EVALUATION OF THE IMPLEMENTATION OF STROKE UNITS: THE CASE OF KORLE-BU TEACHING HOSPITAL, GHANA

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This thesis is dedicated to my husband John for supporting me in all my endeavours and to my supervisor Dr. Raphael Lencucha for his dedication to see me succeed.

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ABSTRACT

Organised Stroke unit care is the most recommended stroke care policy to improve stroke outcomes. There is sufficient evidence supporting the effectiveness of stroke unit care compared to care on medical or neurological wards. The research on and wide spread implementation of organised stroke unit care has mainly been conducted in high income countries with advanced research environments and well-resourced health care systems. Nevertheless, there is some, although limited evidence that stroke unit care is effective in lower resource setting. Many low- and middle-income countries (LMICs) are beginning to adopt organised stroke unit care as their stroke care policy to improve stroke outcomes.

In 2014, the Korle-Bu Teaching hospital, in partnership with Wessex took steps in restructuring acute stroke care by establishing a stroke unit. The adoption of stroke unit care as a key component of stroke care policy in Ghana must be based on evidence of efficacy, effectiveness, efficiency and applicability. The efficacy and effectiveness of stroke units have been well established. The questions that still remain are, can stroke units implemented in Ghana realize similar outcomes as those implemented elsewhere? Is there evidence over time in Ghana, that restructuring stroke care from care in the general medical wards to a dedicated stroke unit changed outcomes? With the prospect of replicating the implementation of the stroke unit in other regions, it is important to estimate the effectiveness of the stroke unit to inform local stroke care policy in Ghana.

Objectives

The global aim is to contribute evidence towards the effectiveness of stroke units in Ghana, a country representative of LMICs. This aim was achieved through five interrelated manuscripts.

The objective of the first manuscript was to estimate the extent to which outcomes of mortality and length of stay changed following the implementation of stroke unit care in KBTH. This was a historically controlled study comparing the pre-stroke unit period (2011-2013) to the post stroke unit period (2014-2016). Patients treated at the stroke unit had a 61% lower risk of dying and shorter length of stay compared to the general medical wards.

The objective of the second manuscript was to estimate the extent to which resource use at the stroke unit was associated with functional independence amongst patients admitted to the stroke unit. This was a study of an admission-to-discharge cohort from the stroke unit. For people

surviving the acute care period, resource use was associated with an increase in functional independence from time of admission to discharge.

The third manuscript estimated and compared the construct validity of a stroke specific preference measure, the Preference Based Stroke Index (PBSI), to a generic preference measure, the EuroQol Five Dimension (EQ-5D-3L). The PBSI demonstrated significantly higher construct validity compared to the EQ-5D-3L and could discriminate amongst known groups. Its use is recommended in the stroke population as it covers dimensions particularly relevant to the stroke population. Furthermore, patient's ratings can be used to identify areas of further assessment and rehabilitation.

The objective of the fourth manuscript was to compare estimates of recovery at 3 months post stroke, among three measures, the Barthel Index (BI) for ADL, the EQ-5D-3L, and the PBSI. This was an observational study of a consecutive series of patients discharged alive from the stroke unit from 2014 to 2016. In summary, the EQ-5D-3L and the PBSI had comparable estimates on recovery. However, the PBSI had a larger effect size. Furthermore, the concordance between the EQ-5D-3L and the PBSI was low, with higher scores resulting from the PBSI when compared with the EQ-5D-3L.

The objective of the last manuscript was to explore the meaning of recovery post stroke from the perspective of a sample of stroke survivors in Ghana. This study was a qualitative analysis based on interpretive description methodology. The meaning of recovery from stroke was unique to each individual, however seven common themes were identified. Results from this study emphasizes the need for clinicians to engage patients to understand what recovery means to them and their expectations of recovery in order to truly meet patients' needs and desires.

This thesis provides evidence on the effectiveness and applicability of stroke unit care in Ghana. In addition, it shows that resource-use in providing stroke unit care is associated with an increase in functional independence. Furthermore, results from this thesis show that estimates of recovery is dependent on the measure used. Lastly, it highlights the importance of having a discussion with patients on what recovery means to them and their expectations of recovery in order to meet patients' needs.

RÉSUMÉ

Les soins des unités d'Accident Vasculaire Cérébrale (AVC) organisé est la politique de soins d'AVC la plus recommandée pour améliorer les résultats d'AVC. Il existe des preuves suffisantes à l'appui de l'efficacité des soins de l'unité d'AVC par rapport aux soins dispensés dans les services médicaux ou neurologiques. La recherche sur la mise en œuvre à grande échelle des unités de soins d'AVC organisées a été principalement menée dans des pays à revenu élevé dotés d'environnements de recherche avancés et de systèmes de soins de santé bien dotés en ressources. Néanmoins, il existe quelques preuves, bien que limitées, que les soins en unité d'AVC sont efficaces dans les milieux de ressources inférieures. De nombreux pays à revenu faible ou intermédiaire commencent à adopter les soins des unités d'AVC organisé comme politique de soins d'AVC afin d'améliorer les résultats d'AVC.

En 2014, l'Hôpital d'Enseignement Korle-Bu (HEKB), en partenariat avec Wessex, a entrepris des démarches de restructuration des soins d'AVC aigu en créant une unité de soin d'AVC. L'adoption des soins des unités d'AVC en tant qu'élément clé de la politique en matière de soins des AVC au Ghana doit reposer sur des preuves d'efficacité, d'efficience et d'applicabilité. L'efficacité des unités de soins d'AVC ont été bien établies. Les questions qui restent sans réponse sont, les unités d'AVC mises en place au Ghana peuvent-elles obtenir des résultats similaires à ceux mis en place ailleurs? Y a-t-il des preuves, au fil du temps au Ghana, que la restructuration des soins d'AVC parmi les soins de services de médecine générale à une unité spécialisée en AVC, d'avoir changé les résultats ? Dans la perspective de reproduire la mise en œuvre de l'unité d'AVC dans d'autres régions, il est important d'estimer l'efficacité de l'unité d'AVC pour informer la politique locale en matière de soins d'AVC au Ghana.

Objectifs:

L'objectif global est de contribuer des données probantes sur l'efficacité des unités d'AVC au Ghana, un pays représentant un revenu faible ou intermédiaire. Cet objectif a été atteint à travers cinq manuscrits interdépendants.

L'objectif du premier manuscrit était d'estimer la mesure dans laquelle les résultats en termes de mortalité et de durée de séjour ont changé à la suite de la mise en œuvre des soins d'unité des accidents vasculaires cérébraux en HEKB. Il s'agissait d'une étude historiquement contrôlée comparant la période de l'unité pré-AVC (2011-2013) à la période de l'unité post-AVC (2014-

2016). Les patients traités à l'unité d'AVC avaient 61% moins de risque de décès et une durée de séjour plus courte par rapport aux salles de médecine générale.

Le deuxième manuscrit avait pour objectif d'évaluer dans quelle mesure l'utilisation des ressources dans l'unité d'AVC était associée à l'indépendance fonctionnelle des patients admis dans cette unité. Il s'agissait d'une étude d'une cohorte de l'admission jusqu'au congé de l'unité d'AVC. Pour les personnes ayant survécu à la période des soins aigus, l'utilisation des ressources était associée à une augmentation de l'indépendance fonctionnelle entre le moment de l'admission et du congé.

Le troisième manuscrit a estimé et comparé la validité conceptuelle d'une mesure de préférence spécifique à un AVC, l'indice d'AVC basé sur la préférence, à une mesure de préférence générique, l'EuroQol Cinq Dimensions. L'indice d'AVC basé sur la préférence a démontré une validité conceptuelle significativement supérieure à celle du EQ-5D-3L et a pu discriminer les groupes connus. Son utilisation est recommandée chez la population atteinte d'AVC car elle couvre des dimensions particulièrement pertinentes pour la population atteinte d'AVC. D'autant plus, les évaluations des patients peuvent être utilisées pour identifier les aspects d'évaluation ultérieure et de réhabilitation.

L'objectif du quatrième manuscrit était de comparer les estimations de la récupération trois mois post-AVC, parmi trois mesures, l'indice de Barthel pour les AVQ, l'EQ-5D-3L et l'indice d'AVC basé sur la préférence. Il s'agissait d'une étude d'observation d'une série consécutive de patients ayant eu un congé et étant en vie de l'unité d'AVC de 2014 à 2016. En résumé, l'EQ-5D-3L et l'indice d'AVC basé sur la préférence avaient des estimations comparables en matière de récupération. Cependant, l'indice d'AVC basé sur la préférence avait un effet très important. De plus, la concordance entre le EQ-5D-3L et l'indice d'AVC basé sur la préférence était faible, les scores les plus élevés étant dus à l'indice d'AVC basé sur la préférence par rapport au EQ-5D-3L.

L'objectif du dernier manuscrit était d'explorer la signification de récupération post-AVC du point de vue d'un échantillon de survivants d'AVC au Ghana. Cette étude était une analyse qualitative basée sur la méthodologie de description interprétative. La signification de récupération d'un AVC était propre à chaque individu, mais sept thèmes communs ont été identifiés. Les résultats de cette étude soulignent la nécessité pour les cliniciens d'engager les patients à comprendre ce que la récupération signifie pour eux et leurs attentes en matière de récupération afin de réellement répondre aux besoins et aux désirs des patients.

Cette thèse fournit des preuves sur l'efficacité et l'applicabilité des soins d'unités d'AVC au Ghana. De plus, elle montre que l'utilisation des ressources dans les soins de l'unité d'AVC est associée à une indépendance fonctionnelle accrue. D'autant plus, les résultats de cette thèse montrent que les estimations de la récupération dépendent de la mesure utilisée. Enfin, cette thèse souligne l'importance d'une discussion avec les patients sur ce que signifie la récupération pour eux et sur leurs attentes en matière de récupération afin de répondre à leurs besoins.

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STATEMENT OF ORIGINALITY

Coming from an economics background, I have always had interest in the evaluation of implemented interventions to inform policy decision making. This thesis work was motivated by a news article I read in 2014 about the implementation of a stroke unit in Ghana. In the article, the Head of the Stroke Unit although enthusiastic about the progress being made in acute stroke care expressed concern about the applicability of the stroke unit seen as foreign concept from high income countries. This sparked my interest in designing a study that aims to evaluate the effectiveness of the stroke unit in Ghana. As part of my protocol course with Dr. Nancy Mayo, I developed a first draft of the protocol. Through deeper engagement with the literature on stroke care in Ghana and the need to undertake a feasible comprehensive evaluation, I identified objectives that led me to five linked manuscripts.

CONTRIBUTION OF AUTHORS

The five manuscripts of this thesis are the work of Adriana B. Appau the PhD Candidate with extensive guidance from Dr. Raphael Lencucha and Dr. Nancy Mayo.

Manuscript 1: Data collation, statistical analysis and writing of first draft was conducted by the PhD Candidate under the supervision of Dr. Raphael Lencucha and Dr. Nancy Mayo. Dr. Nandini Dendukuri, a committee member provided her extensive expertise on technology assessment and effectiveness studies. Dr. Raphael Lencucha, Dr. Nancy Mayo, Dr. Alfred Akpalu and Dr. Nandini Dendukuri are co-authors on this manuscript. They contributed to the refinement of this manuscript

Manuscript 2: Data collation, statistical analysis and writing of first draft was conducted by the PhD Candidate. Dr. Raphael Lencucha and Dr. Nancy Mayo are co-authors on this manuscript. They provided continual feedback on the interpretation of results and the refinement of the manuscript for journal publication.

Manuscript 3: The data for the third manuscript was obtained from a previous study conducted by Dr. Lois Finch on functional outcomes of stroke survivors in Canada. I conducted the statistical analysis and wrote the first draft of this manuscript under the supervision of Dr. Nancy Mayo. Dr. Lois Finch, Dr. Nancy Mayo and Dr. Raphael Lencucha extensively reviewed this manuscript and are co-authors. They also contributed to responding to reviewers' comments.

Manuscript 4: Data collection, statistical analysis and writing of first draft was conducted by the PhD Candidate and Dr. Nancy Mayo. Both Dr. Raphael Lencucha and Dr. Nancy Mayo are co-authors of this manuscript. They contributed to the interpretation of result, revision of the first draft and provided continual feedback.

Manuscript 5: Face-to-face semi-structured interviews and transcribing of interviews were conducted by the PhD Candidate. Dr. Raphael Lencucha and Dr. Nancy Mayo contributed to the data analysis. The first draft of the manuscript was written by the PhD Candidate. All authors contributed to the refinement of the manuscript and responding to reviewer's comments.

THESIS ORGANISATION AND OVERVIEW

This thesis consists of five manuscripts. Following the guidelines of Graduate and Postdoctoral Studies (GPS), additional chapters have been incorporated into the thesis. As this is a manuscript-based thesis, there are repetitions. The organisation of the thesis is found below.

Chapter 1 presents the introduction and a summary of the literature on models of stroke care

Chapter 2 presents the literature review on stroke unit care in developing countries

Chapter 3 outlines the rational and research objectives of this thesis

Chapter 4 presents the first manuscript entitled "Stroke Unit Care is Effective in Ghana-The Case of The Korle-Bu Teaching Hospital Stroke Unit". This manuscript has been submitted to Stroke

Chapter 5 links manuscripts one and two

Chapter 6 presents the second manuscript entitled "Resource use and function recovery from Stroke in Ghana: The Case of Korle-Bu Stroke Unit". This manuscript will be submitted to Stroke Journal

Chapter 7 links manuscripts two and three

Chapter 8 presents manuscript three entitled "Further Validation of the Preference Based Stroke Index (PBSI) Three Months After Stroke". This manuscript has been published at Clinical Rehabilitation

Chapter 9 links manuscripts three and four

Chapter 10 presents manuscript four entitled "Quantifying Recovery Post Stroke in Ghana-Measures Matter". This manuscript will be submitted to Clinical Rehabilitation

Chapter 11 links manuscripts four and five

Chapter 12 presents the fifth manuscript entitled "The Meaning of Recovery from The Perspective of Stroke Survivors in Ghana". This manuscript is under review at Disability and Rehabilitation

Chapter 13 presents the global discussion of the entire thesis and the conclusion of the thesis

Corresponding references, tables, figures and supplementary material are presented at the end of each manuscript. Referencing styles are according to journal requirements. A complete reference list of the thesis is provided at the end of the thesis. Ethics approval was obtained from the McGill University, Faculty of Medicine Institutional Review Board and the Institutional Review Board of the Korle-Bu Teaching Hospital.

ABBREVIATIONS

LMICs-Low- and Middle-Income Countries

PBSI-Preference Based Stroke Index

DALY- Disability-Adjusted Life Years

YLL- Years of Life Lost

ESD- Early Supportive Discharge

KBTH- Korle-Bu Teaching Hospital

CT- Computed Tomography

HRQL- Health-Related Quality of Life Measures

EQ-5D-3L- EuroQol-5D Three Level

ADL- Activities of Daily Living

NIHSS- National Institutes of Health Stroke Scale

BI- Barthel Index

CNS- Canadian Neurological Scale

FIM-Functional Independence Measure

SF-6D- Short Form-6D

HUI- Health Utilities Index

AQOL-8D- Australian developed Assessment of Quality of Life

ClinROs- Clinician Reported Outcomes

PerfOs- Performance tests

PROMs- Patient-Reported Outcome Measures

SIS- Stroke Impact Scale

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CHAPTER 1: MODELS OF ACUTE STROKE CARE

1.1 Introduction

Stroke is the second leading cause of death and the third leading cause of disability worldwide (1). The burden of stroke for developing countries paints an alarming picture. Approximately 87% of stroke deaths occur in developing countries (2). Stroke has risen to become the fifth leading cause of death in Africa, going up two levels since the year 2000 (1). It is the third leading cause of both disability-adjusted life years (DALY) and years of life lost (YLL), moving up one level since 2000. Even though malaria and tuberculosis continue to be the leading cause of death in most developing countries, DALY of stroke is expected to be three times higher than that of tuberculosis and four times higher than that of malaria in the near future (3). While research shows that there is a decrease in the incidence of stroke in developed countries, incidence of stroke continues to increase in Africa (4). The increase in cardiovascular diseases such as stroke in Africa has been associated with industrialization and urbanisation which has led to changes in diets, tobacco consumption and physical inactivity (5). These have led to an increase in the incidence of risk factors such as hypertension, obesity and dyslipidemia (4,6). Furthermore, health systems in Africa have mainly focused on addressing communicable diseases to the neglect of noncommunicable disease (5). It is projected that mortality and disability due to stroke will double worldwide by the year 2035 indicating that stroke will remain a leading cause of death over the next 15 years at least (7). In addition to preventative measures, it is essential for health care providers to implement evidence-based stroke interventions to improve stroke outcomes, especially in developing countries.

Stroke in Ghana

In Ghana, stroke is the second leading cause of death and the fourth leading cause of in-patient death (death that occurred during admission). A study on stroke admission and case-fatality in one of the major tertiary hospitals in Ghana showed that stroke admissions per 1000 hospital admissions had increased over the last three decades (8). Stroke admissions per 1000 hospital admissions increased from 5.32 in 1983 to 7.58 in 2000 to 14.7 in 2013. Furthermore, 62.1% of stroke deaths occurred within the first seven days of stroke onset (8). In a recent study in the same hospital, in-patient case fatality rate was 43.3% (9). Furthermore, 81% of stroke survivors had moderate to severe disability at time of discharge (9). The burden of stroke is anticipated to be

larger as these data represent the small number of people who are able to access medical facilities. In addition, information on death upon arrival as a result of stroke is not included. Apart from mortality, stroke impacts all components of disability from motor, emotional, and cognitive impairments, to activity limitations, to restriction in participating in life roles, all of which greatly affects return to work and overall quality of life. An estimated 50% of stroke survivors in Ghana encounter problems returning to paid or voluntary work and an even greater proportion are restricted in socializing with family members and the community (10). The increasing burden of stroke is not limited to patients but creates a strain on families and to the already limited resources of fragile health care systems. It is worth noting that 25% of family caregivers report a diminished quality of life (11). Considering the looming burden of stroke in Ghana, it is crucial for the health care system to implement effective and efficient evidence-based interventions to improve stroke outcomes.

1.2 Models of Acute Stroke Care

This section summarizes the lessons learned from research on how to optimize the organization of acute stroke care to improve outcomes for stroke patients. Stroke patients were traditionally cared for in hospital departments such as the neurology department or general medical wards (12). The increasing incidence and disability impact of stroke led to the study and implementation of different models of care specifically designed to target stroke outcomes. The efficacy and effectiveness of stroke care models have been extensively studied (12–14). Notable amongst these are stroke care pathways, early supported discharge, and stroke unit care.

