibikubiye mu nyandiko y'ibisobanuro bigenewe usabwa kugira uruhare mu bushakashatsi bwavuzwe hejuru yo ku wa_____ (kopi_____) kandi ndemeza ko nahawe umwanya wo kubaza ibibazo ☐

Numvise ko kugira urahare kwanjye muri ubu bushakashatsi ari ubushake kandi ko mfite uburenganzira bwo kwivanamo igihe icyo ari cyo cyose, ntabanje gutanga ibisobanuro, kandi uburenganzira bwanjye buteganywa n'amategeko ntibubangamirwe. ☐

Nemeye kugira uruhare muri ubu bushakashatsi ☐

_____	_____	_____
Izina ry'ugira uruhare mu bushakashatsi	Italiki	Umukono/Igikumwe
_____	_____	_____
Izina ry'umuhamya w'uko ibyasomwe ari ukuri (mu gihe inyandiko zasomewe usabwa Kugira uruhare mu bushakashatsi)	Italiki	Umukono
_____	_____	_____
Izina ry'uwakiriye ukwemera kugira uruhare mu bushakashatsi (niba atandukanye n'ukora ubushakashatsi)	Italiki	Umukono
Gerard Urimubenshi _____	_____	_____
Ukora ubushakashatsi	Italiki	Umukono

(Kopi 1 y'ugira uruhare mu bushakashatsi; Kopi 1 y'ukora ubushakashatsi)

Appendix 5. 14: Assent form (Kinyarwanda)

University of Glasgow | College of Medical, Veterinary & Life Sciences

Nimero y'ibitaro: **101/102**

Nimero y'ubushakashatsi: **200160048**

Nimero y'ugira uruhare mu bushakashatsi:

INYANDIKO Y'UHAGARARIYE USABWA KUGIRA URUHARE MU BUSHAKASHATSI

Izina ry'ubushakashatsi: Ishyirwa mu bikorwa ry'ubuvuzi bwihariye bwa sitoroke mu bitaro byo mu Rwanda

Izina ry'ukora ubushakashatsi: Gerard Urimubenshi

Shyira akamenyetso "V" mu gasanduku ku byo wemera

Ndemeza ko nasomye, cyangwa nasomewe kandi numvise ibikubiye mu nyandiko y'ibisobanuro bigenewe usabwa kugira uruhare mu bushakashatsi bwavuzwe hejuru yo ku wa_____ (kopi_____) kandi ndemeza ko nahawe umwanya wo kubaza ibibazo ☐

Numvise ko kugira uruhare k'uwo mpagarariye muri ubu bushakashatsi ari ubushake kandi ko afite uburenganzira bwo kwivanamo igihe icyo ari cyo cyose, atabanje gutanga ibisobanuro, kandi uburenganzira bwe buteganywa n'amategeko ntibubangamirwe. ☐

Nemeye ko uwo mpagarariye agira uruhare muri ubu bushakashatsi ☐

_____	_____	_____
Izina ry'uhagarariye ugira uruhare mu bushakashatsi	Italiki	Umukono/Igikumwe
_____	_____	_____
Izina ry'umuhamya w'uko ibyasomwe ari ukuri (mu gihe inyandiko zasomewe uhagarariye usabwa kugira uruhare mu bushakashati)	Italiki	Umukono
_____	_____	_____
Izina ry'uwakiriye inyandiko y'uhagarariye ugira uruhare mu bushakashatsi (niba atandukanye n'ukora ubushakashatsi)	Italiki	Umukono
Gerard Urimubenshi _____	_____	_____
Ukora ubushakashatsi	Italiki	Umukono

(Kopi 1 y'uhagarariye ugira uruhare mu bushakashatsi; Kopi 1 y'ukora ubushakashatsi)

Appendix 5. 15: Consent to continue form (Kinyarwanda)

Nimero y'ibitaro: **101/102**

Nimero y'ubushakashatsi: **200160048**

Nimero y'ugira uruhare mu bushakashatsi:

INYANDIKO YO KWEMERA GUKOMEZA KUGIRA URUHARE MU BUSHAKASHATSI

Izina ry'ubushakashatsi: Ishyirwa mu bikorwa ry'ubuvuzi bwihariye bwa sitoroke mu bitaro byo mu Rwanda

Izina ry'ukora ubushakashatsi: Gerard Urimubenshi

Shyira akamenyetso "V" mu gasanduku ku byo wemera

Ndemeza ko nasomye, cyangwa nasomewe kandi numvise ibikubiye mu nyandiko y'ibisobanuro bigenewe usabwa kugira uruhare mu bushakashatsi bwavuzwe hejuru yo ku wa _____ (kopi_____) kandi ndemeza ko nahawe umwanya wo kubaza ibibazo. ☐

Numvise ko kugira urahare kwanjye muri ubu bushakashatsi ari ubushake kandi ko mfite uburenganzira bwo kwivanamo igihe icyo ari cyo cyose, ntabanje gutanga ibisobanuro, kandi uburenganzira bwanjye buteganywa n'amategeko ntibubangamirwe. ☐

Nemeye gukomeza kugira uruhare muri ubu bushakashatsi ☐

Izina ry'uwemera gukomeza kugira uruhare mu bushakashatsi	Italiki	Umukono/Igikumwe
Izina ry'umuhamya w'uko ibyasomwe ari ukuri (mu gihe inyandiko zasomewe usabwa Kugira uruhare mu bushakashatsi)	Italiki	Umukono
Izina ry'uwakiriye ukwemera gukomeza kugira uruhare mu bushakashatsi (niba atandukanye n'ukora ubushakashatsi)	Italiki	Umukono
Gerard Urimubenshi Ukora ubushakashatsi	Italiki	Umukono

(Kopi 1 y'uwemera gukomeza kugira uruhare mu bushakashatsi; Kopi 1 y'ukora ubushakashatsi)

Appendix 6. 1: Publications

Review article

EUROPEAN STROKE JOURNAL

European Stroke Journal
2017, Vol. 2(4) 287–307

DOI: 10.1177/2396987317735426
journals.sagepub.com/home/eso
SAGE

Association between patient outcomes and key performance indicators of stroke care quality: A systematic review and meta-analysis

Gerard Urimubenshi[1,2], Peter Langhorne[1], Dominique A Cadilhac[3,4], Jeanne N Kagwiza[2] and Olivia Wu[5]

Abstract

Purpose: Translating research evidence into clinical practice often uses key performance indicators to monitor quality of care. We conducted a systematic review to identify the stroke key performance indicators used in large registries, and to estimate their association with patient outcomes.

Method: We sought publications of recent (January 2000–May 2017) national or regional stroke registers reporting the association of key performance indicators with patient outcome (adjusting for age and stroke severity). We searched Ovid Medline, EMBASE and PubMed and screened references from bibliographies. We used an inverse variance random effects meta-analysis to estimate associations (odds ratio; 95% confidence interval) with death or poor outcome (death or disability) at the end of follow-up.

Findings: We identified 30 eligible studies (324,409 patients). The commonest key performance indicators were swallowing/nutritional assessment, stroke unit admission, antiplatelet use for ischaemic stroke, brain imaging and anticoagulant use for ischaemic stroke with atrial fibrillation, lipid management, deep vein thrombosis prophylaxis and early physiotherapy/mobilisation. Lower case fatality was associated with stroke unit admission (odds ratio 0.79; 0.72–0.87), swallow/nutritional assessment (odds ratio 0.78; 0.66–0.92) and antiplatelet use for ischaemic stroke (odds ratio 0.61; 0.50–0.74) or anticoagulant use for ischaemic stroke with atrial fibrillation (odds ratio 0.51; 0.43–0.64), lipid management (odds ratio 0.52; 0.38–0.71) and early physiotherapy or mobilisation (odds ratio 0.78; 0.67–0.91). Reduced poor outcome was associated with adherence to swallowing/nutritional assessment (odds ratio 0.58; 0.43–0.78) and stroke unit admission (odds ratio 0.83; 0.77–0.89). Adherence with several key performance indicators appeared to have an additive benefit.

Discussion: Adherence with common key performance indicators was consistently associated with a lower risk of death or disability after stroke.

Conclusion: Policy makers and health care professionals should implement and monitor those key performance indicators supported by good evidence.

Keywords
Stroke, indicator, care quality, patient outcome

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Introduction

In recent years, there have been concerted efforts to develop and implement clinical practice guidelines for the management of patients with acute stroke.[1] Clinical guidelines are written to promote diagnostic or therapeutic interventions applicable to the majority of patients in most circumstances. However, the use of guideline recommendations for individual patients has

traditionally been left to the discretion of individual clinicians.[2] A recognised approach to assist the translation of research evidence into clinical practice is to monitor the quality of care using standardised performance indicators[3] also called quality indicators, process of care measures or key performance indicators (KPIs). Performance indicators are standards of care which imply that health care professionals are providing inadequate care if eligible patients do not receive that standard of care. Performance indicators can be used to monitor the adherence to current guidelines, and support the transfer of new evidence into everyday clinical practice.[4]

There are now numerous stroke interventions that have been shown to improve patient outcomes in research trials; admission to specialised stroke units, use of intravenous thrombolysis, mechanical thrombectomy, antiplatelet drugs, anticoagulants and management of fever, hyperglycaemia and swallowing dysfunction for selected patient groups.[5–9] However, application into routine practice is challenging and regular monitoring is important.[10] Ideally, implementation of clinical evidence can be demonstrated using a range of stroke KPIs, which offer proxy measures for ideal care being delivered. In turn, this would lead to evidence of better patient outcomes.[11]

In a previous systematic review of the association between stroke quality (performance) indicators and patient-centred outcomes, out of 14 studies that met the eligibility criteria; 9 had mostly positive associations, whereas 5 reported little or no association with a lower risk for mortality, disability, medical complications, stroke recurrence or patient dissatisfaction.[12] A limitation of this review was the exclusion of stroke unit care as a performance indicator. With the ongoing developments in clinical guidelines and quality indicators for monitoring the application of these guidelines,[10,13] we believe that there is a need for up-to date comprehensive information on KPIs for stroke care.

We aimed to conduct a systematic literature review to identify the KPIs that have been described in stroke care and to summarise their association with patient outcomes. We intend that information gathered from this review will provide decision makers and health care professionals with information on reliable and meaningful KPIs that can be implemented to improve outcomes post stroke.

Methods

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[14] This review was registered in Prospero Database (CRD42016050798).

Search strategy

Searching sources were Ovid Medline, Embase and PubMed databases, and relevant references from screening the bibliographies of the initial articles included in the search.

We used Medical Subject Headings (MeSH) and all subheading terms including 'stroke', 'cerebrovascular accident', 'cerebrovascular disease', 'cerebrovascular disorders', 'brain hemorrhage', 'intracranial hemorrhages', 'brain infarction', 'subarachnoid hemorrhage', 'health care quality', 'quality of health care', 'quality indicators, health care', 'quality assurance, health care', 'quality control', 'quality indicator', 'performance indicator', 'register', 'registries', 'clinical audit', 'treatment outcome', 'case fatality rate', 'mortality', 'survival', 'disability', 'functional status', 'hospitalization', 'cost', 'quality of life', 'complication', 'hospital discharge' and 'stroke recurrence'. Our search was restricted to full-text manuscripts published in English from 1 January 2000 to 24 May 2017.

The search strategies for different databases are detailed in the *Online Supplement*.

Inclusion criteria. We included national or regional registers that recorded the independent association (after adjusting for at least age and a measure of stroke severity) between the KPIs and stroke patient outcomes, and involved patients from at least three hospitals.

Exclusion criteria. We excluded reports that were reviews or did not provide odds ratio (OR), hazard ratio (HR) or rate ratio (RR) data.

Screening and quality assessment

One author (GU) reviewed each title and excluded obviously irrelevant studies. Articles identified as potentially relevant underwent a full review by two authors (GU and PL) to determine if they met the inclusion criteria. In cases of disagreement, final determination was by discussion and consensus.

Data extraction

We used a standardised form to record information on country, main inclusion or exclusion criteria for the recruitment of participants, sample size, stroke severity measure, KPIs and outcome(s) reported, and reported results (and 95% confidence interval (CI)).

