CHAPTER 14

STROKE
IN SOUTH AFRICA

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1. INTRODUCTION

Stroke is the second commonest cause of death worldwide,[1] with two-thirds of these deaths occurring in developing regions of the world, such as sub-Saharan Africa (SSA). The burden of stroke does not only lie in the high mortality but the high morbidity also leaves up to 50% of survivors chronically disabled.[2] The incidence of stroke in developing countries is also expected to rise in the future as the populations undergo what has been referred to as the "health transition."[3] At present, the major health burdens in SSA are infectious diseases, including HIV/AIDS, and diseases related to poverty and malnutrition. However, urbanisation is predicted to increase the risk factors for vascular disease and hence lead to a sharp increase in stroke, such as is found in developing countries.

The pattern of vascular disease changes during this transition; in its early stage stroke is likely to be more common than heart disease.[3] However, stroke is a heterogeneous condition consisting of different types (cerebral haemorrhage and cerebral infarction) and subtypes of infarction (broadly classified as large vessel and small vessel infarcts); the relative importance of these changes depending on the risk factor profile prevalent in the population, and hence the stage of the population in the health transition. The causes of the various stroke types and subtypes differ, as does their management. Therefore, it is important to understand the profile of stroke and the common causes within a population, and appropriately equip the health service to deal with population-specific needs.

Accurately understanding the burden and nature of stroke in the population therefore allows one insight into where the population is along the health transition, and allows for appropriate health service planning for acute services and 1° and 2° prevention. In South Africa, this task is complicated by our different population groups and socio-economic structure. Not only does the relative importance of risk factors for stroke and cardiovascular disease differ between population groups globally,[4,5] but as a result of socio-economic and past political influences we have population groups that, in general, reflect different stages of the health transition.

While a great deal is known about stroke in the high-income countries, very little, if anything, is known about the burden and nature of stroke for most of SSA. In South Africa we can probably extrapolate fairly accurately from the findings of stroke studies done elsewhere that included whites and to some extent Asians, but we are totally reliant on doing our own studies to obtain accurate data on coloured and black South Africans. Fortunately, since the last edition of this report, several studies have advanced our knowledge of the burden and nature of stroke in South Africa. Our present knowledge is reviewed in this chapter. We will then briefly highlight what is being done to advance the treatment and prevention of stroke in the country, and end with the state of current and future research on stroke in South Africa.

2. BURDEN AND NATURE OF STROKE IN SOUTH AFRICA

2.1 Burden of stroke

The burden of stroke on a population includes the mortality, the prevalence, the incidence, and the long-term outcome of patients.[6] Ideally, one would also like to know what the cost or economic burden of the disease is in terms of its impact on the health service directly, and on the individual, family and community, both directly and indirectly, financially, and psychosocially. Unfortunately, very little is known about the socio-economic impact of stroke in South Africa and we have not considered this aspect further, although some investigators are researching this important issue.

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2.2 Mortality of stroke

Traditionally, mortality figures are derived from vital registration data. However, the HIV/AIDS epidemic has caused dramatic changes in demographic features and mortality profiles.[7] As a result, a more complex model has been devised to estimate causes of death, including stroke. From these 'Initial burden of disease estimates for South Africa, 2000',[7] stroke was found to be the fourth most common cause of death, accounting for 6% of all deaths in 2000. Estimations showed more females (18 184) than males (13 930) died of stroke, and the overall age-standardised mortality rate for stroke was 124.9/100 000. Stroke is thus the most important non-communicable disease which causes death in females, compared to ischaemic heart disease in males.[8] Population group-specific figures are not available.

