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# A RACIAL AND URBAN-RURAL COMPARISON OF THE NATURE OF STROKE IN SOUTH AFRICA

**Myles Dean Connor**

**A thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfilment of the requirements for the degree of Doctor of Philosophy**

**Johannesburg, 2007**

**DECLARATION**

I, Myles Dean Connor declare that this thesis is my own work. It is being submitted for the degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

…….....

……...day of …….., 2007.

***This thesis is dedicated to my partner Charles, without whose support and encouragement, it would never have been started or completed***

## PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS STUDY

### PUBLICATIONS

Connor, M. & Warlow, C. 2001. Stroke in the young in South Africa (letter). **S Afr Med J**, vol. 91, pp. 273-274.

SASPI Project Team 2004a. Prevalence of stroke survivors in rural South Africa: results from the Southern Africa Stroke Prevention Initiative (SASPI) Agincourt field site. **Stroke**, vol. 35, pp. 627-632.

SASPI Project Team 2004b. Secondary prevention of stroke - results from the Southern Africa Stroke Prevention Initiative (SASPI) study. **Bulletin of the World Health Organisation**, vol. 82, pp. 503-508.

Connor, M.D., Thorogood, M., Modi, G. et al. 2007. The burden of stroke in Sub-Saharan Africa. **Am J Prev Med**, vol. 33, pp. 172-173.

Connor, M.D., Walker, R., Modi, G. et al. 2007. Burden of stroke in black populations in sub-Saharan Africa. **Lancet Neurology**, vol. 6, pp. 269-278.

Connor, M.D., Modi, G. & Warlow, C.P. 2007. Accuracy of the Siriraj and Guy's Hospital Stroke Scores in Urban South Africans. **Stroke**, vol. 38, pp. 62-68.

**PRESENTATIONS**

Neurological Association of South Africa, Millenium Congress. 2000. Drakensburg, South Africa. **Stroke in Africa: a systematic review.** Connor, M.D., Warlow, C.P., Fritz, V.U.

World Stroke Congress. 2000. Melbourne, Australia. **Stroke in Sub-Saharan Africa: a systematic review.** Connor, M.D., Warlow, C.P., Fritz, V.U.

Neurological Association of South Africa, Annual Congress. 2001. Wild Coast, South Africa. **The usefulness of clinical rating scales in distinguishing stroke types in African stroke patients.** Connor, M.D., Rascher, C., Heard, V., Mavrodaris, L., Osman, S., Pearl, J., Kaplan, T., Fritz, V.U.

Neurological Association of South Africa, Annual Congress, 2002. Johannesburg, South Africa. **The Tintswalo Hospital Stroke Register (THSR): analysis of the first 50 patients.** Connor, M.D., Casserly, B.L., Modi, G., Warlow, C.P.

Southern African Hypertension Society Conference. 2003. Johannesburg. **The prevalence of stroke survivors in rural South Africa: findings from the Southern African Stroke Prevention Initiative (SASPI) rural Agincourt field site.** Connor, M.D., Casserly, B.L., Dobson, C., Thorogood, M., Warlow, C.P. on behalf of the SASPI team

European Stroke Conference. 2003. Valencia, Spain. **The Tintswalo Hospital Stroke Register: A rural South African Stroke Register.** Connor, M.D., Casserly, B., Thorogood, M., Modi, G., Warlow, C.P. on behalf of the SASPI Project Team

European Stroke Conference. 2003. Valencia, Spain. **The prevalence of stroke survivors in rural South Africa: results from the Southern African Stroke Prevention Initiative rural Agincourt Field Site.** Connor, M., Casserly, B., Dobson, C., Thorogood, M., Warlow, C., on behalf of the SASPI Project Team

European Stroke Conference. 2003. Valencia, Spain. **Secondary stroke prevention, prophylaxis and health seeking behaviour in stroke survivors in rural South Africa: report from the SASPI study.** Thorogood, M., Connor, M., Casserly, B., Dobson, C., Warlow, C. on behalf of the SASPI Project Team

Combined meeting of the Neurology Association of South Africa and Association of British Neurologists. 2003. Cape Town, South Africa. **Stroke in rural South Africa.** Connor, M.D., on behalf of the SASPI Project Team

Neurological Association of South Africa. 2004. Pretoria, South Africa. **Clinical diagnosis of cerebral haemorrhage using the Allen and Siriraj scores in black South African stroke patients.** Connor, M.D., Modi, G., Warlow, C.P.

Association of British Neurologists Spring Meeting. April 2004. London. **Measuring the emerging burden of stroke in black South Africans, with difficulty.** Warlow, C., and Connor, M.

World Congress of Neurology. November 2005. Sydney, Australia. **Stroke in the developing world compared to western countries.** Warlow, C.P., and Connor, M.

Joint World Congress on Stroke. October 2006. Cape Town, South Africa. **Pathological stroke type and ischaemic stroke subtype differs between population groups in urban hospital-based South African stroke patients: the Johannesburg Hospital Stroke Register (JHSR).** Connor, M.D., Modi, G., Warlow, C.P.

Joint World Congress on Stroke. October 2006. Cape Town, South Africa. **Risk factors in urban hospital-based South African stroke patients: the Johannesburg Hospital Stroke Register (JHSR).** Connor, M.D., Modi, G., Warlow, C.P.

**ABSTRACT**

Sub-Saharan Africa is thought to be undergoing a health (or epidemiological) and demographic transition, moving from a pattern of disease dominated by infection, perinatal illness and other diseases of poverty, to one dominated by non-communicable disease, in particular vascular disease. If such a transition is occurring, then the burden of vascular disease including stroke will increase. Stroke is a heterogeneous condition and it is likely that the nature of stroke (pathological types, subtypes, and causes) will change during this transition. However, little is known about the burden and nature of stroke in Sub-Saharan Africa, as it is now. This information is essential to inform health services to appropriately plan and deliver health care for the future, to develop strategies for stroke prevention, and to test the theory of the health and demographic transition.

My overall aim was to assess and compare the burden and nature of stroke in rural and urban South Africa, and to establish whether there is any evidence of a health transition. Specifically I aimed to:

- review what is known about stroke in Sub-Saharan Africa;
- establish the prevalence and nature of prevalent stroke in rural South Africa;
- compare the nature of hospital-based stroke in urban and rural stroke patients;
- compare the nature of urban hospital-based stroke in different population groups; and

- validate two stroke scores in the urban stroke register to enable us to diagnose pathological stroke type in rural stroke patients who do not have access to brain imaging.

**Methods:** The following methods were used to achieve these aims:

- I systematically searched the literature for, and critically reviewed, studies of stroke from Sub-Saharan Africa (literature review).
- The rural Agincourt Health and Population Unit demographic surveillance site was screened for stroke using two questions during the annual census. Anyone who screened positive for stroke was examined to decide whether they had had a stroke (stroke prevalence study).
- The Tintswalo Hospital Stroke Register was established to ascertain and assess rural stroke patients over 20 months (rural hospital-based stroke), and
- The Johannesburg Hospital Stroke Register similarly established to assess urban stroke patients over 23 months (urban hospital-based stroke).
- The accuracy of the Siriraj and Guy's Hospital stroke scores was compared to the CT brain scan "gold-standard" in the Johannesburg Hospital Stroke Register.

**Results:** Using these approaches I found that:

- Very little is currently known about the burden and nature of stroke in Sub-Saharan Africa.
- The prevalence of rural stroke was about half that found in high-income countries, and double that found in Tanzania. However, *disabling* stroke was at least as prevalent as it is in high-income countries.
- Both rural and urban black South Africans are probably in early phases of the health transition, and this is impacting on the nature of stroke, particularly the cause of cardioembolic stroke.
- Neither the Siriraj nor Guy's Hospital stroke score are sufficiently accurate for use in epidemiological studies or clinical management of stroke in Sub-Saharan Africa.

**Conclusion:** There is already a heavy burden of stroke in Sub-Saharan Africa, and there is some evidence of a health transition in the black population. However, it is not possible to accurately assess the burden and nature of stroke without community-based incidence studies using early brain imaging to distinguish ischaemic stroke from cerebral haemorrhage. Until we have these studies, we will never know the precise burden and nature of stroke, the effect of the health transition, or the optimal approach to preventing a stroke epidemic in our population.

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**NOMENCLATURE**

All abbreviations that are not part of common usage are abbreviated in the text, but outlined here for reference.

| | |
|---|---|
| % | percentage |
| ADA | adenosine deaminase |
| ADL | activities of daily living |
| AHPU | Agincourt Health and Population Unit |
| AIDS | Acquired Immunodeficiency Syndrome |
| AMMP | Adult Mortality and Morbidity Project |
| ANOVA | analysis of covariance |
| BHF | British Heart Foundation |
| BI | Barthel Index |
| BP | blood pressure |
| CD 4 cells | cluster of differentiation molecule 4 containing cells |
| CH | cerebral haemorrhage |
| CI | confidence interval |
| CSF | cerebrospinal fluid |
| CT scan | Computerised tomography scan |
| DHSA | South African Demographic and Health survey |
| DSDB | Durban Stroke Data Bank |
| DSS | demographic surveillance site |
| ECG | electrocardiogram |
| ELISA | enzyme-linked immunosorbent assay |
| F (in tables) | Female |

| | |
|---|---|
| g/L | grams per litre |
| GCNKSS | Greater Cincinnati / Kentucky Stroke Study |
| GHSS | Guy's Hospital Stroke Score |
| HDL | high-density lipoprotein |
| HIV | human immunodeficiency virus |
| HTHD | hypertensive heart disease |
| IHD | ischaemic heart disease |
| INDEPTH | International Network of field sites with continuous Demographic Evaluation of Populations and Their Health in developing countries |
| IS | ischaemic stroke |
| JHSR | Johannesburg Hospital Stroke Register |
| L | litre |
| LACI | lacunar infarction |
| LACS | lacunar syndrome |
| M (in tables) | Male |
| Medunsa | Medical University of Southern Africa |
| MeSH | Medical Subject Headings |
| mmHg | millimetres of mercury |
| mmol/L | millimoles per liter |
| MR angiogram | magnetic resonance angiogram |
| mRankin | modified Rankin scale |
| MRC | Medical Research Council |
| MRI scan | Magnetic resonance imaging scan |
| MSDB | Medunsa Stroke Data Bank |
| MUGA | multigated blood pool scanning |
| NIHSS | National Institutes of Health stroke score |
| NMSS | Northern Manhattan Stroke Study |
| OCSP | Oxfordshire Community Stroke Project |

| | |
|---|---|
| OXVASC | Oxford Vascular Study |
| PACI | partial anterior circulation infarction |
| PACS | partial anterior circulation syndrome |
| POCI | posterior circulation infarction |
| POCI | posterior circulation syndrome |
| PROGRESS | Perindopril prevention against recurrent stroke study |
| PVD | Peripheral vascular disease |
| QECH | Queen Elizabeth Central Hospital |
| RPR | rapid plasma reagin |
| SAH | Sub-arachnoid haemorrhage |
| SD | standard deviation |
| SD | standard deviation |
| SSA | Sub-Saharan Africa |
| SSS | Siriraj Stroke Score |
| SSS | Scandinavian Stroke Score everywhere except chapter 6, where it is used to abbreviate Siriraj Stroke Score |
| STI | sexually transmitted infection |
| TACI | total anterior circulation infarction |
| TACS | total anterior circulation syndrome |
| THSR | Tintswalo Hospital Stroke Register |
| TIA | transient ischaemic attack |
| TOAST | Trial of Org 101725 in Acute Stroke Treatment |
| UK | United Kingdom |
| UNAIDS | Joint United Nations Programme on HIV/AIDS |
| VDRL | Venereal Disease Research Laboratory |
| WHO | World Health Organisation |

# CHAPTER 1 INTRODUCTION

## 1.0 The purpose of this study

In high-income countries stroke has been recognised as an important cause of death and disability for many years. Recently the importance of stroke in low- and middle-income (developing) countries has also been appreciated, highlighted by the Global Burden of Disease study that two-thirds of stroke deaths occur in low and middle-income regions of the world (Murray & Lopez, 1997; Bovet, 2002). Moreover, the burden of stroke and other vascular disease is likely to increase dramatically over the next few decades in these lower income countries because of their expected health and demographic transition (see section 1.6 for description of the health and demographic transition), so adding to the infectious and poverty related diseases already affecting these populations (Howson, Reddy, Ryan et al, 1998; Vorster, 2002; Bovet, 2002).

Health services in Sub-Saharan African countries are used to dealing with acute disease such as infection and trauma. However, it is essential to encourage these health services and the governments that control them to adjust health services to take on chronic non-communicable disease management and prevention (Leeder, Raymond, Greenberg et al, 2004). This is not an easy task, given the limited resources available in most countries in Sub-Saharan Africa. Thus, to convince these

health services of the need for change, we need persuasive epidemiological evidence highlighting the growing burden of chronic non-communicable disease, and the changing nature of vascular diseases such as stroke which leads the way in the health transition. Furthermore, most Sub-Saharan African countries are faced with an enormous human immunodeficiency virus (HIV) epidemic, and the impact of HIV on the emergence and development of vascular and other non-communicable disease is not known.

There is little high quality epidemiological data on stroke and particularly on the effect of the health transition on stroke, both in South Africa and in Sub-Saharan Africa in general. South Africa's multi-ethnic population provides the opportunity to compare the nature of stroke (pathological stroke types, ischaemic stroke subtypes, risk factors and causes of stroke) in populations at different stages of the health transition. At least three hospital-based stroke registers have investigated stroke in South Africa, two of these in urban black South Africa populations (Kalafong n=212 and Medunsa n=304) before the HIV era (Rosman, 1989; Joubert, 1991), and one predominantly in white South Africans (n=1298). There are no community-based stroke studies from South Africa, nor any hospital-based studies that have investigated rural stroke or compared stroke across a representative sample of the country's population (see chapter 2 and 5).

The diagnosis of pathological stroke type (cerebral haemorrhage, ischaemic stroke and subarachnoid haemorrhage) is best made using computer tomography (CT) or

magnetic resonance imaging (MRI) scanning. Unfortunately scanners are seldom available outside major centres in South Africa or indeed the whole of Sub-Saharan Africa. Bedside scores to assist in diagnosing pathological stroke type have been produced but not validated in Sub-Saharan Africa. For many reasons (discussed in chapter 6) these scores may not work as well in Sub-Saharan Africans as in the populations in which they were developed.

**The purpose of this study was to:**

1. Systematically review the literature of stroke in Sub-Saharan Africa, in particular in South Africa

2. Establish the prevalence of stroke in rural South Africa

3. Establish the nature of prevalent stroke in rural South Africa

4. Compare the nature of hospital-based stroke in different population groups in urban South Africa

5. Assess the performance of two stroke scores in black South Africans for use in diagnosing pathological stroke type when brain imaging is not available

6. Assess the nature of hospital-based stroke in rural South Africa

7. Compare the nature of stroke in urban and rural black South Africans.

## 1.1 The rationale for the design of the study

The ideal study to investigate stroke in a population is a community-based stroke incidence study (Warlow, 1998). However, these studies are expensive to perform and we did not have sufficient funding to conduct one in South Africa, though we applied for grants unsuccessfully on several occasions. We then decided to start the work presented here. It is less expensive to measure stroke prevalence in a community provided one has an accurate denominator. We were fortunate enough to have access to a defined population who were part of the University of the Witwatersrand / Medical Research Council (Agincourt) Rural Public Health and Health Transitions Research Unit, a demographic and surveillance site in the north-east of South Africa. This enabled us to accurately assess the prevalence of stroke in approximately 70 000 people, by screening for stroke using two questions during the annual unit census. We were then able to assess people who had likely had a stroke in detail, to determine both the nature of prevalent stroke in rural South Africa and the pattern of health seeking behaviour.

We assessed the nature of stroke in a representative sample of urban South Africans by establishing a stroke register at Johannesburg Hospital, one of the University of the Witwatersrand's teaching hospitals. This hospital is attached to the University of the Witwatersrand, Faculty of Health Sciences, and close to our Division of Neurology. While it is a tertiary referral hospital, it also provides an extensive secondary care service to the Johannesburg inner city and surrounding suburbs. The population admitted to the hospital is representative of an urban South African population. We carefully ascertained all stroke patients, made a detailed clinical assessment and documented all available investigations on the patients.

The Johannesburg Hospital had a CT brain scanner and this allowed us to validate the Guy's Hospital and Siriraj Stroke Scores, which are used to assign the pathological type of stroke, in a black South African population. We were then able to use these scores in the Tintswalo Hospital stroke register, where CT scanning was not available.

We chose to establish our rural hospital stroke register at Tintswalo Hospital in the Bohlabela region of Limpopo Province, because it is one of three hospitals that provides a service to the Agincourt community studied in the stroke prevalence study. The hospital also has close ties with the University of the Witwatersrand and many medical students visit this hospital as part of their rural medicine programme. As in the Johannesburg Hospital, we did not have sufficient funding to freely investigate stroke patients, though mid-way through the running of the register we did receive

funding for blood investigations. We therefore focused on the complete ascertainment of stroke patients, thorough clinical assessment and documentation of any investigations that were performed as part of their routine care.

The individual components, i.e. the rural stroke prevalence study, the urban stroke register at Johannesburg Hospital, and the rural stroke register at Tintswalo Hospital, all ran separately. We made a concerted effort to ensure that our method of assessing stroke patients in each component was the same or very similar. I established and ran each component, trained all staff who assisted with patient assessment and reviewed all cases prior to including them into the study data. All three components of the study used the same questionnaire which was modified and adapted for each component, e.g. by including questions regarding which village people came from in the Agincourt Unit for the prevalence study (Appendices B, D and G).

We were then able to compare the nature of urban and rural stroke, the nature of stroke in different population groups, and more broadly the nature of prevalent rural stroke to assess whether there was any evidence to support a vascular health transition in South Africa.

## 1.2 The overlap between the Southern African Stroke Prevention Initiative (SASPI) study and other components of this study

The Southern African Stroke Prevention Initiative is a collaborative study originally between the University of the Witwatersrand and the London School of Hygiene and Tropical Medicine, with collaborators from the University of Edinburgh. The University of Warwick later replaced the London School of Hygiene and Tropical Medicine. The study included a multidisciplinary team of neurologists, epidemiologists, public health specialists, social anthropologists and an occupational therapist. The aim of the SASPI study was to quantify the impact of stroke on the rural Agincourt community, understand the social setting of stroke, understand the nature of stroke in people admitted to hospital with stroke and in stroke survivors in the community, and to identify problems related to the prevention, diagnosis and management of stroke in the Agincourt population. The initial SASPI study included: a stroke prevalence study, a hospital-based stroke register run at Tintswalo Hospital, a community survey of vascular risk factors in adults over the age of 35 years, assessment of the social impact of stroke on stroke survivors, and the lay-beliefs and understanding of stroke and its related symptoms in Agincourt.

I am an investigator on SASPI and was responsible for the stroke prevalence study and the Tintswalo Hospital Stroke Register. These two components, which form part of this thesis, were part of the SASPI study, while the Johannesburg Hospital Stroke

Register was not a component of the SASPI study. SASPI was funded by the Wellcome Trust (reference number 064762/Z/01/2).

## 1.3 My role in the various components of the study

Epidemiological stroke studies are invariably collaborative efforts, and the various components of this study could not have been performed by one person. However, as this work forms part of my thesis, it is prudent to outline exactly what my role was in each component.

- **Literature review (chapter 2):** I compiled the systematic literature review (chapter 2) after receiving useful advice and training on methodology of systematic reviews and designing a literature search from the Cochrane Stroke Group in Edinburgh, United Kingdom.
- **Stroke prevalence study and nature of prevalent stroke (chapters 3 and 4):** I initiated and designed the prevalence study and together with the SASPI team wrote the grant application and obtained funding for this study. I trained the field-workers who screened the Agincourt population for stroke during the annual census, and performed an initial pilot study of stroke prevalence. I trained the two research fellows who assisted me with the assessment of individuals who screened positive for the stroke. As well as spending approximately 3 months in the field seeing people who had screened positive on my own, I also visited the research fellows approximately weekly and

reviewed all patients who the research fellows assessed as having had a stroke in person, any individuals in whom they were not sure of the diagnosis, and any individuals with neurological disease who required further assessment. I then reviewed all the questionnaires / data and discussed specific individuals with my supervisors (Professor Charles Warlow, University of Edinburgh, United Kingdom, and Professor Girish Modi, University of the Witwatersrand, South Africa), to ensure that we correctly diagnosed and assessed the stroke patients prior to data entry. I cleaned the database and analysed the data with the help of Professor Margaret Thorogood the principal investigator of SASPI (Professor of Epidemiology, University of Warwick, United Kingdom).

- **Johannesburg Hospital Stroke Register (JHSR) (chapter 5):** I designed the JHSR study and raised funding for the study. I trained the stroke register assistant who ascertained our stroke cases, and trained the doctors who formed part of the stroke team in the assessment of stroke patients. I assessed over a quarter of the patients referred to the JHSR without any assistance, and reviewed the majority of the remainder in person together with the other stroke team members who had assessed them initially. I reviewed all case notes prior to data entry and inclusion in the register to ensure that we accurately diagnosed and classified stroke patients. Again, I discussed difficult cases with my supervisors. I entered all the data, cleaned the database and analysed the data with occasional assistance from Professor Thorogood.

- **Tintswalo Hospital Stroke Register (THSR) (chapter 7):** I designed the THSR, and raised funds to start the study and later to continue it with further funding raised as part of the SASPI study. I trained the THSR nurse co-ordinator who ascertained stroke cases and performed the initial assessment of the patients. On my approximately weekly visits to the hospital, I assessed the majority of the patients. Some patients died or rarely were transferred to other hospitals before I could assess them. I reviewed all the questionnaires and assessments as in the JHSR. I entered the data, cleaned the data base and analysed the data.
- **The validation of the Guy's Hospital and Siriraj Stroke scores (chapter 6):** This component is an integral part of the JHSR and my involvement is as stated for the JHSR.

## 1.4 Time taken to complete the work

We started the grant application process and literature review in January 1999. The Johannesburg Hospital Stroke Register commenced in mid-July 2000, the Tintswalo Hospital Stroke Register in mid-2001 and the stroke prevalence study in mid-2001. The work was completed in 2003 but I only completed the analysis of the data and writing up of this thesis in May 2006 as I did this in addition to a full time clinical neurology and teaching post. Figure 1.1 is a Gantt diagram of the work.

## 1.5 Organisation and style of the thesis

Figure 1.2 shows the organisation of the thesis. The literature review (chapter 2) deals only with the burden and nature of stroke in black Sub-Saharan Africans. Stroke in white and Indian / Asian population groups living in Africa is likely to be similar to that found in studies from outside Africa. However, we have discussed relevant stroke studies including other population groups in South Africa in chapter 5.