1.2.1 Stroke Care Pathways

A stroke care pathway is a detailed plan of care developed and used by a multidisciplinary team to achieve organised and efficient stroke care (13). The plan of care is grounded in evidence-based practice and involves the use of multidisciplinary guidelines. Stroke care pathways can be categorized as acute stroke management, stroke rehabilitation or a combination of acute stroke management and stroke rehabilitation (13). The main aim of care pathways is to promote the use of best practice guidelines and evidence in making clinical decisions, to standardize patient care by reducing variation in the care provided, promote and improve communication amongst health practitioners and between health practitioners and patients, and finally to improve documentation (15). Care pathways outline the specific interventions needed for a condition and the timeline for

expected progress and or the achievement of stroke outcomes (13). In addition, the optimal timing for clinical assessments and specific interventions or treatments is also indicated in a care pathway. An integral part of most care pathways is variance reporting (13). Variance reporting allows health care professionals to record changes in both treatment procedure and patient recovery that are contrary to those planned or predicted in the care pathway. When using care pathways, changes in treatment plans must be justified by clinical evidence or guidelines (15). Substantial research has been done on the effectiveness of care pathways. A Cochrane review on care pathways has shown that there were no differences between patients treated under care pathways and patients treated in conventional care in terms of death, independence at time of discharge and need for institutional care (13). Furthermore, care pathways led to an increase in quality of documentation and clinical data. However, there were no significant differences in death and length of stay for people who received stroke care pathways compared to conventional care.

Table 1: Stroke Outcomes Comparing Stroke Care Pathways to Standard Care (Kwan J, Sandercock PAG, 2004)

Outcome by end of scheduled follow up	Care Pathway (%)	Control (%)	OR* [95% OR]
Death	15.5	16.6	0.88 [0.49, 1.57]
Death or Institutional Care	47.0	52.7	0.8 [0.61, 1.05]
Death or Dependency	72.4	65.8	1.36 [0.68, 2.72]

*OR=Odds Ratio

1.2.3 Early Supportive Discharge

Early supportive discharge (ESD) is the provision of stroke care services that accelerate the discharge of a patient from the hospital to home followed by providing rehabilitation and support in the home setting (14). In conventional care, stroke patients usually receive acute care and rehabilitation followed by discharge, after which very little to no rehabilitation or support is provided to the patient at home (16). However, under ESD, discharge occurs earlier than usual, followed by active rehabilitation and support in the patient's home. A meta-analysis on ESD showed that, ESD frees up hospital beds, reduces hospital cost and increases independence 6 months post stroke. However, ESD was shown to put a lot of strain on caregivers because it requires active participation of caregivers and adjusting home setting to facilitate rehabilitation.

Table 2: Stroke Outcomes Comparing Early Supportive Discharge to Standard Care (Langhorne et al, 2005)

Outcome by end of scheduled follow up	ESD (%)	Control (%)	OR* [95% OR]
Death			0.90 [0.64, 1.27]
Death or Institutional Care			0.74 [0.56, 0.96]
Death or Dependency	44.7	50.2	0.79 [0.64, 0.97]

*OR=Odds Ratio

1.2.2 Organised Stroke Unit

A stroke unit is defined by the Stroke Unit Trialists' Collaboration as *"focusing of care for stroke patients in hospital under a multidisciplinary team who specialize in stroke management*" (12). Different models of organised stroke care are provided in the form of stroke wards, mixed rehabilitation wards and mobile stroke teams depending on the level of stroke specific service organization (12). There is overwhelming evidence of the short- and long-term benefits of stroke units. Randomized control trials comparing the efficacy of stroke units to stroke care provided in the general medical ward have shown that stroke units lead to lower mortality rates, higher levels of independence, and shorter length of stay in hospitals (12). Table 3 summarizes the results of a review comparing stroke units to the general ward. According to the Cochrane review of organised stroke unit care, by the end of scheduled follow-up, the patient mortality rate on the stroke unit was 17% compared to 24.2% of patients in the general ward. For death or dependency, these proportions were 50.4% among those assigned to the stroke unit compared with 60.2% for those assigned to care in general wards. Stroke unit care was also associated with a reduction in the length of stay, and a benefit in terms of independence, physical function after stroke, participation and quality of life. Results from the Cochrane review demonstrated that, patients who received care at a stroke unit had the highest potential to survive, recover and gain their independence compared to patients receiving other forms of stroke care. Today, organized stroke unit care continues to be the most recommended intervention for improving stroke outcomes at the population level for both developed and developing countries (3,17,18).

The research on stroke units and its wide spread implementation has mainly been carried out in developed countries within well-established research environments, efficient health systems, and

with access to advanced medical technologies. These conditions likely contribute to the lower rates in stroke mortality and disability caused by stroke in developed countries. It has been estimated that 2/3 of the deaths due to stroke in developing countries are attributed to lack of resources and appropriate stroke care (19). Although stroke unit care has been shown to reduce stroke mortality and increase functional independence, there is a dearth of research on the applicability of stroke units in lower resource settings especially in Africa. In addition, most of the research on stroke unit effectiveness comes from randomized controlled trials and not from evaluation in real-world clinical settings. Little is known about the effectiveness and applicability of implementing stroke units into clinical practice in low resource settings. It is also important to estimate the cost associated with stroke unit care to ensure effective use of health care resources, particularly in an environment with limited resources and other possible approaches to care.

Table 3: Stroke Outcomes Comparing Organized Stroke Unit to General Medical Ward (Stroke Unit Trialists' Collaboration, 2013)

Outcome by end of scheduled follow up	Stroke unit (%)	General Ward (%)	OR* [95% OR]
Death	17.9	24.2	0.75 [0.63, 0.90]
Death or Institutional Care	32.08	38.35	0.74 [0.63, 0.87]
Death or Dependency	50.4	60.2	0.75 [0.64, 0.88]

*OR=Odds Ratio

Despite evidence supporting stroke unit care, there are a number of barriers to implementing stroke units in developing countries. First, concerns have been raised about the applicability of stroke units (seen as a "foreign concept" from developed nations) in developing countries as a result of the paucity of evidence on implementation in low resource settings (3). Other major barriers include: (i) limited health care resources, especially in clinical staff and medical equipment; (ii) limited and/or difficult access to the available medical facilities; (iii) limited knowledge of stroke and stroke symptoms; and (iv) cultural and social beliefs (20). These factors make it challenging for developing countries to implement stroke unit care. Nevertheless there is empirical evidence to suggest that the most basic organised stroke care in the form of dedicated beds for stroke patients has the potential to achieve better stroke outcomes than care received at the general medical ward in low resource settings (3,11).

As of 2013, Ghana had no stroke unit care. After a series of visits, workshops and training sessions, a team made up of health professionals from England and two hospitals in Ghana; Ridge Hospital and Korle-Bu Teaching Hospital (KBTH) drew up strategic plans to establish a stroke unit as a key step towards improvement in stroke care delivery (21). Through a partnership with WESSEX and financial support from Tropical Health Education Trust, a stroke unit was opened in January 2014 at the KBTH in Accra (22). The unit, which is headed by a neurologist, is managed by a multidisciplinary team made up of doctors and nurses, a physiotherapist, occupational therapist, speech and language therapist, dietician and clinical psychologist (22). The team meets weekly and one of its outcomes has been the development of an Acute Stroke Checklist. The stroke unit in KBTH has the key characteristics of organized stroke care: dedicated beds, a multidisciplinary team and regular team meetings (12,23).

As noted, the adoption of stroke unit care as a stroke care policy in developing countries must be based on evidence of efficacy, effectiveness, efficiency and applicability. The efficacy and effectiveness of stroke units have been well established in developed countries. The questions that still remain are: Can stroke units implemented in developing countries realize similar outcomes as those implemented elsewhere? Is there evidence over time in Ghana, that restructuring stroke care from care in the general medical wards to a dedicated stroke unit changed outcomes? This being the first established stroke unit in Ghana, and with the prospect of replicating the implementation of the stroke unit in other regions, it is important to estimate the effectiveness of the stroke unit to inform local stroke care policy. To date there has not been a comprehensive evaluation of the stroke unit in KBTH. It is important to evaluate the effect of the stroke unit on stroke outcomes if stroke units are to become the model for care. The ultimate aim of this study was to contribute evidence towards the effectiveness and applicability of stroke unit care in developing countries.

CHAPTER 2- EFFECTIVENESS AND APPLICABILITY OF STROKE UNIT CARE IN ROUTINE AND LOWER RESOURCE SETTINGS

In the introductory chapter I discussed the main models of acute stroke unit care and their impact on mortality, independence and discharge into institutional care. The literature, based mostly on randomised trials, provides evidence supporting the effectiveness of organised stroke unit care in reducing mortality and the need for institutional care and improving functional independence at the end of scheduled follow-up. Despite this improvement in outcomes from stroke unit care, there are still major concerns about the applicability of a complex intervention such as a stroke unit outside a strictly controlled research environment and if whether similar outcomes can be realized in existing stroke units over time. Seenan et al. (2007) (24) conducted a systematic review on the effectiveness of stroke units as implemented in clinical settings, including 25 observational studies, 18 of which had useable outcome data. Out of the 18 studies, 12 were single-center studies and 6 were multi-centered. Stroke unit care was associated with a 21% [OR:0.79, CI:0.73 0.86] decreased odds of death compared to usual care within 1 year of scheduled follow-up. Looking at multicenter studies only, stroke unit care was associated with an 18% [OR:0.82, CI:0.77 0.89] decreased odds of death within 1 year of follow-up compared to usual care. Similarly, the stroke unit was associated with an 18% [OR:0.82, CI:0.69 0.97] less odds of death one year or more post stroke. Furthermore, patients treated in the stroke unit had a reduced odds of death, need for institutional care and/or functional dependence in comparison to odds of these outcomes for patients treated in usual care settings [OR: 0.87; 95% CI: 0.80 0.95]. The results from this systematic review of observational studies confirm that stroke unit care as implemented in clinical settings produce similar outcomes with respect to death, need for institutional care and independence as observed in randomised trials.

2.1 Literature on Stroke Unit Care in Low- and Middle-Income Countries

Nevertheless, there is still a dearth of literature on the effectiveness and applicability of stroke units in low- and middle-income countries (LMICs). Only 1 (Turkey) out of the 25 studies identified in the systematic review is from a LMIC. It has often been argued that organised stroke unit care is a complex intervention with evidence supporting its effectiveness mostly from high-income countries with efficient health care systems, well developed research environments and greater resources. It is still unclear whether the effectiveness estimated from clinical trials (25) and

routine setting (24) in high-income countries can be realised in lower resource settings which has implication on the applicability of organised stroke unit care in LMICs.

2.1 Methods

In order to appraise the current state of research on stroke unit care in LMICs, I conducted a literature search on using a combination of the following search terms: stroke *(economics, mortality, therapy), stroke unit, developing countries, organised stroke*. The search was conducted using the following databases: Ovid Medline, PubMed and google scholar. This was followed by citation chaining and hand searching to identify related studies.

A total of 9 studies were identified that estimated the effect of stroke unit care on stroke outcomes in low-and-middle income countries (26–34). Full text of 2 studies (31,34) were unavailable leaving 7 studies for this review. Out of the 7 studies, 3 were from Asia (China, Thailand, India), 2 from Europe (Turkey, Croatia), and 1 each from South America (Brazil) and Africa (South Africa). Three of the studies were historically controlled, 2 prospective studies and 2 randomised trials. The total sample size was 13,076 (SU:6356, Control: 6720). All studies compared outcomes from the stroke unit to either the general medical ward or the neurological ward. The primary outcomes of the studies identified were mortality, length of stay and rate of complication. Secondary outcomes reported included prevalence of risk factors amongst patients who died, proportion of independence at discharge, transfer to tertiary hospital, referral to inpatient rehabilitation, number of Computed Tomography scans (CT scans), use of rehabilitation services and initiation of secondary prevention drugs.

2.2 Results

2.2.1 Primary Outcomes

Mortality

All studies reported on the in-hospital mortality rate. In all studies, the stroke unit had a lower in-hospital mortality rate compared to either the general medical ward or the neurological ward, ranging from the highest difference of 35.1% (29) to the lowest of 7.3% (30). Cabral et al. (2003) reported on mortality rate at 10 days and at 1 month. Mortality rate at 10 days for the stroke unit (8.5%) was lower than that of the medical ward (12.8%). Similarly, the mortality rate at 1 month

for patients receiving treatment at the stroke unit (14.2%) was lower than that of patients receiving treatment in the general ward (28.2%).

Length of Stay

Length of hospital stay was reported by 4 out of 7 studies. Two studies (29,32) reported a longer mean length of stay for the stoke unit while the other two studies (26,27) reported a shorter mean length of stay for the stroke unit. The mean length of stay for stroke unit care ranged from 6.8 days to 13.7 days and from 5.1 to 16.7 days in the control groups.

Rate of medical complication

Four studies compared the rate of medical complication between the stroke unit and the control group (26,27,29,33). Three of these studies reported a lower rate of medical complications for the stroke unit group (differences in rate of complication: 22.6% (29), 9.9% (26) and 29.2% (33)) compared to their control while one study reported a higher rate of medical complication for the stroke unit group compared to the control group (difference in rate of complication: 1.2% (27)).

Table 1: Literature on Stroke Units in Developing countries

Author (Year)	Country [Year of Data Collection]	Study design [Comparison]	Sample Sizes	Source of Data	Measures Used
Cabral et al. (2003)	Brazil [Mar-Dec 2000]	RCT [Medical Ward]	SU:35, GW:39	Unclear	Scandinavian Scale, Barthel Index
	Outcomes: Mortality rate, death/independence/ independence at 10 days, 1 month, 6 months				
Krespi et al. (2003)	Turkey [Jan 1997-Mar 1999/After April 1999]	Prospective [Neurological Ward]	SU:352, NW:352	Stroke Registry	OCSP Criteria Modified Rankin Scale
	Outcomes: In-hospital case fatality rate, length of stay, proportion of independence at discharge, rate of medical complication				
Ma et al. (2004)	China [Dec 2001-Jan 2003]	RCT [Neurological Ward]	SU:195, NW:197	Unclear	Barthel Index, NIHSS and Oxford Handicap Scale
	Outcomes: Change in Functional Independence, stroke severity, OHS, rate of medical complication				
Suwanwela et al. (2007)	Thailand [2001-2003]	Prospective [Medical Ward]	SU:301, MW:106	Unclear	N/A
	Outcomes: In-hospital mortality, rate of neurological and medical complication, length of stay				
de Villiers et al. (2009)	South Africa [Dec 2001-Feb 2002/ Mar 2002-May 2002]	Historically Controlled	Pre:94, Post:101	Ward Registry	N/A
	Outcomes: In-hospital mortality, length of stay, transfer to tertiary hospital, referral to inpatient rehabilitation, number of CT scans				
Supanc et al. (2009)	Croatia [1995-2006]	pre and post-Historically controlled [Neurological Ward]	SU:5171, NW:5730	medical records and hospital registry	N/A
	Outcomes: In-hospital case fatality, prevalence of risk factors amongst patients who died				

Pandian et al. (2011)	India [Mar 2008-sep 2009]	Historically Controlled [Medical Ward]	SU:201, MW:202	Medical Records	N/A
	Outcomes: In-hospital Mortality, Length of Stay, Rate of medical Complication, Use of rehabilitation services, initiation of secondary prevention drugs				

Table 2: Literature comparing stroke outcomes between stroke unit care and conventional care in developing countries

Author (year)	In Hospital Mortality Rate	Percent Independent	Length of Stay	Rate of Complications
Cabral et al. (2003)	At 10 Days- SU:8.5% GW:12.8 At 1 Month - SU:14.2%, GW:28.2%	SU:48.6%, GW:42%		
Krespi et al (2003)	SU:10.5%, NW:19.6%(9.1)	SU:45.2%, NW 43.8%	SU:13.76±10.1 NW:16.72±15.38	SU:23.9%, NW:22.7%
Ma et al. (2004)				SU:25.1, NW 54.3
Suwanwela et al(2007)	SU: 2.1%, GW:8.9% (12.1)		SU:8.09, GW:11.26	SU:15.7%, GW:25.6%
de Villiers et al. (2009)	SU:16%, GW:33% (17)		SU:6.8, GW:5.1	
Supanc et al. (2009)	SU:12.8% ± 0.34, GW:20.1% ± 0.4			
Pandian et al. (2011)	SU:11.9%, MW:47% (35.1)		SU:9.4 ± 6.7, MW: 7.7 ± 8.1	SU:42.2%, GW 64.8%

2.3 Secondary outcomes

Four studies reported on secondary outcomes (29,30,32,33) that are not reported in the table. Three studies reported on the level of independence at different time points. Krespi et al. (2003) estimated the percentage of patients independent at time of discharge. At time of discharge, 45.2% of patients from the stroke unit were independent compared to 43.8% of patients from the general medical ward. Cabral et al. (2003) reported on the level of independence at 6 months post stroke. A larger percentage of patients receiving care at the stroke unit (48.6%) were independent at 6 months compared to patients receiving care at the general medical ward (42%).

Pandian et al. (2011) compared the use of rehabilitation services and the initiation of secondary prevention drugs between the two groups. Amongst patients receiving care at the stroke unit, 93.5% had seen a physiotherapist compared to 53.9% of patients receiving care in the general medical ward. In addition, a higher percentage of patients in the stroke unit (57.2%) were using Antiplatelets compared to the general medical ward (27.7%). De Villiers et al. (2009) also reported on the rate of referral to inpatient rehabilitation, rate of referral to tertiary institution and the number of CT scans performed. The stroke unit group had a 10% higher rate of referral to inpatient rehabilitation while the control group had a 3% higher rate of referral to a tertiary institution. For patients admitted to the stroke unit, 16% had a CT scan performed compared to 13% of participants from the medical ward. Supanc et al. (2009) calculated the proportion of patient with risk factor who died for each group. The percentage of patients with hypertension who died was lower in the stroke unit group (78%) compared to the general medical ward (82.2%). On the other hand, the percentage of patients with diabetes Mellitus who died was higher in the stroke unit group (27.6%) compared to the general medical ward group (20.8%).

A limitation of this review was the use of a limited number of search words to search for studies conducted particularly in developing countries. As there were limited search words to capture this group of countries, I may have missed some studies that were not categorised under the search terms used.

2.4 Conclusion

In summary, all studies consistently demonstrated that stroke unit care in developing countries was associated with lower mortality compared to care in the general medical ward or neurological

ward. There is also evidence to support that care at the stroke unit is associated with higher functional independence and lower rates of medical complications. Furthermore, a higher proportion of patients admitted to the stroke unit were referred to inpatient rehabilitation compared to patients admitted to the general ward. These findings suggest that stroke unit care may be applicable in lower resource settings in the absence of advance health care systems and medical facilities. I was unable to conduct a meta-analysis due to the small number of studies identified and the heterogeneity. Only one study was identified from Sub-Saharan Africa. This indicates a dearth of research on the effectiveness of stroke units in Sub-Saharan Africa and the need to generate evidence on the applicability of stroke units in that context. The next chapter presents the rational for this thesis.

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CHAPTER 3-RATIONAL AND OBJECTIVES

As mentioned in previous chapters, organised stroke unit care is the most recommended stroke care policy to improve stroke outcomes. The evidence supporting the effectiveness of stroke unit care compared to care at the medical or neurological ward is substantial. The research on and wide spread implementation of organised stroke unit care has mainly been conducted in high income countries with advanced research environments and well-developed health care systems. Nevertheless, there is some, although limited evidence that stroke unit care is effective in lower resource setting. Many developing countries are beginning to adopt organised stroke unit care in their stroke care policy to improve stroke outcomes.

