Audit of the quality and cost of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital

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Faculty of Health Sciences Declaration of originality

This research report is my original work. Neither the whole work nor any part of it has been, is being, or is to be submitted for another degree to any other university. None of this work has been published in any format prior to registration for the above-mentioned degree.

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I, **Charle André Viljoen**, hereby declare that the work on which this dissertation / thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

Permission was obtained from the chairs of the Doctoral and Masters Committee for Research and the Postgraduate Masters Committee of UCT to report and discuss the results of this study in the format of two publications in Chapter 2, instead of the usual standard of one publication.

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Thesis abstract

Thesis abstract word count: 500 words

Introduction

Stroke is the leading cause of death and disability amongst South Africans older than 60 years. The majority of stroke patients in South Africa are managed in general medical wards where little is known about the quality and cost of care. The aim of this study was to determine the cost of stroke care and to identify factors associated with increased expense, as well as to evaluate the quality of stroke care in general medical wards in order to identify areas where quality of care could be improved.

Methods

We conducted a retrospective folder review of all acute stroke admissions to the general medical wards at Groote Schuur Hospital from 1 January to 31 December 2012. Patients younger than 45 years and those that received thrombolysis were excluded. The hospital's finance department provided the bed costs, as well as expenditure on consumables, pharmacy, laboratory and radiology for each subject. The quality of care was measured according to the South African Stroke Guidelines.

Results

The inpatient care of 261 patients was evaluated. Although neuroradiology was performed on 95% of patients, carotid duplex Doppler ultrasonography and echocardiography were not often done. Although all patients with ischaemic stroke received inpatient antiplatelet or anti-coagulation therapy, not all risk factors were adequately addressed on discharge. The median cost of a stroke admission was R19,072.07 (IQR R10,899.85 to R27,789.43). The strongest correlation with cost

was with length of stay (LOS), r = 0.9977. The median LOS was 6 days (IQR 3 to 9 days). Using non-parametric univariable analysis, clinical factors prolonging LOS were previous stroke ($P = 0.028$) and inpatient complications: fever ($P < 0.001$), urinary tract infections ($P < 0.001$) and acute kidney injury ($P < 0.001$). The LOS increased as the number of inpatient complications increased ($P = 0.059$). Mortality was 20% and 68% of patients experienced at least one medical complication during admission. Fever and pneumonia were predictors of death. Pneumonia was less prevalent amongst patients who were mobilised early ($P = 0.002$). Early nutritional support was beneficial in reducing the incidence of acute kidney injury ($P < 0.001$). The median LOS was significantly prolonged by delaying speech therapy ($P < 0.001$), nutritional support ($P < 0.01$), physiotherapy ($P < 0.01$) and occupational therapy ($P < 0.001$). Discharge to inpatient rehabilitation centres significantly prolonged LOS as compared with patients discharged home ($P < 0.001$).

Conclusions

This is the first study evaluating the cost of acute stroke care in South Africa. Length of stay was the greatest determinant of cost. Improving the quality of care to reduce the number of complications, early referral to allied health professionals and effective discharge planning would result in shorter length of hospital stay and therefore cost saving. There is a need for increased access to stroke unit beds, albeit dedicated stroke beds in the general medical wards, to ensure specialised nursing care and early inpatient rehabilitation to reduce the number of inpatient complications, as well as implementation of protocols to allow for better adherence to national guidelines.

Chapter 1: Structured literature review

Structured literature review word count, excluding references: 3847 words

Introduction

This literature review was conducted to explore the international and local stroke guidelines, the recommended management and expected quality of stroke care, as well as the economic impact that stroke has internationally and on South African health care systems.

Methods

Literature search

Full-text articles and publications from 1989 to 2014 were identified by conducting a literature search in Google Scholar and PubMed/MEDLINE databases through the University of Cape Town's online library access. The terms used for the electronic search included "stroke and cost", "stroke and length of stay", "stroke and quality of care", "stroke and South Africa", "stroke and guidelines", "stroke and epidemiology", "stroke and risk factors", "stroke and subtypes", "stroke and management", "stroke and complications" and "stroke and rehabilitation". The search was restricted to articles published in English, but included articles from Africa, Europe, North and South America, Asia and Australia.

Articles were imported into Mendelay Desktop version 1.10.3 and categorized according to the above search criteria. Citations and referencing to articles used in the literature review were done through the Mendelay citation plugin in Microsoft Word for Mac 2011 version 14.3.9.

Results

A total of 115 articles were identified through the online search, of which 22 discussed the cost of stroke care and 16 reviewed the length of stay in stroke care. Stroke management was dealt with in 11 articles and 7 reviewed methods of assessing quality of stroke care. Four stroke guidelines were reviewed (including South African Stroke Guidelines, American Heart/Stroke Association Guidelines, European Stroke Organisation Guidelines, the World Health Organisation (WHO) guidelines). Moreover, 15 publications explored epidemiology of stroke and non-communicable diseases of which 4 focused on South Africa. The risk factors and comorbidities of stroke were reviewed in 8 publications. Stroke subtypes and stroke classifications were discussed in 6 articles, whereas 22 publications explored the complications of stroke. A further 10 articles were reviewed for its discussion on stroke rehabilitation.

Discussion

Introduction

Cerebrovascular accidents remain the second leading cause of mortality and most frequent cause of permanent disability in the world.[1-5] Worldwide, stroke accounted for 5.7 million deaths and contributed to 46.6 million Disability Adjusted Life Years (DALYs) in 2008.[2,6] In South Africa, stroke accounts for 17.7% of female and 12.2% of male deaths in persons of 60 years of age and older, making it the leading cause of death in this age group.[7] In a report published by the Western Cape Department of Health and the City of Cape Town in 2008, it was estimated that the stroke mortality in females ranged from 108.1 to 131.5 deaths per 100 000 in Mitchell's Plain and Khayelitsha respectively, whereas in males the deaths per 100 000 ranged from 125.8 in Khayelitsha to 136.6 in Mitchell's Plain.[8] From this can be inferred that cerebrovascular disease places a considerable burden on local

acute and chronic health care resources. Mayosi et al reported that this burden of disease is the result of the increase of cardiovascular risk factors present in urban and rural South Africa, and is predicted to increase considerably if the appropriate action is not taken.[9-13]

Due to the high incidence of acute stroke, stroke care imposes a major economic burden on health care services around the world.[14-16] The International Comparison of Stroke Cost Studies estimated that health care costs for stroke represented between 2% and 7% of total healthcare expenditures.[17,18] In addition to the direct costs to health care services, there are indirect costs incurred by the loss of productivity resulting from post stroke functional disability and death.[19,20] In the United States of America, the total cost of stroke in 2008 was $65.5 billion, of which $43.8 billion (67%) were direct costs related to stroke care and $21.7 billion (33%) were indirect costs.[20] In the European Union, a total of €27 billion is spent on stroke yearly, of which €18.5 billion (68.5%) relates to the direct cost of stroke care and €8.5 billion (31.5%) relates to indirect costs of functional impairment.[20]

Although little is known about the health care expenditure on stroke in South Africa, it is estimated that stroke is 20% more prevalent in low and middle-income countries than in high-income countries, where the impact on limited health care resources would be greater than in developed countries.[6] Cost containment and rationalisation of health care resource allocation is therefore of paramount importance in face of escalating health care costs worldwide.[21,22]

Cost is predicted by length of stay

The inpatient treatment of acute stroke and post-stroke rehabilitation are expensive.[23] Amongst all the predictors of inpatient cost, length of stay (LOS) has the strongest association with the total cost of an admission, and is therefore the most important determinant of hospitalisation costs in patients with acute stroke.[14,15,24,27]

Length of stay is not only the major determinant of the cost of acute stroke care, but the factors influencing LOS and their management can be used as indicators of the quality of stroke care.[28] In light of the health care resource constraints and inexorably growing demand for inpatient beds in developing countries, it is therefore very important to identify the factors that prolong LOS and how they can be modified to ensure that bed use is cost-efficient and remains efficacious.[14,29,30]

Demographic influence on length of stay

Although many studies have shown that age and gender do not have an influence on LOS,[14,26,31] Chow et al found that younger patients were likely to have more expensive stroke care than their elder counterparts.[32] This is explained by the need for more extensive investigations in younger stroke patients.[32]

The influence of risk factors and comorbidities on length of stay

Hypertension remains the most important modifiable risk factor for stroke and continues to rise in prevalence.[33,34] Similarly, there is an increase in the prevalence of diabetes mellitus worldwide, which is an important independent risk factor for stroke.[33,34] In addition, there is an increased prevalence of ischaemic heart disease and atrial fibrillation in ageing populations, which are important risk factors for stroke.[34] Studies have shown that comorbidities such as hypertension, diabetes mellitus and ischaemic heart disease do not significantly contribute to prolonged LOS.[14,26,31] However, Koton et al reported that patients with atrial fibrillation or congestive heart failure prior to their admission for acute stroke had a prolonged LOS.[15]

Arboix et al reported that health care campaigns promoting smoking cessation resulted in an increased public awareness of the dangers of smoking and could be contributing to the decline of smoking as a risk factor for stroke.[34,35] There is

controversy with regards to the impact of smoking on LOS of patients with stroke. Appelros et al reported a prolonged LOS for acute stroke in smokers, whereas Chang et al found a shorter LOS.[14,28] However, Edjoc et al reported smoking was associated with poorer functional outcomes at discharge, as well as an increased mortality within one year of the acute cerebrovascular event.[36]

Stroke recurrence has been reported to be associated with prolonged LOS.[37] This could be explained by the greater neurological impairment in patients with acute stroke who have had previous strokes.[37]

The influence of stroke severity on length of stay

Stroke severity is strongly associated with LOS.[14,28] Appelros et al reported that for each point the National Institute of Health Stroke Scale (NIHSS) score is increased the LOS was prolonged by 0.8 days.[28] Similarly, Chang et al showed that this held true for a NIHSS score of up to 15, from which point the LOS decreased by 1 day for every point increase in the NHISS score.[14] The decreased LOS that was observed in patients with high NIHSS scores (i.e. patients with severe strokes) can explained by an increase in mortality.[14,26] It was reported by Koton et al that patients with severe strokes are at increased risk of early death.[15]

Amongst the clinical parameters used in calculating the NIHSS score, Appelros et al reported that unilateral neglect, leg paresis and level of consciousness were the most important clinical factors influencing LOS.[28]

Stroke subtypes and their influence on length of stay

Huang et al reported that stroke subtypes impacted significantly on LOS and health care cost.[37] In that study, patients with total anterior circulation infarcts (TACI) or posterior circulation infarcts (POCI) had mean lengths of stay of 17.8 and 16.1 respectively, whereas patients with partial anterior circulation infarcts (PACI) and

lacunar infarcts (LACI) stayed for a mean of 11.69 and 11.6 days respectively ($P < 0.001$).[37] Similarly, Dodel et al reported that large vessel infarcts affecting more than 50% of the volume of a cerebral hemisphere were more likely to have a longer LOS.[38]

In studies by Reed et al and Dodel et al it was reported that there is no statistically significant difference in LOS in patients with ischaemic stroke and those with haemorrhagic stroke.[38,39]

It was reported by Dodel et al that stroke laterality has no influence on the length of stay or cost of an acute admission for stroke.[39]

The influence of medical complications on length of stay

Davenport et al reported that complications are found in up to 59% of patients admitted with acute stroke, amongst which 60% of patients have more than one complication during their admission.[40] These complications include cardiovascular dysfunction, hyperglycaemia, pneumonia, urinary tract infections, pressure ulcers, venous thromboembolism and gastro-intestinal bleeding.[40-42] Complications are more frequently encountered in the elderly, in patients with severe strokes and in patients with pre-stroke disability.[40]

Ingeman et al reported that patients who developed inpatient complications were more likely to have a worse outcome.[41] Medical complications are largely preventable and are therefore considered as a negative indicator of quality of stroke care.[43,44] Complications significantly contribute to a prolonged LOS, as demonstrated by Lee et al who reported that the occurrence of infections was associated with a 5.24 higher risk of prolonged hospital admission.[30] Furthermore, complications contribute to deconditioning, which delays rehabilitation and hinders successful functional recovery and which ultimately has a negative impact on the quality of life (QOL) of patients who have had a stroke.[29,40,41,44,45]

Zorowitz et al reported that stroke is often accompanied by cardiovascular dysfunction, with as much as 90% of patients having an abnormal ECG during admission.[42] The treatment of blood pressure after acute stroke remains controversial, but hypotension and systolic pressures greater than 220mmHg should be avoided.[46] Severe hypertension may predispose to myocardial ischaemia and decompensated cardiac failure after stroke, which contribute to unfavourable outcomes and prolong LOS.[42,45]

Langhorne et al reported that hyperglycaemia has been associated with poor outcome after stroke.[47] However, evidence to support tight glycaemic control with insulin infusions after stroke remains limited.[33] The current recommendations by the South African Stroke Society is to treat hyperglycaemia with insulin if the blood glucose is more than 10 mmol/L.[33]

In studies by Katzan et al and Heuschman et al it was estimated that a third of deaths after acute stroke could be related to pneumonia, which makes it the most common non-neurological cause of death.[42,48,49] Vermeij et al reported that pneumonia has an association with poor outcome at one year after an acute cerebrovascular event.[50]

Cerebral, cerebellar as well as brain stem strokes can impair the physiology of swallowing.[51] A third of patients with dysphagia develop pneumonia, but not all patients with pneumonia have dysphagia and aspiration.[48,52] Katzan et al reported that the crude relative risks for developing pneumonia were 2.7 in patients with haemorrhagic stroke, 5.8 in patients with coma and 2.69 in patients with paralysis ($P = 0.001$).[48] Hinchley et al reported that a formal dysphagia screening tool for acute stroke reduced the occurrence of pneumonia three fold.[52] International guidelines suggest that patients with impaired swallowing should receive nasogastric feeding.[33,46,47,52-54] Furthermore, patients with dysphagia should be nursed in a semi-upright position and be offered oropharyngeal suctioning if they are unable to handle their own secretions.[45]

Dysphagia is associated with worse outcomes following acute stroke, as it not only increases the risk of developing pneumonia, but it also predisposes the patient to malnutrition and the risk of developing a catabolic state, as well as dehydration which results in acute kidney injury.[33,42,45,46,54,55] These complications could be avoided by timeous insertion of a nasogastric tube and the initiation of appropriate feeding.[33,46]

Urinary tract infections (UTI) are frequently encountered in patients with acute stroke, particularly in patients with severe stroke.[54] Aslanyan et al reported that UTI after stroke does not increase the risk of mortality,[53] but that UTI was associated with poorer functional recovery, as evidenced by an odds ratio of 4.8 for having a Rankin score more than 2 three months after the acute cerebrovascular event.[53] Urethral catheters should be used conservatively, and when used, patients should be monitored closely for urinary tract infections.[33,46,53,54] Antibiotics should best be reserved for patients with evidence of infection.[33,54]

Weimar et al reported that fever, which is a marker of infections such as pneumonia and urinary tract infections, has an odds ratio of 2.931 as an independent predictor of incomplete functional recovery or mortality.[56] Careful temperature monitoring would assist in rapid detection of fever, which would expedite the investigation and treatment of underling infective processes.[54] The South African Stroke Society recommends antipyretic treatment if the temperature is greater than 37.5°C, as experimental studies have shown that fever increases infarct size.[33]

Pressure ulcers are prevented by rigorous nursing care, which includes frequent turning and incontinence care. Pressure ulcers should be treated by relieving pressure on the affected area by more frequent turning and the application of the appropriate dressings.[42,47]

Venous thromboembolism is an uncommon complication following acute stroke, but remains an important contributor to mortality.[41] Heuschmann et al reported that 0.4% of patients in the German Stroke Registry had venous thromboembolism;

46.8% of these patients died from pulmonary embolism.[57] The hazards ratio for death in venous thromboembolism in that study is 14.3 (P = 0.001).[57] Zorowitz et al reported that deep vein thrombosis (DVT) occurred in up to 75% of patients who were not given thrombo-prophylaxis during their admission.[42] Early mobilisation has been shown to reduce the risk of DVT in patients with acute stroke five fold.[42]

Zorowitz et al reported that gastrointestinal bleeding occurred in 1 to 3% of patients in their study admitted for acute stroke.[42] Erosive gastric changes were found in up to 50% of patients in that cohort.[42] Aspirin is thought to contribute to gastritis.[42] Patients who received thrombolysis or receive dual anti-platelet therapy are at risk of life threatening gastro-intestinal bleeds, and gastric protection with proton pump inhibitors is indicated in these patients.[42,45]

The influence of neurological complications on length of stay

Neurological complications include cerebral oedema, secondary haemorrhagic conversion and seizures.[58] Balami et al reported that neurological complications occur less commonly than medical complications, but has potentially serious short term and long term effects on outcome.[58] Neurological complications contribute to delayed rehabilitation and worse functional recovery, as well as prolonged hospital stays with increased cost and death.[58]

Cerebral oedema occurs in up to 10 to 20% of anterior circulation infarcts.[54] The extent of oedema is largely determined by the volume of the infarct.[54,58] Cerebral oedema and the resultant raised intracranial pressures remain an important risk factor of death.[58] Heuschmann et al reported that the hazards ratio for death in patients with raised intracranial pressure was 16.8 (P < 0.001).[57] Patients with cerebral oedema following acute stroke should be closely monitored within the first few days and are best managed with the head of the bed elevated by 20 to 30 degrees to facilitate venous drainage.[33,46,58] Decompressive surgery can be life

saving, but is only indicated in selected patients with substantial cerebral oedema resulting in brain shift.[33,54,58]

Balami et al reported that secondary haemorrhagic conversion is uncommon (0.6%) in patients who did not receive thrombolysis.[58] There is no treatment to reduce the risk of developing haemorrhagic conversion.[58] Neurosurgery, i.e. clot evacuation, can be considered in patients with expanding haematomas.[58]

Adams et al reported that early seizures (occurring within two weeks after the acute stroke) occur in up to 33 % of patients and late seizures in up to 67% patients.[54] Balami et al reported that 2.5 to 4% of patients develop epilepsy, i.e. recurrent seizures, after acute stroke.[58] There is no evidence to suggest the routine prescription of anti-convulsant therapy for the prophylaxis of seizures.[33,54,58] Current guidelines recommend that seizures should be treated in accordance with general principles of seizure management.[33,46,54,59]

Preventing neurological and medical complications after stroke, as well as early identification and effective treatment of such complications contribute to a reduction in morbidity and mortality.[40]

Quality care proves to be cost-efficient

There is an association between good quality care and shorter length of stay in the stroke unit.[60] Schouten et al reported that the LOS was reduced from 18.3 to 13.3 days by implementing a quality improvement programme for patients admitted with acute stroke in Sweden.[61] In that study, the stroke service teams that scored higher in the team functioning scores achieved the shortest LOS amongst stroke patients.[61] Similarly, Svendsen et al reported that LOS was reduced by 50% by effecting high quality care in Denmark.[62] The criteria used to measure the quality of stroke care in Svendsen et al's study included early admission to a dedicated stroke unit, early introduction of antiplatelet therapy or anticoagulation, early radiological

investigation by means of CT or MRI, early dysphagia screening, early nutritional assessment and identifying those at risk of constipation, early intermittent catherisation, early DVT prophylaxis and mobilisation and early assessment by the physiotherapist and occupational therapist.[62]

Lim et al reported that patients with physical disability benefit from early physiotherapy by preventing deconditioning and thereby resulting in shorter LOS.[29] In a study by Feys et al it was reported that patients that received early intensive physiotherapy for severe motor deficit in the arm had a significant improvement in motor function as compared with the control group in that study.[63] Christensen et al suggested that better functional recovery may result in a lesser chance of readmission, thus decreasing long term cost of health care.[64]

Ingeman et al reported that early mobilisation also reduced the risk of developing inpatient complications.[65] In that study, mobilising within the first day of admission was associated with an adjusted odds ratio of 0.43 for developing pneumonia, 0.56 for developing urinary tract infection and 0.43 for developing pressure ulcers.[65]

Organised stroke unit model of care has been shown to reduce complications and result in better functional outcomes following stroke.[66,67] Although treating patients in a stroke unit is more expensive than treating patients in a conventional ward, the outcome in stroke units by far exceeds that of conventional wards.[18] Epifanov et al reported that admission to a stroke unit in Germany was 13.4% more expensive for ischaemic stroke than admission to a general neurological ward in the same hospital for the same condition.[18] The increase in cost could largely be accounted for by expenditures on the increased numbers of medical personnel needed to work in the stroke unit. However, the same study reported that the length of stay per admission was significantly shorter in the stroke unit, 11.9 days in the stroke unit as compared to 16.9 days in the general neurology wards.[18]

In a systematic review by Seenan et al, stroke units had superior outcomes to conventional wards.[68] In that review the stroke unit was associated with an odds

ratio for death of 0.79 ($P < 0.001$).[68] A systematic review by Govan et al reported that patients managed in a stroke unit developed less complications when compared to those managed in general medical wards.[67] The odds ratios were reported to be 0.6 for developing pneumonia, 0.81 for dehydration and 0.44 for having bedsores when managed in the stroke unit as compared with general medical wards.[67]

Improved outcomes in stroke units are achieved by improved diagnostic accuracy, appropriate monitoring and the prevention of complications resulting from efficient management by a multidisciplinary team, specialised nursing care, early rehabilitation and better discharge planning.[18,47,66,69,70]

The impact of investigations and procedures on length of stay

De Carvalho et al reported that delays in complementary evaluations and procedures such as endoscopy and surgery resulted in increased cost of care through prolonged LOS and an increase in inpatient complications.[71]

Kim et al reported that patients with stroke who underwent surgery had a 2.1 times longer LOS than patients that did not have surgery.[23] Tu et al it reported that surgery contributed significantly to the cost of an admission, as evidenced by the mean crude hospital charges amounting to $15 249 in patients that underwent surgery compared with $7 594 in patients that did not have surgery during their admission ($P < 0.001$).[72]

The influence of discharge destination on length of stay

In a recent French study, Schnitzler et al reported that up to 50% of patients admitted with stroke require rehabilitation.[73] Luengo-Fernadez et al reported that although hospital admission is usually shorter than the admission to a rehabilitation centre, the cost of a hospital admission bed cost per day (£331 per day in a stroke

unit and £269 per day in a general ward) exceeds that of rehabilitation centres (£213 per day).[15] For this reason, Lee et al suggested that it is more cost efficient to arrange for timeous transfer to a rehabilitation centre in patients who require rehabilitation.[30]

The reasons for prolonged length of hospital stay in patients discharged to rehabilitation centres or nursing homes are two fold. Firstly, LOS in hospital is influenced by the availability of beds at rehabilitation centres and step down facilities to which patients are discharged.[22] Secondly, stroke severity and complications influence whether patients are discharged to institutions.[28,31,74] Saxena et al reported that patients that are discharged to rehabilitation centres are those that had more severe strokes and that experience greater functional disability.[31] Furthermore, as reported by Indredavik et al, stroke severity predisposes patients to developing complications,[75] which in itself not only prolongs LOS, but it also delays the initiation of effective rehabilitation as reported by Davenport et al.[40]

Lim et al stated that one could achieve a shorter LOS by starting effective discharge planning early in the admission.[29] Bryer et al, De Villiers et al and Langhorne et al suggested that early assessment by a multidisciplinary team, comprising of social workers, physiotherapists, occupational and speech therapists, results in shorter LOS by facilitating the early application and efficient transfer to rehabilitation centres.[47,55,66]

In their Cochrane systematic review, the Early Supported Discharge Trialists have reported that by developing an early discharge support group that would assist with continued rehabilitation at home resulted in a 9 day shorter LOS after acute stroke ($P < 0.001$).[76]

Conclusion

Identification of gaps and need for further research

Even though stroke is a leading cause of morbidity and mortality, very little is known about the quality and cost of stroke care in South Africa.[66] Sposato et al suggested that knowledge of the quality of stroke care is of critical importance in forming interventions to improve stroke care.[77] With stroke prevalence and its incurred costs that are predicted to continue to increase in future, the health sector will be faced with increasing financial challenges in providing optimal care for inpatients with acute stroke.[9,77,78] For this reason, De Villiers et al suggested further study in cost analysis of stroke care in South Africa.[66]

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Chapter 2: Journal ready manuscripts

This study generated an extensive database, as elaborated in the research protocol. However, to keep the manuscript focussed, the results of this study were divided into two manuscripts in publishable format.

Permission was obtained from the chairs of the Doctoral and Masters Committee for Research and the Postgraduate Masters Committee of UCT to report and discuss the results of this study in the format of two publications in Chapter 2, instead of the usual standard of one publication.

The first article concentrates on the cost of acute stroke care, whereas the second article focuses on the quality of stroke care in the general medical wards at Groote Schuur Hospital.

As stipulated in the University of Cape Town's regulations for master's degrees, manuscripts are to be formatted to comply with the instructions to authors of a journal appropriate to the subject matter of the dissertation. The author guidelines for the journal "Stroke" were followed for these manuscripts. However, for the purposes of readability of this dissertation, tables and graphs were placed in the text rather than appended.

Title page of first manuscript

Manuscript word count, including abstract and references: 4414 words

Cost of acute stroke care in South Africa

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Key words: acute stroke care, cost, length of stay

Abstract

Abstract word count: 250 words

Background and purpose

Stroke remains the leading cause of death amongst South Africans older than 60 years, yet little is known about the cost of stroke care in South Africa. The aim of this study was to determine the cost of acute stroke care in general medical wards in Cape Town and to identify factors associated with increased expense.

Methods

We conducted a retrospective folder review of all patients admitted with acute stroke to general medical wards at Groote Schuur Hospital from 1 January to 31 December 2012. Patients younger than 45 years and those that received thrombolysis were excluded. The hospital's finance department provided the bed costs, as for expenditure on consumables, pharmacy, laboratory and radiology for each subject.

Results

The inpatient care of 261 patients was reviewed. The median cost of a stroke admission in this study was R19,072.07 (IQR R10,899.85 to R27,789.43). The strongest correlation with cost was with length of stay (LOS), r = 0.9977. The median LOS was 6 days (IQR 3 to 9 days). LOS was significantly prolonged in patients with recurrent stroke ($P = 0.028$), fever ($P < 0.001$), urinary tract infections ($P < 0.001$), acute kidney injury ($P < 0.001$), delayed assessment by allied health professionals ($P < 0.01$) and discharge to rehabilitation centres ($P < 0.001$).

Conclusions

Improving the quality of acute stroke care to reduce the number of complications, early referral to allied health professionals and effective discharge planning would result in shorter length of stay and therefore cost saving.

Introduction

Stroke remains the second leading cause of mortality and most frequent cause of permanent disability in the world.[1] Internationally, stroke places a considerable burden on acute and chronic health care services, representing between 2% and 7% of total healthcare expenditure.[2] Even though stroke is the leading cause of death in South Africans older than 60 years, accounting for 17.7% of female and 12.2% of male deaths in this age group, very little is known about the cost of acute stroke care in South Africa.[3,4] With stroke incidence that is predicted to continue to rise in face of an increase in life expectancy and escalation in non-communicable diseases in urban and rural South Africa, the health sector will be faced with increasing financial challenges in providing optimal care for inpatients with acute stroke.[5-9] Cost containment and rationalisation of health care resource allocation is therefore of paramount importance if quality care is to be affordable for patients with acute stroke.[10]

This study was conducted to determine the cost of acute stroke care and factors contributing to that cost. This study also aims to identify patient characteristics, inpatient complications and management factors influencing the cost of stroke care. The identification of modifiable factors associated with increased costs could inform changes in management which would lead to cost savings.

Methods

Data collection

A retrospective folder review was conducted after approval by the Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town. Data was collected using a standardized template. All patient data in this study remains anonymous.

Study population and dates of enrolment

Groote Schuur Hospital is an 893 bed tertiary academic hospital associated with the University of Cape Town, which has 121 secondary level general medical ward beds and a 6 bed specialist stroke unit. Stroke patients who are not admitted to the stroke unit are managed in general medical wards.

Patients were identified by reviewing emergency unit admission registers. All patients admitted by the Department of Internal Medicine to the general medical wards over a 12 month period (1 January to 31 December 2012) with a diagnosis of acute stroke, as defined by the World Health Organization, were included in the study.[11]

Patients excluded from study

Patients were excluded if, after folder review it was determined that acute stroke was not the primary reason for admission, if they were younger than 45 years of age on the day of admission, if they received thrombolysis or were admitted by a neurologist to the stroke unit. Patients with subarachnoid or subdural haemorrhage were not included into the study.

Demography and clinical background of patients entered into study

Data collected included the demographic details of subjects, a history of previous stroke, preceding transient ischaemic attacks prior to admission and vascular risk factors defined as smoking (current smoker or within the 5 years prior to admission), hypertension (on the history, use of regular anti-hypertensive treatment or in-hospital diagnosis), diabetes mellitus (on the history, regular use of oral anti-diabetic medication or subcutaneous insulin, or in-hospital diagnosis),

hypercholesterolaemia (on history or a total cholesterol level of more than 5 mmol/L during the admission), atrial fibrillation (ECG), ischaemic heart disease (history of angina or prior myocardial infarction), valvular heart disease (echocardiography), HIV (positive serology) and neurosyphilis (cerebrospinal fluid analysis).

Stroke subtype and clinical presentation

Computerised tomography (CT) scans of the brain were reviewed by a stroke specialist and patients were classified as haemorrhagic or ischaemic stroke. The latter were classified according to the Oxfordshire Community Stroke Project (OCSP) clinical classification into total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI) and posterior circulation infarcts (POCI).[12] Clinical records were reviewed to identify patients with decreased level of consciousness, aphasia (further classified into receptive and/or expressive aphasia), dysphagia and hemiparesis of the arms and/or legs and its laterality.

Special investigations done during admission

Laboratory examinations done were identified from the hospitals electronic reporting system using patients' hospital numbers. Investigations recorded included full blood count, renal function (electrolytes, urea and creatinine), INR, lipid profile, thyroid stimulating hormone (TSH), liver function tests, C-reactive protein (CRP), ELISA for human immunodeficiency virus (HIV), syphilis serology and blood cultures. Urinalysis and cerebrospinal fluid analysis with its respective microscopy, culture and sensitivities were also recorded. Radiological investigations recorded included CT or MRI of the brain, angiogram of the intracranial vessels, Doppler ultrasound of the carotid vessels, chest X-rays and compression ultrasound of the calves, CT angiogram of pulmonary vessels or ventilation/perfusion scan. Cardiac investigations recorded included ECGs and echocardiograms.

Inpatient treatment

Prescription charts were reviewed to identify the use of antiplatelet agents, anticoagulants, antihypertensives, diabetic drugs, statins and antibiotics as well as its route of administration and duration of therapy.

Involvement of allied health professionals

The time interval between admission and assessment by a speech therapist, dietician, physiotherapist or occupational therapist was recorded. Patients were categorised according to whether they were first seen within 72 hours of admission, thereafter or not seen.

Complications during admission

The following complications were recorded: death, fever (defined as core body temperature > 37.5°C), pneumonia (diagnosed clinically or radiographically), urinary tract infection (based on urinalysis results), drip site sepsis, hyperglycaemia (defined as blood glucose > 7mmol/L), acute kidney injury (defined by 50% rise of creatinine from baseline within 7 days or 26.1µmol/L rise in creatinine within 48 hours),[13] bedsores, deep vein thrombosis (ultrasonographic confirmation), pulmonary embolism (confirmed on ventilation/perfusion scan or CT angiogram of pulmonary vessels), gastro-intestinal bleeds and seizures.

Discharge destination

Stroke survivors' discharge destinations from hospital were classified according to whether they went home or to an inpatient rehabilitation centre.

Length of stay

The length of stay (LOS) was calculated in days from the day of admission to the day of discharge or death.