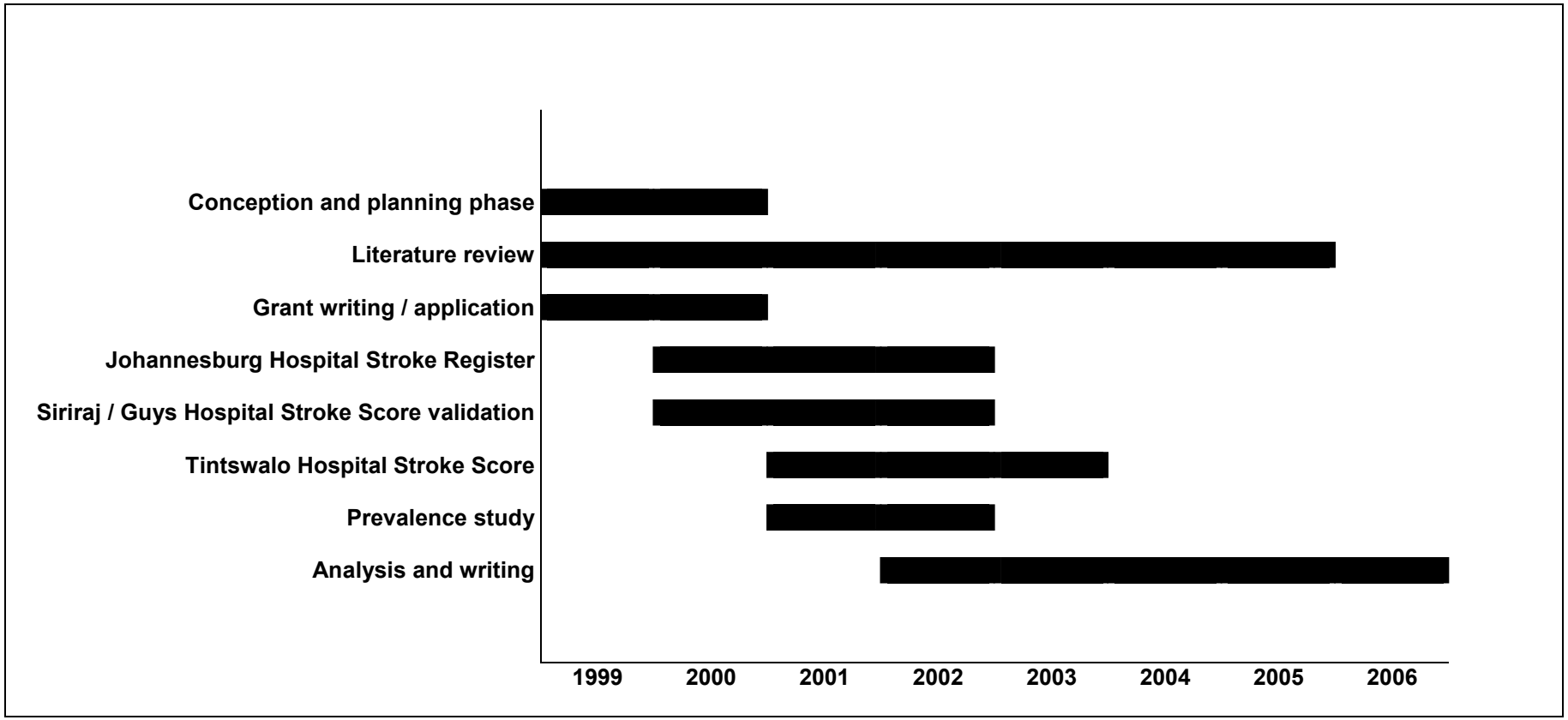



**Figure 1.1 Gantt Diagram showing the time taken for each component of the thesis (note the mid-year detail is not shown)**

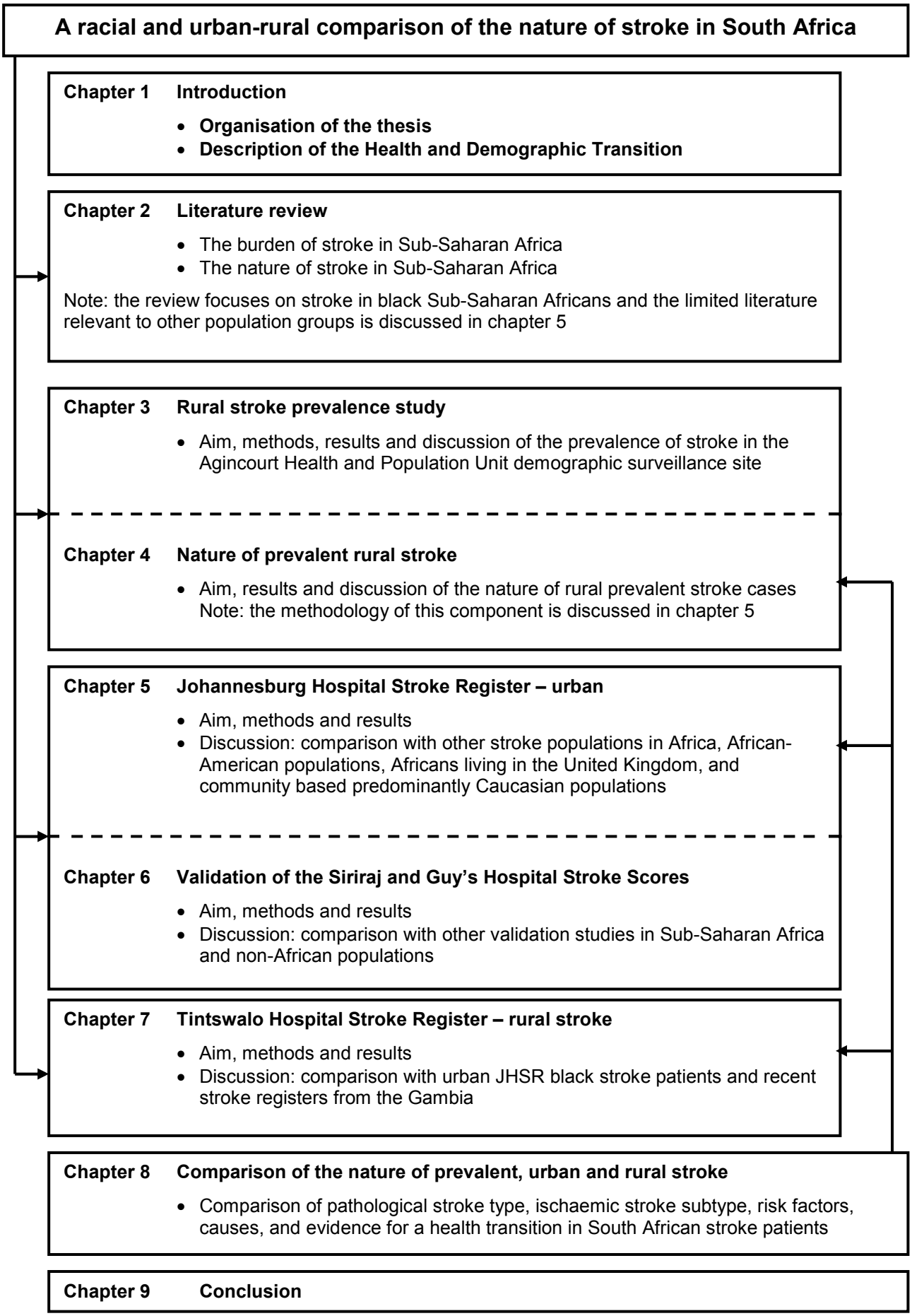



**Figure 1.2 Organisation of the thesis**

### 1.5.1 Terminology regarding population groups

I have used the same terms to describe ethnic or population groups in South Africa as used by Statistics South Africa (Lehohla, 2005): black Africans (abbreviated to blacks), whites, coloureds (mixed ancestry), and Indian / Asians. Instead of referring to ethnic groups we will follow the example of Statistics South Africa and the South African Demographic and Health Survey and refer to population groups (Medical Research Council, 1998; Lehohla, 2005). I assigned population groups based on a stroke patient's (or their carer's) self-identified classification.

### 1.5.2 Style of writing

I have made every effort to use a modern active language style of writing throughout this thesis. Use of the personal pronoun is therefore inevitable. However, much of this work has been collaborative (as discussed in sections 1.2 and 1.3) and use of the pronoun 'I' is not only inappropriate but sounds jarring in my opinion. I have thus rarely used the pronoun 'I' and so from now on have chosen to use 'we' instead, even when quite obviously the thoughts and decisions have been my own.

## 1.6 Stroke and the health and demographic transition

The concept of 'health transition' (also termed epidemiologic transition) provides a framework for understanding changes in the pattern of disease that has taken place in all countries over the last few centuries (Bonita, 2001) (table 1.1). In low-income countries that start with a disease burden dominated by nutritional, perinatal, and infectious diseases, economic development results in transition to a disease burden dominated by non-communicable disease, particularly vascular disease (Omran, 1971; Caldwell, 2001). Four phases of health transition were originally described by Omran (table 1.1). The initial pattern of cardiac and vascular disease changes from one dominated by rheumatic heart disease and cardiomyopathies caused by infection and nutritional deficiencies, to a pattern dominated by hypertension related disease. Then, as life expectancy improves, so atherosclerotic related disease including ischaemic heart disease and peripheral vascular disease emerge. A fifth stage of 'health regression and social upheaval' has been suggested by Yusuf et al to explain the resurgence of conditions seen in the first two stages, in regions where war or social upheaval break down existing social or health structures (Yusuf, Reddy, Ounpuu et al, 2001). This probably represents a separate subgroup rather than part of a natural transition for all populations.

The population within a country or a region may be at different stages of the health transition. An 'early-adopter' community is one that is undergoing rapid socioeconomic development and has an earlier increase in vascular disease than other parts of the population (Yusuf et al., 2001).

**Table 1.1 Stages of the health transition (adapted from Howson *et al.*, 1998; Bonita, 2001; Omran, 1971 and Yusuf, 2001)**

| Stage of Transition | Percentage of all deaths caused by cardiac and vascular disease | Predominant cardiac and vascular diseases | Predominant nature of stroke | Likely regional examples |
|---|---|---|---|---|
| Age of pestilence and famine | 5-10 | Rheumatic heart disease, infections, and nutritional cardiomyopathies | Cardioembolic | Sub-Saharan Africa, rural India, and South America |
| Age of receding pandemics | 10-35 | As above, plus hypertension, hypertensive heart disease; stroke more common than ischaemic heart disease. High rheumatic heart disease to atherosclerotic heart disease ratio | As above, plus haemorrhagic stroke due to hypertension. Stroke occurring at relatively young age. Emergence of atherothrombotic stroke | China |
| Age of degenerative and man-made diseases | 35-55 | Ischaemic heart disease at relatively young ages. Heart disease more common than stroke. Very low rheumatic heart disease to atherosclerotic heart ratio | Proportion of strokes due to haemorrhage decreases and atherothrombotic stroke increases | Urban India, former socialist economies |
| Age of delayed degenerative diseases | <50 | Stroke and ischaemic heart disease at older ages | Atherothrombotic stroke; cardioembolic stroke often secondary to effects of ischaemic heart disease (atrial fibrillation, mural thrombi, cardiomyopathy) | Western Europe, North America, Australia, New Zealand |

Gillum has suggested six stages to explain the evolution of patterns of vascular disease among people of Sub-Saharan African (SSA) origin (Gillum, 1996a). Stage 1 represents the situation in pre-colonial Africa and the few remaining traditional African societies. Stage 2 is found in modern urban Sub-Saharan Africans. Stage 3 occurs in the modern black populations of the West Indies, and is similar to stage 4 which is found in rural black populations in the United States. Stage 5 characterises poor, inner city black Americans and stage 6 represents affluent suburban or urban black Americans. Therefore, there is a steady increase in acculturation, urbanisation and affluence from stage 1 to 6. Vascular risk factors increase (saturated-fat intake, salt intake and cigarette smoking) from stage 1 to stage 5, with an associated increase initially in hypertensive vascular disease and from stage 3 onwards in atherosclerotic disease. In stage 6, however, there is a reduction in vascular risk factors, a marked reduction in hypertensive vascular disease and a less marked reduction in atherosclerotic disease.

Stroke **burden** increases during health transition and is initially much more common than heart disease (Reed, 1990). Stroke also changes in **nature** (type and cause) as the population undergoes transition. Initially when hypertension is the major vascular risk factor, haemorrhagic stroke is common. Then as cholesterol levels increase, so ischaemic stroke due to atherothrombosis increases (Howson et al., 1998). Presumably, the early phase of the transition is also accompanied by small vessel ischaemic stroke caused by hypertension, cardioembolic stroke caused by rheumatic heart disease, nutritional cardiomyopathies, and perhaps by alcohol and idiopathic dilated cardiomyopathy. Hypertensive heart disease may add to ischaemic stroke by causing atrial

fibrillation in a small number of cases. If one accepts the entity of an end-stage dilated cardiomyopathy of hypertensive heart disease then this too may be an embolic source (Lip, Felmeden, Li-Saw-Hee et al, 2000). Unfortunately, the effect of the early stage of the transition on stroke was never well documented in the current high-income countries, and unless we document it accurately in populations currently undergoing transition much of the effect of the transition on vascular disease will remain mere conjecture.

The changing structure of populations, or demographic transition, will also increase the burden of stroke (Walker, Unwin, & Alberti, 1998). Stroke predominantly affects an older population and, because it is estimated that in low and middle-income countries the number of adults aged 30-69 from 1990 to 2020 will almost double, stroke incidence should increase dramatically for that reason alone (Murray & Lopez, 1996; Smith & Mensah, 2003).

We will refer to the framework of the health transition frequently in the following sections, and relate our findings to this framework.

# CHAPTER 2 LITERATURE REVIEW – A SYSTEMATIC REVIEW OF STROKE IN SUB-SAHARAN AFRICA

## 2.0 Introduction

There are no systematic reviews of the existing knowledge of stroke in Sub-Saharan Africa (SSA). My aim was to systematically gather all the publications that relate to stroke in SSA and to assess what is known about the burden (mortality, prevalence, incidence and case-fatality) and nature (pathological types, sub-types, causes and risk factors) of stroke in the region.

## 2.1 Critical appraisal of the literature

We searched Medline from 1966 to December 2004 and Embase from 1980 to December 2004, using detailed search terms for stroke or related disease combined with terms relevant to SSA. We used forty-two terms to describe symptoms and signs of stroke, stroke types or subtypes, related cerebrovascular conditions such as migraine, as well as 'exploding' specific terms such as 'cerebrovascular disease' and 'stroke' (Appendix A). We then combined this search with the articles retrieved from a second search designed to find all publications of any type related to Africa. This second search included 91 terms which might have been used in articles relevant to SSA and included terms for race (including terms that come from a previous political era), regions of Africa e.g. central Africa, countries in SSA (including former names of countries), with

particular but not exclusive use of MeSH terms used by Medline and Embase (Appendix A).

We obtained articles from before 1966 and other relevant published articles by perusing reference lists from articles already obtained, from theses, discussions with colleagues working in Africa, and conference proceedings. Finally, the two journals with the highest yield were hand searched (*East African Medical Journal* and *South African Medical Journal)* for relevant publications during the last ten years that might have been missed by the other methods.

This search yielded 3238 publications. We screened all abstracts, and read in full all articles that might contain relevant information. All articles and published abstracts in all languages, relevant to the burden and nature of stroke in SSA were included. In an attempt to obtain all useful information, we included publications whether they included original data or not.

Conducting epidemiological studies in SSA is fraught with practical difficulties and so, while we considered it important to evaluate the available studies against accepted quality criteria, we also considered it important to include an accurate representation of the published literature on the subject. We highlighted the strengths and weaknesses of publications in each section, however, and in the section on the nature and risk factors for stroke, we detailed the reasons for including and excluding studies. Thus we combined a thorough search of the literature with critical evaluation of the literature (Stroup, Berlin, Morton et al, 2000)

with a narrative review (Slavin, 1995), and highlighted the quality of the evidence throughout.

This resulted in 448 references germane to the scope of this review. We then excluded studies dealing with stroke in Africans living outside Africa unless they included comparisons with a population living in Africa, as well as publications dealing with stroke in non-African populations living in SSA. We also excluded studies that did not provide separate data for Black Africans and Africans from other populations. Finally, we excluded any published data from this thesis, which was already available at the time of the final literature search update. We specified our selection criteria in each section of the review when relevant.

**We have presented our findings using the following scheme:**

Section 2.2 The burden of stroke in Sub-Saharan Africa – mortality, incidence, case fatality, and prevalence

Section 2.3 The nature of stroke in Sub-Saharan Africa – pathological stroke type, subtype, causes (including autopsy studies), and risk factors

## 2.2 What is the burden of stroke in Sub-Saharan Africa?

The **burden** of stroke in a community **includes stroke mortality, incidence, prevalence, and long-term outcome of stroke survivors** (Warlow, 1998). Although it is an important part of the burden of stroke on the individual and community, the estimation of the economic cost of stroke is beyond the scope of this review. We will now discuss each component making up the burden of stroke in depth.

### 2.2.1 Mortality

This section includes mortality data derived from vital registration, verbal autopsy studies and studies that have focused on stroke mortality in SSA populations.

#### 2.2.1.1 Vital registration based data

In high-income countries death certificate data provide easily available, but not very accurate, information on stroke mortality (Warlow, 1998). The Global Burden of Disease study used available vital registration data from SSA and other regions to estimate mortality in 1990. However, vital registration data are unreliable and seldom available in SSA (Walker, McLarty, Kitange et al, 2000a). Indeed, Murray and Lopez found SSA to be the region with the lowest coverage of vital registration in the world (1.1%). As a result the Global Burden of Disease findings for southern SSA, and to a lesser extent northern SSA, were based on modelling of vital registration data from South Africa collected during the apartheid years (Murray et

al., 1997). However, during the apartheid era vital registration for Africans was particularly unreliable (Wyndham, 1982; Botha & Bradshaw, 1985; Disler, Epstein, Buchanan-Lee et al, 1987). Despite these difficulties, and so rather surprisingly, the global Burden of Disease findings are supported by demographic surveillance sites (population-monitoring laboratories) throughout Africa (Murray et al., 1997).

In 1999 the WHO estimated, using similar methodology to the Global Burden of Disease study and vital registration data from member states, that there were about 5 million stroke deaths (5% of all deaths) in Africa compared to almost 8 million (14% of all deaths) in Europe. Stroke caused an estimated 45% of all vascular deaths in Africa compared to 25% of vascular deaths in high-income Europe (The WHO, 1999) – in other words Africa was at an earlier stage of health transition.

#### 2.2.1.2 Verbal autopsy data

In many low-income regions where there is a void of health information and vital registration for the population, demographic and health surveillance sites have been established (INDEPTH network, 2002). Cause of death data on a sample of the population is derived from careful recording of all deaths during population census rounds and from verbal autopsies. Verbal autopsies consist of a questionnaire completed during an interview of a close caregiver who is able to describe - retrospectively - what happened during the hours, days or months preceding a death. A most likely cause of death is inferred from the sequence and

combination of systems and events, either by physicians or by computer algorithms (INDEPTH network, 2002).

Two sites in SSA have published information on stroke deaths specifically. The Agincourt Health and Population Unit, based in Bohlabelo in the rural north-east of South Africa, found stroke caused 6% of all deaths in a population of 63 000 between 1992 and 1995. Stroke was the second most common cause of death in the 35 – 54 year age group and over 75-year age group, and the most common cause in the 55 – 74 year age group (Kahn & Tollman, 1999a). The overall crude stroke mortality was 127 per 100 000 (95% CI, 93 to 160).

In a much larger verbal autopsy study in Tanzania, the Adult Morbidity and Mortality Project found stroke caused 5.5% of *adult* deaths in three regions (urban, fairly prosperous rural and rural) with a total population of 307 820 (Walker et al., 2000a). Age-adjusted mortality for individuals over the age of 15 in the prosperous rural and urban regions in Tanzania were higher than United Kingdom figures. This discrepancy was most striking in younger age groups (15-64 years) where rates age-adjusted to the Segi world population were three to ten times greater in Tanzania than in England and Wales, but the numbers were so small that any difference could be due to chance (Walker et al., 2000a).

Figures 2.1 and 2.2 show age-specific stroke mortality in Agincourt, South Africa, the three regions of Tanzania mentioned above, for Tanzania and South Africa combined, and for England and Wales in the early 1990s.

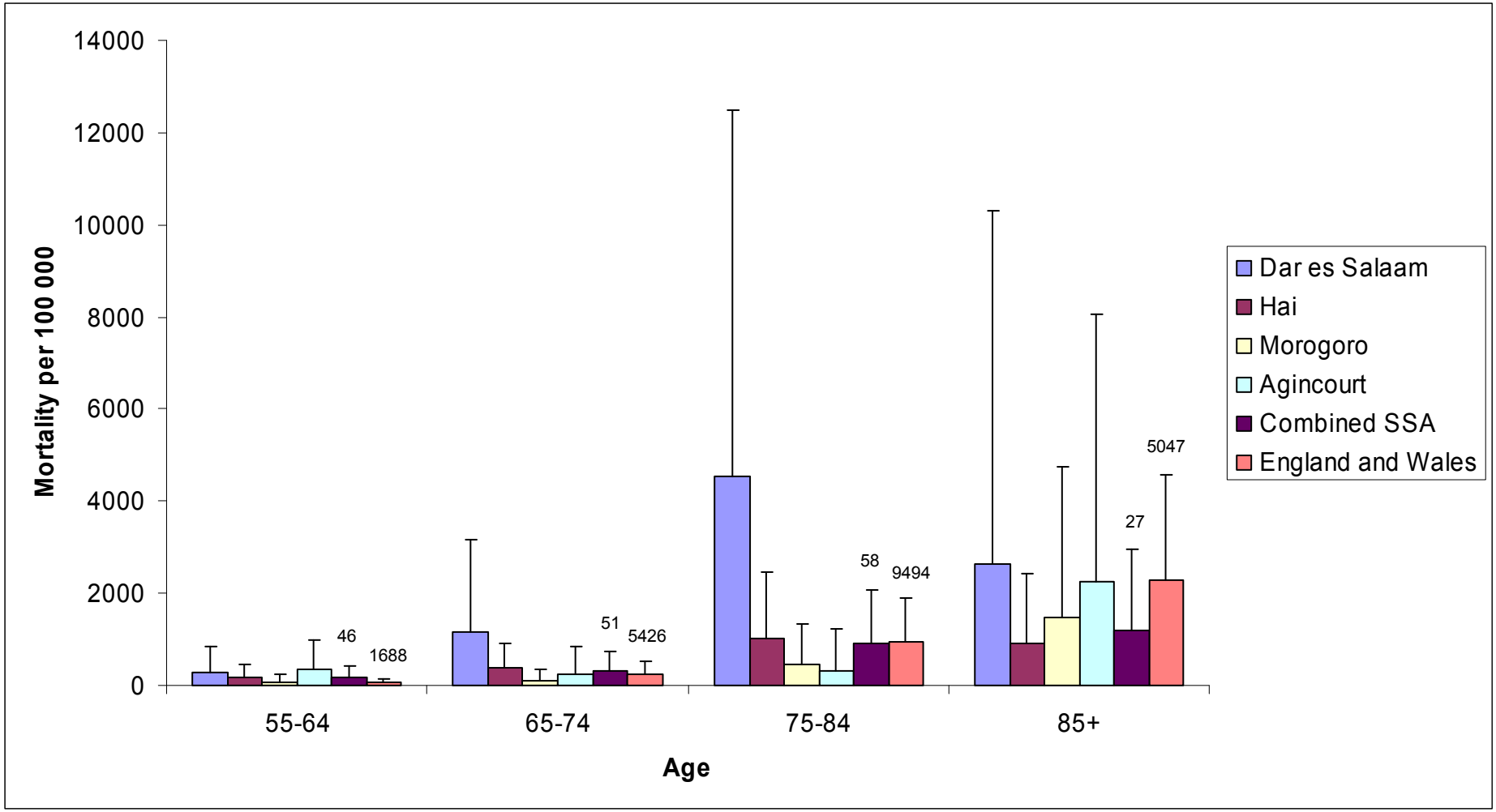



Figure 2.1 Comparison of age-specific stroke mortality in males over 55 years of age in three regions of Tanzania (Dar es Salaam – urban, Hai – prosperous rural, and Morogoro – rural), in Agincourt South Africa, the SSA regions combined and England and Wales
The numbers above the upper 95% confidence interval indicate the total numbers of strokes for SSA combined and England and Wales in each age group; SSA - Sub-Saharan Africa

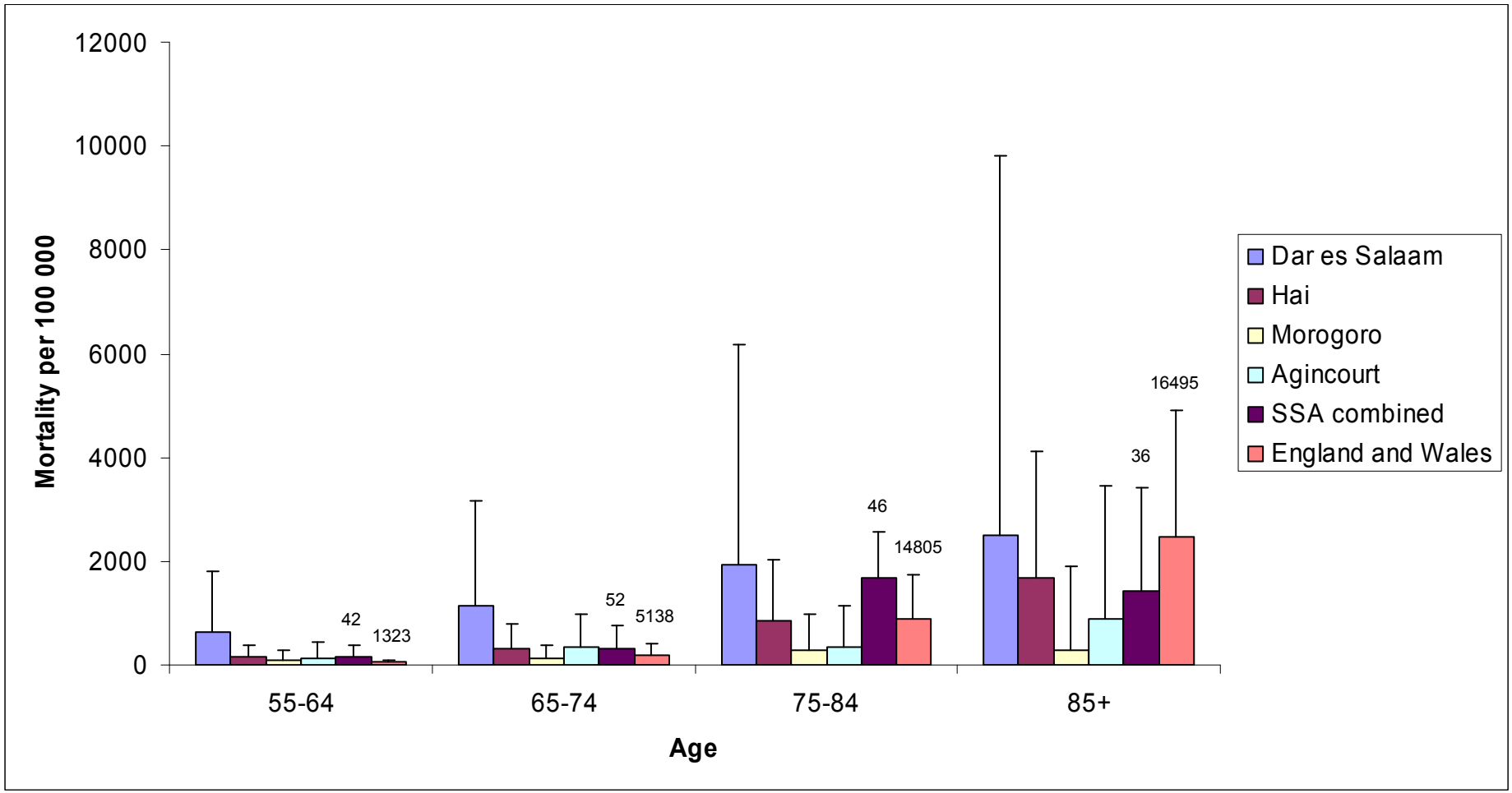



Figure 2.2 Comparison of age-specific stroke mortality in females over 55 years of age in three regions of Tanzania (Dar es Salaam – urban, Hai – prosperous rural, and Morogoro – rural), in Agincourt South Africa, the SSA regions combined and England and Wales
The numbers above the upper 95% confidence interval indicate the total numbers of strokes for SSA combined and England and Wales in each age group; SSA - Sub-Saharan Africa

The figures demonstrate that age-specific mortality data from SSA are based on small numbers with associated large confidence intervals. Age-specific mortality in SSA may be as high as in England and Wales, and perhaps higher in younger age groups, but larger studies are clearly needed.