Vital registration is limited, if available at all, for most of SSA.[1] To overcome this void in health information, demographic health and surveillance sites (DSS) have utilised the verbal autopsy, a tool that consists of a questionnaire completed during a retrospective interview of individuals who are able to describe what happened during the hours, days or months preceding a death. A most likely cause of death is inferred from this information, either by physicians or by computer algorithms.[9]

The MRC/Wits (Agincourt) Rural Public Health and Health Transition Research Unit, using verbal autopsies, found stroke caused 5.5% of all deaths in a rural population of 63 000 in Limpopo Province between 1992 and 1995. The sensitivity and specificity for stroke in this study was 87% and 97%, respectively.[10] Stroke was the commonest cause of death in the 55-74-year-old age group. While in the 35-54-year-old and ≥ 75-year-old age groups, it was the second commonest cause of death after assault and congestive heart failure, respectively. The overall crude stroke mortality rate was 127/100 000 (95% CI, 93 to 160).

Based on England and Wales in 1993, where the age-adjusted mortality rate (per 100,000) was 122 in males and 115 in females,[11] stroke mortality in South Africa is at least as high, if not higher. (Obviously, a direct comparison must be made with caution, as the South African figures are not age-adjusted to Segi's world population in this case, and the figures for England and Wales are adjusted. However, as the South African rural population demographic structure is typical of a developing country population, one might expect the mortality figures to increase on adjustment).[12,13] However, a high mortality may reflect either a high incidence of stroke or a high case fatality rate or both.[14]

2.3 Prevalence of stroke

It is useful to know the prevalence of stroke in a population (i.e., the number of people with stroke in the community at any one time) in order to help plan health services. In high-income countries, stroke prevalence studies are usually conducted using telephone or postal surveys. However, in South Africa identifying people with stroke at home, particularly outside urban areas, is fraught with difficulty.

The Southern African Stroke Prevention Initiative (SASPI) has recently published the first stroke prevalence study from South Africa. The study was conducted in the Agincourt demographic and health surveillance site in Limpopo, with a population of 70 000. During the Unit's annual door-to-door census of the population in 2001, the census fieldworkers were trained to ask two additional screening questions for stroke. They requested each household informant to name every individual over the age of 15 years in the household, and then asked whether the named person(s) 1) ever had weakness down one side of the body, and 2) ever had a stroke. If the answer to either or both questions was positive, then a neurologist or one of two clinicians trained in stroke assessment, accompanied by an interpreter, visited the individual in his or her home and assessed whether or not the individual had had a stroke. The diagnosis of stroke was based on the World Health Organization definition and people with transient ischaemic attacks were excluded. If the person had had a stroke, then they were fully assessed clinically and their blood pressure was taken.

The crude prevalence was 300/100 000 (95% CI, 250 to 357)[15] after a correction was made by sex and 10-year age band for those not examined who screened positive. Labour migration added an element of complexity to the study as one would expect in any prevalence study in rural South Africa. Stroke prevalence was higher in females, 348 (95% CI, 276 to 436), than males, 246 (95% CI, 181 to 323). The age-standardised prevalence using the Segi standard population was 290.[13]

Of particular interest is the comparison of the prevalence of all strokes with the prevalence of stroke survivors 'needing help with at least one activity of daily living' and comparing this with similar data from Tanzania and Auckland, New Zealand. Overall, rural stroke prevalence in South Africa is about three times lower than in New Zealand and more than double that in Tanzania. But,

despite fewer people with stroke in the community, the prevalence of people 'needing help with at least one activity of daily living' was higher in South Africa than in New Zealand (200/100 000 compared to 173).[15] This is a significant finding because this group of people need the most help and places the greatest burden on the family, community, and health services.

2.4 Stroke incidence and case fatality

While stroke prevalence studies are useful, they have shortcomings in that they under-represent cases that die soon after the stroke, and people with very mild strokes who recover quickly and may not be included in a survey months or years later. Yet both groups may utilise health services and add to the overall disease burden. Neither stroke mortality, nor stroke prevalence, studies provide accurate data on the nature of stroke types and subtypes, and the exact cause of the stroke, all of which are best assessed within hours or days after the onset of a first-ever stroke. So the best epidemiological studies of stroke are community-based incidence studies of first-ever-in-a-lifetime stroke, with long-term follow up of case fatality.[6]