As noted previously, Ghana implemented its first stroke unit in 2014 at the Korle-Bu Teaching hospital. It is an opportune time to now examine the efficacy, effectiveness, efficiency and applicability of the unit. The efficacy and effectiveness of stroke units have been well established. The questions that still remain are, can stroke units implemented in Ghana realize similar outcomes as those implemented elsewhere? Is there evidence over time in Ghana, that restructuring stroke care from care in the general medical wards to a dedicated stroke unit changed outcomes? With the prospect of replicating the implementation of the stroke unit in other regions, it is important to estimate the effectiveness of the stroke unit to inform local stroke care policy in Ghana.

Objectives

The global aim of this project was to contribute evidence towards the effectiveness of stroke units in Ghana, a country representative of lower middle-income countries. This aim was achieved through five interrelated manuscripts.

The objective of the first manuscript was to estimate the extent to which outcomes of mortality and length of stay changed following the implementation of stroke unit care in KBTH. This was a historically controlled study comparing the pre-stroke unit period (2011-2013) to the post stroke unit period (2014-2016). The stroke unit was associated with lower mortality and shorter length of stay compared to the general medical wards after controlling for year of admission, age and sex. Stroke severity predicted both time to death and time to discharge for patients who received care at the stroke unit.

The objective of the second manuscript was to estimate the extent to which resource use at the stroke unit was associated with functional independence amongst patients admitted to the stroke unit. For people surviving the acute care period, resource use was associated with an increase in functional independence from time of admission to discharge.

One of the challenges in estimating effectiveness of stroke units is that the outcomes are not patient-centered assessing very basic function or disability from a clinician's view point. More complex stroke outcomes such as those falling under the rubric of stroke-specific health-related quality of life measures (HRQL) are often very long and not culturally adapted nor translated to the target populations in LMICs. This was true for Ghana where I found it difficult to imagine using most of the existing measures in this setting. The exception was the Preference Based Stroke Index (PBSI) and the generic HRQL measure, the EuroQol-5D (EQ-5D-3L). Both of these measures are short and the items relevant to this population. However, the validity of the PBSI had not been independently established and so, before choosing it for Ghana, I undertook a validation study.

The third manuscript estimated and compared the construct validity of the PBSI to the EQ-5D-3L using data previously collected from a study in Canada. The premise was that, if there was limited evidence of validity in the country of origin, it would not be suitable for use in Ghana. The PBSI demonstrated greater construct validity with respect to other stroke outcome measures than did the EQ-5D-3L and could discriminate amongst known groups. Its use was therefore recommended as it covered dimensions particularly relevant to the stroke population in Ghana. Furthermore, patients' ratings can be used to identify areas of further assessment and rehabilitation. Based on this positive assessment, it was translated into Twi.

Now, I had a selection of relevant stroke outcome measures, recovery after stroke in Ghana could now be measured. In the fourth manuscript I undertook this assessment. Estimates of recovery at 3 months post stroke, were compared among three measures, the Barthel Index for Activities of Daily Living (ADL), the EQ-5D-3L, and the PBSI. This was an observational study of a consecutive series of patients discharged alive from the stroke unit from 2014 to 2016.

The objective of the last manuscript was to explore the meaning of recovery post stroke from the perspective of a sample of stroke survivors in Ghana. This study was a qualitative analysis based on interpretive description methodology.

The five manuscripts provide a varied appreciation of stroke care and outcomes in Ghana from stroke onset to reintegration into the community.

CHAPTER 4- MANUSCRIPT 1

Stroke Unit Care is Effective in Ghana-The Case of The Korle-Bu Teaching Hospital Stroke Unit

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Abstract

Background

Organised stroke unit care is one of the most recommended models of providing acute stroke care. There is substantial evidence supporting the short- and long-term benefits of stroke unit care. Compared to care in a general medical ward, stroke unit care is associated with lower mortality and functional independence. However, the research and wide spread implementation of stroke unit care has been conducted largely in high income countries with advanced research environments and well-resourced health care systems. There is a dearth of research on the applicability of stroke unit care in lower resource settings. The objective of this study is to estimate the extent to which outcomes of mortality and length of stay changed following the implementation of stroke unit care at the Korle-Bu Teaching Hospital in Ghana.

Methods

This is a historically controlled study. Time to death and time to discharge alive was modelled using Cox proportional hazards regression, comparing the pre-stroke unit period (2011-2013) to the post stroke unit period (2014-2016).

Results

The stroke unit was associated with a lower hazard ratio of 0.39 [CI:0.28,0.55]. Thus, patients who received care at the stroke unit had a lower probability of dying compared to patients who received care at the medical wards. Furthermore, patients admitted to the stroke unit had a greater probability of being discharged at any point in time than patients admitted to the general medical ward. [HR:1.25, CI: 1.04 1.50].

Conclusion

The stroke unit was associated with lower mortality and shorter length of stay. These results demonstrate that stroke units are applicable and can be effective in lower resource settings.

Introduction

Stroke is the second leading cause of death and the third leading cause of disability worldwide (1). Approximately 87% of stroke mortality is believed to occur in low and middle income countries (LMIC) (2). In Africa, stroke is the fifth leading cause of death, moving up two levels since the year 2000 (1). It is the third leading cause of both disability-adjusted life years (DALY) and years of life lost (YLL), moving up one level since 2000 (3). Even though malaria and tuberculosis continue to be the leading causes of death in most LMIC, DALY of stroke is expected to be three times higher than that of tuberculosis and four times higher than that of malaria in the near future (4). While research shows that there is a decrease in the incidence of stroke in high income countries (HIC), incidence of stroke continues to increase in Africa (5).

In Ghana, stroke is the fifth leading cause of death (6). A study on stroke admission and case-fatality in one of the teaching hospitals in Ghana, showed that, stroke admission per 1000 hospital admissions has increased over the last three decades (7). Stroke admission per 1000 hospital admissions increased from 5.32 in 1983 to 7.58 in 2000 to 14.7 in 2013. Furthermore, 62.1% of stroke deaths occurred within the first seven days of stroke onset (7). In a recent study in the same hospital, in-patient case fatality was 43.3% (8). In addition, 81% of stroke survivors had moderate to severe disability at time of discharge (8). In another study in southern Ghana, they estimated a 28 days case fatality of 41% (9). The burden of stroke is anticipated to be larger since this data represents the number of people who are able to access medical facilities. In addition, it does not include death upon arrival as a result of stroke.

It has been estimated that 2/3 of the deaths due to stroke in LMIC are attributed to lack of resources and appropriate stroke care (10). There is substantial evidence supporting that stroke unit care is associated with lower mortality and functional independence (11). The research on stroke units and its wide spread implementation has mainly been carried out in HIC within well-established research environments, efficient health systems, and access to advanced medical technologies. There is a dearth of research on the applicability of stroke units in lower resource settings, especially in Africa. In a recent systematic review on stroke care in Africa (12), only 3 countries: South Africa, Ghana and Central African Republic reported having stroke units. In two of these three countries, stroke unit care was associated with 17% and 30% reduction in inpatient mortality rate in Central African Republic and South Africa respectively (12). In another review on the application of acute stroke care interventions in Africa, only 4 studies were identified; three on

thrombolytic therapy and one on stroke unit care (13). This is an indication of the wide evidence-to-practice gap in Africa and the paucity of published studies on stroke units on the continent.

A major concern and barrier to the implementation of stroke units is the lack of empirical evidence to support the applicability of stroke units in Africa (4). Other barriers include high infrastructure and medical equipment costs, limited health care and clinical staff, limited and expensive medical transportation, limited knowledge of stroke and stroke symptoms, and cultural and social beliefs (12,14). These factors make it challenging for LMIC to implement stroke unit care. In addition, most of the research involves randomized controlled trials and not stroke unit evaluation in real world clinical settings. There has been one systematic review summarizing the observational studies (n=18 of 25 with useable data) (15). In comparison to the odds of death among people with stroke managed in general medical wards, the odds of death among people managed in specialized stroke units was lower [OR:0.79; CI 0.73,0.86]. Stroke unit care was also associated with lower odds of a poor outcome defined as death, institutional care or dependency [OR:0.87; CI 0.80,0.95]. None of the studies included in this review were from Africa. Little is known about the effectiveness and applicability of implementing stroke units into clinical practice in low resource settings. Nevertheless there is empirical evidence to suggest that the most basic organised stroke care, in the form of dedicated stroke beds in low resource settings, has the potential to achieve better stroke outcomes than care received at the general ward (4,16).

In 2014, the Korle-Bu Teaching Hospital (KBTH) in Ghana implemented its first stroke unit as a major step towards improving stroke care in Ghana. The stroke unit, which is headed by a neurologist and managed by a multidisciplinary team has dedicated beds for stroke rehabilitation and provides acute stroke care to patients. Currently there has not been a comprehensive evaluation of the stroke unit in KBTH. It is important to evaluate the effect of the stroke unit on stroke outcomes if stroke units are to become the model for care. The global objective of this study is to contribute evidence towards the effectiveness and applicability of stroke unit care in LMICs. The specific objective is to estimate the extent to which outcomes of mortality and length of stay changed following the implementation of stroke unit care in KBTH.

Methods

Study Design

This is a historically controlled study comparing outcomes pre- and post-introduction of a stroke unit in KBTH. Stroke outcomes of mortality and length of stay were gathered for all people admitted to the hospital over two time periods (two years in each time period): pre-stroke unit introduction, January 2011 to December 2013; and post-stroke unit introduction, January 2014 and December 2016.

Study Site

This study was conducted at the stroke unit and the general medical wards at the KBTH. The KBTH, situated in the southwestern part of Accra is the leading national referral hospital in Ghana. Most of its operations are government funded however cost of care at the KBTH is either covered by the National Health Insurance Scheme, paid out of pocket or covered by a private insurance company. The stroke unit has 20 beds. It is equipped with a hoist, wheel chairs and a ripple bed. The stroke unit is managed by a multidisciplinary team (doctors, nurses, physiotherapist, occupational therapist, speech therapist and clinical psychologist) headed by a neurologist. Member of the multidisciplinary team have stroke specific training. The stroke unit also has an inhouse physiotherapy unit that provides physiotherapy to admitted patients and some discharged patients. The multidisciplinary team conducts clinical rounds everyday while patients receive physiotherapy at least once a day. The medical department has a bed capacity of 277. The study focuses on the four general medical wards which are comprised of the Gastroenterology Unit, Endocrinology Unit, Neurology Unit, Cardiology Unit and Rheumatology Unit. The study was conducted according to the declaration of Helsinki. Ethics approval was obtained from McGill University, Faculty of Medicine Institutional Review Board and the Institutional Review Board of the Korle-Bu Teaching Hospital.

Study Population

The target population was stroke patients receiving care at the KBTH in Ghana during the time period when stroke care transitioned from care in a general medical ward to care in a newly created stroke unit. Patients must have been admitted for acute stroke according to WHO definition of stroke and admitted within 2 weeks of stroke onset during the study period (2011-2016). The

World Health Organization defines stroke as "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" (17). Based on this definition, patients who had suffered a transient ischemic attack and subdural haematoma were excluded. In a study conducted in 2012 in the same hospital, in-patient case fatality proportion was 43% and 81% of stroke survivors had moderate to severe disability at time of discharge (8). The sample size was calculated to detect an absolute risk reduction of at least 10% in mortality with a 95% confidence interval that excludes 0 (18). Based on this, a sample size of 200 patients from each group (Stroke Unit and Historical Control) was required.

Outcomes

The primary outcomes were mortality and length of stay. Data on stroke deaths and length of stay was obtained through a review of the admission and discharge books of the stroke unit (January 2014 to December 2016) and the four general medical wards (January 2011 to December 2013). When the data was missing, individual patient records were reviewed if available. Other variables such as stroke severity, age of patient, and type of stroke was also collected when available. Stroke severity, measured using the National Institutes of Health Stroke Scale (NIHSS) (19), was only available once the stroke unit was in place. Mild stroke was defined by NIHSS score of less than 5, mild to moderate a NIHSS score of 5 to 14, severe a NIHSS score of 15 to 24 and very severe a NIHSS score greater than 24. A special data abstraction form was developed to standardize the data collection.

Statistical Methods

Time to death and time to discharge was modelled over the entire study period (2011 to 2016) using Cox Proportional Hazards Regression with the main effect being stroke unit care or not, considering age, sex, and year of admission. A subsequent analysis focused only on the stroke unit period (2014-2016) where the main effect was year of admission and adjustment was for age, sex and stroke severity.

Results

Characteristics of patients admitted under the two models of care at KBTH are provided in Table 1. Patients admitted in the stroke unit were of similar age to those admitted to the medical ward.

There were more men than women admitted into both models of care. The average length of stay for patients was similar for both, however a higher proportion of patients were discharged alive from the stroke unit (83.2) than the medical ward (70.0). With respect to mortality, 93% of deaths occurred within 14 days with only 3% occurring after 21 days for the stroke unit, while 83% of deaths occurred within 14 days with 9% occurring after 21 days for the medical wards.

INSERT TABLE 1 HERE

Table 2 presents the results of the Cox model of the effect of the stroke unit care on time to death. Patients admitted to the stroke unit had a lower probability of dying compared to patients admitted to the medical ward [HR:0.39; CI: 0.28,0.55]. On the other hand, patients on the stroke unit had a greater probability of being discharged at any point in time than patients in the previous period when only general medical care was available [HR:1.25, CI: 1.04,1.50]. This indicates a shorter length of stay as the probability of being discharged is a positive outcome. The related survival curves for time to death and time to discharge comparing the two models of care are presented in Figures 1 and 2.

INSERT TABLE 2 HERE

Figure 1: Probability of Surviving for patients admitted to the two models of care

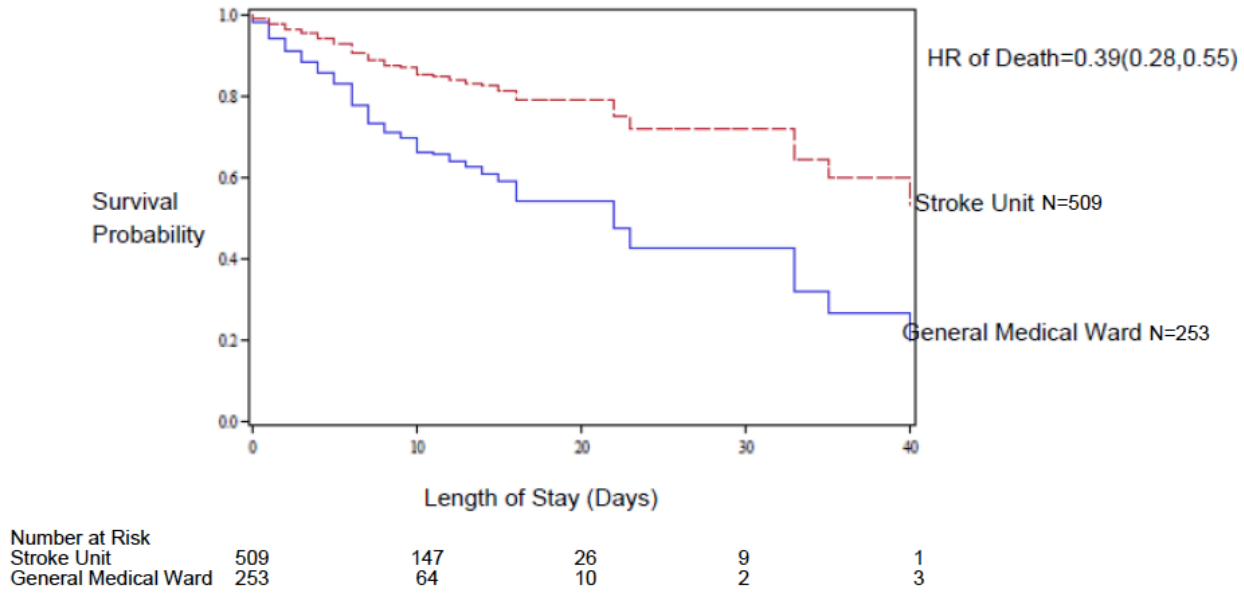
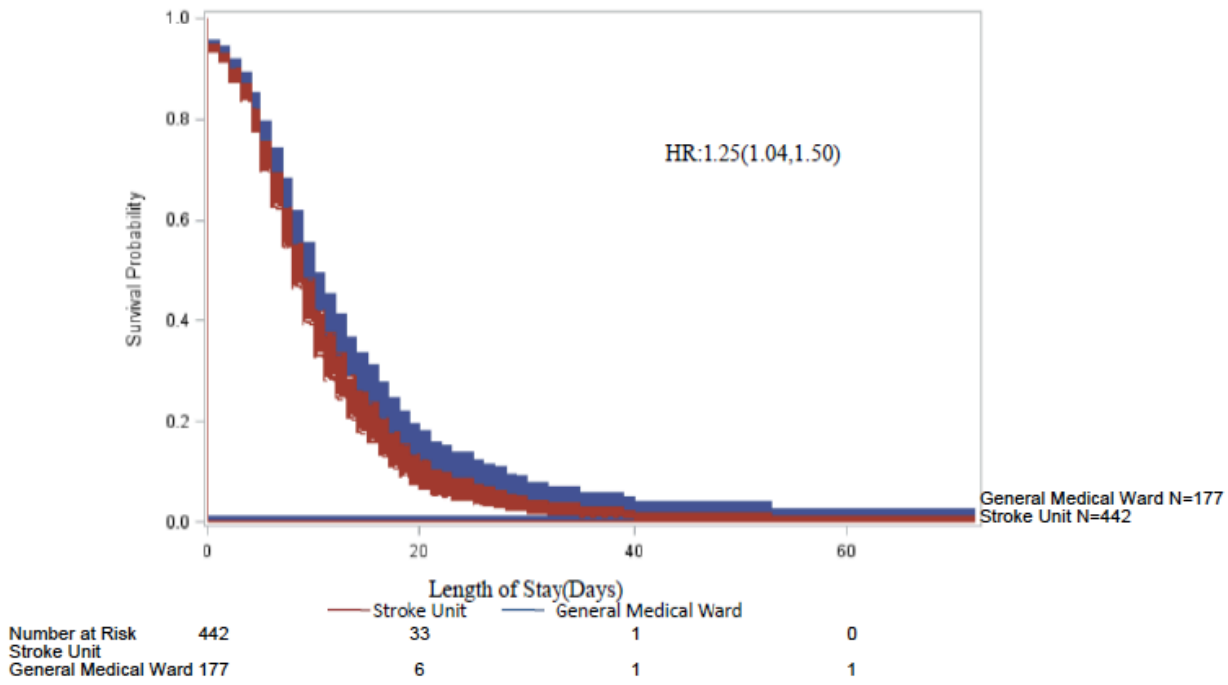


Figure 2: Time to discharge alive for patients admitted to the two models of care



Among only those patients admitted to the stroke unit, time to death and time to discharge was modeled as a function of year of admission: 2014 as reference year. Table 3 presents the characteristics of the patients over time.

INSERT TABLE 3 HERE

Table 4 presents the result of the Cox model on time to death and time to discharge alive by year. There was no effect of year, sex or age on time-to-death or time-to-discharge but stroke severity was a factor.