While the sensitivity and specificity for the Tanzanian study verbal autopsy was 100% and for Agincourt, South Africa, 87% and 97% respectively, these figures are based on small numbers (twelve strokes in the case of the Tanzanian study) and doubt has been cast on the accuracy of verbal autopsy data (Snow, Armstrong, Forster et al, 1992). In both studies the gold standard was a hospital diagnosis of stroke. This did not include brain imaging for the South African study. It is not clear whether the assessment included brain imaging for the Tanzanian study. But despite their shortcomings, verbal autopsies provide the only detailed mortality data for most of the SSA region and stroke is likely to be one of the conditions most accurately diagnosed by verbal autopsy.

#### 2.2.1.3 Other studies

Between 1975 and 1980 a five-year follow-up study of 4075 people aged 15 – 64 years in Accra, Ghana, found stroke caused about 8% of all deaths in that age group (Chukwumeka, Pobee, Larbi et al, 1982). This study probably underestimated stroke deaths because an undetermined number of subjects died outside the area. Cause of death was diagnosed using death certificates, health nurse inquiry and lay recorders. It is not clear whether the authors had validated their method of diagnosing stroke.

We excluded a review of death certificates in Sierra Leone between 1983 and 1992 because only stroke caused by hypertension was included (Lisk & McEwen, 1996). Published stroke mortality for Harare, Zimbabwe (Razum, 1996) and South African MRC mortality figures (Bradshaw, Schneider, Dorrington et al, 2002) have not been included as the figures were not classified by ethnicity. For many socio-political reasons there are likely to be large differences in disease rates between whites and blacks living in Zimbabwe and South Africa.

We also excluded studies that estimated stroke mortality on hospital-based figures because it is highly unlikely that these are representative of the community. Even in developed regions a large proportion of stroke patients are not admitted to hospital (Dennis, Bamford, & Warlow, 1994; Sudlow & Warlow, 1996). In SSA there are many factors that may increase this proportion including: limited access to healthcare, transport difficulties, non-biomedical interpretation of symptoms of stroke, and use of traditional and alternative healers (Hundt, Stuttaford, & Ngoma, 2004).

#### 2.2.1.4. Is stroke mortality changing in Sub-Saharan Africa?

Older studies based on vital registration data in South Africa suggest that stroke mortality was not always as high as in developed countries. The age-standardised cerebrovascular disease mortality for 45-64 year old Africans in Johannesburg between 1953 and 1956 was 108 per 100 000, *similar* to both white South Africans (128 per 100 000) and England and Wales (111 per 100 000) (Walker & Grusin,

1959; Walker, 1963). By 1970, however, age-standardised mortality for Blacks between 15 and 64 years of age (males: 65 per 100 000, females 92 per 100 000) was much higher than for whites in South Africa (males: 41 per 100 000, females: 43 per 100 000) and in England and Wales (Wyndham, 1979; Wyndham, 1982). It is tempting to conclude that these figures demonstrate a progression along the health transition, but vital registration and census figures for Blacks living in South Africa were highly inaccurate (Botha et al., 1985). As long as accurate vital registration data remains unavailable for most of SSA, evidence of any change in stroke mortality in SSA is only likely to come from demographic surveillance sites using verbal autopsy data, although the inevitably small numbers of deaths in such areas will render any estimates rather imprecise.

Although higher *age-adjusted* mortality is seen in SSA compared to developed regions, overall the absolute numbers of deaths due to stroke remain low. The population structure in SSA typically has far more young than elderly people with about 44% of the population under the age of 15-years and only about 3-6% over the age of 65-years (Kahn et al., 1999a; INDEPTH network, 2002). So total numbers of stroke and deaths due to stroke are small at present, but are likely to increase as the population undergoes economic development and the number of elderly increase (Omran, 1971; Walker et al., 1998; Warlow, 1998; Unwin, 2001; Caldwell, 2001).

Of course, a high mortality is only one component reflecting the burden of disease and it may be caused by either a high *incidence* of stroke or a high *case fatality* or both (Warlow, 1998).

### 2.2.2 Stroke incidence

#### 2.2.2.1 Community-based incidence

Stroke incidence, based on representative community samples, and with rigorous case ascertainment and accurate diagnosis, provides far more information about stroke burden than either mortality or prevalence (Warlow, 1998), but such studies require considerable resources and rigorous methods (Feigin & Carter, 2004). Standardised criteria for the 'ideal' stroke incidence study have been established (Sudlow et al., 1996) and these have recently been updated (Feigin & Hoorn, 2004) (table 2.1). Against these criteria there are no even nearly ideal stroke incidence studies available for SSA (Feigin, Lawes, Bennett et al, 2003b).

Although their study does not fulfil the criteria, there has been one serious attempt at a community-based incidence study from SSA. Osuntokun and his colleagues (Osuntokun, Bademosi, Akinkugbe et al, 1979) established and ran a stroke registry in Ibadan, Nigeria for two years (1973-1975) as part of the international multicentric programme of the Cardiovascular Diseases Unit of the WHO. They attempted to cover the whole of Ibadan (803 098 people). They based population figures on the 1963 census projected for 1973 using a 2.5% annual growth rate. They ascertained stroke cases by notification from hospitals, general practitioners, private nursing homes, coroner's offices and the office of the Medical Officer of Health for the city. First-ever-in-a-lifetime and recurrent strokes were included. One nurse visited these various institutions once a week to find the

**Table 2.1 Criteria for an ideal study of stroke incidence, from (Sudlow and Warlow, 1996), (Feigin and Hoorn, 2004) and (Feigin and Carter, 2004)**

| |
|---|
| **Standard definitions** |
| WHO definition of stroke |
| Availability of data on first-ever-in-a-lifetime strokes |
| At least 80% verification of stroke type by CT or MRI brain scan |
| Classification of ischaemic stroke subtype* |
| Availability of data on recurrent strokes* |
| **Standard methods** |
| Complete, community-based ascertainment, based on multiple overlapping sources |
| Prospective study design, ideally with 'hot pursuit' of cases |
| Large, well-defined, stable population allowing at least 100 000 person-years of observation |
| Reliable method for estimating the denominator (census data ≤ 5 years old) |
| Follow up of patients' vital status for at least 1 month |
| Ascertainment of patients with TIA, recurrent strokes and those referred for brain, carotid, or cerebral vascular imaging* |
| Direct assessment of under-ascertainment by checking of alternative sources e.g. general practitioner databases, hospital admissions or referrals for vascular imaging or interventions* |
| **Standard data presentation** |
| Whole years of data |
| Not > 5 years of data averaged together |
| Men and women presented separately |
| No upper age limit for the population studied |
| Standard mid-decade age bands used in publications |
| Presentation of 95% confidence intervals around incidence rates |
| Unpublished 5-year age bands available for comparison with other studies* |

Criteria marked (*) are considered supplementary rather than 'core' criteria (Feigin and Carter, 2004)

cases, who were then invited to return to a clinic for evaluation by a neurologist. In situations where the cases were not assessed by the neurologist a diagnosis was based on case histories and results of available investigations. Computer tomography (CT) scanning was not available in those days.

Over the two-year period 318 stroke patients were registered, resulting in a very low crude incidence of 25 per 100 000 for males and 13 per 100 000 for females (total 20 per 100 000). It is likely, however, that this figure is an underestimate because of difficulties with case ascertainment resulting from the very large, and likely mobile, population covered by a very small study staff.

#### 2.2.2.2. Hospital-based 'incidence'

The vast majority of the studies available on stroke in SSA are hospital-based case series. Most often these studies document the proportion of patients admitted to medical and neurology services that have had strokes. While it is very difficult to conclude anything from individual case series with respect to stroke burden in the community (Feigin et al., 2004), some institutions have monitored their stroke admissions over time and shown a steady increase. In Tanzania statistics from the Ministry of Health (Haddock, 1965) indicate that stroke admissions increased from 23 per 100 000 in 1935 to 86 per 100 000 in 1962. Nyame and his colleagues compared stroke admissions to Korle Bu Teaching Hospital in Accra, Ghana, during three periods: 1960-1968, 1976-1983 and 1990-1993 (Nyame, Bonsu-Bruce, Amoah et al, 1994) and found that the number of strokes admitted per year increased from about 50 in 1960 to 622 in 1993. The percentage of total adult

medical admissions due to stroke increasing from less than 2% in 1960 to about 12% in 1993. This may have been the result of population aging, a change in admission policy or criteria for diagnosing stroke, or a real increase in stroke incidence.

Two hospital-based studies, from Southern Africa (Rosman, 1986; Matenga, 1997), both urban, have attempted to estimate stroke incidence. Matenga ascertained cases for a year (1991) from all four general hospitals in Harare, Zimbabwe, the capital city with a population of 887 768 black Zimbabweans. The post-mortem register was also inspected monthly as were hospital discharge summaries. Stroke was defined according to the WHO definition and only first-ever-in-a-lifetime strokes were included. The attending physician diagnosed stroke and in difficult cases reviewed the diagnosis with the investigator. None of the cases had CT scans of the brain. The crude stroke incidence was 31 (95% CI, 27 to 34) per 100 000 per year. Standardised to the world population the incidence was 68 per 100 000.

Rosman included all strokes (first-ever-in-a-lifetime and recurrent), excluding subarachnoid haemorrhage, admitted to Kalafong Hospital in Atteridgeville and suburban Pretoria, South Africa. Seventy-nine percent of all stroke cases had CT scans. The crude stroke incidence for over 20 year olds was 101 per 100 000 per year.

The different methodology used in the South African and Zimbabwean hospital-based studies, and in community-based studies from outside SSA, precludes

accurate comparison of incidence. Despite this, it is interesting to note that age-specific stroke incidence is much higher in younger age groups in the SSA studies compared to the United Kingdom Oxford Vascular Study (Rothwell, Coull, Giles et al, 2004), but lower than figures for African-Americans from the North of Manhattan Stroke Study (Sacco, Boden-Albala, Gan et al, 1998) (table 2.2). Furthermore, stroke admissions to hospital are clearly rising in SSA although this could be due to changes in attitudes towards allopathic medicine, easier access to medical care, or ageing of the population, as much as to increasing incidence. While *total* stroke incidence is lower in SSA than in other parts of the world this may simply be because the population is so much younger.

The available hospital-based SSA studies almost certainly under estimate stroke incidence. In order to accurately determine stroke incidence in SSA now and in the future, incidence studies fulfilling as many of the ideal criteria as possible (table 2.1) are needed.

**Table 2.2 Comparison of age and sex specific annual stroke incidence per 100 000 population (rates are not standardised). NB the South African and Zimbabwean studies are hospital-based**

| | **Males (rate)** | | | **Females (rate)** | | | **Total** | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Age (years) | South Africa (Rosman, 1986) | Zimbabwe (Matenga, 1997) | OXVASC (Rothwell *et al.*, 2004) | South Africa (Rosman, 1986) | Zimbabwe (Matenga, 1997) | OXVASC (Rothwell *et al.*, 2004) | South Africa (Rosman, 1986) | Zimbabwe (Matenga, 1997) | NMSS (Sacco *et al.*, 1998) | OXVASC (Rothwell *et al.*, 2004) |
| 20-24 | 8 | - | - | - | - | - | - | - | - | - |
| 25-34 | 9 | 7 | - | 10 | 13 | - | - | 10 | 0 | - |
| 35-44 | 37 | 23 | 27 | 43 | 66 | 16 | - | 41 | 54 | 22 |
| 45-54 | 107 | 126 | 73 | 109 | 102 | 54 | - | 118 | 184 | 64 |
| 55-64 | 249 | 174 | 177 | 239 | 237 | 175 | 280 | 194 | 366 | 176 |
| 65-74 | 643 | 402 | 646 | 583 | 563 | 408 | 837 | 469 | 636 | 526 |
| >75 | 445 | 619 | - | 611 | 957 | - | 726 | 788 | - | - |
| **Total** | **84** | **30** | **134** | **90** | **32** | **156** | **101** | **31** | **223** | **145** |

OXVASC – Oxford Vascular Study; NMSS – North of Manhattan Stroke Study

### 2.2.3 Case fatality

Because of the heterogeneity of stroke type and severity, and the likelihood that many stroke patients are not admitted to hospital, one ideally needs to know case fatality from community-based studies. We excluded all *retrospective* hospital based studies of case fatality (Dada, Johnson, Araba et al, 1969; Abraham & Abdulkadir, 1981; Bahemuka, 1985; Bwala, 1989; Ndiaye, 1989; Lisk, 1993; Nyame et al., 1994; M'Buyamba-Kabangu, Longo-Mbenza, Tambwe et al, 1995) because these are likely to be hampered by missing and variably recorded data as well as hospital admission bias. We also excluded studies that did not provide the time after stroke when case fatality was assessed (Osuntokun, Odeku, & Adeloye, 1969; Abraham et al., 1981; Abebe & Haimanot, 1990; Kwasa & Lore, 1990; Lisk, 1993; Nyame et al., 1994; Longo-Mbenza, Phanzu-Mbete, M'Buyamba-Kabangu et al, 1999; Longo-Mbenza, Tonduangu, Muyeno et al, 2000; Sokrab, Sid-Ahmed, & Idris, 2002).

The only community-based study, the Ibadan stroke register (Osuntokun et al., 1979), found the case fatality at three weeks to be 35%, higher for cerebral haemorrhage and subarachnoid haemorrhage, 61% and 62% respectively, but stroke types, other than SAH, must have been diagnosed unreliably without CT scanning. Furthermore, the investigators had great difficultly with follow up and at three months only 76 of 318 patients could be traced. As a result, this case fatality figure is likely to be unreliable.

Early stroke (haemorrhagic and ischaemic) case fatality i.e. up to about one month, derived from *prospective* hospital case series, is about 33% (Rosman, 1986; Joubert, 1991; Matenga, 1997). Rosman found a higher case fatality in patients with cerebral haemorrhage (58%) than cerebral infarction (22%) but patients who died before they had a CT scan were assumed to have had an intracerebral haemorrhage which would have inflated that figure (Rosman, 1986).

Only one study provided long-term follow up over four years to determine case-fatality, time to death and likely cause of death. This study from the Gambia (Walker, Rolfe, Kelly et al, 2003) included all patients admitted to hospital with a diagnosis of stroke or who had a stroke as an inpatient over a one-year period. Both first-ever-in-a-lifetime and recurrent strokes were included and patients with subarachnoid haemorrhage were excluded. None of the patients had a CT scan. Patients were followed up at home or hospital at one and six months and again between three and four years after their stroke. Case fatality in the 106 cases at one and six months was 27% and 44% respectively, and 75% of patients had died by the final follow up. At the end of follow up cause of death in all patients was the initial stroke in 61%, further stroke in 7%, infection in 12% and another vascular cause (hypertensive encephalopathy) in only 1 patient. None of the patients had angina or myocardial infarction and only one patient died of a cardiac cause, a cardiomyopathy. Remarkably only four cases were lost to follow up.

While this study provides the only available data on long-term follow-up of stroke patients, it is hospital-based and CT scanning was not available. As such, severe and mild strokes may have been excluded and it is not possible to differentiate

case fatality between haemorrhagic and ischaemic strokes. It does, however, provide the best data available of stroke case fatality and cause of death in SSA and suggests that in the Gambia at least one month case fatality is not much higher (27%) than in comparable stroke studies from the rest of the world (23%) (Feigin et al., 2003b). But the risk of a cardiac death following stroke was much lower than is found in high-income regions of the world (Dennis, Burn, Sandercock et al, 1993).

Detailed stroke type specific (infarct versus haemorrhage) community based case fatality data are not available for SSA. Considering the importance of this figure in estimating stroke burden and quality of stroke care it is essential that studies and funders address this issue in the future.

### 2.2.4 Stroke prevalence

Estimating the prevalence of stroke survivors in the community is complicated by the difficulty in making a retrospective yet accurate diagnosis of stroke and stroke type months or years after the event. It is also biased by under-representation of fatal cases, and even by disabling stroke which can be difficult to assess because of overlapping disability caused by other conditions such as osteoarthritis and dementia. Prevalence, which depends on incidence and case fatality, is therefore better estimated from incidence studies of first-ever-in-a-lifetime stroke and survival (Warlow, 1998). But in SSA high quality incidence studies are unavailable and anyway difficult to perform, so stroke prevalence studies in demographic surveillance sites which provide an accurate denominator have arguably provided the most accurate measures of stroke burden in recent years despite the limitations.

In developed countries most studies of stroke prevalence have used a screening postal questionnaire for case finding (Aho, Reunanen, Aromaa et al, 1986; Mahony, Dobson, Rodgers et al, 1995; Geddes, Fear, Tennant et al, 1996). Poor or non-existent postal services in SSA make this approach unfeasible and, as in most low-income countries, door-to-door surveys have mainly been used (Walker, McLarty, Masuki et al, 2000b) .

In 1982 and 1987 Osuntokun and colleagues published the results of three studies designed to establish the prevalence of neurological disease in rural Nigeria using door-to-door surveys performed by nurses, primary health care attendants and

medical students. In Aiyete, a community of about 2000, 903 individuals were screened to pilot a research protocol for measuring the prevalence of neurological disease in the community. Four people were found to have had a stroke (Osuntokun, Schoenberg, & Nottidge, 1982). In Udo, 2925 people were screened and two found to have had a stroke (Longe & Osuntokun, 1989). The largest study - in Igbo-Ora - took place in 1982. Teams drawn from teacher and non-doctor primary health care workers were trained for a month to administer the screening questionnaire for neurological disorders piloted in Aiyete and to make a simple neurological examination in everyone over the age of 7 years. Those who screened positive for neurological disease were examined by an adult or paediatric neurologist or neurosurgeon. Stroke was diagnosed in 11 of 18 954 people screened, resulting in a crude prevalence of 58 per 100 000 (Osuntokun, Adeuja, Schoenberg et al, 1987).

Although these studies were a brave attempt to assess the prevalence of stroke and neurological disease under difficult circumstances, the populations screened were far too small to establish stroke prevalence accurately, particularly as typically 44% of the population in SSA are under the age of 15 years old and stroke mainly affects older age groups. Furthermore, very little information was given in the publications about the criteria used to diagnose stroke. The accuracy of the stroke prevalence found is therefore questionable.

Between 1986 and 1988 a door-to-door survey was conducted on a random sample of 60 820 rural Ethiopians of all ages. Lay health workers who had been trained by neurologists, conducted a census and identified cases with symptoms

and signs of neurological disorders, using a previously piloted questionnaire (Tekle-Haimanot, Abebe, Gebre-Mariam et al, 1990). Neurologists regularly visited the villages to examine people identified and validate diagnoses. Stroke was found in 9 people ranging in age from 28 to 85 years (crude prevalence: 15 per 100 000). The authors suggested that the low prevalence was the result of a high case fatality, but case fatality figures were not in fact available. In view of their seemingly sound methodology under difficult circumstances, the low prevalence may also reflect a low stroke incidence in rural Ethiopia in the mid-1980s, or simply that mild strokes that had recovered were not detected.

The largest study, which was of the prevalence of disabling hemiplegic stroke, in SSA was conducted in 1994 in the rural Hai district of Tanzania (population 148 135) (Walker et al., 2000b). This is one of the demographic surveillance system (DSS) project areas of the Adult Morbidity and Mortality Project, one of the members of INDEPTH (International Network for the continuous Demographic Evaluation of Populations and Their Health) (INDEPTH network, 2002), where a yearly census is carried out. In each village a specially trained ‘enumerator’ is responsible for data collection. During the 1994 census three questions were included to try to identify anyone who may have been disabled by a stroke viz.: ‘Is there anyone in the household with a history of stroke?’; ‘Is there anyone in the household with weakness down one side of the body?’; ‘Does anyone in the household require assistance with: dressing, eating or toileting?’ Everyone with one or more positive responses was seen by a physician with extensive experience of stroke who confirmed the diagnosis based on a detailed history and examination according to the WHO definition of stroke. 108 people were identified

as fitting the criteria for the study. This provided an age standardised (to the Segi World population) prevalence of disability resulting from stroke of 154 per 100 000 in males and 114 per 100 000 in females over the age of 15 years (Walker et al., 2000b). This study has the advantage of an accurate denominator and careful assessment of people who screened positive for stroke. But the accuracy of the census screening questions was not assessed and verification of this method of establishing stroke prevalence in SSA would be difficult and unreliable (Walker et al., 2000b). The investigators also assessed the prevalence of stroke survivors 'who required help with at least one activity of daily living' for comparison with findings of a similar assessment performed in a study of stroke prevalence in Auckland, New Zealand (Bonita, Solomon, & Broad, 1997). This is an important measure because these people probably place the greatest burden on the family and health service.

The prevalence of disabling hemiplegic stroke in Tanzania was about six times lower than that found in New Zealand, and the prevalence of stroke survivors 'who required help with at least one activity of daily living' about half. This may be because of a lower incidence of stroke or higher case fatality in Tanzania, or because of methodological differences. The prevalence of stroke in Auckland was modelled on the results of two community based incidence studies and therefore far more likely accounted for people with very mild strokes and those who recovered completely from their stroke. Only population-based incidence studies with long term follow up and assessment of case fatality will clarify these questions in SSA. **(We discuss these two studies further in Chapter 3 following the results of the prevalence of stroke in rural South Africa).**

## 2.3 The nature of stroke in Sub-Saharan Africa

### 2.3.1 Stroke types and subtypes

#### 2.3.1.1 Methodological problems associated with stroke series in SSA

Stroke is a heterogeneous condition consisting of three pathological types, ischaemic stroke, cerebral haemorrhage (CH) and subarachnoid haemorrhage (SAH). Ischaemic stroke is further divided into subtypes such as intracranial small vessel disease, large-vessel atherosclerotic disease, and embolism from the heart (Warlow, 1998). Haemorrhagic stroke too can be subtyped, but with more difficulty because so often more than one 'cause' appears to be acting in any one individual (for example, hypertension and presumed amyloid angiopathy). Pathological stroke types and ischaemic subtypes differ in terms of cause, outcome and appropriate treatment policies (Warlow, Dennis, van Gijn et al, 2001). The nature (pathological stroke type, ischaemic and haemorrhagic stroke subtype, risk factors, and causes) of stroke is also likely to change as SSA undergoes health transition – from haemorrhagic stroke to ischaemic stroke caused by atherosclerosis in large and medium sized arteries (table 1.1) (Gillum, 1996a; Howson et al., 1998).