No community-based stroke incidence studies have ever been done in Southern Africa because of the difficulty of performing them.[16] There have been urban hospital-based studies from South Africa and Zimbabwe that have attempted to estimate stroke incidence in the region. However, there are many reasons why people may not be admitted to hospital with stroke and often people who are admitted represent a particular spectrum of stroke patients, possibly more severe cases.[17] These studies provide valuable information regarding the nature of stroke in the community, and are discussed later (see Table 14.1). International criteria now exist for acceptable methodology for comparable stroke incidence studies.[17,18]

There are also no case fatality data for stroke in South Africa from community-based studies. The only case fatality data available come from hospital-based urban stroke registers. All three registers (two South African and one from Zimbabwe) found very similar stroke case fatality, ranging between 33% and 35% at one month following the stroke.[19-21] But because stroke is a heterogeneous condition, it is important to know the case-mix and stroke types if possible. Rosman[19] found the case fatality to be 22% at one month for cerebral infarction and 58% for cerebral haemorrhage in Pretoria.

In a recently published study with longer follow up in The Gambia, Walker *et al*.[22] found hospital-based all stroke case fatality to be 27% at one month and 44% at six months.

3. NATURE OF STROKE

Stroke is a heterogeneous condition made up of three pathological types: cerebral infarction, cerebral haemorrhage and subarachnoid haemorrhage. Cerebral infarction or ischaemic stroke is then further divided into various subtypes, such as intracranial small vessel disease, large-vessel atherosclerotic disease, and embolism from the heart.[6] These types and subtypes differ in terms of cause, outcome and treatment.[14]

The proportions of the various stroke types and subtypes change within populations as they undergo the health transition. For example, early in the transition, when the prevalence of hypertension is high, but smoking, blood cholesterol and atherosclerotic disease are low, cerebral haemorrhage forms a greater proportion of all strokes.[23,24] However, later, as the other risk factors become more common, and cerebral atherosclerosis increases, there is a decrease in the rate of cerebral haemorrhage and an increase in the rate of cerebral infarction. The causes of ischaemic stroke also change. For example, early in the transition, cardio-embolic stroke may be related to a high prevalence of rheumatic heart disease, and later this may be superseded by ischaemic heart disease.[24]

3.1 Stroke types and subtypes in South Africa

To accurately understand the true nature of stroke community-based incidence studies are needed with early brain imaging and investigations of risk factors and cause. Unfortunately, these studies require large budgets and take years to plan and develop. Hospital-based stroke registers with overlapping case ascertainment, entering consecutive stroke patients admitted to hospital, and all patients who develop stroke while in hospital, where patients are assessed by clinicians experienced in the subtlety of stroke diagnosis, typing and management, add greatly to our knowledge of the nature of stroke within the population. There have been three such studies published from South Africa, one from Zimbabwe and a further three registers are either in progress or have recently been completed. Table 14.1 compares the findings of stroke type and subtype from the published studies that used brain imaging. Matenga's[21] study from Zimbabwe included a larger number of patients in the Harare stroke study, but only the patients in this substudy were scanned and are therefore included in the Table.[25] All the studies are either exclusively urban or in the case of Hoffmann's[26-28] studies predominantly urban.

Table 14.1. Comparison of pathological stroke types and subtypes from hospital-based stroke studies

				Stroke type (%)			Ischaemic stroke subtype (%)				Comments
Study (site/author/year)	**n**	**Population group/s**	**Scan rate (%)**	**CH**	**CI**	**SAH**	**LV**	**SV**	**CE**	**Other/ unknown**	
Kalafong/Rosman/1986[19]	116	Black	79	33	66	n/i	47	31	21	1	Recurrent and first-ever-in-a-lifetime strokes included.
Harare/Matenga/1986[25]	100	Black	100	31	67	2	-	-	19	-	100 consecutive patients with presumed stroke studied. Seven were found to have non-stroke lesions.
Medunsa/Joubert/1991[20]	304	Black	82	26	71	3	-	1	46	-	All first-ever-in-a-lifetime strokes.
Durban/Hoffmann/ 2000[26-28]	1000	White : 781 Asian : 104 Black : 100 Coloured : 14 Uncertain : 1	100	5	95	0	26	26	12	35	Register based on referrals to author's practice, i.e., personal series. Very detailed investigations and focus on cognitive assessment of patients. See section on HIV and stroke.