Cost of admission

The hospital's finance department provided the bed costs, as for expenditure on consumables, pharmacy, laboratory and radiology for each subject. The cost of an admission to a general medical ward was calculated by multiplying the total length of stay in days with the sum of goods and services cost per patient day equivalent (PDE) (R2250) and agency cost per PDE (R28), medicine cost per PDE (R300), medical supplies per PDE (R233), which is a total of R2811 per day.

Chronic medication was included in ward cost, but acute medication such as antibiotics were calculated based on the cost per drug per day multiplied by the length of the treatment. The daily cost of parenterally administered antibiotics given to patients in this study included ampicillin of R12.96, ceftriaxone of R4.55, co-amoxiclav of R39.60, ertapenem of R368.33, gentamycin of R11.61 and penicillin G of R44.64 per day. Oral antiobiotics included amoxicillin of R0.83, co-amoxiclav of R2.98, ciprofloxacin of R0.88, flucloxacillin of R3.57 and metronidazole of R0.56 per day.

Each special investigation done during the admission was counted. The cost of each investigation was multiplied by the number of times each test was done. Radiological cost included chest X-ray of R122, CT brain of R1628, MRI brain of R1628, CT angiogram of intracranial vessels of R4096, carotid doppler of the carotid arteries of R340 and compression ultrasound of the calf of R340. An ECG was billed at R151 and echocardiogram would cost R340. Laboratory costs were based on the cost of a full blood count of R50.22, urea, creatinine and electrolytes of R105.08, INR of R40.95, total cholesterol of R39.12 and lipid profile of R148.06, TSH of

R220.89, CRP of R63.18, HIV ELISA test of R47.77, syphilis serology (RPR) of R29.19. A blood culture would cost R104.61 and urine microscopy and culture with sensitivities R84.40 per test.

Statistical analysis

Coded data was entered into an Excel computerised database. Statistical analysis was performed by using the statistical software R version 3.0.2. Non-parametric Mann-Whitney U (for dichotomous variables) or Kruskal-Wallis (for categorical variables) tests were used to identify whether demography, comorbidities, stroke subtypes, clinical presentation, special investigations, medical complications and management factors influenced length of stay. Only *P* values of less than 0.05 were considered significant in the analysis.

Results

A total of 344 patients with an admission diagnosis of stroke were identified in emergency unit registers, of which 261 were included in the study. Amongst the 83 patients excluded, 43 had intracranial pathology other than acute stroke, 9 were readmitted with complications of immobility from previous strokes, 9 were admitted to the stroke unit, 3 were younger than 45 years of age and 16 patients had incomplete patient records.

The demography, type of stroke, clinical presentation and comorbidities of the study sample are described in table 1.

Table 1: demography, type of stroke, clinical presentation and comorbidities.

	Number	Percentage
Age		
45 – 59 years	85	32.57%
60 – 74 years	111	42.53%
> 75 years	65	24.90%
Gender		
Male	121	46.36%
Female	140	53.64%
Type of stroke		
Ischaemic stroke	216	82.76%
Haemorrhagic stroke	26	9.96%
Infarct with haemorrhagic conversion	6	2.30%
Unknown	13	4.98%
Infarcts classified by OCSP criteria [12]		
Total anterior circulation infarct (TACI)	46	20.72%
Partial anterior circulation infarct (PACI)	110	49.55%
Lacunar infarct (LACI)	51	22.97%
Posterior circulation infarct (POCI)	15	6.76%
Clinical presentation		
Decreased level of consciousness	63	24.14%
Receptive aphasia	34	13.03%
Expressive aphasia	75	28.74%
Dysphagia	125	47.89%
Paresis of right arm	146	55.94%
Paresis of right leg	148	56.70%
Paresis of left arm	108	41.38%
Paresis of left leg	109	41.76%
Comorbidities		
Previous Stroke	94	36.02%
TIA prior to admission	23	8.81%
Smoking	94	36.02%
Hypertension	223	85.44%
Diabetes mellitus	99	37.93%
Hypercholesterolaemia	128	49.04%
Atrial fibrillation	34	13.03%
Ischaemic heart disease	52	19.92%
Valvular Heart Disease	9	3.45%
HIV	5	1.92%
Neurosyphilis	3	1.15%

Cost of admission

The total expenditure on all stroke admissions in this study was R5,636,998.11, of which R3,988,838.23 (70.76%) was spent on the ward admission, R408,038.86 (7.23%) on medical supplies, R525,183.91 (9.32%) on chronic medicine, R19,473.56 (0.35%) on antibiotics, R162,831.55 (2.89%) on laboratory related costs and R532,632.00 (9.45%) on radiological costs.

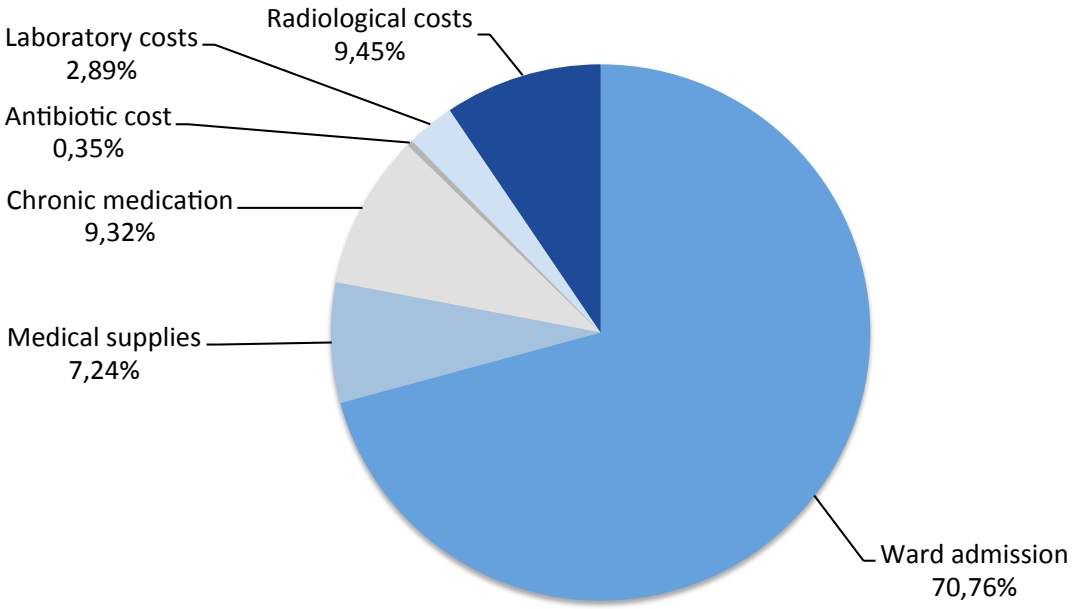

Figure 1: *this chart illustrates how the total cost of acute stroke care of all patients (n = 261) in this study was divided amongst ward cost, consumables, pharmacy cost, laboratory cost and radiological cost.*

The median cost of stroke admissions was R19,072.07 (range R5,136.85 to R100,343.62, IQR R10,899.85 to R27,789.43). The greatest variation in cost was observed with ward cost, with a median cost of R16,866.00 (IQR R8,433.00 to R25,299.00). Median laboratory related cost was R505.37 (IQR R387.76 to R745.32) and median radiology cost was R1,901.00 (IQR R1,901.00 to R2,023.00).

Correlation between cost and length of stay

Stepwise multiple regression analysis revealed that length of stay (LOS) was the key determinant of total cost of admission ($P < 0.001$). Correlation between LOS and total cost was 0.9977 with 99.55% of the variation in total cost accounted for by variation in the LOS, as demonstrated in figure 2.

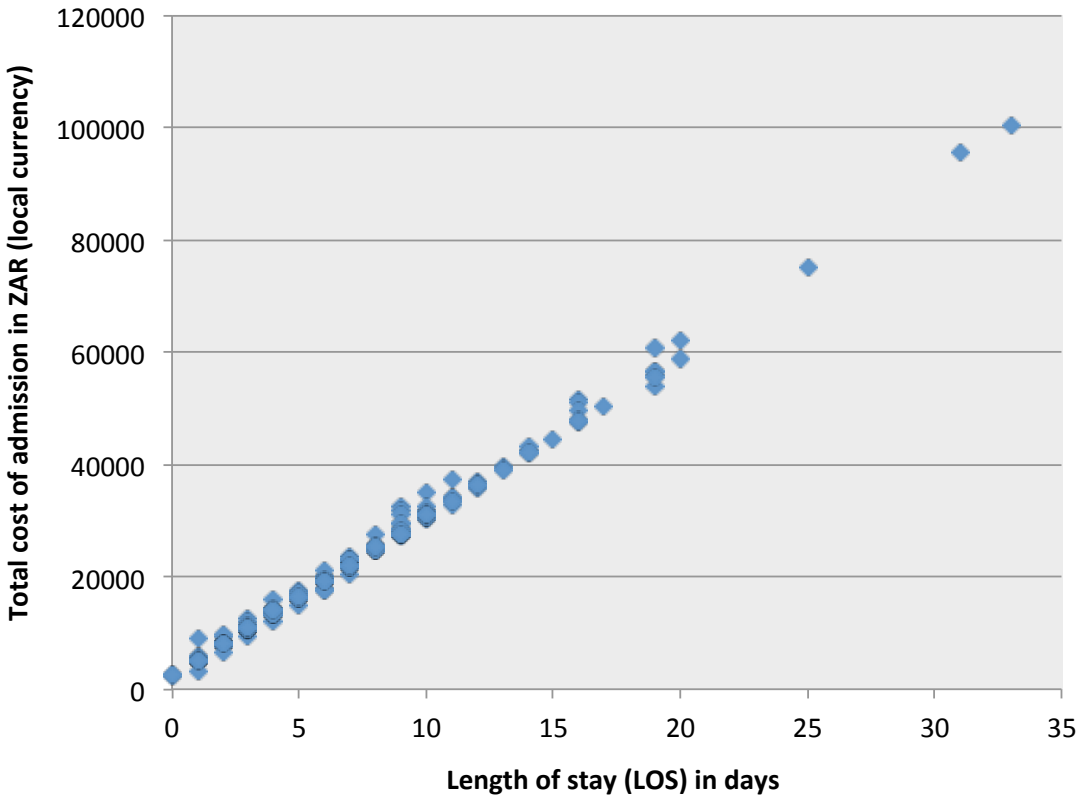

Figure 2: *This scatter plot illustrates the correlation between length of stay as measured in days and total cost of admission (n = 261) (R^2 = 99.55%).*
R^2 is the percentage of total variance explained by the model.

The median length of stay (LOS) was 6 days (range 1 to 33 days, IQR 3 – 9 days). Non-parametric tests established that demography, the different stroke types and neurological deficits on presentation did not significantly influence LOS. The only comorbidity associated with prolonged LOS was stroke recurrence ($P = 0.028$). Valvular heart disease ($P = 0.031$) and HIV ($P < 0.001$) displayed significance, but this inference cannot be accurately made due to the small sample size within these categories.

Delayed assessment by allied health professionals, inpatient complications and discharge to inpatient rehabilitation lead to a significant increase in LOS, as demonstrated in table 2.

Table 2: the influence of delayed first assessment by allied health professionals, inpatient complications and discharge destination on length of stay.

		N (%)	Median LOS	*P* value
First assessment by allied health professionals *				
Speech therapy	within 72 hours	127 (48.66)	7	< 0.001
	after 72 hours	26 (9.96)	10	
Dietary assessment	within 72 hours	94 (36.02)	6.5	< 0.01
	after 72 hours	18 (6.9)	10	
Physiotherapy	within 72 hours	150 (57.47)	6	< 0.01
	after 72 hours	40 (15.33)	9	
Occupational therapy	within 72 hours	134 (51.34)	6	< 0.001
	after 72 hours	39 (14.94)	9	
Complications during admission *				
Death	yes	53 (20.31)	3	< 0.001
	no	208 (79.69)	6	
Fever	yes	108 (41.38)	7	< 0.001
	no	153 (58.62)	5	
Pneumonia	yes	57 (21.84)	5	0.769
	no	210 (80.46)	6	
UTI	yes	57 (21.84)	7	< 0.001
	no	204 (78.16)	5	
Acute kidney injury	yes	25 (9.58)	10	< 0.001
	no	236 (90.42)	5	
Discharge destination †				
Home		102 (40.23)	4	< 0.001
Rehabilitation centre		105 (39.08)	8	
Died		54 (20.69)	3	

Non-parametric analyses were performed by Mann Whitney U (*) or Kruskal-Wallis tests (†) as indicated.

Similarly, delays in special investigations were associated with a significant increase in LOS (delays in angiogram, $P = 0.035$; carotid artery Doppler ultrasound, $P = 0.021$; echocardiogram, $P = 0.007$), however the sample size of patients that underwent these tests in this study is not large enough to accurately make this inference (only 6 patients (2.29%) underwent angiogram of the intra-cranial vessels, 11 patients (4.21%) had carotid artery Doppler ultrasound, 16 patients (6.13%) had an echocardiogram).

Table 3 demonstrates the influence of the number of inpatient complications on the median LOS (*P* = 0.059), as calculated by Kruskal-Wallis non-parametric testing.

Table 3: the influence of the number of complications on the length of stay.

	N (%)	Median LOS	*P* value
Number of inpatient complications			
None	93(35.63%)	5	0.059
1 complication	58 (22.22%)	6	
2 or 3 complications	82 (31.42%)	5.5	
More than 3 complications	28 (10.73%)	8.5	

Analysis performed by Kruskal-Wallis non-parametric testing

Death was statistically significant in shortening LOS. A logistic regression analysis was performed to determine the factors that predicted for death in this study. Table 4 illustrates the factors and their odds ratios that predicted death.

Table 4: multivariate logistic regression analysis of the risk of death.

Predictor of death	Odds ratio	95% Confidence interval		*P* value
		Lower bound	Upper bound	
TACI [12]	4.803	2.403	9.629	< 0.001
Decreased level of consciousness	6.916	3.607	13.517	< 0.001
Fever	3.240	1.745	6.174	< 0.001
Pneumonia	4.929	2.512	9.714	< 0.001

The following variables that were analysed according to this model did not reach statistical significance: patient characteristics (all variables in table 1, except if indicated above) and inpatient complications (urinary tract infection, drip site sepsis, hyperglycaemia, acute kidney injury, bedsores, deep vein thrombosis, pulmonary embolism, gastro-intestinal bleeds and seizures).

A sub-analysis was performed amongst patients referred to inpatient rehabilitation centres, which showed that patients assessed within 72 hours of admission by allied health professionals had significantly shorter LOS, as summarised in table 5.

Table 5: Median length of stay amongst patients that were discharged to rehabilitation centres according to when they were first seen by allied health professionals

	N	%	Median LOS	IQR	*P* value
Speech therapy *					0.007
Seen within 72 hours of admission	61	79.22%	8	5 – 10	
Seen after 72 hours of admission	16	20.78%	10.5	8.5 – 15	
Dietician *					0.084
Seen within 72 hours of admission	43	82.69%	8	5 – 9.5	
Seen after 72 hours of admission	9	17.31%	10	8 – 16	
Physiotherapy *					< 0.001
Seen within 72 hours of admission	76	79.16%	7	6 – 9	
Seen after 72 hours of admission	20	20.84%	10.5	8.5 – 15	
Occupational therapy *					0.059
Seen within 72 hours of admission	62	74.7%	8	6 – 9	
Seen after 72 hours of admission	21	25.3%	10	7 – 16	

** Analyses performed by Mann Whitney U test*

In corroboration with the above analysis, multivariate stepwise regression was used to identify the key predictors for LOS. The results are shown in table 6, wherein fever, acute kidney injury and delayed management by allied health professionals were associated with longer length of stay. This model explains 38% of variance in LOS (*P* value < 0.001).

Table 6: multivariate stepwise regression demonstrating how complications and delayed management by allied health professionals predict longer LOS.

Predictor	Beta	*P* value
Fever	0.311	0.001
Acute kidney injury	0.385	0.016
Speech therapy	0.266	< 0.001
Nutritional support	0.165	0.091
Physiotherapy	0.293	0.001
Occupational therapy	0.335	< 0.001

This model with F statistic of 27.71 (P value < 0.001) has an adjusted R squared of 0.38.

Discussion

To our knowledge, this is the first study of the cost of acute stroke care in South Africa. Inpatient treatment of acute stroke and its ensuing rehabilitation are expensive.[14] Amongst all the predictors of inpatient cost, length of stay (LOS) has the strongest association with the total cost of an admission, and is therefore used as the key determinant of hospitalisation costs of patients with acute stroke.[15-17] In light of the health care resource constraints and growing demand for inpatient beds that clinicians in developing countries are faced with, it is therefore very important to identify the factors that prolong LOS and identify those that are modifiable in order to make acute stroke care more cost-efficient.[15,18,19]

In our study, we investigated whether unmodifiable patient factors such demography, stroke subtype and clinical presentation or modifiable factors such as inpatient management, delays in special investigations, inpatient complications and treatment thereof, and discharge destination played a role in determining the LOS in patients with acute stroke.

As was reported by previous studies by Chang et al, Jorgensen et al and Saxena et al,[15,17,20] we found that age and gender did not have a significant influence on LOS amongst patients admitted with stroke. Chow et al demonstrated that younger patients were likely to have more expensive stroke care than their elder counterparts, which could be explained by the more extensive set of investigations that are usually done in the younger stroke population.[21] For this reason we excluded patients younger than 45 years as we wanted to quantify the cost of the average stroke patient admitted to general medical wards.

In our study we found that patients presenting with a recurrent stroke had a median LOS of 7 days as compared with a median LOS of 5 days in patients with first time stroke ($P = 0.028$), which is in accordance with a study by Huang et al that showed that stroke reccurrence is associated with prolonged LOS.[22] This could be

explained by the fact that patients with stroke recurrence have greater neurological impairment than patients with a first time stroke.[22] Comparable to previous studies by Chang et al and Saxena et al,[15-20] comorbidities such as hypertension, diabetes, dyslipidaemia and ischaemic heart disease did not influence LOS amongst patients in our study. In this study patients with valvular heart disease and HIV had statistically significant increases in LOS, but the sample sizes in these groups were small and this finding should be interpreted with caution. In a study by Koton et al, however, it was reported that valvular heart disease and heart failure were associated with increased LOS.[23]

Results from our study are in keeping with studies by Reed et al and Dodel et al which showed that there is no statistically significant difference in LOS between haemorrhagic and ischemic strokes.[24,25] Huang et al found patients with TACI to have prolonged LOS.[22] In our study however, there was no statistically significant difference in LOS between the infarct subtypes as classified by the TOAST criteria,[12] which could be explained by the increased risk of death amongst the TACI group in this study, as demonstrated in table 4.

Acute stroke patients are at risk of developing medical complications during their hospital stay.[27] In line with the publication by Davenport et al,[28] two thirds of the patients in our study had at least one medical complication during their admission. Inpatient medical complications are not only considered to be a negative indicator of quality of stroke care, as these complications are largely preventable,[29,30] but complications were reported to increase the LOS and cost of care in studies by Lim et al and Lee et al.[18,19] In this study, as in that by Kim et al,[14] LOS increased as the number of complications increased ($P = 0.059$).

Death was associated with shorter length of stay in this study. Patients with TACI, depressed level of consciousness at presentation, fever, pneumonia and multiple complications had significantly increased mortality in this study (table 4).

This study showed that patients who were seen by allied health professionals within 72 hours of admission had a significantly shorter LOS, which could be due to the prevention of deconditioning as reported by Lim et al and by early mobilization which reduced the risk of complications in a study by Ingeman et al.[18,31] Complications contribute to deconditioning, which delays rehabilitation and hinders successful functional recovery.[18,27,28,30,32]

Lee et al suggested that is more cost efficient to transfer acute stroke patients to rehabilitation centres as soon as possible, since the cost of a hospital admission exceeds that of rehabilitation centres.[19,33] In this study patients transferred to rehabilitation centres had significantly longer LOS than those discharged home. Results from our study (table 5) are in line with those of Bryer et al, De Villiers et al and Langhorne et al who suggested that early assessment by a multidisciplinary team, comprising of social workers, physiotherapists, occupational and speech therapists, results in shorter LOS by facilitating the early application and efficient transfer to rehabilitation centres.[4,34,35]

Limitations

We encountered limitations in conducting our study. Although from previous studies we know that stroke severity is associated with prolonged LOS,[15,36] we could not include stroke severity in the analysis of our data. As this study is a retrospective folder review, we relied on the clinical notes of the enrolled patients for data used in our study and the NHISS stroke scoring system was not consistently recorded in the patients' notes.

Conclusion

This is the first study evaluating the cost of acute stroke admissions in general medical wards in South Africa. As expected, length of stay was the greatest determinant of cost. This study has shown that length of stay was predominantly influenced by modifiable factors, such as the occurrence of inpatient complications, delay in special investigations, delayed assessment and management by allied health professionals and discharge to rehabilitation centres. Improving the quality of care to reduce the number of inpatient complications, reducing the waiting time for special investigations, early referral to allied health professionals and effective discharge planning in which transfer to rehabilitation centres is expedited would result in shorter length of hospital stay and therefore cost saving.

Abbreviations

AKI for acute kidney injury, CT for computerized tomography, LACI for lacunar infarct, LOC for level of consciousness, LOS for length of stay, MRI for magnetic resonance imaging, PACI for partial anterior circulation infarct, PDE for patient day equivalent, POCI for posterior circulation infarct, TACI for total anterior circulation infarct.

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Authors contributions

Author contributions: CAV and LDV designed the study; CAV collected the data; LD and MB analysed the data; CAV was involved in the manuscript preparation; LD, MB and LDV edited the manuscript.

Competing interests

The authors declare that they have no competing interests.

Disclosures

None

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Audit of the quality of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital

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Abstract

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Background and purpose

Organised stroke units with multi-disciplinary care have superior outcomes than conventional medical wards, but are not yet fully integrated in South Africa. The aim of this study was to assess the quality of acute stroke care in general medical wards and to identify areas where quality of care could be improved.

Methods

We conducted a retrospective folder review all patients admitted with acute stroke to the general medical wards at Groote Schuur Hospital from 1 January to 31 December 2012. The positive indicators of quality of care included the investigations and management as recommended by the South African Stroke Guidelines. The negative indicators of quality of care were inpatient complications.

Results

Although neuroradiology was performed on 95% of patients, carotid duplex Doppler ultrasonography and echocardiography were not often done. Although all patients with ischaemic stroke received inpatient antiplatelet or anti-coagulation therapy, not all risk factors were adequately addressed on discharge. Mortality was 20% and 68% of patients experienced at least one medical complication. Fever and pneumonia were predictors of death. Early mobilisation proved to be beneficial in pneumonia reduction ($P = 0.002$) and early nutritional support was beneficial in reducing the incidence of acute kidney injury ($P < 0.001$).

Conclusions

There is a need for increased access to stroke unit beds, albeit dedicated stroke beds in general medical wards, to ensure specialised nursing care and early inpatient rehabilitation to reduce the number of inpatient complications and to implement protocols to allow for better adherence to national guidelines.

Introduction

Stroke is the leading cause of disability around the world, and remains the second most important reason for death internationally.[1-5] South Africa is no exception, with stroke being the most common reason for death amongst South Africans older than 60 years.[6] It is estimated that 50 000 of the 75 000 annual strokes in South Africa are not fatal.[7] Stroke survivors are at risk of long-term disability and place a considerable burden on health care services and health care budgets.[7]

Even though major advances have been made in thrombolytic therapy of acute ischaemic stroke,[8] much of acute stroke care still depends on rehabilitation and the prevention of complications and stroke recurrence after the acute cerebrovascular event.[9] High quality acute stroke care has been convincingly shown to be associated with decreased mortality and morbidity, as well as with shorter length of hospital stay.[10-12]

Organised stroke units with multi-disciplinary care have superior outcomes than conventional wards,[13,14] but there are few such units in South Africa.[15,16] Patients managed in general medical wards are frequently not managed according to National recommendations due to lack of protocols, bed pressure and staff shortages.[16] Since little is known about the quality of stroke care in developing countries, a better understanding of current practices would be of value in facilitating interventions to improve the quality of stroke care.[17]

We therefore conducted this study to review current practices in the general medical wards at Groote Schuur Hospital and to identify areas where quality of care could be improved. Groote Schuur Hospital is an 893 bed tertiary academic hospital associated with the University of Cape Town, which has 121 secondary level general medical ward beds and a 6 bed specialised stroke unit. When the hospital's stroke unit has reached capacity, patients with acute stroke are managed in the general medical wards.

Methods

Data collection

The Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town approved this retrospective folder review. Data was collected using a standardised template and remains anonymous.

Study population and dates of enrolment

All patients with a diagnosis of acute ischaemic or haemorrhagic stroke who were admitted to the general medical wards at Groote Schuur Hospital from 1 January 2012 to 31 December 2012 were considered for this study.

Patients excluded from study

Patients were excluded if they were under the age of 45 on the day of admission, received thrombolytic therapy for acute stroke, were admitted to the specialised stroke unit or had a discharge diagnosis other than acute stroke.

Demography and clinical background of patients entered into study

The patient's age and gender were recorded, as were comorbidities, which included previous stroke (from history of clinical notes), transient ischaemic attacks (TIAs) prior to the index admission (from history), smoking (based on current or previous history), hypertension (based on history or regular use of anti-hypertensives), diabetes mellitus (based on history, regular use of diabetic agents, hyperglycaemia during admission), hyperlipidaemia (based on history, regular statin use, total cholesterol > 5 mmol/dL on admission), atrial fibrillation (ECG), ischaemic heart disease (based on history of angina or prior myocardial infarction), valvular heart

disease (based on clinical notes or echocardiography), HIV (history, serology or regular use of anti-retroviral therapy) and neurosyphilis (based on cerebrospinal fluid analysis).

Stroke subtype

A stroke specialist reviewed all brain computer tomography (CT) and magnetic resonance imaging (MRI) of included patients and classified patients as haemorrhagic strokes or infarcts. Patients with infarcts were further classified according to the Oxfordshire Community Stroke Project (OCSP) clinical classification into total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI) and posterior circulation infarcts (POCI).[18]

Clinical presentation

The following clinical parameters were recorded: decreased level of consciousness, aphasia (further classified as receptive aphasia or expressive aphasia), dysphagia and hemiparesis affecting the arm or leg and its laterality.

Positive indicators of quality of care

We identified positive indicators of quality of stroke care and grouped them under investigations and management.

The essential investigations of all stroke patients that were identified were CT or MRI brain within 24 hours of admission, glucose on admission, full blood count, renal function, CRP, ECG and chest X-ray.[19] Additional investigations in selected patients that were identified included a lipid profile, HIV testing, syphilis serology, lumbar puncture, CT angiogram of intracranial vessels, Duplex Doppler ultrasonography of carotid arteries and echocardiogram.[19]

With regards to acute stroke management, it was recorded whether patients with ischaemic stroke received aspirin or anticoagulation during their hospital stay.[19] It was also recorded whether patients with infarcts were discharged on antiplatelet therapy or warfarin if in atrial fibrillation. The management of risk factors at discharge that were evaluated included blood pressure control, glucose control and prescription of statin therapy.

It was recorded whether patients underwent formal dysphagia screening within or after 72 hours by speech therapy, and whether patients received nutritional support from a dietician within or after 72 hours. It was furthermore recorded whether patients received nasogastric feeding and intravenous fluids. Nursing notes were reviewed to record whether patients received pressure care. Prescription charts were evaluated to identify sub-cutaneous heparin as part of deep venous thrombosis (DVT) prophylaxis, regular oral diabetic treatment or sub-cutaneous insulin sliding scales in patients with diabetes, antibiotics with its route of administration and paracetamol in the presence of fever.

With regards to inpatient rehabilitation, the time interval between admission and assessment by a physiotherapist and occupational therapist was recorded. Patients were categorised according to whether they were first seen within 72 hours of admission, thereafter or not seen.

Negative indicators of quality of care

The following inpatient complications were recorded: death, fever (temperature > 37.5°C), pneumonia (radiological confirmation or documented clinical findings), urinary tract infection (UTI) (based on urinalysis), hyperglycaemia (blood glucose > 7mmol/L), bedsores (documented in notes), deep vein thrombosis (DVT) (ultrasonographic confirmation), pulmonary embolism (PE) (confirmed by CT of the pulmonary arteries or V/Q scanning), dehydration (recorded in notes), acute kidney

injury (50% in rise of creatinine or 26.1 µmol/L rise in creatinine),[20] seizures, drip site sepsis and gastro-intestinal bleeds (recorded in notes).

Discharge destination

All stroke survivors in this study were classified whether they went home or to inpatient rehabilitation centres directly after the acute hospital admission.

Statistical analysis

Coded data was entered into an Excel computerised database. Statistical analysis was performed by using the software SPSS, version 22. Multivariate logistic regression was performed to assess which variables were associated with death, a categorical variable. The strengths of association of the predictors were expressed as the odds ratio (OR) and their 95% CI. Chi-square tests were used to analyse categorical values, to compare the incidence of complications among patients seen within 72 hours, after 72 hours or not seen by allied health professionals. *P* values of less than 0.05 were considered statistically significant in the analysis.

Results

Review of emergency unit registers for patient referred for medical admission identified 344 with an initial diagnosis of stroke of which 261 patients were included in this study. Amongst the 83 patients excluded, 43 had intracranial pathology other than acute stroke, 9 were readmitted with complications of previous strokes, 9 were transferred to the stroke unit, 3 were younger than 45 years of age and 16 patients had incomplete patient records.

The demographic details, type of stroke, clinical presentation and comorbidities of patients in our study are summarised in table 1.

Table 1: demography, type of stroke, clinical presentation and comorbidities.

	Number	Percentage
Age		
45 – 59 years	85	32.57%
60 – 74 years	111	42.53%
> 75 years	65	24.90%
Gender		
Male	121	46.36%
Female	140	53.64%
Type of stroke		
Ischaemic stroke	216	82.76%
Haemorrhagic stroke	26	9.96%
Infarct with haemorrhagic conversion	6	2.30%
Unknown	13	4.98%
Infarcts classified by OCSP criteria [18]		
Total anterior circulation infarct (TACI)	46	20.72%
Partial anterior circulation infarct (PACI)	110	49.55%
Lacunar infarct (LACI)	51	22.97%
Posterior circulation infarct (POCI)	15	6.76%
Clinical presentation		
Decreased level of consciousness	63	24.14%
Receptive aphasia	34	13.03%
Expressive aphasia	75	28.74%
Dysphagia	125	47.89%
Paresis of right arm	146	55.94%
Paresis of right leg	148	56.70%
Paresis of left arm	108	41.38%
Paresis of left leg	109	41.76%
Comorbidities		
Previous Stroke	94	36.02%
TIA prior to admission	23	8.81%
Smoking	94	36.02%
Hypertension	223	85.44%
Diabetes mellitus	99	37.93%
Hypercholesterolaemia	128	49.04%
Atrial fibrillation	34	13.03%
Ischaemic heart disease	52	19.92%
Valvular Heart Disease	9	3.45%
HIV	5	1.92%
Neurosyphilis	3	1.15%

The positive indicators of quality of care of patients in our study are summarised in tables 2 and 3. Table 2 indicates the number and percentage of patients in this study that underwent the respective special investigations as part of their stroke

work-up, as recommended by the South African Stroke guidelines, whereas table 3 summarises the management that patients received whilst being admitted.

Table 2: positive indicators of quality of stroke care: work-up of acute stroke

	N	Percentage
Essential investigations		
CT brain within 24 hours of admission	228	87,36%
Blood glucose tested on admission	235	90%
Full blood count	259	99.23%
Creatinine, urea and electrolytes	260	99,62%
CRP	12	4.60%
ECG	228	87.36%
Chest X-ray	244	93.49%
Additional investigations		
Lipid profile	190	73.07%
HIV	29	11.11%
Syphilis serology	74	28.35%
CSF analysis	10	3.83%
Angiogram of intracranial vessels	6	2.29%
Doppler of carotid arteries	11	4.21%
Echocardiogram	16	6.13%

Although 90% of patients had their blood glucose measured on presentation (table 2), only half of stroke survivors in this study had their blood glucose measured on the day of discharge. Amongst the group that had their glucose measured on discharge, 92.23% were diabetic. Amongst all patients discharged and glucose measured, 73.78% of patients had a serum glucose of less than 10mmol/L. With regards to diabetic treatment 66 (66.67%) patients received concomittant subcutaneous insulin and oral diabetic treatment (table 3).