INSERT TABLE 4 HERE

Discussion

This study estimated the extent to which mortality and length of stay changed following the implementation of stroke unit care at the KBTH. We found that the introduction of the stroke unit was associated with lower mortality and shorter length of stay compared to the general medical wards. These results were unaffected by year of admission, age or sex but stroke severity predicted both time to death and time to discharge for patients admitted into the stroke unit.

These results are compatible with those observed in other studies. In the literature on the effect of stroke unit care in LMIC, stroke unit care was associated with a lower in-hospital mortality (ranging from the lowest of 2.1% to the highest of 16%) compared to the general ward (20–26). Furthermore, in two systematic reviews on the effectiveness of stroke unit care based on RCTs (11) and observational studies (15), the stroke unit was associated with lower odds of death (odds ratio of 0.75 and 0.79 respectively). The results on length of stay is mixed. Similar to our study, Pandian et al. (2011) and De Villiers et al. (2009) reported a shorter length of stay for patients receiving care at the stroke unit compared to the general medical ward, while Suwanwela et al. (2007) and Krespi et al. (2003) reported a longer length of stay for the stroke unit.

The effectiveness and applicability of stroke unit care in LMIC especially in Sub-Saharan Africa has been questioned as a result of the many barriers faced in its implementation in lower resource setting. These barriers include poor access to medical facilities as a result of inadequate medical transportation, lack of stroke experts, inadequate skilled staff, lack of medical equipment, insufficient hospital infrastructure and high cost of medication (4,27). Despite these barriers, this study contributes to the evidence that stroke unit care implemented in lower resource settings improves stroke outcomes. Key components of an effective stroke unit include having dedicated beds for acute stroke care, a well-coordinated multidisciplinary team (comprising of a neurologist, doctors, nurses, physiotherapist, occupational therapist, speech therapist and social worker), access to diagnostic facilities and medication. In LMICs, reorganisation of already available health resources to provide organised stroke unit care has the potential to reap great benefits compared to care at the medical or neurological ward. Replication should be well planned to address the different contextual factors that may impact the effectiveness of the stroke unit (28). For instance, in settings where there is a lack of stroke experts or rehabilitation therapists, establishing evidence-based stroke protocols of care that are tailored to the local context and providing supplementary training to available staff (e.g. nurses, medical assistants) can be one way of supplementing the multidisciplinary team needed. Furthermore, based on the resources available, different models of organised stroke care can be adopted. For example, in settings where resources are very limited, mobile stroke teams can manage stroke patients in the general medical ward using evidence-based stroke protocols. As stroke unit care has the potential of reducing the length of stay and has been shown to be associated with lower rate of medical complications, providing organised stroke unit care may be a more resource efficient model of care in lower resource settings.

Limitations

This study has some limitations. The information on stroke severity for patients admitted to the medical wards was limited. Due to this, we were unable to control for the effect of stroke severity on time to discharge and time to death before and after the implementation of the stroke unit. In addition, we were unable to estimate the effect of stroke unit care on any outcome of recovery or long-term outcome as there was no information on recovery after discharge. Future research should estimate the effect of stroke unit care on other stroke outcomes such as recovery.

Conclusion

This study demonstrates that stroke units are applicable and can be effective in lower resource settings. The reduction in morality and shortened length of stay indicates that this resource allocation was of benefit to the population.

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Table 1: Characteristics of Stroke Patients Admitted under the Two Models of Care

Variables	**Stroke Unit (n=509)** Mean (SD) [Median] of N (%)	**Medical Wards (n=253)** Mean (SD)[Median] or N (%)
Age	58 (13.7)	60(14.5)
Men / Women	326/205 (61.0/39.0)	156/100 (61.0/39.0)
NIHSS (0 – 42; higher is worse)	10.9 (7.6)	-
Type of Stroke:		
Haemorrhage	204 (40.3)	-
Infarct	296 (58.5)	-
Multiple Infarct	1 (0.2)	-
Subarachnoid	5 (1.0)	-
Length of stay	8.5 (6.9) [7]	8.6(8.1) [7]
Discharged alive		
Proportion	442 (83.2)	177 (70.0)
Time to discharge (days):		
Mean (SD) [Median]	9.2(7.0)[8]	9.3(8.0)[8]
≤7	202 (46)	98(55)
8 to 14	163 (37)	54 (30)
15 to 21	54 (12)	19 (11)
> 21	23 (5)	6 (3)
Deceased		
Mean (SD) [Median]	6.8(5.4)[6]	7.3(8.3)[5]
Proportion	67 (12.6)	76 (30.0)
Missing	21 (4)	
Time to death (days):		
≤7	48(72)	53(70)
8 to 14	14(21)	12(16)
15 to 21	3(4)	4(5)
> 21	2(3)	7(9)
Transferred	1 (0.2)	

Table 2: Effect of Stroke Unit Care in Comparison to Medical Ward Care on Time-to-Death and on Time-to-Discharge Alive (n=730)

Outcome	β(SE)	HR[#]	95% CI
Time to death (n=139)	-0.94(0.17)	0.39	0.28, 0.55
Time to discharge alive (n=509)	0.223 (0.094)	1.25	1.04, 1.50

[#]Hazard ratio (HR) is for Stroke Unit care vs. Medical Ward care adjusted for age and sex. Note time to death is a negative outcome and time to discharge alive is a positive outcome.

Table 3: Characteristics of the Patients admitted to the Stroke Unit over Time (n=509)

Variables	2014 (n=71)	2015 (n=199)	2016 (n=239)
Age: mean (SD)	55.5(14.2)	59.4(14.6)	56.8(14.4)
Men (%)	59.2	60.8	62.8
Stroke Severity (NIHSS):mean (SD)[%]			
Mild	2.5(1.95)[31]	2.2(1.7)[25]	2.8(1.7) [20]
Moderate	9.6(2.6)[35]	9.9(2.5)[42]	10.2(2.6) [39]
Severe	18.9(2.8)[26]	18.8(2.7)[26]	18.6(2.6) [26]
Very Severe	27.7(3.8)[4]	31.0(4.5)[2]	28.1(3.5) [6]
Missing	[4]	[5]	[9]
Length of stay: mean (SD) days	8.2 (4.8)	9.7(7.7)	8.5(6.6)

Table 4: Effect of Year on Time-to-Death and Time-to-Discharge

Variables	Time to Death Hazard Ratio (95% Hazard Ratio CI)	Time to Discharge Hazard Ratio (95% Hazard Ratio CI)
Year (2014)	Reference	Reference
2015	0.80(0.40 1.61)	0.83(0.61 1.12)
2016	0.65(0.33 1.28)	1.01(0.76 1.36)
Stroke Severity (NIHSS)		
Mild	Reference	Reference
Missing	4.52(1.07 19.06)	0.49(0.32 0.76)
Moderate	1.58(0.44 5.67)	0.64(0.51 0.82)
Severe	6.82(2.08 22.37)	0.40(0.31 0.53)
Very Severe	18.84(5.26 67.46)	0.18(0.09 0.36)
Women vs. Men	0.77(0.46 1.30)	0.93(0.77 1.13)
Age (per decade)	0.88(0.76 1.02)	1.00(0.94 1.07)

CHAPTER 5-INTEGRATION OF MANUSCRIPT 1 AND 2

Manuscript 1 demonstrated that stroke unit care at the Korle-Bu Teaching Hospital is associated with a reduction in in-hospital mortality compared to the general medical wards. Furthermore, patients receiving care at the stroke unit had a shorter length of stay at the stroke unit compared to the general medical ward. The literature on stroke unit care in developing countries has focused on providing evidence on the impact of stroke unit care on stroke outcomes. A major barrier to the implementation of stroke unit care in LMICs is the lack of financial and medical resources. Yet, less focus has been paid to the association between resource use and stroke outcomes. In the presence of limited resources and competing interests, it is vital to estimate the extent to which available resource used is associated with favourable stroke outcomes in Ghana. This is important to ensure that the limited health care resources allocated to providing stroke unit care is efficiently used to realise optimum outcomes. The next manuscript entitled "Resource use and functional recovery from stroke in Ghana: The Case of Korle-Bu Stroke Unit" estimates the extent to which resource use is associated with stroke outcome of functional independence at discharge from the stroke unit.

CHAPTER 6 – MANUSCRIPT 2

Resource use and functional recovery from Stroke in Ghana: The Case of Korle-Bu Stroke Unit

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This manuscript will be submitted to Stroke

Abstract

Purpose

To estimate the extent to which stroke unit resource use (direct medical cost) is related to recovery of functional independence at time of discharge.

Methods

This is a study of an admission-to-discharge cohort of patients admitted to the Korle-Bu Teaching Hospital stroke unit in Ghana from 2014 to 2016. Regression analysis was used to estimate the association between direct cost and recovery of functional independence measured by the Barthel Index. Two estimators of recovery: absolute change from admission to discharge: and proportional change were used.

Results

Direct medical cost had a positive and significant association with recovery in functional independence. When absolute change is modelled, a dollar increase in cost results in a 0.04 unit change in functional independence. On the other hand, when proportional change is modelled, a dollar increase in cost results in a 0.002 or 0.2% increase in functional independence. Therefore, when absolute change of the outcome variable is used, the evidence suggests treating everyone the same regardless of their functional independence. However, when proportional change of the outcome variable is used, the evidence favours treating patients with the lowest functional independence as long as they are making improvements.

Conclusion

For patients admitted with higher levels of functional independence (BI of 85 and above), it may be more resource efficient to stabilize them medically and discharge home or to a rehabilitation center.

Introduction

Cardiovascular disease is the leading cause of death and disability adjusted life years (DALY) (1). Ischemic heart disease and stroke account for 85.1% of all deaths attributed to cardiovascular disease (1). The burden of stroke continues to increase especially in low and middle income countries (LMICs) (1). For instance, cardiovascular disease moved up four levels since 1990 to become the second leading cause of death in Africa (2). The increase in cardiovascular disease in Africa is placing an added burden on health care systems. It is important to identify the most cost-effective approaches to respond to this new challenge.

Organised stroke units are the most recommended way of delivering acute stroke care. Studies on the effectiveness of stroke unit care in LMICs has shown a benefit for mortality, medical complications, and independence (3–9) of similar magnitude to counties with highly resourced health systems. Although these studies provide evidence on outcomes of stroke units from LMICs, there is limited information on how resource use relates to stroke outcomes. This is important information that could guide allocation of resources to those who would benefit the most from organised stroke unit care taking into account the limited resources available. Supplementary table 2 summarizes studies that were found reporting on outcomes of stroke units. Of the 7 studies that we could report on, 3 did not include indicators of resource use. The other four studies had length of stay as the common resource indicator although two studies also had use of computed tomography scans, services and drugs as resource indicators. Furthermore, the most common outcome of these studies was case-fatality (n=6/7) and complications (n=4/7); three studies reported on some aspect of function, two using the Barthel Index (BI).

In Ghana, stroke is the 5th leading cause of death. Stroke related death increased by 16.9% in the last decade (2). As part of wider efforts to strengthen stroke prevention and care, a stroke unit was established at the Korle-Bu Teaching Hospital, Accra, Ghana in 2014. An earlier study reported on the changes in stroke outcomes observed following implementation of the unit, for the common outcome, mortality and length of stay (pre-implementation period: 2012-2013, post-implementation period: 2014-2016) (10). The results showed that patients receiving treatment at the stroke unit had a 61% less risk of dying compared to patients receiving treatment at the medical wards (10). To the best of our knowledge, there is no information on how resource use at the stroke unit is associated with stroke outcomes. The purpose of this study is to estimate the extent to which

stroke unit resource use (direct medical cost) is related to recovery of functional independence at discharge.

Methods

Study Design

This is a study of an admission-to-discharge cohort from a stroke unit at the KBTH in Ghana. From the inception of the stroke unit, the BI was collected at admission and discharge. Functional independence was measured using the BI at admission and discharge. This information was gathered for patients admitted to the stroke unit between January 2014 and December 2016. Direct cost of stroke unit care was calculated using information from the accounting department. Ethics approval was obtained from McGill University, Faculty of Medicine Institutional Review Board and the Institutional Review Board of the Korle-Bu Teaching Hospital.

Population

The target population was stroke patients receiving care at the stroke unit at KBTH from January 2014 to December 2016. To be included, patients must have been diagnosed of acute stroke and admitted within 2 weeks of stroke onset. Patients who had suffered a transient ischemic attack and subdural haematoma were excluded. A total sample of 383 patients was included in the analysis.

Measurement

The outcome was functional independence measured at admission and discharge using the BI. The BI, developed to measure functional independence has 10 items on bathing, grooming, feeding, dressing, toilet use, ascend/descend stairs, bowel management, bladder management, bed/wheel chair transfer and mobility. The total score ranges from 0-100**,** with 0-20 indicating total dependence, 21-60 indicating severe dependence, 61-90 indicating moderate dependence and 91-99 indicating independence. Direct medical cost was defined as cost due to resource use associated to receiving care at the stroke unit. The aggregate cost of hospitalization included accommodation, feeding, sanitation cost, use of medical supplies, admissions cost and documentation. Data on direct cost was obtained using information from the admission and discharge books and the accounting department. A data abstraction form was developed to standardize data collection.

Statistical Analysis

Two estimators of recovery were used: (i) absolute change from admission to discharge: and (ii) proportional change calculated as the absolute change divided by the average of the two measurements. In modeling change scores, there is concern that baseline scores exerts a great influence on the score a person obtains post-intervention and consequently on the change. It is, therefore, recommended that the baseline score be adjusted for in a regression analysis (11). However, including the baseline score on the right side of the regression equation violates an assumption of linear regression: that is the x variables should be measured without error or at least the error in an x variable should not be associated with the error in the y variable (12). One way of removing some of the error by adjusting for baseline, is to create a categorical variable much like what would be done if a stratified analysis was to be considered, stratified by baseline value. Therefore, baseline BI was categorized into four groups BI≤30, BI 31-60, BI 61-90 and BI>90.

Others have proposed dividing the difference by the mean to obtain proportional change (13–16). The proportional change is unbiased as the two sources of error in the numerator (pre and post measures) is cancelled out as these sources of error also occur in the denominator. As there is no consensus on the best approach, we estimated four models all of which included adjustment for age and gender:

Model 1: $\Delta BI = cost + age + gender$

Model 2: $\Delta BI = baseline\ BI + cost + age + gender$

Model 3: $\Delta BI = baseline\ BI_x + cost + age + gender$

Model 4: $\frac{\Delta BI}{mean\ BI} = cost + age + gender$

Where ΔBI is change in BI and x is 1-4 representing levels of functional independence.

Results

A total sample of 383 patients had data on the BI at both admission and discharge. Out of 383, 3 patients were missing BI at admission, 45 at discharge, and 55 both. Table 1 describes the sample.

INERT TABLE 1 HERE

Table 2 presents the results on the association of direct medical cost on recovery of functional independence over the stroke unit period. Direct medical cost in USD had a positive and significant

association with functional outcome in all four models. Model 1 demonstrated that a one dollar increase in cost results in a 0.04 unit change in the BI.

Models 2 and 3 adjusted for baseline BI as a continuous and categorical variable respectively. Model 2 illustrates that a 1 unit difference in baseline BI was associated with a -0.07 change (less change) in BI score. To make these parameters more interpretable, a 5-unit difference in BI at baseline was considered showing an association with BI change of -0.35 units.

Results from model 3, with the BI categorized into four levels, shows that a higher level of functional independence at admission is associated with less change by an average of -5 units. The estimate of cost did not change across these three models. In model 4, the outcome variable was proportional change in BI. A dollar increase in cost was associated with a 0.002 or 0.2% increase in functional independence.

INSERT TABLE 2 HERE

Discussion

This study estimated the extent to which resource use measured by direct medical cost was associated with functional independence at discharge at the Korle-Bu stroke unit in Ghana. It also demonstrated how the modeling of change in outcome may result in different policy decisions. In general, results from the study suggests that, for people surviving the acute care period, resource use is associated with a gain in functional independence from admission to discharge.

Although resource use at the stroke unit is associated with a gain in functional independence, results from the four models have different implications on recourse allocation. For example, assuming that $125 worth of stroke care was available per person, results from models 1 to 3 indicate that for every $125, the associated change in function on the BI was 5 points (one level of independence on 1 item). To put this in context, everybody who has a baseline BI up to 95 can change 5 points and theoretically would benefit from treatment on the stroke unit. On the other hand, model 4 implies that for every $125 available, a 25% increase in BI is obtained. However, people with a BI greater than 85 do not have the room to change by 25% (this will imply a total BI over 100). Therefore, if absolute change of the outcome variable, BI, is used, the implication

from models 1 to 3 is that everyone would be given the same resources regardless of their functional independence.

However, the model for proportional change (model 4) favours treating patients with the lowest functional independence as long as they are making improvements. For patients admitted with higher levels of functional independence (BI of 85 and above), it may be more resource efficient to stabilize them medically at the stroke unit and discharge home or to a rehabilitation center as it is not cost-efficient to treat them in acute-care (they cannot make the requisite gain, change of 25%, with the resource envelop). Thinking this way will relieve more resources for the treatment of patients with lower functional independence who have greater room to improve for the same amount of resources. This is because, at the lower level of functional independence, a 5-point increase in BI score for example from 25 to 30 is indicative of greater improvements in activities of daily living compared to a 5-point increase from 85 to 90 on the BI. It is important to note that due to the ceiling effect of the BI, patients who appear to have a high BI (although may not have enough room to change in the BI) are most likely to still benefit from being treated at the stroke unit.

The results of this study must be interpreted with caution. Due to unavailable data on functional outcomes for stroke patients receiving care at the general medical wards, we were unable to calculate the cost effectiveness of stroke unit care. As it stands, we are unable to conclude whether stroke unit care is more cost effective than care at the general medical ward. In addition, the scope of direct cost included in this study was limited. A broader definition of cost which includes cost of diagnostic tests, medication and other patient related cost would provide more information on the cost associated with stroke unit care. Future research should aim to estimate this. In summary, modeling absolute change would indicate a policy to treat everyone the same. Modeling proportional change would indicate a different policy. As the BI is a hierarchical measure, what a person can do at each level can be predicted. Once someone has reached a BI of 85, they can do all of the functional items except walking up stairs and may still need assistance with bathing but are not dependent. At the lower end, the meaning of gains that are insufficient to move a person out of the dependent range (60/100) may be queried. For people who reach a recovery plateau that is still below 60, discharge to another level of care may be indicated, if such a facility is available.