CH: cerebral haemorrhage; CI: cerebral infarction; SAH: sub-arachnoid haemorrhage; LV: large vessel; SV: small vessel; CE: cardio-embolic; n/i: not included

The three ongoing or recently completed stroke registers are: the University of Cape Town and Groote Schuur Hospital database, the Johannesburg Hospital Stroke Register, and the Tintswalo Hospital Stroke Register. The first two urban registers will provide cross-population group comparisons of the nature of stroke during a time of rapid health transition and high HIV/AIDS prevalence, and the Tintswalo Hospital Stroke Register will provide the first glimpse of the profile of stroke in a rural hospital in South Africa. All three registers have similar methodology to aid in future comparisons.

Table 14.1 shows that cerebral haemorrhage occurs in about 30% of black stroke patients and it is tempting to infer that this is in keeping with the anticipated impact of the health transition and subsequent hypertension in the absence of much atherosclerosis. One has to be cautious in the interpretation of hospital-based series, however, as cerebral haemorrhages have a more dramatic clinical presentation and are therefore more likely to be admitted to hospital and then to be imaged. The low proportion of cerebral haemorrhage in the Durban Stroke Register may reflect the population groups included, but as 5% would be low anywhere in the world, it more likely reflects the pattern of referral to the register.

It is very difficult to interpret the differences in stroke subtypes found in the series shown in Table 14.1. Not all studies provided sufficient detail on ischaemic stroke subtypes to complete the Table. From earlier studies, it is also not clear how small and large vessel disease was defined. Patients with small vessel or lacunar strokes often experience very mild strokes and may not have been admitted to hospital. This may also have added to the low percentage of small vessel strokes in the Medunsa Stroke Register (Table 14.1).

The prevalence of extracranial carotid disease, measured by Doppler or indirectly implied by the presence or absence of carotid bruits and pulses, is generally low in studies of black South Africans (<1-4%)[20,29,30] and higher in series with a large proportion of white South Africans, e.g. 25% in the Durban Stroke Register.[26]

Patients entered into the Durban Stroke Register were investigated in detail, and the focus of the study was on higher cortical deficits following stroke. Hoffmann[27] reached the conclusion that cognitive impairment is present in the majority of stroke types and may be the sole presentation of stroke even when unaccompanied by long-tract signs.

Although multiple population groups were included, all 100 black stroke patients were young,[28] and there is insufficient published data to compare stroke subtypes across groups and make inferences regarding the health transition.

Two studies have specifically considered TIA or stroke in young South Africans. Between 1981 and 1991 Giovannoni and Fritz[31] investigated 75 young (< 45 years old) TIA patients seen at the Johannesburg Hospital TIA clinic and compared them with older patients in terms of risk factors and cause of their TIA. They found that the younger patients were more likely to have migraine and valvular heart disease, and the older group were more likely to have hypertension, ischaemic heart disease, peripheral vascular disease and a previous smoking history. Although the commonest aetiology in both groups was atherosclerosis, younger patients were also more likely to have conditions such as fibromuscular dysplasia and mitral valve prolapse, and to use the oral contraceptive pill.[31]

Hoffmann[28] analysed the 320 young (15-49 years) stroke patients in the Durban Stroke Register and found that race and endemic disease were important determinants of the underlying cause and risk factor profile. Whites presented with the more traditional risk factors, such as hypertension, hyperlipidaemia, alcohol abuse and smoking, while blacks more often had had an infection in the two weeks prior to the stroke. The TOAST classification of 'other' stroke causes, included HIV-associated stroke in 20%, tuberculosis vasculitis, neurocysticercosis, syphilis, bilharzia, Takayashu's disease, a large number of coagulopathies, and dissection and cerebral venous thrombosis.[28]