Amongst the stroke survivors in this study, 49.3% of patients were discharged home and 50.7% were transferred to inpatient rehabilitation centres.

Table 3: positive indicators of quality of stroke care: management of acute stroke

			N	Percentage
Acute stroke management				
Aspirin *			212 / 216 *	98.15%
Warfarin †			4 / 34 †	8.82%
DVT prophylaxis / sub-cutaneous heparin *			120 / 216 *	55.56%
Pressure care			169	64.75%
Regular oral diabetic medication ‡			70 / 99 ‡	70.7%
Sub-cutaneous insulin sliding scale ‡			69 / 99 ‡	69.7%
Formal dysphagia screening				
Formal dysphagia screening within 72 hours			127	48.66%
Speech therapist only consulted after 72 hours			26	9.96%
Nutritional support				
Dietician	consulted within 72 hours of admission		94	36.02%
	consulted after 72 hours of admission		18	6.90%
Nasogastric feeding in patients with dysphagia §			116 / 125 §	92.8%
Intravenous fluid administration			56	21.46%
Inpatient rehabilitation				
Physiotherapy	within 72 hours of admission		150	57.47%
	after 72 hours of admission		40	15.33%
Occupational therapy	within 72 hours of admission		134	51.34%
	after 72 hours of admission		39	14.94%
Management of complications				
Paracetamol given in the presence of fever ||			26 / 108 ||	24.07%
Antibiotics administered	orally		25	9.58%
	intravenously		38	14.56%
	intravenously and orally		20	7.66%
Management of risk factors at discharge (excluding 54 patients that died)				
Blood pressure control (SBP < 140mmHg)			141	68.11%
Glucose control #	serum glucose 4 – 6.9mmol/L		40 / 103 #	38.83%
	serum glucose 7 – 9.9mmol/L		36 / 103 #	34.95%
Discharged on statin therapy *			185 / 216 *	85.64%
Discharged on single antiplatelet therapy *			151 / 216 *	87.79%
Discharged on dual anti-platelet therapy *			3 / 216 *	1.74%
Discharged on warfarin †			12 / 34 †	35.29%

** management of the 216 with ischaemic stroke patients in this study*
† management of 34 patients with atrial fibrillation
‡ management of the 99 patients with diabetes mellitus in this study
§ management of 125 patients with dysphagia in this study
|| *management of 108 patients with fever (defined as temperature > 37,5°C) in this study*
 # glucose only measured in 103 patients on day of discharge

The negative indicators of quality of care were inpatient complications and death, which are summarised in table 4. In this study, 168 (64%) patients developed at least one inpatient complication.

Table 4: negative indicators of quality of care

	N	Percentage
Inpatient complications		
Death	53	20.31%
Fever	108	41.38%
Pneumonia	51	19.54%
Urinary tract infection	57	21.84%
Drip site sepsis	2	0.77%
Hyperglycemia	59	22.61%
Dehydration	7	2.68%
Acute kidney injury	25	9.58%
DVT	2	0.77%
Bedsores	8	3.07%
GI bleed	4	1.53%
Seizures	2	0.77%

Amongst the 63 patients with a depressed level of consciousness, 42 (66.67%) developed fever, 20 (31.74%) developed pneumonia, 14 (22.22%) developed urinary tract infection, 8 (12.69%) developed acute kidney injury and 30 (47.61%) patients died. Of the 125 patients who had dysphagia, 77 (61%) developed fever, 39 (31.2%) developed pneumonia, 17 (13.6%) developed acute kidney injury and 43 (34.4%) died.

Table 5 illustrates the factors and their odds ratios that predicted death for patients in this study, as calculated by a logistic regression analysis.

Table 5: multivariate logistic regression analysis of the risk of death

Predictor of death	Odds ratio	95% Confidence interval		*P* value
		Lower bound	Upper bound	
TACI [18]	4.803	2.403	9.629	< 0.001
Decreased level of consciousness	6.916	3.607	13.517	< 0.001
Fever	3.240	1.745	6.174	< 0.001
Pneumonia	4.929	2.512	9.714	< 0.001

The following variables that were analysed according to this model did not reach statistical significance: patient characteristics (all variables in table 1, except if indicated above) and inpatient complications (urinary tract infection, drip site sepsis, hyperglycaemia, acute kidney injury, bedsores, deep vein thrombosis, pulmonary embolism, gastro-intestinal bleeds and seizures).

The odds ratio for patients that received physiotherapy was 0.324 for developing pneumonia, with a 95% confidence interval of 0.171 to 0.614 ($P < 0.001$), and 0.209 for death with a 95% confidence interval of 0.111 to 0.396 ($P < 0.001$). Table 6 demonstrates that pneumonia was less frequent in patients who received physiotherapy and significantly reduced in the cohort that received physiotherapy within 72 hours of admission ($P = 0.002$). Speech therapy was not statistically significant in reducing the incidence of pneumonia in this study (P value 0.238).

Table 6: comparison of occurrence of pneumonia according to when patients started physiotherapy

		Physiotherapy			$P = 0.002$
		Cohort seen within 72 hours	Cohort seen after 72 hours	Cohort not seen	Total
Pneumonia	Number	20	7	24	51
	% within cohort	**13.3%**	**17.5%**	**33.8%**	**19.5%**
No pneumonia	Number	130	33	47	210
	% within cohort	**86.7%**	**82.5%**	**66.2%**	**80.5%**
Total	Number	150	40	71	261
	% within cohort	100.0%	100.0%	100.0%	100.0%

$\chi^2 = 12.968;\ df\ 2;\ P = 0.002$

Amongst the 25 patients that developed acute kidney injury, 17 (68%) had dysphagia and received nasogastric tube feeding. As demonstrated in table 7, acute kidney injury was significantly reduced in patients who received early nutritional support, instituted by a dietician, as compared to those assessed by a dietician only after 72 hours of admission ($P < 0.001$).

Table 7: comparison of the occurrence of acute kidney injury (AKI) according to when patients started were first assessed by a dietician and started nutritional support

		Dietician / nutritional support			
		Cohort seen within 72 hours	Cohort seen after 72 hours	Cohort not seen	Total
AKI	Number	14	5	6	25
	% within cohort	**14.9%**	**27.8%**	**4.0%**	**9.6%**
No AKI	Number	80	13	143	236
	% within cohort	**85.1%**	**72.2%**	**96.0%**	**90.4%**
Total	Number	94	18	149	261
	% within cohort	100.0%	100.0%	100.0%	100.0%

$\chi^2 = 15.252;\ df\ 2;\ P < 0.001$

Discussion

Stroke is a leading cause of mortality and morbidity in South Africa.[6,7,16] Although class 1 level A evidence suggests that all stroke patients should be treated in organised stroke units,[19] the majority of South African patients with stroke are treated in general medical wards due to constraints in public health care resources.[16] General medical wards often do not fulfil the criteria of high quality stroke care due to the lack of implementation of protocols or adherence to national stroke care guidelines.[16]

The positive indicators of quality of care that were examined in this study included the work-up and management of acute stroke, as recommended by the South African Stroke Guidelines.[19] Inpatient complications, which contribute to worse outcome, are largely preventable and can be reduced by implementing higher quality care.[15,21-23] The incidence of complications can thus be used as negative indicators of the quality of care.[21,22]

Neuroimaging enables clinicians to differentiate between haemorrhagic and ischaemic stroke as well as to exclude non vascular intra-cranial pathology.[19] Although 87% of patients in this study had neuroimaging within 24 hours of admission and 7% thereafter, which is an indicator of good care, very few patients had investigations such as echocardiography and carotid artery duplex Doppler, as indicated in table 2, and consequently were not adequately investigated for stroke aetiology. Improving access to special investigations would thus be beneficial.

All patients with cerebral infarcts that were not anti-coagulated with warfarin, received aspirin. However, only 8.82% of patients with atrial fibrillation in this study were anti-coagulated as recommended.[19] Two international trials have shown that that aspirin started within 48 hours of the acute ischaemic stroke has beneficial effects.[24-25] However, the IST trial failed to show similar benefits with anti-coagulation, but showed an increased risk of haemorrhage instead.[19,26]

The South African Stroke Society recommends antipyretic treatment if the temperature is greater than 37.5°C, as experimental studies have shown that fever increases infarct size.[19] Fever is a marker of infections and is as an independent predictor of incomplete functional recovery and mortality after stroke.[27] In our study fever was significantly associated with death, as demonstrated in table 5. Amongst the patients in our study that had fever, 37% developed pneumonia and 41% had urinary tract infections. From this study it is apparent that antipyretic treatment was often neglected, as demonstrated in table 3, indicating a lack of awareness amongst clinicians.

In our study, 31.2% of patients with dysphagia developed pneumonia, which is in line with previous studies showing that a third of patients with dysphagia will develop pneumonia.[28,29] Additionally, our study found that pneumonia was significantly associated with death, as presented in table 5. Studies have shown that pneumonia, accounting for a third of post stroke mortality, is the most common non-neurological cause of death following a stroke.[29-31] In ensuring high quality stroke care, all efforts should be made to prevent pneumonia. In our study pneumonia occurred less frequently amongst patients who received physiotherapy, with a further reduction if initiated within 72 hours of admission indicating that care would be improved if all patients requiring physiotherapy received it as soon after admission as possible.

Formal dysphagia screening performed by speech therapists has been shown to significantly reduce the risk of pneumonia.[28] We were not able to determine whether those patients who did have dysphagia screening were fed orally prior to the assessment, which may have increased their risk of pneumonia and thus accounting for our failure to demonstrate a benefit in reducing the incidence of pneumonia. Although there is currently no evidence to suggest when a formal dysphagia screen should be performed, care would be improved if formal dysphagia assessment by a speech therapist was done before oral feeding.[19] In order to maintain nutrition this should be done as soon as possible.[19] In this study there was

a significant reduction in acute kidney injury in patients with dysphagia who received nutritional support within 72 hours of admission, but only 83% of patients with dysphagia were seen by a dietician within that timeframe.

Urinary tract infections (UTI) are common in patients with acute stroke, particularly severe stroke and are associated with poor functional recovery.[27] UTI was a common complication in our study (table 4) but was not a significant predictor of death (table 5). The incidence of both UTI and pneumonia was higher in this study than in others,[23] indicating that stroke care could be improved.

Pressure care was implemented in two thirds of patients in this study (table 3) and bedsores were uncommon (table 4). Venous thromboembolism is an uncommon complication following acute stroke, but remains an important contributor to mortality.[23] Deep vein thrombosis (DVT) has been reported to occur in up to 75% of patients not given thrombo-prophylaxis.[30] Early mobilisation has been shown to reduce the risk of DVT in patients with acute stroke fivefold.[30] It is thus surprising that only two DVTs were diagnosed in our study despite only 56% of patients with infarcts receiving thrombo-prophylaxis. Awareness of thrombo-prophylaxis recommendations and surveillance for DVTs should be increased.

Previous studies have shown that hyperglycaemia is associated with poor outcome after stroke.[9] However, evidence to support tight glycaemic control with insulin infusions after stroke remains limited.[20] The current recommendations by the South African Stroke Society suggest treating hyperglycaemia with insulin if the blood glucose is more than 10 mmol/L.[20] In this study hyperglycaemia occurred in 60% of diabetics indicating a need for more aggressive glycaemic control. Sustained systolic blood pressures over 140 mmHg at the time of discharge were observed in 37% of hypertensive patients indicating sub optimal control. Better adherence to secondary prevention recommendations would reduce the risk of stroke recurrence.[19]

This study highlights the high mortality and morbidity rate of patients with acute stroke managed in general wards. The stroke unit model of care has been shown to reduce complications and result in better functional outcomes following stroke.[13-15] Improved outcomes in stroke units are achieved by improved diagnostic accuracy, appropriate monitoring and the prevention of complications resulting from efficient management by a multidisciplinary team, specialised nursing care, early rehabilitation and better discharge planning.[9,15,32-34] Organised stroke care has successfully been implemented and shown to improve outcomes in low resource settings and if introduced at this hospital would facilitate improving the quality of stroke care.[15]

Limitations

We encountered several limitations in this study. Due to the retrospective nature of this study we relied on the quality of the clinicians' and nursing staff record keeping for data collection. Furthermore, a clinical scoring system such as the Rankin score was not consistently recorded in the notes and functional outcomes could therefore not be measured.

Conclusion

This study indicates the need for organised stroke care with protocols for management within the general medical wards. This would also facilitate more timeous initiation of rehabilitation by the physiotherapist and occupational therapist, as well as expedite early formal dysphagia screening by speech therapy and nutritional support of patients with the help of dietetics. Early rehabilitation prevents deconditioning after stroke and reduces the risk of developing inpatient complications.[35,36] Our study clearly shows the benefit of early mobilisation by the help of physiotherapy in reducing the incidence of pneumonia and early nutritional support to reduce the incidence of acute kidney injury.

Abbreviations

AKI for acute kidney injury, CT for computerized tomography, DVT for deep vein thrombosis, IQR for interquartile range, LACI for lacunar infarct, LOC for level of consciousness, LOS for length of stay, MRI for magnetic resonance imaging, OR, for odds ration, PACI for partial anterior circulation infarct, PE for pulmonary embolism, POCI for posterior circulation infarct, TIA for transient ischaemic attack, TACI for total anterior circulation infarct, UTI for urinary tract infection.

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Authors contributions

Author contributions: CAV and LDV designed the study; CAV collected the data; MB and LD analysed the data; CAV was involved in the manuscript preparation; MB, LD and LDV edited the manuscript.

Competing interests

The authors declare that they have no competing interests.

Disclosures

None

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Chapter 3: Appendices and supporting material

Chapter index

Research protocol

Audit of the quality and cost of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital.

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Background

Although South Africa is at present overwhelmed by infectious diseases such as HIV and TB, there has also been a substantial increase in non-communicable diseases amongst South Africans over the past 15 years.[1,2] The WHO suggests that South Africa has a two to three times higher incidence of non-communicable diseases than that is found in the developed world.[1] This burden of disease is the result of the increase of cardiovascular risk factors present in urban and rural South Africa, and is predicted to increase considerably if the appropriate action is not taken.[1,3,4]

Cerebrovascular accidents remain the second leading cause of mortality and most frequent cause of permanent disability in the world.[5] In South Africa, stroke accounts for 17.7% of female and 12.2% of male deaths in persons of 60 years of age and older, making it the leading cause of death in this age group.[6] In a report published by the Western Cape Department of Health and the City of Cape Town in 2008, it was estimated that the stroke mortality in females ranged from 108.1 to 131.5 deaths per 100000 in Mitchell's Plain and Khayelitsha respectively, whereas in males the deaths per 100000 ranged from 125.8 in Khayelitsha to 136.6 in Mitchell's Plain.[7] This illustrates the burden that cerebrovascular accidents have on the acute and chronic health care facilities.

Even though stroke is a leading cause of morbidity and mortality, very little is known about the quality of stroke care and its incurred cost in South Africa.[8] Knowledge of the quality of stroke care that our patients are currently receiving is of critical importance in order to improve current practices and plan future protocols.[8,9,10] Widespread implementation of optimal stroke care continues to pose enormous challenges on health care systems.[10] Furthermore, with stroke prevalence that is predicted to continue to increase in the near future, the health sector will be faced with even more financial difficulties to maintain optimal care for inpatients with acute stroke.[1,9,10]

Aim

The aim of this project is to establish the quality and cost of acute stroke care in the general medical wards at Groote Schuur Hospital, as a tertiary hospital in the South African setting.

Objective

The objective of this study is to establish the quality of care offered to patients admitted with an acute cerebrovascular attack to general medical wards at Groote Schuur Hospital and to identify specific management practices that could be improved. Data generated by this study will be useful in informing recommendations for stroke management and the development of protocols for acute stroke care in this setting. The study will also establish the cost of stroke care and examine to which extent patient demographics (age and gender), clinical factors (i.e. comorbidities, neurological deficits of the stroke, complications during the admission) and management factors influence the cost of stroke care. This would identify areas where rationalisation of resources could lead to cost savings without a negative impact on stroke care.

Methods

Study design

This study is a retrospective audit of all acute stroke patients admitted to the general medical wards at Groote Schuur Hospital over a 12 month period.

Study sites

The study sites for our project will include the general medicine wards at Groote Schuur Hospital.

Study population and sampling

We intend to include all patients that were admitted with acute ischaemic or haemorrhagic stroke to the general medical wards.

Patients that will not be included in the study are

- Patients in which acute stroke is not the primary reason for admission, or developed stroke in hospital whilst being admitted for another reason
- Patients under the age of 45 on the day of admission
- Patients that received thrombolytic therapy for acute stroke
- Patients that were transferred to the stroke unit
- Patients that suffered from sub-arachnoid haemorrhage

The reason for the above exclusions is that these patients have additional investigations as part of work-up, prolonged hospital stays, a different set of complications, all which may skew the analysis of the data that we wish to collect.

Patients will be identified from admission registers in the emergency unit of Groote Schuur Hospital. In-patient medical records by medical doctors, nursing staff and members of allied health will be reviewed and data will be extracted. Investigations done will be identified using the National Health Laboratory Service (NHLS) and radiology databases, and the relevant results and reports will be included.

Measurements

Data collection to establish quality and cost of acute stroke care will include:

1.1. Demographic data of patients

a. age
b. gender

1.2. Risk factors for cerebrovascular attack (CVA)

a. previous CVA (from history of clinical notes)
b. transient ischaemic attacks (TIAs) prior to admission (from history)
c. smoking (based on current or previous history)
d. hypertension (based on history, notes or regular use of anti-hypertensives)
e. diabetes mellitus (based on history, regular use of diabetic agents, hyperglycaemia)
f. hyperlipidaemia (based on history, regular statin use, total cholesterol > 5 mmol/dL)
g. atrial fibrillation (from history or ECG)
h. ischaemic heart disease (based on history of angina or myocardial infarction)
i. valvular heart disease (based on history or clinical notes)
j. HIV (history, serology or regular use of anti-retroviral therapy)
k. neurosyphilis (based on cerebrospinal fluid analysis)

1.3. Stroke subtype

a. infarct
    I. classified by TOAST criteria (by expert review of CT brain)
        i. total anterior circulation infarct
        ii. partial anterior circulation infarct
        iii. lacunar infarct
        iv. posterior infarct
    II. classified according to pathogenesis of infarct
        i. atherosclerotic
        ii. cardio-embolic
        iii. lacunar
        iv. vasculitis
        v. other
b. haemorrhagic
c. unknown

1.4. Clinical presentation

a. decreased level of consciousness
b. aphasia
    i. receptive aphasia
    ii. expressive aphasia
c. dysphagia
d. hemiparesis
    i. right or left arm
    ii. right or left leg

1.5. Special investigations done during admission (and quantify how many)

a. Blood pressure measured (on admission and discharge)
b. Glucose measured (on admission and discharge)
c. Full blood count
d. Renal function
e. INR
f. Lipid profile
g. TSH
h. Liver function tests
i. CRP
j. Human Immunodeficiency Virus (HIV)
k. Venereal Disease Research Laboratory test (VDRL)
l. Blood culture
m. Chest X-ray (CXR)
n. Electrocardiogram (ECG)
o. Computerised Tomography (CT) of the brain
p. MRI of the brain
q. Angiogram of the intracranial vessels

r. Doppler ultrasound of the carotid arteries
s. Echocardiogram
t. Urinalysis (Dipstix)
u. Urine microscopy, culture and sensitivities
v. Lumbar puncture

1.6. Indicators of poor inpatient care / number of complications

a. Death
b. Fever
c. Pneumonia
d. Urinary tract infection (UTI)
e. Hyperglycaemia
f. Bedsores
g. Deep vein thrombosis (DVT) / pulmonary embolism (PE)
h. Dehydration
i. Acute kidney injury (50% in rise of creatinine or 26.1 µmol/L rise in creatinine)[11]
j. Seizures
k. Drip site sepsis
l. Gastro-intestinal bleeds

1.7. Management

a. Time between admission and CT brain
b. Aspirin given
c. Warfarin given
d. Heparin prophylaxis given
e. Nasogastric tube (NGT) feeding
f. Intravenous fluids administered
g. Fever managed
h. Antibiotics given

i. Pressure care done
j. Regular diabetic medication given
k. Insulin sliding scale prescribed

1.8. How soon patients were assessed by allied health professionals during admission

a. Speech therapy
b. Physiotherapy
c. Occupational therapy
d. Dietician

1.9. Management of risk factors at discharge

a. Blood pressure control at discharge
b. Glucose control at discharge
c. Discharged on antiplatelet therapy
d. Discharged on warfarin if in AF
e. Discharged on a statin if increased cholesterol

1.10. Discharge destination

a. Home
b. Rehabilitation centre

The length of stay will be calculated from the day of admission until the day of discharge, counted in days.

The cost of each stroke included in the study will be determined by accessing the Groote Schuur Hospital financial records through the hospital finance department and case management to determine the bed cost, as well as the radiology, laboratory and pharmacy bills for each subject as identified by their folder number.

Statistical analysis

Coded data will be entered into an Excel computerised database.

Statistical Analysis will be performed using the statistical software R version 3.0.2. Univariate analysis using non-parametric tests and multivariate regression analysis will be used to identify risk factors, stroke characteristics, medical complications and management associated with increased length of stay and cost of admission.

Univariate logistic regressions will be used to identify the risk factors, stroke characteristics and inpatient complications associated with increased risk of death during admission.

Budget

No budget is required for this retrospective study.

Timeline

February 2012 – July 2013	complete project design data collection from medical folders
August 2013	data collection on financial records
September – December 2013	data processing
February – March 2014	data analysis report writing preparation for journal articles

Benefits of this clinical audit

Analysis of data obtained from this audit will identify areas of stroke care where the quality of care could be improved and inform the development of guidelines and protocols of care.

In establishing the cost of stroke care and by identifying those factors that increase the cost of stroke care, we may be able to identify areas where resource utilisation could be rationalised without negatively impacting on stroke care.

Ethics

There are no ethical conflicts in this study, since this project is a retrospective audit of patient information, which will be kept anonymous. Furthermore, this retrospective study would not interfere with the current practice and stroke care patients are receiving.

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Data collection sheet

Audit of the quality and cost of acute inpatient stroke care in general medical wards at Groote Schuur Hospital.

Drs Viljoen / de Villiers

Data sheet

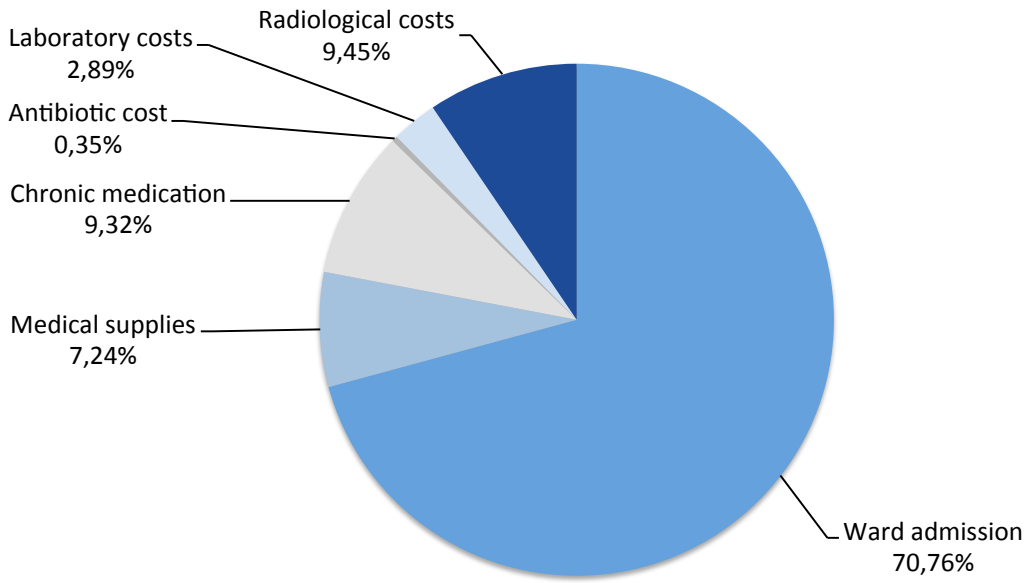
Patient number in study		GSH Folder number					Gender	M	F	
Name			Date of birth				Prev CVA	Y	N	
Risk factors	Smoking	HPT	DM	↑ chol	TIA	A fib	IHD	VHD	HIV	Syphilis
Admission date			BP	/			Glucose			
Investigations (indicate number)	Blood	FBC	U&E	INR	Chol	TSH	LFT	CRP	HIV	RPR	B/C
	CXR	ECG	CT brain	MRI	Carotid	Echo	Angiogram	Dipstix	U-MCS	LP	
	Other									
Time to CTB		Type	Haemorrhage	Infarct	Unknown	TOAST	TACI	PACI	LACI	POCI	
Infarct subtype	Lacunar	Atherosclerosis	Embolic	Vasculitis	*Other:*					
Deficit (on admission)	↓ level of consciousness	Receptive aphasia	Expressive aphasia	Dysphagia						
	Right hemi arm	Right hemi leg	Left hemi arm	Left hemi leg						
Complications	Death	Fever	Pneumonia	UTI	Bedsores	Hyperglycemia				
	DVT	PE	Dehydration	Acute kidney injury (creat up 50% or 26umol/L)						
	Drip site sepsis	Seizures	Upper GI bleed	Number of complications						
Prevention	Aspirin	Warfarin	Heparin prophylaxis	NGT if dysphagia	IV fluids					
	Fever managed	Antibiotics	Pressure care	Regular DM meds	Sliding scale					
Assessed by Allied health	Speech	< 72 hrs	> 72 hrs	none	Dietician	< 72 hrs	> 72 hrs	none		
	Physio	< 72 hrs	> 72 hrs	none	O.T.	< 72 hrs	> 72 hrs	none		
Discharge date			BP	/			Glucose			
Discharge to	Rehab	Home		Reason for delay						
Discharge meds	aspirin	warfarin	statin							
Comments (e.g. which day death, fever occurred)										

		Date				Treatment whilst admitted
FBC	WCC	4 – 10				
	HB	14.3 – 18.3				
	MCV	79 – 96				
	PLTS	137 – 373				
DIFF	Neutro	2.0 – 7.5				
	Mono	0.18 – 0.8				
	Lymph	1.0 – 4.0				
	Eosinophils	0 – 0.45				
CLOT	INR					
	PTT patient					
	PTT control					
RENAL	Na^+	135 – 147				
	K^+	3.3 – 5.3				
	Urea	2.6 – 7.0				
	Creatinine	60 – 120				
	GFR	> 120				
LIVER	Bili total	0 – 21				Treatment on discharge
	Bili conj	0 - 6				
	Total prot	60 – 85				
	Albumin	35 – 52				
	ALP	40 – 120				
	GGT	0 – 60				
	ALT	5 – 40				
	AST	5 - 40				
INFLAM	ESR	0 - 15				
	CRP	0 - 10				
THYR	TSH	0.27 – 4.2				
	T_4	12 - 22				
	T_3					
LIPIDS	Total chol	<5.0				
	Trigs	<3.0				
	HDL	>1.0				Additional comments
	LDL	<1.7				
INFX	RVD					
	CD_4					
	RPR					
	Blood culture					
CSF	Polymorphs					
	Lymphocytes					
	Erythrocytes					
	Protein					
	Glucose					
	Bacteria					
	Culture					
	FTA / TPHA					
	CLAT					

Results and data analyses

The abbreviation **LOS** for "**length of stay**" is often used in the appendix.

Figure 1: Breakdown of cost of all acute stroke admissions in this study



Ward admission	R 3 988 838.23
Medical supplies	R 408 038.86
Chronic medication	R 525 183.91
Antibiotic cost	R 19 473.56
Laboratory costs	R 162 831.55
Radiological costs	R 532 632.00
Total	**R 5 636 998.11**

Figure 2: Correlation between cost and length of stay (LOS)

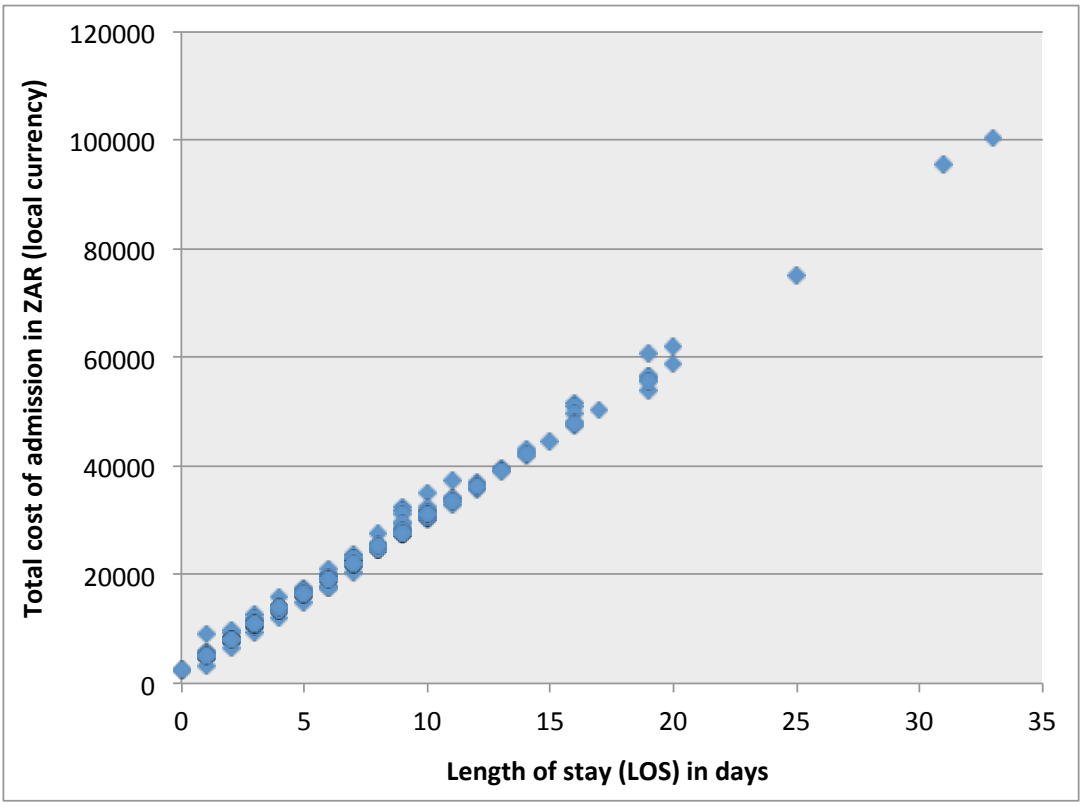


Figure 1: *This scatter plot illustrates the correlation between length of stay as measured in days and total cost of admission in ZAR (r = 0.9977).*

Regressing the total cost of admission by the length of stay (LOS) demonstrated that LOS is highly significant in determining the total cost of admission (p value < 0.001). In support of this regression, the correlation between LOS and total cost is seen to be 0.9977. The adjusted R-squared shows that 99.55% of the variation in total cost is accounted for by variation in the LOS.

Because of the strong correlation between LOS and total cost of admission, we looked at the factors that prolonged LOS to determine what impacts on a more costly admission.