Data analysis

Initially, the identified KPIs and their association with the patient outcomes were categorised on whether the authors reported a significant association between the

KPI and patient outcome. There was then a further quantitative analysis (meta-analysis) of the relationship (adjusted for at least age and stroke severity) between the KPIs identified and patient outcomes. Some checking of the consistency of KPIs and outcomes was required with grouping of similar KPIs. For the meta-analysis, we sought information on case fatality and poor outcome (death and disability or requiring support) after stroke.

The meta-analysis was done using the Review Manager (version 5.3) software. Log ORs were combined using an inverse variance analysis (random effects model). First, we assumed that HRs and RRs approximate the ORs and performed the primary meta-analysis including all studies reporting on association of KPIs with case fatality and poor outcome. Second, we performed sensitivity meta-analysis by excluding studies that used HR or RR as measures of association.

Results

The review profile is shown in Figure 1. We identified 3606 references from which 30 studies[15–44] were eligible for the qualitative review. Among these, only 22 were eligible for the meta-analysis.

Included studies

Table 1 shows the studies considered for our systematic literature review. Most of the included studies[15–29] were conducted in Europe: One European study[15] was multinational (across ten countries), the rest were conducted in Denmark (n = 6), Sweden (n = 2), United Kingdom (n = 3) (one in England and two in Scotland), Italy (n = 1), Spain (n = 1) and Greece (n = 1). The non-European studies were conducted in the USA, Canada, Chile, Australia, New Zealand, China, Thailand and Taiwan. Two reports from Denmark[17,18] and two from Scotland[24,25] were based on the same datasets but since they provided associations with different outcomes, they were all included in this systematic review.

The majority (23/30) of the included studies used prospective recruitment while the rest[25,26,28–30,35,37] consisted of retrospective audits. Thirteen[16,19,20,23,24,29,30,32,34,35,40,41,43] included only patients with ischaemic stroke, and

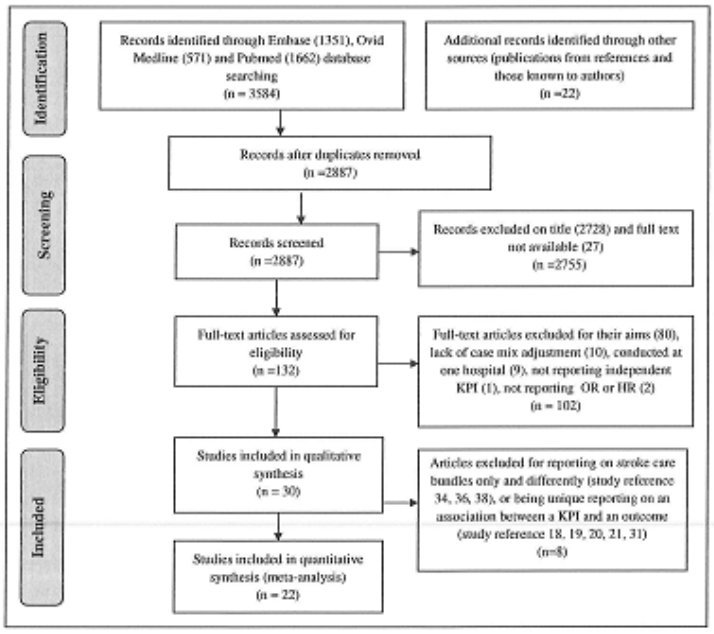

Figure 1. Review profile showing selection of studies. HR: hazard ratio; KPI: key performance indicator; OR: odds ratio.

Table 1. Studies eligible for the systematic literature review.

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
Europe[15]	SAH excluded	Level of consciousness, incontinence, dysphagia, dysphasia and paralysis	1847 (10 countries)	Brain imaging	3-month case fatality	0.7	0.4–1.3
					3-month disability (BI ≤ 18)	1.45	0.39–7.4
				Organised stroke care[a]	3-month case fatality	0.5	0.3–0.8
					3-month disability (BI ≤ 18)	1.3	0.6–1.76
Denmark[16]	Ischaemic stroke	SSS scale (SSS)	22,179 (all Danish hospitals)	Anticoagulants for IS with AF	4-year survival	1.91	1.44–2.52
Denmark[17]	SAH excluded	SSS	29,573 (40 hospitals)	Specialised stroke unit by 2nd day	90-day case fatality	0.76	0.69–0.83
				Antiplatelet therapy by 2nd day		0.71	0.62–0.81
				Anticoagulants for IS with AF by 14th day		0.41	0.31–0.52
				CT/MRI scan by first day		1.35	1.24–1.46
				Assessment by a PT by 2nd day		0.81	0.73–0.88
				Assessment by an OT by 2nd day		0.83	0.75–0.91
				Nutritional risk assessment by 2nd d.		0.69	0.61–0.76
				Number of criteria fulfilled			
				1 vs 0		0.94	0.65–1.49
				2 vs 0		0.78	0.54–1.02
				3 vs 0		0.60	0.42–0.78
				4 vs 0		0.61	0.42–0.79
				5 vs 0		0.45	0.31–0.60
				6 vs 0		0.48	0.31–0.65
Denmark[18]	SAH excluded	SSS	2636 (7 stroke units)	Stroke unit (2nd day)	Prolonged LoS	0.71	0.65–0.77
				Antiplatelet for IS (2nd day)		0.80	0.73–0.87
				Anticoagulant for IS with AF (14th day)		0.78	0.62–0.98

(continued)

Table 1. Continued

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
				CT/MRI scan (2nd day)		0.82	0.74–0.91
				PT assessment (2nd day)		0.87	0.81–0.93
				OT assessment (2nd day)		0.85	0.80–0.91
				Nutritional risk assessment (2nd day)		0.83	0.77–0.90
				Swallowing assessment (2nd day)		0.78	0.69–0.87
				Constipation risk assessment (2nd day)		0.70	0.63–0.78
				Mobilisation (2nd day)		0.67	0.61–0.73
				Intermittent catheterisation (2nd day)		0.77	0.64–0.92
				DVT prophylaxis (2nd day)		0.82	0.71–0.95
				Percentage of criteria fulfilled			
				25%–49% vs 0%–24%		0.77	0.69–0.86
				50%–74% vs 0%–24%		0.67	0.60–0.75
				75%–100% vs 0%–24%		0.53	0.48–0.59
Denmark [19]	All ischaemic strokes	SSS	4292 (all Danish hospitals)	Thrombolysis	1.4 years mortality	0.66	0.49–0.88
					1.4 years recurrent stroke	1.05	0.68–1.64
					1.4 years major bleeding	0.59	0.24–1.47
Denmark[20]	First ever ischaemic strokes	SSS	5070 (Aarhus County)	Antidepressants during hospitalisation	30-day case fatality	0.28	0.18–0.43
Denmark[21]	All stroke types	SSS	11,757 (10 stroke units in two counties)	Early admission to a stroke unit	Any medical complication[b] during admission (LoS = 13 days)	0.79	0.68–0.92
				Antiplatelet therapy for IS		0.95	0.79–1.15
				Anticoagulant therapy for IS with AF		0.59	0.45–0.76
				CT/MRI scan		1.52	1.35–1.72
				Assessment by a PT		1.10	0.94–1.28
				Assessment by an OT		1.10	0.94–1.27
				Assessment of nutritional risk		0.87	0.70–1.07
				Swallowing assessment		0.97	0.84–1.11
				Early mobilisation		0.43	0.35–0.53

(continued)

Table 1. Continued

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
				Percentage of criteria fulfilled			
				25%–49% vs 0%–24%		0.77	0.67–0.88
				50%–74% vs 0%–24%		0.57	0.46–0.70
				75%–100% vs 0%–24%		0.50	0.36–0.68
Sweden[22]	SAH excluded	Level of consciousness	8194 (all hospitals in Sweden)	Stroke unit (Independent before stroke)	2-year case fatality	0.81	0.72–0.92
					2-year functional dependency	0.79	0.66–0.94
Sweden[23]	First ever ischaemic strokes	ADLs function	14,529 (all hospitals in Sweden)	Antiplatelet therapy for IS	3-month case fatality	0.83	0.68–1.01
				ACE inhibitors therapy		1.00	0.87–1.14
				Statins therapy		0.78	0.67–0.91
				Anticoagulants therapy for IS with AF		0.58	0.44–0.76
UK (England)[24]	Ischaemic stroke	Level of consciousness and neurological deficit	36,197 (106 hospitals)	Seen by a stroke consultant or associate specialist within 24 h	30-day case fatality	0.88	0.80–0.97
				Brain scan within 24 h		0.96	0.86–1.07
				Bundle 1: seen by nurse and one therapist within 24 h and all relevant therapists within 72 h		0.90	0.82–0.99
				Bundle 2: nutrition screening and formal swallow assessment within 72 h where appropriate		0.76	0.67–0.87
				Bundle 3: patient's first ward of admission was stroke unit and they arrived there within 4 h of hospital admission		0.99	0.90–1.08
				Bundle 4: patient given antiplatelet therapy where appropriate and had adequate fluid and nutrition for first 72 h		0.46	0.42–0.50
				Number of criteria fulfilled			
				Quality score 5 or 6 v 0–4		0.74	0.66–0.83

(continued)

Table 1. Continued

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
UK (Scotland)[25]	All stroke types	SSV	36,055 (36 hospitals)	Stroke unit on day 0 or 1	6-month case fatality	0.79	0.74–0.85
				Swallow screen on day 0		0.95	0.86–1.04
				Brain scan on day 0		0.95	0.88–1.03
				Aspirin on day 0 or 1		0.54	0.49–0.58
				Number of criteria fulfilled	6-month case fatality		
				0 vs 4		2.26	1.60–3.21
				1 vs 4		1.67	1.45–1.93
				2 vs 4		1.44	1.31–1.59
				3 vs 4		1.17	1.08–1.27
				Number of criteria fulfilled	Discharge to home/ usual residence at 6 months		
				0 vs 4		0.70	0.50–0.98
				1 vs 4		0.74	0.65–0.84
				2 vs 4		0.84	0.76–0.91
				3 vs 4		0.91	0.85–0.98
UK (Scotland)[26]	All stroke types	SSV	41,692 (36 hospitals)	Admission to stroke unit	1-year survival	1.43	2.71–3.56
					6-month discharged home	1.19	1.11–1.28
Italy[27]	All stroke types	Level of consciousness	11,572 (424 stroke units and 260 hospitals)	Stroke unit	2-year case fatality	0.79	0.68–0.91
					2-year death or disability (mRS > 2)	0.81	0.72–0.91
					2 year not living at home	0.85	0.74–0.97
Spain[28]	SAH excluded	NIHSS	1767 (47 hospitals)	Brain imaging < 24 h	1-year case fatality risk for noncompliance	1.4	0.71–2.76
				Screening of dysphagia		1.23	0.88–1.71
				Antiplatelets < 48 h for IS		1.3	0.84–2.02
				Early mobilisation		1.54	1.05–2.24
				Assessment of rehabilitation needs		1.48	1.06–2.07
				DVT prevention		0.98	0.60–1.60
				Management of hyperthermia		0.67	0.25–1.79
				Management of hypertension		1.87	1.22–2.86
				Management of dyslipidemia		1.29	0.86–1.93

(continued)

Table 1. Continued

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
				Anticoagulants for IS with AF		1.70	0.95–3.05
				Antithrombotics at discharge (IS)		2.79	1.41–5.54
Greece[29]	First-ever acute ischaemic stroke	SSS	794 (different Athenian hospitals)	Statin at discharge	10-year case fatality	0.43	0.29–0.61
					10-year stroke recurrence	0.65	0.39–0.97
USA[30]	Ischaemic stroke	NIHSS	1363 (5 hospitals)	Neurology assessment	In-hospital mortality, discharge to hospice, or discharge to a skilled nursing facility	1.13	0.59–2.17
				Swallowing evaluation		0.64	0.43–0.94
				DVT prophylaxis		0.60	0.37–0.96
				Early mobilisation		0.69	0.42–1.14
				Blood pressure management		1.00	0.67–1.50
				Fever management		0.71	0.35–1.41
				Hypoxia management		0.26	0.09–0.73
USA[31]	All stroke types	Weakness and altered level of consciousness	18,017(222 hospitals from 6 States)	Dysphagia screening	Higher risk of pneumonia for no screening	2.15	1.74–2.66
Canada[32]	Ischaemic stroke	CNS	3631 (11 hospitals)	OCI[c] 1 vs 0	1-year case fatality	0.69	0.44–1.09
				OCI 2 vs 0		0.39	0.25–0.62
				OCI 3 vs 0		0.40	0.25–0.64
				Antithrombotic therapy		0.33	0.22–0.50
Canada[33]	Intracerebral haemorrhage stroke	CNS	2466 (11 hospitals)	Statin use in hospital	6 months case fatality	0.2	0.1–0.3
					Poor outcome (mRS4–6.) at discharge	0.6	0.4–0.9
Canada[34]	Ischaemic stroke	CNS	6223 (12 centres)	OCI[c] 2–3 vs 0–1	30-day case fatality	0.23	0.19–0.28
Chile[35]	Ischaemic stroke	Aphasia, hemiplegia, reduced level of consciousness, and speech disturbance	677 (7 hospitals)	Neurological evaluation on admission	30-day case fatality	2.02	0.77–5.30
					In-hospital pneumonia	1.07	0.79–1.44
				Dysphagia screening within 48 h	30-day case fatality	0.52	0.26–1.04
					In-hospital pneumonia	1.58	0.60–4.15