Theoretically at least, the cause of embolic stroke is also likely to change as the population undergoes health transition. Rheumatic heart disease and the dilated form of cardiomyopathy which results from hypertension as well as nutritional

deficiency are the predominant causes of heart failure in populations in early transition. Later as ischaemic heart disease and extracranial atherosclerosis of large vessels develop, so these together with atrial fibrillation are likely to become the major sources of emboli (Howson et al., 1998). While this theory makes sense, there is little epidemiological evidence in the literature to support it; probably because most developed regions passed through the transition before documentation of change was possible.

Ideally studies that distinguish between stroke types should have a high neuroimaging rate and patients should be scanned within days of symptom onset to reliably distinguish between cerebral haemorrhage and infarction if CT rather than MR brain scans are used (Sudlow et al., 1996). Clinical scoring systems such as the Guy's hospital or Siriraj scores are sometimes used to complement a high but incomplete CT scan rate (Sudlow et al., 1996). These scores have not been validated by large prospective studies in SSA. **(Chapter 6 covers a literature review of clinical scoring systems in general and the literature pertaining to SSA specifically).** Subarachnoid haemorrhage is easier to differentiate because of the characteristic clinical syndrome backed up with blood in the cerebrospinal fluid, if CT is not available.

The only community-based stroke study, the Ibadan stroke registry (Osuntokun et al., 1979) was undertaken before CT scanning was available. This lack of community-based studies limits the usefulness of the data on the type and subtype of stroke from SSA, so hospital-based studies are more likely to include severe strokes and cerebral haemorrhages which have a more dramatic clinical

presentation than mild ischaemic strokes (Bamford, Sandercock, Warlow et al, 1986; Dennis et al., 1994).

Many retrospective and prospective hospital-based case series from SSA have documented stroke types and subtypes, but few have used neuroimaging. Retrospective studies while sometimes adding interesting anecdotal information may add to the bias of hospital-based series. Moreover, poor documentation often results in insufficient detail on stroke diagnosis, type and subtype, particularly in patients who die soon after admission (Walker & Ogungbo, 2003). We therefore excluded retrospective series and hospital-based series that did not use brain imaging when evaluating stroke types and subtypes.

Table 2.3 lists all the prospective hospital-based stroke registers that have made use of CT scanning. We have not included a prospective hospital based study of 1214 individuals from Kinshasa, Congo which did use brain imaging (Longo-Mbenza et al., 1999; Longo-Mbenza et al., 2000). The main aim of that study was to assess the relationship between haematocrit and stroke and various meteorological variations and so 15% of the patients were excluded because they did not have demographic data or measurements of haematocrit available. Furthermore, although brain imaging was performed, it was not stated how many of the patients actually had a CT brain scan. We also excluded a prospective hospital based study of 96 stroke patients from Sudan from table 2.3, because only 18 had a CT brain scan (19%), well below the recommended 70 to 80% scan rate for stroke studies to differentiate pathological type (Sudlow et al., 1996; Feigin et al., 2004).

## Table 2.3 Comparison of stroke types and selected subtypes from prospective hospital-based studies in SSA that used brain imaging

| | | | | Pathological stroke types<br>No. (% of all strokes imaged for all but the Kalafong study in which % is of all strokes) | | | | Subtypes of ischaemic stroke<br>(% is of ischaemic strokes)* | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Study details | Number of strokes | Brain scan No. (%) | Time of stroke onset to scan | CH (%) | Ischaemic stroke (%) | SAH (%) | Unspecified (%) | Small vessel No. (%) | Cardio-embolic No. (%) | Comment |
| Kalafong, South Africa (Rosman, 1986) | 116 | 92 (79) (CT) | ? | 38 (33) | 77 (66) | Not included | 1 (1) | 24 (31) | ? | Recurrent and first-ever-in-a-lifetime strokes included |
| Harare, Zimbabwe (Matenga, 1986) | 93 | 93 (100) (CT) | ? | 29 (31) | 62 (67) | 2 (2) | 0 (0) | ? | 12 (19) | 100 consecutive patients with presumed stroke studied. 7 found to have non-stroke lesions |
| Medunsa, South Africa (Joubert, 1991) | 304 | 250 (82) (CT) | Median 4 days (range 1 to 39) | 64 (26) | 178 (71) | 80 (3) | 0 (0) | 4 (2) | 47 (46)† | All first-ever-in-a-lifetime strokes |
| Durban Stroke Data Bank, South Africa (Hoffmann, 2000) | 100 | 100 (100) (CT, MRI or both) | See text | 10 (10) | 90 (90) | 0 (0) | 0 (0) | 3 (3) | 7 (8) | Durban Stroke Data Bank included 1298 patients, 151 of whom were Black. Separate information on stroke type and subtype only available for 100 Blacks, all of whom were young (Hoffmann,1998; Hoffmann, Nath et al., 2000) |

CT – computer tomography; MRI – Magnetic resonance imaging; CH - Cerebral Haemorrhage; SAH – Subarachnoid haemorrhage; ? - data not provided
*The lack of data and use of different classification systems and methodologies in the studies makes the comparison of ischaemic stroke subtypes inaccurate. It is not possible to compare large vessel disease across the studies. See text for detail.
† A subgroup of 102 patients underwent detailed cardiac assessment (what this entailed is not clear) and of these 47 had cardiogenic sources of embolism diagnosed. See text for detail.

Although, the Durban Stroke Data Bank (DSDB) included 1298 patients, only 151 were black Africans (Hoffmann, Berger, Nath et al, 2000b). Brain imaging and stroke type and subtype data were only available for the 100 young (less than 50 years of age) stroke patients within this group (Hoffmann, 2000) and these were included in table 2.3.

#### 2.3.1.2 Cerebral haemorrhage

Table 2.3 shows the proportion of cerebral haemorrhages in all the prospective hospital-based stroke series from SSA that used imaging. All were based in urban settings, three from South Africa and one from Zimbabwe.

The low proportion of cerebral haemorrhages in **the Durban Stroke Data Bank** is surprising. In community-based studies of stroke incidence in young white stroke patients cerebral haemorrhage is relatively more common than it is in older patients (Marini, Totaro, De Santis et al, 2001). This Durban finding may reflect referral bias or late brain scanning. Although the timing to assessment and scanning is not available for the 100 young patients in table 2.3, only 44% of the entire DSDB were assessed within 7 days and 62% within 4 weeks (Hoffmann, 1998). Thus some haemorrhages may have been missed in the approximately one third of patients who had a CT and not an MRI brain scan (Dennis, Bamford, Molyneux et al, 1987).

Ninety-three strokes were confirmed following brain scan in a series of 113 consecutive adult patients admitted to two Harare hospitals with a clinical diagnosis of stroke in the mid-1980s (Matenga, Kitai, & Levy, 1986). 13 died before being having a CT scan. The seven non-stroke lesions included subdural haematoma (4), cysticercosis (1), malignant glioma (1), and metastatic deposits (1). 27 of the 29 intracerebral haemorrhages were presumed to be the result of hypertension. It is not clear whether the haemorrhages occurred in what are assumed to be typically hypertensive sites, or whether angiography was

performed to exclude other potential causes of intracerebral haemorrhage. Of the two remaining patients, one had a mycotic aneurysm and no cause was found for the haemorrhage in the other. Two of the 13 patients who died underwent autopsy and both had intracerebral haemorrhage with subarachnoid extension. Of the remainder, 10 were thought to have had cerebral haemorrhages on clinical grounds (Matenga et al., 1986).

Although the aetiology of cerebral haemorrhage was not discussed in detail in the Kalafong study, 82% of patients presenting with cerebral haemorrhage had associated hypertension diagnosed on the basis of a history of sustained elevated blood pressure (defined as >160/95 mmHg) requiring medical treatment and confirmed by medical records, or if hypertensive end organ damage was found (Rosman, 1989). No detail on the nature of cerebral haemorrhages was provided in the Medunsa study (Joubert, 1991).

The high proportion (approximately a third of all strokes) of cerebral haemorrhages found in most studies (table 2.3) may fit with SSA being in an early phase of health transition, but may equally be influenced by hospital-admission bias. Haemorrhagic strokes are more dramatic in onset and more likely to be severe. In SSA, where for most people there are numerous barriers to accessing health care (Hundt et al., 2004), it is likely that the more severe presentation of a cerebral haemorrhage increases the likelihood of hospital admission.

#### 2.3.1.3 Subarachnoid Haemorrhage

Subarachnoid haemorrhage occurred infrequently (3% of stroke cases or less) in studies in SSA (table 2.3). This is within the range of 0.9% to 7% found in community-based stroke incidence studies outside SSA (Feigin et al., 2003b), but based on very small numbers. Therefore, one can say little about SAH other than it seems to be rare, or maybe it is more common than we found but rarely diagnosed for lack of CT scanning and even lumbar puncture availability. Moreover, stroke series may have missed subarachnoid haemorrhages if they were referred directly to neurosurgical departments on admission.

#### 2.3.1.4 Ischaemic stroke

Ischaemic strokes may be subtyped using clinical classifications as in the Oxfordshire Community Stroke Project (OCSP) (Bamford, Sandercock, Dennis et al, 1991), or aetiopathogenic classifications as in the Trial of Org 10172 (TOAST) (Adams, Jr., Bendixen, Kappelle et al, 1993). Table 2.3 shows the ischaemic stroke subtypes reported in prospective studies that used brain imaging.

The standardised OCSP and TOAST criteria were only used in the DSDB and all patients were extensively investigated (Hoffmann, 2000). Unfortunately, the level of investigation needed to assess patients using the TOAST criteria renders this classification unhelpful in the SSA setting as such a large proportion of stroke patients fall into the unclassified category (Connor & Warlow, 2001). Indeed, despite extensive investigation, 47 of the 90 young stroke patients with ischaemic

stroke (52%) were classified as having had strokes due to unknown causes using the TOAST classification.

Stroke subtypes were classified according to the Harvard Cooperative Stroke Registry diagnostic criteria in the Kalafong study (Mohr, Caplan, Melski et al, 1978) and according to the Stroke Data Bank criteria in the Medunsa study (Kunitz, Gross, Heyman et al, 1984). In the study from Zimbabwe, the only subtype reported was cardioembolic stroke in patients with ischaemic stroke who presented with a potential cardiac source of embolism and without any other obvious cause for their stroke. Thus the assessment of subtypes was not uniform across studies.

To add to the difficulty in interpreting the differences in ischaemic stroke subtypes, hospital-referral bias and age differences, notably the young patients in the DSDB, may have influenced the case mix in these studies. For example, cardioembolic strokes are usually more severe than small vessel lacunar strokes, hospital series are likely to over-represent severe stroke, and young stroke patients are less likely to have hypertensive small vessel disease and more likely to have 'other' less common causes of stroke, such as vasculitis. As a result, we recommend treating a direct comparison of the subtypes found in these studies with caution.

#### 2.3.1.5 Large artery atherosclerosis

##### 2.3.1.5.1 Extracranial carotid atherosclerosis

While atherosclerosis of the extracranial carotid arteries does occur in black Africans (Madiba & Robbs, 1990; Kadwa & Robbs, 1993) it is not as common as in whites (Moossy, 1993; Wityk, Lehman, Klag et al, 1996). This view is supported by autopsy (Reef & Isaacson, 1962; Lemercier, Quenum, Richir et al, 1970; Lemercier, Collomb, N'Diaye et al, 1970; Anim, 1987), angiographic (Inzitari, Hachinski, Taylor et al, 1990), and carotid Doppler studies (Kingue, Kuaban, Dongmol et al, 1998), all in people who have *not* had strokes. However, even in African *stroke* patients, carotid atherosclerosis is not common.

It is not possible to assess directly atherosclerotic involvement of the carotid arteries in stroke patients in the prospective stroke studies from SSA that used imaging (table 2.3). There was no clinical evidence of carotid artery disease in the Zimbabwean study, though no detail is provided on how this was assessed (Matenga et al., 1986). The study from Kalafong found 37 ischaemic stroke cases (48% of ischaemic strokes) to have been caused by 'large artery thrombosis,' however, only two patients were investigated with carotid Doppler in the Kalafong study, and no comment was made on the findings in the 11 patients who had angiograms, so it is not possible be sure of the extent of extracranial atherosclerotic carotid disease in these patients (Rosman, 1989).

On the other hand the DSDB found only 5 (5%) of their young stroke patients to have ‘large artery atherosclerosis’ using the more rigid TOAST classification which required documented stenosis of the extracranial carotid artery. Thus the low frequency probably reflects both the rigid diagnostic criteria (Adams, Jr. et al., 1993; Adams, Jr., Kappelle, Biller et al, 1995) and the age (most less than 40 years old) of the stroke cases (Bogousslavsky & Pierre, 1992). In the Medunsa Stroke Data Bank, 30 of the patients with carotid territory cerebral infarctions underwent angiography. Of these 4 (13%) had some evidence of atherosclerosis (plaques, stenosis or occlusion) (Joubert, 1991).

Most studies from SSA have not commented on the presence or absence of cervical arterial bruits. In high-income populations they are present in about 5% of normal people over the age of 75 years (Sandok, Whisnant, Furlan et al, 1982), and in about 14% of patients with ischaemic stroke (Sandercock, Warlow, Jones et al, 1989). Those studies from SSA that have documented cervical bruits found them in only 1 to 4%, suggesting a very low prevalence of extracranial atherosclerosis (Rosman, 1989; Joubert, 1991).

#### 2.3.1.5.2 Intracranial carotid atherosclerosis

None of the prospective stroke studies using brain imaging in SSA (table 2.3) have attempted to document intracranial atherosclerotic disease. There is, however, autopsy data that addresses this issue and this will be discussed later.

#### 2.3.1.5.3 Peripheral vascular disease in stroke patients

Large artery disease, if found in one arterial system, is likely to be found in others (Warlow et al., 2001; Duvall & Vorchheimer, 2004). Therefore, we looked at the prevalence of peripheral vascular disease (PVD) in stroke patients in SSA. There is very little. Two studies found none at all (Aho, Harmsen, Hatano et al, 1980; Matenga et al., 1986), one found clinical evidence of PVD in just 1% of stroke patients (Joubert, 1991) and in the Kalafong study 15% of patients had diminished or absent dorsalis pedis pulses (Rosman, 1989). Even this figure of 15% which is more than double that found in any other study, is low compared to the 9 to 25% found in high-income stroke populations (Sandercock et al., 1989; Rothwell et al., 2004). In community-based prevalent stroke cases PVD was found in 1% in Tanzania (Walker et al., 2000b).

As far as we can tell, therefore, stroke patients in SSA have very little evidence of large vessel atherosclerosis, either as the cause of stroke or elsewhere in the circulation.

#### 2.3.1.6 Cardioembolic stroke and ischaemic heart disease

Ischaemic heart disease (IHD) is uncommon in Sub-Saharan Africans (Walker, 1963; Seedat, Pillay, & Marcoyannopoulou-Fojas, 1976; Wyndham, 1979; Walker, 1980; Isles & Milne, 1987; Bertrand, 1995; Kahn, Tollman, Garenne et al, 1999b; Bradshaw et al., 2002; Walker, Walker, Sci et al, 2002; Akinboboye, Idris, Akinboboye et al, 2003). However, non-ischaemic heart disease such as cardiomyopathy and rheumatic valvular heart disease is common and an important cause of death, especially in the elderly (Wyndham, 1979; van der Horst, 1984; Kahn et al., 1999b; Bradshaw et al., 2002). The causes of cardioembolic stroke are likely to reflect this pattern.

In the Ibadan Stroke Register (Aho et al., 1980) that did not have brain imaging but did attempt to ascertain community-based stroke cases, none of the 318 patients had a history of myocardial infarction, while 15% of females and 14% of males had a history of 'other types' of heart disease. It is not clear whether people with a history of ischaemic heart disease other than causing myocardial infarction were included in this 'other types' group.

Stroke was thought to be due to cardiac embolism in 8-46% of the hospital-based stroke registers that used brain imaging (table 2.3). In the Kalafong study from South Africa, none of the patients had IHD and atrial fibrillation was the presumed cause of the ischaemic stroke in 8 of the 77 patients (10%) (Rosman, 1986). The likely cause of the atrial fibrillation is not clear from the study. In the extended Kalafong study which included 152 ischaemic strokes, cardioembolic causes included: 27 (18%) presumed to be due to rheumatic valvular heart disease, 5

(3%) due to infective endocarditis, 5 (3%) due to cardiomyopathy and the remainder 14 (7%) due to atrial fibrillation. In the Zimbabwean study, 12 of 62 ischaemic strokes (19%) were cardioembolic, due to atrial fibrillation, cardiomyopathy or valvular heart disease (Matenga et al., 1986). Again the cause of the atrial fibrillation was not clear. Cardioembolic causes were responsible for 7 (8%) of 90 ischaemic strokes in the DSDB, but no further detail specific to the black patients was provided (Hoffmann, 2000).

In SSA, most hospital-based studies using imaging, and community-based studies, have found a low prevalence of IHD in stroke patients ranging from 0-7% (Aho et al., 1980; Matenga et al., 1986; Rosman, 1989; Joubert, 1991; Hoffmann, 2000; Walker et al., 2000b). This is much lower than the 38% found in the Oxfordshire Community Stroke Project in the 1980s (Sandercock et al., 1989).

However, the Medunsa Stroke Data Bank (MSDB) group have challenged this notion of a low prevalence of IHD in SSA stroke patients using an extended version of their data i.e. different numbers to those shown in table 2.3. 555 stroke patients (72% ischaemic stroke and 28% cerebral haemorrhage) underwent detailed cardiac investigation including clinical assessment and resting ECG, and a subgroup of 102 (78% ischaemic stroke; 22% cerebral haemorrhage) consecutively admitted patients underwent echocardiography, and multigated blood pool scanning (MUGA) (group 1) (Joubert, McLean, Reid et al, 2000). Sixty other, randomly selected patients (88% with ischaemic stroke and 12% with cerebral haemorrhage), underwent myocardial scintigraphic perfusion studies (group 2). Twenty-three patients (70% with ischaemic stroke; 30% cerebral

haemorrhage) underwent autopsy (group 3). The ECG assessment revealed evidence of presumed coronary artery disease (myocardial ischaemia, previous or acute myocardial infarction) in 17% of patients. In the first group, 13% of patients were found to have myocardial ischaemia and 6% evidence of previous MI. This figure rose to 32% for myocardial ischaemia and 13% for MI in the scintigraphic study (group 2). Seventeen percent of autopsied patients (group 3) had evidence of previous MI and 50% had evidence of >50% stenosis in 1, 2 or 3 coronary arteries. But, despite the significant prevalence of IHD, less than 1% of the 741 stroke patients from which this sample originated complained of angina and none was aware of a previous diagnosis of myocardial infarction. Nonetheless, the authors concluded that black stroke patients might have a similar risk of coronary artery disease to that of their white counterparts. In the light of the low prevalence of IHD found in other SSA stroke series, and in the population in general, these findings will probably only become widely accepted if confirmed by other studies.

In a separate publication from the MSDB (Joubert, Van Gelder, Darazs et al, 1989) 102 consecutive stroke patients, 24% with cerebral haemorrhage, were evaluated as in the first group above (it is not clear from either publication whether these are the same patients), and a structural or functional cardiac abnormality was found in 27 of the 102 stroke patients of all types (27%). 'Possible' sources of cardiac embolism (mainly congestive, restrictive, and hypertrophic cardiomyopathy, mitral valve prolapse, sclerotic aortic valves and hypertension associated with myopathic ventricles) were found in 23 (23%) and definite sources in 24 (24%) of the 102 stroke patients. Of those with definite sources of cardiac emboli: 5 had atrial fibrillation caused by rheumatic heart disease (2), hypertensive heart disease (1),

non-obstructive hypertrophic cardiomyopathy (1) and in 1 the cause was not known. A further 11 were caused by rheumatic heart disease, 4 by congestive cardiomyopathy, 2 by valvular heart disease and left ventricular thrombus, 1 by left ventricular thrombus alone and 1 by left atrial thrombus and a calcified mitral valve annulus. In 3 patients the rheumatic heart disease was associated with bacterial endocarditis. None of the patients had complained of a myocardial infarction but ischaemic heart disease was presumed to be present on ECG or echocardiography in 7 (7%) of the 102 stroke patients. Unfortunately, it is not clear from the study what proportion of the ischaemic stroke patients had likely cardioembolic sources.

Thus, cardioembolic stroke probably occurs about as often in SSA as in developed regions. However, the underlying cardiac lesion is more likely to be due to rheumatic or other non-ischaemic cardiac disease than ischaemic heart disease at present. If the health transition theory holds (table 1.1), then the cause of cardiac embolism should gradually shift towards ischaemic heart disease and atrial fibrillation.

#### 2.3.1.7 Lacunar infarction / complex small vessel disease

In high-income countries about a quarter of all ischaemic strokes are lacunar. Most of these are caused by 'complex' small vessel disease or atheroma of the proximal parts of intracranial perforating arteries (Warlow et al., 2001). Occlusion of these arteries results in small deep, not cortical infarcts. While the majority of clinical lacunar syndromes are the result of infarction, haemorrhage also is responsible and imaging is needed for differentiation.

If indeed Sub-Saharan Africans do have more intracranial than extracranial atherosclerosis, then one might anticipate lacunar infarction to be a common ischaemic stroke subtype. However, there is considerable disagreement on the proportion of lacunar strokes in the hospital-based series from SSA (table 2.3). 24 (31%) ischaemic strokes in the Kalafong study (Rosman, 1986), 4 (2%) in the Medunsa study (Joubert, 1991) and 3 (3%) in Durban (Hoffmann, 2000) were thought to be due to intracranial small vessel disease. Of course, the discrepancy between these figures may be the result of different diagnostic criteria or case mix differences. It is not clear how rigidly the Medunsa Stroke Data Base group enforced the Stroke Data Bank (Kunitz et al., 1984) criteria for lacunes, which required evidence of infarction when a CT scan was performed. If they did apply the criteria rigidly then this would have reduced the frequency of small vessel disease in their study as it has in others (Kunitz et al., 1984). Small vessel disease is less common in young stroke patients than in older patients (Warlow et al., 2001), which may in part explain the low frequency in the DSDB.

### 2.3.2 Other causes of stroke

Of the studies included in table 2.3, only the Kalafong study and DSDB included details on strokes caused by infection, coagulopathy or causes usually classified as 'other.' In the extended Kalafong study six of 211 patients were considered to have meningovascular syphilis based on positive cerebrospinal fluid (CSF) serology, in the presence of inflammatory cells and an appropriate clinical picture (Rosman, 1989).

All 100 patients in the DSDB young stroke series were between the ages of 15 and 49 years. It was difficult to identify the causes of stroke within the young black patients, but 20 were HIV-positive. In three alternative explanations for the stroke were cardiac valvular disease, cryptococcal meningitis and tuberculosis related vasculopathy (Hoffmann, 2000).

Many studies and case reports that did not meet our criteria for inclusion in table 2 have described other less common causes of stroke in Africa. Two broad groups of causes are prominent, sickle cell disease and infection.

#### 2.3.2.1 Sickle cell disease

Studies from Europe and the United States have reported ischaemic stroke and less commonly cerebral haemorrhage in children and young adults with homozygous sickle cell disease. The overall stroke risk is about 1% per annum (Ohene-Frempong, Weiner, Sleeper et al, 1998). Silent cerebral infarcts are more

common than overt stroke and are noted in about 20% of children by 14 years of age (Buchanan, DeBaun, Quinn et al, 2004). Heterozygous disease (sickle cell trait) rarely causes stroke in children and young adults unless there is an associated hypoxia-provoked sickle cell crisis (Greenberg & Massey, 1985; Partington, Aronyk, & Byrd, 1994).