3.2 Stroke risk factors in South Africa – in people who have had strokes

Stroke risk factors are divided into those that are modifiable and those that are not, such as sex. Increasing age is a major unmodifiable risk factor for stroke in all studies, whether in developed or developing countries. Of importance, though, is that data from hospital-based studies suggest that age-specific stroke incidence is higher in younger (35-54-year-old) age groups in South Africa than in high-income regions.[19,21]

Hospital-based studies have found the following prevalence of modifiable stroke risk factors in people admitted with stroke:[19,20,26]

hypertension in patients with cerebral infarction 32-76%,

hypertension in patients with cerebral haemorrhage 76-93%,

diabetes mellitus 3-10%,

hypercholesterolaemia <2-10% (although the definition used is not given in the study by Hoffmann,[25] and 10% is at least double the finding of any other study),

atrial fibrillation 1-7%,

cigarette smoking 15-28%, and

previous stroke or transient ischaemic attack 2-7%.

In the SASPI study of stroke prevalence in rural South Africans, hypertension was again the most common risk factor: hypertension 71%, diabetes mellitus 12%, cigarette smoking 9%, and current alcohol use 20%.[30]

3.3 The impact of human immunodeficiency virus (HIV) on stroke in South Africa

There is no accurate way of knowing what the impact of HIV has been on stroke in South Africa. Anecdotally, many clinicians mention increasing numbers of young HIV-positive stroke patients in our hospitals, and there are many reasons why someone who is immunosuppressed with HIV may present with a stroke (e.g., as a result of tuberculous meningitis, toxoplasmosis affecting cerebral blood vessels or even cardiac disease).[32] HIV has been associated with coagulation abnormalities, such as Protein S deficiency, but this does not seem to be an important cause of stroke in our population and in a case series from Chris Hani Baragwanath Hospital. Mochan *et al*.[33] found the causes of stroke in HIV-positive stroke patients to be similar to those in HIV-negative stroke patients.

So does HIV itself actually cause or independently increase the risk of stroke? It certainly causes an intracranial small vessel vasculopathy,[32] and an extra-cranial large artery 'vasculitis' of sorts,[34,35] but only one study has fairly convincingly found HIV to be an independent risk for stroke.[36]

There have not been many prospective series published during the 'HIV-era' in South Africa. The Durban Stroke Register found 20% of young black stroke patients to be HIV positive and have HIV-associated stroke,[28] but in the older rural SASPI stroke prevalence study only 2% of stroke patients were thought to be HIV positive.[15] In both studies, these figures probably reflect the HIV prevalence in the general population; what is needed is a case-controlled study to answer the question.

Of more immediate concern, though, is the impact that an increasing burden of stroke is likely to have on the country's middle-aged and elderly population. In a population affected by HIV, where many families have lost their parents, that role is then taken on by grandparents. This group is at most risk for stroke and vascular disease.

3.4 Summary of the burden and nature of stroke in South Africa

Stroke mortality is already high in South Africa, and although stroke prevalence is not yet at developed country levels in rural areas, the prevalence of people requiring help with activities of daily living is already higher than that found in high-income countries. These findings suggest that we are well into the health transition and that stroke is adding significantly to the burden of disease facing our health service. However, knowing about stroke mortality and prevalence is not enough, and we certainly do not know nearly enough about the nature of stroke in the community in South Africa. We need high quality community-based stroke incidence studies with accurate assessment of stroke type, subtype, risk factors and causes, and long-term follow up to inform us about risk factors, causes, true stroke burden and outcome, and to help us develop appropriate treatment and prevention strategies.

4. THE TREATMENT AND PREVENTION OF STROKE IN SOUTH AFRICA

4.1Treatment of acute stroke

There have been major advances in the treatment of acute stroke in recent years.[15] Fundamental to these advances have been the use of thrombolysis in ischaemic stroke, protocol driven multi-disciplinary care in stroke units, and development of national guidelines to assist in protocol development and standardisation of care.[15] Since the last edition of this report, the South African Stroke Management Guidelines have been published under the auspices of the South African Medical Association and edited by Professor Vivian Fritz.[37] The South African

Hypertension Guidelines also specifically deal with the management of hypertension in stroke patients.[38]

There is currently only one academic stroke unit, which is located at Groote Schuur Hospital, Cape Town, established by Professor Alan Bryer, and a second provincial unit at the GF Jooste Hospital in Cape Town. However, the South African Government has accepted the Stroke Management Guidelines, which are now policy, and the intention of government is that every province will have at least one stroke unit.