(continued)

Table 1. Continued

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
Australia[36]	SAH excluded	GCS, ability to lift both arms, ability to walk, and urinary incontinence	468 (8 hospitals)	Thorough (n-I ≤ 1)[d] adherence to 15 processes of stroke care[e]	Independent at 28 weeks	1.78	0.93–3.38
					Being at home at 28 weeks	1.69	0.86–3.32
					Alive at 28 weeks	2.10	0.92–4.82
				Complete (n-I ≤ 0) adherence to 15 processes of stroke care	Independent at 28 weeks	2.61	0.96–7.10
					Being at home at 28 weeks	3.09	0.96–9.87
					Alive at 28 weeks	3.22	0.66–15.86
Australia[37]	All stroke types	FIM	2119 (108 rehabilitations units)	ADLs rehabilitation	Discharged home (Median LoS = 26 days)	1.01	0.33–3.13
				DVT prevention		0.58	0.41–0.81
				Home assessment		6.15	3.70–10.22
				Balance rehabilitation		0.54	0.35–0.83
				Secondary prevention on discharge[f]		1.99	1.12–3.53
				Education to patients[g]		2.37	1.30–4.29
				Discussing post-discharge needs with patients		1.27	0.66–2.43
Australia[38]	All stroke types	Ability to walk on admission	16,665 (42 hospitals)	1 process received vs 0	180-day case fatality	0.63	0.41–0.97
				2 processes received vs 0		0.46	0.31–0.68
				3 processes received vs 0		0.30	0.18–0.47
				1 process received vs 0	90- to 180-day Quality of Life (QoL)	12.53	−2.22 to 27.28
				2 processes received vs 0		16.67	0.30–33.05
				3 processes received vs 0		18.70	1.86–35.55
New Zealand[39]	All stroke types	Age, initial FIM, pre-stroke FIM, and being European	181 (3 hospitals)	Swallowing assessment	1-year poor outcome (death or moved from home) for swallowing recorded 'no'	3.2	0.97–10.7
China[40]	Ischaemic stroke	NIHSS	1951 (23 hospitals in 11 major cities of China)	Antiplatelet therapy for IS	1-year case fatality	0.42	0.21–0.86
					Recurrent cerebrovascular event	0.58	0.36–0.92
					Functional improvement	1.25	1.02–1.52

(continued)

Table 1. Continued

Study	Stroke type	Stroke severity measure	Sample size	Performance indicator	Patient outcome	OR/HR/RR	95% CI
China[41]	First ever ischaemic stroke	NIHSS	7455 (132 hospitals)	Stain use during hospitalisation	3-month case fatality	0.51	0.38–0.67
					3-month dependency	0.95	0.81–1.11
China[42]	Intracerebral haemorrhage stroke	NIHSS	3218 (132 hospitals)	Stain use during hospitalisation	1-year case fatality	0.49	0.27–0.86
					1-year good functional outcome	2.04	1.37–3.06
Thailand[43]	Ischaemic stroke	NIHSS	1222 (76 hospitals)	Stroke unit admission	Poor outcome (mRS 5–6 at discharge) (LoS = 4 days)	0.54	0.33–0.87
				Thrombolysis		0.09	0.03–0.23
				Aspirin within 48 h		1.25	0.73–2.15
Taiwan[44]	All stroke types	NIHSS	30,599 (39 hospitals)	IV tPA for 2 h	6-month functional dependency (mRS ≥ 2)	0.52	0.35–0.76
				Antithrombotics at discharge	6-month risk of cardiovascular events and death	0.41	0.35–0.47
				Anticoagulation for IS with AF at discharge		0.59	0.44–0.80
				Lipid-lowering agents at discharge		0.94	0.78–1.13

[a]Organised stroke care included wards which encompassed multidisciplinary team-working, a physician with an interest in stroke, as well as taking into account the proportion of time spent (>50% of their length of stay) in such an environment. The wards that encompassed organised stroke care included neurology, elderly care, stroke specific unit and intensive care unit.
[b]The complications that were considered in the analysis included pneumonia, urinary tract infection, pressure ulcer, falls, venous thromboembolism and constipation.
[c]OCI is a summary score based on the presence of occupational therapy or physiotherapy, stroke team assessment and admission to a stroke unit. A score of zero indicates that stroke patients received none of these services, and higher scores indicate access to more services. The 'organised care' index was classified as having received 0, 1, 2 or 3 services.
[d]n indicates number of applicable PoC; i, number of PoC adhered to.
[e]The 15 processes of care consisted of CT scan < 24 h since admission, swallow < 24 h since admission, allied health < 24 h since admission, incontinence addressed, discharged on antiplatelet agent, fever > 38.5 managed, documented premorbid function, documented discharge needs, regular neurology observations for the first 24 h of admission, physiotherapist within 24 h, occupational therapist within 24 h, speech pathologist within 24 h, enteric feeding if nil by mouth > 48 h, aspiration avoidance and DVT prophylaxis if not ambulant.
[f]Secondary prevention included deep vein thrombosis prophylaxis, discharged on lipid-lowering medication, discharged on blood-pressure–lowering medication and discharged on antithrombotics.
[g]Education to patients consisted of lifestyle advice, information on sexuality poststroke, information about peer support, information on self-management programs, carer training and providing contact to patient.
ACE: angiotensin-converting enzyme; ADLs: Activities of Daily Living; AF: atrial fibrillation; BI: Barthel Index; CNS: Canadian neurological scale; CT: computerised tomography; MRI: magnetic resonance imaging; CI: confidence interval; DVT: deep vein thrombosis; FIM: functional independence measure; GCS: Glasgow coma scale; HR, hazard ratio; IS: ischaemic stroke; LoS: length of hospital stay; mRS: modified Rankin Scale; NIHSS: national institute of health stroke scale; PT: physiotherapy; OR: odds ratio; OT: occupational therapy; RR: rate ratio; SAH: subarachnoid haemorrhage; SSS: Scandinavian stroke scale; SSV: six simple variable; OCI: organised care index; PoC: processes of care.

two[33,42] included only patients with intracerebral haemorrhage. The remainder included both ischaemic and haemorrhagic stroke. Among those studies that included both types of stroke, six[15,17,18,22,28,36] excluded patients with subarachnoid haemorrhage.

For the association between KPIs and patient outcomes, the majority[22] of the included studies used OR, six studies[16,19,23,29,38,40] used HR while the remaining two[17,18] used rate RR. The included studies also used different measures for stroke severity as a case mix variable for adjustment to estimate the independent association between a KPI and a patient outcome. Twenty of the included studies used validated tools including National Institute of Health Stroke Scale,[28,30,40–44] Scandinavian Stroke Scale,[16–21,29] Canadian Neurological Scale,[32–34] Six Simple Variables[25,26] and Glasgow Coma Scale,[36] while the remainder used stroke severity proxies such as level of consciousness, incontinence, dysphagia, dysphasia, paralysis and disability.

Reporting of published KPIs

As there were some variations in data definitions and analysis methods, several assumptions were made to allow easy comparison between the studies:

Swallow/nutritional assessment – This single KPI comprised an assessment of swallowing, dysphagia and/or nutritional risk. If separate data for both swallow and nutritional risk assessment[18,21] were reported, we preferentially included data for swallow assessment.

Antiplatelet drugs for ischaemic stroke (IS) – Aspirin administration reported in two studies[25,43] was combined with a KPI for antiplatelet drugs for ischaemic stroke reported in seven studies.[17,18,21,23,24,28,40]

Early nurse/rehabilitation assessment – This combined indicator of early assessment by a nurse[24] and early assessment of rehabilitation needs.[28]

Early physiotherapy/mobilisation – This combined five reports of early mobilisation[18,21,28,30] with one[17] about early physiotherapy assessment.

Selection of outcome measures

As there were minor variations in the approach to outcome analysis adjustments were made to the reported OR, HR, RR and CI to allow comparisons between the studies. The *online supplement Table S1* provides a summary of the adjustments made.

Data reported in terms of poor outcome,[33,39,43] disability,[15,22,41,44] death or disability[17,30] or not returning home[27] post stroke were all combined as a 'poor outcome' post stroke. Finally, the results on the association between KPIs and stroke case fatality were categorised at the end of scheduled follow-up although the timing of follow-up was included in sensitivity analyses.

KPIs

There were 25 reported KPIs in total. The KPIs that were reported by at least a quarter of the eligible studies were swallow/nutritional assessment, stroke unit admission and antiplatelets for ischaemic stroke.

Stroke unit admission was variably defined across the related studies.[15,17,18,21,22,24–27,43] Two Danish studies[17,18] defined a 'stroke unit' as a hospital department/unit that exclusively or primarily is dedicated to patients with stroke and which is characterised by multidisciplinary teams, a staff with a specific interest in stroke, involvement of relatives and continuous education of the staff. In the Italian study,[27] stroke unit was defined as a hospital ward with dedicated beds (at least 80% stroke admission) and with a dedicated stroke staff (at least one physician and one nurse) who work exclusively in the care of stroke patients.

The online supplement Table S2 provides a list of reported KPIs and their frequencies out of the 30 studies. Table 2 indicates the reported KPIs and their association with patient outcomes.

Association between individual KPIs and lower risk for case fatality at the end of scheduled follow-up

The median time of scheduled follow-up for the studies reporting on the association between individual KPIs and case fatality was 1 year; range from 1 month to 10 years. Significant reductions in case fatality were observed across multiple studies for stroke unit admission,[15,17,22,25–27] swallow/nutritional assessment,[17,24] antiplatelets for ischaemic stroke,[17,40,24,25] anticoagulants for ischaemic stroke with atrial fibrillation,[16,17,23] lipid management,[23,29,33,41,42] early nurse/rehabilitation assessment[24,28] and early physiotherapy/mobilisation.[17,28] In addition, significant associations within single studies were observed for DVT prophylaxis[32] and blood pressure lowering therapy.[28]

In contrast, several studies reported wide CIs and no statistically significant association between the reported KPIs and stroke case fatality; stroke unit admission,[24] swallow/nutritional assessment,[25,28,35] antiplatelets for ischaemic stroke,[23,28] anticoagulants for ischaemic stroke with atrial fibrillation, lipid management,[28] DVT prophylaxis[28] and blood pressure lowering therapy.[23] In one study,[17] the CT/MRI brain imaging was associated with increased risk of early case fatality (RR: 1.35, 95% CI: 1.24–1.46), while in other

Table 2. Reported KPIs and their association patient outcomes.