In a case-control study from Nigeria with 180 non-embolic strokes and 100 age and sex matched controls, none of the stroke patients had homozygous sickle cell disease (haemoglobin SS) and the frequencies of haemoglobin AS and AC (heterozygotes) were similar in strokes and controls (Danesi, Oyenola, & Ontiri, 1983). All the participants were adults with an average age of 56 years in the stroke group and 55 years in the control group, which probably explains the absence of any sickle cell homozygotes as sickle cell disease usually results in death before 30 years of age in most parts of SSA (Diallo & Tchernia, 2002). The lack of association between sickle cell heterozygosity and stroke may be the result of the small sample size.

Although both sickle cell disease and sickle cell trait are very common in Western, Central and Eastern SSA (Akinyanju, 1989; Diallo et al., 2002) neither have formed a prominent part of the stroke literature in adults in SSA. None of the prospective stroke series in table 2.3 or the WHO-Nigerian community-based stroke incidence study (all in adults) examined the role of sickle cell trait. Two retrospective and one more recent prospective hospital-based adult stroke series found that sickle cell disease and trait were uncommon causes of stroke (Haddock, 1970; Billinghurst, 1970; Longo-Mbenza et al., 1999). On the other

hand in a mixed prospective and retrospective series of stroke in 35 *children* admitted to two hospitals in the Cameroon over a six month period, homozygous sickle cell disease was the commonest cause of stroke (31%) (Obama, Dongmo, Nkemayim et al, 1994).

In summary, sickle cell disease in SSA appears to play the same role in stroke as it does elsewhere in the world. However, this conclusion is based on very limited evidence from inadequately designed studies.

#### 2.3.2.2 Meningovascular syphilis

The diagnosis of meningovascular syphilis is not simple. In the context of stroke it is diagnosed either at autopsy or if the syphilis serology is positive in the blood and the VDRL (Venereal Disease Research Laboratory) is positive in the cerebrospinal fluid (CSF) of a patient with a recent stroke (Timmermans & Carr, 2004). However, false positive VDRL results caused by contamination from serum are possible, and false negative results have also been described. A positive FTA-abs (fluorescent treponemal antibody) in the CSF is very sensitive but results in many false positives and is more useful when negative to exclude syphilis as a cause of disease. Unfortunately, co-infection with human immunodeficiency virus (HIV) complicates the interpretation of the serological tests further. HIV positive individuals are more likely to have false negative blood serology and CSF VDRL results than HIV negative individuals, and repeat testing and a careful interpretation of the rest of an individual's CSF findings, brain imaging and clinical

presentation is required to make the diagnosis of meningovascular syphilis (Lynn & Lightman, 2004).

Few hospital-based stroke series have documented the CSF serology in patients with stroke and positive blood serology. Those that have, quote a low frequency of meningovascular neurosyphilis, in the same range as the Kalafong study (3%): 2 of 150 (1%) in a study from Ethiopia (Abebe et al., 1990), 4 of 96 (4%) in Sudan (Sokrab et al., 2002), 1 of 44 (2%) in a retrospective study from Sierra Leone (Lisk, 1993), and 3 of 105 autopsy cases of ischaemic stroke (3%) in Uganda (James, 1975). In the Zimbabwean study of 93 stroke patients, all of whom had brain imaging (table 2.3), the stroke was attributed to neurosyphilis in 8 patients (all ischaemic strokes) (Matenga et al., 1986).

#### 2.3.2.3 Human immunodeficiency virus (HIV)

There are many reasons why individuals who are infected with HIV may present with a stroke or stroke mimic, e.g. secondary to various opportunistic causes of meningitis, intracranial infective mass lesions, infective vasculitides or following cardiac manifestations of HIV (Connor, Lammie, Bell et al, 2000). Ischaemic stroke in HIV-infected individuals is not common in the absence of a non-HIV infection, or lymphoma in the brain or embolic sources, despite an underlying HIV related vasculopathy (Connor et al., 2000). Moreover, there is limited support for the role of HIV on its own as a cause for stroke (Cole, Pinto, Hebel et al, 2004).

Two studies in SSA have examined the association between HIV and stroke. In the DSDB (table 2.3) 20 out of the 100 young stroke patients were HIV-positive and in all but three this was the only identified cause for the stroke (Hoffmann, 2000; Hoffmann, Berger, Nath et al, 2000a). The seropositivity rate was similar to the background population, however. In a case series of 35 predominantly young (mean age 32 years) HIV-positive urban South African stroke patients, an underlying non-HIV cause of the stroke was found in 30 of the 35 patients and included protein S deficiency, meningitis, cardiac embolism and hypertension (Mochan, Modi, & Modi, 2003). The authors felt that these causes were not significantly different to what one might expect to find in HIV-negative stroke patients in urban Johannesburg.

So it is not clear whether HIV is an independent risk factor or cause for stroke in Sub-Saharan Africans and a large prospective case-control study as well as high quality post mortem studies are needed to resolve this confusion.

### 2.3.3 Autopsy studies of stroke and cerebral atherosclerosis in Africa

Autopsy series can be very useful, particularly for formulating hypotheses of what may cause stroke, but they are clearly subject to multiple selection biases. For example, haemorrhagic strokes which are more often fatal are likely to be overrepresented and lacunar strokes underrepresented. Therefore, they do not reflect stroke types and subtypes in the community. The autopsy studies from SSA have seldom provided a detailed description of selection criteria for autopsy, such as whether patients who had died of atherosclerosis related disease were included

or excluded, and techniques for assessing the degree of atherosclerosis were often subjective and varied from study to study. All of this made the interpretation of the results and comparison of studies challenging. We have included studies that specifically focused on the distribution of atherosclerosis in the cerebral vasculature in stroke populations in SSA and studies that have described the causes of ischaemic stroke and cerebral haemorrhage in SSA. We excluded studies that did not clearly distinguish between the pathological stroke types when assessing the cause of stroke.

#### 2.3.3.1 Atherosclerosis

Although studies reporting on atherosclerosis in African populations (Baker, Flora, Resch et al, 1967; Walker, 1974) have been conflicting, most of the disagreement has come from South African studies (Reef et al., 1962; Meyer, Pepler, Meyer et al, 1964; Strong, 1972) and one Ugandan study (Owor, Resch, & Loewenson, 1976) and may result from differences in populations across Africa (Anon., 1971), perhaps influenced by their stage in the health transition.

From various autopsy studies in black Sub-Saharan Africans and studies that have compared this group with white SSA populations, African Americans and white Americans, a pattern of intracranial, carotid and coronary atherosclerosis emerges (table 2.4). This pattern suggests there is a progression from minimal intracranial or coronary atherosclerosis found in populations from Nigeria (Williams, Resch, & Loewenson, 1969; Williams, Loewenson, Lippert et al, 1975),

## Table 2.4 Comparison of the pattern of atherosclerosis found in autopsy studies from populations in Sub-Saharan Africa and the United States of America

| | Autopsy studies in unselected populations | | | Autopsy studies in Stroke populations | |
|---|---|---|---|---|---|
| | Atherosclerosis in: | | | Atherosclerosis in: | |
| Region | Intra-cranial arteries | Extra-cranial carotid arteries | Coronary arteries | Intra-cranial arteries | Coronary arteries |
| Nigeria, (Williams et al., 1969; Williams et al., 1975)<br><br>Senegal, (Collomb, Dumas, Lemercier et al, 1967; Lemercier et al., 1970; Resch, Williams, Lemercier et al, 1970)<br><br>Ghana (Edington, 1954; Anim, 1987; Anim & Kofi, 1989) | - | - * | - | + | - |
| South Africa, (Higginson & Pepler, 1954; Laurie & Woods, 1958; Sacks, 1960; Reef et al., 1962; Meyer et al., 1964; Strong, 1972)<br><br>Uganda (Owor et al., 1976) | - / + | - | - | + | ? |
| White Africans (Sacks, 1960; Meyer et al., 1964)<br><br>White Americans (Solberg & McGarry, 1972; Strong, 1972; McGarry, Solberg, Guzman et al, 1985) | + | ++ † | ++ | | |
| African Americans (Williams et al., 1969; Resch et al., 1970; Solberg et al., 1972; Strong, 1972; Williams et al., 1975; Owor et al., 1976; McGarry et al., 1985) | ++ | ++ | ++ | | |

- \- little atherosclerosis
- \+ atherosclerosis present but at low to moderate levels
- ++ marked atherosclerosis

* One study from Senegal found some atherosclerosis in extracranial carotid arteries (see text for detail)
† no reference for autopsy studies in White Africans

Senegal (Resch et al., 1970), and Ghana (Anim, 1987; Anim et al., 1989) to similar amounts of intracranial atherosclerosis in blacks in South Africa (Meyer et al., 1964) and Uganda (Owor et al., 1976) and whites in South Africa (Meyer et al., 1964), though still without any evidence of an increase in coronary or carotid atherosclerosis in blacks (Higginson et al., 1954; Sacks, 1960; Reef et al., 1962). There is, however, one study from Senegal that found >50% stenosis of at least one carotid artery in 7 of 112 (6%) patients at autopsy (Collomb, Sankale, Courson et al, 1971). Finally, the most severe intracranial, carotid and coronary atherosclerosis has been found in African Americans (Solberg et al., 1972; Strong, 1972; McGarry et al., 1985; Anim, 1987). In comparative studies both within South African and intercontinental, intracranial atherosclerosis in all populations is seen to increase in extent and severity with age and male gender (Williams et al., 1975; Anim, 1987). A history of hypertension (and increased heart mass) and diabetes mellitus has also been associated with an increase in the severity of intracranial atherosclerosis in SSA populations (Williams et al., 1975; Anim, 1987).

In autopsy populations from SSA who had had a stroke, three studies found significant intracranial atherosclerosis (Laurie et al., 1958; Collomb et al., 1967; Lemercier et al., 1970). Perhaps people with increased intracerebral atherosclerosis who develop ischaemic strokes represent the vanguard of the health transition and in time populations in SSA will develop atherosclerotic disease in the carotids and coronaries similar to that seen in African Americans. Only further community-based studies with detailed imaging, and autopsy studies will be able to resolve this confusion.

#### 2.3.3.2 Autopsy causes of stroke

As mentioned above autopsy studies do not accurately reflect the nature of stroke in the community. However, a recent autopsy study from Accra, Ghana compared the proportion of ischaemic and haemorrhagic strokes (including cerebral haemorrhage and subarachnoid haemorrhage), reaching autopsy during two different time periods, 1972-1981 and 1994-1998 at the same institution (Wiredu & Nyame, 2001). The proportion of haemorrhagic stroke had fallen from 89% in 1981 to 61% in 1998. This may reflect a downward trend in the number of haemorrhagic strokes in the population, altered referral patterns, or other influences which are not clear from the study. However, the decline in haemorrhagic stroke would be compatible with the health transition.

Autopsy series of course may provide more detail on what causes strokes (or at least fatal strokes) in a population. The same study from Accra provided a retrospective analysis of the cause of 666 haemorrhagic strokes (7% subarachnoid haemorrhage), 397 ischaemic strokes and 23 in a poorly defined group termed ‘combined strokes’ which presumably included both haemorrhages and ischaemic strokes in the same patient. Haemorrhagic strokes were caused by: hypertension (90%), hypertension plus cerebral atherosclerosis (3%), other causes including ruptured berry aneurysm, bleeding disorder and vascular malformations (3%), bacterial endocarditis (0.5%) and miscellaneous conditions in 4%. Ischaemic strokes were caused by: hypertension (24%) though the exact mechanism by which this was thought to have occurred is not clear, hypertension plus cerebral atherosclerosis (25%), cerebral atherosclerosis alone (35%),

cerebrovascular thrombosis (in the absence of atherosclerosis) (3%) and cardiac mural thrombi (2%), bacterial endocarditis (2%) and was undetermined in 8%. In the group with ischaemic and haemorrhagics strokes combined in the same patient the cause was hypertension in 96% and undetermined in the remainder (Wiredu et al., 2001). Unfortunately the authors did not comment on extracranial atherosclerosis or the role of artery-to-artery or cardiac embolism to the brain in this series. However, an autopsy study performed at the same centre about ten years previously found almost no significant atherosclerosis in the extracranial carotid or coronary arteries (Anim, 1987).

The same centre from Ghana had previously used the arteriographic technique of Ross Russell in 284 consecutive non-traumatic, unselected autopsy cases over 20 years of age (Anim & Kofi, 1984). The authors suggested that the prevalence of microaneurysms was lower than in similar studies of white patients, even in hypertensive patients with haemorrhagic strokes, and suggested that the mechanism of hypertensive haemorrhage may be different in young black Africans. However, microaneurysms are very difficult to detect and there are numerous methodological pitfalls with this type of study (van Gijn, 2001).

In a much earlier autopsy series in the 1950s, again from Ghana, hypertension was thought to be responsible for 23 of 53 cerebral haemorrhages, atherosclerosis for 13, unclassified causes for 12 and pregnancy, syphilis and sickle cell disease for 5 (Edington, 1954).

In Uganda stroke was the cause of death in 207 of a retrospective review of 5497 autopsies performed between 1967 and 1971: 75 (48 males, 27 females) had cerebral haemorrhages, 105 (74 males, 31 females) ischaemic strokes and 27 (17 males and 10 females) subarachnoid haemorrhages (James, 1975). The presumed cause of the cerebral haemorrhages was hypertension in 32 of the 75 (43%) (essential hypertension in 24, hypertension secondary to renal disease in 7 and 'possible' hypertension in 8). It is not clear exactly how the diagnosis of hypertension was made, however. The remainder were caused by: eclampsia (6), sickle cell disease (2), coagulation defects (7), unspecified 'heart disease' and 'other causes' in 5, and in 9 no obvious cause was found. In the 105 ischaemic strokes the causes were: essential hypertension and secondary hypertension in 19 (18%), cardioembolic in 47 (45%), atherothromboembolic in 5 (5%), syphilis in 3 (3%), and in 31 (30%) the cause was not clearly identified. The cardioembolic sources, as previously found in SSA, were seldom related to ischaemic heart disease, and myocardial infarction was only present in 5 of 105 (5%) of ischaemic strokes. Other causes were: endocarditis in 25 (24%), endomyocardial fibrosis in 6 (6%), rheumatic heart disease in 5 (5%), cardiomyopathy (unspecified) in 4 (4%) and myocarditis in 2 (2%). Finally, in the 27 cases of subarachnoid haemorrhage the cause was: berry aneurysm in 10 (37%), mycotic aneurysm in 2 and an aneurysm of uncertain origin in 1. Five were associated with either possible or definite hypertension, and in a further 5 no cause was found. The remaining 4 included one case each of sickle cell disease, aplastic anaemia, anticoagulant therapy and bacterial endocarditis.

### 2.3.4 Major Vascular Risk Factors – Unmodifiable

#### 2.3.4.1 Age and Sex

In SSA, as in high-income countries, increasing age is a major risk factor for stroke (table 2.2). Stroke incidence in the younger 35-54 year-old age groups, even in hospital series, is higher than in the United Kingdom, but not quite as high as in African-Americans.

Early SSA hospital case series and the Ibadan Stroke Registry (Osuntokun et al., 1979) found the male:female sex ratio to be as high as 3:1 (Osuntokun, 1994). Some authors considered this excess of males to reflect cultural practices in which men were more likely to go to or be admitted to hospital than woman (Osuntokun, 1977). A recent stroke registry from Zimbabwe found a sex ratio closer to 1:1 (Matenga, 1997), while others from Sudan**,** the Congo and the Gambia continue to find a higher proportion of men admitted with ratios ranging from 1.4 to 1.7:1 (Longo-Mbenza et al., 2000; Sokrab et al., 2002; Walker et al., 2003). An exception to the male predominance was found in the MEDUNSA stroke data bank in South Africa where the male to female ratio was 0.8:1 (Joubert, 1991). This is not a consistent feature of South African registries though, because there was a male predominance in the Kalafong study, with a ratio of 1.3:1 a year previously in the same part of the country (Rosman, 1986).

The community-based rural stroke prevalence study from Tanzania found age-standardised stroke prevalence to be higher in men than women (ratio 1.4:1)

(Walker et al., 2000b), Some of the discrepancies seen across studies may be age related and reflect a younger population when an increased male predominance is found. In both the Oxfordshire Community Stroke Project and the OXVASC community stroke incidence studies males had a higher incidence of stroke in middle age but the incidence was similar in men and women over the age of 75 (Rothwell et al., 2004).

### 2.3.5 Modifiable Risk Factors

There is only one published but small case-control study of 180 patients and 100 controls investigating non-cardioembolic ischaemic stroke risk factors in SSA (Danesi et al., 1983). The authors found a significantly elevated relative risk (in brackets) of ischaemic stroke from diastolic hypertension (5.5) defined as a pressure of $\geq$ 100 mmHg, systolic hypertension (5.2) defined as a pressure of $\geq$ 160 mmHg, diabetes mellitus (2.5), low socio-economic status (2.2) and obesity (3.2). Random serum cholesterol, haemoglobin and random blood glucose were significantly higher in the cases than in the controls. The serum cholesterol in the cases was 5.0 mmol/l compared to 4.4 mmol/l in the controls ($p<0.05$). The haemoglobin was 13.9 g/dl in the cases and 13.2 in the controls ($p<0.05$) and the random blood glucose was 6.5 mmol/l in the cases and 5.1 mmol/l in the controls ($p<0.01$). Small numbers and the absence of brain imaging limit the study. It is also not clear whether patients were indeed hypertensive or simply had elevated blood pressure associated with acute stroke.

In the absence of any other case control studies, we are reliant on assessing risk factors from their prevalence in stroke registers and case series. Studies containing information on risk factors were included in our assessment if they were community-based stroke studies or prospective hospital-based stroke studies that included consecutive stroke admissions. We excluded studies without clearly defined risk factors. We found that risk factors were seldom if ever reported by stroke type. Where they were we have used pathological type specific data, otherwise results refer to the percentage of all strokes combined affected by the risk factor.

#### 2.3.5.1 Hypertension

Hypertension is an important risk factor for stroke but definitions vary and it is not always clear whether investigators have relied on blood pressure measurements at the time of presentation which are more likely to reflect transient hypertension related to the acute stroke (Bath & Bath, 1997). Ideally one would like to know whether a stroke patient had a history of hypertension prior to their stroke or had ever been on treatment for hypertension. Unfortunately, the vast majority of people with hypertension in SSA are undiagnosed and so this is not a particularly helpful definition in this setting. Another way of determining whether a stroke patient had pre-existing hypertension is to look for clinical signs of end-organ damage such as left ventricular hypertrophy or hypertensive retinal changes (Warlow et al., 2001).

In hospital-based studies that used brain imaging (table 2.3), hypertension was diagnosed in 43-70% (Matenga et al., 1986; Rosman, 1986; Joubert, 1991) of

strokes, although this was not surprisingly higher (93%) in patients presenting with cerebral haemorrhage in Zimbabwe (Matenga et al., 1986).

In a community-based study that did not use brain imaging, hypertension was present in 68% of incident stroke cases in Nigeria (defined as sustained blood pressure >160/100 mmHg for at least one week or end organ damage) (Osuntokun et al., 1979). Other prospective hospital stroke series that did not use imaging have found a prevalence of hypertension in stroke admissions of about 65% (Abebe et al., 1990; Roberts, Opare-Sem, & Acheampong, 1994).

#### 2.3.5.2 Diabetes mellitus

In hospital-based studies using imaging diabetes mellitus was diagnosed in 3-10% of all strokes (Matenga et al., 1986; Joubert et al., 1989; Rosman, 1989). It was found in 5% of young stroke patients in the Durban Stroke Data Bank (Hoffmann, 2000). In community-based studies the range was a similar 3-10% (Osuntokun et al., 1979; Walker et al., 2000b) with the lower figure from Tanzania and the higher one from Nigeria. Prospective hospital series have found diabetes mellitus in 3-5% of stroke admissions (Abebe et al., 1990; Walker et al., 2003). So diabetes mellitus is not particularly common in SSA when compared to the finding of diabetes mellitus in about 10% of community-based incident stroke cases in the United Kingdom between 1981 and 2004 (Rothwell et al., 2004).

**Atrial fibrillation**

In one hospital series atrial fibrillation was found in 2% of strokes (Abebe et al., 1990) though it is seldom commented on in studies from SSA. It was found in 5-7% of strokes in hospital series using imaging (Rosman, 1986; Joubert et al., 1989) and in 7% of prevalent cases in Tanzania (Walker, 2002). So atrial fibrillation occurs less frequently in SSA than in high-income country stroke populations, but this may be because stroke occurs at a younger age in SSA than in high-income populations.

### 2.3.5.4 Cholesterol

None of the community-based studies have investigated blood cholesterol levels and it is difficult to interpret the results of the hospital-based studies as few define what is meant by hypercholesterolaemia or dyslipidaemia or how and when specimens were taken. As a result, findings vary widely. For example in a similar population at a similar time in South Africa total cholesterol was found to be elevated in <2% of stroke patients in one study (Rosman, 1989) and in 10% in another (Joubert et al., 1989). In a hospital series in Ethiopia the proportion of stroke patients with elevated cholesterol levels was 7% (Abebe et al., 1990). Despite this variation, the proportion is substantially lower than the 58% of incident strokes with total cholesterol $\geq$ 6 mmol/L found in the high-income UK population in Oxfordshire in the 1980s or even the 30% found in the same population in the OXVASC study twenty years later (Rothwell et al., 2004).

#### 2.3.5.5 Smoking

Current cigarrette smoking was found in 6-28% in hospital-based studies that used imaging (Matenga et al., 1986; Rosman, 1989; Joubert, 1991; Hoffmann, 2000). In Ethiopia cigarette smoking was found in 7% of stroke patients admitted to hospital (Abebe et al., 1990). In a hospital cohort study from The Gambia, half of the stroke patients had a history of smoking and 23% were current cigarette smokers at the time of their stroke. Smoking was significantly less common in age and sex matched controls selected from among hospital visitors, of whom 14% had a history of smoking, but only 8% were current smokers at the time they were seen (Walker et al., 2003). In Oxfordshire, UK, about 30% of all incident stroke cases were current smokers in the early 1980s, but this had declined to 18% in 2002 in the OXVASC study.

#### 2.3.5.6 Alcohol

A number of studies have assessed alcohol use (Rosman, 1989; Nwosu, Nwabueze, & Ikeh, 1992; Walker et al., 2003). Unfortunately, few if any have attempted to quantify the amount of alcohol consumed (Joubert, 1991), which is particularly difficult in many parts of SSA where alcohol is brewed at home and the strength varies (Greenhalgh, 2004). The exact role of alcohol as a risk factor in SSA is not clear and none of the studies have used controls

## 2.4 Summary of the literature on stroke in SSA

The literature on the burden and nature of stroke in SSA is limited (often because of a lack of brain imaging) and there are no community based incidence studies of stroke that come close to meeting accepted 'ideal' standards. Stroke mortality appears to be increasing, but there are no accurate longitudinal data from regions with good vital registration or where verbal autopsies were performed. The prevalence of stroke is lower than in high-income regions. Of course without community based incidence studies with follow up it is not possible to assess whether the low prevalence is the result of low incidence or high case fatality or both.

The only stroke studies in SSA that provide information on the nature of stroke type and subtype, as well as causes and risk factors - because of the availability of brain imaging - are hospital-based and therefore are likely to be biased. Moreover, most of these studies lack clear definitions of risk factors and descriptions of how stroke subtypes were diagnosed. As a result, the nature and causes of strokes in SSA are very unclear.

The literature does provide some support for the concept of the health transition. Stroke in hospital series is found at a relatively younger age than it is in high-income regions. At present cerebral haemorrhage, in hospital studies at least, is more common than one would expect in a high-income region, constituting about a third of all strokes. Cardioembolic strokes account for about one fifth of ischaemic strokes but there is little evidence of ischaemic heart disease in stroke patients.

Indeed, extracranial atherosclerotic disease is uncommon in any form with carotid artery disease and peripheral vascular disease seldom found in stroke patients in SSA. This pattern of relative lack of atherosclerotic disease, particularly in the extracranial arteries is generally supported by autopsy studies. All of this would suggest that SSA has entered the health transition but has not yet developed a large burden of atherosclerotic disease and its clinical consequences.

The pattern of risk factors in stroke patients likely reflects this pattern of stroke. Hypertension is by far the most common risk factor, while elevated cholesterol is found in fewer than 10% of stroke survivors. Diabetes mellitus is less common than one would expect in high-income populations but not markedly so, and in most studies current smoking was generally less common than in high-income populations. Based on small studies, homozygous sickle cell disease appears to be an important cause of stroke in children but not adults in endemic regions of SSA. The role of HIV / AIDS as a risk factor or cause for stroke has not been adequately investigated in this region.