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Table 1: Characteristics of Patients Admitted to the Stroke Unit

Variable	Mean (SD)
Age	57.9(13.7)
Gender: Women	197
Men	316
Cost	145.0(72.2)
Barthel Index at Admission	31.6(30.4)
Barthel Index at Discharge	41.3(31.9)

Table 2: The Relationship Between Resource Use and Functional Outcome at Discharge

Variables	Model 1 (N=383)	Model 2 (N=383)	Model 3 (N=383)	Model 4 (339)
Cost (USD)	**0.04(0.01)**	**0.04(0.01)**	**0.04(0.01)**	**0.002(0.0005)**
Baseline Barthel		**-0.07(0.03)**	**-5.02(1.89)**	
Age (Decade)	-0.60(0.64)	-0.78(0.64)	-0.73(0.64)	0.04(0.03)
Women	-0.98(1.75)	-1.07(1.74)	-1.13(1.74)	0.10(0.07)
R-Squared	0.03	0.04	0.05	0.07

Model 1: $\Delta BI = cost + age + gender$; Model 2: $\Delta BI = baseline\ BI + cost + age + gender$; Model 3: $\Delta BI = Baseline\ BI_x + cost + age + gender$; Model 4: $\frac{\Delta BI}{mean\ BI} = cost + age + gender$

Supplementary Table 1: Distribution of Barthel Index at Admission and Discharge

Distribution	BI at Admission	BI at Discharge
10 Percentile	0	0
25 Percentile	10	17.5
50 Percentile Median	20	35.5
75 Percentile	45	60
90 Percentile	90	95
100 Percentile	100	100

Supplementary Table 2: Resource Indicators and Outcome measures used in studies of Stroke Unit in Developing Countries

Author (Year)	Country [Year of Data Collection]	Source of Data	Resource Indicators	Outcomes [Measures]
Pandian et al. (2011)	India [Mar 2008-sep 2009]	Medical Records	Length of Stay, Use of rehabilitation services, initiation of secondary prevention drugs	In-hospital Mortality, Rate of medical complications.
de Villiers et al. (2009)	South Africa [Dec 2001-Feb 2002/ Mar 2002-May 2002]	Ward Registry	length of stay, number of CT scans	In-hospital mortality, referral to inpatient rehabilitation, transfer to tertiary hospital,
Suwanwela et al. (2007)	Thailand (2001-2003)	Unclear	length of stay	In-hospital mortality, rate of neurological and medical complication,
Krespi et al. (2003)	Turkey [Jan 1997-Mar 1999/After April 1999]	Stroke Registry	length of stay,	In-hospital case fatality rate, proportion of independence at discharge, rate of medical complication OCSP Criteria for stroke severity Modified Rankin Scale-functional status
Ma et al. (2004)	China (Dec 2001-Jan 2003)	Unclear		Change in Functional Independence, stroke severity, OHS, rate of medical complication Barthel Index, NIHSS and Oxford Handicap Scale

Cabral et al. (2003)	Brazil [Mar-Dec 2000]			Mortality rate, death/independence/ independence at 10 days, 1 month, 6 months Scandinavian Scale, Barthel Index
Supanc et al. (2009)	Croatia [1995-2006]	medical records and hospital registry		In-hospital case fatality, prevalence of risk factors amongst patients who died

CHAPTER 7-INTEGRATION OF MANUSCRIPT 2 AND 3

In Manuscript 1 and 2, we examined the effect of stroke unit care on primary outcomes of death and length of stay and the extent to which resource use is associated with functional outcome as measured by the Barthel Index, all at time of discharge. Empirical studies suggest that recovery from stroke can continue past 6 months post stroke with most functional recovery taking place within the first 3 to 6 months. To comprehensively evaluate the effectiveness of stroke unit care on stroke outcomes in Ghana, one of my objectives was to consider longer term stroke outcomes such as HRQL.

One of the challenges in estimating effectiveness of stroke units is that the measures are not patient-centered assessing very basic function or disability from the clinician's view point. In addition, most existing measures of stroke impact or HRQL are long and include items that are not culturally relevant or easily translated into the local language. For example, the Stroke Impact Scale, though stroke specific includes 59 items. After carefully considering the items in a number of measures, the Preference Based Stroke Index (PBSI) and the generic HRQL measure, the EuroQol-5D three level (EQ-5D-3L) were short and included items relevant to the Ghanaian population. However, the validity of the PBSI had not been independently established and so, before choosing it for Ghana, I undertook a validation study.

The object of the next chapter is to estimate the construct validity of the PBSI on a sample of stroke survivors 3 months post stroke.

CHAPTER 8- MANUSCRIPT 3

Further Validation of the Preference Based Stroke Index (PBSI) Three Months After Stroke

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Abstract

Objective: To estimate the construct validity of the Preference Based Stroke Index and its value added over a generic measure, the EuroQol-5D-3L at 3 months after stroke.

Design: Secondary analysis of an existing inception cohort. Pearson correlation coefficients were estimated to test construct validity and Generalized Estimating Equation analysis was conducted to compare the strength of the correlations of the Preference Based Stroke Index and EuroQol-5D-3L with other measures.

Setting: Community

Subjects: Participants (n=488) with confirmed diagnosis of stroke hospitalized within 72 hours

Main Measures: Health Related Quality of Life was measured using Preference Based Stroke Index and Euroqol-5D-3L. For validation purposes, the Stroke Impact Scale, Short Form-36 V1, Walking Speed, Two-Minute Walk Test, Berg Balance Scale and the Mini-Mental State Examination were used. The Barthel Index and Canadian Neurological Scale were used to define known groups.

Results: Preference Based Stroke Index correlated moderately with the EuroQol-5D-3L (r=0.73), Walking Speed (r=0.68), Two Minutes Walk Test (r=0.73) and Berg Balance Scale (r=0.70) and strongly with Stroke Impact Scale Activities of Daily Living (r=0.80). Correlations were significantly higher for the Preference Based Stroke Index than EuroQol-5D-3L. Participants with mild stroke had a higher mean Preference Based Stroke Index score (77.9±20.6) than participants with severe stroke (62.8±20.3). Participants with functional independence had higher Preference Based Stroke Index (85.7±11.9) than those dependent for activities of daily living (60.8±19.7).

Conclusion: Preference Based Stroke Index demonstrated significantly higher construct validity compared to the EQ-5D-3L at 3 months post stroke and can discriminate amongst known groups.

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Further validation of the Preference-Based Stroke Index three months after stroke

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Abstract

Objective: To estimate the construct validity of the Preference-Based Stroke Index and its value added over a generic measure, the EuroQol-5D-3L at three months after stroke.

Design: This is a secondary analysis of an existing inception cohort. Pearson correlation coefficients were estimated to test construct validity and Generalized Estimating Equation analysis was conducted to compare the strength of the correlations of the Preference-Based Stroke Index and EuroQol-5D-3L with other measures.

Setting: Community.

Subjects: Participants ($n = 488$) with confirmed diagnosis of stroke hospitalized within 72 hours.

Main measures: Health-related quality of life was measured using Preference-Based Stroke Index and EuroQol-5D-3L. For validation purposes, the Stroke Impact Scale, Short Form-36 V1, Walking Speed, Two-Minute Walk Test, Berg Balance Scale, and the Mini-Mental State Examination were used. The Barthel Index and Canadian Neurological Scale were used to define known groups.

Results: Preference-Based Stroke Index correlated moderately with the EuroQol-5D-3L ($r = 0.73$), Walking Speed ($r = 0.68$), Two-Minute Walk Test ($r = 0.73$), and Berg Balance Scale ($r = 0.70$) and strongly with Stroke Impact Scale Activities of Daily Living ($r = 0.80$). Correlations were significantly higher for the Preference-Based Stroke Index than EuroQol-5D-3L. Participants with mild stroke had a higher mean Preference-Based Stroke Index score (77.9 ± 20.6) than participants with severe stroke (62.8 ± 20.3). Participants with functional independence had higher Preference-Based Stroke Index (85.7 ± 11.9) than those dependent for activities of daily living (60.8 ± 19.7).

Conclusion: Preference-Based Stroke Index demonstrated significantly higher construct validity compared to the EuroQol-5D-3L at three months post stroke and can discriminate among known groups.

Keywords

Measurement, stroke, utility, condition specific preference measure

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Introduction

The measurement of stroke outcomes has had two main aims: describing the impact of stroke and evaluating the effects of interventions.[1,2] Little focus has been paid to the measurement of the impact of organizational or policy changes that need outcomes linked to cost. In a recent topical review on home rehabilitation for stroke,[1] Mayo identified the value of using utility measures for evaluation of these system-wide changes. The most widely used utility measures are generic, meaning that they are developed for use in the general population to identify the life impact of common health states. The best known of these generic utility measures are the EuroQol-5D (EQ-5D),[3] Short Form-6D[4] derived from the Short Form-36, and Health Utilities Index.[5] All have been used in stroke, some extensively.[6–8] A key feature and potential limitation of these measures is that, while patients rate themselves on the domains yielding a health profile, these profiles are valued by members of the general population not the people with stroke.

There is now an emerging literature that patient preferences for health states differ from the general population in important ways that would render the use of generic measures less appropriate for evaluation of policy changes that apply to stroke.[9] As a result, condition-specific preference-based measures are being developed. Stroke has one of the earliest preference-based measures, the Preference-Based Stroke Index, developed by presenting people with stroke and caregivers with outcomes from existing measures and having them rate the importance and impact of these outcomes.[10] The 10 most impactful items were walking, stairs, physical activities, recreational activities, work/activity, driving, memory, speech, coping, and self-esteem, evaluated on a three-point scale. Rating scale method was used to obtain a weight for the best and worst levels of each dimension.

A preliminary assessment of validity of the Preference-Based Stroke Index, carried out on the same sample used for its development, showed moderate to high convergent validity with the EuroQol-Visual Analog Scale ($r=0.68$), all Short Form-36 domains ($r=0.4-0.78$) except Role Emotional ($r=0.32$) and could discriminate between known groups.[11] Although the developmental study provided support for the validity of the Preference-Based Stroke Index, only chronic stroke patients were evaluated. Further validation is warranted on an independent sample at an earlier point of recovery, a period when policy changes are often initiated particularly in the hyperacute and acute period of stroke. While long-term outcomes after stroke are of value, from a policy perspective, many events and circumstances can affect longer term stroke outcomes which may mask the impact of the policy innovation implemented in the early period after stroke.

Thus, the global aim of this study is to contribute further evidence for the construct validity (convergent and discriminant validity) of the Preference-Based Stroke Index and its value added over a generic utility measure, EQ-5D-3L. Specifically, the objectives are to estimate, at three months post stroke, the degree of association between the Preference-Based Stroke Index and other measures of stroke impact including the EQ-5D-3L, Stroke Impact Scale, Short Form-36 Health Survey, and performance-based measures of physical and cognitive ability, compare these associations with those from the EQ-5D-3L, and assess the ability of the Preference-Based Stroke Index to discriminate among known groups.

Methods

This is a secondary analysis of an existing inception cohort of people with stroke. The methods and study sample have been described previously.[12] Briefly, subjects with a confirmed diagnosis of stroke hospitalized within 72 hours were included. Excluded were people with subarachnoid hemorrhage, coexisting severe illness, and cognitive or comprehension impairments. Data collection was carried out from June 2002 to March 2005. Assessments were done within three days and at three months by trained professionals. This analysis is restricted to the three-month survivors. Ethics approval was obtained from the McGill University review board.

Measures

The two measures of interest are the Preference-Based Stroke Index and the EQ-5D-3L. The Preference-Based Stroke Index is described in section "Introduction." It has 10 dimensions evaluated on a three-point scale. Preference weights were elicited from 32 stroke survivors and 28 caregivers. To facilitate its use, a valid simple score was generated from the rating scale values.[11] The EQ-5D-3L is a descriptive system of health-related quality-of-life states with five dimensions: mobility, self-care, usual daily activity, pain and discomfort, and anxiety/depression with three response levels of severity. The EQ-5D-3L produces 243 health states. For validation purposes, the most well-known outcomes for stroke were chosen. The Stroke Impact Scale,[13] the Short Form-36 Version One,[14] Walking Speed,[15] Two-Minute Walk Test,[16] Berg Balance Scale,[17] and the Mini-Mental State Examination[18] were included in the analysis. Known group validity is the ability of a measure to discriminate among groups of people known to differ on a trait.[19] For known-groups validity, the categories of stroke severity from the Canadian Neurological Scale (CNS)[20] and the Barthel Index[21] were contrasted. Where available, age-specific normative data were included for comparison.[22–24]

Data analysis

Because the distribution of the measures was normal and the relationships between variables on visual inspection were linear, Pearson correlation coefficients (r) were estimated. For validation purposes, values of $r \geqslant 0.8$ are considered strong, $0.4 \leqslant r < 0.8$ moderate, and $r < 0.4$ as weak.[25] To compare the strength of the correlations of the Preference-Based Stroke Index and EQ-5D-3L with other measures, Generalized Estimating Equation analysis was conducted, which accounted for the non-independence of the Preference-Based Stroke Index and EQ-5D-3L. To test the known-groups validity of the Preference-Based Stroke Index, two groups were defined based on the level of stroke severity measured by the CNS ($CNS < 9$ and $CNS > 11$), while three groups were defined based on participant's level of functional independence measured by the Barthel Index (<60, 65–95, and 100). Known groups were tested using linear regression. All statistical analyses were conducted using SAS V9.3.

Results

Table 1 shows the characteristics of the 488 participants (mean age: 71.5; SD: 12.8; predominantly men) on all stroke outcomes at three months post stroke. The mean score on the Preference-Based Stroke Index was higher compared to the EQ-5D-3L. Considering the value of 100 on the Stroke Impact Scale subscales as optimal, the subscale with the lowest score was Participation, despite a mean score on the Stroke Impact Scale Activities of Daily Living of 71 and a score on Communication of over 90. This sample judged their overall recovery at near 69. The Short Form-36 subscales are presented with normative values. Physical Function and Role Physical showed the most disparity from the norm. For the performance outcomes, the values for both Walking Speed and Two-Minute Walk Test were both lower than norms and the balance score indicated that almost half had only acceptable balance.

Also shown are the correlations with Preference-Based Stroke Index and EQ-5D-3L, which are strongly intercorrelated. The Preference-Based Stroke Index correlated strongly with the Stroke Impact Scale Activities of Daily Living and the Short Form-36 Physical Function component and moderately with Walking Speed, Two-Minute Walk Test, and Berg Balance Scale. Correlations were highest for constructs related to Physical Function and Participation and always significantly higher for Preference-Based Stroke Index than EQ-5D-3L.

Table 2 presents the results of comparing Preference-Based Stroke Index scores across known groups of people with different stroke severities as measured by CNS and Barthel Index. Participants with less severe stroke ($CNS > 11$) had a higher mean Preference-Based Stroke Index score compared to participants with more severe stroke. Similarly, participants with functional

Table 1. Characteristics of participants ($n = 488$) on all stroke outcomes and Pearson correlation coefficients.

Variable	Mean ± SD (quartile range)	Correlation [95% CI] with Preference-Based Stroke Index	Correlation [95% CI] with EQ-5D-3L
Preference-based measures (0–100)			
Preference-Based Stroke Index Total Score	68.3 ± 20.8		
EQ-5D-3L	63.1 ± 21.6	0.73 [0.7, 0.8]	
Stroke Impact Scale (SIS; 0–100)			
Activities of Daily Living	71.2 ± 27.4	**0.80 [0.74, 0.84]**	**0.73 [0.67, 0.79]**
Communication	91.1 ± 15.4	0.42 [0.35, 0.50]	0.33 [0.24, 0.41]
Participation	56.6 ± 31.8	**0.77 [0.72, 0.82]**	**0.66 [0.58, 0.73]**
Recovery VAS	68.8 ± 21.6	0.56 [0.47, 0.64]	0.47 [0.36, 0.57]
Short Form-36-V1 (normative value), range: 0–100			
Physical Function (75.7)	49.1 ± 32.4	**0.79 [0.75, 0.82]**	**0.73 [0.47, 0.61]**
Role Physical (76.2)	30.8 ± 39.0	0.51 [0.41, 0.59]	0.46 [0.35, 0.56]
Pain (74.0)	73.6 ± 28.3	0.27 [0.15, 0.38]	0.52 [0.41, 0.61]
General Health Perception (73.5)	61.9 ± 19.8	0.38 [0.27, 0.49]	0.41 [0.29, 0.51]
Vitality (67.7)	53.2 ± 22.6	0.44 [0.33, 0.53]	0.43 [0.31, 0.53]
Social Function (87.0)	62.4 ± 31.2	**0.60 [0.54, 0.66]**	**0.54 [0.22, 0.46]**
Role Emotional (83.4)	57.5 ± 43.7	0.49 [0.38, 0.58]	0.39 [0.27, 0.50]
Mental Health Index (79.3)	69.6 ± 21.8	0.47 [0.37, 0.56]	0.39 [0.27, 0.49]
Performance outcomes (normative value)			
Walking Speed (≈0.94), m/s	0.8 ± 0.5 [0.6]	**0.68 [0.60, 0.7]**	**0.62 [0.53, 0.70]**
Two-Minute Walk Test (159), m	85.8 ± 54.6 [82]	**0.73 [0.66, 0.79]**	**0.66 [0.58, 0.73]**
Berg Balance Scale (0–56)	43.3 ± 16.0	**0.70 [0.63, 0.76]**	**0.67 [0.59, 0.74]**
Mini-Mental score (0–22)	19.0 ± 3.2	0.54 [0.42, 0.63]	0.45 [0.32, 0.56]

CI: confidence interval; EQ-5D-3L: EuroQol-5D-3L; VAS: Visual Analog Scale.
Normative values reported are only age specific.
Bolded values indicate statistically different correlation coefficients for the Preference-Based Stroke Index and EQ-5D-3L.

independence (Barthel score: 100) had higher Preference-Based Stroke Index than those with the lowest independence (Barthel score < 60).

Discussion

The Preference-Based Stroke Index demonstrated strong convergent validity with the EQ-5D-3L, Stroke Impact Scale, and the Short Form-36 Physical and Social Function components with correlation coefficients greater than 0.7. The Preference-Based Stroke Index demonstrated moderate convergent validity with the Mental Health, General Health Perception, Vitality, Role Emotional, and Role Social components of Short Form-36 and Mini-Mental State Examination. The Preference-Based Stroke Index also demonstrated divergent validity with the Short Form-36 Pain domain with a weak correlation coefficient of 0.27. This was expected as pain was not an area nominated by stroke survivors and hence not included in the Preference-Based Stroke Index. Furthermore, the Preference-Based Stroke Index correlated more strongly than the EQ-5D-3L with Stroke Impact Scale Activities of Daily Living and Participation, the Short Form-36 Physical and Social Function, Walking Speed, Two-Minute Walk Test, and Berg Balance Scale. Furthermore, it was able to discriminate among patients with different levels of stroke severity and functional independence.

The Preference-Based Stroke Index is a stroke-specific preference-based measure that generates

Table 2. Difference in mean values on the Preference-Based Stroke Index according to known groups of stroke severity.

Measure	*N*	Preference-Based Stroke Index score, mean (SD)	*B* [95% CI]
Canadian Neurological Scale score			
⩽9	302	62.8 (20.3)	Reference
9 < CNS ⩽ 10	70	75.7 (14.1)	12.9 [7.7, 18.0]
>10	116	77.9 (20.6)	15.0 [10.8, 19.3]
Barthel Index score			
<60 (low independence)	308	60.8 (19.7)	Reference
65–95 (moderate independence)	132	79.3 (16.9)	18.5 [14.7, 20.2]
100 (independent)	48	85.7 (11.9)	24.8 [19.2, 30.4]

CI: confidence interval; CNS: Canadian Neurological Scale.
t-test on difference in means between groups (each group compared to the reference indicated) is significant at $P < 0.0001$.

310 theoretical health states (59,049: number of response options$^{\text{number of items}}$) that can be used for studies linked to cost. The Preference-Based Stroke Index total score is generated by multiplying the value for the response options (e.g.1, 2, 3) by the preference weight derived during the initial evaluation[11] and rescaled to range from 0 to 100. This simple score is valid because, during the development of the Preference-Based Stroke Index, the response options were selected to have interval properties.