KPI	Study	Treatment time	End follow-up period	OR/HR/RR	95% CI
1. Reported KPIs and their association with case fatality					
CT/MRI brain imaging	Europe[15]		3 months	0.70	0.40–1.30
	Denmark[17]	1st day of LoS	3 months	1.35	1.24–1.46
	UK (England)[24]	≤24 h	1 month	0.96	0.86–1.07
	UK (Scotland)[25]	day 0	6 months	0.95	0.88–1.03
	Spain[28]	<24 h	1 year	0.71	0.36–1.41
Neurological assessment	Chile[35]	On admission	1 month	2.02	0.77–5.30
Thrombolysis	Denmark[19]		1.4 year	0.66	0.49–0.88
Stroke unit admission	Europe[15]		3 months	0.50	0.30–0.80
	Denmark[17]	2nd day of LoS	3 months	0.76	0.69–0.83
	Sweden[22]		2 years	0.81	0.72–0.92
	UK (England)[24]	≤4 h	1 month	0.99	0.90–1.08
	UK (Scotland)[25]	day 0 or 1	6 months	0.79	0.74–0.85
	UK (Scotland)[26]		1 year	0.70	0.65–0.75
	Italy[27]		2 years	0.79	0.68–0.91
Swallow/nutritional assessment	Denmark[17]	2nd day of LoS	3 months	0.69	0.61–0.76
	UK (England)[24]	≤72 h	1 month	0.76	0.67–0.87
	UK (Scotland)[25]	day 0	6 months	0.95	0.86–1.04
	Spain[28]		1 year	0.81	0.58–1.14
	Chile[35]	≤48 h	1 month	0.52	0.26–1.04
Antiplatelets for IS	Denmark[17]	2nd day of LoS	3 months	0.71	0.62–0.81
	Sweden[23]	–	3 months	0.83	0.68–1.01
	UK (England)[24]	≤72 h	1 month	0.46	0.42–0.50
	UK (Scotland)[25]	day 0 or 1	6 months	0.54	0.49–0.58
	Spain[28]	< 48 h	1 year	0.77	0.50–1.19
	China[40]	LoS	1 year	0.42	0.21–0.86
Anticoagulants for IS with AF	Denmark[16]	Acute LoS	4 years	0.52	0.40–0.69
	Denmark[17]	By 14th day	3 months	0.41	0.31–0.52
	Sweden[23]	–	3 months	0.58	0.44–0.76
	Spain[28]		1 year	0.59	0.33–1.05
Blood pressure lowering therapy	Sweden[23]	–	3 months	1.00	0.87–1.14
	Spain[28]		1 year	0.53	0.35–0.82
Hyperthermia management	Spain[28]		1 year	1.50	0.56–4.00
Lipid management	Sweden[23]	–	3 months	0.78	0.67–0.91
	Spain[28]		1 year	0.78	0.52–1.16
	Greece[29]	At discharge	10 years	0.43	0.29–0.61
	Canada[33]	Acute LoS	6 months	0.2	0.1–0.3
	China[41]	LoS	3months	0.51	0.38–0.67
	China[42]	Acute LoS	1 year	0.49	0.27–0.86
DVT prophylaxis	Spain[28]		1 year	1.02	0.63–1.67
	Canada[32]	Acute LoS	1 year	0.33	0.22–0.50
Early medical assessment	UK (England)[24]	≤24 h	1 month	0.88	0.80–0.97
Early nurse/rehabilitation assessment	UK (England)[24]	≤24 h	1 month	0.90	0.82–0.99
	Spain[28]		1 year	0.68	0.48–0.94
Early physiotherapy/mobilisation	Denmark[17]	2nd day of LoS	3 months	0.81	0.73–0.88
	Spain[28]		1 year	0.65	0.45–0.95

(continued)

Table 2. Continued

KPI	Study	Treatment time	End follow-up period	OR/HR/RR	95% CI
Occupational therapy assessment	Denmark[17]	2nd day of LoS	3 months	0.83	0.75–0.91
Antidepressant therapy	Denmark[20]	LoS	1 month	0.28	0.18–0.43
2. Reported KPIs and their association with poor outcome					
CT/MRI brain imaging	Europe[15]		3 months	1.45	0.39–7.4
Thrombolysis	Thailand[43]		LoS = 4 days	0.09	0.03–0.23
	Taiwan[44]	3 h of onset	6 months	0.52	0.35–0.76
Neurological Assessment	USA[30]		LoS	1.13	0.59–2.17
Stroke unit admission	Thailand[43]		LoS = 4 days	0.54	0.33–0.87
	Europe[15]		3 months	1.3	0.6–1.76
	Italy[27]		2 years	0.85	0.74–0.97
	UK (Scotland)[26]		6 months	0.84	0.78–0.90
	Sweden[22]		2 years	0.79	0.66–0.94
Swallow/nutritional assessment	Thailand[43]		LoS = 4 days	0.54	0.33–0.87
	New Zealand[39]		1 year	0.31	0.09–1.03
	USA[30]		LoS	0.64	0.43–0.94
Antiplatelets for IS	China[40]	LoS	1 year	0.80	0.66–0.98
	Thailand[43]	48 h	LoS = 4 days	1.25	0.73–2.15
Blood pressure lowering therapy	USA[30]		LoS	1.00	0.67–1.50
Hyperthermia management	USA[30]	All episodes	LoS	0.71	0.35–1.41
Hypoxia management	USA[30]	All episodes	LoS	0.26	0.09–0.73
DVT Prophylaxis	USA[30]		LoS	0.60	0.37–0.96
	Australia[37]		26 days	1.72	1.23–2.44
Early physiotherapy/mobilisation	USA[30]		LoS	0.69	0.42–1.14
ADLs rehabilitation	Australia[37]		26 days	0.99	0.32–3.03
Home assessment	Australia[37]		26 days	0.16	0.10–0.27
Balance rehabilitation	Australia[37]		26 days	1.85	1.20–2.86
Secondary prevention on discharge	Australia[37]		26 days	0.50	0.28–0.89
Education to patients	Australia[37]		26 days	0.42	0.23–0.77
Discussing post-discharge needs with patients	Australia[37]		26 days	0.79	0.41–1.52
Lipid management	China[41]	Acute LoS	3 months	0.95	0.81–1.11
	China[42]	Acute LoS	1 year	0.49	0.33–0.73
	Canada[33]	Acute LoS	At discharge	0.6	0.4–0.9
3. Reported KPIs and their association with prolonged length of hospital stay					
Stroke unit admission	Denmark[18]	2nd day		0.71	0.65–0.77
Antiplatelets for IS	Denmark[18]	2nd day		0.80	0.73–0.87
Anticoagulants for IS with AF	Denmark[18]	14th day		0.78	0.62–0.98
CT/MRI brain imaging	Denmark[18]	2nd day		0.82	0.74–0.91
Swallow/nutritional assessment	Denmark[18]	2nd day		0.78	0.69–0.87
Constipation risk assessment	Denmark[18]	2nd day		0.70	0.63–0.78
Early physiotherapy/mobilisation	Denmark[18]	2nd day		0.67	0.61–0.73
Occupational therapy assessment	Denmark[18]	2nd day		0.85	0.80–0.91
Intermittent catheterisation	Denmark[18]	2nd day		0.77	0.64–0.92
DVT prophylaxis	Denmark[18]	2nd day		0.82	0.71–0.95

(continued)

Table 2. Continued

KPI	Study	Treatment time	End follow-up period	OR/HR/RR	95% CI
4. Reported KPIs and their association with medical complications					
CT/MRI brain imaging	Denmark[21]		LoS = 13 days	1.52	1.35–1.72
Neurological assessment	Chile[35]	On admission	30 days	1.07	0.79–1.44
Stroke unit admission	Denmark[21]		LoS = 13 days	0.79	0.68–0.92
Swallow/nutritional assessment	Chile[35]	≤48 h	30 days	1.58	0.60–4.15
	Denmark[21]		LoS = 13 days	0.97	0.84–1.11
	USA[31]		LoS = 5 days	0.47	0.38–0.57
Antiplatelets for IS	Denmark[21]		LoS = 13 days	0.95	0.79–1.15
Anticoagulants for IS with AF	Denmark[21]		LoS = 13 days	0.59	0.45–0.76
Early physiotherapy/mobilisation	Denmark[21]		LoS = 13 days	0.43	0.35–0.53
Occupational therapy assessment	Denmark[21]		LoS = 13 days	1.10	0.94–1.27
Thrombolysis	Denmark[19]		1.4 years	0.59	0.24–1.47
5. Reported KPIs and their association with stroke recurrence					
Antiplatelets for IS	China[40]	LoS	12 months	0.58	0.36–0.92
Anticoagulants for IS with AF	Taiwan[44]	At discharge	6 months	0.59	0.44–0.80
Lipid management	Taiwan[44]	At discharge	6 months	0.94	0.78–1.13
	Greece[39]	At discharge	10 years	0.65	0.39–0.97
DVT prophylaxis	Taiwan[44]	At discharge	6 months	0.41	0.35–0.47
Thrombolysis	Denmark[19]		1.4 year	1.05	0.68–1.64

ADLs: activities of daily living; AF: atrial fibrillation; CT: computerised tomography; MRI: magnetic resonance imaging; CI: confidence interval; DVT: deep vein thrombosis; HR: hazard ratio; IS: ischaemic stroke; KPI: key performance indicator; LoS: length of hospital stay; OR: odds ratio; RR: rate ratio.

studies,[15,24,25,28] no evidence for an association of CT/MRI brain imaging and stroke case fatality was found.

Figure 2 summarises the primary meta-analysis results regarding the associations between individual KPIs and stroke case fatality at the end of follow-up. The KPIs that were associated with lower risk for case fatality include stroke unit admission (OR: 0.79, 95% CI: 0.72–0.87), swallow/nutritional assessment (OR: 0.78, 95% CI: 0.66–0.92), antiplatelets for ischaemic stroke (OR: 0.61, 95% CI: 0.50–0.74), anticoagulants for ischaemic stroke with atrial fibrillation (OR: 0.51, 95% CI: 0.43–0.61), lipid management (OR: 0.52, 95% CI: 0.38–0.71) and early physiotherapy/mobilisation (OR: 0.78, 95% CI: 0.67–0.91). However, the significant associations of stroke unit admission, swallow/nutritional assessment, antiplatelets for ischaemic stroke and lipid management were complicated by substantial heterogeneity ($I^2 > 50\%$). When analysed at a fixed time point, swallow/nutritional assessment (OR: 0.72, 95% CI: 0.66–0.79), antiplatelets for ischaemic stroke (OR: 0.64, 95% CI: 0.44–0.93) and lipid management (OR: 0.64, 95% CI: 0.42–0.97) were associated with a lower risk for early case fatality (up to 3 months post stroke), but the heterogeneity was reduced for swallow/nutritional assessment ($I^2 = 1\%$) only. Stroke unit admission (OR: 0.77, 95% CI: 0.71–0.82), antiplatelets for ischaemic stroke (OR: 0.57, 95% CI: 0.45–0.72) and lipid management (OR: 0.45, 95% CI: 0.27–0.74) were associated with lower risk for late case fatality (beyond 3 months post stroke), but the heterogeneity was reduced for antiplatelets for ischaemic stroke ($I^2 = 34\%$) only.

The meta-analysis showed no evidence for the association between the stroke case fatality and DVT prophylaxis, blood pressure lowering therapy, early nurse/rehabilitation assessment and CT/MRI brain imaging.

The sensitivity analysis excluding those that used HR or RR produced results that were similar to those in Figure 2 (data not shown): stroke unit admission (OR: 0.79, 95% CI: 0.71–0.89), swallow/nutritional assessment (OR: 0.82, 95% CI: 0.69–0.98), antiplatelets for ischaemic stroke (OR: 0.53, 95% CI: 0.44–0.63) and lipid management (OR: 0.47, 95% CI: 0.30–0.74) remained associated with lower risk for case fatality, and there was no evidence for the association between the stroke case fatality and DVT prophylaxis, early nurse/rehabilitation assessment and CT/MRI brain imaging.

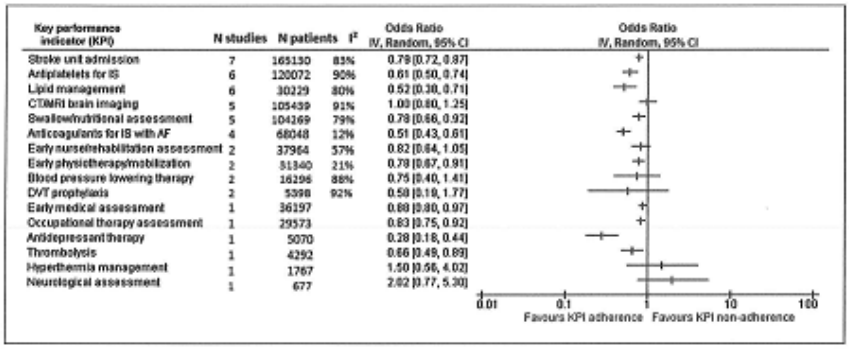

Figure 2. Association between individual KPIs and lower risk for case fatality. AF: atrial fibrillation; CT: computerised tomography; MRI: magnetic resonance imaging; CI: confidence interval; DVT: deep vein thrombosis; I^2: heterogeneity; IS: ischaemic stroke; IV: inverse variance; KPI: key performance indicator; N: number of.