## 2.5 Discussion and comment

Without intervention, vascular and cardiac disease related deaths are set to increase from 3 million in 1998 to 5 million in 2020 in WHO developing regions (The WHO, 2001; Leeder et al., 2004). As risk factors for vascular disease increase, so the burden of vascular disease will increase. Typically the pattern of vascular disease fits the basic outline given by Omran's theory of the health or epidemiologic transition (Omran, 1971) and stroke leads the way. However, the type and subtype of stroke and the relative proportion of extracranial atherosclerotic diseases (ischaemic heart disease, stroke due to carotid artery disease, and peripheral vascular disease) will probably change as the vascular risk factors change within the population. Stroke in SSA is entering the health transition and as the burden of risk factors increases, so the burden of stroke will increase to epidemic proportions unless interventions are set in place now.

Many reports from influential groups have highlighted this impending epidemic and called for low and medium-income countries and research funders to act (Howson et al., 1998; The WHO-Wellcome Trust, 2001; The WHO, 2001; The WHO, 2002; The WHO, 2003; Leeder et al., 2004). Many have highlighted the need for high quality epidemiological research to establish the burden of stroke in SSA and monitor the effect of interventions.

Unfortunately we have found little high quality epidemiological data on stroke in SSA. Stroke research has focused on hospital based studies, few with imaging and most retrospective. It is time to move on and 'ideal' community based

incidence and case fatality studies are needed, at least in a few sites, perhaps at different stages in the transition, to clarify both the burden and nature of stroke. While these studies are relatively expensive and logistically difficult to perform, and SSA particularly in rural and more remote regions is a difficult place to work in, the potential exists to do this type of research in demographic surveillance sites such as those that are part of the INDEPTH group (INDEPTH network, 2005). These sites provide not only an accurate denominator, but also very often a research infrastructure which supports the research. In countries and areas where this type of study is not feasible, surveillance of stroke in a STEPwise form as developed by the WHO will provide useful local and longitudinal information (Bonita, Mendis, Truelsen et al, 2004). But only detailed community studies of the nature of stroke in the region, with brain imaging, will provide insight into where the region is along the health transition and help direct the focus of interventions to the appropriate risk factors and causes. They would also help to clarify the effect of HIV / AIDS on stroke.

While combating stroke and vascular disease will require action on a range of fronts, including government initiatives to change population risk by for example legislating against cigarette advertising and smoking, and interventions will have to be developed in consultation with local populations, it is essential that action be taken now to reduce the future burden (Leeder et al., 2004). The remarkable drop in stroke incidence found in the recent OXVASC study in Oxfordshire, UK, done in the same population twenty years after the OCSP study and associated with a drop in vascular risk factors, suggests that stroke prevention is both possible and effective, and can be surprisingly rapid (Rothwell et al., 2004). The challenge now

is to accurately document the burden and nature of stroke, to implement stroke prevention appropriately, and to measure the outcome in Sub-Saharan Africa.

# CHAPTER 3 THE PREVALENCE OF STROKE IN RURAL SOUTH AFRICA

## 3.0 Introduction

There are no stroke prevalence data available for South Africa and only very limited reliable data available for the rest of sub-Saharan Africa (see section 2.2.4). The aim of this study was to establish the prevalence of stroke, and nature of prevalent strokes, in the University of the Witwatersrand / Medical Research Council (Agincourt) Rural Public Health and Health Transitions Research Unit demographic site, hereafter referred to as the 'Agincourt Health and Population Unit' (AHPU) or simply as Agincourt. The study formed one component of the Southern African Stroke Prevention Initiative (SASPI) study. This chapter will describe the methods used and the prevalence of stroke in the region, while the nature of prevalent stroke in the region will be described in chapter 4.

Although I have presented the literature pertaining to the prevalence of stroke in Sub-Saharan African Africa in section 2.2.4, I will highlight the literature relevant to stroke prevalence studies elsewhere in the world in the discussion.

## 3.1 Setting and population

The Agincourt Health and Population Unit, located in a deprived rural area of South Africa (figures 3.1 and 3.2), has been monitoring the causes of death, births and inward and outward migration by means of a health and demographic

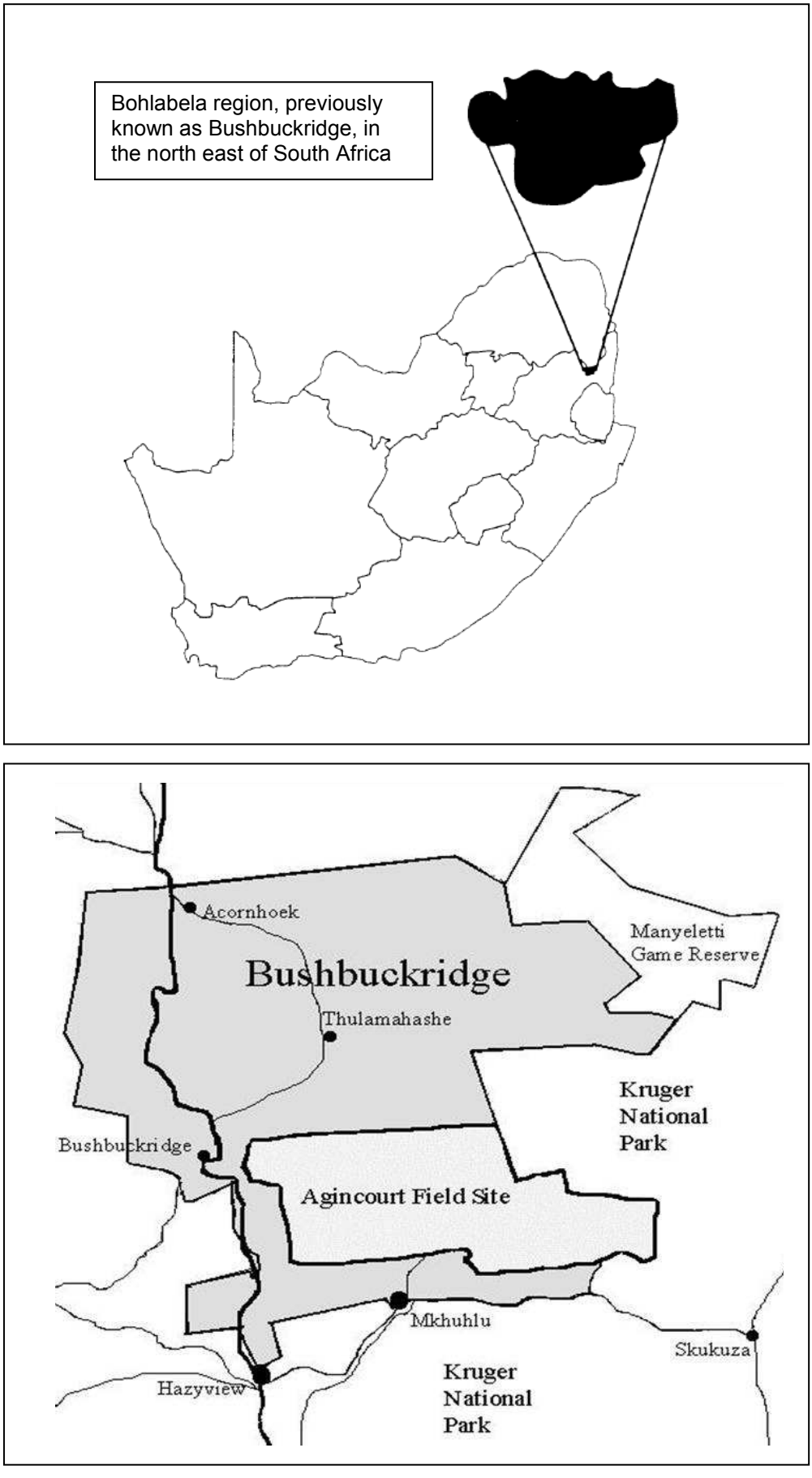



Figure 3.1 Situation of Agincourt Health and Population Unit field site



Figure 3.2 Houses in the Agincourt Health and Population Unit (AHPU) field site

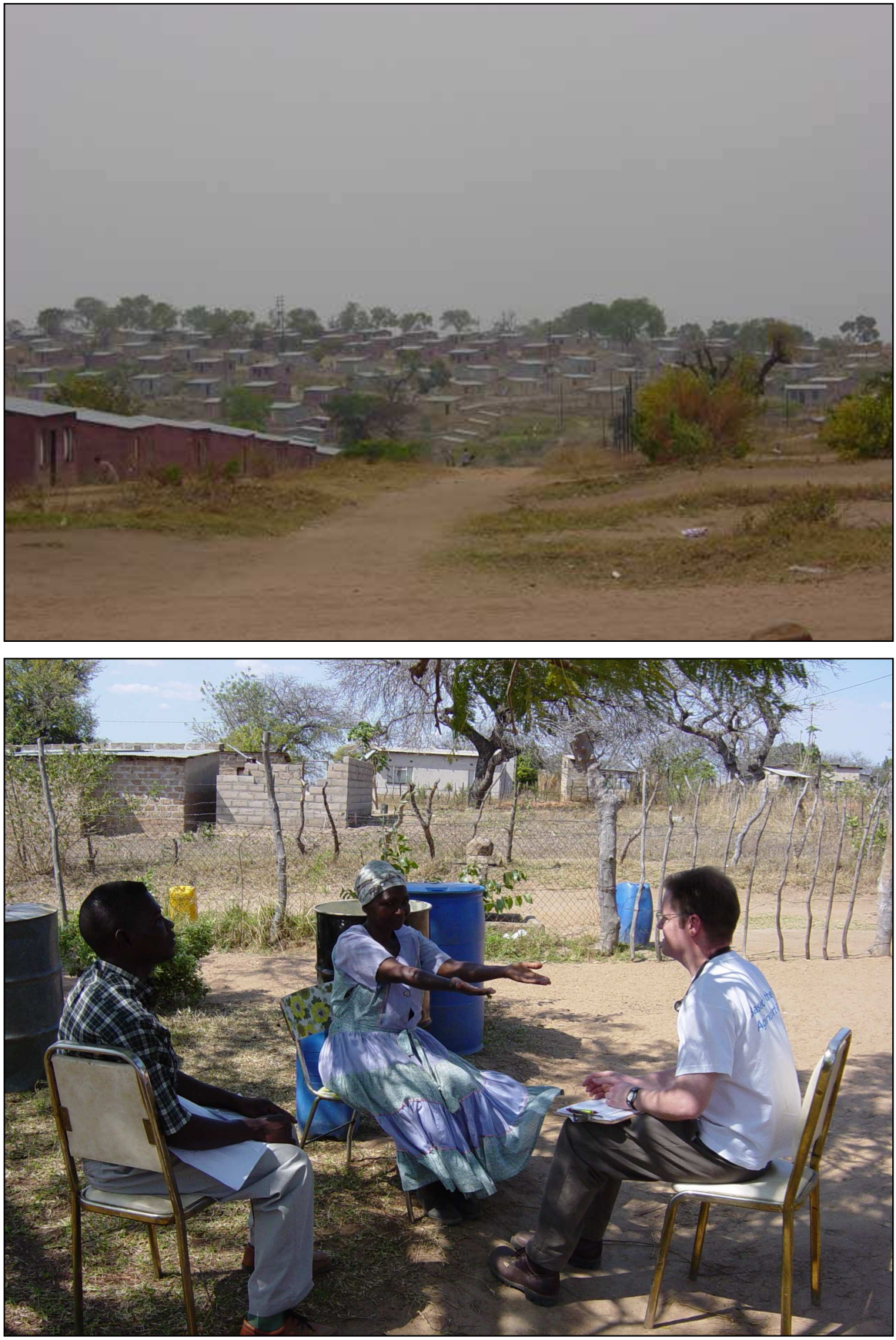


Figure 3.3 The government's new Reconstruction and Development Project housing in the AHPU (above), and the team interviewing a woman who screened positive for stroke during the census but had hypocalcaemia with severe muscle cramping not stroke (below, with permission)

surveillance system in a population of around 70,000 people since 1992 (Tollman, Herbst, & Garenne, 1995).

The Agincourt sub-district of Limpopo Province, in the northeast of South Africa, was formerly part of the homeland of Gazankulu. The population is Shangaan, although Mozambican refugees who settled in the area after the 1980s civil war in Mozambique, who are also Shangaan speaking and culturally affiliated with the South African population, make up about a third of the population. There are limited amenities. Although electricity is recently available in most villages, it does not reach all households, and access to clean water is severely restricted. As part of the legacy of the apartheid system, there is considerable labour migration, especially amongst men. Some migrant workers return home only at Christmas and Easter; while others return more frequently. Migrants are included in the annual census as they would consider 'home' to be the Agincourt Health and Population Unit villages, and almost all of them maintain a household in the area. If they become ill and unable to work, they usually return here. Figures 3.2 – 3.3 include photographs of the Agincourt field site showing the range of dwellings from the typical Mozambican refugee hut to the new relatively high density government reconstruction and development programme housing.

## 3.2 Case finding

Each year, the Agincourt Health and Population Unit carries out a door-to-door census survey of all the households in the 21 villages in the area using an interview questionnaire administered by trained census workers (Collinson,

Mokoena, Mgiba et al, 2002). In 2001, we added two screening questions similar to those asked in the then recent stroke prevalence study in Tanzania (Walker et al., 2000b) (see section 2.2.4). The fieldworker questioned each household informant, named every individual in the household and asked: 'Has ……. (person) ever had weakness down one side of the body?' and 'Has ……. (person) ever had a stroke?' In the Tanzanian study, three questions were posed to each household: 'Is there anyone in the household with a history of stroke?'; 'Is there anyone in the household with a weakness down one side of the body?' and 'Does anyone in the household require assistance with: a) dressing, b) eating and c) toileting?' The Tanzanian investigators found that question three was very sensitive but not very specific and did not yield significantly more strokes than the first two questions (personal communication R W Walker). In Agincourt the term 'stroke' has multiple interpretations and prior to the SASPI study we thought that it might perhaps be interpreted as bewitchment and influence the participant's response. As a result we asked about weakness down one side *before* asking whether the person had had a stroke. In an effort to detect all prevalent strokes rather than to limit the findings to people with current disability or functional impairment, we asked whether people had 'ever' had weakness rather than currently had weakness as in the question used in Tanzania. Finally, in contrast to the Tanzanian study our fieldworkers asked the household informant whether each member of the household had weakness or a stroke, rather than asking about the household in general.

We gave the census workers, an experienced team of trained local fieldworkers, specific training on stroke, including information on its causes and manifestations,

as well as instruction and practice in using the questions in the vernacular. We conducted a pilot study in 20 households and found a significant number of children with birth trauma related neurological conditions and cerebral palsy but almost none with stroke. The causes of stroke in children differ from those in adults and accurate diagnosis requires relevant paediatric skills (deVeber, Roach, Riela et al, 2000). As a result stroke prevalence studies seldom if ever include children (Feigin et al., 2003b). We planned to compare our findings with those from a similar stroke prevalence study from Tanzania (Walker et al., 2000b) and with a study from New Zealand (Bonita et al., 1997). Both these studies used 15 years of age as the lower limit for inclusion. So for several reasons we selected the same threshold for inclusion. The census ran between August and November 2001, and the date chosen for point prevalence was the day before the census started, the 31$^{st}$ July 2001.

If either screening question was answered positively, then, accompanied by an interpreter, we (myself or one of two research fellows I trained in the assessment of stroke) visited the relevant individual in their home between January and October 2002 (see figure 3.3). We obtained informed consent before taking a detailed history and examining the individual. We held regular meetings (approximately weekly) to discuss and agree on the diagnosis in all cases. Where there was diagnostic doubt, I visited and assessed individuals, and made a final diagnosis.

In this remote region, there are no reliable means of postal or other communication so we had to visit the households. If the relevant individual was not

available, we tried to arrange a future visit through other household members or neighbours. If initially unsuccessful, we made at least two further attempts on different occasions to visit any individual who on the basis of the census questions might have had a stroke.

## 3.3 Clinical assessment

We defined stroke according to the WHO criteria as 'rapidly developing signs of focal (or global) disturbance of cerebral function, leading to death or lasting longer than 24 hours, with no apparent cause other than vascular' (Hatano, 1976a; Asplund, Tuomilehto, Stegmayr et al, 1988), with one modification - we did not include any individuals who died prior to assessment. We also excluded people with transient ischaemic attacks. Computer Tomography (CT) and Magnetic Resonance (MR) scanning were far from readily available and the diagnosis of stroke was therefore made clinically. Indeed the nearest CT scanner was about 300 km or four hours drive away by road. In making the diagnosis, we emphasised the sudden onset of focal neurological symptoms and lack of progression of the illness, to avoid including infective processes or space occupying lesions that mimic stroke. If the individual had suffered multiple events, we focused on their first-ever-in-a-lifetime event. We defined an individual as 'needing help with at least one activity of daily living' if they needed assistance with any of washing, dressing, bathing, feeding, transfer, or toileting. We used this definition of disability to compare our findings with a stroke prevalence study from New Zealand (Bonita et al., 1997) (mentioned in section 2.2.4) and the stroke prevalence study from Tanzania, discussed in section 2.2.4 (Walker et al., 2000b).

We asked individuals found to have had a stroke about their demographic details, symptoms at onset and since the stroke, symptoms of other vascular disease, and risk factors for stroke, including smoking and alcohol intake (appendix B). If a stroke patient was uncertain of their age, we checked this both against the census

data and against their identity card when available. We listened for carotid bruits and felt all peripheral pulses, examined the heart for evidence of likely embolic sources, looked for hypertensive end-organ damage, and did a neurological examination.

Although it was often months or even years since the first stroke event, we attempted to assess the likely stroke type based on the person's symptoms at the time of the stroke. We were more likely to diagnose cerebral haemorrhage than ischaemic stroke if the person gave a history of severe headache, seizure (Burn, Dennis, Bamford et al, 1997) or loss of consciousness at the onset, as these presentations are unusual in ischaemic stroke (Warlow et al., 2001). We assessed the likely ischaemic stroke subtype using the Oxfordshire Community Stroke Project (OCSP) classification (Bamford et al., 1991).

We also assessed the person's current modified Rankin score (Rankin, 1957; Bamford, Sandercock, Warlow et al, 1989) and Barthel score (Mahoney & Barthel, 1965). We recorded any medication that the stroke survivor was using and specifically noted whether they were using aspirin, whether they had experienced any complications of the stroke, as well as any other relevant findings on examination.

We measured the blood pressure in the sitting position after five minutes rest with the appropriate cuff size using an OMRON 705CP or OMRON M5-I blood pressure monitor. We defined hypertension as systolic blood pressure greater than 139 mmHg, or diastolic blood pressure greater than 89 mmHg, using the mean of

two measurements, or if the stroke survivor was taking antihypertensive treatment. We used two measurements as one measurement is generally considered inaccurate, and we felt that more than two measurements would unnecessarily add to an already lengthy assessment. We were reassured that a large international study investigating the role of antihypertensive agents following stroke required two measurements (Neal & MacMahon, 1995) at that time, and later by a similar recommendation by the European Society of Hypertension (O'Brien, Asmar, Beilin et al, 2003). We defined hypertensive subgroups as 'mild hypertension', if the systolic pressure was greater than 139 mmHg and less than 160 mmHg and/or the diastolic pressure was greater than 89 mmHg and less than 95 mmHg; and 'moderate or severe hypertension' if either the systolic pressure was greater than 159 mmHg or the diastolic pressure was greater than 95 mmHg. We defined *'any evidence of hypertension*' as all hypertensive individuals plus those with clinical evidence of hypertensive end organ damage or previous antihypertensive treatment. Although clinical evidence of hypertensive end-organ damage would usually include electrocardiograph evidence as well as urine analysis for microalbumin / creatinine ratios, we were unable to perform these assessments. We based our evaluation on fundoscopic changes of hypertension and auscultation and palpation of the stroke survivor's heart.

We defined diabetes as a history of diabetes mellitus or treatment with oral hypoglycaemic agents or insulin. We did not perform electrocardiograms and we diagnosed angina and myocardial infarction on history, and atrial fibrillation on history or on examination of the pulse and auscultation of the heart. Peripheral

vascular disease was defined as a history of calf claudication, femoral artery bruits or both foot pulses absent on examination.

Previous alcohol or cigarette smoking use was defined as no use during the last year; while current use was defined as use of either within the last year.

Human immunodeficiency virus (HIV) infection has reached epidemic proportions in South Africa (Bradshaw et al., 2002) and HIV infection is associated with stroke (Connor et al., 2000; Mochan et al., 2003; Patel, Sacoor, Francis et al, 2005). Although we did not do any blood tests, at the end of the clinical examination we documented whether we had any reason to suspect HIV infection in the individual (appendix B). We considered a history of recurrent infections, recurrent diarrhoea, unexplained weight loss, or examination findings of oral candidiasis, generalised wasting, generalised lymphadenopathy, or HIV-related skin and hair disease as suggestive of HIV infection, particularly when we found these features in a young stroke survivor.

Finally, we asked stroke survivors or their carers whether they had sought assistance from health care providers or healers following the stroke including: clinics, hospitals, traditional healers, or church groups, and if relevant, which they had visited first. Where appropriate, we referred individuals to local clinics or hospitals with suggestions for secondary stroke prevention or management of other specific conditions.

## 3.4 Data analysis

We calculated the age specific prevalence of stroke survivors both according to the number of stroke survivors identified, and also with an adjustment factor to allow for the likely number of strokes among the individuals who screened positively but who we were not able to examine. For this calculation we assumed that the prevalence of stroke survivors in each 10-year age and sex stratum was the same amongst those examined and those not examined. We then calculated age-standardised prevalence in 10 year gender specific bands using the Segi standard population to enable comparison with published work, and with the new WHO standard population to permit comparison with future work in this area (Ahmad, Boschi-Pinto, Lopez et al, 2002). We used STATA software for the analyses including calculation of the confidence intervals for age-standardised prevalence (StataCorp, 2001). We calculated the 95% confidence intervals for crude stroke prevalence using Confidence Interval Analysis (CIA) software (Bryant, 2000).

## 3.5 Ethics

Ethics committee approval was granted by both the London School of Hygiene and Tropical Medicine (755) and the University of the Witwatersrand (M02-04-63) (appendix C).

## 3.6 Results

Figure 3.4 shows the screening process, the numbers of individuals examined and their diagnoses, both of stroke and other conditions.

### 3.6.1 Response rates

The population of the Agincourt subdistrict under health and demographic surveillance was 68,525 in 2001. Of these, 42,378 were 15 years of age or over. There were 982 positive responses to the screening questionnaire, and 724 (74%) of these individuals were examined (figure 3.4). Reasons for failure to examine were that people had moved away (39), died (37) or refused (2). In addition, we were unable to locate one person, 101 were migrant workers, and we were unable to make contact with 73 despite at least 3 attempts. In 5 cases the reason for failure to examine was not recorded.