4.2 Treatment and prevention of stroke in South Africa

The key to advancing the treatment of stroke and improving primary and secondary prevention is enhanced public and health practitioner awareness or education. This role has been taken on by the Southern African Stroke Foundation (SASF). The SASF, under the leadership of Professor Vivian Fritz, has promoted stroke awareness through the annual stroke awareness week, using multiple media modalities, pamphlets, fun activities and various other events. Doctors, nurses and allied professionals have been educated through congresses, workshops, continuing education meetings, television programmes and print media.

The SASF is therefore a fundamental part of both the 'mass' and 'high' risk strategies for lowering risk for stroke. The high-risk strategy involves the more costly identification and treatment of people at high risk for stroke (e.g., those with high cholesterol, high blood pressure and those who have had a stroke). The 'mass' strategy is less costly, but requires huge numbers of the population to change their lifestyle and, for example, eat less salt and exercise more, and so lower their risk.

The SASPI prevalence study has recently highlighted the very poor level of secondary prevention in our rural stroke patients. Of 103 stroke patients, only one person was taking daily aspirin, and of the 73 who had hypertension, only eight were on treatment and only one was controlled.[30]

The importance of good treatment and prevention strategies was recently highlighted with the publication of the Oxfordshire Community Stroke Project / OXVASC follow-up study. This study demonstrated that a 40% age-specific drop in stroke incidence over 20 years is possible in a population, almost certainly due in large part to the impact of preventive strategies.[18,19,39]

5. CURRENT AND FUTURE STROKE RESEARCH IN SOUTH AFRICA

Although we cannot claim to be aware of all stroke research activities underway in the country, major research activities planned, recently completed or currently underway include:

- Hospital-based registers at Groote Schuur, Johannesburg Hospital and Tintswalo Hospital.
- Southern African Stroke Prevention Initiative (SASPI) – a multi-disciplinary collaborative study between the University of the Witwatersrand, University of Warwick and University of Edinburgh (and others). Work takes place in the MRC/ Wits (Agincourt) Rural Public Health and Health Transition Research Unit, Limpopo Province. Topics being researched are the prevalence of vascular risk factors, qualitative research regarding perception of health and illness, the socio-economic impact of stroke, and other components mentioned in the text. Planned future projects include a stroke incidence study, the development of a long-term cohort study and interventions to reduce stroke/ vascular disease.
- UCT/ Wits/ Swedish Collaboration (Sida-Sarec): A study for the development of a community-based stroke care model for use in urban and rural South Africa.
- Cardiovascular disease research funded study to assess the role of discharge planning post-stroke. This is based at GF Jooste Hospital and will be followed by a community study to assess post-stroke outcome.
- The development of acute stroke management protocols appropriate to various levels of care in South Africa (SASF).
- Research to clarify the impact of HIV on stroke and help guide the management of HIV-infected patients is continuing in a number of centres.

6. CONCLUSION

Stroke is the forerunner of vascular disease in the epidemiologic or health transition, and all evidence suggests that South Africa is well into the transition. It is a devastating condition with high levels of disability and case fatality. Yet stroke is readily prevented. It is not, however, a uniform, one-size-fits-all disease. It is a heterogeneous condition made up of different types and subtypes, each with its own profile of risk factors and causes and management. Furthermore, the types and subtypes are not uniformly represented across all sections of the population. If we are to develop

appropriate strategies to treat and prevent stroke in South Africa, we need to find out more about stroke burden and nature in order to develop locally relevant interventions and facilities capable of handling these conditions. The benefits have been shown to be enormous. If we fail, we will be facing a rapidly increasing burden of stroke adding to our health service burden.

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