Figure 3: Age distribution of patients admitted for acute stroke

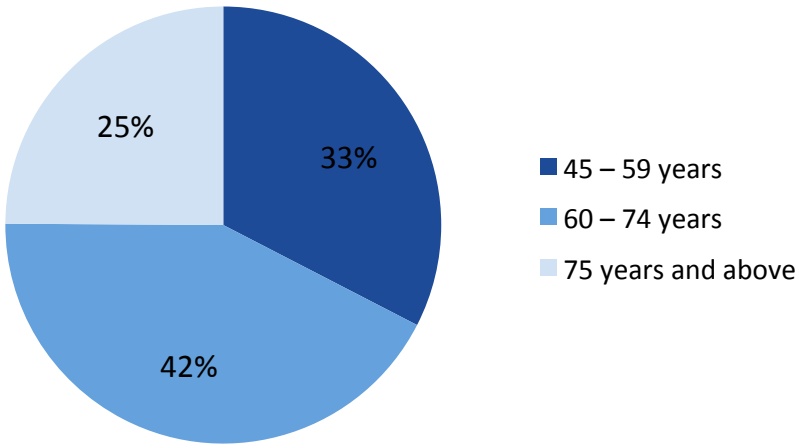
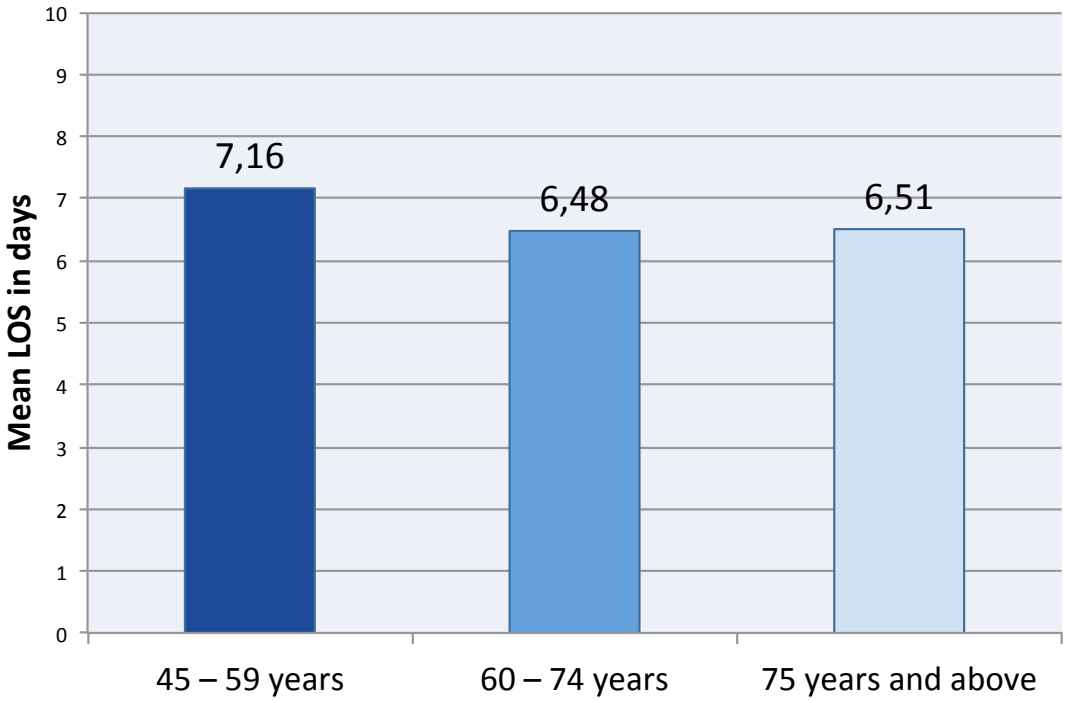


Table 1: Univariate analysis of LOS as influenced by age

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Age (*P* value 0.9191) by Kruskal-Wallis test					
45 – 59	85	32.57%	7.164	6	1 – 20
60 – 74	111	42.53%	6.477	6	1 – 19
> 75	65	24.90%	6.507	5	1 – 17.2

Figure 4: Mean LOS amongst different age groups



Age was not statistically significant in influencing length of stay in this study (refer to table 1)

Figure 5: Percentage males and females in this study

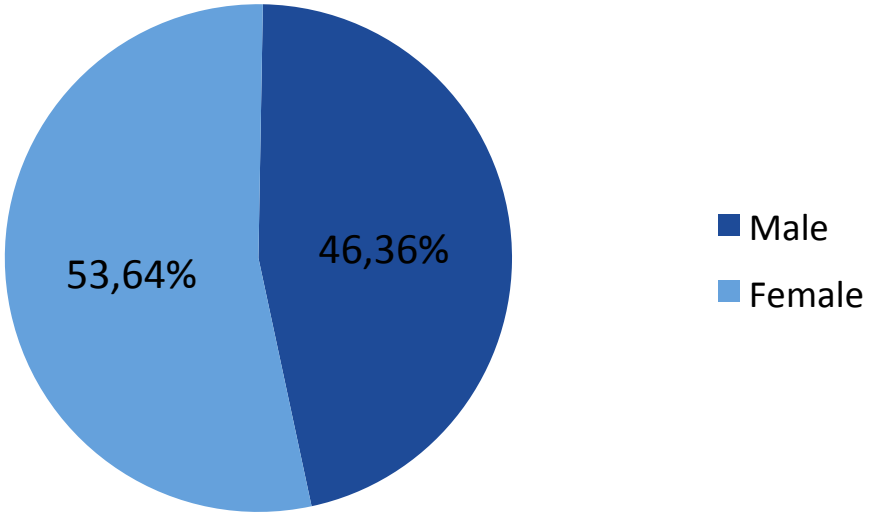
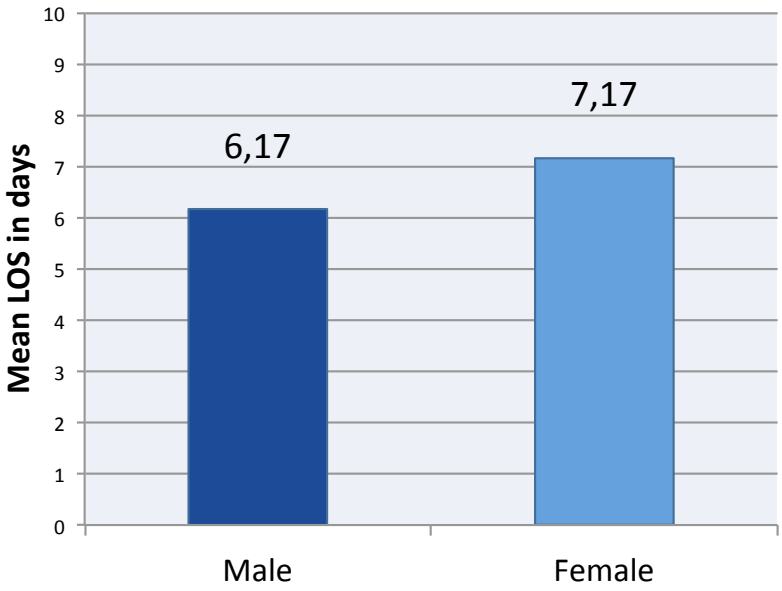


Table 2: Univariate analysis of LOS as influenced by gender

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Gender (*P* value 0.285) by Mann-Whitney *U* test					
Male	121	46.36%	6.165	6	1 - 16
Female	140	53.64%	7.17	6	1 - 19.525

Figure 6: Mean LOS amongst males and females in this study



Gender was not statistically significant in influencing length of stay in this study (refer to table 2).

Figure 7: Incidence of comorbidities in this study

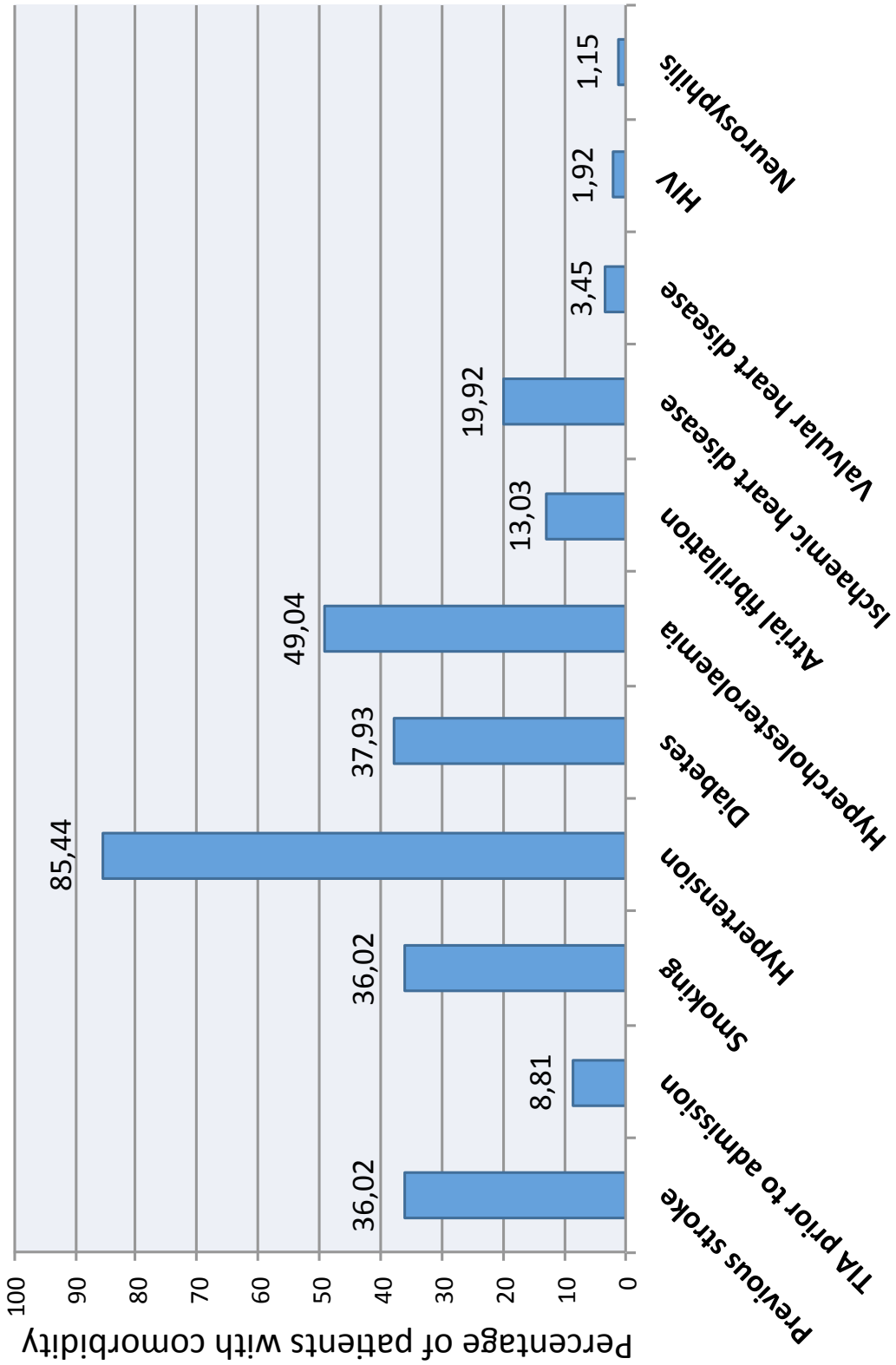


Table 3: Univariate analysis of LOS as influenced by comorbidities

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Previous Stroke (*P* value 0.028) Mann-Whitney *U* test					
Yes	94	36.02%	7.319	7	1 – 19
No	167	63.98%	6.365	5	1 – 19
Transient ischaemic attack (TIA) prior to admission (*P* value 0.953) Mann-Whitney *U* test					
Yes	23	8.81%	6.478	6	1 – 16.15
No	238	91.19%	6.731	6	1 – 19
Smoking (*P* value 0.072) Mann-Whitney *U* test					
Yes	94	36.02%	6.138	5	1 – 19.675
No	167	63.98%	7.029	6	1 – 19
Hypertension (*P* value 0.589) Mann-Whitney *U* test					
Yes	223	85.44%	6.713	6	1 – 19
No	38	14.56%	6.684	5	1 – 19.075
Diabetes mellitus (*P* value 0.910) Mann-Whitney *U* test					
Yes	99	37.93%	6.585	6	1 – 19
No	162	62.07%	6.783	5.5	1 – 17.65
Hypercholesterolaemia (*P* value 0.687) Mann-Whitney *U* test					
Yes	128	49.04%	6.718	5.5	1 – 19
No	133	50.96%	6.699	6	1 – 19
Atrial fibrillation (*P* value 0.263) Mann-Whitney *U* test					
Yes	34	13.03%	7.147	6.5	1.65 – 16.525
No	227	86.97%	6.643	6	1 – 19
Ischaemic heart disease (*P* value 0.678) Mann-Whitney *U* test					
Yes	52	19.92%	6.423	5	1.275 – 16
No	209	80.08%	6.779	6	1 – 19
Valvular Heart Disease * (*P* value 0.031) Mann-Whitney *U* test					
Yes	9	3.45%	9.333	9	2.8 – 15.6
No	252	96.55%	6.615	6	1 – 19
HIV * (*P* value 0.001) Mann-Whitney *U* test					
Yes	5	1.92%	19	19	8.9 – 29.9
No	256	98.08%	6.648	6	1 – 19
Neurosyphilis * (*P* value 0.096) Mann-Whitney *U* test					
Yes	3	1.15%	12	10	6.2 – 19.5
No	258	98.85%	6.647	6	1 – 19

* small sample size, results to be interpreted with caution

The only comorbidities that were statistically significant in influencing LOS were previous stroke, valvular heart disease and HIV.

However, the sample sizes of valvular heart disease and HIV were very small, and the results should therefore be interpreted with caution.

Figure 8: LOS as influenced by comorbidities

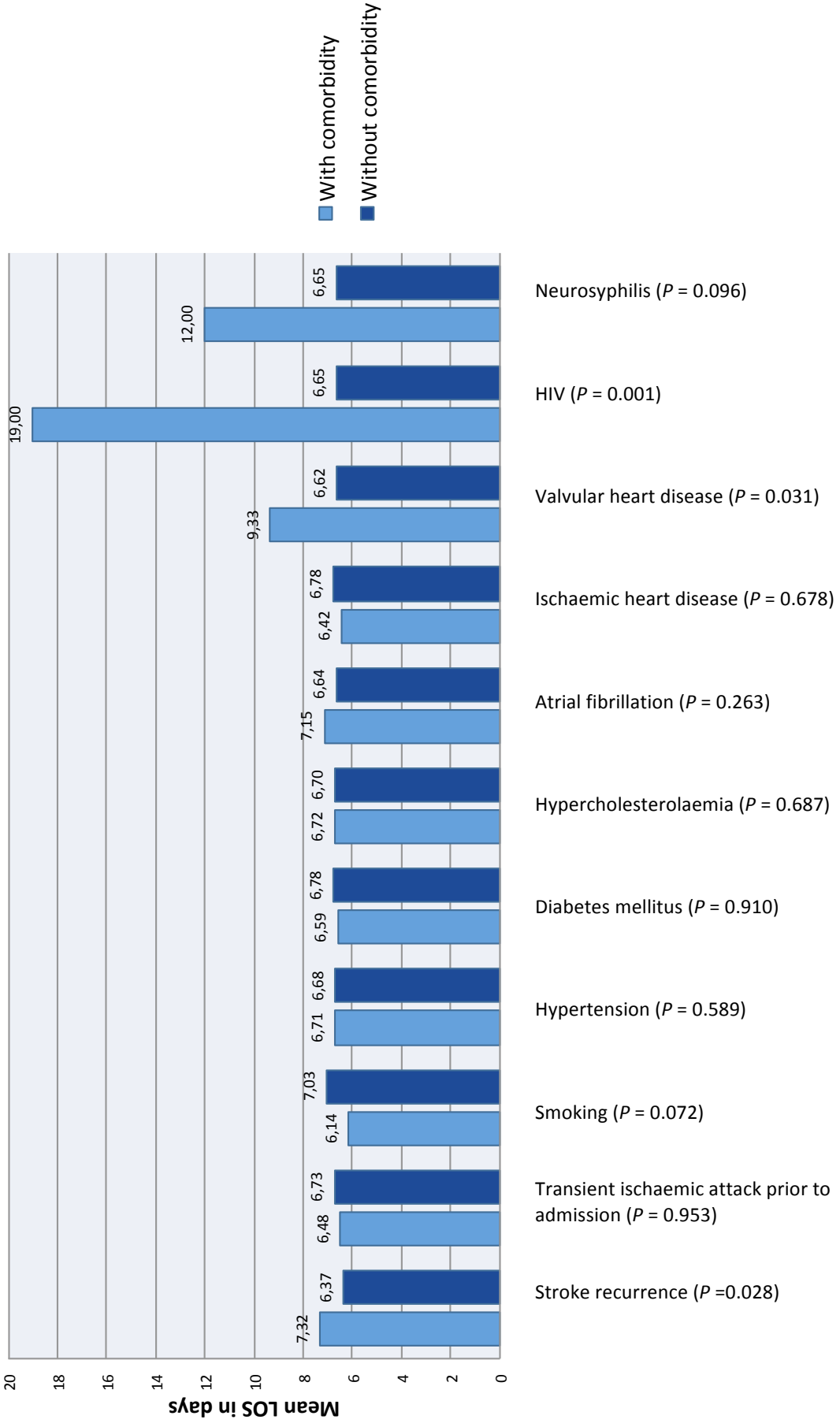


Table 4: Stepwise regression analysis of LOS with comorbidities

Predictor	Number	%	Beta	*P* value
Previous stroke	94	36.02%	0.184	0.022
Smoking	94	36.02%	- 0.154	0.055
HIV *	5	1.92%	1.122	< 0.001

Adjusted R squared: 0.08
F statistic: 8.08 (*P* value < 0.001)

* small sample size, results to be interpreted with caution

Figure 9: Stroke subtypes in this study

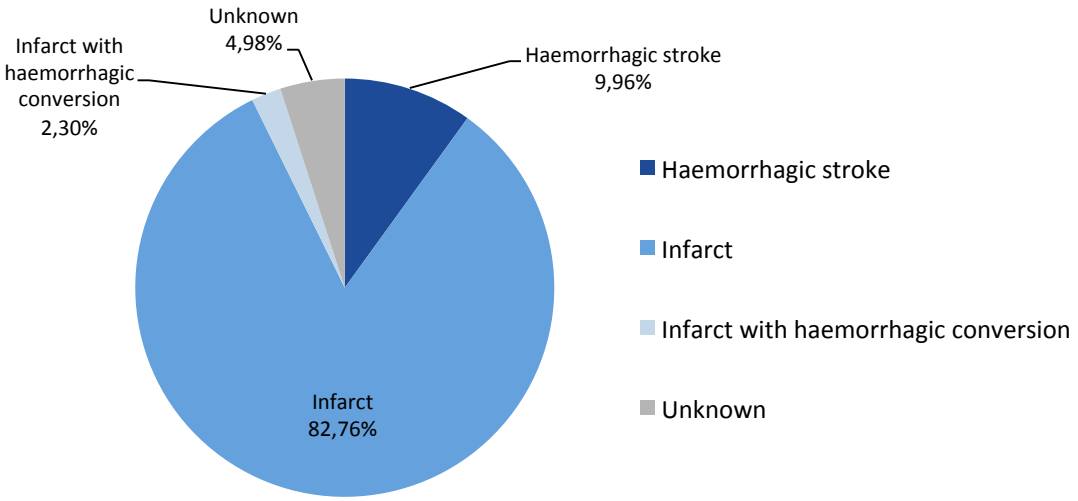
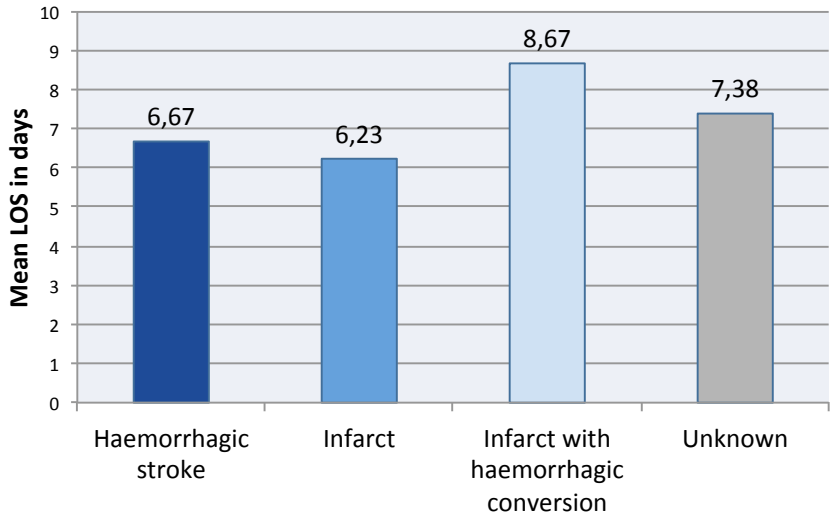


Table 5: Univariate analysis of LOS amongst different stroke types

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Type of stroke (*P* value 0.567) by Kruskal-Wallis test					
Ischaemic	216	82.76%	6.671	6	1 – 19
Haemorrhagic	26	9.96%	6.230	4	1 – 19.37
Infarct with haemorrhagic conversion *	6	2.30%	8.666	7	2.5 – 18
Unknown	13	4.98%	7.384	6	1.3 – 17.5

Figure 10: LOS as influenced by the different stroke subtypes



The difference in stroke subtype was not statistically significant in influencing LOS in this study (refer to table 5).

Figure 11: Infarct subgroups as classified by OCSP clinical classification

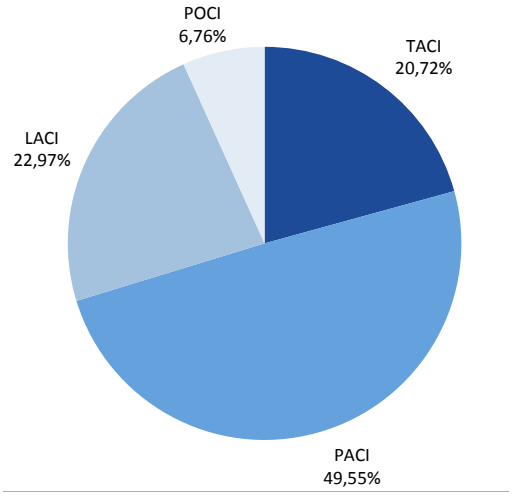
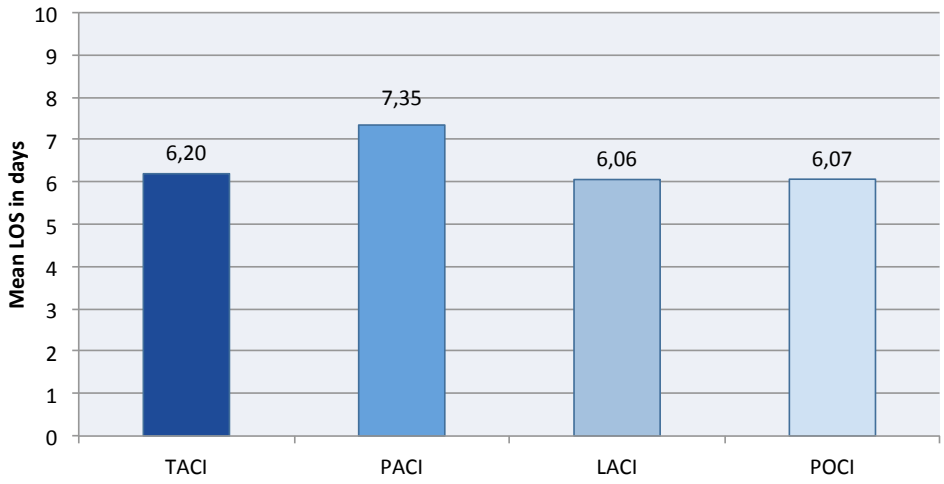


Table 6: Univariate analysis of LOS amongst infarcts as classified by OCSP clinical classification

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Infarcts classified by TOAST criteria (*P* value 0.151) by Kruskal-Wallis test					
TACI	46	20.72%	6.195	4.5	1 – 19.875
PACI	110	49.55%	7.345	7	1 – 19
LACI	51	22.97%	6.058	5	1 – 15
POCI	15	6.76%	6.066	6	1 – 14.25

Figure 12: LOS as influenced by infarct subtypes classified by OCSP clinical classification



The different infarcts classified according to the TOAST criteria were not statistically significant in influencing LOS in this study (refer to table 6).

Figure 13: Infarct subgroups as classified by underlying pathogenesis

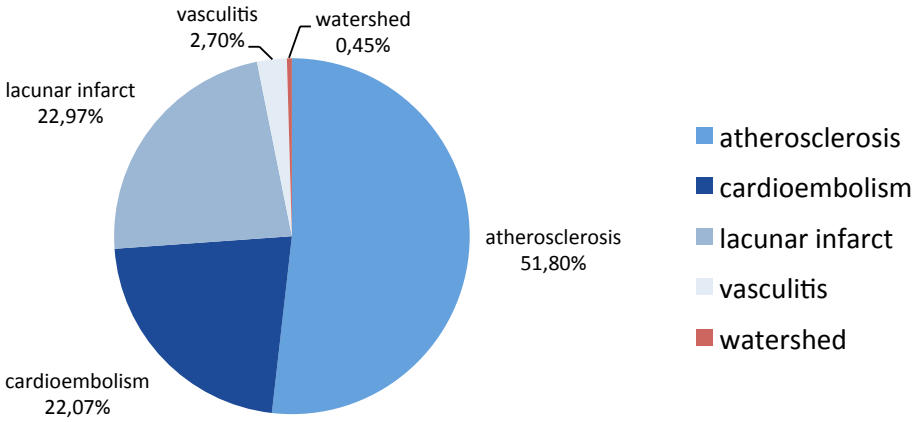
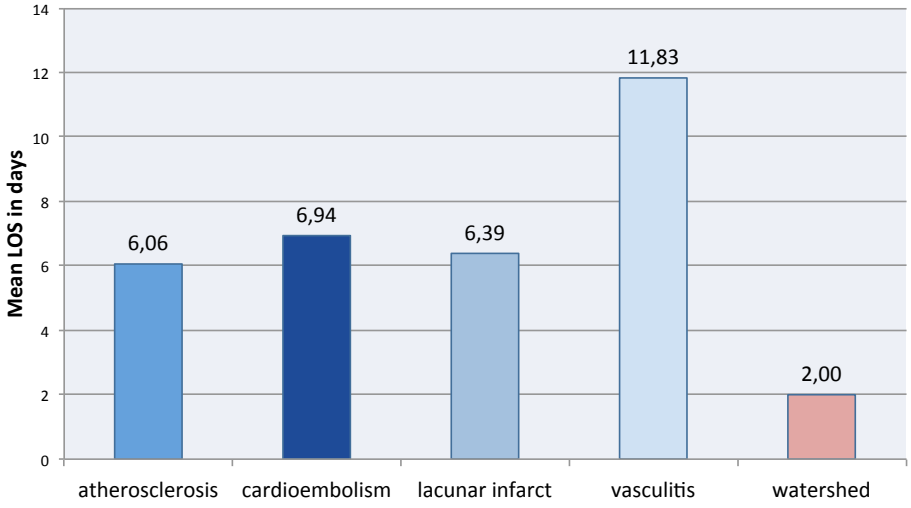


Table 7: Univariate analysis of LOS amongst infarcts as classified according to pathogenesis

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Pathogenesis of infarction (*P* value 0.438) by Kruskal-Wallis test					
Lacunar	51	22.97%	6.058	5	1 – 15
Atherosclerosis	115	51.80%	6.939	6	1 – 19.15
Cardio-embolic	49	22.07%	6.387	5	1 – 16
Vasculitis *	6	2.70%	11.833	12.5	1.625 – 19.875
Watershed *	1	0.45%	2	2	2

* small sample size, results to be interpreted with caution

Figure 14: LOS as influenced by infarct subtypes classified by pathogenesis



The different infarcts classified according to pathogenesis were not statistically significant in influencing LOS in this study (refer to table 7).

Figure 15: Incidence of neurological deficits on admission

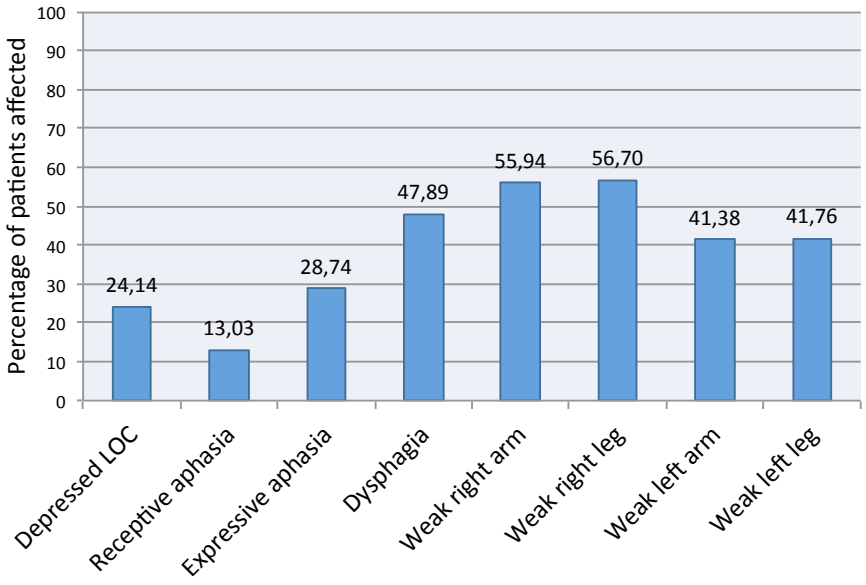
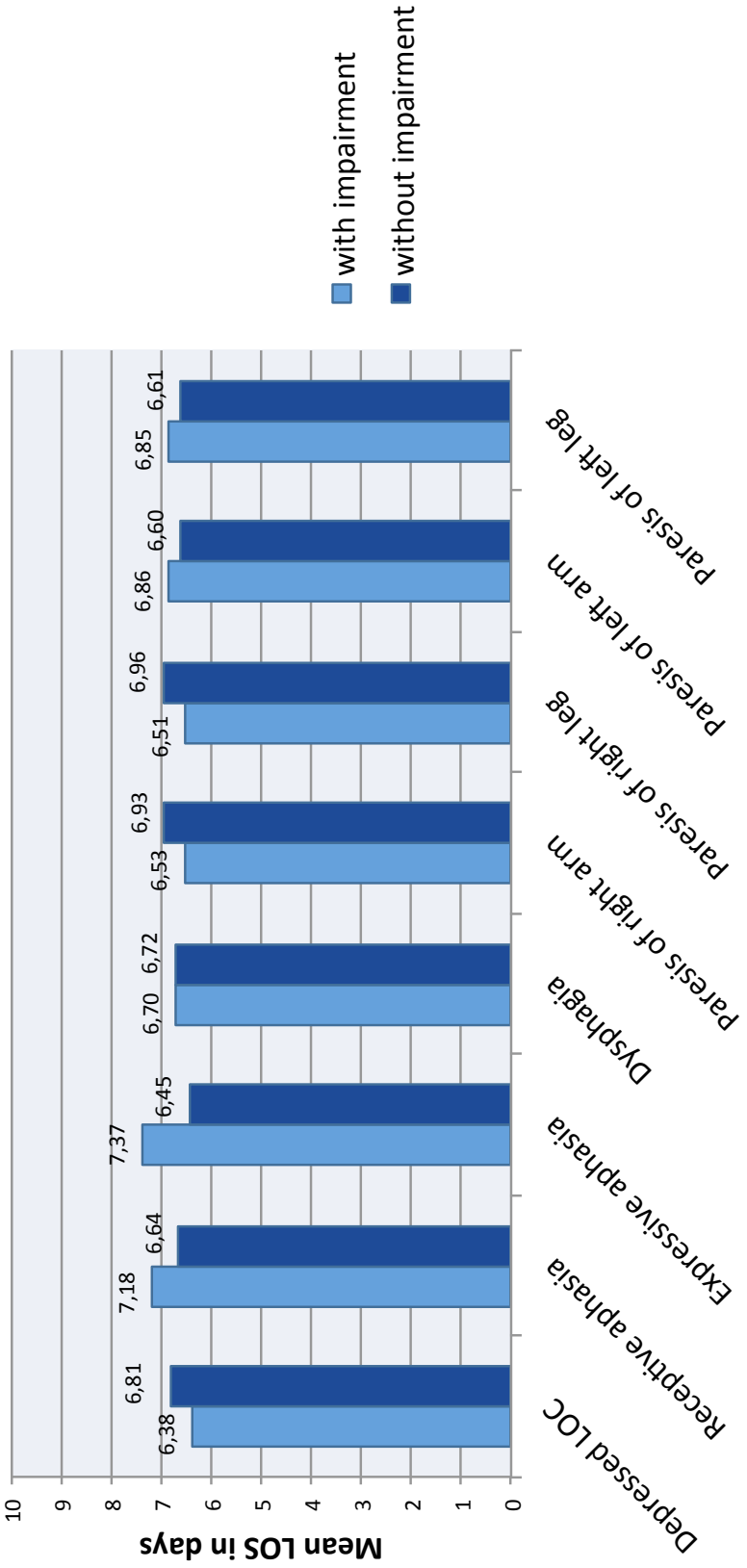


Table 8: Univariate analysis of LOS as influenced by clinical presentation / neurological deficit on admission

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Decreased level of consciousness (*P* value 0.194) Mann-Whitney *U* test					
Yes	63	24.14%	6.380	4	1 – 19
No	198	75.86%	6.813	6	1 – 19
Receptive aphasia (*P* value 0.627) Mann-Whitney *U* test					
Yes	34	13.03%	7.176	6	1 – 21.45
No	227	86.97%	6.638	6	1 – 19
Expressive aphasia (*P* value 0.616) Mann-Whitney *U* test					
Yes	75	28.74%	7.360	6	1 – 25.9
No	186	71.26%	6.446	6	1 – 16.375
Dysphagia (*P* value 0.886) Mann-Whitney *U* test					
Yes	125	47.89%	6.696	6	1 – 19
No	136	52.11%	6.720	6	1 – 19
Paresis of right arm (*P* value 0.162) Mann-Whitney *U* test					
Yes	146	55.94%	6.534	5	1 – 19.37
No	115	44.06%	6.930	6	1 – 16.15
Paresis of right leg (*P* value 0.145) Mann-Whitney *U* test					
Yes	148	56.70%	6.51	5	1 – 19.325
No	113	43.30%	6.964	6	1 – 16.2
Paresis of left arm (*P* value 0.281) Mann-Whitney *U* test					
Yes	108	41.38%	6.861	6	1 – 16.325
No	153	58.62%	6.601	5	1 – 19.2
Paresis of left leg (*P* value 0.289) Mann-Whitney *U* test					
Yes	109	41.76%	6.853	6	1 – 16.3
No	152	58.24%	6.605	5	1 – 19.225

Clinical presentation was not statistically significant in influencing LOS in this study

Figure 16: LOS as influenced by neurological deficit on presentation



Clinical presentation was not statistically significant in influencing LOS in this study (refer to table 8).