Significant associations within single studies were observed for thrombolysis,[19] early medical assessment,[24] OT assessment[17] and antidepressant therapy,[20] but there was no evidence for the association between stroke case fatality and hyperthermia management,[28] and neurological assessment.[35]

Association between individual KPIs and the risk for poor outcome

For studies reporting on the association between individual KPIs and poor outcome, the available follow-up periods were between 4 days and 2 years, with a mean of 282 days.

KPIs that were reported to be associated with the lower risk for poor outcome included thrombolysis,[43,44] stroke unit admission,[22,26,27,43] swallowing/nutritional assessment,[30,43] antiplatelets for ischaemic stroke,[40] DVT prophylaxis,[30] and lipid management management.[33,42] However, some studies found no evidence of an association with poor outcome and stroke unit admission[15]; swallowing/nutritional assessment,[39] antiplatelets for ischaemic stroke,[43] DVT prophylaxis[37] and lipid management.[41]

As summarised in Figure 3, the meta-analysis showed that the KPIs associated with the lower risk for poor outcome were stroke unit admission (OR: 0.83, 95% CI: 0.77–0.89) and swallowing/nutritional assessment (OR: 0.58, 95% CI: 0.43–0.78), while there was no evidence for the association with poor outcome for thrombolysis, antiplatelets for ischaemic stroke, DVT prophylaxis and lipid management.

Several individual studies reported significant associations between lower risk for poor outcome and hypoxia management[30]; home assessment, secondary prevention on discharge and education to patients.[37] No association with poor outcome was found for CT/MRI brain imaging[15]; neurological assessment, blood pressure lowering therapy, hyperthermia management and early physiotherapy/mobilisation[30]; ADLs rehabilitation, balance rehabilitation and discussing post-discharge needs with patients.[37]

All the studies included for the primary meta-analysis about the association of KPIs with poor outcome used ORs, except one Chinese study.[40] After excluding that study, antiplatelets for ischaemic stroke remained with a single study,[43] which showed no association with poor outcome (OR: 1.25, 95% CI: 0.73–2.14).

Association between individual KPIs and relative length of hospital stay

A single Danish study[18] reported that a shorter relative length of hospital stay was associated with stroke unit admission, antiplatelets and anticoagulants for ischaemic stroke with atrial fibrillation, CT/MRI brain imaging, early physiotherapy/mobilisation, occupational therapy assessment, swallowing/nutritional assessment and DVT prophylaxis, with rate ratio ranging from 0.67 (0.61–0.73) for early physiotherapy/mobilisation to 0.85 (0.80–0.91) for occupational therapy assessment.

Association between individual KPIs and the risk for medical complications and stroke recurrence

Stroke unit admission, anticoagulants for ischaemic stroke with atrial fibrillation and early physiotherapy/mobilisation,[21] as well as swallow/nutritional assessment[31] were found to be associated with lower risk for medical complications (OR: 0.79; 0.68–0.92; 0.59,

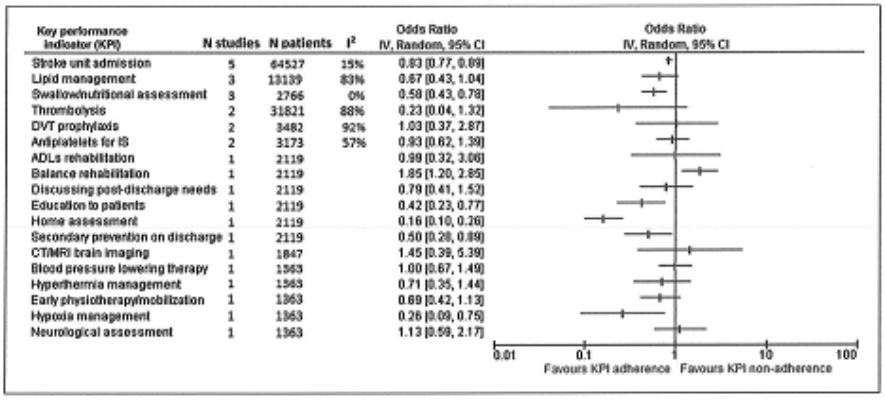

Figure 3. Association between individual KPIs and lower risk for poor outcome. ADLs: activities of daily living; CT: computerised tomography; MRI: magnetic resonance imaging; CI: confidence interval; DVT: deep vein thrombosis; I^2: heterogeneity; IS: ischaemic stroke; IV: inverse variance; KPI: key performance indicator; N: number of.

0.45–0.76 and 0.43, 0.35–0.53; 0.47, 0.38–0.57, respectively). By contrast, CT/MRI brain imaging was associated with a greater risk for medical complications with (1.52, 1.35–1.72).[21] Other studies with wide CIs did not show evidence for the association between the occurrence of medical complications and neurological assessment[35]; swallow/nutritional assessment[21,35]; antiplatelets for ischaemic stroke, occupational therapy assessment[21]; and thrombolysis.[19]

KPIs that were reported to be associated with lower recurrence rate for stroke included antiplatelets for ischaemic stroke,[40] anticoagulants for ischaemic stroke with atrial fibrillation and DVT prophylaxis[44] and lipid management.[29] However, in one study,[21] evidence for the association between lipid management and stroke recurrence was not found,[44] and there was no evidence of an association with thrombolysis.[19]

Association between adherence to groups of KPIs and the risk for case fatality

Seven studies[17,24,25,32,34,36,38] had consistent findings whereby adherence to a combination of several KPIs ('bundle') was associated with a greater decrease in stroke mortality. A lower risk for poor outcome was also reported when full stroke care bundle was achieved.[25,36] An Australian study[38] also showed that achieving full care bundle was associated with better quality of life at 3 to 6 months post stroke. Increased adherence to stroke care KPIs[18] was associated with shorter length of hospital stay (data are not shown in Table 3).

Overall (see *Online Supplement Table 3*), only stroke unit admission, swallow/nutritional assessment, antiplatelets for ischaemic stroke, anticoagulants for ischaemic stroke with atrial fibrillation, lipid management and early physiotherapy/mobilisation were found to be significantly associated with improved outcomes after a meta-analysis of two or more studies. Thrombolysis results were associated with reduced poor outcome in two studies, but the combined analysis was not significant due to substantial heterogeneity. Data were very limited for the outcomes of length of stay, stroke recurrence or medical complications.

Discussion

The publications we have reviewed provide a large and diverse body of evidence on whether quality of care, as measured by adherence with a KPI, is associated with improved clinical outcomes in patients hospitalised with stroke. Our primary meta-analysis indicated that several KPIs including stroke unit admission, swallowing/nutritional risk assessment, antiplatelets for ischaemic stroke, anticoagulants for ischaemic stroke with atrial fibrillation, lipid management and early physiotherapy/mobilisation were associated with a reduction in case fatality or poor outcome. However, although our meta-analysis showed significant associations between lower risk for case fatality and several individual KPs at the end of scheduled follow-up, there was substantial heterogeneity ($I^2 > 50\%$) for stroke unit admission, swallowing/nutritional risk assessment, antiplatelets for ischaemic stroke and lipid

Table 3. Association between the number of KPIs achieved and patient outcomes.

	Case fatality				Poor outcome				Quality of life			
Study	FU period	Number of processes	HR	95% CI	FU period	Number of processes	OR/HR/RR	95% CI	FU period	Number of processes	OR/HR/RR	95% CI
Denmark[17]	3 months	1 vs 0	0.94	0.65–1.49								
		2 vs 0	0.78	0.54–1.02								
		3 vs 0	0.60	0.42–0.78								
		4 vs 0	0.61	0.42–0.79								
		5 vs 0	0.45	0.31–0.60								
		6 vs 0	0.48	0.31–0.65								
UK (England)[24]	1 month	5–6 vs 0–4	0.74	0.66–0.83								
UK (Scotland)[25]	6 months	0 vs 4	2.26	1.60–3.21	6 months	0 vs 4	1.43	1.02–2.00				
		1 vs 4	1.67	1.45–1.93		1 vs 4	1.35	1.19–1.54				
		2 vs 4	1.44	1.31–1.59		2 vs 4	1.19	1.10–1.32				
		3 vs 4	1.17	1.08–1.27		3 vs 4	1.10	1.02–1.18				
Canada[32]	12 months	OCI 1 vs 0	0.69	0.44–1.09								
		OCI 2 vs 0	0.39	0.25–0.62								
		OCI 3 vs 0	0.40	0.25–0.64								
Australia[36]	6 months	All or n-1	0.48	0.21–1.09	6 months	All or n-1	0.59	0.30–1.16				
		All	0.31	0.06–1.52		All	0.32	0.10–1.04				
Australia[38]	6 months	1 vs 0	0.63	0.41–0.97					3–6 months	1 vs 0	12.53	−2.22 to 27.28
		2 vs 0	0.46	0.31–0.68						2 vs 0	16.67	0.30–33.05
		3 vs 0	0.30	0.18–0.47						3 vs 0	18.70	1.86–35.55
Canada[34]	1 month	2–3 vs 0–1	0.23	0.19–0.28								

CI: confidence interval; FU: follow-up; HR: hazard ratio; *n*: number of applicable processes of care; OCI: organised care index; OR: odds ratio; RR: rate ratio.

management. Therefore, our meta-analysis results need to be interpreted with caution.

The strong association of stroke unit care with improved outcomes could be anticipated from a substantial number of RCTs.[45] Our review confirms this across a range of studies in routine care. Given the evidence for specialised multidisciplinary stroke unit care in stroke,[45] one might also expect to see benefits associated with early nurse or rehabilitation assessment and early medical assessment,[24] as well as occupational therapy assessment.[17] These indicators lack direct evidence from randomised trials, but may possibly be markers for admission to a stroke unit and multidisciplinary stroke care. However, there were no comparable data from many studies about early medical assessment, early nurse or rehabilitation assessment or early occupational therapy assessment for our review.

Our finding of a reduced risk of case fatality after early physiotherapy/mobilisation was in accordance with the literature about stroke unit care,[45] and some small RCTs[46] but not consistent with recent RCTs of very early mobilisation.[47] However, the recent AVERT trial tested mobilisation at an earlier stage than in routine care, so the optimal timing of mobilisation remains unclear, and very early intensive mobilisation within 24 h may carry some hazard.[47]

Our meta-analysis showed that swallow or nutritional assessment was associated with lower risk for both mortality and disability post stroke. This finding was consistent with a randomised controlled trial,[9] which found that reinforcement of multidisciplinary management of swallowing dysfunction was significantly associated with lower risk for death or dependency. Thus, swallowing or nutritional assessment may be of paramount importance. The current meta-analysis also showed that early antiplatelet use for ischaemic stroke was associated with reduction in case fatality, and this was consistent with the results from a previous systematic review[48] of eight randomised trials. It showed that early antiplatelet therapy was associated with mortality reduction at a final follow-up between 1 and 6 months. However, our review showed greater apparent benefit than the 8% reduction in case fatality that was reported in the review of randomised trials.[48] However, a recent individual patient data meta-analysis of aspirin trials[49] confirms an important short-term benefit of aspirin therapy in preventing recurrent cerebral ischemia and that benefits may be greater than previously estimated. Our meta-analysis finding of a reduced risk of stroke case fatality associated with lipid management was consistent with the results from a meta-analysis[50] of 42 randomised trials.

One major disagreement with the RCTs is that our meta-analysis also showed that early anticoagulant use for ischaemic stroke with atrial fibrillation was associated with a reduction in early and late case fatality. However, this finding was not supported by a review[51] of 24 randomised clinical trials. This disagreement may be explained by the participants' inclusion criteria. In fact, while the randomised trials included in the review[51] recruited patients with presumed or confirmed ischaemic stroke, the studies included in our review considered only patients with ischaemic stroke and atrial fibrillation. Additionally, as the studies included in our review were neither randomised nor blinded, the apparent effects of antiplatelets and anticoagulants for ischaemic stroke may have been overestimated due to selection bias and incomplete adjustment for confounders. Alternatively, KPIs may also reflect other important and unmeasured aspects of care, which would not be tested in a well-designed RCT. Additionally, the duration of follow-up for the studies included in our meta-analysis varied between 3 and 48 months (mean: 16.5 ± 21.4 months) while the duration of follow-up in the trials was generally shorter. This short-term follow-up may lead to missing a significant proportion of deaths that occur after 1 month, and disability is best assessed between 3 to 6 months when most of the recovery has taken place.[51]

Our review has also identified some areas with inconsistent evidence of the association of KPIs with outcome. Deep vein thrombosis (DVT) prophylaxis was found to be associated with significant benefits in studies in Canada[32] and the USA[30] but not in Spain.[28] However, a meta-analysis of RCTs has failed to show improvements in survival or independence.[51]

Regarding thrombolysis, in two studies included for our review,[43,44] thrombolysis was associated with a lower risk for poor functional outcome, and this was consistent with the systematic review of the RCTs.[52] However, because of high heterogeneity ($I^2 = 88\%$) between the two studies reviewed, the summary effect was not statistically significant.