This study used a larger sample and evaluated seven outcome measures at three months post stroke. This period was chosen as it is relevant for the evaluation of policy- or clinical-level changes implemented in the early phase of stroke. If the effects of these innovations are not seen early on, it is unlikely that they will emerge later on as most would be implemented to improve the immediate health state of the patient. This study adds to a growing body of literature supporting the validity of the Preference-Based Stroke Index as a stroke-specific preference measure that would be suitable for evaluating the cost effectiveness of stroke interventions. Similar results were obtained in the original development and validation study[11] where the correlations between the Preference-Based Stroke Index and the Short Form-36 subscales (range: 0.4–0.78) were stronger than those between the EQ-5D-3L subscales (range: 0.35–0.60) for all subscales except Pain and Role Emotional. Further validation of content and responsiveness was provided from a trial of community program targeting reintegration for people several years post stroke.[26] The Preference-Based Stroke Index showed the highest degree of responsiveness of any of the nine measures used in the trial over the 15 months of the program (effect size by 12 months: 0.27). In another study comparing the association between scores from Patient-Generated Index and preference-based measures, participants with stroke ($n = 249$) were asked to nominate the most important areas of their life affected by stroke; these were balance, memory, arm impairment, speech, walking, housework, vigorous activities, sports, driving, work, and recreation and leisure. Seven of the Preference-Based Stroke Index items were spontaneously nominated in this new sample.[27]

Both the current and original studies provide evidence of convergent validity and value added for the Preference-Based Stroke Index. This study has some limitations. The preferences elicited for the development of the Preference-Based Stroke Index were made over a decade ago. It is possible that although there is little evidence to suggest so,[28] that preference for health states may change slowly over time. However, while stroke severity may have changed over time as reflected by the average scores or proportions of people at specific recovery levels, secular changes in treatment should not affect the scoring structure and validity of the measure itself which is the main focus of this study.

Implications of findings and future research

The Preference-Based Stroke Index demonstrated higher construct validity with stroke-specific and performance-based measures than the EQ-5D-3L at three months post stroke. Unlike generic preference-based measures, the Preference-Based Stroke Index covers dimensions particularly relevant to the stroke population and, thus, usually assessed for research and clinical uses. For policy-level considerations where cost is often of major concern, the Preference-Based Stroke Index is useful to compare across treatments for stroke. For clinical use, the ratings on dimensions can be used to identify areas of further in-depth assessment, streamlining and tailoring the assessment process. For example, response to the driving item could stimulate a driving assessment.

At this stage, the Preference-Based Stroke Index can be used for the purpose for which it was developed using the simple weighted linear score. However, future research should develop a valuation function. The rating scale method was used to weigh the contribution of a limited set of health states (the corner states) for their detriment to perfect health. Although not all multidimensional health states were evaluated, the corner state ratings provide a relative weight for the item at the lowest level and this was used to derive the total score. The strength of this approach was that the values came from patients themselves, which is needed to compare across stroke interventions. Currently, ordinal methods are recommended (discrete choice or best–worst) for obtaining valuations from patients as these methods are much less cognitively challenging than the cardinal methods using direct elicitation such as standard gamble or time trade-off. Future work in this area is planned.

Clinical Messages

- The Preference-Based Stroke Index has moderate-to-strong evidence of construct validity as an outcome measure for stroke and stronger evidence than the EQ-5D-3L at three months post stroke.

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A.A. and N.M. designed the study and conducted the analysis. All authors contributed to writing of the manuscript.

Declaration of Conflicting Interests

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Table 1: Characteristics of Participants (n=488) on all stroke outcomes and Pearson Correlation Coefficients

Variable	Mean ± SD [Quartile Range]	Correlation [95% CI] with Preference Based Stroke Index	Correlation [95% CI] with EQ-5D-3L
Preference-Based Measures (0-100)			
Preference Based Stroke Index Total Score	68.3 ±20.8		
EQ-5D-3L	63.1 ±21.6	0.73 [0.7 0.8]	
Stroke Impact Scale (SIS; 0-100)			
Activities of Daily Living	71.2 ±27.4	**0.80 [0.74 0.84]**	**0.73 [0.67 0.79]**
Communication	91.1±15.4	0.42 [0.35 0.50]	0.33 [0.24. 0.41]
Participation	56.6 ±31.8	**0.77 [0.72 0.82]**	**0.66 [0.58 0.73]**
Recovery VAS	68.8±21.6	0.56 [0.47 0.64]	0.47 [0.36 0.57]
Short Form-36-V1 (0-100)[Normative Value]			
Physical Function [75.7]	49.1±32.4	**0.79 [0.75 0.82]**	**0.73 [0.47 0.61]**
Role Physical [76.2]	30.8±39.0	0.51 [0.41 0.59]	0.46 [0.35 0.56]
Pain [74.0]	73.6±28.3	0.27 [0.15 0.38]	0.52 [0.41 0.61]
General Health Perception [73.5]	61.9±19.8	0.38 [0.27 0.49]	0.41 [0.29 0.51]
Vitality [67.7]	53.2±22.6	0.44 [0.33 0.53]	0.43 [0.31 0.53]
Social Function [87.0]	62.4±31.2	**0.60 [0.54 0.66]**	**0.54 [0.22 0.46]**
Role Emotional [83.4]	57.5±43.7	0.49 [0.38 0.58]	0.39 [0.27 0.50]
Mental Health Index [79.3]	69.6±21.8	0.47 [0.37 0.56]	0.39 [0.27 0.49]
Performance Outcomes [Normative value]			
Walking Speed (meters per second) [≈0.94]	0.8±0.5 [0.6]	**0.68 [0.60 0.7]**	**0.62 [0.53 0.70]**
Two Minute Walk Test (meters) [159]	85.8±54.6 [82]	**0.73 [0.66 0.79]**	**0.66 [0.58 0.73]**
Berg Balance Scale (0-56)	43.3±16.0	**0.70 [0.63 0.76]**	**0.67 [0.59 0.74]**
Mini Mental Score (0-22)	19.0±3.2	0.54 [0.42 0.63]	0.45 [0.32 0.56]

Normative values are reported age-specific only. Bolded coefficients indicate statistically different correlation coefficients for the Preference Based Stroke Index and EQ-5D-3L

Table 2: Difference in Mean Values on The Preference Based Stroke Index according to Known Groups of Stroke Severity

Measure	N	Preference Based Stroke Index Score Mean (sd)	β [95% CI]
Canadian Neurological Scale Score			
<=9	302	62.8 (20.3)	Reference
9<CNS<=10	70	75.7 (14.1)	12.9 [7.7, 18.0]
>10	116	77.9 (20.6)	15.0 [10.8, 19.3]
Barthel Index Score			
<60 (low independence)	308	60.8 (19.7)	Reference
65-95 (moderate independence)	132	79.3 (16.9)	18.5 [14.7, 20.2]
100 (independent)	48	85.7 (11.9)	24.8 [19.2, 30.4]

T-test on difference in means between groups (each group compared to the reference indicated) is significant at $p<0.0001$

CHAPTER 9- INTEGRATION OF MANUSCRIPT 3 AND 4

In manuscript 3, we estimated the construct validity of the PBSI at 3 months post stroke in a sample of stroke survivors from Canada. The PBSI demonstrated construct validity and could discriminate amongst known groups in this sample. In Ghana, there has been no systematic way of measuring recovery from stroke. The Modified Rankin Scale or The Barthel Index have been used routinely to judge functional recovery from stroke usually at time of discharge. However, these measures are restricted to functional recovery and provide very little information on other domains of recovery and HRQL.

Considering the limited resources and the burden of using multiple measures to estimate recovery, we anticipate that short, generic and stroke-specific preference-based measures may fill this gap. In the next manuscript we compare estimates of recovery at 3 months post stroke, among three measures, the Barthel Index for ADL, a commonly used generic preference-based measure of HRQL, the EQ-5D-3L, and a stroke specific, preference-based, HRQL measure, the PBSI.

CHAPTER 10-MANUSCRIPT 4

Quantifying Recovery Post Stroke in Ghana-Measures Matter

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Abstract

Purpose: To compare estimates of recovery at 3 months post stroke among three measures, the Barthel Index (BI), the EuroQol-5D-3L (EQ-5D-3L), and the Preference Based Stroke Index (PBSI).

Methods: This is an observational study of a consecutive series of patients discharged from the stroke unit at the Korle-Bu Teaching Hospital, Accra, Ghana (N=82). Data collection was conducted from March 2017 to February 2018. Descriptive statistics, inter-measure correlations, and known-groups variability using generalized linear models was conducted.

Results: The measures were strongly intercorrelated with a correlation coefficient of 0.87 between the BI and PBSI, 0.83 between the BI and EQ-5D-3L and 0.82 between the PBSI and the EQ-5D-3L. Compared to the lowest level of functional independence (BI<30), people with a BI from 61-90 showed higher EQ-5D-3L and PBSI scores of 35.28 and 33.68 units respectively. People with a BI>90 also showed a higher EQ-5D-3L score of 54.54 units and a higher PBSI score of 54.23 units. In addition, the concordance between the two measures was 0.38 (31/82; 95% CI: 0.28-0.49). When the measures were discordant, the PBSI was most often higher than the EQ-5D-3L.

Conclusion: The EQ-5D-3L and PBSI provided similar estimates of recovery for functionally independent patients, however, the PBSI showed more variation for functionally dependent patients.

Introduction

Recovery from stroke often refers to a return to normal function and activities (1). Neurological, recovery has been classified as normal, near normal, compensatory, or minimal (2). These definitions imply that people are rated on tests of motor and cognitive function and activities and their "performance" on these tests indicates their level of recovery. Common tests and measures of recovery include the Modified Rankin Scale, Barthel Index (BI), and Functional Independence Measure (FIM) in addition to other performance-based measures (3,4). Although these measures provide interpretable information for purposes of evaluating change towards recovery, these measures do not reflect the health-related quality of life (HRQL) of patients or their preferred health states. The determination of whether a patient has recovered or not is highly dependent on the measure used. For instance, in a study of 495 stroke survivors (5), the BI was used to measure recovery based on independence in activities of daily living. The study found that 57% of participants had recovered. However, using the same sample, only 37% of participants were classified as recovered when the Fugl-Meyer measure of motor and sensory impairments was used. An estimate of HRQL may be a more comprehensive reflection of recovery.

HRQL measures can be generic (across health conditions) or condition specific (stroke for example). In addition, there are two main types of HRQL measures: profile measures that provide scores on multiple domains such as the Short Form-36 or the Stroke Impact Scale; or indices that provide one value across domains based on preferences which provide utilities useful for evaluation of costs. The most widely used generic utility measures are the Euroqol-5D (EQ-5D) (6), Short Form-6D (SF-6D)(7) derived from the SF-36, Health Utilities Index (HUI) (8), and the Australian developed Assessment of Quality of Life (AQOL-8D)(9). The most widely used utility measure in stroke is the EuroQol-5D (10,11). These measures have an advantage over profile measures in that they are usually short (5 to 10 items).

Generic utility or preference-based measures have been shown to have construct and content validity in conditions such as mental illness (13), visual disorders (14), COPD and asthma (15) but lack content and construct validity in stroke (16), multiple sclerosis (17) and dementia (18). Empirical evidence has shown the superiority of condition specific preference based measures for discrimination across levels of severity and for responsiveness to change (19). In a recent topical review on home rehabilitation for stroke (12), Mayo identified the value of using utility measures for evaluation of system wide changes such as providing stroke unit care.

It is common for stroke survivors to experience impairments of motor function, cognitive impairment, aphasia, lack of arm and hand function, and restrictions in participation (20,21). However most existing measures used in the stroke population do not include all the relevant domains important for the assessment of HRQL in the stroke population. A condition specific measure of HRQL, the Preference Based Stroke Index (PBSI) (16) was developed to address this concern specific to the stroke population.

There is a need to identify useful stroke specific measures in the context of Ghana. Ghana implemented the first stroke unit in 2014 and there are prospects of scaling up stroke care. Because resources are often insufficient to put in multiple measures, there is a need to identify valid, short stroke-specific preference-based measures for clinical and research purposes. Therefore, the purpose of this study is to compare estimates of recovery at 3 months post stroke, among three measures, the BI for ADL, a commonly used generic preference-based measure of HRQL, the EQ-5D-3L, and a stroke specific, preference-based, HRQL measure, the PBSI.

Methods

Study Design

This is an observational study of a consecutive series of patients discharged from the stroke unit at the Korle-Bu Teaching Hospital, Accra, Ghana during a time period 2 months preceding the targeted data collection (3 months post-stroke). A total of 172 patients were eligible, out of which 82 were recruited for this study. Dependency and HRQL were assessed at 3 months post stroke. Data collection was conducted from March 2017 to February 2018. Ethics approval was obtained from the McGill University, Faculty of Medicine Institutional Review Board and the Institutional Review Board of the Korle-Bu Teaching Hospital.

Outcomes

The primary outcomes were dependency and HRQL three months post stroke. Dependency is defined as the loss of autonomy in undertaking ADL which leads to the need for help and support to undertake these activities. Dependency at 3 months was measured using the BI. HRQL is defined as "a measure of the value assigned to duration of life as modified by impairments, functional state, perceptions and opportunities, as influenced by disease, injury, treatment and policy" (22). There are a number of measures that assess HRQL. In order to choose measures that were feasible to use and included items that were culturally relevant to Ghana, we reviewed the

items of 5 measures of HRQL; AQOL-8D, HUI, EQ-5D-3L, PBSI and SF-6D. HRQL was measured using the EQ-5D-3L, a generic measure and the PBSI, a stroke specific measure as they were short, simply worded and could be translated into the local language and had culturally relevant items. The EQ-5D-3L includes 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety and depression measured on a 3-point scale. The PBSI includes 10 dimensions: walking, stairs, physical activities, recreational activities, work/activity, driving, memory, speech, coping and self-esteem also measured on a 3-point scale. The two measures were translated into the local language (Twi) by two linguists, and back translated into English by the principal investigator. Both the English and Twi versions of the measures were available based on participants' preferences.

Data Analysis

Apart from basic descriptive statistics and inter-measure correlations, the first analysis was of known-groups variability using generalized linear models. Three estimators of difference over levels of dependence were used, the regression coefficients which provided an adjusted means difference from each level with respect to the lowest level, an adjusted t-statistic (β/se) which is an effect size, and Cohen's D effect size across adjacent categories (difference / pooled SD). We categorized participants into four levels of functional independence in ADL; BI<30, BI 31-60, BI 61-90 and BI>90. In the second analysis we calculated the concordance between the two measures of HRQL. All analyses were done using the SAS statistical software (v9.4).

The study was powered to detect a moderate effect size between the measures even in the presence of other variables using the formula provided by Green (1991): 50 + 8m, where m is the number of other variables to be considered (23). We originally planned to include age, sex, type of stroke, and stroke severity requiring an additional 32 subjects. In the end, stroke severity was not available.

Results

A total sample of 82 participants were recruited into the study with a mean age of 57±11.7. There were more men (60%) than women. Participants had a mean BI of 74.3±27.9 and a lower mean EQ-5D-3L (63±27.9) compared to the PBSI (64.7±27). The PBSI had a lower coefficient of variation of 41.75 compared to the EQ-5D-3L of 44.31. The PBSI also had a lower percent at floor (0%) and ceiling (6.67%) compared to the EQ-5D-3L (percent at floor =2.6% and ceiling= 23.68%). The three measures were strongly correlated with each other with a correlation

coefficient of 0.87 between the BI and PBSI, 0.83 between the BI and EQ-5D-3L and 0.82 between the PBSI and the EQ-5D-3L.

Table 1 shows the differences in values on the PBSI and EQ-5D-3L across levels of independence in ADL measured by the BI. Compared to the lowest level of functional independence (BI<30), for participant with a BI from 61-90, a unit increase in the BI increases HRQL measured by the EQ-5-3L by 35.28 units and HRQL measured by the PBSI by 33.68 units. For participants with a BI>90, a unit increase in the BI increases EQ-5D-3L score by 54.54 units and the PBSI score by 54.23 units. The PBSI had a larger effect size than the EQ-5D-3L for participants with a Barthel less than 90.

The concordance between the EQ-5D-3L and the PBSI is presented in Table 2. Figures 1A and 1B also shows the distribution across EQ-5D-3L and PBSI according to functional independence 3 months after stroke. The two measures correlate strongly (correlation is 0.82) across values of the BI.

The crude agreement between the two measures was 0.38 (31/82; 95% CI: 0.28-0.49), however, when discordant, the PBSI was more often higher than the EQ-5D-3L (66%; 34/51 of discordant pairs; 95% CI: 0.53-0.78).

Figure 1A: Distribution across PBSI and EQ-5D-3L according to functional independence 3 months after stroke

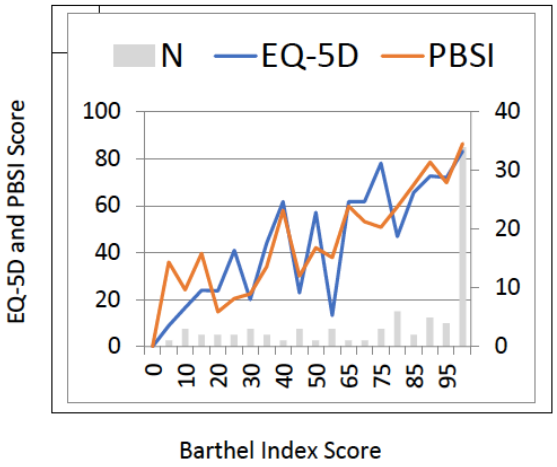
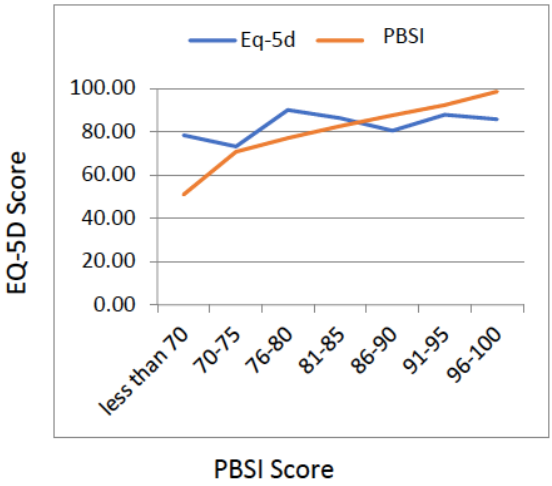


Figure 1B: Distribution of PBSI and EQ-5D-3L among functionally independent participants (Barthel = 100)



Discussion

In this study, we compared estimates of recovery 3 months after stroke using three measures; the BI, EQ-5D-3L and PBSI. All three measures were strongly correlated. However for participants functionally independent in ADL (BI=100), the PBSI and EQ-5D-3L showed more variability in HRQL. On average, both the EQ-5D-3L and the PBSI provided similar information on recovery 3 months post stroke however, the EQ-5D-3L had a ceiling effect. Furthermore, the PBSI had a larger effect size than the EQ-5D-3L. The degree of agreement between the EQ-5D-3L and the PBSI was low, with PBSI scores often higher than those of the EQ-5D-3L.