Table 9: Stepwise regression analysis of LOS with clinical presentation

Predictor	Number	%	Beta	*P* value
Expressive aphasia	75	28.74%	0.194	0.062
Paresis of right leg	148	56.70%	- 0.182	0.056

Adjusted R squared: 0.01
F statistic: 2.339 (*P* value 0.099)

Figure 17: Systolic blood pressure on presentation

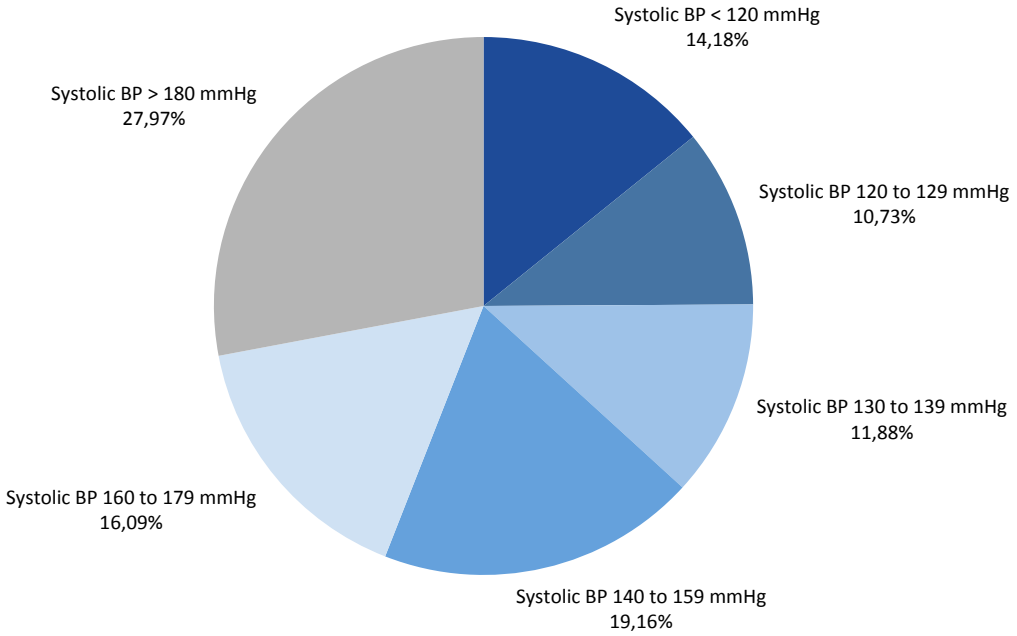


Table 10: Univariate analysis of LOS associated with systolic blood pressure on admission

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Blood pressure on admission (*P* value 0.118) by Kruskal-Wallis test					
SBP < 120	37	14.18%	8.567	8	1.9 – 19.6
SBP 120 – 129	28	10.73%	7.071	5	1 – 23.55
SPB 130 – 139	31	11.88%	5.387	5	1.5 – 12.5
SBP 140 – 159	50	19.16%	6.6	6	1 – 14.78
SBP 160 – 179	42	16.09%	7.024	5	1 – 19.98
SBP > 180	73	27.97%	6.082	5	1 – 16.6

Systolic blood pressure on admission was not statistically significant in influencing LOS in this study.

Figure 18: Blood glucose on presentation

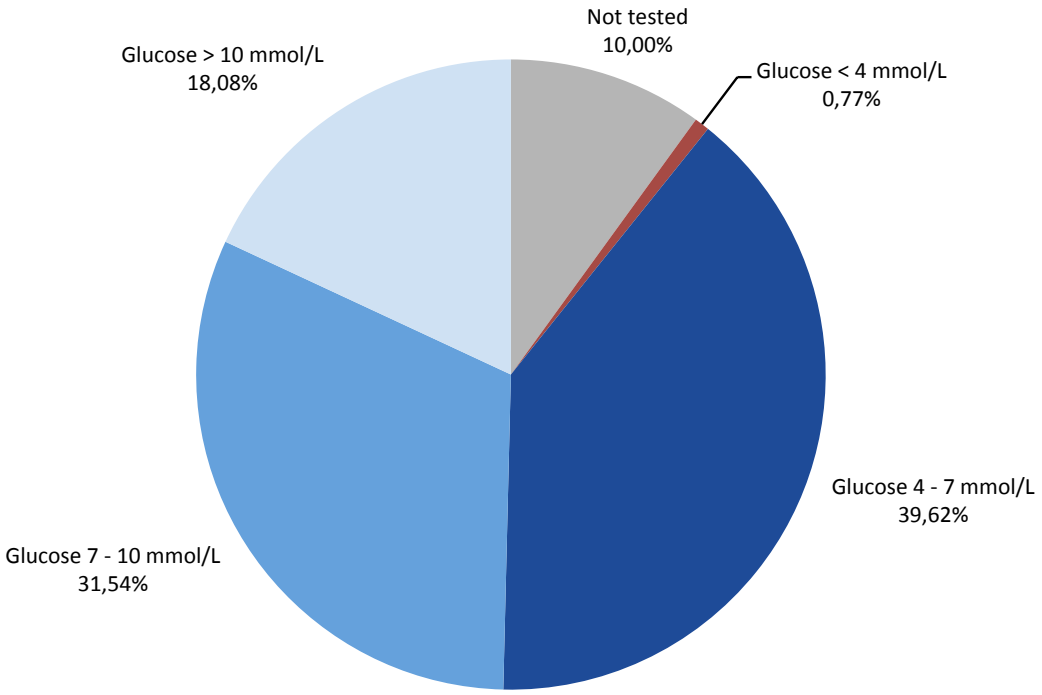


Table 11: Univariate analysis of LOS associated with blood glucose as measured on admission

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Glucose measured on admission (*P* value 0.454) by Kruskal-Wallis test					
Not tested	26	10%	7.615	6	1 – 20
Glucose < 4	2	0.77%	5.5	5.5	4.075 – 6.925
Glucose 4 - 7	103	39.46%	6.592	5	1 – 19
Glucose 7 - 10	82	31.42%	7.341	6	1 – 19
Glucose > 10	47	18.01%	5.438	5	1 – 11.825
Total tested	235	90%			

Blood glucose on admission was not statistically significant in influencing LOS in this study.

Figure 19: Laboratory related investigations done during admission

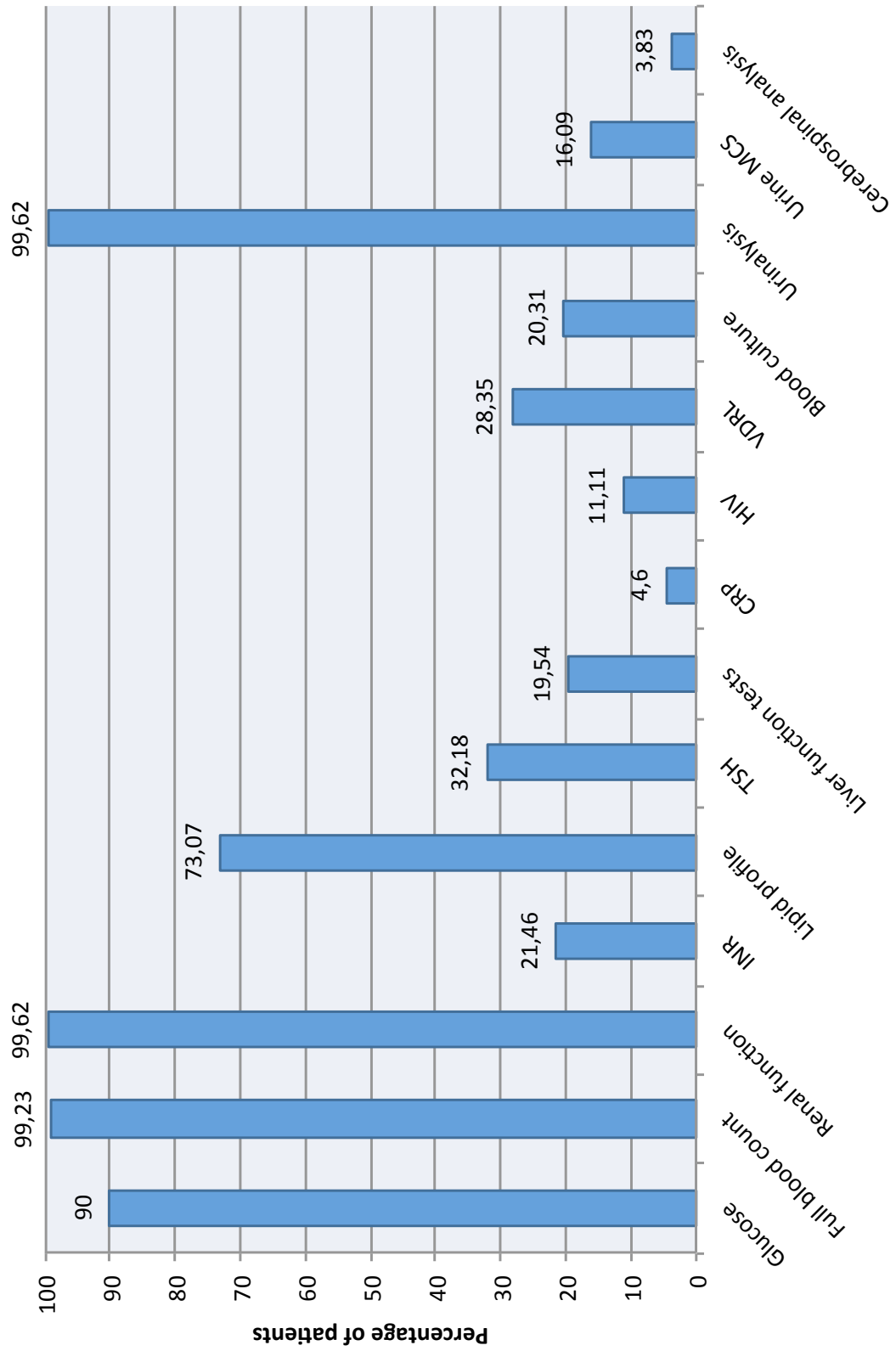


Table 12: Univariate analysis of LOS associated with laboratory related special investigations done during admission

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Full blood count measured (*P* value < 0.001) by Kruskal-Wallis test					
Not tested	2	0.77%	6.5	6.5	4.125 – 8.875
1 test	166	63.60%	5.771	5	1 – 16.875
2 tests	63	24.14%	7.063	6	1 – 19.45
> 2 tests	30	11.49%	11.167	10	3.45 – 26.65
Total tested	*259*	*99.23%*			
Renal function measured (*P* value < 0.001) by Kruskal-Wallis test					
Not tested	1	0.38%	9	9	9
1 test	135	51.72%	5.215	4	1 – 15.65
2 tests	74	28.35%	7.108	6	1 – 19.175
> 2 tests	51	19.54%	10.039	9	2.25 – 23.5
Total tested	*260*	*99,62%*			
INR measured (*P* value 0.042) by Kruskal-Wallis test					
Not tested	205	78.44%	6.492	6	1 – 19
1 test	48	18.39%	6.583	5	1 – 18.475
2 tests	2	0.77%	9.5	9.5	3.325 – 15.675
> 2 tests	6	2.30%	14.167	11	8 – 29.125
Total tested	*56*	*21.46%*			
Lipid profile measured (*P* value 0.127) by Kruskal-Wallis test					
Not tested	71	26.93%	7.056	7	1 – 17.5
1 test	177	67.82%	6.452	5	1 – 19
2 tests	12	4.60%	8.75	9.5	1.55 – 17.07
> 2 tests	1	0.38%	3	3	3
Total tested	*190*	*73.07%*			
TSH measured (*P* value 0.715) by Mann Whitney *U* test					
Not tested	177	67.82%	6.841	6	1 – 19.6
Tested	84	32.18%	6.429	6	1 – 15.85
Liver function test measured (*P* value 0.093) by Kruskal-Wallis test					
Not tested	210	80.46%	6.567	6	1 – 19
1 test	48	19.39%	6.875	6	19
2 tests	2	0.77%	13	13	12.05 – 13.95
> 2 tests	1	0.38%	16	16	16
Total tested	*51*	*19.54%*			
CRP measured (*P* value 0.154) by Kruskal-Wallis test					
Not tested	249	94.40%	6.57	6	1 – 19
1 test	11	4.21%	8.727	6	2.25 – 22.25
2 tests	0	0	0	0	0
> 2 tests	1	0.38%	19	19	19
Total tested	*12*	*4.60%*			

HIV tested (*P* value 0.607) by Mann Whitney *U* test					
Not tested	232	88.89%	6.582	6	1 – 19
Tested	29	11.11%	7.724	7	1 – 23.3
VDRL tested (*P* value 0.462) by Kruskal-Wallis test					
Not tested	187	71,65%	6.254	5	1 – 19
1 test	73	27.97%	7.178	6	1 – 19.2
2 tests	1	0.38%	7	7	7
> 2 tests	0	0	0	0	0
Total tested	*74*	*28.35%*			
Blood culture done (*P* value < 0.001) by Kruskal-Wallis test					
Not tested	208	79.69%	6.091	5	1 – 18.25
1 test	39	14.94%	8.436	8	1.95 – 19.05
2 tests	8	3.07%	9.375	8	3.350 – 22.375
> 2 tests	6	2.30%	13.333	15	5.5 – 19.5
Total tested	*53*	*20.31%*			
Urinalysis (dipstix) analysed (*P* value 0.095) by Mann Whitney *U* test					
Not tested	1	0.38%	2	2	2
Tested	260	99.62%	6.645	6	1 – 19
Urine MCS done (*P* value of 0.621) by Mann Whitney *U* test					
Not tested	219	83.91%	6.562	6	1 – 19
Tested	42	16.09%	7.778	6	1.88 – 20.5
Lumbar puncture and CSF analysis (*P* value 0.020) by Mann Whitney *U* test					
Not tested	251	96.17%	6.566	6	1 – 19
Tested	10	3.83%	10.3	9.5	2.68 – 19.78

Figure 20: Comparing LOS and number of laboratory tests done

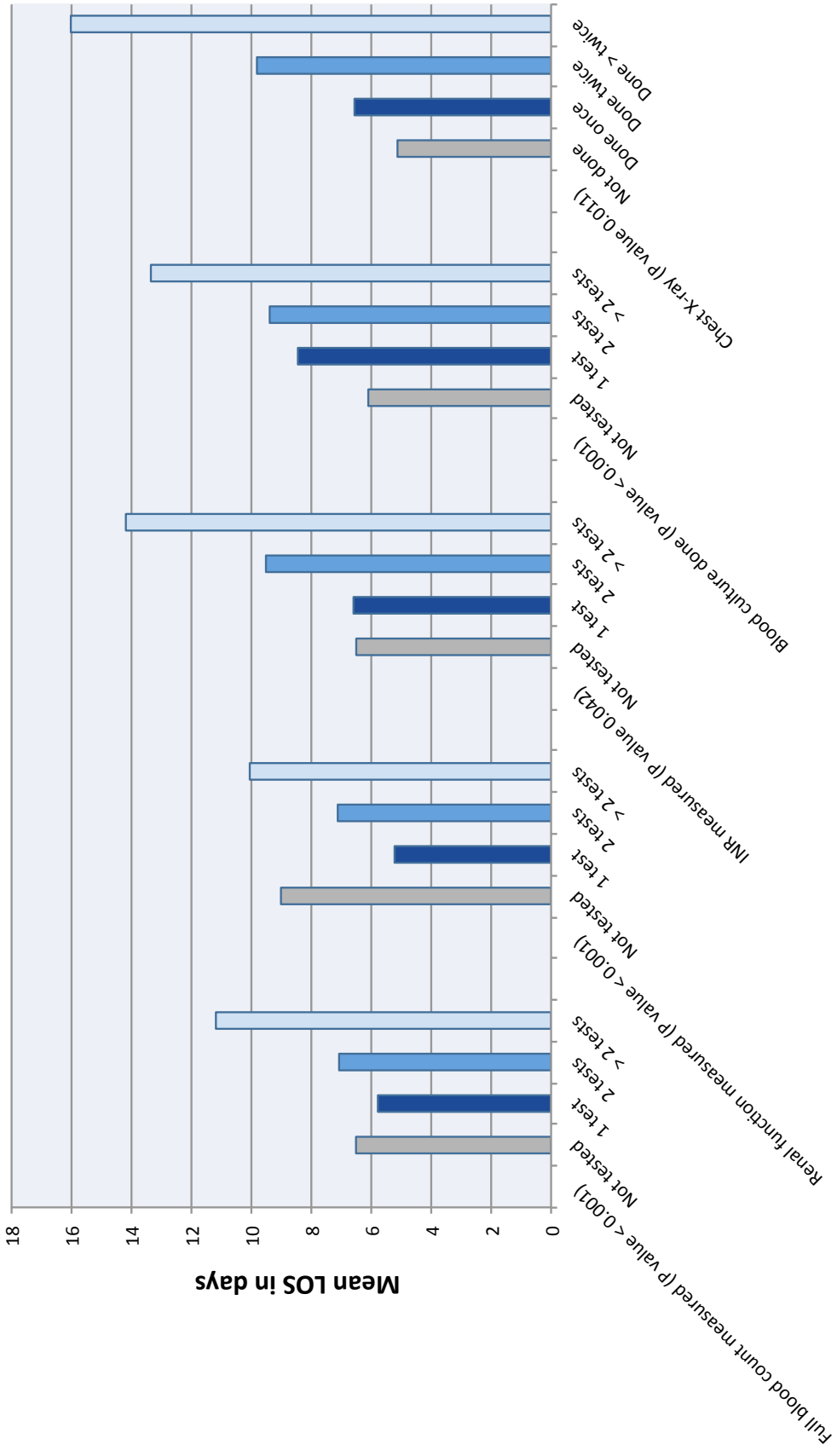


Figure 21: Radiological and cardiac investigations done during admission

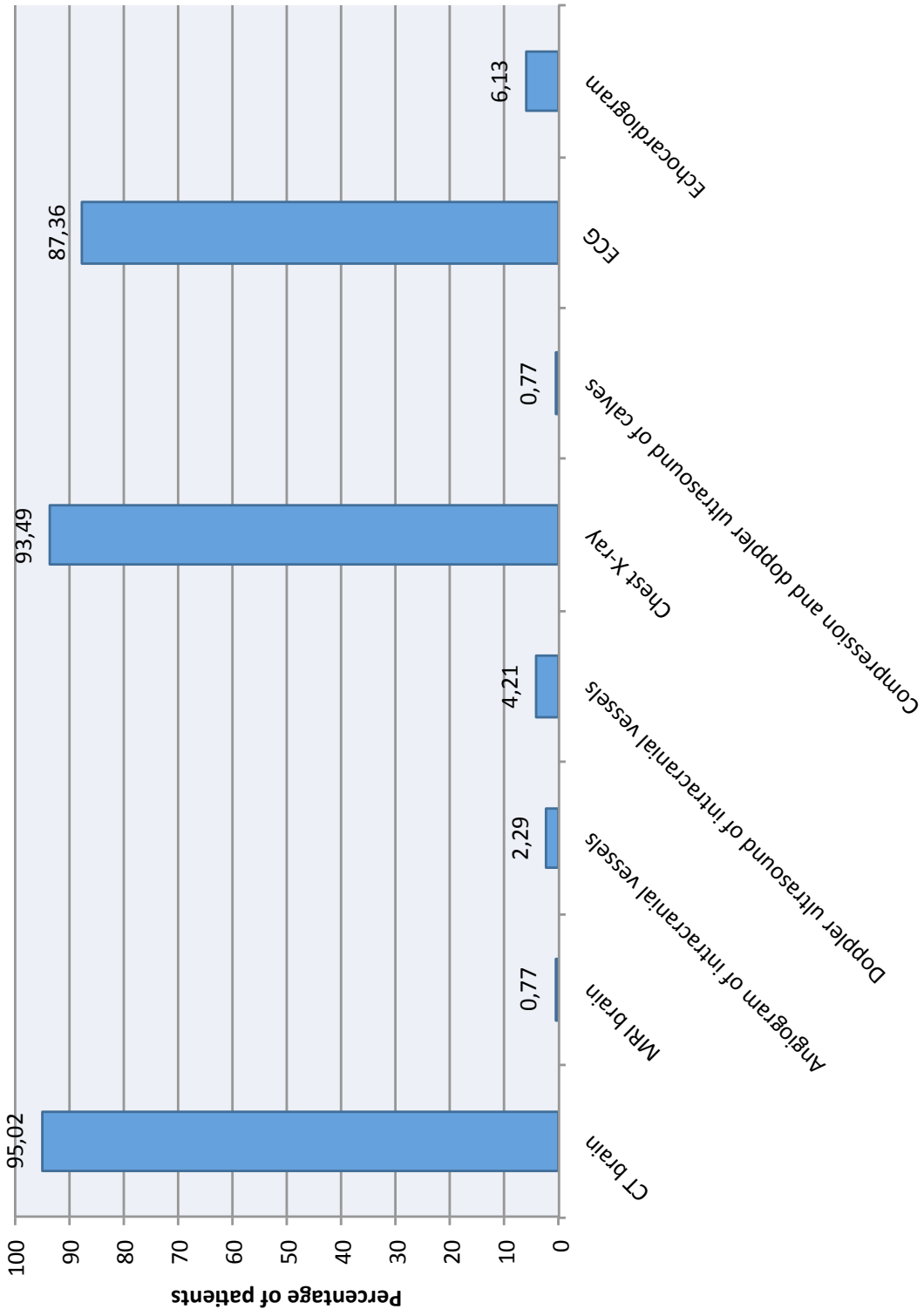


Table 13: Univariate analysis of LOS associated with radiological and cardiac investigations done during admission

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
CT brain (*P* value 0.759) by Kruskal-Wallis test					
Not done	13	4.98%	7.385	6	1.3 – 17.5
Done once	237	90.80%	6.620	6	1 – 19
Done twice	10	3.83%	7.7	6.5	2 – 19.1
Done > twice	1	0.38%	9	9	9
Total done	*248*	*95.02%*			
MRI brain * (*P* value 0.053) by Mann Whitney *U* test					
Not done	259	99.23%	6.649	6	1 – 19
Done	2	0.77%	14.5	14.5	10.23 – 18.78
Total done	*2*	*0.77%*			
Angiogram of intracranial vessels * (*P* value 0.035) by Mann Whitney *U* test					
Not done	255	97.71%	6.494	6	1 – 19
Done once	6	2.29%	15.833	10.5	2 – 32.75
Total done	*6*	*2.29%*			
Doppler of carotid arteries (*P* value 0.021) by Mann Whitney *U* test					
Not done	250	95.79%	6.448	6	1 – 19
Done once	11	4.21%	12.636	9	3.25 – 32.5
Total done	*11*	*4.21%*			
Chest X-ray (*P* value 0.011) by Kruskal-Wallis test					
Not done	17	6.51%	5.118	3	1 – 17
Done once	222	85.06%	6.550	6	1 – 19
Done twice	16	6.13%	9.8	9	5.4 – 15.4
Done > twice	6	2.30%	16	16	16
Total done	*244*	*93.49%*			
Compression ultrasound of calves * (*P* value 0.185) by Mann Whitney *U* test					
Not done	259	99.23%	6.687	6	1 – 19
Done once	2	0.77%	9.5	9.5	8.08 – 10.93
Total done	*2*	*0.77%*			
ECG (*P* value 0.486) by Kruskal-Wallis test					
Not done	33	12.64%	6.484	5	1 – 20.2
Done once	207	79.31%	6.633	6	1 – 19
Done twice	16	6.13%	7.688	7	2.38 – 17.87
Done > twice	5	1.92%	8.2	5	4 – 18.8
Total done	*228*	*87.36%*			
Echocardiogram * (*P* value 0.007) by Mann Whitney *U* test					
Not done	245	93.87%	6.4	5	1 – 19
Done once	16	6.13%	11.438	8.5	2.75 – 32.25
Total done	*16*	*6.13%*			

Delays in CT angiogram and echocardiogram were associated with prolonged LOS, however, the sample sizes in these groups were to small to accurately interpret the results.

Figure 22: Percentage of patients that went to CT brain within or after 24 hours

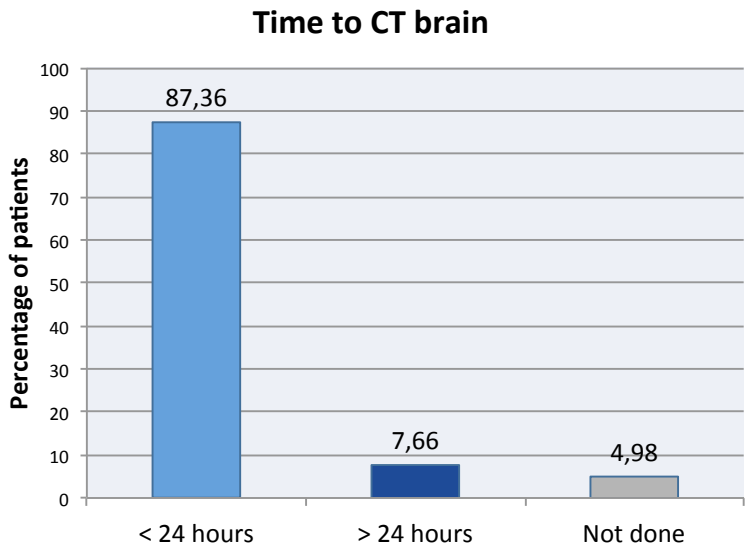
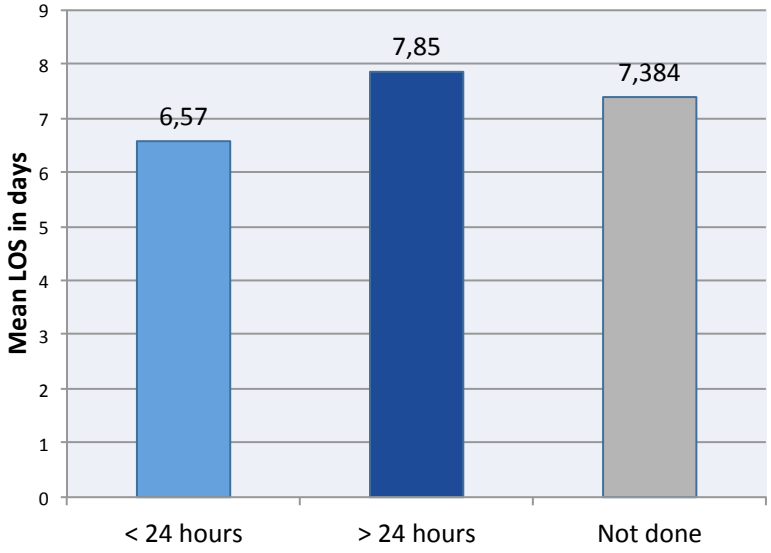


Table 14: Univariate analysis of LOS as influenced by time to CT brain

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Time to CT or MRI of brain (*P* value 0.230) by Kruskal-Wallis test					
< 24 hours	228	87,36%	6.570	5.5	1 – 19
> 24 hours	20	7,66%	7.85	8	1.475 – 16.675
Not done	13	4,98%	7.384	6	1.3 – 17.5

Figure 23: Influence of time to CT brain on LOS



Time to CT brain was not statistically significant in influencing LOS in this study (refer to table 14).