Our review showed that CT/MRI brain imaging and neurological assessment were not associated with any reported patient outcomes. This may be due to several reasons. First, the assessment itself, if not combined with adequate care, is unlikely to show any difference in outcome. For instance, once ischaemic stroke is diagnosed with brain imaging, further management by intravenous tissue plasminogen activator was found to be effective. It was however recently reported that only 3% of low-income, 19% of lower-middle-income, 33% of upper-middle-income and 50% of high-income-countries use it.[53] Second, the increased risk of early case fatality[17] and medical complications[21] that were reported after early CT/MRI brain imaging in two Danish studies was most likely due to reverse causality; patients who deteriorated during the first hours after hospitalisation were more likely to receive an early CT/MRI brain

imaging, and also had a greater risk of death or medical complications.[21] Third, some of the analyses of data may have been hampered by small sample sizes, and lack of statistical power to show the differential benefit.

Adherence to an individual measure in isolation may not have a clinically detectable impact on outcomes, making determination of an effect more difficult.[54] However, adherence to several KPIs was always associated with improved outcomes.

Strengths and weaknesses

Our systematic review has several strengths including searching a wide range of databases using standardised methodology. Furthermore, the review report was based on the PRISMA guidelines. The studies that were included in our review involved large sample sizes in general, allowing sufficient statistical power and enhancing the external validity of the results. One study[15] was multinational, and 12 studies[16,17,19,22,23,27,37,38,41–44] involved nationwide datasets. The remaining studies were conducted regionally with the recruitment of participants from between three[39] to 222 hospitals.[31] Additionally, we only conducted analyses using data from studies that corrected for patient casemix (age and stroke severity). Our approach to meta-analysis has used a conservative random-effects approach to acknowledge the diversity of studies identified. Finally, we performed a sensitivity analysis to evaluate the robustness of our findings.

We must acknowledge some weaknesses. We did not use any scoring system to assess risk of bias in included studies, but simply included large register studies reporting independent association of KPIs with patient outcomes after adjusting at least two variables including age and stroke severity. Second, the review was based on data from observational studies with different follow-up time periods and designs. Third, although we have only included data that used a multivariable analysis to correct for patient casemix, there remains the possibility that the patient outcomes were influenced by unmeasured or residual confounding factors such as indication bias or factors related to the nonrandomised study design rather than the reported KPIs themselves. Fourth, our review could be subject to publication bias because our search strategy was limited to electronic databases and references known to the authors, and manuscripts published in English only. Fifth, there is a potential concern about combining results from studies from different settings and using different research methodologies. For instance, there were different measures for stroke severity for case mix adjustment, different models of stroke unit and different models of implementing or measuring the KPIs. Finally, we were limited to a few studies reporting data on important outcomes such as the length of hospital stay and quality of life, and none of the studies considered the cost of care, which is clearly important in a disabling condition such as stroke.

Conclusion

Our review found that the most frequently reported KPIs for stroke care were swallow/nutritional assessment, stroke unit admission, antiplatelets for ischaemic stroke, CT/MRI brain imaging, anticoagulants for ischaemic stroke with atrial fibrillation, lipid management, DVT prophylaxis and early physiotherapy/mobilisation. Stroke unit admission and early interventions including swallowing/nutritional risk assessment, antiplatelets for ischaemic stroke, anticoagulants for ischaemic stroke with atrial fibrillation, lipid management and early physiotherapy/mobilisation were all associated with better patient outcomes. Achieving a combination of several KPIs was always associated with a better outcome. Both policy makers and health care professionals should be encouraged to implement the KPIs for stroke management that are reliable and meaningful for regularly monitoring the quality of stroke care. Future research could focus on novel stroke care quality indicators, particularly in the post-acute period.

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Ethical approval

Not applicable.

Informed consent

Not applicable.

Guarantor

GU and PL.

Contributorship

GU and PL conceived the study, researched literature, analysed data and wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Review

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Stroke care in Africa: A systematic review of the literature

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Abstract

Background: Appropriate systems of stroke care are important to manage the increasing death and disability associated with stroke in Africa. Information on existing stroke services in African countries is limited.

Aim: To describe the status of stroke care in Africa.

Summary of review: We undertook a systematic search of the published literature to identify recent (1 January 2006–20 June 2017) publications that described stroke care in any African country. Our initial search yielded 838 potential papers, of which 38 publications were eligible representing 14/54 African countries. Across the publications included for our review, the proportion of stroke patients reported to arrive at hospital within 3 h from stroke onset varied between 10% and 43%. The median time interval between stroke onset and hospital admission was 31 h. Poor awareness of stroke signs and symptoms, shortages of medical transportation, health care personnel, and stroke units, and the high cost of brain imaging, thrombolysis, and outpatient physiotherapy rehabilitation services were reported as major barriers to providing best-practice stroke care in Africa.

Conclusions: This review provides an overview of stroke care in Africa, and highlights the paucity of available data. Stroke care in Africa usually fell below the recommended standards with variations across countries and settings. Combined efforts from policy makers and health care professionals in Africa are needed to improve, and ensure access, to organized stroke care in as many settings as possible. Mechanisms to routinely monitor usual care (i.e., registries or audits) are also needed to inform policy and practice.

Keywords

Stroke, awareness, health care, stroke unit, rehabilitation, secondary prevention, Africa

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Introduction

Stroke is the second most common cause of death,[1] and the third most common cause of disability-adjusted life-years (DALYs) lost worldwide.[2] In contrast to high-income countries (HICs) where stroke mortality rates have declined, the burden of stroke in developing countries has risen in recent years and is expected to accelerate.[3] Eighty-six percent of all stroke deaths around the world take place in low- and middle-income countries (LMICs).[4] Further, LMICs account for over 87% DALYs lost from stroke, which is about seven times the DALYs lost in HICs.[5]

African countries are undergoing an epidemiological transition driven by sociodemographic and lifestyle changes related to unchecked industrialization and a rise in many modifiable vascular disease risk factors. These include smoking, harmful use of alcohol, physical inactivity, and unhealthy diets resulting in an increased prevalence of hypertension, diabetes, and obesity.[6] Consequently, the burden of noncommunicable diseases (NCDs) including stroke is growing.[6]

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A recent systematic review[7] of community-based studies revealed an age-standardized annual stroke incidence rate of up to 316 per 100,000 population, and age-standardized prevalence rates of up to 981 per 100,000 in Africa. However, health systems in many African countries are characterized by geographical and financial inaccessibility, rapid turnover of people in key positions, lack of continuity in policy, lack of resources, poor management of available resources, and poor implementation.[8]

It is recommended that appropriate systems of stroke care be established in Africa and other LMIC regions to control the increasing death and disability associated with stroke.[9,10] We need information about the existing resources and current practices for stroke care in Africa. There have been some international reviews and surveys (not offered in languages other than English) on stroke care, but few studies included Africa. Several have relied on self-reported information which may be biased or had a very narrow focus.[10–13] This motivated us to conduct a systematic literature review on systems of stroke care in Africa to inform policy makers and health care professionals about areas for improvement across the whole stroke care pathway.

Methods

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[14]

Search strategy

Studies for this review were identified through searches of Ovid Medline, Embase, Amed, CINAHL, PubMed, and African Journals Online (AJOL) databases. There was no language restriction, but the search was limited to contemporary full-text publications (from 1 January 2006 to 20 June 2017). The search strategies for different databases were developed in consultation with a medical literature search specialist and are detailed in the online Supplement. Additional searching was conducted on reference lists of relevant studies to identify publications that could have been omitted in the database searches.

Inclusion criteria

Publications describing stroke care in an African country.

Exclusion criteria

Reviews and clinical trial publications.

Screening and quality assessment

All publications were screened and assessed for eligibility for narrative synthesis by GU in discussion with PL. Publications identified as potentially relevant underwent a full review by two authors (GU and PL) to determine if they met the inclusion criteria. In cases of disagreement, final determination was by discussion and consensus.

Data extraction

Data were extracted using the World Stroke Organisation (WSO) Stroke Services Framework[15] which consists of six phases of the continuum of stroke care: systems for stroke recognition and response, hyperacute stroke care, acute inpatient care, stroke rehabilitation, secondary stroke prevention, and longer-term stroke recovery.

The draft form was pilot tested on five studies for further refinement. The final version allowed extracting data regarding the country, year of publication, study setting, study design, sample size, key element(s) investigated, and the main results.

Thereafter, data from each publication relevant to the current review were systematically extracted by GU. PL crosschecked a subsample of 10 studies to ensure accuracy and consistency.

Data analysis

We anticipated that there would be limited and heterogeneous data identified. Therefore, we used a narrative synthesis to summarize the information from the included studies. Information was reported according to the phase of patient journey as conceptualized by the WSO framework.[15]

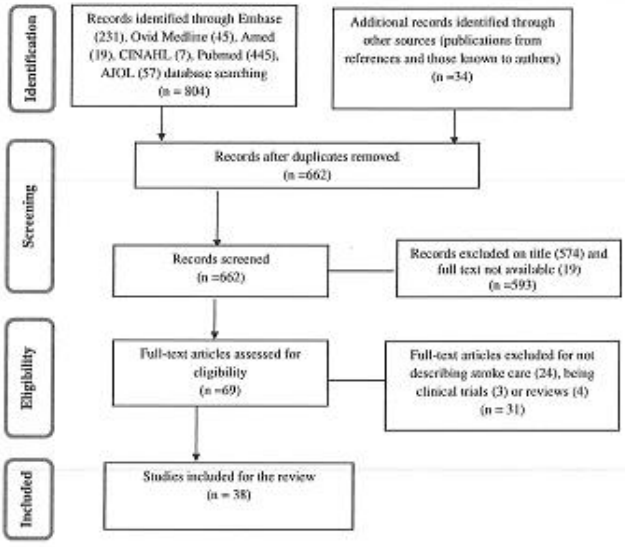
Results

The review profile is shown in Figure 1. We identified 838 references from which 38 publications[16–53] were eligible for our review following de-duplication and screening.

The included publications represent 14/54 African countries from all the main regions (east, west, central, north, and south) (Figure 2).

The data ranged from 2008 to 2017, with most (24/38) published between 2013 and 2017. The publications included single and multi-site studies with varying numbers of respondents (1 (case study)–15,155 population survey of stroke knowledge). Nigeria and South Africa provided 10 (27.8%) and 9 (25.0%) of the selected publications, respectively. The majority (30/38) of the studies were conducted in urban hospitals or urban

Figure 1. Review profile showing selection of studies.



communities. Two publications[34,42] were written in French and the remainder were in English.

Table 1 provides a list of the number of publications with information on each stroke care phase from 2008 to 2017.

Some publications[26,28,34,39,44] provided information on more than one stroke care phase. Only the first and second phases of stroke care were reported in at least a quarter of the included publications. Secondary stroke prevention and longer-term stroke recovery were rarely reported. The reported core elements related to the stroke care phases are summarized in the online Supplement Table S1.

Systems for stroke recognition and response

The main core elements related to systems for stroke recognition and response were knowledge of stroke signs and symptoms, perception of adequate response to stroke signs and symptoms, availability and accessibility of stroke care policies and services.[16–31]

Regarding the awareness about stroke signs and symptoms, the greatest proportion of participants who knew any of the established stroke signs and symptoms ranged between 18% for paralysis in Uganda[17] and 66% for weakness in Nigeria.[22] The most preferred response to stroke signs and symptoms (range: 41–94%) was bringing the patient to the hospital,[20–24] but some participants, between 1% and 13%, identified seeking spiritual intervention as the first option.[19,21–24] In several studies, higher education level was significantly associated with better knowledge[16,19,21,22] of, and better response[19,21] to, stroke signs and symptoms.