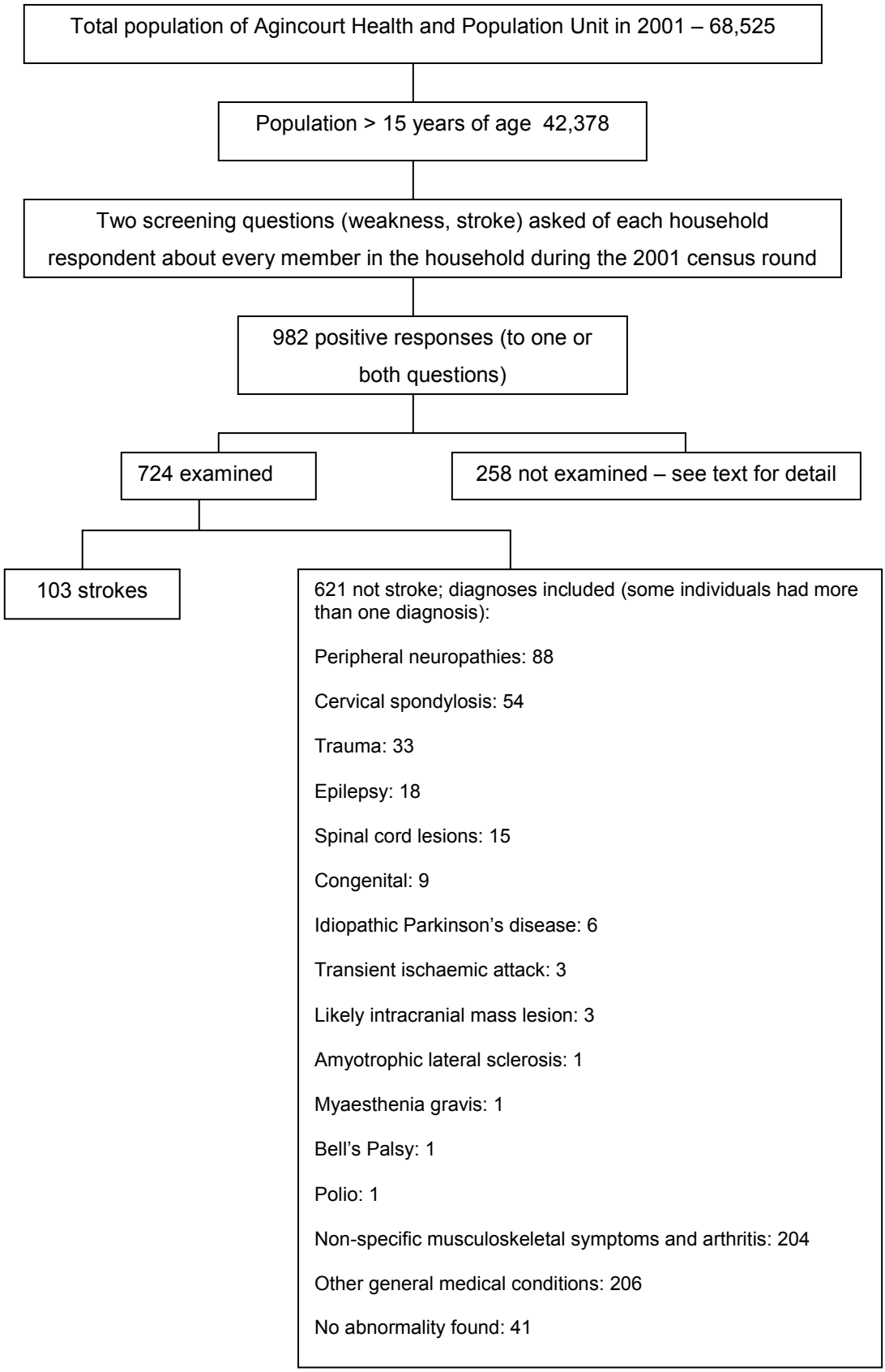



**Figure 3.4 Scheme of prevalence study outline including diagnoses in participants without stroke**

## Table 3.1. Prevalence of positive answers to the two screening questions, and prevalence of stroke survivors by sex and age

| | Population | Number +ve respondents (prevalence / 100 000) | Number (%) +ve respondents examined | Number of stroke survivors diagnosed | Prevalence of stroke survivors (95% CI) / 100 000 | Prevalence of stroke survivors (95% CI) adjusted for proportion not examined /100,000* |
|---|---|---|---|---|---|---|
| Total population >15 years | 42 378 | 982 (2 317) | 724 (74) | 103 | 243 (198 to 295) | 300 (250 to 357) |
| Males | 20 042 | 339 (1 691) | 213 (63) | 37 | 185 (130 to 255) | 246 (181 to 323) |
| Females | 22 336 | 643 (2 879) | 511 (79) | 66 | 296 (229 to 376) | 348 (276 to 436) |
| Age: 15-24 | 15 358 | 41 (267) | 32 (78) | 2 | 13 (2 to 47) | 16 (2 to 47) |
| 25-34 | 10 315 | 88 (853) | 50 (57) | 6 | 58 (21 to 127) | 83 (34 to 153) |
| 35-44 | 6 855 | 137 (1 999) | 75 (55) | 8 | 117 (50 to 230) | 170 (80 to 287) |
| 45-54 | 4 340 | 203 (4 677) | 155 (76) | 21 | 484 (300 to 740) | 598 (373 to 850) |
| 55-64 | 2 497 | 198 (7 930) | 150 (76) | 19 | 761 (458 to 1 188) | 945 (584 to 1 382) |
| 65-74 | 1 925 | 166 (8 623) | 136 (82) | 22 | 1 143 (716 to 1 730) | 1 349 (882 to 1 979) |
| 75-84 | 901 | 131 (14 539) | 112 (85) | 22 | 2 442 (1 530 to 3 697) | 2 796 (1,796 to 4 096) |
| ≥85 | 187 | 18 (9 626) | 14 (78) | 3 | 1 604 (331 to 4 688) | 1 961 (583 to 5 477) |

* calculated using the same proportion of stroke survivors diagnosed among those examined for each 10-year age-sex stratum

### 3.6.2 Prevalence of stroke

We identified a total of 103 cases of stroke, including six Mozambican refugees, giving a crude prevalence of 243 / 100 000 aged over 15 (table 3.1), 300 / 100 000 after adjustment for the individuals who screened positive but we did not examine.

Of the 103 stroke cases 62 had answered positively to both screening questions, 40 only to the question about weakness and 1 only to the question about whether they had ever had a stroke. The crude male to female ratio was 1:1.8. There was a steep age gradient (figure 3.5). Table 3.2 shows, after the adjustment for those we did not examine, the age-standardised prevalence using both the Segi (290 / 100 000) and the new WHO (330 / 100 000) standard populations. After age standardisation the male / female ratio was about one. Sixty-eight (66%) stroke survivors seen needed help with at least one activity of daily living, giving a Segi age-standardised prevalence of 200 / 100 000 over the age of 15 (table 3.2) when adjusted for those that we did not examine. (The age specific crude prevalence of disabling stroke not adjusted for those we did not examine is shown in the following chapter (table 4.5) and will be discussed under the section on disability and handicap – section 4.2)

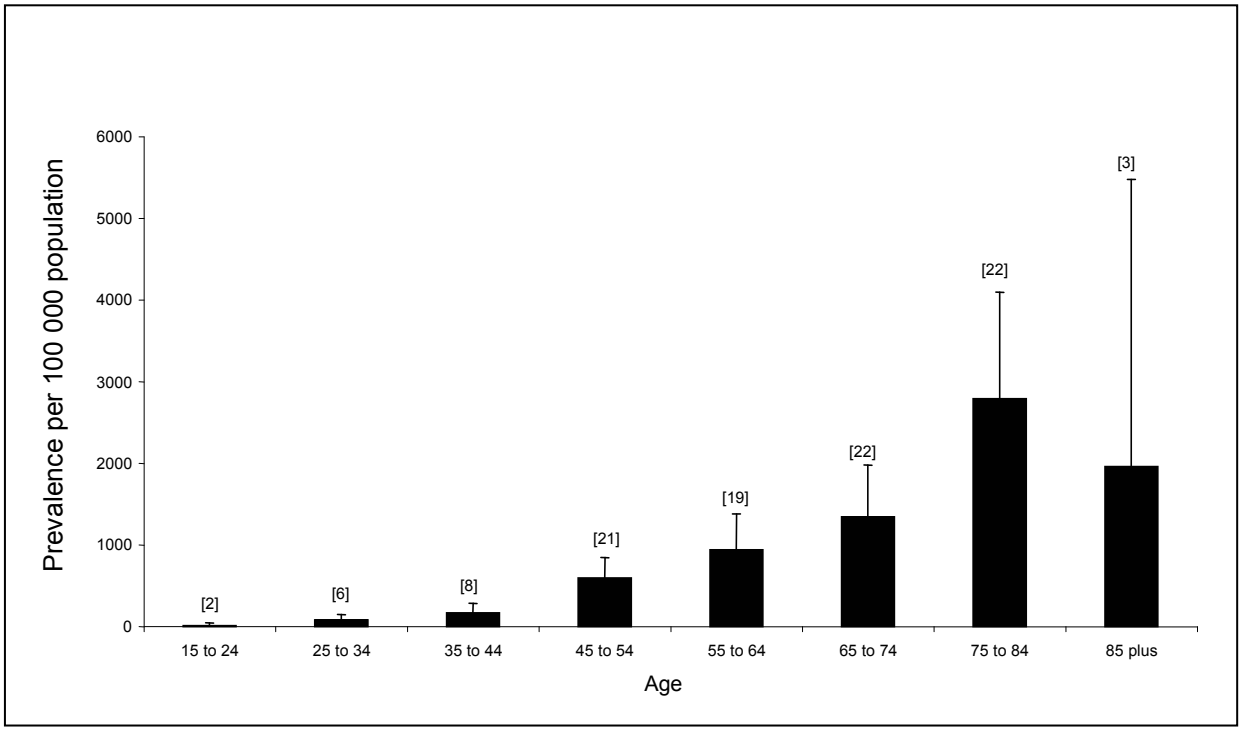



**Figure 3.5 Prevalence of stroke by age group adjusted for the proportion not examined.**
**(whiskers represent the upper 95% confidence interval and the number above the whisker is the number of stroke survivors in the age group)**

**Table 3.2. Age standardised prevalence of stroke survivors and of stroke survivors 'needing help with at least one activity of daily living' by sex, using both the Segi and the new WHO standard populations*.**

| | Population | Age standardised using Segi population (95% CI) / 100,000 | Age standardised using new WHO population (95% CI) / 100,000 |
|---|---|---|---|
| All stroke survivors: | Male | 281 (200 to 362) | 324 (232 to 416) |
| | Female | 315 (243 to 387) | 354 (275 to 434) |
| | **Total** | **290 (238 to 343)** | **330 (271 to 389)** |
| Stroke survivors needing help with at least one activity of daily living: | Male | 218 (145 to 291) | 247 (165 to 328) |
| | Female | 188 (132 to 243) | 221 (157 to 284) |
| | **Total** | **200 (156 to 244)** | **232 (182 to 282)** |

* using estimated prevalence of stroke survivors adjusted for proportion not examined

## 3.7 Discussion

### 3.7.1 Strengths and limitations of our study

Our study had an accurate denominator because it was based in a demographic surveillance site with rigorous annual census surveys. However, we were not able to examine every individual identified as a possible stroke from the screening questionnaire. We had to assume an equal stroke prevalence in those examined (74% of those screening positive were examined) and not-examined and then adjust the crude prevalence figures accordingly. Of course, as it would be anywhere else, diagnosing stroke sometimes long after the event, and without the benefit of CT, is difficult and can be inaccurate (Warlow, 1998). However, in this study clinicians were skilled in diagnosing stroke and conducted detailed assessments. We carefully reviewed and discussed all cases before we accepted a stroke diagnosis.

We do not know the sensitivity of the screening questions, since we did not have the resources to study a group who did not report either one-sided weakness or stroke. Furthermore, we do not know whether the screening questions missed posterior circulation strokes that did not present with typical ‘weakness down one side of the body’ as well as other strokes that did not involve long-term weakness e.g. speech loss, ataxia, isolated visuospatial problems, bilateral weakness, hemianopia, cortical blindness, retinal artery occlusion, isolated hemisensory lacunar strokes and amnesic syndromes. However, from the list of false positive diagnoses it is clear that many people with bilateral weakness or other forms of

neurological weakness answered yes to the question. Further, it is also possible that people with more unusual neurological manifestations sought medical help and may have been told that they had had a stroke and therefore answered that question. Certainly, we may have missed very mild strokes with symptoms that people had forgotten or that had not presented with weakness as a prominent manifestation.

Our finding that 102 of 103 people with stroke answered 'yes' to unilateral weakness at some time in their lives suggests that we missed stroke survivors who did not have significant weakness caused by their stroke and that we underestimated stroke prevalence. In an attempt to correct for this we assessed the proportion of patients in the Tintswalo (rural) Hospital Stroke Register (THSR) (chapter 7) and black stroke patients in the Johannesburg Hospital Stroke Register (JHSR)(chapter 5) without motor weakness (THSR: 6 (4%) of 135 patients and JHSR: 28 (9%) of 305 patients). We then assumed that these hospital data reflected the nature of stroke in the community (an unlikely assumption as previously discussed) and applied the corrections of between four and nine percent to our prevalent stroke data. We found that this increased our crude prevalence of stroke to: 250 per 100 000 (95% CI 205 to 303) using the rural THSR data and 264 (218 to 318) using the urban JHSR data. At most, therefore, we have underestimated the crude prevalence by 21 per 100 000 over the age of 15 years.

Many studies of stroke prevalence in high income countries have used a screening postal or telephonic questionnaire (O'Mahony, Dobson, Rodgers et al, 1995;

Geddes et al., 1996; O'Mahony, Thomson, Dobson et al, 1999), but this was not possible in our population because there is no postal or reliable telephone service. Stroke prevalence studies in general are limited, not only by the difficulty in diagnosing stroke long after the event, but also by accurate case finding and under representation of fatal cases and very minor strokes. As prevalence depends on incidence and case fatality, arguably the most accurate way of assessing stroke prevalence is from an incidence study with follow up of patients to assess case fatality (Warlow, 1998).

Despite these shortcomings and given the challenging environment in which the study was conducted, we believe this study design with an accurate denominator and extensive effort to achieve an accurate numerator represents a reasonable starting point in estimating the prevalence and nature of prevalent stroke in rural Sub-Saharan Africa. The problem of migrant labour, which had a large influence on our response rate is likely to be experienced in any similar setting in South Africa.

### 3.7.2 Comparison of our findings with other stroke prevalence studies

The age-standardised prevalence of stroke in high-income countries in a recent review of studies since 1990 ranged from 461 to 733 per 100 000 (Feigin et al., 2003b) for people aged 65 years or more. The largest of these came (Bonita et al., 1997) from Auckland, New Zealand where it was estimated that about 461 per 100 000 people aged over 15 years had made an incomplete recovery from a previous stroke, of whom 173 per 100 000 needed assistance with at least one self-care activity. The total age-standardised prevalence for the population aged 15 years and older was 833 per 100 000. While the age-standardised overall prevalence of stroke survivors adjusted for those we could not examine was much lower in our study (table 3.3), the prevalence of survivors needing help with at least one activity of daily living (200 / 100 000) was higher, and even higher than in Tanzania (Walker et al., 2000b). The *proportion* of stroke survivors who needed help with at least one activity of daily living was similar to that found in Tanzania (66% compared with 60%), both much higher than in New Zealand (22%). (Note: as described in 3.3. all three studies used the same definition of 'needing help with at least one activity of daily living.')

## Table 3.3. Comparison of age standardised rates (Segi population / 100,000) in three prevalence studies

| | New Zealand (Bonita, Solomon & Broad, 1997) | Tanzania (Walker, McLarty, Masuki, et al., 2000) | Agincourt (SASPI) |
|---|---|---|---|
| All stroke survivors | 833 | n/a | 290 |
| Males | 991 | 154 | 281 |
| Females | 706 | 114 | 315 |
| Male / female ratio | 1.4 | 1.4 | 0.9 |
| Stroke survivors 'needing help with at least one activity of daily living' | 173 | n/a | 200 |
| Males | 156 | 69 | 218 |
| Females | 188 | 90 | 188 |
| Male / female ratio | 0.8 | 0.8 | 1.2 |

n/a – not available

Note: The studies in Tanzania and South Africa (Agincourt - SASPI) used similar methodology to determine stroke prevalence i.e. screening questions asked of individuals during a census round in a demographic surveillance site, followed by clinical assessment of everyone who gave a positive answer. Stroke prevalence in Auckland was *calculated* using an actuarial model from two incidence studies conducted 10 years apart.

The lower prevalence of stroke in our population compared to Auckland, and other high-income countries (Feigin et al., 2003b), may reflect a lower incidence at this early stage of health transition, or a higher case fatality. Both are plausible, but there are no reliable population-based data on either incidence or case-fatality in Sub-Saharan Africa (section 2.3.2 and 2.3.3). Methodological differences must also account for some of the disparity. For example, in Auckland (Bonita et al., 1997) prevalence was modelled from the results of two incidence studies and therefore would have included very mild strokes that recovered completely. We must have missed some mild strokes that had recovered and strokes that did not cause hemiparesis. This would also have been a problem in the Tanzanian study (Walker et al., 2000b), which used similar methodology to find strokes, but would not have occurred in Auckland as all incident strokes were included. That we missed some mild strokes is further suggested by the higher proportion of all identified strokes who were dependent in our study, although the cultural interpretation of 'needing help with every day activities,' including even the interpretation of the specific questions about needing help with specific activities, must be highly variable. Another explanation is that inadequate care after stroke in our study area leaves more survivors disabled.

Our higher prevalence of stroke than in rural Tanzania might be explained by a higher case fatality in Tanzania. Some authors have pointed out that the methodology used in the Tanzanian study (Walker et al., 2000b) was likely to find people with residual hemiplegic impairment or disability rather than all prevalent strokes (Feigin, Lawes, Bennett et al, 2003a). Our screening questions asked about weakness and stroke at any time, while the Tanzanian study asked about a

history of stroke but **current** weakness. The prevalence of disabiling stroke in our study is, however, still two to three times higher than in the Tanzanian study; this difference is unlikely to be simply the result of the difference in the wording of the question in the two studies. Another possibility is that the rural South African population has been exposed to lifestyle risk factors for longer than the Tanzanians, is further along the health transition and so has a higher stroke incidence. Only population-based incidence studies will clear this up.

The stroke prevalence we found in Agincourt is much higher than has been found previously in other studies from Africa. This is likely to be because of differences in the diagnosis of stroke used and completeness of case ascertainment in the three smaller Nigerian studies described in section 2.2.4 (Osuntokun et al., 1982; Osuntokun et al., 1987; Longe et al., 1989). The very much lower crude prevalence of 15 per 100 000 found in Ethiopia in the mid-1980s may be the result of incomplete ascertainment of mild strokes, but it may also reflect a low stroke incidence in Ethiopia as suggested above for Tanzania.

There are very few studies that have investigated the prevalence of stroke in African-Americans, particularly in recent years (Gorelick, 1998). In older studies from the 1950s to 1970s the prevalence of stroke in African-Americans was consistently higher than in their white counterparts (Gillum, 1988; Gillum, Gorelick, & Cooper, 2003). In a household survey in Copiah County, Mississippi, neurologists examined all individuals who screened positive and identified 250 strokes. The prevalence of stroke was 1341 per 100 000 in African-American men and 1228 per 100 000 in African-American women. In a more recent study of self

reported stroke from the 1999 to 2001 National Health Interview Study, the age-adjusted prevalence of stroke in African-Americans over the age of 18 years was 366 per 100 000 in males, and 313 per 100 000 in females (unadjusted crude prevalence: 287 and 274 per 100 000 respectively) (McGruder, Malarcher, Antoine et al, 2004). These findings are closer to the typical figures seen in high income countries. Indeed, although the prevalence was significantly higher in African-Americans than in whites or Hispanic Individuals, it is lower than the range previously quoted for high income regions. Apart from other potential difficulties with case ascertainment in a self-reported survey, this is probably because the study excluded institutionalised stroke survivors.

African-Americans are considered to be further along the health transition than Africans living in Africa (Gillum, 1996b). The large burden of stroke seen in African-Americans may represent an inevitable level that South Africans are headed towards, if appropriate interventions are not set in place to prevent an increase in stroke risk factors.

The sex ratio of the survivors that we identified was different from that found in Tanzania and in New Zealand. Both of those studies found an overall male to female ratio of 1:1.4, declining to a ratio of 1:0.8 when only those survivors needing help with activities of daily living were considered (table 3.3). Indeed male stroke prevalence has consistently been higher than female prevalence in studies performed since 1990 in high income countries (Feigin et al., 2003a). By contrast, the overall sex ratio in our population was 1:0.9, and increased to 1:1.1 when only those needing help were considered (table 3.3). There is considerable labour

migration, predominantly in men, but these migrant labourers, are included in the local population denominator. They consider the region home, maintain their families by sending money home and usually return to use local health resources when too ill to work. We had a higher rate of 'non-contact' in men aged between 25 and 44 years (49 men, 54%) than in any other age and gender group. However, we adjusted our figures for each 10-year age strata and sex group to allow for those we had not examined, assuming the same proportion of stroke survivors as in those examined. Thus, we have assumed that there is the same proportion of stroke survivors in men in employment as amongst predominantly unemployed men. As a result, we have probably overestimated, rather than underestimated, prevalence of stroke in men.

## 3.8 Conclusion

The prevalence of stroke in the rural Agincourt Health and Population Unit in north-east South Africa is about a half to a third of that typically found in high income regions of the world and about double that found in Tanzania using similar methodology. Based on limited data, it is lower than stroke prevalence in African-Americans. However, the prevalence of stroke survivors 'needing help with more than one activity of daily living' is already at similar levels to that previously found in a high-income setting. Although, as in all prevalence studies, this study can only provide limited information on the burden of stroke in the region in the absence of data on the incidence and case fatality of stroke, it suggests that there is already a considerable burden of stroke, particularly disabling stroke, in the rural South African population. Further, if the theory of the health transition holds, then it is likely that this burden will increase as the population's exposure to vascular risk factors increases.

The prevalence we found, intermediate between that found in Tanzania and typical high income region prevalence figures, may suggest that rural South Africa is already further advanced along the health transition than Tanzania. Indeed South Africa may represent an 'early-adopter' region (see section 1.6) (Yusuf et al., 2001) within Sub-Saharan Africa. The high prevalence of stroke in African-Americans may represent a potential 'end-point' to which our population is headed in the absence of appropriate intervention to reduce risk factors for stroke.

### 3.8.1 What this study adds to the literature

This is the first community based study of stroke performed in South Africa. It is also the first stroke prevalence study and first rural stroke study to be performed in South Africa. While it is the second, large community based stroke prevalence study from Sub-Saharan Africa, our methodology attempted to ascertain the prevalence of all strokes and not only disabling stroke. Furthermore, our finding of a much higher prevalence of stroke (including disabling stroke) in South Africa compared to Tanzania emphasises the need for stroke epidemiology studies across Sub-Saharan Africa. Varying socioeconomic influences are likely to impact on risk factor profiles in different countries and influence their progression through the health transition. Single country studies of the burden of stroke, be they prevalence, incidence or mortality studies will not give a true representation of the diversity of Sub-Saharan Africa's population nor their health needs.

# CHAPTER 4 THE NATURE OF PREVALENT STROKE IN RURAL SOUTH AFRICA

## 4.0 Introduction

Chapter 3 described the prevalence of stroke in the rural population of the Agincourt Health and Population Unit in north-east South Africa. This chapter describes the characteristics of the stroke survivors identified, including the nature of their strokes (pathological stroke type, ischaemic stroke subtype, risk factors and causes), their use of secondary stroke prevention, and their health seeking behaviour.

The nature of prevalent stroke is seldom if ever reported. Prevalent strokes are usually assessed by self-reporting of individuals who have suffered a stroke, using postal or telephonic surveys (Aho et al., 1986; O'Mahony et al., 1995; Geddes et al., 1996), and the assessment of stroke type is likely to be inaccurate when based on self reported information. Even when studies have attempted to validate stroke type using hospital records this has seldom been successful for the majority of cases (Huang, Chiang, & Lee, 1997). Indeed, the assessment of stroke type, subtype, risk factors and causes, months and even years after the event is likely to be very inaccurate as stroke survivors and their family or caregivers will have forgotten the detail of what happened. Furthermore, survivors may have developed entirely new conditions unrelated to the original event, so confusing the clinical picture. Despite these potential short-comings, we decided to take a

detailed history and perform a detailed examination on the stroke survivors in our study. However, we considered it inappropriate to subject the stroke survivors to detailed investigations given the limited clinical yield in prevalent stroke cases. We then made every effort to assess the nature of their strokes in an attempt to add to the very limited data available on stroke in the community in Sub-Saharan Africa (section 2.2.4).

As a result of the limited data available on the nature of prevalent stroke (Osuntokun et al., 1982; Osuntokun et al., 1987; Longe et al., 1989; Tekle-Haimanot et al., 1990; Huang et al., 1997; Prencipe, Ferretti, Casini et al, 1997; O'Mahony et al., 1999; Nicoletti, Sofia, Giuffrida et al, 2000; Bermejo, Gabriel, Vega et al, 2001), we have compared our findings to the nature of stroke in Oxfordshire in the United Kingdom, using either the Oxfordshire Community Stroke Project (OCSP) (Sandercock et al., 1989; Bamford et al., 1991; Warlow et al., 2001) findings or those of the more recent Oxford Vascular Study (OXVASC) conducted in the same population twenty years later (Rothwell et al., 2004). We also compared our findings with those in African-American incident stroke patients in the Northern Manhattan stroke study (NMSS) or Greater Cincinnati / Kentucky Stroke Study (GCNKSS) (Broderick, Brott, Kothari et al, 1998; Sacco et al., 1998; White, Boden-Albala, Wang et al, 2005). The Rochester Study (Brown, Whisnant, Sicks et al, 1996; Petty, Brown, Jr., Whisnant et al, 1999; Feigin et al., 2003b), recognised as fulfilling ideal stroke incidence study criteria (Feigin et al., 2003b) consists predominantly of white Americans (96%) and does not include sufficient African-Americans to provide a comparison with our findings. We have also compared our findings to data on non-institutionalised African-Americans with

stroke from the 1999 to 2001 National Health Interview Survey of self reported stroke (McGruder et al., 2004) in the discussion section.