Similar results have been obtained in other studies. The EQ-5D-3L has been shown to have a ceiling effect across different patient populations (24) . In other studies comparing the EQ-5D-3L to the PBSI, the PBSI had no ceiling effect (16) and was able to discriminate among known-groups of functional independence (16).

Among people who are functionally independent, the EQ-5D-3L and PBSI provide similar results. However, among persons who are functional dependent, there is more variation across levels of dependence when using the PBSI. As most stroke intervention would target people within this

range of dependence, this implies that the PBSI may be more suitable as an outcome measure for recovery in Ghana.

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Table 1: Differences in values on the PBSI and EQ-5D-3L Across Levels of Independence in ADL Measured by the Barthel Index.

Variable	**Barthel≤30 Mean (SD)**	**Barthel:31-60 Mean (SD)**	**Barthel:61-90 Mean (SD)**	**Barthel>90 Mean (SD)**
N (%)	16 (20)	10(12)	18(22)	38(46)
EQ-5D-3L	27.0 (25.2)	33.5 (24.3)	64.0 (16.8)	82.4 (9.2)
Effect size[#]		0.3	1.5	1.5
β (se)*	Reference	6.5 (7.2)	36.9 (6.1)	55.4(5.5)
β (se)	Reference	9.6 (8.2)	**35.3 (6.9)**	**54.5 (6.2)**
t*	Reference	0.9	6.03	10.33
t	Reference	1.17	5.14	8.75
PBSI	28.18(18.57)	37.18(13.26)	64.88(14.16)	84.66(13.87)
Effect size[#]		0.6	2.1	1.4
β (se)*	Reference	7.03 (7.37)	**33.68 (6.01)**	**54.23 (5.51)**
β	Reference	9.0(6.4)	36.7(5.4)	56.5(4.8)
t*	Reference	0.95	5.61	9.85
t	Reference	1.4	6.74	11.82

*adjusted for age, sex, and type of stroke; # between adjacent categories

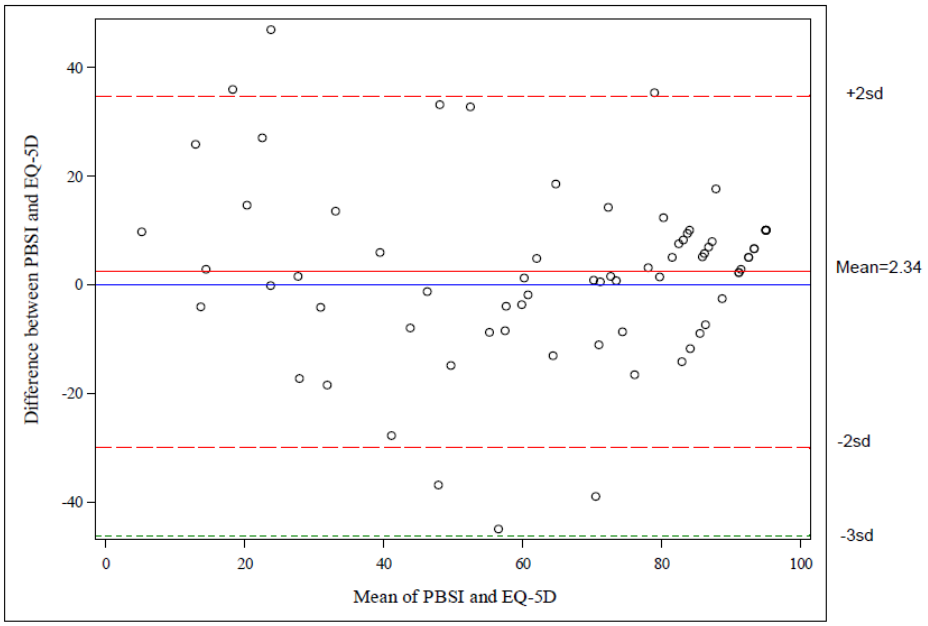
Table 2: Degree of Agreement between the EQ-5D-3L and PBSI

	PBSI						
EQ-5D-3L	0-30	30-50	50-70	71-80	81-90	90-100	Total
0-30	12	4	2	0	0	0	18
30-50	3	3	2	0	0	0	8
51-70	2	1	7	3	0	1	14
71-80	2	1	3	4	7	1	18
81-90	1	0	2	2	5	14	24
90-100						0	0

Crude Agreement rate=38%
Number where PBSI>EQ-5D-3L=34

Supplementary Material

Supplementary Figure 1: Bland Altman Plot for the PBSI and EQ-5D-3L



Mean of diff=2.34
Sd=16.18

Supplementary Table 1: Correlation amongst BI, PBSI and EQ-5D-3L 3 months after stroke

Measures	PBSI	EQ-5D-3L
BI	0.87	0.83
PBSI	1	0.82
EQ-5D-3L		1

Supplementary Table 2: Characteristics of Participant According to Functional Independence 3 Months After Stroke

Variable	**Barthel≤30 Mean (SD)(15)**	**Barthel:31-60 Mean (SD)(8)**	**Barthel:61-90 Mean (SD)(18)**	**Barthel>90 Mean (SD)(34)**
Age	67.7 (13)	62.25(7.5)	53.06(12.3)	54.6(9.8)
Gender				
Women	56	40	39	34
Men	44	60	61	65
Stroke Type				
Infarct	47	70	33	41
Haemorrhagic	33	10	50	41
Missing	20	20	17	19
Length of Stay	11.4(7.7)	10.6(4.0)	9.00(7.3)	7.38(6.1)
Fixed Cost	824.9(389.6)	836.1(256.3)	677.39(376.7)	621.81(327.3)

CHAPTER 11 - INTEGRATION OF MANUSCRIPTS 4 AND 5

The preceding chapter measured recovery from the clinician perspective. We estimated the effect of stroke unit care on HRQL 3 months after stroke using patient reported outcome measures. Results from this chapter indicate that the choice of measure has influence on the level of recovery measured. Furthermore, although these measures are patient reported, they are still based on predetermined categories. There may be differences in the meaning of recovery from the patient or clinician perspective. With the rising need for patient centered care, it is important to understand the meaning of recovery from the perspective of patients. The next chapter presents a qualitative analysis of the meaning of recovery from the perspective of a sample of participants in Ghana.

CHAPTER 12 - MANUSCRIPT 5

The Meaning of Recovery from The Perspective of Stroke Survivors in Ghana

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Abstract

Purpose: To gain insights on the meaning of recovery from the perspective of a sample of stroke survivors in Ghana.

Method: Face-to-face qualitative interviews were conducted with 11 stroke survivors who received care at the Korle-Bu Teaching Hospital in Accra, Ghana. All interviews were recorded and transcribed verbatim. A thematic analysis was guided by interpretative description methodology.

Results: Seven themes were identified representing the meaning of recovery: recovery as improvement in physical impairment, recovery as function and independence, recovery as acceptance and adaptation, recovery as progressive, recovery from a reference point, recovery and gratefulness to God and recovery as staying connected. Participants indicated that improvement in physical impairments such as walking was indicative of recovery however they focused more on their ability to perform activities most important to them. Maintaining relationships with family and friends was an important contributor to recovery. Furthermore, individual religious belief served as a resource during recovery. Participants who expressed gratefulness to God noted satisfaction with their level of recovery.

Conclusion: The meaning of recovery from stroke is unique to each individual, however most participants prioritised their ability to perform activities most important to them. Focusing on task-oriented rehabilitation based on meaningful activities may truly support patients' needs and recovery.

Introduction

Recovery has been defined as the "*process of regaining health or a normal condition after an illness, injury or a period of difficulty"* (1). For stroke survivors, recovery has often been conceptualized as regaining independence in undertaking activities of daily living and returning to work as a result of improvement in physical function such as motor control and speech (2).

Recovery from stroke depends on whose perspective it is taken and different perspectives have different measures. For example, widely used measures of stroke recovery, Modified Rankin Scale, Barthel Index, and Functional Independence Measure, (3,4) are classified as Clinician Reported Outcomes (ClinROs) (5) as the clinician rates the person on different activities considered to reflect recovery of the brain. Performance tests (PerfOs) have limited value in judging recovery as pre-stroke values are usually not available.

Qualitative studies on recovery from stroke suggest that patients and clinicians may have different perspectives on recovery (6,7). While clinicians may focus on improving physical impairments over time (7), studies have suggested that patients tend to focus more on regaining function and the ability to independently participate in activities that matters most to them (8–11). In addition, patients prioritise their ability to perform previous roles (8,12), social interaction (9,12–14) and emotional wellbeing (9,15). The difference in perspectives on the meaning of recovery has implications for how recovery is measured and the focus of care, especially during rehabilitation. For instance, in a study on patient's expectations for recovery after stroke, Wiles et al. (2002) (16) noted that, there was a lack of communication on what recovery meant to the clinician and the patient. Patients therefore assumed their service providers shared and were aware of their expectation of recovery, when this was not the case (16). This misalignment contributed to disappointment and frustration for patients.

Care that focuses on what patients' value has been termed patient-centered care (1) and this approach has been shown to improve quality of care and health outcomes, increase patient satisfaction while reducing the cost of providing this care (17). The use of patient-centered outcomes is a key element of patient-centered care and stroke care models are beginning to emphasize the use of these with the aim of focusing on what improvements matter to patients. (18–20).

Apart from differences that may exist between clinicians and patients, there is extensive research illustrating that culture and personal belief systems shape how individuals experience an illness and the meaning of recovery (21–23). Culture and belief systems have been shown to have a direct impact on how people cope and adapt post stroke (6,25), their openness to rehabilitation (24) and the role they play in their recovery (6). Additionally, different cultures value dimensions differently when it comes to recovery from stroke or measuring the impact of stroke on quality of life (6,27). For instance, Awolabi's (2011) study comparing the quality of life between a sample of stroke patients and healthy adults in Nigeria and Germany found that although stroke patients in both countries value physical domains similarly, patients in Nigeria rated the spiritual domains higher than those in Germany (27). As it stands, most of the literature on recovery from stroke has been conducted in Europe and North America. It is important to consider cultural and geographic variations in the meaning of recovery from stroke in order to provide culturally sensitive care. This is particularly important given the rising burden of stroke in Africa and the corresponding efforts to reform stroke care policies to improve stroke outcomes.

Patients care about symptoms and function (1) and there are well validated patient-reported outcome measures (PROMs) widely used in stroke outcomes research. For example, the Measuring Outcomes Study, Short-Form 36 (SF-36) (28) and the Stroke Impact Scale (SIS) (29) cover domains affected by stroke are used to estimate and predict patient recovery as the top score is the "recovery" target. Although PROs aim to measure recovery from the patient's point of view, they are still based on a fixed set of items and predetermined categories for response. These measures provide the ability to quantify changes used to indicate progress towards recovery. However, there remains a pressing need to explore the unique meaning of recovery for patients. This type of exploration can contribute to a deeper understanding of the patient's unique experiences of and meaning attributed to recovery, preferences that will be important when designing interventions and allocating services.

Stroke is one of the leading causes of death in Ghana (30,31). In the last decade, Ghana has embarked on a journey to improve stroke care. This initiative has involved sensitizing the general public on ways to prevent stroke, recognizing signs of stroke and finally the establishment of a stroke unit in the Korle-Bu Teaching Hospital in the capital city of Accra in 2014. The stroke unit was established with the aim of improving stroke outcomes (32). As Ghana restructures its stroke care policies, it is essential to understand the meaning of recovery from the patient's perspective.

First, understanding what recovery means to patients will allow clinicians to tailor stroke care to meet patient needs and support recovery. Second, a better understanding of recovery from the patient's perspective can illuminate both shared perspectives and unique meanings of recovery. The latter can sensitize caregivers to explore the unique experiences of patients and may facilitate more targeted support from family members. Finally, by understanding the meaning of recovery from the patient's perspective, decision makers will be able provide and include services and interventions that facilitate recovery and increases quality of life of patients. The aim of this qualitative study is to gain insights on the meaning of recovery from the perspective of a sample of stroke survivors in Ghana.

Methods

To gain insight on the meaning of recovery from the perspective of individuals who have experienced a stroke, our research is informed by an interpretive description methodology. Interpretive description aims at generating practical knowledge that allows us to "deconstruct the angle of vision" upon which current knowledge on the meaning of recovery from stroke has been based. This angle is particularly important for this study as recovery has generally been defined and viewed from a biomedical or clinician perspective (33). In interpretative description, "reality" is contextual and subjective, however Thorne (1996) notes that realities can be shared, and patterns of subjective experience can be identified (34). For this reason, we aim to provide a description of the meaning of recovery from stroke by identifying themes and commonalities from individual perspectives, yet still account for the inevitable differences that participants will have in their reflection on the meaning of recovery. This perspective assumes that the researcher is intimately connected to the research itself and shapes both the data being generated and how the data is interpreted (35). The principal investigator is a researcher in stroke rehabilitation and from Ghana, interpretative descriptions was suitable for this study because the methodology acknowledges the researcher's prior theoretical and practical knowledge on the phenomena being studied. In light of this prior knowledge on stroke and recovery, we aim to gain insights into the novel perspectives on recovery from a group of participants in Ghana (35). To ensure that reflections on the research process are documented, and the perspective of participants are foregrounded, a reflexive log was kept during data analysis. In addition, the interview guide was created and modified by co-investigators.

Data Collection

Semi-structured face-to-face interviews were conducted with 11 participants. The use of semi-structured qualitative interviews allows for the elicitation of experiences and self-reflections by participants on what recovery means to them (36). In addition, individual interviews allow participants to express their thoughts and feelings freely and at a comfortable pace. All interviews were conducted using an interview guide meant to stimulate discussion. The interview guide included questions like: "Would you mind describing a typical day prior to your stroke?", "Can you describe to me what happened between when you were admitted and when you were discharged from the hospital?", "Would you mind describing a typical day now that you have been discharged from the hospital?". A member of the research team at the stroke unit approached eligible participants explaining to them the purpose of the study. Interested participants were then contacted by the principal investigator to schedule a time for the interviews. Interviews were scheduled to coincide with patient's hospital appointments and were conducted in a private room at the Korle-Bu Teaching Hospital. Before the interview, the purpose of the study was explained once again to the participant and a written/oral consent was obtained. Interviews were conducted in English or Akan based on the participant's preference. All interviews were recorded.

Sample

Criterion purposive sampling was used to select participants for interviews (37). We aimed to recruit both men and women at different levels of stroke recovery. The participant must have had a confirmed stroke. A sample of at least 10 participants is often recommended for a study of this nature (38). Based on this, we recruited 11 participants.

Analysis

The data were coded inductively to identify themes that represented the meaning of recovery for participants. First, all English interviews were transcribed verbatim. Interviews conducted in Akan language were translated into English by the lead author. All transcripts were thoroughly read. This was followed by a thematic analysis of individual transcripts. In the context of this study a theme was defined as a common description of recovery (36). In other words, themes encapsulate the meanings of recovery from participants' description and self-reflection which could be common across participants or not. This analytic approach was used to identify participant descriptions that seemed to represent an important aspect of the meaning of recovery. This process

was repeated for every transcript. The transcripts were read for a third time. The principal investigator and RL met to review the initial themes and through dialogue and a further review of the transcripts, generated overarching categories that seemed to best answer the research question. We present a description of these overarching categories and their sub themes using direct quotes from participants. All analysis was conducted using NVivo 12 software.

The study was carried out according to the declaration of Helsinki (39). Ethics approval was obtained from McGill University, Faculty of Medicine Institutional Review Board and the Institutional Review Board of the Korle-Bu Teaching Hospital.

Results

Recovery as Improvement in Physical Impairment

Some participants expressed that recovery was related to improvement in physical impairments. When some participants reflected on indications that they were recovering from stroke, they often cited instances where their walking or speech had improved.

"since I was able to walk before I was discharged, it means I recovered here at the hospital before leaving for home" (Participant 2, 61 years)

Participant 4, 54 years - "oh but now I have recovered!

I: (Laughing) You rated your recovery as 6 so I am wondering what needs to be done to get you to 10.

Participant 4, 54 years - It is the walking"

The absence of the physical signs of stroke as seen by others was also an important indication of stroke recovery for some participants. These participants indicated that if others could not tell they had had a stroke from their outward appearance, this was indicative of recovery. For instance, a participant who had not returned to work although he had mentioned he was functionally independent shared:

"....I want everyone to see that I have never had a stroke. I want everyone to see me as if I have never had a stroke. So when I went there the man asked me to pick a chair, to use my left hand to pick a chair. I was able to life it up (gesturing to show the level)…Yes I lifted it up for him to see.

And when I am walking I don't want it (arm) to be laying on my side, so If I am doing something I have to do….either I pocket it or…" (Participant 1, 61 years)

Another participant noted:

"I do, I live my normal life as I used to, do you understand. I am able to go to everywhere. Even if I don't tell you I was affected by that sickness you will never know unless I tell you myself. Because nothing shows that I was affected. Nothing. Unless I open my mouth. Do you understand? So I can tell you I have, I have. I walk normal like I used to, so everything is normal" (Participant 9, 33 years)

"I was talking with a lady and she asked why are you coming to Korle-bu. She thought my husband was the one who got ill. She was surprised when I told her I had been seriously ill and admitted here for almost a month. She said nothing shows I was ever ill. It is God. She was soo shocked." (Participant 8, 60 years)

Recovery as Function and Independence

For some participants, recovery from stroke was related to function and independence. These participants viewed their recovery as being able to engage in personally meaningful activities. They situated physical improvements, such as mobility or improvement in hand movement, in relation to the ability to do necessary and desired daily activities independently. This was illustrated by their strong rejection of being helped by family members and the need for being independent even at early stages of stroke recovery.

"The very first day I could remember… I wasn't able to you know, they had to help me in taking my shower and even to help me to put on my boxer shorts and … but I think after three days I told them no, I will do everything myself." (Participant 9, 33 years)

"Movement, being able to lift it myself, and I can scratch. Because the other day mosquito was biting me and I couldn't do anything. I just looked on and after biting it left me. So if I can do scratching, at least scratch myself and then put on my shirt then I will see there is much improvement especially if I can fend for myself. … Not necessarily going back to work … But at least being able to walk to the washroom to bath, to put on my dress and can move about." (Participant 5, 62 years)

For most participants, recovery from stroke was tied to activities meaningful to them. For these participants, although they acknowledge major improvements in impairments, being unable to perform certain tasks that they deemed important was a key aspect in their understanding of recovery.

"In another weeks time I wanted to sing and pray but I could not as well as I wanted to. But now I feel its better." (Participant 7, 59 years)

"Thinking…its all about the memory. Them trying to see if the memory will come back. Because I like doing things with the memory. I preach in the church, I teach bible, but now you see I can't do anything. I am eager to do it but the memory is not there. I can't go and stand in front of the congregation and begin to mumbling stumbling, you see that is not good." (Participant 8, 60 years)

"You see when I go to physio, you see I have a band on my toe. When I walk my slippers keep coming off. The therapist says it will get better so that is that. Apart from that I don't have anything else I can think of…. When I am going to work I can wear sandals. If I wear sandals I should be fine. The last time I came for follow-up I wore sandals. But today I wanted to try wearing slippers." (Participant 1, 61 years)

Recovery as Acceptance and Adaptation

Acceptance and adaptation were components of recovery expressed by some participants. Older participants viewed stroke and subsequent recovery as part of the different stages in life in relation to their age. As a result of this acceptance, recovery from stroke was not necessarily going back to their life pre-stroke, but a continuation of the different stages one goes through. This may include their acceptance of not being able to do some activities that they were able to do before having a stroke.