Figure 24: Medical management of patients in this study

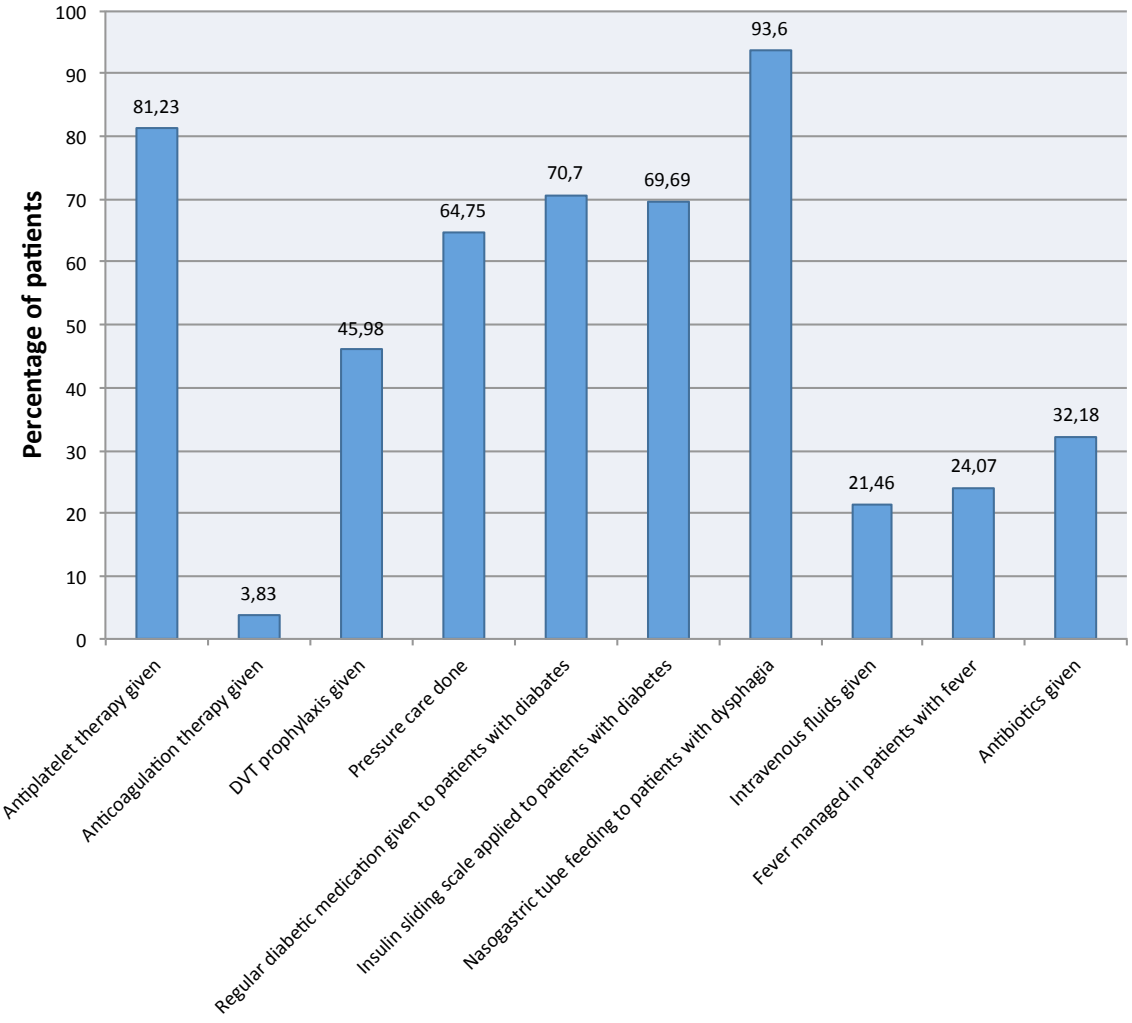


Figure 25: Percentage of patients managed by allied health professionals, and when first assessed

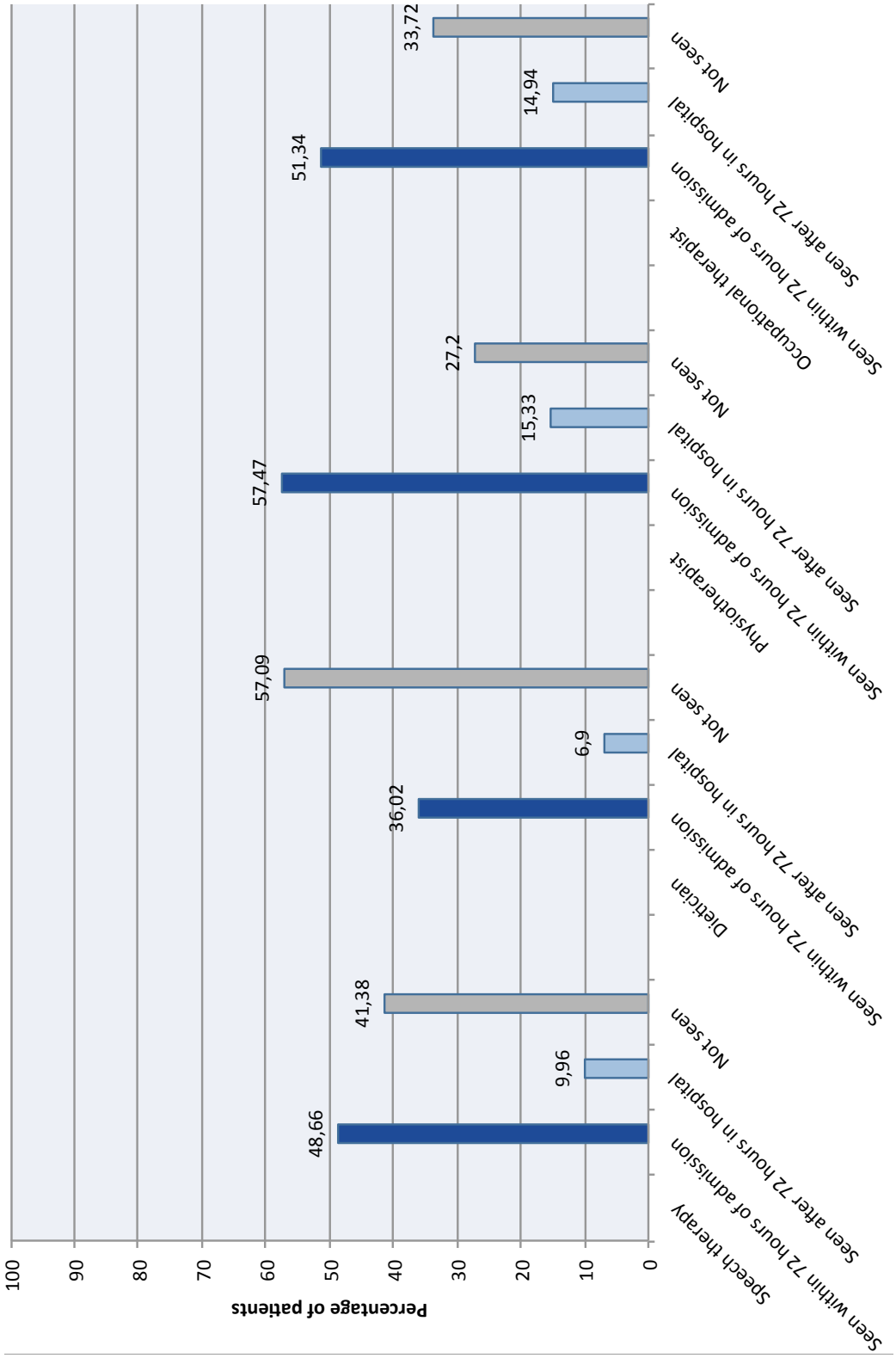


Table 15: Univariate analysis of LOS as influenced by when patients were first assessed by allied medical services

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Speech therapy (*P* value < 0.001) by Mann Whitney *U* test					
Seen within 72 hours of admission	127	48.66%	7.637	7	2 – 19.85
Seen after 72 hours in hospital	26	9.96%	10.461	10	4.250 – 19.370
Dietician (*P* value < 0.01) by Mann Whitney *U* test					
Seen within 72 hours of admission	94	36.02%	7.308	6.5	1.325 – 19
Seen after 72 hours in hospital	18	6.90%	10.555	10	4.275 – 19.575
Physiotherapist (*P* value < 0.01) by Mann Whitney *U* test					
Seen within 72 hours of admission	150	57.47%	7.220	6	2 – 19
Seen after 72 hours in hospital	40	15.33%	9.300	9	4 – 19.025
Occupational therapist (*P* value < 0.001) by Mann Whitney *U* test					
Seen within 72 hours of admission	134	51.34%	7.291	6	2 – 19
Seen after 72 hours in hospital	39	14.94%	9.846	9	4 – 19.05

Figure 26: Mean LOS as influenced by when patients were first assessed by allied health professionals

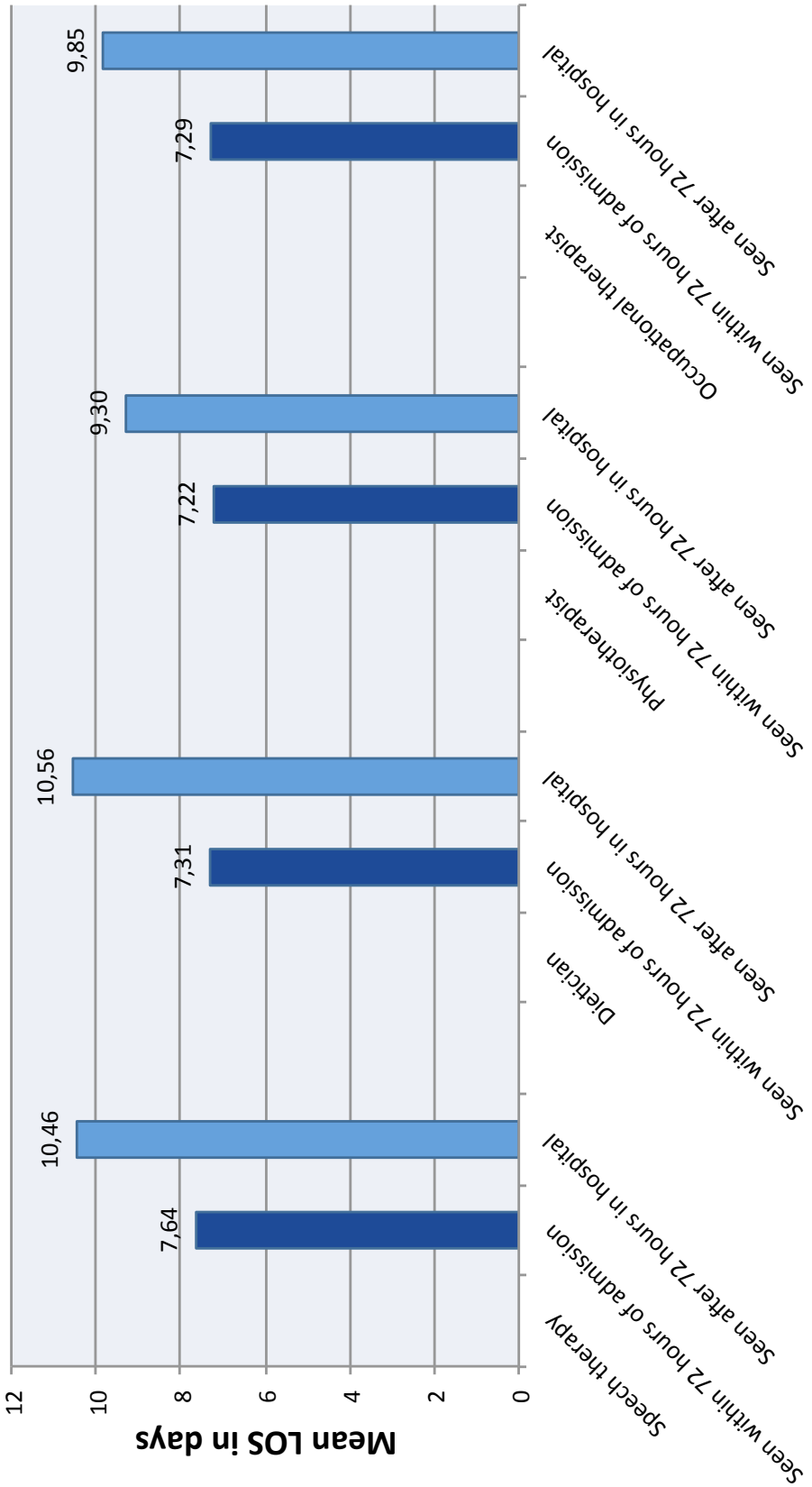


Figure 27: Percentage of patients that developed inpatient complications

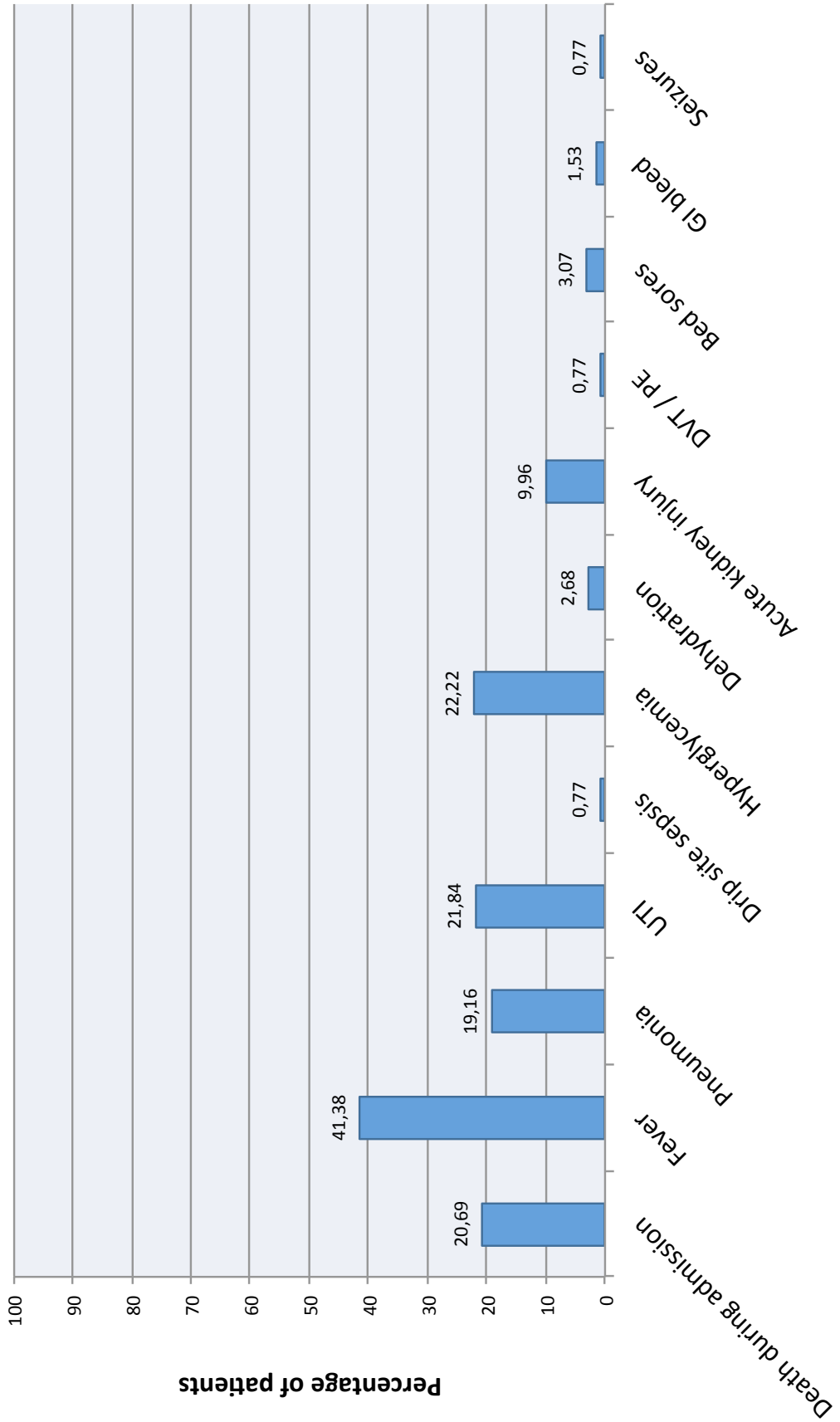


Table 16: Univariate analysis of LOS as influenced by medical complications during admission

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Death during admission (*P* value < 0.001) by Mann Whitney *U* test					
Yes	53	20.31%	4.320	3	1 – 11.7
No	208	79.69%	7.317	6	1 – 19
Fever (*P* value 0.001) by Mann Whitney *U* test					
Yes	108	41.38%	7.851	7	1.675 – 19.325
No	153	58.62%	5.901	5	1 – 16
Pneumonia (*P* value 0.769) by Mann Whitney *U* test					
Yes	51	19.54%	7.117	5	1 – 19.5
No	210	80.46%	6.609	6	1 – 19
UTI (*P* value < 0.001) by Mann Whitney *U* test					
Yes	57	21.84%	8.122	7	2 – 16
No	204	78.16%	6.313	5	1 – 19
Drip site Sepsis * (*P* value 0.037) by Mann Whitney *U* test					
Yes	2	0.77%	15.5	15.5	11.225 – 19.775
No	259	99.23%	6.640	6	1 – 19
Hyperglycaemia (*P* value 0.258) by Mann Whitney *U* test					
Yes	59	22.61%	7.016	6	1.45 – 17.65
No	202	77.39%	6.618	5	1 – 19
Dehydration * (*P* value 0.629) by Mann Whitney *U* test					
Yes	7	2.68%	7.285	7	2 – 13.7
No	254	97.32%	6.692	6	1 – 19
Acute kidney injury (*P* value < 0.001) by Mann Whitney *U* test					
Yes	25	9.58%	9.480	10	3.6 – 17.2
No	236	90.42%	6.415	5	1 – 19
DVT / PE * (*P* value 0.185) by Mann Whitney *U* test					
Yes	2	0.77%	9.5	9.5	8.075 – 10.925
No	259	99.23%	6.687	6	1 – 19
Bedsores * (*P* value 0.242) by Mann Whitney *U* test					
Yes	8	3.07%	8.375	7	2.35 – 17.6
No	253	96.93%	6.656	6	1 – 19
GI Bleed * (*P* value 0.594) by Mann Whitney *U* test					
Yes	4	1.53%	10	10	1.225 – 18.775
No	257	98.47%	6.657	6	1 – 19
Seizures * (*P* value 0.116) by Mann Whitney *U* test					
Yes	2	0.77%	10	10	10 – 10
No	259	99.23%	6.683	6	1 – 19

* small sample size, results to be interpreted with caution

Inpatient complications that were significant in prolonging LOS were fever, UTI and acute kidney injury. Drip site sepsis had a small sample size and the results should therefore be interpreted with caution. Death was significant in shortening LOS.

Figure 28: Mean LOS as influenced by inpatient complications

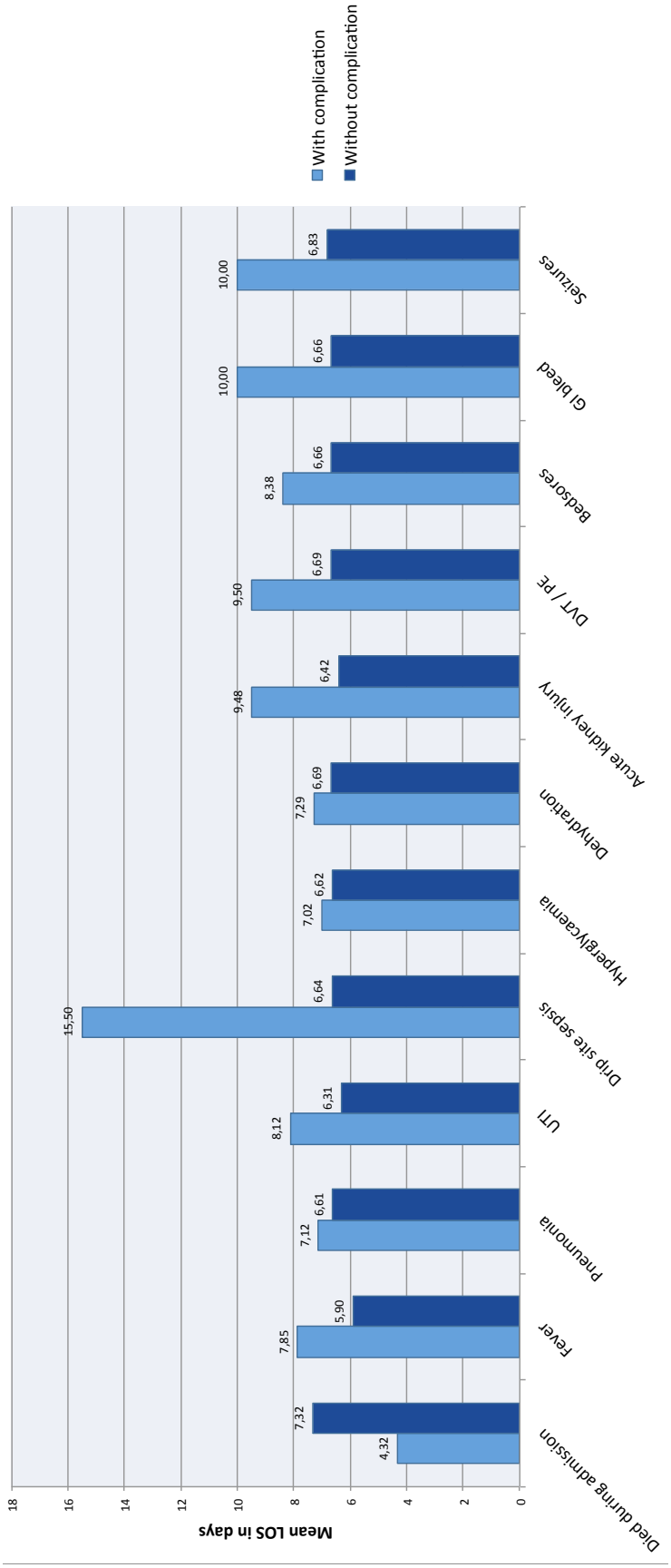


Table 17: Stepwise regression analysis of LOS against complications

Predictor	Beta	*P* value
Fever	0.281	< 0.001
UTI	0.166	0.084
AKI	0.303	0.017
Death	- 0.574	< 0.001

R adjusted squared: 0.1922
F statistic: 16.47 (*P* value < 0.001)

On stepwise regression analysis, inpatient complications that were significant in prolonging LOS were fever and acute kidney injury.

Death was significant in shortening LOS.

Figure 29: The number of inpatient complications that patients developed

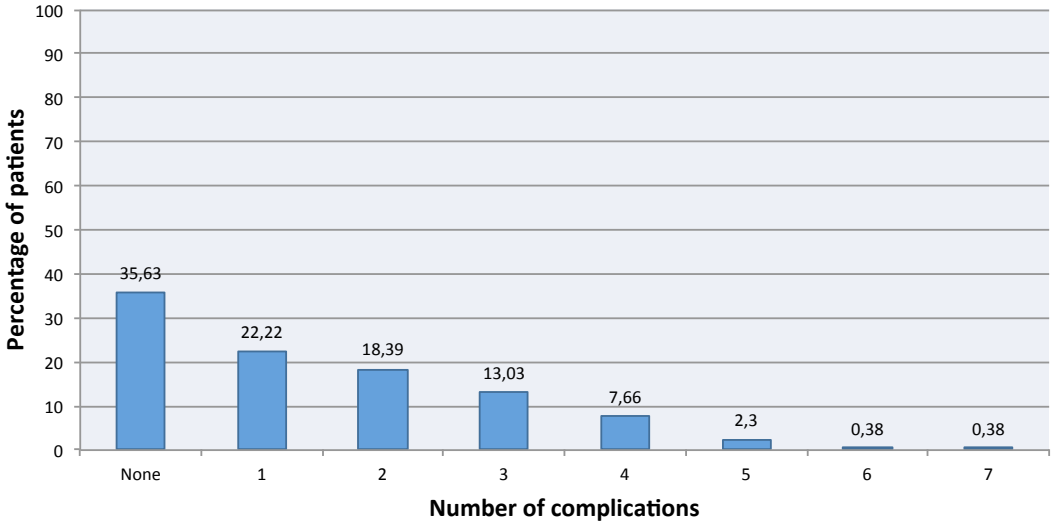


Table 18: Univariate analysis of LOS as influenced by the number of complications patients developed during admission

	Number	Percentage	Mean LOS	Median LOS
Number of complications (*P* value 0.22) by Kruskal-Wallis testing				
0	93	35.63%	6.247	5
1	58	22.22%	6.310	6
2	48	18.39%	7.166	5.5
3	34	13.03%	6.500	5.5
4	20	7.66%	8.3	8
5	6	2.30%	7.666	8
6	1	0.38%	11	11
7	1	0.38%	16	16

Figure 30: Mean LOS increased as the number of inpatient complications increased

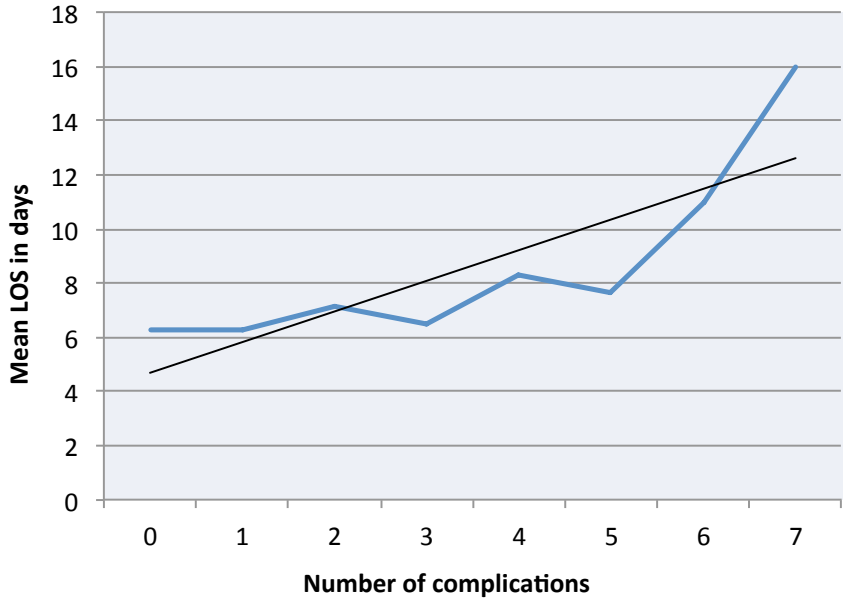


Table 19: Univariate analysis of LOS as influenced by the number of complications patients experienced during admission, categorised

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Number of complications (*P* value 0.059) by Kruskal-Wallis testing					
0	93	35.63%	6.247	5	1 – 16.7
1	58	22.22%	6.310	6	1 – 17.725
2-3	82	31.42%	6.890	5.5	1 – 19
4>	28	10.73%	8.535	8.5	2 – 18.925

Table 20: Incidence of complications amongst ischaemic and haemorrhagic stroke

	Ischaemic stroke N = 216		Haemorrhagic stroke N = 26	
	Number	%	Number	%
Death	43	19.9	5	19.2
Fever	81	37.5	14	53.84
Pneumonia	41	18.89	7	26.92
UTI	35	16.2	3	11.53
Acute kidney injury	8	3.7	1	3.8

Table 21: Incidence of complications amongst patients with depressed level of consciousness

	Depressed level of consciousness N = 63	
	Number	%
Death	30	47.61
Fever	42	66.67
Pneumonia	20	31.74
UTI	14	22.22
Acute kidney injury	8	12.69

Table 22: Incidence of complications amongst patients with dysphagia

	Dysphagia N = 125	
	Number	%
Death	43	34.4
Fever	77	61
Pneumonia	39	31.2
Acute kidney injury	17	13.6

Table 23: Chi squared test (χ^2) comparing occurrence of pneumonia amongst patients that received early, late and no physiotherapy

		Physiotherapy			
		Cohort seen within 72 hours	Cohort seen after 72 hours	Cohort not seen	Total
Pneumonia	Number	20	7	24	51
	% within cohort	**13.3%**	**17.5%**	**33.8%**	**19.5%**
No pneumonia	Number	130	33	47	210
	% within cohort	**86.7%**	**82.5%**	**66.2%**	**80.5%**
Total	Number	150	40	71	261
	% within cohort	100.0%	100.0%	100.0%	100.0%

$\chi^2 = 12.968$; df 2; P = 0.002

Table 24: Chi squared test (χ^2) comparing occurrence of bedsores amongst patients that were seen by the occupational therapist within 72 hours of admission with those managed only after 72 hours

		Occupational therapy		
		Cohort seen within 72 hours	Cohort seen after 72 hours	Total
Bedsores	Number	2	5	8
	% within cohort	**1.5%**	**12.8%**	**3.1%**
No bedsores	Number	132	34	253
	% within cohort	**98.5%**	**87.2%**	**96.9%**
Total	Number	134	39	261
	% within cohort	100.0%	100.0%	100.0%

$\chi^2 = 9.984$; df 1; P = 0.002

Table 25: Chi squared test (χ^2) comparing occurrence of acute kidney injury (AKI) amongst patients that were assessed by the dietician within 72 hours of admission with those receiving nutritional support only after 72 hours

		Dietician / nutritional support			
		Cohort seen within 72 hours	Cohort seen after 72 hours	Cohort not seen	Total
AKI	Number	14	5	6	25
	% within cohort	**14.9%**	**27.8%**	**4.0%**	**9.6%**
No AKI	Number	80	13	143	236
	% within cohort	**85.1%**	**72.2%**	**96.0%**	**90.4%**
Total	Number	94	18	149	261
	% within cohort	100.0%	100.0%	100.0%	100.0%

$\chi^2 = 15.252$; df 2; P < 0.001

Table 26: Logistic regression analysis of the risk of death

Predictor of death	Odds ratio	95% Confidence interval		*P* value
		Lower bound	Upper bound	
TACI	4.803	2.403	9.629	< 0.001
Decreased level of consciousness	6.916	3.607	13.517	< 0.001
Fever	3.240	1.745	6.174	< 0.001
Pneumonia	4.929	2.512	9.714	< 0.001

The following variables that were analysed according to this model did not reach statistical significance: patient characteristics (except if indicated above) and inpatient complications (urinary tract infection, drip site sepsis, hyperglycaemia, acute kidney injury, bedsores, deep vein thrombosis, pulmonary embolism, gastro-intestinal bleeds and seizures).

Figure 31: Discharge destinations in this study

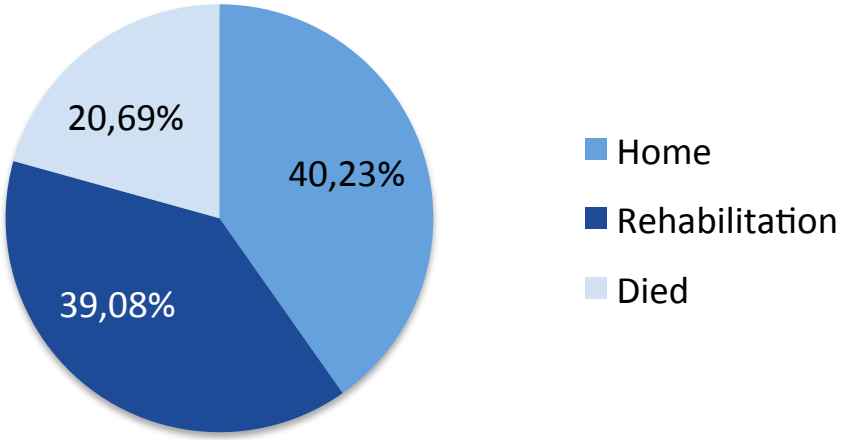
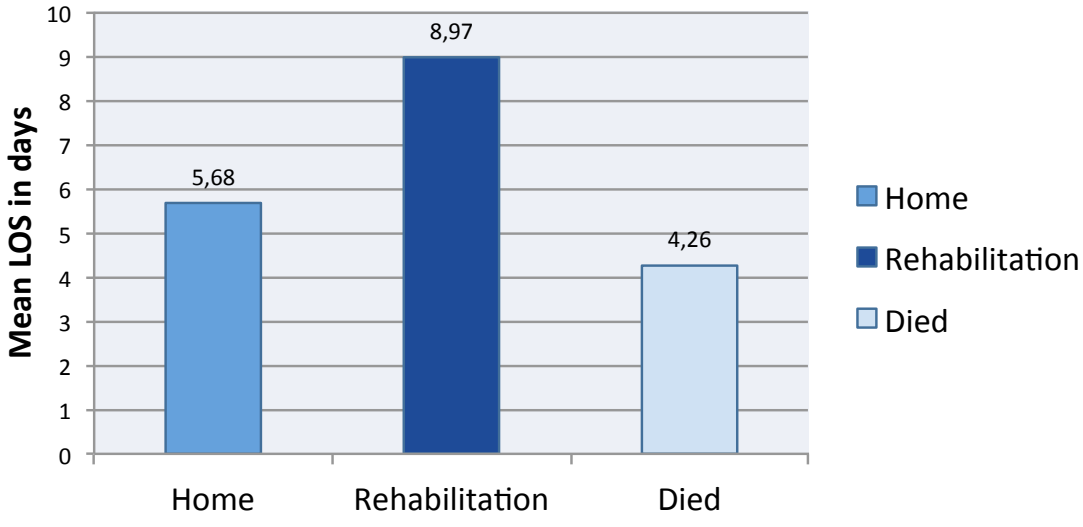


Table 27: Univariate analysis of LOS as influenced by discharge destination

	Number	Percentage	Mean LOS	Median LOS	2.5 – 97.5% quartiles
Discharge destination (*P* value < 0.001) by Kruskal-Wallis testing					
Home	102	40.23%	5.676	4	1 – 16.475
Rehabilitation	105	39.08%	8.971	8	3 – 20
Died	54	20.69%	4.259	3	1 – 11.675

Figure 32: LOS as influenced by discharge destination



Discharge destination was significant in influencing LOS (refer to table 27).