Gaps were reported in the availability of stroke care services with variations across countries and settings. The areas in which shortage was commonly reported included medical transportation,[27,33,34,36] computerized tomography (ct)/magnetic resonance imaging (MRI) scanning machines,[26–28,31] stroke units,[30,31] thrombolysis,[27,31,38] inpatient and long-term rehabilitation services,[27] and health care personnel in overall number and specialties.[26,28,31,38]

The high cost of infrastructure resources where they exist such as CT scanners,[26,27,37] medications such as thrombolysis,[39] and outpatient physiotherapy rehabilitation services[49] were reported as major barriers for stroke care in Africa. In addition, a study from

Figure 2. African map showing countries (in blue) with included publications. NS: number of studies. [a]One study[44] was conducted in three countries including Rwanda, South Africa, and Tanzania.

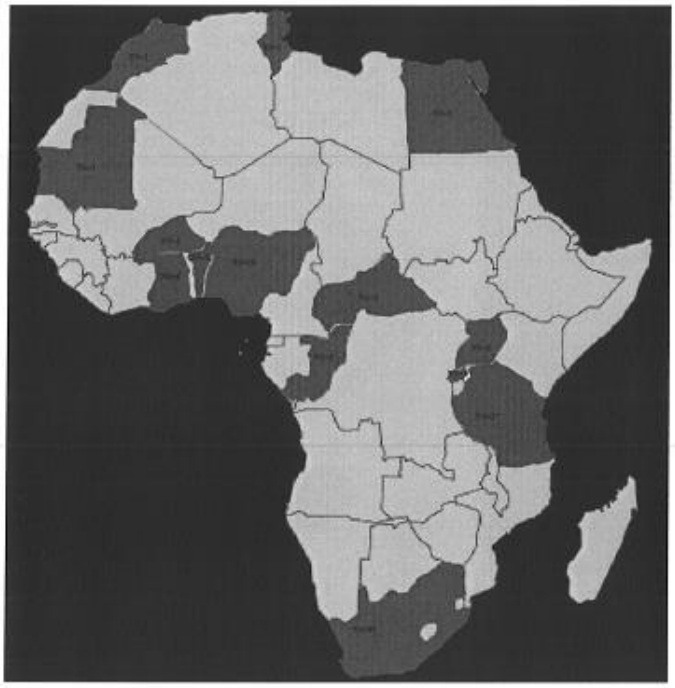


Table 1. Availability of information reported by stroke care phase from the publications by year

WSO template	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Systems for stroke recognition and response	2	2	0	1	3	0	2	3	2	1	**16**
Hyperacute stroke care	1	1	0	0	1	2	1	2	2	1	**11**
Acute inpatient care	2	2	0	0	1	0	0	1	1	0	**7**
Stroke rehabilitation	0	1	0	0	1	2	0	1	0	2	**7**
Secondary stroke prevention	0	1	0	0	0	0	0	0	1	2	**4**
Longer-term stroke recovery	0	1	0	0	0	0	0	0	0	0	**1**

Ghana[29] identified the lack of direct regional or national health policy to support stroke care, including a lack of a national stroke policy framework and national stroke clinical guidelines.

Hyperacute stroke care

The most common elements related to hyperacute stroke care reported included time from stroke onset to hospital arrival and patient access to CT/MRI brain imaging.[28,32–41]

Several publications consistently identified that patients with stroke in Africa were late in arriving to hospital. The highest reported proportion of stroke patients who arrived at hospital within 3 h from stroke onset was 43% in Tunisia[34] while the lowest proportion (10%) was reported in Nigeria.[32] The reported proportions of stroke patients who received CT brain imaging within 3 h of stroke onset varied between 0%[35] and 13%,[34] and where operational CT/MRI scan machines existed, the reported proportion of patients who received CT/MRI brain imaging varied between 13%[28] and 36%.[36]

Acute inpatient care

The main core elements related to acute inpatient care for stroke patients that were reported included the time from stroke onset to hospital admission, and access to stroke units.[26,28,34,39,42–44]

The interval between time of stroke onset and hospital admission varied between 7.2 h and 6.8 days,[34,42,44] with a median of 1.3 day. Few patients, 1% in Tunisia[34] and 17% in Benin,[26] were reported to have been admitted within 3 h of stroke onset. Regarding access to stroke units, South Africa was reported to have 21 stroke units,[29] and the only other countries reported to have a stroke unit were Ghana[31] and the Central African Republic.[39] Two studies[39,43] included in our review reported that stroke unit admission was associated with a decrease in inpatient mortality rate of 17–30%.

Stroke rehabilitation

The proportion of patients reported to receive inpatient physiotherapy rehabilitation was greatest in South Africa (98%) and smallest in Rwanda (40%).[44] A South African publication describing access to outpatient physiotherapy rehabilitation[48] identified low attendance rates (14%) as being associated with lack of finances (95%), patient migration to other areas (36%), and living a long distance from the hospital (38%).[48] In a study from Nigeria[49] the majority (59%) of patients were highly satisfied with outpatient physiotherapy services, however, the high cost of these services and lack of continuity of care were sources of dissatisfaction.

Three South African studies[46,47,51] reported information on rehabilitation after discharge from the acute inpatient settings. It appeared that patients treated in a specialized rehabilitation facility received a variety of rehabilitation services from medical doctors, nurses, physiotherapists, social workers, occupational therapists, and speech therapists, although few of them received dietetics (17%) or psychology (11%) services.[47] In contrast, services offered in community health centers were mostly limited to physiotherapy and medical rehabilitation services.[46]

Secondary stroke prevention

A retrospective observational study[52] involving 418 stroke survivors enrolled into a neurology clinic in Ghana showed that, at 1-year post stroke, 92% of subjects were persisting with secondary prevention medications. However, in two publications[28,50] included in our review, evidence of poor compliance with secondary prevention medications was reported. In one study[28] of stroke survivors living in a rural South African community who were prescribed aspirin for secondary prevention, 9/20 (45%) reported taking this medication at 3 months poststroke. In a similar study conducted in Uganda[50] which involved 112 participants, only 17% were adhering to anti-hypertensive medications as prescribed. The main reasons for poor drug adherence were lack of knowledge of the chronicity of hypertension (73%) and cost of the drugs (63%). Other factors that were reported to be associated with poor compliance with secondary prevention medications were alcohol abuse[52] and average number of antihypertensive medications prescribed.[53]

Longer-term stroke recovery

Regarding longer-term stroke recovery, many challenges were identified in a South African study.[28] Three months poststroke, 20 survivors living in a rural community had no access to a rehabilitation facility, and did not get support from government or local authorities, leaving the responsibility to some local nongovernmental organizations which also had limited resources to provide stroke survivors support.

Discussion

Overall, very few studies on stroke care have been published about the vast continent of Africa, and only two studies[28,50] included information on secondary stroke prevention or longer-term stroke recovery. From the

available data, we identified only a small proportion of patients with stroke that arrived at a hospital within 3 h from symptom onset[32,34] and, consequently, less than 20%[26,34] of patients were admitted within 3 h of stroke onset. Studies from other non-African LMICs showed a similar delay.[54,55] Late presentation to hospital has been reported to be associated with poor awareness of stroke signs and symptoms, late referral from private hospitals, transportation problems, visit to traditional healers before coming to hospital, and treatment at home.[33,36] These were also identified in our review. Delays in presentation to hospital prevent patients from benefiting from emergency interventions such as brain imaging and thrombolysis for ischemic stroke among others. Also, although diagnostic CT or MRI scan imaging is important when antithrombotic treatments are being considered, our review showed that the CT/MRI brain imaging services were rare or too expensive for many patients in Africa.[28,36] Our review showed that no patients in a Nigerian hospital[35] and only 13% of stroke patients in Tunisia[34] received a CT scan within 3 h of stroke onset. This is a major barrier to meet the recommended standard of thrombolysis for ischemic stroke within 4½ h of stroke onset.[15]

Despite the evidence that thrombolysis can improve outcome in ischemic stroke,[56] our review indicates that intravenous thrombolysis remains "a desirable dream" in many African countries.[38,39] This finding was consistent with the results of a survey[12] whereby none of the African centers surveyed in 2012 administered acute revascularization therapy to patients with acute stroke. In another systematic review,[37] only 3% of low-income countries were found to use thrombolysis for acute ischemic stroke. The most important barrier of thrombolysis therapy in Africa, as in other low-income countries, is reported to be cost.[36,39] This emphasizes the need for governments and health systems of developing countries to develop strategies to enhance accessibility to thrombolysis.

Despite the available evidence for the benefits associated with stroke unit admission, the stroke unit model for stroke care appeared to be rare in Africa. In fact, collectively we identified that there were only 23 stroke units from the available publications we reviewed. Fortunately, there is the intention for the establishment of more stroke units in Africa in the next few years.[29,30]

The WSO recommended early adequate rehabilitation to reduce the social and economic costs related to long-term care.[15] However, it appeared that only medical and physiotherapy rehabilitation services are common in Africa,[31,44,47] and that the physiotherapy services are accessible to a limited number of patients. We need to address the identified barriers for inpatient and outpatient physiotherapy rehabilitation including high cost, geographical inaccessibility, and lack of continuity of care.

While aspirin and antihypertensive drugs were found to be associated with lower risk for stroke recurrence,[58,59] our review findings indicated poor compliance with secondary prevention anti-hypertensive medications in Uganda[50] and aspirin in South Africa[28] most likely because of cost and lack of knowledge about the risk of stroke recurrence. This issue should be addressed in education sessions for stroke patients and their caregivers.

Other important challenges that were raised were shortage or high cost of medical transportation, brain imaging infrastructure, stroke units, and healthcare personnel.[26–28,31,33,34,36–38] To address this gap, politicians in most African countries need to invest in stroke care by developing and implementing direct health policies for stroke, training, and staffing key rehabilitation professionals, making available and accessible the appropriate infrastructure, equipment, and medications for quality stroke care, building national insurance systems to reduce the cost for care,[60] and establishing partnerships with international experts to improve stroke care in African countries as they appeared to be effective in South Africa.[29]

Strengths and weaknesses

To the best of our knowledge, this is the first review on delivery of stroke care with focus on Africa. It provides a systematic, up-to-date overview of the available data on this topic. We searched many relevant databases, with no language restriction. Additionally, data from eligible publications were extracted and analyzed based on the WSO Stroke Services Framework[15] while the review report is based on the PRISMA guidelines. However, our review may well be subject to publication bias as only the electronic databases and references were considered. Furthermore, the investigators of the identified studies were not contacted to confirm data. Among the studies that were considered for our review, nine were retrospective and the shortcomings of this study design needs to be considered while interpreting the results. Furthermore, most of the publications were conducted in cities, and some of them were single studies and generalizability to rural settings or whole countries is limited. Therefore, national or regional prospective observational studies on the provision of stroke care in African countries are needed. The lack of data from many African countries is also a limitation and highlights the urgent need to establish systems of routine and reliable data monitoring across this continent. Finally, there were limited data on important phases of stroke care including secondary prevention

and longer-term recovery. More studies about these two phases are required.

Conclusion

Overall, the reported provision of stroke care in Africa is below the recommended standards with variations across countries and settings. Combined efforts from policy makers and health care professionals in Africa are needed to ensure greater access to essential infrastructure such as stroke units. More high-quality studies are needed to inform how to establish infrastructure in African settings where there are limited resources and diverse sociocultural contexts. Mechanisms to routinely monitor usual care (i.e., registries or audits) would be invaluable to inform policy and practice.

Declaration of conflicting interests

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Authors' contributions

GU and PL conceived the study, researched literature, analyzed data, and wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Background and Aims: The aim of this meta-analysis was to test if multidomain interventions, addressing several modifiable vascular risk factors simultaneously, is more effective than usual post-stroke care for the prevention of cognitive decline after stroke.
Method: This individual patient data one-stage meta-analysis includes two randomised controlled trials using a multidomain approach to target vascular risk factors in stroke patients and cognition as primary outcome. Changes from baseline to 12 months in trail making test (TMT) A, B and the 10-word test were analysed using step-wise backward linear mixed models with study as random factor. Two analyses were based on the intention-to-treat (ITT) principal using different imputation approaches, and one on complete cases. Electronic literature was searched (as update of a previous systematic search until March 2011) in Pubmed from April 2011 to May 2016.
Results: Data from 322 patients (157 assigned to multidomain intervention, 165 to standard care) were analysed. Differences between randomisation groups for TMT-A scores were found in one ITT model ($p=0.014$) and approached significance in the second ITT model ($p=0.087$) and for complete cases ($p=0.091$). No significant intervention effects were found for any of the other cognitive variables.
Conclusion: We found indications that multidomain interventions compared with standard care can improve the scores in TMT-A one year after stroke but not those for TMT-B or the 10-word test. These results have to be interpreted with caution due to the small number of patients.