"Your life changes. And as man grows your situation and everything will change. So me, recovery will not go back to where I was first. I think there will be a change in everything." (Participant 3, 62 years)

"Because of my age, as human beings at a certain age you don't expect to be as strong as a young person. Considering what I went through during the illness period, I think I am ok" (Participant 8, 60 years)

Related to this acceptance was the adaptation of lifestyle to promote recovery. This included taking preventive medication, exercising and improving eating habits. Although adaptation involved significant lifestyle changes, the participants did not view it as an effect of the stroke on their life. For example, asking a participant who had initially stated that he had recovered from his stroke whether he had made any changes because of the stroke he stated *"oh like if first I eat late, as I was telling you, before I fell sick normally I was eating like 10pm you see me eating, 1 am you see me eating. I don't do that again. Latest by 4 o'clock I have finished anything I have to eat. If you see me eating after 5, then it should be fruits.*" However, when we later asked if the stroke had affected his life he said: *"no no no no.it has never affected my life. I am still living my normal life … yes I am still living my life but I do know what to do and what not to do"* (Participant 9, 33 years).

Recovery as progressive

Participants also acknowledged that recovery from stroke was progressive. They expressed that recovery occurs over time, beginning with improvements in some domains and gradually attaining functional independence. They expressed in great detail that:

Participant 8, 60 years: I could see, at first I could not even straighten my neck. But now I am able to eat very well. I am able to walk and do certain things

I: Can you please tell me when you will say your recovery started? And what was the process?

Participant 8, 60 years: After I was able to eat well, I could walk too. Initially I could wash my clothes. When I was first discharged they were bathing me. But later when I decided to bath myself I was sitting on a chair. However, later I did not need the chair.

"Well now I can get up from bed. What is important now is my walking. Like I said, being able to do activities like washing would not be instant. Gradually I will be able to do it. I really can't answer your question. Even with God, he does things gradually. He has shown in the bible to let us know that He can do certain things. That is why I am saying I have recovered. If I was bed ridden then … but even now when I am visiting the washroom, at first I could not, but now I am able to manage and go. So what else do I want? So I am good" (Participant 4, 54 years)

Recovery from a reference point

Most participants reflected on their recovery using a reference point. Some participants used their pre-stroke life as a reference point for recovery, while others compared themselves to other stroke survivors. To these participants, being "better" than other stroke survivors meant they had recovered from their stroke because they thought that it could have been worse. Therefore, moderate improvements in their functional independence meant recovery from stroke.

"Because if I look some people, I have been seeing some people..ahmmm how it takes them before they can recover and comparing to mine, I am better." (Participant 10, 57 years)

"Because Madam, not everyone was lucky as me. See a friend's friend had a stroke it has been three years now and he is unable to talk or do anything. He is immobile." (Participant 1, 61 years)

"Because sometimes you see people and their state and realise that you are in heaven (a better state)." (Participant 6, 45 years)

For others, the reference point was their level of stroke severity and level of impairment post stroke. They seemed content and believed they had recovered based on family and friend's description of their level of stroke severity (for those who could not remember):

"The way they were describing my state, it took a very short period for me to recover. The way they were describing what happened and how they brought me in…" (Participant 6, 45 years)

"Considering what I went through during the illness period, I think I am ok." (Participant 8, 60 years)

Recovery and gratefulness to God

A recurring theme identified was participants' association of recovery to their belief in God. Participants at different stages of recovery often referred to their gratefulness to God. This sense of gratitude to God seemed to be an expression of their thankfulness for any improvement in their health, well-being or functioning. Participants often felt that they would be ungrateful to God for their life if they said they had not recovered because of the improvements they had seen.

"In the name of God I have recovered (laughter) God has done a lot for me." (Participant 2, 61 years)

"If I am being fair to my Maker, I will say that I have recovered" (Participant 3, 62 years)

"Even with God, he does things gradually. He has shown in the bible to let us know that He can do certain things. That is why I am saying I have recovered." (Participant 4, 54 years)

Recovery as staying connected

Social interaction played a major role in recovery according to participants. Majority of participants indicated that maintaining relationships and interacting with family and friends as they had prior to the stroke contributed immensely to their recovery. Friends interacted with them "normally" and continued to involve them in recreational and social activities. Staying connected reduced the chances of feeling isolated or stuck for these participants.

"I think friends too were around talking, we talk normal. Because I like football a lot do you understand me, so we talk about football a lot. They helped me to forget about what ever happened…They talk as if there is nothing happening, and they were visiting me (stresses on visiting me). Days that they know our football team is going to play they come around and we will all watch it together, we eat together." (Participant 9, 33 years)

"Oh they (family) were very supportive, and they took really good care of me. Even when I could do certain things, they will insist on not letting me do it." (Participant 8, 60 years)

However, some participants noted how their stroke impacted their ability to maintain their relationships. One participant expressed displeasure with their inability to visit friends. To him, recovery from stroke included being able to maintain social relationships and activities such as visiting friends and returning to work. He expressed:

"Yes I wash my own things but can I stay at home all the time?...Can I always be at home every single day? I will stay at home. Sometimes I go and sit with my friend. Maybe at the end of the month I will start work." (Participant 1, 61 years)

Limitations

This study has some limitations. First, interviews were shorter than anticipated. Due to patient safety reasons, all interviews were conducted at the Korle-Bu Teaching hospital to coincide with follow-up appointments. As a result, most patients and their caregivers had a limited amount of

time for the interviews and for some instances had to leave for personal reasons. Secondly, some participants that needed to be interviewed for a second time were lost to follow up. Attempts to clarify certain aspects of their interviews were unsuccessful. As a result, these aspects were not included in the analysis. This may have led to the omission of important aspects of the meaning of recovery. Thirdly, this study reports result from a sample of stroke survivors from one tertiary hospital in Accra, Ghana. This may not reflect the meaning of recovery from stroke for individuals from different regions with markedly different cultures and religions. While we acknowledge that these limitations may have limited the depth of interviews and information on the meaning of recovery, this study is one of the first to explore the meaning of recovery from the patient's perspective in Ghana.

Discussion

This study explored the meaning of recovery from stroke from the perspective of a sample of stroke survivors in Accra, Ghana. It provides an interpretive description of the meaning of recovery by highlighting not only similarities but also the differences in the meaning of recovery. According to the participants, recovery represented an improvement in physical impairment and was reflected in the lack of visible signs of stroke. Participants seemed to prioritize their ability to perform personally meaningful activities independently. Recovery from stroke was seen as progressive, thus making improvements over a period of time. Most participants conceptualized their level of recovery based on either their pre-stroke life, their level of impairment at time of admission or the level of impairment of other stroke survivors. Therefore, depending on the individuals reference point, recovery could mean returning to pre-stroke life or not. Furthermore, this meaning of recovery was influenced by the participant's belief in God.

Participants focused on their ability to perform meaningful activity. The emphasis on meaningful activity has been described in other studies on recovery from stroke where participants were more interested in improving their ability to undertake activities that matter most to them rather than the component processes in for example improving hand function or mobility (8,9). This finding suggests that focusing on improving physical or other impairments can be thought of in relation to participation. There is an important relationship between participation and improvement in physical, cognitive and visual impairment. However, task-oriented training based on what matters most to the individual may be more effective in improving physical impairment and functional capacity to meet patients' needs. Focusing on a meaningful activity may also be a way of

motivating participants during rehabilitation and the recovery process. This may also increase their willingness for rehabilitation, personal engagement and self-management to improve stroke outcomes.

Similar to results from Faircloth et al. (2004), (40) the effect of stroke was not always seen as a "biographic disruption" to life by participants in this study. Especially for older participant, it was seen as part of life in light of their age. The sequela of stroke and recovery from stroke was therefore seen as an accepted part of life. This acceptance did not seem to mean that participants conceded to the impacts of the stroke. Most patients took personal initiatives to improve their health after the stroke by researching, exercising, managing their emotions or adopting better eating habits to help with their recovery or prevent another stroke. This finding also suggests that stroke survivors express an eagerness to adapt to their new situation and to make life changes to improve their health post-stroke. Considering that knowledge on stroke is low in Ghana (41), stroke care policies in Ghana can include education of stroke survivors and caregivers on secondary prevention and other self-management interventions that will help them improve long term outcomes.

There was a great focus on gratitude to God in the understanding of recovery from stroke. Most participants showed satisfaction and a general positive attitude towards their recovery regardless of their level of recovery in terms of functional independence. Other studied have found similar associations of faith to recovery and quality of life. Prayer and connecting to God has been shown to be a source of strength and confidence post stroke (5). In addition, Lev and Owen (1996) study concluded that participants who expressed higher faith in God and prayed had higher quality of life post stroke compared to patients who expressed little faith in God (42). A study on barriers to evidence-based acute stroke care in Ghana from the perspective of stroke care professionals identified sociocultural and religious beliefs of patients as a barrier to optimal care (43). According to stroke care professionals, certain cultural and religious beliefs hinder patients from seeking medical attention and in some cases patients resorted to alternative herbal or traditional medicine before seeking medical attention (43). On the contrary, our study identified religion as an important resource during the recovery process which seemed to have a positive influence on how participants experienced recovery from stroke. Being aware of individual faith systems and how it influences individual experiences of recovery can help both clinicians and patients achieve their goals and improve stroke outcomes.

Our study confirms that participants viewed recovery from unique points of reference as seen in other studies. Participants from different studies saw recovery from stroke as returning to their pre-stroke life while other participants did not use their pre-stroke life as a reference. (8,9,13) This discrepancy suggests that pursuing normality or returning to pre-stroke life may not be a suitable reference point to capture experiences of recovery for all stroke survivors. It will be important for clinicians to explore with patients what recovery means to them as their reference point has implications on their expectation of recovery. For instance, in the current study, participants who defined recovery based on their pre-stroke life expected to be able to return to their normal life while participants whose reference point was their level of stroke severity were more open to adaptation and coping. Being aware of these differences is valuable in managing patient's expectations and planning goals that foster motivation and decrease disappointment or hopelessness at the end of rehabilitation services. This may have implications for the rate of dissatisfaction expressed by patients in relation to their recovery seen in other studies at the time rehabilitation services are withdrawn (16).

The literature on stroke recovery has been predominantly from countries outside Africa. There are some differences in the meaning of recovery identified from other studies that we do not find in the current study. For example, a number of qualitative studies found that there was a general sense of shock, frustration and negative emotions in terms of stroke and recovery from stroke which we do not find in our current study (8,13). This difference was also found during the elicitation of preference values in Zimbabwe for health states where most participants from Zimbabwe were unwilling to rate any health state as worse than death and preferences for worse health states were higher than those elicited from other countries (44). Another major finding from other studies that was not reflected in the meaning of recovery in Ghana was social interaction (8,9,15,45). For example, in O'Connel et al's (2001) study on recovery after stroke, participants prioritized social interaction because friends stopped visiting or talking with them especially because of difficulty in communication (45). Although one participant in our study mentioned that his social interaction declined after his stroke, a larger number of participants stated that social interaction and relationships where one of the factors that contributed and improved their recovery from stroke. It was not surprising to see this as an important contributor to recovery because Ghana has a strong social and family-oriented culture where members of the extended families and friends continued to participate in the lives of participants by visiting and offering continual support. This expressed

importance of social relationships corresponds with literature across contexts while suggesting that social isolation was not as prominent in the Ghanaian context.

In the last five years, major strides have been made to restructure stroke care policies in Ghana. This has included providing timely evidence-based acute stroke care interventions, however this has been limited to a few tertiary hospitals. This study highlights the different facets of recovery from stroke and the need to be aware of the different perspective between patients and clinicians and amongst patients. This requires a personal approach to stroke care and rehabilitation starting from open communication with patients on what recovery means to them, what their expectations for recovery are and what is most important to them. These results can also help shape stroke care policy to be culturally and religiously sensitive. In addition, one of the barriers to the implementation of evidence-based acute stroke care policy identified in Ghana was the lack of a national stroke care protocol and policy (43). It is important to take into account the patient's perspective on stroke and stroke recovery to develop stroke care policies that truly supports patient needs to improve their quality of life post stroke.

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CHAPTER 13: GLOBAL DISCUSSION

The global aim of this thesis was to contribute evidence towards the effectiveness of stroke unit care in lower resource settings, the KBTH in Ghana being the case study. The current thesis presents the results of an evaluation of the implementation of the stroke unit in Ghana. Considering that the results presented in this thesis may inform local stroke care policy, it was important to choose outcomes that were relevant for stroke units in the context of the health care system in lower resource settings. Hence this study focused on three categories of outcomes: 1) outcomes from the perspective of the health system/policy makers, 2) outcomes from the perspective of the clinician and 3) outcomes from the perspective of persons with stroke. This global aim of the thesis was achieved in five interrelated manuscripts.

In the first manuscript, I estimated the extent to which outcomes of mortality and length of stay changed after the implementation of the stroke unit, comparing the pre-implementation period (2011-2013) to the post implementation period (2014-2016). There was a 17% absolute risk reduction in in-hospital mortality after the implementation of the stroke unit. Furthermore, patients receiving care at the stroke unit had a shorter length of stay compared to patients receiving care at the general medical wards. The stroke unit at the KBTH is managed by a multidisciplinary team. Although the unit has 20 well equipped beds, due to lack of medical staff, the unit is not operating at full capacity. Nevertheless, results from this study suggest that even in the absence of advanced medical and research environments, coupled with inadequate medical staff, stroke unit care implemented in lower resource settings has better stroke outcomes than care at the general medical ward.

Particularly for Ghana, it may be more resource efficient to provide organised stroke unit care for acute stroke management. This may entail reorganising already available health care resources to provide some form of organised stroke unit care. One may argue that the KBTH being a leading referral tertiary hospital is well equipped to support the implementation of organised stroke unit care and therefore this study may not be generalizable to smaller hospitals and clinics.

During the conduct of this study, I was on site at the KBTH stroke unit. I, therefore, had the opportunity to make observations. Apart from having a geographically dedicated ward to care for stroke patients (which may reduce medical complications), the presence of a multidisciplinary team working together with an evidence-based stroke protocol, early mobilization and

rehabilitation seemed to be key contributors to the effectiveness of the stroke unit. Previous studies on the important components of stroke unit care have arrived at similar conclusions (1–3). While it is understandable that not all hospitals will have a dedicated unit, and not all stroke units may have the full multidisciplinary team, a national stroke protocol implemented at major hospitals and some supplementary stroke specific training to staff members may be one way of providing care to patients who do not have access to stroke units (2,4). A systematic review of "portable" stroke care showed that this approach is superior to care in general medical wards, but not superior to stroke unit care although the latter conclusion was based on one study only (5).

A major barrier to the implementation of stroke unit care is the associated cost. With limited resources and competing interests, it is important to know if the cost of providing stroke unit care is associated with better outcomes. The second manuscript presents results on the relationship between resource use measured by direct medical cost and functional independence at discharge measured by the BI amongst patients receiving care at the stroke unit. Resource use was associated with improvement in functional independence. In this analysis, it was observed that how the outcome is measured has different policy implications. When absolute change of BI was used as the outcome, it appeared efficient to treat all patients at the stroke unit regardless of their baseline BI. When proportional change of the BI was used a different conclusion emerged. It was not efficient to treat people with a baseline BI ≥85 and that alternative models of organised stroke care such as telestroke or other forms of remote care, would likely be more resource efficient.

A major challenge and a limitation of this study was the inability to calculate the association between resource use and functional outcome for patients receiving care at the general medical ward. There was a general lack of data on stroke outcomes for patients receiving care at the general medical ward. This made it impossible to calculate the incremental cost effectiveness of the stroke unit. As a result, we are unable to conclude that the stroke unit care is more cost effective than care at the general medical ward. This experience points to the importance of documenting and collecting data on stroke outcomes in stroke units and other units where stroke patients receive care.

The first four manuscripts were a challenging yet great learning experience in quantitative research in rehabilitation science considering I have a predominantly economics background. I learnt the characteristics of and used four different study designs (historically controlled study, validation analysis, observational study of a consecutive series, and an admission-to-discharge cohort study)

all with different types of data and data collection processes. I gained experience on how to collect, organise and analyse both primary and secondary data. In addition, I learnt 6 different types of regression analysis. Throughout this research, I also learnt the importance of how modeling outcome variables such as change in functional independence can shape information that would then be used by policymakers. This drew my attention to the importance of looking beyond the picture of research and considering how results presented for the purposes of research may have different policy implications.

It can be said that the ultimate aim of stroke care interventions is to achieve recovery from stroke, however there is no definite definition for recovery. Recovery from stroke has often been measured from the biomedical or clinician perspective with clinicians focusing on improving physical impairment or functional independence, emotional wellbeing and in some instances, participation using measures such as the BI, PBSI, EQ-5D-3L or the SIS. However, results from manuscript 4 suggests that different measures have different cut off points and hence different operational definitions of recovery.

In the last manuscript I explored the meaning of recovery from stroke from a sample of stroke survivors in Accra Ghana. The participants had different reference points that they used to judge their recovery, where some participants made a judgement based on a comparison to their life before experiencing a stroke while others judged recovery based on comparing themselves to others they know who had experienced stroke. The reference point of recovery was an important influence on what recovery meant to each participant. Furthermore, to participants, recovery meant improvements in physical impairment but more importantly achieving functional independence in carrying out activities that matters most to them. They were also of the view that recovery from stroke was progressive and may take some time to achieve. A major finding was the importance of social and family relationships to recovery from stroke. In the literature on recovery from stroke, participants from HIC stated they were socially isolated and unable to participate in social activities they used to and hence making it an important aspect of recovery. Contrary in our study, participants had very good social support from friends and family. They stated that it was one of the main contributors to their recovery. This highlights the importance of social relationships in recovery from stroke. Clinicians and health care professionals can emphasize the important role family and friends play in promoting recovery for the patient. It will be worthwhile to have a conversation with the patient to understand what recovery means to them, their goals for recovery

and how they can harness all these contributors and components of recovery to support their needs and recovery from stroke.

This study exposed me to qualitative research methodology and the different qualitative research methods. I gained first-hand experience in conducting semi-structured face to face interviews both in English and the local language. In the beginning, it was difficult to draw out participant's experience with recovery however as the interviews progressed, I felt more comfortable stimulating discussions in the topic, following up with questions and picking up on important ques. In addition, being new to qualitative research, I learnt how to code using NVIVO software and conduct thematic analysis. All in all, this thesis provided me an enriched learning experience in two of the major branches of research methodologies.

Conclusion

In conclusion, this thesis provides evidence on the effectiveness and applicability of stroke unit care in Ghana. It also highlights the importance of engaging patients in the recovery process to understand what recovery means to them and their expectation of recovery post stroke in order to meet their needs. Results of this study are generalizable to lower resource settings and indicates that stroke unit care may be an optimum and resource efficient stroke care policy to improve stroke outcomes in Ghana.

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