Table 28: Median LOS of group that was referred to inpatient rehabilitation according to whether they were seen within or after 72 hours by allied health professionals

	Number	Percentage	Median LOS	IQR
Speech therapy by Mann Whitney *U* test (*P* value 0.007)				
Seen within 72 hours of admission	61	79.22%	8	5 – 10
Seen after 72 hours of admission	16	20.78%	10.5	8.5 – 15
Dietician by Mann Whitney *U* test (*P* value 0.084)				
Seen within 72 hours of admission	43	82.69%	8	5 – 9.5
Seen after 72 hours of admission	9	17.31%	10	8 – 16
Physiotherapy by Mann Whitney *U* test (*P* value < 0.001)				
Seen within 72 hours of admission	76	79.16%	7	6 – 9
Seen after 72 hours of admission	20	20.84%	10.5	8.5 – 15
Occupational therapy by Mann Whitney *U* test (*P* value 0.059)				
Seen within 72 hours of admission	62	74.7%	8	6 – 9
Seen after 72 hours of admission	21	25.3%	10	7 – 16

Figure 33: Median LOS of patients referred to inpatient rehabilitation centres as influenced by when they were first seen by allied health professionals

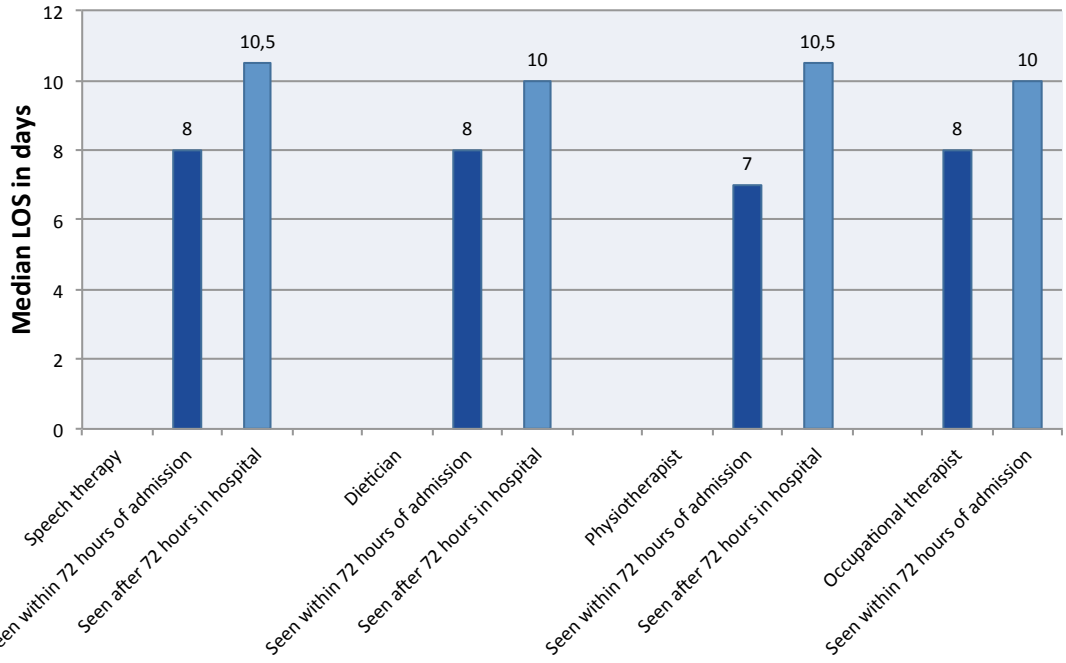


Table 29: Blood pressure control at discharge

Excluding the 54 patients (20.69%) that died

	Number	Percentage
SBP < 120	56	27.05%
SBP 120 – 129	50	24.15%
SPB 130 – 139	35	16.91%
SBP 140 – 159	34	16.43%
SBP 160 – 179	24	11.59%
SBP > 180	8	3.86%

Figure 34: Blood pressure control at discharge

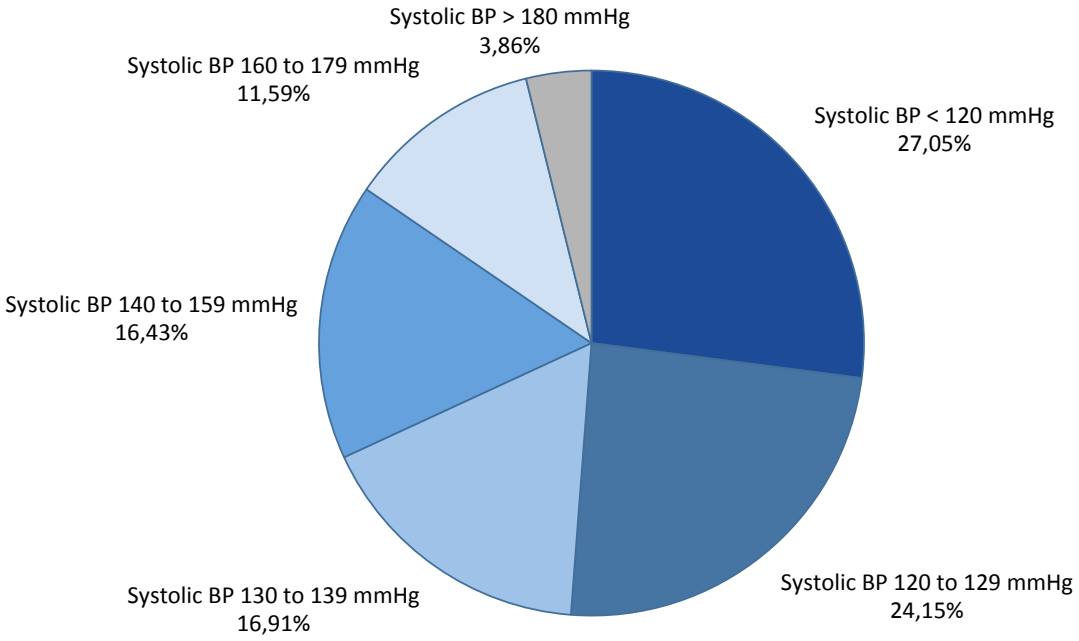


Table 30: Blood glucose control amongst all patients at discharge

Excluding the 54 patients (20.69%) that died

	Number	Percentage
< 4	0	
4 – 6,9	40	19.32%
7 – 9,9	36	17.39%
> 10	27	13.04%
Not done	104	50.24%

Figure 35: Blood glucose amongst all patients at discharge

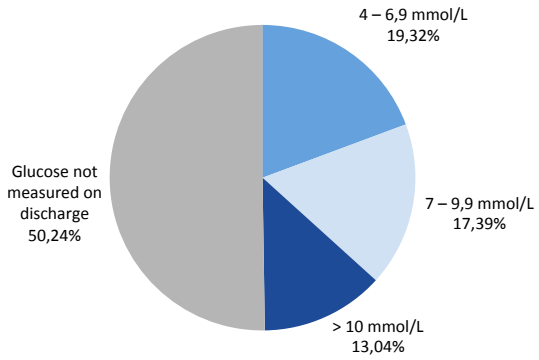


Table 31: Glucose control of diabetic patients at discharge

Excluding the 18 patients (18.19%) admitted with diabetes mellitus that died

	Number	Percentage
< 4	0	
4 – 6,9	24	29.63%
7 – 9,9	28	34.57%
> 10	25	30.86%
Not done	4	4.94%

Figure 36: Blood glucose amongst diabetic patients at discharge

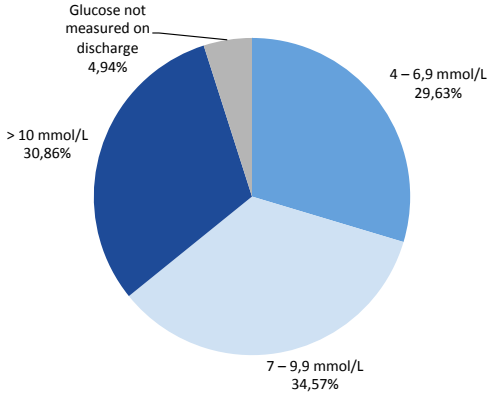


Table 32: Patients with ischaemic stroke discharged on antiplatelet therapy

Excluding the 54 patients (20,69%) that died

	Number	Percentage
Single	163	78.74%
Dual	3	1.45%
Not given	41	19.81%

Figure 37: Patients with ischaemic stroke discharged on antiplatelet therapy

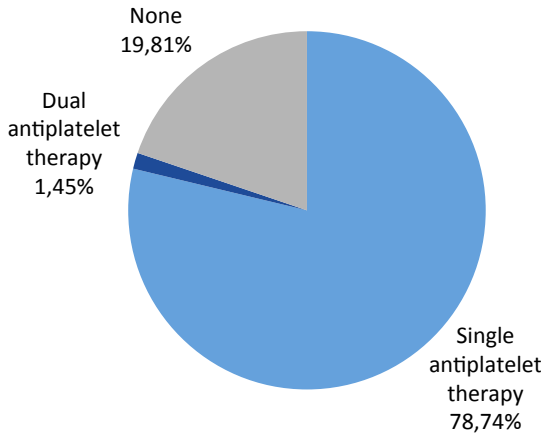


Table 33: Patients with ischaemic stroke discharged on warfarin

Excluding the 44 patients (20.37%) admitted with ischaemic stroke that died

	Number	Percentage
Given	11	6.4%
Not given	161	93.6%

Figure 38: Patients with ischaemic stroke discharged on warfarin

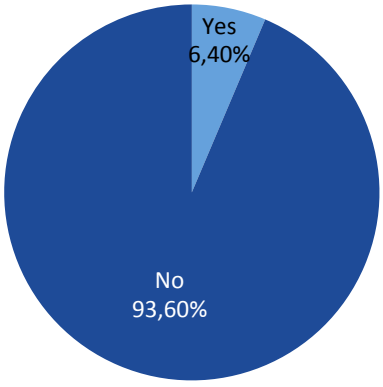


Table 34: Patients with hypercholesterolaemia discharged on a statin

Excluding 17 patients with hypercholesterolaemia that died

	Infarcts	Haemorrhagic stroke	All patients
Given	96 (86.5%)	6 (5.4%)	102 (91.9%)
Not given	5 (4.5%)	4 (3.6%)	9 (8.1%)

Instructions to authors

Stroke: A Journal of Cerebral Circulation publishes reports of clinical and basic investigation of any aspect of the cerebral circulation and its diseases from many disciplines, including anesthesiology, critical care medicine, epidemiology, internal medicine, neurology, neuro-ophthalmology, neuropathology, neuropsychology, neurosurgery, nuclear medicine, nursing, radiology, rehabilitation, speech pathology, vascular physiology, and vascular surgery.

Updated February 4, 2014

Notices

- Any contributor who needs to be cross-referenced in PMC should be listed either as an individual author (part of the writing group) in the manuscript processing system or, for study groups with non-writing group contributors, in the main manuscript file as an Appendix. Please be sure that all contributor names are spelled correctly and presented in the format the contributor wishes to appear in PMC. This information is included in the word count. If contributors do not need to be listed as authors or cross-referenced in PMC, then they may be included in a PDF Data Supplement to the manuscript.

Features

- eComments. This exciting feature allows for the rapid online appearance of appropriate comments related to content in the Controversies in Stroke section. All comments are reviewed by the editors, who will decide on their acceptability. Only those comments deemed by the editors to contribute substantially to the topic under discussion will be posted. It is our goal to publish all comments within 10 days of submission. Copyright forms will be required. eComments are not submitted to PMC or any other index. They appear on the journal website only. To avoid points that have already been made, please read other people's remarks before submission. For those interested in participating, please go to the Controversy that you wish to comment on and select the link to Submit a Comment (in the right hand column under Comments).
- Free Webinars. Stroke initiated a series of educational webinars that occur on a bimonthly basis. These webinars cover important topics in the cerebrovascular disease field, especially those with recent advances that will impact clinicians and researchers. For current information on our series, please visit Stroke Webinars.
- Blogging Stroke. Written by invited stroke fellows throughout the country, Blogging Stroke, comments on selected articles soon after they appear online ahead of print. Comments from bloggers participating in conferences are also featured. Please join the conversation at Blogging Stroke.

Article Categories

- Original Contributions. For preparation, see "Instructions for New Submissions." Maximum length for manuscripts is 4,500 words. Please note that the 4,500-word limit includes title page, abstract, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, tables, and appendices intended for print publication. Please note the publication fees in the Costs to Authors section. Authors should eliminate redundancy, emphasize the central message, and provide only the data necessary to convey that message. The total number of figures and/or tables is limited to 6. Each figure may contain up to 4 panels (i.e., parts A to D) and must conform to the requirements for figures described in that section of the instructions to authors. Additional figures and tables up to a combined total of 4 may be submitted for publication but will appear as an online data supplement. The use of the online data supplement is strongly encouraged not only for additional tables and figures but for complex methodology, large tables, and complex figures. They must be clearly labeled as data supplement on the title page and in references throughout the paper and the file should be uploaded as a separate supplemental PDF.
- Brief Reports. These articles highlight important research in stroke. Maximum length is 1,800 words. The 1,800-word limit includes title page, abstract, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, and tables. The total number of references is limited to 15. The total number of figures and/or tables is limited to 3.
- Clinical and Research Innovations (Online-Only Publication). These articles provide a broad opportunity to communicate innovative new ideas that comprise solutions to problems in acute stroke that are currently viewed as impediments to progress in stroke research and clinical care. Submissions may cover a wide spectrum of potential advances including new technologies that accelerate progress; articles delineating the need for new potential collaborations; solutions to workflow problems; as well as solutions and innovations related social, ethical and legal matters impacting stroke care and research. Format: Please do NOT include an abstract. The initial paragraph should center on the specific problem that is being addressed. It may contain a limited amount of literature review related to the problem itself in order to clearly set out the issues at hand. The rest of the article should focus on the solution but not on the problem. Please structure the manuscript using these subheadings as guidelines. You may modify or omit subheadings as appropriate: Brief description on the problem/challenge; Description of the innovation/solution; Results of pilot testing; and Conclusion/Limitations/next steps. Articles are not limited to innovations that can result in intellectual property or other assets with commercial potential. However, in the process of describing the solution, the generation of intellectual property, filing for patents, of the development of

products and/or companies and industry collaborations are recognized to be natural aspects of innovation, and are welcome attributes and should be mentioned if applicable. (Please note that the journal is not responsible for protection of intellectual property). Subheadings may be used as necessary. Please include a Conclusion that comments on the implications of this latest work on the overall stroke and research are encouraged. In addition, authors may consider discussing future plans, expectations of collaboration etc. Maximum length for this article is 2,000-2500 words. The word limit includes title page, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, and tables. Subheadings may be used as appropriate. Please see the recent editorial intriducing this new article type: "Bottlenecks in Acute Stroke Care and Research: Solutions and Innovations."

- Progress or Topical Reviews. This category presents a review of advances related to important research and clinical topics relevant to some aspect of cerebrovascular disease. They will generally be invited by the editors but unsolicited reviews will also be accepted for editorial review. Invited reviews will also undergo peer review but except in rare circumstances will not be subject to rapid triage and early rejection. Manuscripts should not exceed 4,500 words including the title page, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, and tables and contain up to 6 figures/tables. Please do not include an abstract in review papers. An introduction or background section will suffice.
- Comments and Opinions. In this category, authors summarize the present state of knowledge in some aspect of cerebrovascular disease without the objectivity required in a Progress Review. Maximum length is 4,500 words and 6 figures/tables, including the title page, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, and tables. Please do not include an abstract in review papers. An introduction or background section will suffice.
- Special Reports. These articles may summarize an event or a topic of interest to the readers of Stroke. Authors must query the editors before writing Special Reports to determine possible interest in such articles. The length is limited to 4,500 words inclusive with a maximum of 6 tables/figures.
- Letters to the Editor (Online-Only Publication). This forum expresses views about articles published in Stroke or presents ideas or findings of scientific interest that do not constitute original research. Letters must be reference a Stroke article published in print within the past 4 weeks. The maximum length is 750 words including no more than 5 references and 3 authors. Tables, figures, and data supplements are prohibited. Authors must double-space text and references, and provide a brief title. Please use the journal formatting for titles of Letters to the Editor. Example: Letter by Author et al. Regarding Article, "Article Title." Letters may be shortened or edited by the Editorial Office. The editor invites responses to letters as appropriate. Response Letter titles use this format: Response to Letter Regarding Article, "Article Title."
- Case Reports (Online-Only Publication). The editors will in very rare circumstances consider case reports for publication only if they present important and unique clinical experience. Authors should limit descriptions of negative and normal findings. Maximum length is 1,500 words with only the most relevant references. Please use the abstract headings Background and Purpose, Summary of Case, and Conclusion. Authors should limit figures to those that enhance the study.

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Online Manuscript Submission

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Initial Review Process

Submitted manuscripts will be evaluated initially by the editor-in-chief and an associate editor. A rapid initial decision of whether to have a manuscript formally reviewed by two or more reviewers with appropriate expertise or rejected without a formal review will be determined by the senior editor and a second reviewer (assistant editor, section editor, member of the editorial board, or invited reviewer with topic-related expertise) based on the quality, originality, scientific rigor and data presentation/analysis of the manuscript. It is anticipated that approximately 50% of the submitted manuscripts will undergo formal review and 50% will be rejected without evaluation by external reviewers. This policy reflects the stringent requirements for the acceptance of manuscripts submitted to Stroke.

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Instructions for New Submissions

The following items should be uploaded with the manuscripts file(s):

- A cover letter that includes the following statement: “All authors have read and approved the submitted manuscript, the manuscript has not been submitted elsewhere nor published elsewhere in whole or in part, except as an abstract (if relevant).” The cover letter may include the names of up to 3 potential reviewers whom the authors would like to suggest, especially members of the editorial board. The authors may also include the names of up to 3 reviewers whom they would like to not evaluate their submission. The editor ultimately decides who reviews the manuscript.
- Authorship Responsibility and Copyright Transfer Agreement Forms are now ONLINE ONLY. Forms will be required PRIOR to resubmission, or if the manuscript has only one version (e.g., a letter to the editor) after acceptance. Each author will be sent an email containing a link to the form as an appropriate time.
- Acknowledgement release signatures, if applicable. Please see the Acknowledgment Permission Form . (Note: The lead author is responsible for collecting these and indicating such on the Copyright Transfer Agreement.)

- One copy of any in-press article that is cited in the references, if applicable.
- One copy of any abstracts published or submitted for publication, if applicable.

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Manuscript Formatting

- Only Microsoft Word files will be accepted for review.
- Manuscripts must be double-spaced, including references, figure legends, and tables.
- We recommend using Times New Roman 12-point font.
- Leave 1-inch margins on all sides. Number every page, beginning with the abstract page, including tables, figure legends, and figures.
- Cite each figure and table in text in numerical order.
- Manuscripts should be presented in the following sequence:

1. Title page
2. Abstract
3. Text, including Introduction, Methods, Results, Discussion and Summary/Conclusions
4. Acknowledgments
5. Sources of Funding
6. Conflict(s)-of-Interest/Disclosure(s)
7. References
8. Figure Legends
9. Tables
10. Figures

- Cite each reference in text in numerical order and list in the References section. In text, reference numbers may be repeated but not omitted. Do not duplicate references either in text or in the reference list.
- Use SI units of measure in all manuscripts. For example, molar (M) should be changed to mol/L; mg/dL to mmol/L; and cm to mm. Units of measure previously reported as percentages (e.g., hematocrit) are expressed as a decimal fraction. Measurements currently not converted to SI units in biomedical applications are blood and oxygen pressures, enzyme activity, H+ concentration, temperature, and volume. The SI unit should be used in text, followed by the conventionally used measurement in parentheses. Conversions should be made by the author before the manuscript is submitted for peer review.
- Consult the AMA Manual of Style: A Guide for Authors and Editors, 10th ed, Oxford: Oxford University Press; 2007, for style.
- Please provide sex-specific and/or racial/ethnic-specific data, when appropriate, in describing outcomes of epidemiologic analyses or clinical trials; or specifically state that no sex-based or racial/ethnic-based differences were present. See the Uniform Requirements for Manuscripts Submitted to Biomedical Journals for more details.
- Please review the correct usage "sex" and "gender." "Gender" is a social construct and "sex" describes a biological status. Please use the terms appropriately.
- Consult current issues for additional guidance on format.

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Title Page

The title page (first page) must include:

- Full title of the article, limited to 120 characters.
- Authors' names, highest academic degree earned by each, authors' affiliations, name and complete address for correspondence, and address for reprints if different from address for correspondence. Please also include any study group or collaborative in the author list, i.e., " . . .Last Author, on behalf of the Stroke Study Group."
- Fax number, telephone number, and e-mail address for the corresponding author.
- Cover title (total characters must not exceed 50, including spaces) to be typeset on the top of the journal page.
- Itemized list of the tables and figures
- 3 to 7 key words for use as indexing terms
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- Specify the number of words on your title page. Word count should include all parts of the manuscript (i.e., title page, abstract, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, tables, and appendices intended for print publication). Over-length manuscripts will NOT be accepted for publication without an additional page charge. See the Costs to Authors below.

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Abstract

- Do not cite references in the abstract.
- Limit use of acronyms and abbreviations.
- Be concise (250 words, maximum).
- The abstract should have the following headings:

1. Background and Purpose (description of rationale for study)
2. Methods (brief description of methods)
3. Results (presentation of significant results)
4. Conclusions (succinct statement of data interpretation)
5. When applicable, include a fifth heading: "Clinical Trial Registration Information." Please list the URL, as well as the Unique Identifier, for the publicly accessible website on which the trial is registered. If the trial is not registered, please indicate the reason in the heading. Example 1: Clinical Trial Registration-URL: http://www.clinicaltrials.gov. Unique identifier: NCT00123456. Example 2: Clinical Trial Registration-

URL: http://www.controlled-trials.com. Unique identifier: ISRCTN70000879. Example 3: Clinical Trial Registration-URL: http://www.chictr.org. Unique identifier: ChiCTR-RCH-14004884. Example 4: Clinical Trial Registration-This trial was not registered because enrollment began prior to July 1, 2005.

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Text

- Follow the instructions in "Manuscript Formatting."
- The following are typical main headings: Materials and Methods, Results, Discussion, and Summary.
- Abbreviations must be defined at first mention in the text, tables, and figures.
- Introduction: This section should briefly introduce the context of the results to be presented and should duplicate what is contained elsewhere in the manuscript
- Methods:

A. For any apparatuses used in Methods, the complete names of manufacturers must be supplied.
B. For human subjects or patients, describe their characteristics.
C. For animals used in experiments, state the species, strain, number used, and other pertinent descriptive characteristics.
D. When describing surgical procedures on animals, identify the preanesthetic and anesthetic agents used, and state the amount or concentration and the route and frequency of administration for each. The use of paralytic agents, such as curare or succinylcholine, is not an acceptable substitute for anesthetics.
E. For other invasive procedures on animals, report the analgesic or tranquilizing drugs used. If none were used, provide justification for such exclusion.
F. Manuscripts that describe studies on humans must indicate that the study was approved by an institutional review committee and that the subjects gave informed consent.
G. Manuscripts involving animals must indicate that the study was approved by an institutional animal care and use committee.
H. Reports of studies on both animals and humans must indicate that the procedures followed were in accordance with institutional guidelines.
I. All drugs should be referred to by their generic names rather than trade names. The generic chemical identification of all investigational drugs must be provided.
J. A statistical subsection must be provided at the end of the Methods section describing the statistical methodology employed for the data presented in the manuscript.
K. The Methods section should provide essential information related to the conduct of the study presented in the manuscript. For methodology previously published by the authors, the prior publication should be referenced and a copy of the paper provided to the reviewers, if necessary.
L. The Methods section should only contain material that is absolutely necessary for comprehension of the results section. Additional (more detailed) methods can be provided as a data supplement.
M. Prevention of bias is important for experimental stroke research (see Macleod et al, Stroke. 2009;40:e50–e52). For studies where the primary objective is the preclinical testing of therapies, the following checklist items must be adhered to:

1. Animals: Species, strains and sources must be defined. For genetically modified animals, wildtype controls including background and back-crossing must be defined.
2. Statistics and sample size: Specific statistical methods must be defined, including parametric versus nonparametric and multigroup analyses, and sample size powering based on expected variances and differences between groups.
3. Inclusions and exclusions: Specific criteria for inclusions and exclusions must be specified. For example, only animals where blood flow reductions fall below a certain threshold are included. Or only animals with a certain degree of neurological deficits are included. Once animals are randomized (see below), all excluded animals must be reported, including explicit presentation of mortality rates.
4. Randomization, allocation concealment and blinding: All animals must be randomized. Investigators responsible for surgical procedures or drug treatments must be blinded. End point assessments must be performed by investigators blinded to the groups for which each animal is assigned.

- Results: This section should succinctly report the results of experimental studies and clinical research or clinical series/observations.
- Guidelines for Human Phenotype–Genotype Association or Linkage Studies:

A. Reporting issues

1. Report process for selecting genes and SNPs.
2. Report Hardy-Weinberg statistics or P values and method of calculating same.
3. Refer to existing public domain websites for the Human Gene Ontology name and the rs number for SNPs.
   - http://www.gene.ucl.ac.uk/nomenclature/
   - http://www.ncbi.nlm.nih.gov/projects/SNP/
   - http://www.ncbi.nlm.nih.gov/snp
4. Describe genotyping methods. If numerous primers have been used, please include them in an online supplement.

B. False-positive and false-negative concerns. Given well-described problems with both false-positive and false-negative associations, phenotype–genotype association studies should meet some or all of the criteria below:

1. Phenotype is clearly defined, is heritable, and if a quantitative phenotype is reported, reproducibility data are provided.
2. The sample size is adequate to detect a SNP or haplotype with a modest effect. For genotype-trait

associations, provide an estimate of the effect size that could be detected with power 0.80 or higher with the allele frequency and sample size reported.

3. Since multiple statistical testing methods are frequently used in genotyping-phenotyping studies, please include specifics of the primary model(s) tested. Nonessential secondary models may be published as electronic data supplements. Clinically relevant confounders should be included in multivariable models or residuals.

C. Review criteria for human linkage studies. Manuscripts should include the following:

1. Identifying plausible candidate genes under the linkage peak.
2. Follow-up fine mapping to narrow the region of linkage, and/or genotyping some of the candidate genes under the linkage peak.
3. Replication data from another sample.

- Guidelines for Genomic and Proteomic Studies:

A. Preparation of Data Submitted: Data should follow the MIAME checklist (for more information see http://www.mged.org/Workgroups/MIAME/miame_checklist.html).

B. Accessibility of Data: Authors of papers that include genomic, proteomic, or other high-throughput data are required to make their data easily accessible for the reviewers and the editors during the review process.

1. You may submit your data to the NCBI gene expression and hybridization array data repository (GEO, http://www.ncbi.nlm.nih.gov/geo/) and provide the GEO accession number; or,
2. You may provide a link to a secure or publicly accessible Web site which hosts the data. Prior to publication, the data must be submitted and an accession number obtained. Access to the information in the database must be available at the time of publication. GEO has a Web-based submission route, suitable for a small number of samples, or a batch submission tool (called SOFT). GEO is accessible from http://www.ncbi.nlm.nih.gov/geo/ The submission FAQ is available at (http://www.ncbi.nlm.nih.gov/projects/geo/info/faq.htm l)

- Guidelines for Proteins and Nucleic Acid Sequences:

A. Newly reported nucleotide or protein sequences must be deposited in GenBank or EMBL databases, and an accession number must be obtained. Access to the information in the database must be available at the time of publication. Authors are responsible for arranging release of data at the time of publication. The authors must also provide a statement in the manuscript that this sequence has been scanned against the database and all sequences with significant relatedness to the new sequence identified (and their accession numbers included in the text of the manuscript).

1. GenBank GenBank Submissions National Center for Biotechnology Information 8600 Rockville Pike, Building 38A Room 8N-805 Bethesda, MD 20894 Tel: (301) 496-2475 On the web at: http://www.ncbi.nlm.nih.gov/Genbank/index.html
2. EMBL Nucleotide Sequence Submissions European Bioinformatics Institute Hinxton Hall Hinxton, Cambridge CB10 1SD, UK Tel.: 44-1223-494401; Fax: 44-1223-494472 e-mail: support@ebi.ac.uk On the web at: http://www.ebi.ac.uk
3. DNA Data Bank of Japan Center for Information Biology National Institute of Genetics Mishima, Shizuoka, 411, Japan Tel.: 81-559-81-6853; Fax: 81-559-81-6849 On the web at: http://www.ddbj.nig.ac.jp

B. Submission to any data bank is sufficient to ensure entry in all.

- Discussion: This section should not reiterate the results but put the results in appropriate context regarding relevant literature and the importance of new observations contained in the manuscript.
- Summary/Conclusions: A brief paragraph summarizing the results and their importance may be included but is not required.

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Acknowledgments, Sources of Funding, and Disclosures

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representing such corporations. The corresponding author should collect Conflict of Interest information from all co-authors before submitting a manuscript online.

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References

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- References with more than 6 authors should list the first 6 authors followed by et al.
- Cite references in numerical order according to first mention in text.
- Personal communications, unpublished observations, and submitted manuscripts must be cited in the text, not in the references, as "([name(s)], unpublished data, 20XX)."
- References must be from a full-length publication in a peer-reviewed journal.
- Abstracts may be cited only if they are the sole source and must be identified in the references as "Abstract."
- "In-press" citations must have been accepted for publication and the name of the journal or book publisher included. Please provide a copy of any potentially overlapping manuscript that has been submitted to another journal or is in press or published elsewhere.
- Example of a journal reference: Mith AR, Asai Y, Kim M, Dirk TR, Karrus HF, Yang YS, et al. This is the title. Stroke. 2012;30:2407–2408.
- Example of an Online Journal Reference: Nakagawa T, Hasegawa Y, Uekawa K, Ma M, Katayama T, Sueta D, et al. Renal Denervation Prevents Stroke and Brain Injury via Attenuation of Oxidative Stress in Hypertensive Rats. J Am Heart Assoc. 2013;2:e000375.
- Example of a publish-ahead-of-print reference: Authors. Article Title. [published online ahead of print date]. Stroke. Year. URL. Access date.
- Example of a book chapter reference: Amstand RR, Smithy RS, Kim LY. Chapter Title. In: Wong YT, Khan S, eds. Book Title. 3rd Ed. New York, NY: Publisher Name; 2009:456–464.
- Example of a website reference: CDC Chronic Disease Indicators: Indicator Definition. Hospitalization for cerebrovascular accident or stroke. National Center for Chronic Disease Prevention and Health Promotion web site. http://apps.nccd.cdc.gov/cdi/IndDefinition.aspx?IndicatorDefinitionID=83. Accessed November 23, 2010.
- Web sites generally follow this format: Author names (if any). Title of information or page. Name of website. URL. Publication date (if any). Access date.
- Example of a Software Manual Reference: StataCorp. Stata statistical software: Release 12. College Station, TX: StataCorp LP; 2011.