AS06-028

SYSTEMATIC REVIEW AND META-ANALYSIS

ANTITHROMBOTIC TREATMENT AFTER STROKE DUE TO INTRACEREBRAL HAEMORRHAGE: A COCHRANE REVIEW

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Background and Aims: Antithrombotic treatments may lower the risk of thromboembolism after ICH, but they may increase the risks of bleeding. This Cochrane review investigated the overall effectiveness and safety of antithrombotic drugs for survivors of ICH.
Method: We searched the Cochrane Central Register of Controlled Trials, Medline, Embase, DORIS, and online registries of clinical trials from inception to August 2016. We selected all randomised controlled trials (RCTs) of any antithrombotic treatment after ICH and screened references of included studies. Three investigators independently extracted data and appraised risk of bias. We divided our analyses into short- and long-term treatment, and used fixed-effect modeling for meta-analysis.
Results: We included two RCTs ($n=121$) on short-term anticoagulation after ICH; one tested subcutaneous unfractionated heparin and the other enoxaparin. The risk of bias in the included RCTs was generally unclear or low, with the exception of blinding of participants and personnel which was not done. Treatment was not associated with a statistically significant difference in case fatality (RR 1.25, 95% CI 0.38–4.07), growth of ICH (RR 1.64, 95% CI 0.51–5.29), or major ischaemic events (RR 0.54, 95% CI 0.23 to 1.28). There were no new ICH or major extracerebral haemorrhages reported.
We identified seven ongoing RCTs on long-term treatment with oral anticoagulants/antiplatelets.
Conclusion: There is insufficient evidence from RCTs to support or discourage the use of antithrombotic treatment after ICH. RCTs comparing starting vs. avoiding antiplatelet or anticoagulant drugs after ICH seem justified and are needed in clinical practice.

AS06-029

SYSTEMATIC REVIEW AND META-ANALYSIS

KEY PERFORMANCE INDICATORS OF QUALITY STROKE CARE AND THEIR ASSOCIATION WITH PATIENT OUTCOMES: A SYSTEMATIC LITERATURE REVIEW

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Background and Aims: The translation of research evidence into clinical practice often uses key performance indicators (KPIs) to monitor quality of care. We conducted a systematic review to identify which stroke KPIs have been used most often, and to estimate their association with patient outcomes.
Method: We sought recent publications (2000–2016) of national or large regional stroke registers that reported the association of KPIs with patient outcome (after adjusting for age and stroke severity). We searched Medline, EMBASE and PubMed and screened references from bibliographies identified. The association of KPIs with patient outcomes were analysed using an inverse variance random effects meta-analysis (RevMan 5.3 Version).
Results: We identified 20 eligible studies. The most frequently used KPIs were stroke unit admission, swallowing and/or nutritional risk assessment, antiplatelet therapy, brain imaging, anticoagulant therapy, early physiotherapy mobilization, and deep vein thrombosis prophylaxis. A lower case fatality (Odds Ratio; 95% Confidence Interval) was associated with anticoagulant therapy (0.55; 0.46–0.66), antiplatelet therapy (0.62; 0.50–0.77), swallowing/nutritional risk assessment (0.75; 0.68–0.82), stroke unit admission (0.84; 0.76–0.93), lipid management (0.78; 0.68–0.90), early nursing/rehabilitation assessment (0.86; 0.74–0.99), early physiotherapy/mobilization (0.84; 0.73–0.97). A lower risk for poor outcome (death or disability) was found to be associated with adherence to swallowing and/or nutritional risk assessment (OR = 0.57; 0.34–0.96) and stroke unit admission (OR = 0.82; 0.74–0.91).
Conclusion: Adhering to one of several common KPIs was consistently associated with a reduced risk of death or disability after stroke. Policy makers and health care professionals should aim to implement those KPIs that are reliable and meaningful.

swallowing biomechanics, and Functional Oral Intake Scale (FOIS), in which: FOIS 1–3 = tube feeding; 4–5 = oral feeding requiring food consistency changes; and 6–7 = no changes in food consistency. mRs ≥ 3 90 days after discharge was considered disability. The data were adjusted for National Institute of Health Stroke Scale, sex, age, type of stroke, and thrombolysis. The significance level was 5%.

Results: Of the 201 patients evaluated, the 42.8% (86) who presented dysphagia were older and had a higher severity of stroke. The FOIS score 6–7 may be a protective factor for disability (mRs < 3) ($p = 0.007$). Scores 1–3 on FOIS increased by 2.88 times the chance of mRs ≥ 3 after 90 days ($p = 0.03$), as the use of tube feeding at hospital discharge increased by 13.9 times the chance of mRs ≥ 3 ($p = 0.002$). Dysphagia at admission ($p = 0.04$) and tube feeding at hospital discharge ($p = 0.007$) increased the chance of mortality 90 days after stroke.

Conclusion: Dysphagia and tube feeding use during hospitalization are associated with disability and mortality 90 days after stroke.

1027
WSC18-1316
Late Breaking Abstract Submission
Outcomes and Quality of Care

IS MORE BETTER? THE SENTINEL STROKE NATIONAL AUDIT PROGRAMME: INVESTIGATING AND EVALUATING STROKE THERAPY (SSNAPIEST)

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Introduction: The intensity of stroke therapy is an important factor driving recovery. Here we investigate the therapy 'dose-response' using national stroke audit data.

Methods: Data included all in-patient strokes at three days reported (July 2013–2015) to the UK's Stroke Sentinel National Audit Programme (n = 94,925). Robust multilevel mixed effects regression models adjusted for all available confounding factors investigated the association between amount of therapy received and health outcomes (e.g. modified Rankin scale). Amount of Physiotherapy (PT), Occupational Therapy (OT) and Speech and Language Therapy (SALT) was defined as "average minutes/day during in-patient stay". We included each as a linear 'dose-response' model and a 'threshold' model using linear splines to investigate possible changes in association across increasing levels of average therapy received.

Results: In the linear models, increased average of OT and SALT minutes/day were associated with improved outcome. Increasing PT however was associated with worse outcome. The splines approach indicated an optimal threshold point of 5 min/day. Increases in all therapies were associated with improvement up to 5 min/day. Beyond 5 min/day, increasing OT and SALT were associated with continued but slight improvements, whereas increasing PT was associated with a gradual decline such that an average 40 min/day would see a return to baseline health.

Conclusion: Though an average of 5 min/day of therapy appears beneficial, increases beyond this are associated with diminishing returns or even detriment. From our data we cannot distinguish patterns of care (i.e. 5 min/day or one 35 min session/week). Prospective research is urgently required to confirm or refute this finding.

Table 1 – Results associated with an average therapy per day of stay increase of one minute and the health outcome modified Ranking Scale (mRs)

Health Outcome - mRs at Discharge (3 - 6)	PT OR	OT OR	SALT OR
Average Min Therapy per Day of Stay	1.01	0.98	0.98
Average Min Therapy per Day of Stay (0-5 min) *	0.92	0.73	0.89
Average Min Therapy per Day of Stay (5+ min) *	1.01	0.99	0.98

Note: all effect sizes (OR) are significant (p-value ≤ 0.1) and adjusted for all known and measured confounders
*Double linear threshold modelling (set continuous variable to represent increased therapy until time threshold and increased therapy post) met.

1028
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Late Breaking Abstract Submission
Outcomes and Quality of Care

ASSOCIATION BETWEEN KEY PERFORMANCE INDICATORS AND PATIENT OUTCOMES IN LOW AND MIDDLE-INCOME COUNTRIES IN THE INTERSTROKE STUDY

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Key performance indicators (KPIs) of quality stroke care have been used to monitor service improvement in high income countries (HICs), but information regarding their value in low and middle-income countries (LMICs) is limited. We aimed to identify the association of KPIs with patient outcomes in LMICs. We had INTERSTROKE data for 12548 participants and analysed 9766 from LMICs. We performed a multivariate logistic regression analysis to determine the association of KPIs with 30-day patient outcomes. We considered age, baseline level of consciousness, stroke type, and baseline stroke severity for case mix adjustment and, for controlling the family-wise error rate, we used the Bonferroni correction method and considered 0.006 as the p-value of significance. In LMIC participants, stroke unit availability ($p < 0.0001$) and stroke specialist availability ($p < 0.0001$) for the majority of stroke patients, antiplatelet therapy for ischaemic stroke ($p = 0.001$), availability of continuing acute rehabilitation ($p = 0.001$) and post-discharge rehabilitation ($p < 0.0001$) were independently associated with lower risk for 30-day mortality. Brain CT scan by day 1 ($p = 0.001$) and stroke unit availability for the majority of stroke patients ($p = 0.0001$) were independently associated with lower risk for 30-day death or severe disability. There was a dose dependent relationship of number of KPIs with a better outcome. Achieving several common KPIs was associated with a reduced risk of death or disability after stroke in LMICs. Policy makers and health care professionals in all settings even with limited resources are encouraged to implement the commonly established stroke care KPIs.

1029
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Late Breaking Abstract Submission
Public Awareness – Advocacy

STROKE AND CARDIOVASCULAR DISEASE PERCEPTIONS AMONG ADULT SMOKERS AND NON-SMOKERS IN TAIWAN, FROM 2014 TO 2017

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Background: There is a well-established causal link between tobacco smoking and stroke. Smoking is the leading risk factors for stroke, along with hypertension. Smoking increases the risk of stroke from two to four-fold, in both men and women, depending on dose response. Both active smoking and second-hand smoking cause similar effects for stroke. However, there is limited information on public knowledge of smoking as a risk of stroke.

Aims: To investigate the knowledge on smoking as a risk factor of stroke and its change 2014–2017 in national level of Taiwan.

Methods: We used cross-sectional population-based data from the Taiwan Adult Tobacco Survey from 2014 to 2017. Weighted univariate and multivariate analyses were performed using Stata 12.1.

Results: Total participants were 101,691 (49.3% male and 50.7% female) and among them 15.8% were smokers (28.5% in male and 3.4% in female). Awareness of smoking as a risk factor of stroke and other CVD was 8.3%-9.3% among non-smokers and 2.5% –3.6% among smokers ($p < 0.001$). Percentage of awareness among participants decreased from 2015 to 2017; however, the decrease was not statistically significant. Regression analysis shows that gender, and smoking status were significant predictors of awareness of smoking as a risk factor for stroke.

Conclusions: Awareness of smoking as one of the main risk factors of stroke is low, especially among smokers and those with less education. Effective public educating programs on harms of smoking would increase risk awareness and could potentially reduce the incidence of stroke.

1030
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Late Breaking Abstract Submission
Public Awareness – Advocacy

A NOVEL SCHOOL-BASED STROKE EDUCATIONAL INTERVENTION TO STIMULATE, RETAIN AND IMPROVE STROKE AWARENESS IN 11 TO 14 YEARS SCHOOL CHILDREN

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Background: Among middle school students, physical inactivity and poor diet reinforce the risk of lifestyle and a future stroke. Existing didactic educational intervention approaches have not been effective. We tested the effect of a newly developed stroke education program that integrates social interaction with active learning among school children in improving stroke awareness.

Method: Middle school students between the ages of 11 and 14 years attending public school, were recruited to participate in an interventional program to promote stroke knowledge and healthy lifestyle education. We tested the impact of the intervention on students' knowledge immediately after, and extended period following the intervention to assess both immediate and delayed retention of basic knowledge of stroke and healthy lifestyle with stratification by grade.

Result: ANOVA with repeated measures found a significant difference in the immediate retention of the signs of stroke (FAST) between the 6th, 7th and 8th grades [$F(1,109) = 279.67$, $P < 0.001$]. In the delayed testing, there was a significant difference [$F(1,109) = 3.89$, $P = 0.96$] among the 6th, 7th and 8th grades in the retention of the fact that stroke occurs in the brain.

Conclusion: In an educational interventional program that integrates active learning with social interactive activities, middle school children between the ages of 11 and 14 can retain information about stroke and healthy life style. Intervention strategies need to consider social interactive activities with embedded active learning to better enhance the retention of basic knowledge of stroke and healthy life style.

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