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Figure Legends

- Provide figure legends on a separate page of the manuscript.
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Tables

- Each table must be typed on a separate sheet and double-spaced, if possible. The table number should be Arabic, followed by a period and a brief informative title.
- Use the same size type as in text.
- Tables should be cell-based (i.e., constructed using Microsoft Word tables or Excel). Do not use tabs or hard returns. Do not supply tables as graphics.
- Tables should be used to present comparisons of large amounts of data at a glance. Tables with only 1 or 2 rows of data should be incorporated into the text.
- Tables should be as compact as possible. Avoid unnecessary rows and columns.
- Use indenting within the stub column to indicate subgroups. Do not use bold, shading, rules, etc.
- Tables should not contain vertically merged cells; horizontally merged cells are permitted when necessary in the heading row.
- Internal headings are not permitted outside of the stub column. If internal headings are required, the table should be split into 2 tables.
- No internal shading is permitted.
- Units of measure should be in the heading row or stub column rather than the body of the table whenever possible.
- Indicate footnotes in the table in this order: *, †, ‡, §, | |, #, * * . Follow AMA 9th edition for footnote styles.
- A permission is required for all tables that are reused or adapted from another source. To obtain permission, please follow the instructions provided by the copyright holder or listed in the license agreement. Follow the copyright holder or licensor's requirements for credit attributions and provide them in the table footnote. If no language is provided in the permission letter, use the following sample: Reprinted from Butler et al,[19] with permission from Smith Publishing. Copyright 2005, American Society of Medical Research.

—TOP—

Figures

- The combined total number of figures and tables is limited to 6. Each figure may contain up to 4 panels (i.e., parts A to D) and must conform to the requirements for figures described below.
- Authors should be pleased with the figure submission quality before submission. We recommend that you print the figure at its final publication size to check the quality.
- Figures should be submitted as high-resolution TIFF or EPS files. PowerPoint files can be accepted but is a less preferred file format, as elements within the figure (such as axis labels) may shift location or drop out during conversion. JPEG, Word, and Excel files should not be used. See Artwork and Table Guidelines (PDF) for instructions for creating high-quality digital art in various software applications.
- Color figures should be in RGB (red/green/blue) mode. If a figure is supplied in CMYK (cyan/magenta/yellow/black) mode, there may be a shift in the appearance of colors, especially fluorescents. Figures that will appear in black and white should be submitted in black and white.
- Figures should be supplied at the highest resolution possible for optimal clarity. Color figures should be at least 300 dpi; halftones, 600 dpi; and line art, 1200 dpi.
- Figures should be submitted at the final publication size. Please note that most figures will be sized at 1 column wide. Dimensions for figures are:
  - 1 column: 3.25 inches wide
  - 2 columns: 6.80 inches wide
- For line and bar graphs and pie charts, ensure that the colors/lines/symbols used for the different sets of data are easily distinguishable.
- Graphs and charts should have a white background. Do not use dark PowerPoint backgrounds.
- Labels for panels should be uppercase letters (A, B, C, D) in boldface Arial or Helvetica.
- Multipart figures may have no more than 4 panels (i.e., A, B, C, D).
- Multipart figures may be set at 2 columns across the page and should be laid out horizontally if appropriate.
- Use the same font (typeface) throughout the figure. Sans serif fonts, such as Arial and Helvetica, work best.
- Use the largest font size possible without distorting the figures. Text should be no smaller than 6 points.
- Whenever possible, all text within a figure should be the same size. If this is not possible, the font size should vary by no more than 2 points.
- Label units of measure consistently with the text and legend. Follow the AMA for unit abbreviations.
- Incorporate figure keys into the legend rather than including them as part of the figure whenever possible. Titles should be included in the figure legends.
- Any abbreviations or symbols used in the figures must be defined in the figure or figure legend.
- Follow AMA 9th edition for footnote style in legends.
- If the figure is reprinted/adapted from another source, please provide a permission letter and include the source in the legend as noted above.
- Supply a scale bar with photomicrographs.
- Authors are responsible for the cost of printing color illustrations. Authors are also responsible for obtaining from the copyright holder permission to reproduce previously published artwork. Authors can check guidelines online at http://submit-stroke.aha-journals.org/ under Artwork and Table Guidelines (PDF).
- See AMA, 10th edition, Section 4.2 for more information on figures.

—TOP—

Online Supplements

This optional section provides an opportunity for authors to present supporting materials to the manuscript. The manuscript appears both in the print version and online, whereas Online Supplements are independent from the manuscript and appear only online in the format submitted by the authors. Online Supplements undergo peer review and therefore must be submitted simultaneously with original submissions.

Any collaborators who need to be cross-referenced in PubMed should be listed either as authors or, for study groups, in the main manuscript file as an Appendix. This information is included in the word count. If contributers do not need to be listed as authors or cross-referenced in PubMed, then they may be included in a PDF Data Supplement to the manuscript.

Online Supplements may consist of any of the following, in any combination: the expanded materials and methods; additional figures and supporting information; additional tables and supporting information; and, video files.

The guidelines below should be used for online supplements:

- Material to be published as an online only supplement should be uploaded online as a single PDF. An exception to this would be if the online supplement is a video file.
- The online supplement should have a title page with the label of ONLINE SUPPLEMENT above the title. The supplemental material to be included in this PDF is as follows: Supplemental Methods, Supplemental Tables, Supplemental Figures and Figure Legends, and Supplemental References. If applicable, the legends for the Video files should also be included in this PDF.
- The online supplement should be single-spaced.
- If citations are made in the Online Supplement, the Online Supplement must contain its own independent Reference Section with references numbered sequentially, beginning with reference 1, even if some of these references duplicate those in the print version.
- Number supplementary figures and tables as Figure I, Figure II, Table I, Table II, etc.
- Place the supplemental figure legend underneath the corresponding figure.
- When referring to online-only material in the print version of the manuscript, use the phrase "please see

http://stroke.ahajournals.org."

- Data Supplements appear only online and will not appear in reprints of the article. The Editorial Office is not responsible for converting files to a suitable format.

—TOP—

Instructions for Revised Submissions

- In the top right-hand corner, indicate the manuscript number followed by R1 to denote a first revision.
- Please provide a copy of the revised text with changes marked in the text using either track changes or highlighting.
- In your written response to the reviewers' comments, give the page number(s), paragraph(s), and line number(s) where each revision was made.
- Respond to each referee's comments, indicating precisely the changes made in response to the critiques. Also give reasons for suggested changes that were not implemented, and identify additional changes made.
- Revisions not received within 60 days from the date of the decision letter will be administratively withdrawn. For further consideration the manuscript must be resubmitted de novo. At the editors' discretion, and in cases where substantial new data are required, extensions may be granted for revisions. In such cases, every effort will be made to retain the original reviewers.

—TOP—

Journal Policies

Compliance With NIH and Other Research Funding Agency Accessibility Requirements

Several research funding agencies now require or request authors to submit the post-print (the article after peer review and acceptance but not the final published article) to a repository that is accessible online by all without charge. Within medical research, 3 funding agencies in particular have announced such policies:

1. The US National Institutes of Health (NIH) requires authors to deposit post-prints of articles, which have received NIH funding, in its repository PubMed Central (PMC). This deposit should be done within the 12 months after publication of the final article in the journal.
2. The Howard Hughes Medical Institute (HHMI) requires, as a condition of research grants, deposit in PMC, but within 6 months after publication of the final article.
3. The Wellcome Trust requires, as a condition of research grants, deposit in UK PMC within 6 months after publication of the final article.

As a service to authors, the Publisher (Wolters Kluwer Health/Lippincott Williams & Wilkins) of the AHA journals will identify to PMC articles that require depositing. The Copyright Transfer Agreement provides the primary mechanism for identifying such articles. The AHA also requests that, during the submission process in eJournal Press, funding is indicated.

WKH/LWW will transmit the post-print of an article, which is based on research funded in whole or in part by 1 or more of these 3 agencies, to PMC.

On NIH request, it remains the legal responsibility of the author(s) to confirm with the NIH the provenance of their manuscript for purposes of deposit.

- Author(s) will not deposit their articles themselves.
- Author(s) will not alter the post-print already transmitted to NIH.
- Author(s) will not authorize the display of the post-print prior to:
  - 12 months after publication of the final article, in the case of NIH,
  - 6 months after publication of the final article, in the case of HHMI and the Wellcome Trust

For more information, please visit PMC.

—TOP—

Guidelines for Clinical Trials

- In accordance with the Clinical Trial Registration Statement from the International Committee of Medical Journal Editors (ICMJE) (Circulation. 2005;111:1337–1338), all clinical trials submitted for publication in Stroke must be registered in a public trials registry at or before the onset of participant enrollment. This requirement applies to all clinical trials that begin enrollment after July 1, 2005.
- Research is considered to be a clinical trial if it involves prospective assignment of human subjects to an intervention or comparison group to study the relation between a health-related intervention and a health outcome. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. As previously, purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. Those who are uncertain whether their trial meets the expanded ICMJE definition should err on the side of registration if they wish to seek publication.
- The registry must be accessible to the public at no charge, searchable, open to all prospective registrants, and managed by a not-for-profit organization. The registry must include the following information: a unique identifying number, a statement of the intervention(s), study hypothesis, definition of primary and secondary outcome measurements, eligibility criteria, target number of subjects, funding source, contact information for the principal investigator, and key dates (registration date, start date, and completion date). The registries listed below are approved by the

ICMJE:

1. United States National Library of Medicine
2. International Standard Randomized Controlled Trial Number (ISRCTN)
3. University Hospital Medical Information Network (UMIN)
4. Australian Clinical Trials Registry (ACTR)
5. Netherlands Trial Register

- Clinical trials may be listed with Other registries, but these registries must meet the above-mentioned requirements.
- The authors will be requested to provide the exact URL and unique identification number for the trial registration at the time of submission. This information will be published in a footnote on the first page of the article.
- Clinical trial reports should also comply with the Consolidated Standards of Reporting Trials (CONSORT) and include a flow diagram presenting the enrollment, intervention allocation, follow-up, and data analysis with number of subjects for each. Please also refer specifically to the CONSORT Checklist of items to include when reporting a randomized clinical trial.
- Results posted in the same clinical trials registry in which the primary registration resides will not be considered prior publication if they are presented in the form of a brief abstract (500 words or fewer) or a table.

—TOP—

Embargo Policy

- All content information of an accepted paper is strictly confidential and cannot appear in the media (in print or electronic form) before its embargo date and time. Authors/researchers, their respective public relations representatives and funding sponsors may not distribute or promote their work to the media prior to embargo.
- In the event that the American Heart Association/American Stroke Association selects the manuscript for promotion in a news release, news conference, video news release or podcast, AHA/ASA staff will contact the author/researcher to inform him/her of the pending news materials and to notify him/her that he/she may give reporters pre-embargo interviews based upon the media requests generated by the AHA/ASA news materials. Authors/researchers must ensure that the reporter understands and will adhere to the embargo time.
- If an embargo break is the result of any action by an author/researcher, he/she risks withdrawal of publication of his/her manuscript. Violations of the embargo policy may also jeopardize future acceptance of manuscripts to be published in AHA/ASA scientific journals.
- Generally, embargoes on journal articles lift the day and the time the article is published, either on-line or in print (whichever comes first) by the American Heart Association/American Stroke Association.
- Questions about media embargoes should be directed to Bridgette McNeill, Senior Communications Manager, Corporate & Media Communications, AHA National Center, 7272 Greenville Avenue, Dallas, TX 75231-4596; Tel: 214-706-1135; Email: bridgette.mcneill@heart.org.
- Although the Editorial Office will endeavor to notify authors of the anticipated publication date/time, neither the Editorial Office nor the AHA/ASA will be responsible for any consequences of early online posting with regard to the intellectual property rights. To safeguard their intellectual property, authors should ensure that appropriate reports of invention and patent applications have been filed before the manuscript is accepted.

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Permissions

- Requests for permission to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via Rightslink (a service of the Copyright Clearance Center), not the Editorial Office. All permission requests are now processed via the Rightslink online system. Steps for obtaining permission include:

1. On Stroke's home page, either search for the article using the Search feature or locate a copy of the article in the online archives for which you are requesting permission.
2. Next, select the Full Text or PDF version of the article.
3. Then, locate the "Request Permissions" link in the menu on the right side of the Web page (under "Services"). A new Web browser will open, which is Rightslink.
4. Follow the step-by-step instructions in Rightslink for requesting permission by:
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   b. Creating an account, if one does not exist already.
   c. Accepting the terms and conditions for reuse.
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5. Further information can be found in the Permissions and Rights Instructions
6. Note: For AHA Scientific Statements and Guidelines, permission to reprint, modify, alter, enhance, copy, or distribute this content must be obtained from the American Heart Association. Instructions are located at http://www.americanheart.org/presenter.jhtml?id entifier=4431 A link to the "Permission Request Form" appears on the right side of the Web page, in the "Related Items" box.

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Costs to Authors

Authors are charged:

- $70 per published page of an article to defray costs of publication (information is sent with author's proof).
- Authors of papers exceeding 4,500 words (1,800 words for Brief Reports, 1500 words for Case Studies, and 750 words for Letters/Responses to the Editor) will be charged a minimum fee of $425 per additional 1,000 words. The usual $70 page charge will also apply. Word count will be calculated by the editorial office, using the Microsoft Word tool. Title page, abstract, main body of text, acknowledgments, sources of funding, disclosures, references, figure legends, tables, and appendices intended for print publication are included in the total word count.
- Color charges per color page equals $653.00. This is in addition to the page charges. Estimate of cost will be provided for author's approval by the publisher.

- Expense for replacing poor-quality art.
- Expense for reprints (price lists are sent with author's proof).
- $50 per published page for excessive author alterations.
- $100 per published page for printing a correction (erratum after online or print publication of the article) that results from an author's error.

No page charges to authors from the following countries: Armenia, Afghanistan, Bangladesh, Benin, Bhutan, Bolivia, Burkina Faso, Burundi, Cabo Verde, Cambodia, Cameroon, Central African Republic, Chad, Comoros, Congo, Cote d'Ivoire, Djibouti, Arab Rep. Egypt, El Salvador, Eritrea, Ethiopia, The Gambia, Georgia, Ghana, Guatemala, Guinea, Guinea-Bissau, Guyana, Haiti, Honduras, India, Indonesia, Kenya, Kiribati, Kosovo, Kyrgyz Republic, Lao PDR, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Fed. Sts. Micronesia, Moldova, Mongolia, Morocco, Mozambique, Nepal, Nicaragua, Niger, Nigeria, Pakistan, Papua New Guinea, Paraguay, Philippines, Rwanda, Samoa, Sao Tome and Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, Sri Lanka, Swaziland, Tajikistan, Tanzania, Timor-Leste, Togo, Uganda, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Yemen, Rep., Zambia, and Zimbabwe.

—TOP—

Redundant Publication

Manuscripts submitted to Stroke should conform to "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" except as indicated otherwise in the instructions below.

Manuscripts submitted to Stroke should not contain material previously published in other publications, except as an abstract, and must not be currently under consideration for publication in another journal. The editors of Stroke agree with the principles of the HEART Group regarding redundant publication (Circulation. 1997;96:1. Cardiovascular News: "HEART Group Notification Regarding Redundant Publication"). Redundant publication is publication of a paper that overlaps substantially with one already published. When submitting a paper, authors should make a full statement to the editor about all submissions and previous reports that might be regarded as redundant publication of the same or similar work. The authors should alert the editor if the work includes subjects about whom a previous report has been published. Copies of such material should be included with the submitted paper to help the editor decide how to handle the matter. If redundant publication is attempted without such notification, authors should expect editorial action to be taken; at the least, rejection of the manuscript.

—TOP—

Editorial Conflict-of-Interest Policy

Original Contributions submitted by the editor-in-chief and any of the associate editors are handled by a Consulting Editor or by another editor, who makes all decisions about the manuscript (including choice of referees and ultimate acceptance or rejection). The entire process is handled confidentially. All manuscripts submitted from the Editor's home institution are also handled entirely by a Consulting Editor or by another editor from a different institution. The Editor (in Chief) and/or Associate Editors may additionally, from time to time, refer a manuscript to a Consulting Editor to avoid a real or reasonably perceived conflict of interest.

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Expedited Publication

The editors invite submission of manuscripts that have major importance to the scientific community. To be considered for expedited publication, an article must be unique and contain information that could make a significant difference in medical practice or constitute an important advance in basic knowledge. The authors must clearly state reasons for the request in the cover letter. If the editors agree that an article should be an expedited publication, they will arrange an accelerated review and, if accepted, accelerated publication.

—TOP—

Preliminary Reports

The editors discourage submission of preliminary reports that describe a standardized design and progress to date. The editors will not consider publication of such studies unless the article describes new and innovative methodology and/or reports data that might be used independently by other groups in planning similar studies. If a preliminary report is submitted, authors should specify inclusion of material that meets the guidelines of this policy.

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Disclaimer

Statements, opinions, and results of studies published in Stroke are those of the authors and do not reflect the policy or position of the American Heart Association, and the American Heart Association provides no warranty as to their accuracy or reliability.

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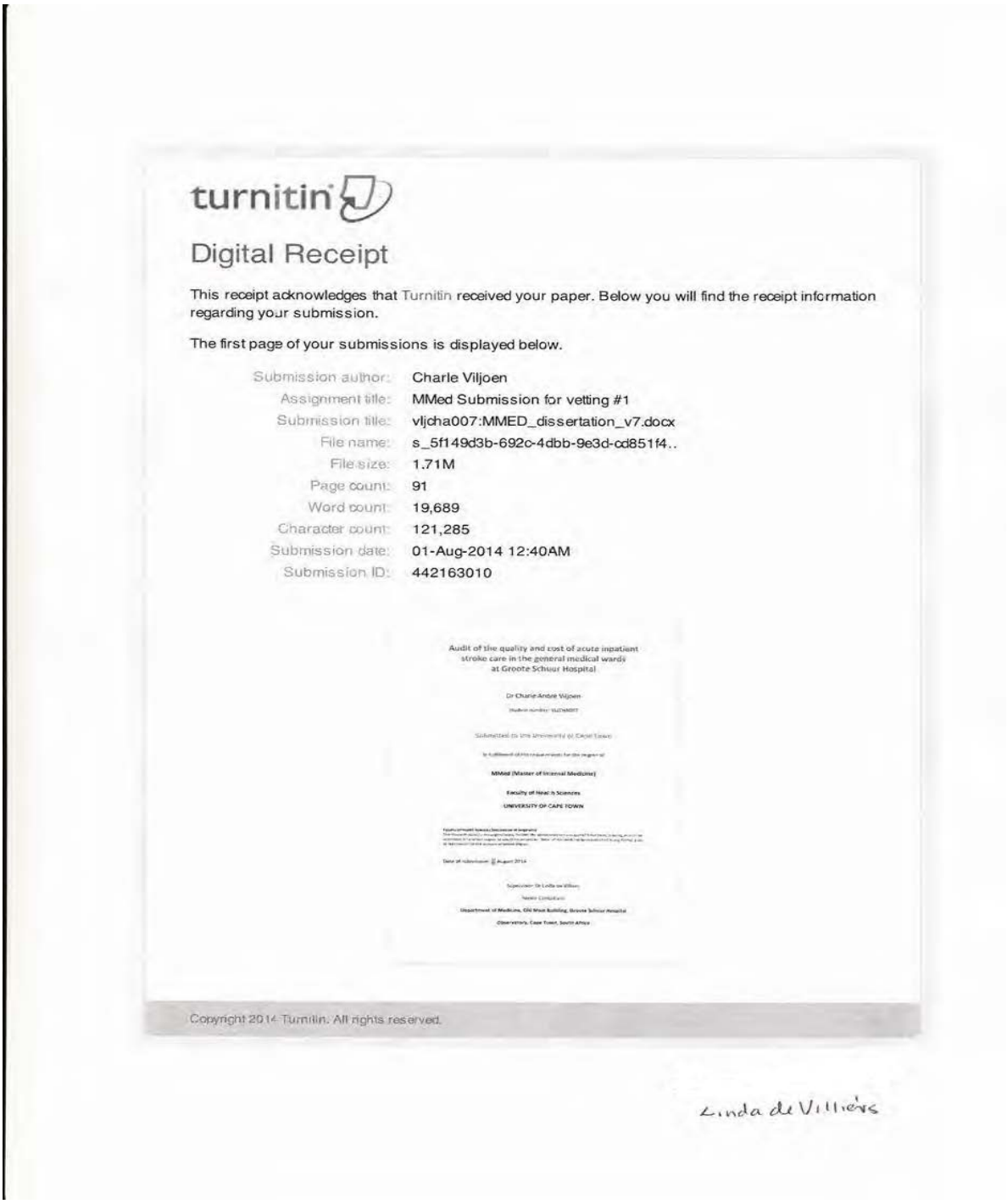
Plagiarism report

As required by the University of Cape Town's regulations for master's degrees, the dissertation was submitted to TurnItIn for a similarity check.



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Audit of the quality and cost of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital

Dr Charle André Viljoen

MMed (Master of Internal Medicine)

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

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Linda de Villiers

Ethics approval

This audit was initially planned to include all patients admitted with acute stroke to the general medical wards at Groote Schuur Hospital and GF Jooste Hospital, under the title *"Audit of the quality and cost of acute inpatient stroke care at district and secondary level hospitals in the Cape Metro"*.

However, GF Jooste Hospital was decommissioned in 2013, which made access to medical folders for review difficult. After consideration with my supervisor, it was felt that the 261 consecutive patients enrolled from the medical wards at Groote Schuur Hospital would suffice for the purposes of a master's degree. The protocol was amended and the title was changed to *"Audit of the quality and cost of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital"*. Approval was obtained from the Faculty of Health Sciences Human Research Ethics Committee after changing the title and amending the protocol accordingly, which was followed by approval by the Dissertations / Doctoral & Masters Committee of the Faculty of Health Sciences at the University of Cape Town.

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za

13 March 2012

HREC REF: 061/2012

Dr CA Viljoen
c/o Dr L De Villiers
Geriatric Medicine
L51, OMB

Dear Dr Viljoen

PROJECT TITLE: AUDIT OF THE QUALITY AND COST OF ACUTE STROKE CARE AT DISTRICT AND SECONDARY LEVEL HOSPITALS IN THE CAPE METROPOLE.

Thank you for responding to the issues raised by the Faculty of Health Sciences Human Research Ethics Committee in your letter dated 9th March 2012.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year till the 30th March 2013.

Please submit a progress form, using the standardised Annual Report Form (FHS016), if the study continues beyond the approval period. Please submit a Standard Closure form (FHS010) if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical

Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

s.thomas

From: **Jackie Cogill** jackie.cogill@uct.ac.za
Subject: Viljoen : Confirmation of Approval of Study Proposal
Date: 29 August 2012 at 10:36 AM
To: charleviljoen@gmail.com, Charle Viljoen ca.viljoen@uct.ac.za
Cc: Linda De Villiers Linda.DeVilliers@uct.ac.za, Lorraine McDonald lorraine.mcdonald@uct.ac.za

Dear Dr Viljoen

Candidature Approval (VLJCHA007)

Degree	MMed in Medicine
Title	Audit of the quality and cost of acute inpatient stroke care at district and secondary level hospitals in the Cape Metro
Department	Medicine
Supervisor	Dr L De Villiers
Ethics Approval	061/2012

I am pleased to advise that the Chair of the Dissertations/Doctoral & Masters Committee has approved your candidature for the above degree on behalf of the Committee. Formal approval was obtained by publication in the Dean's Circular, PG-Med July 2012.

Yours sincerely

Jackie Cogill

Jackie Cogill | Senior Secretary: Postgrad Academic Administration |Faculty of Health Sciences | University of Cape Town | Room N2.19, Wernher & Beit North, Health Sciences Campus, Anzio Rd, Observatory, 7925 ☎ + 27 21 406 6750 🖷 + 27 86 5565 5778 Office Hours: 08h00-16h00 Unavailable Hours: 10h00-11h00 & 13h00-13h30

UNIVERSITY OF CAPE TOWN

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e-mail: sumayah.ariefdien@uct.ac.za
www.health.uct.ac.za/research/humanethics/forms/

04 July 2013

HREC/REF: 061/2012

Dr C Viljoen
Institute of Ageing in Africa
Division of Geriatric Medicine
L-51
OMB

Dear Dr Viljoen

Project Title: AUDIT OF THE QUALITY AND COST OF ACUTE STROKE CARE AT DISTRICT AND SECONDARY LEVEL HOSPITALS IN THE CAPE METROPOLE

Thank you for your letter to the Human Research Ethics Committee dated 26 June 2013.

It is a pleasure to inform you that the Ethics Committee has **approved** the amendment subject to the following:-

1. Permission to access GSH financial records must be obtained from Groote Schuur Hospital, and a copy of this approval must be submitted to the HREC.
2. An annual progress report must be submitted if the study continues beyond the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

pp
PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

sAriefdien

HUMAN RESEARCH ETHICS COMMITTEE
-5 JUL 2013
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

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FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.3.2014
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	pp TJBurgess	Date Signed	05/07/2013

Principal Investigator to complete the following:

1. Protocol information

Date form submitted	05/07/2013		
HREC REF Number	061/2012	Current Ethics Approval was granted until	March 2013
Protocol title	AUDIT OF THE QUALITY AND COST OF ACUTE STROKE CARE AT DISTRICT AND SECONDARY LEVEL HOSPITALS IN THE CAPE METROPOLE		
Principal Investigator	L DE VILLIERS		
Department / Office Internal Mail Address	251 Old Main Building, Groote Schuur		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☑ No

2. Protocol status (tick ✓)

☑	Research-related activities are ongoing
☐	Data collection is complete, data analysis only

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		
Total number of records or specimens collected, reviewed or stored since last progress report		320.
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	☒ No

4. Signature

Signature of PI		Date	5/7/2013
Signature of Supervisor (if PI is a student)		Date	05/07/2013

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bhavna Patel
E-mail : Bhavna.Patel@westerncape.gov.za

Dr Linda De Villiers
Specialist
Geriatrics Department
Groote Schuur Hospital
NGSH

Dear Dr De Villiers

RESEARCH: Permission to access Financial Records for Costing Study as part of MMED.

Your recent letter to the hospital refers.

You are hereby granted permission to proceed with your research until the end of March 2014.

Please note the following:

a) Your research may not interfere with normal patient care
b) Hospital staff may not be asked to assist with the research.
c) No hospital consumables and stationary may be used.
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please introduce yourself to the person in charge of an area before commencing.
f) Confidentiality must be maintained at all times.

I would like to wish you every success with the project.

Yours sincerely

DR BHAVNA PATEL
SENIOR MANAGER: MEDICAL SERVICES
Date: 22 July 2013

c.c. Mr L Naidoo
Ms W Bryant

G46 Management Suite, Old Main Building,
Observatory 7925

Tel: +27 21 404 6288 fax: +27 21 404 6125

Private Bag X,
Observatory, 7935

www.capegateway.go.v.za

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS006: Protocol Amendment

HREC office use only (FWA00001637; IRB00001938)			
☑ Approved	☑ Type of review: Expedited	☐ Full committee	
This serves as notification that all changes and documentation described below are approved.			
Signature Chairperson of the HREC		Date	12/8/2013

Note: All amendments should include a Synopsis justifying the changes for the amendment (please see notice dated 23 April 2012)

Principal Investigator to complete the following:

1. Protocol information

Date	12 August 2013		
HREC REF Number	~~016/2012~~ 061/2013		
Protocol title	Audit of the quality and cost of acute stroke care at district and secondary level in the Cape metropole		
Protocol number (if applicable)			
Principal Investigator	Charle Viljoen		
Department / Office Internal Mail Address	Institute of Ageing, L51 Old Main Building, GSH		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☐ No
1.2 Is this a major or a minor amendment? (see FHS006hlp)		☐ Major	☐ Minor

2. List of Proposed Amendments with Revised Version Numbers and Dates

Please itemise on the page below, all amendments with revised version numbers and dates, which need approval.
This page will be detached, signed and returned to the PI as notification of approval. Please add extra pages if necessary.

Ethics committee approval was granted for data collection at Groote Schuur Hospital and GF Jooste hospital. Data will now only be collected at Groote Schuur hospital.

Title will change to;

.

Audit of the quality and cost of acute stroke care in the general medical wards at Groote Schuur Hospital.

HUMAN RESEARCH ETHICS COMMITTEE
12 AUG 2013
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS006: Protocol Amendment

HREC office use only (FWA00001697, IRB00001938)			
☐ Approved	☒ Type of review: Expedited	☐ Full committee	
This serves as notification that all changes and documentation described below are approved			
Signature Chairperson of the HREC		Date	24/2/2014

Note: All amendments should include a Synopsis justifying the changes for the amendment (please see notice dated 23 April 2012)

Principal Investigator to complete the following:

1. Protocol information

Date	11 February 2014
HREC REF Number	061/2012
Protocol title	Audit of the quality and cost of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital.
Protocol number (if applicable)	
Principal Investigator	Dr Charle André Viljoen (Supervisor: Dr Linda de Villiers)
Department / Office Internal Mail Address	Medicine (Division of Geriatrics) charleviljoen@gmail.com

1.1 Does this protocol receive US Federal funding?	☐ Yes	☒ No
1.2 Is this a major or a minor amendment? (see FHS006hlp)	☐ Major	☒ Minor

2. List of Proposed Amendments with Revised Version Numbers and Dates

Please itemise on the page below, all amendments with revised version numbers and dates, which need approval.
This page will be detached, signed and returned to the PI as notification of approval. Please add extra pages if necessary

The reason for this amendment is to clarify and provide more detail about what we would be including and excluding in our data collection in this **retrospective medical record review**.

Additions are indicated in the amended protocol in *italic*, removals are indicated by ~~strokethrough~~.

1. In the **aim** we have specified that the study is in the *general medical wards* of Groote Schuur Hospital
2. We have given more detail in the **objective** as to what we would like to establish that influences the cost of an acute stroke admission.
3. In the **methods**, with regards to the study population, we have given more clarity to which patients are not eligible to be included in the study (we have *broadened the exclusions* – to exclude patients that would stay longer, have a different set of investigations, and that might skew our data)

From: **Jackie Cogill** jackie.cogill@uct.ac.za
Subject: Viljoen: Change of Title
Date: 10 April 2014 at 9:44 AM
To: charleviljoen@gmail.com
Cc: Dianne Pryce dianne.pryce@uct.ac.za, Lorraine McDonald lorraine.mcdonald@uct.ac.za

Dear Dr Viljoen

The title of your Study Proposal has been changed to: Audit of quality and cost of acute stroke care in the general wards at Groote Schuur Hospital.

The change of title was published in the Dean's Circular No. PG-MedFebruary2014.

Regards
Jackie Cogill

Jackie Cogill | Senior Secretary: Postgrad Academic Administration |Faculty of Health Sciences | University of Cape Town |
Room N2.19, Wernher & Beit North, Health Sciences Campus, Anzio Rd, Observatory, 7925 ☎ + 27 21 406 6750 🖷 + 27 86 556 5778

UNIVERSITY OF CAPE TOWN 18 JUL 2014

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS010: Study Closure Report

HREC office use only (FWA00001637; IRB00001938)			
Noted and filed. This serves as acknowledgement that this study is closed			
☐ Approved	Study closure report		
☐ Not Approved	Study closure report		
Chairperson of the HREC signature		Date	18/7/2014

1. Principal Investigator to complete the following:

Date	18/7/2014
HREC REF Number	061/2012
Protocol Title	Audit of the quality and cost of acute inpatient stroke care in the general medical wards at Groote Schuur Hospital.
Protocol number (if applicable)	
Principal Investigator	Charle André VILJOEN
Department / Office Internal Mail Address	Internal Medicine charleviljoen@gmail.com

2. Please confirm (tick √)

This study is closed to enrollment	☑ Yes	☐ No
Participants have completed all research-related interventions	☑ Yes	☐ No
Participants have completed all research-related follow-up	☑ Yes	☐ No
Data analysis is complete	☑ Yes	☐ No
Your sponsored protocol is closed	☑ Yes	☐ No
If you answered 'no' to any of the above questions, you must keep your study open until all research activity is completed		

3. What is the reason for closing the study? (tick √)

Research completed	✓	No time	
Terminated due to toxicity/adverse event		PI left UCT or affiliated sites	