We described the methods for case finding and assessment of the 103 prevalent stroke cases in Chapter 3.

## 4.1 Results

The mean time from the onset of stroke to our assessment was 7.9 years (range 22 days to 56 years).

### 4.1.1 Pathological stroke types and subtypes

Table 4.1 shows the clinical assessment of stroke type and subtype and compares our findings with incident stroke cases in Oxfordshire in the United Kingdom and in African-Americans in Northern Manhattan in the United States of America. A higher proportion of our prevalent stroke survivors had cerebral haemorrhage than incident stroke patients had in both the UK population and African-Americans in the USA, but far fewer had ischaemic strokes. It is not surprising that we did not detect any subarachnoid haemorrhages as our screening questions would probably have missed this diagnosis unless it was associated with focal weakness. Even then we would probably have attributed it to one of the other two pathological stroke types – most likely to cerebral haemorrhage if we had been given a history of severe headache with neck stiffness at the onset. In nine cases, we could not reach consensus regarding the likely stroke type. We may have over-estimated cerebral haemorrhage, as ischaemic stroke may present with headache and less frequently even neckstiffness and seizures (Warlow et al., 2001). We would have been more likely to diagnose cerebral haemorrhage in the presence of these symptoms, particularly if the headache was severe. (See chapter 6 for further discussion on the accuracy of bedside diagnosis of pathological stroke type)

**Table 4.1 Comparison of pathological stroke type and subtype found in prevalent stroke cases in rural South Africa with incident stroke cases in the United Kingdom and African-Americans (all figures are number of participants with percentages in brackets)**

| Pathological stroke type: | Agincourt (SASPI) (n=103) | OXVASC (n=262 ) (Rothwell, et al., 2004) | NMSS* (1993 - 1996) (n=148) (Sacco, et al., 1998) |
|---|---|---|---|
| Cerebral haemorrhage | 31 (30) | 17 (7) | 21 (15) |
| Ischaemic stroke | 63 (61) | 223 (85) | 120 (81) |
| Subarachnoid haemorrhage | 0 (0) | 16 (6) | 6 (4) |
| Unsure | 9 (9) | 6 (2) | 0 (0) |

| OCSP classification of ischaemic stroke subtype: | Agincourt (SASPI) (n=63) | OCSP (n=543) (Bamford, et al., 1991) | NMSS* (1993 - 1997) (n=155) (White, et al., 2005) |
|---|---|---|---|
| Total anterior circulation syndrome | 4 (6) | 92 (17) | - |
| Partial anterior circulation syndrome | 22 (35) | 185 (34) | - |
| Lacunar syndrome | 30 (48) | 137 (25) | 33 (21) |
| Posterior circulation syndrome | 7 (11) | 129 (24) | - |

SASPI – Southern African Stroke Prevention Initiative; OXVASC - Oxford Vascular Study; OCSP – Oxfordshire Community Stroke Project; NMSS – Northern Manhattan Stroke Study

* Data for the NMSS are only for African-Americans. The NMSS did not classify stroke cases using the OCSP classification and only lacunar strokes overlap with the classification used.

While we found about twice as many lacunar strokes as were found in Oxfordshire or in Northern Manhattan African-Americans, we found a similar number of partial anterior circulation syndromes to the OCSP study. However, we found less than half the number of total anterior circulation and posterior circulation syndromes when compared to the OCSP study. We could only compare lacunar ischaemic stroke subtypes with the NMSS study because they did not use the OCSP classification, and the modified Stroke Data Bank classification (Kunitz et al., 1984; Foulkes, Wolf, Price et al, 1988) used in the NMSS only overlaps with the OCSP (Bamford et al., 1991) in the definition of lacunar stroke (table 4.1). Even in the lacunar stroke group there is a marked difference between the proportion of lacunar strokes in the OCSP (25%) and in whites in the NMSS (16%). This may represent the case mix in the NMSS e.g. milder lacunar strokes not detected, a true difference between the two populations or a difference in the diagnosis and classification of lacunar stroke. So the comparison of lacunar strokes between Agincourt and Oxfordshire, and the Northern Manhattan Study should probably be made with caution.

### 4.1.2 Risk factors in prevalent stroke cases

Table 4.2 shows the major risk factors associated with all strokes combined in our study population. Hypertension stands out as the dominant stroke risk factor in

## Table 4.2 Risk factors for stroke in our prevalent stroke population. Data are number of stroke survivors (%)

| | Male (n=37) | Female (n= 66) | Total (103) |
|---|---|---|---|
| *On history* | | | |
| Diabetes mellitus | 2 (5) | 10 (15) | 12 (12) |
| Symptoms of angina | 5 (14) | 6 (9) | 11 (11) |
| Current cigarette smoker | 8 (22) | 1 (2) | 9 (9) |
| Never smoker | 17 (46) | 62 (94) | 79 (77) |
| Currently drink alcohol | 11 (30) | 10 (15) | 21 (20) |
| *On Examination* | | | |
| Hypertensive* | 24 (65) | 49 (74) | 73 (71) |
| 'Any evidence of hypertension'† | 31 (84) | 56 (85) | 87 (85) |
| Carotid bruit | 1 (3) | 3 (5) | 4 (4) |
| Peripheral vascular disease | 2 (5) | 3 (5) | 5 (5) |

*Hypertension defined as: systolic blood pressure greater than 139 mmHg, or diastolic blood pressure greater than 89 mmHg, using the mean of two measurements, or if the stroke survivor was taking antihypertensive treatment

†'Any evidence of hypertension' defined as: all hypertensive individuals (above) plus those with evidence of hypertensive end organ damage or previous antihypertensive treatment

both men and women. Two blood pressure readings were available for 97 individuals. The mean systolic pressure was 158 mmHg (95% CI, 151 to 165 mmHg), and mean diastolic pressure was 92 mmHg (95% CI, 88 to 95 mmHg). Twenty eight (67%) women and 15 (33%) men (difference not significant) had a blood pressure ≥ 160 mmHg systolic or ≥ 95 mmHg diastolic. Eight stroke survivors were taking anti-hypertensive medication, but only one of them had a blood pressure within the normal range (BP 116/74 mmHg). The mean systolic blood pressure in these eight survivors on medication was 172 mmHg (95% CI, 147 to 198 mmHg), and mean diastolic pressure was 96 mmHg (95% CI, 86 to 107 mmHg). Diabetes mellitus was moderately frequent in woman but not in men.

Cigarrette smoking was not very frequent in the stroke survivors, nor had it ever been, particularly in women. Only six of the eight men who smoked did this daily and the mean daily consumption of cigarettes for the men was five (range 3 to 10). The use of snuff (inhaled tobacco) is more common in Agincourt particularly amongst woman, and we found 16 (16%) stroke survivors were current users of snuff at the time of our assessment (15 females and 1 male). There are conflicting findings from the limited number of reports on the effect of snuff use, ranging from increased risk of stroke death (Henley, Thun, Connell et al, 2005) to no effect on stroke risk (Asplund, 2001; Asplund, Nasic, Janlert et al, 2003). Most have studied the effect of oral not inhaled snuff use. While almost a third of men drank alcohol, half the number of women drank alcohol. It is almost impossible to quantify the amount of alcohol consumed. Even knowing the number of drinks consumed per day is not sufficient to calculate the amount of alcohol ingested, as so much of the

alcohol used is brewed at home in this area and is of varying strength (Greenhalgh, 2004).

Evidence suggesting large vessel atherosclerosis, namely symptoms of angina, carotid bruits and peripheral vascular disease, were not common (table 4.2) and no one gave a history of myocardial infarction. None of the stroke survivors gave a history of elevated cholesterol, eight gave a family history of stroke and none gave a history suggestive of prior transient ischaemic attack. No one had ever used recreational drugs.

#### 4.1.2.1 Risk factors associated with particular stroke types

Table 4.3 compares the frequency of both unmodifiable and modifiable risk factors associated with cerebral haemorrhage and ischaemic stroke. Although hypertension, male sex, a history of angina, current smoking and alcohol use appeared to be more common with cerebral haemorrhage, there was no statistically significant difference between the two groups. This may well be influenced by the difficulty in determining stroke type accurately and in determining risk factors that were relevant at the time the stroke occurred.

## Table 4.3. Presence of risk factors by type of stroke. Data are number of stroke survivors (%) unless otherwise specified

| Variable | Cerebral haemorrhage (n=31) | Ischaemic stroke (n=63) | Significance of difference |
|---|---|---|---|
| Mean age at first stroke (years) | 55 (SE 2.5) | 55 (SE 2.5) | |
| Male | 14 (45) | 19 (30) | p=0.2 |
| Hypertension | 25 (81) | 43 (68) | p=0.2 |
| 'Any evidence of hypertension'* | 27 (87) | 54 (86) | p=0.9 |
| Diabetes mellitus | 3 (10) | 9 (14) | p=0.5 |
| History of angina | 5 (16) | 5 (8) | p=0.2 |
| Current smoker | 5 (16) | 2 (3) | |
| Previous smoker | 5 (16) | 8 (12) | p=0.07 |
| Never smoked | 21 (68) | 52 (84) | |
| Currently uses alcohol | 10 (32) | 9 (14) | |
| Previous alcohol use | 6 (19) | 15 (24) | p=0.125 |
| Has never used alcohol | 15 (48) | 39 (62) | |

* see text for definition

**Table 4.4 A comparison between risk factors in prevalent stroke cases in Agincourt and incident stroke in the OXVASC study (Rothwell, et al., 2004) and in African-Americans in the Greater Cincinnati / Northern Kentucky Stroke Study (GCNKSS) (Kissela, et al., 2004) (Data are the number of patients (%) unless otherwise indicated)**

| Risk Factor | Agincourt (SASPI) (n = 103) | OXVASC (n = 262) | GCNKSS (n = 969) |
|---|---|---|---|
| Male | 37 (36) | 126 (48) | n/a |
| Mean age (SD) | 60.6 ± (16.5)* | 73.6 ± (11.9) | n/a |
| Mean systolic BP mmHg (95% CI) | 158 (151 to 165) | 148 (145 to 150) | n/a |
| Mean diastolic BP (95% CI) | 92 (88 to 95) | 82 (81 to 84) | n/a |
| Proportion with hypertension (see definition below)† | 73 (71) | 118 (46) | 661 (68) |
| Diabetes mellitus | 12 (12) | 25 (10) | 318 (33) |
| History of angina | 11 (11) | 32 (12) | n/a |
| Atrial fibrillation | 1 (1) | 44 (17) | 70 (7) |
| Current smoking | 9 (9) | 47 (18) | 257 (26) |
| Never smoker | 79 (77) | 117 (45) | n/a |
| Peripheral vascular disease | 5 (5) | 22 (9) | n/a |
| Previous myocardial infartion | 0 | 33 (13) | n/a |

* Age at time of stroke
** Mean age for a smaller data set of the African-American subgroup of NMS based on data published in (Di Tullio, et al., 1999); no other separate data on mean age available for the African-American subgroup
† Hypertension defined as: (1) Agincourt (SASPI) >139 / 89 mmHg or on antihypertensive treatment (2) OXVASC: ≥ 150 / 85 mmHg, and (3) hypertension noted on record review (no further detail provided)

#### 4.1.2.2 Comparison of risk factors with other stroke populations

Table 4.4 compares risk factors in our prevalent stroke population with risk factors found in the OXVASC study in the UK (Rothwell et al., 2004) and in African-Americans in the Greater Cincinnati / Kentucky Stroke Study (GCNKSS) (Kissela, Schneider, Kleindorfer et al, 2004). Although we have used the Northern Manhattan Stroke study for previous comparisons, there are no data published of all stroke (ischaemic and haemorrhagic) risk factors found in the NMS and so we used the GCNKSS data for this comparison.

The possible reasons for the lower proportion of men in our study to that found not only in the OXVASC study but in many other studies has been discussed in section 3.7.2. The mean age at the time of stroke in our study was considerably lower than that found in Oxfordshire. This is typical of low-income region population stroke studies, and is the result of both the population demographics with a younger population at risk (only 7% of our adult population was over the age of 65 years), and possibly to a lesser extent an increased incidence of stroke at younger ages in the population (table 2.2).

Both the mean systolic and diastolic blood pressure were 10 mmHg higher in the Agincourt population compared to the Oxfordshire population. This, together with the much higher proportion of hypertensive individuals in Agincourt again highlights the importance of hypertension as a risk factor in our study. However, the different definitions of hypertension used by the three studies should be noted. Our systolic blood pressure cut-off for hypertension was 10mmHg lower than the

OXVASC study and our diastolic blood pressure cut-off was 5 mmHg higher. This may have influenced the comparison, though it is unlikely to have accounted for anything near the 25% difference in the proportion with hypertension. It is not clear exactly how hypertension was defined in the GCNKSS (Kissela et al., 2004).

Diabetes mellitus, diagnosed on history or if the stroke survivor was on treatment in our study, on history or record review in OXVASC, or on nurse record review in GCNKSS, was about as frequent in Agincourt and Oxfordshire, but almost three times as common in African-Americans. In terms of large vessel atherosclerotic disease, a history of angina was about as common in Agincourt and Oxfordshire, though we must point out that it is very difficult obtaining a reliable history of angina in rural South Africa. None of the tools used to diagnose angina at the bedside or in epidemiological studies, such as the Rose Angina Questionnaire (Rose, 1962), have been validated in our population, and the prevalence of ischaemic heart disease remains low in rural areas (Walker & Sareli, 1997; Kahn et al., 1999b). We diagnosed angina when we were unsure whether the pain was of cardiac ischaemic origin based on the history, and so probably over-diagnosed angina. Peripheral arterial disease occurred infrequently and was about half as common as in Oxfordshire. This is particularly significant as we included asymptomatic patients with absent pulses or femoral bruits, and these patients were not included in the OXVASC study.

Atrial fibrillation was rare in our population, only occurring in one individual. In both African-Americans and particularly in whites in the OXVASC study, atrial fibrillation was far more frequent, possibly as a result of a higher prevalence of ischaemic

heart disease and the older age of both populations. Thirteen percent of stroke patients in the OXVASC study had had a previous myocardial infarction and in the ischaemic stroke subgroup of the GCNKSS 100 of 362 (28%) African-American patients had coronary artery disease in some form (coronary artery disease, myocardial infarction, or angina) though it is not clear exactly how this was defined (Schneider, Kissela, Woo et al, 2004). None of the stroke survivors in Agincourt had a history of myocardial infarction.

Our stroke survivors were far less likely to be current smokers or indeed ever to have smoked than either African-American stroke patients who were relatively heavy smokers and even Oxfordshire stroke patients. As mentioned previously (section 4.1.3), even when our stroke survivors did smoke this was not heavy.

### 4.1.3 Likely causes of the prevalent strokes

In the 31 stroke survivors that we diagnosed as having had a cerebral haemorrhage, hypertension was the only identifiable risk factor and deemed the most likely cause in 24 (77%). In one individual who did not have hypertension the stroke followed an alcohol binge which may be relevant, although the role of an alcohol binge as a cause of cerebral haemorrhage is controversial, as most case-control studies that have addressed the issue were subject to bias (van Gijn, 2001). In the remaining six, we could not determine a cause.

In the 63 stroke survivors with ischaemic stroke, 30 were found to have a lacunar syndrome. Of these, hypertension was the only relevant risk factor in 24

individuals (80%). Two of the 30 (7%) had diabetes mellitus without any other vascular risk factors or likely cause for the stroke. One individual had both diabetes mellitus and hypertension.

We found potential cardioembolic sources in five individuals with ischaemic stroke: 2 had valvular lesions, one of whom had been diagnosed at an academic hospital and was on warfarin (the only stroke survivor on anticoagulation), 2 had features of a dilated cardiomyopathy, and 1 had atrial fibrillation.

Three individuals gave histories suggestive of arterial dissection. Four strokes were associated with pregnancy or the puerperal period. Although we could not determine the mechanism of the stroke in this study, stroke has been associated with both pregnancy and the puerperal period in multiple ways including: cerebral venous thrombosis, paradoxical embolism and arterial dissection during labour (Mas & Lamy, 1998). Two people gave histories suggestive of migrainous stroke (Bousser & Welch, 2005).

#### 4.1.3.1 Human immunodeficiency virus in stroke survivors

Although we did not test the stroke survivors for human immunodeficiency virus (HIV) infection, we added a question at the end of the questionnaire which asked the examining clinician whether they had any reason to believe that the individual may have retroviral disease based on their history and examination findings (appendix B). We only suspected HIV infection in two individuals, one aged 26 and the other 42 years. Although HIV is often associated with intracranial space

occupying lesions which may present as stroke (Connor et al., 2000; Kumwenda, Mateyu, Kampondeni et al, 2005), in these two patients the deficit had not changed in 2 and 3 years respectively, making stroke the more likely diagnosis.

### 4.1.4 Disability and handicap in prevalent stroke cases

We assessed the prevalence of disabled stroke survivors who 'needed help with at least one activity of daily living' as described in section 3.3. The age standardised prevalence of disabling stroke was presented in table 3.2. Table 4.5 shows more detailed results for the age specific prevalence of disabling stroke. The prevalence of disabling stroke increases with age, with a marked increase over the age of 55 years and then again in the over 75 year old age groups. Of course it is unlikely that we were simply measuring stroke related disability, particularly in the elderly who are likely to suffer from other disabling conditions such as arthritis.

Figure 4.1 shows the percentage of males and females who required help with specific activities of daily living (ADL). Men had less impairment and disability than women using this assessment, though they were more likely to require help with transfer, climbing stairs and bathing. In both males and females incontinence was not common, but loss of independence in dressing, grooming and feeding was very common. It is difficult to know to what extent the pattern seen in figure 4.1 reflects cultural differences (Ali & Mulley, 1998) in the interpretation of 'needing help' with these specific activities or indeed reflects difficulties we may have had with the process of interpretation and understanding the response from the stroke survivor or their carer.

We used both the Barthel Index (Mahoney et al., 1965) and the modified Rankin scale (Rankin, 1957; Bamford et al., 1989) also known as the Oxford Handicap Scale, to assess disability and handicap in our stroke survivors.

## Table 4.5 Age specific crude prevalence of stroke survivors needing help with at least one activity of daily living (ADL), by sex (not adjusted for the proportion we did not examine)

| | Population | Number of stroke survivors needing help with ADL | Prevalence of stroke survivors needing help with ADL (95% CI) / 100 000 |
|---|---|---|---|
| Total population >15 years | 42 378 | 68 | 161 (125 to 203)* |
| Males | 20 042 | 27 | 135 (89 to 196) |
| Females | 22 336 | 41 | 184 (132 to 249) |
| Age: 15-24 | 15 358 | 1 | 7 (0 to 36) |
| 25-34 | 10 315 | 0 | 0 |
| 35-44 | 6 855 | 4 | 58 (16 to 149) |
| 45-54 | 4 340 | 9 | 207 (95 to 394) |
| 55-64 | 2 497 | 16 | 641 (366 to 1041) |
| 65-74 | 1 925 | 16 | 831 (475 to 1350) |
| 75-84 | 901 | 19 | 2109 (1270 to 3293) |
| ≥85 | 187 | 3 | 1604 (331 to 4688) |

* Age standardised (Segi World Population) prevalence (95% CI) per 100 000: 200 (100 to 200)

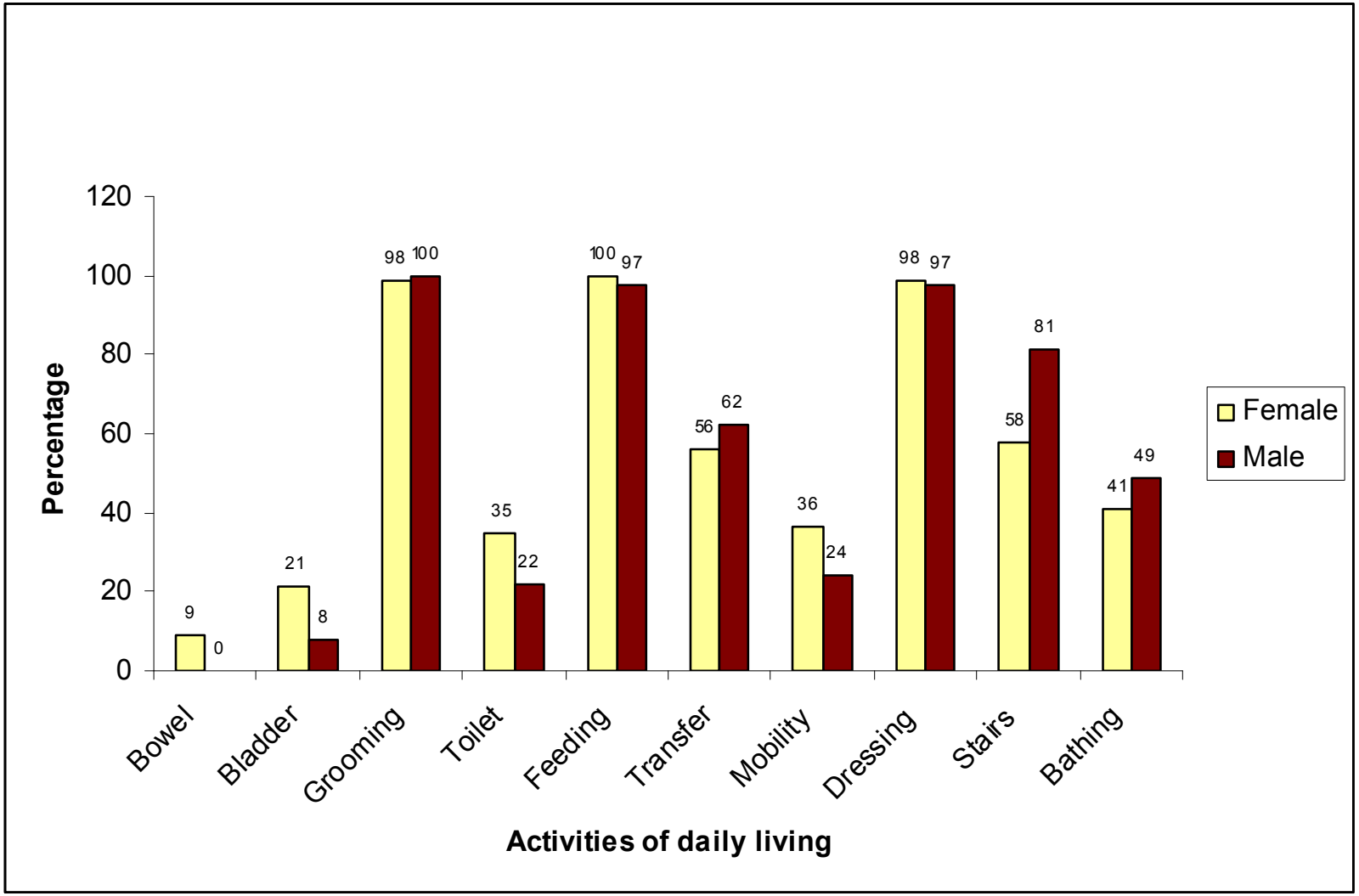



Figure 4.1 Percentage of male and female survivors requiring help with activities of daily living (actual percentages shown above the bars)

Although the Barthel Index is useful as a measure of disability and dependence in ADL, it does demonstrate a 'ceiling' effect (Dennis, 2001) and does not describe difficulties in key areas such as language. The modified Rankin scale, although designed as a measure of handicap, measures a combination of symptoms, dependency and change in lifestyle (Bamford et al., 1989; Dennis, 2001). It is often used as a measure of independence in everyday activities. A score of 0 to 2 is associated with independence.

To add to the profile of disability and handicap in our stroke survivors, table 4.6 provides further detail on the proportion of individuals with specific Barthel Index and modified Rankin scale scores, as well as specific disabilities that would interfere with function and independence. All but one of the stroke survivors (modified Rankin scale 3) had been independent at the time of their stroke. Although 68 (66%) individuals needed help with at least one activity of daily living (table 4.5 and figure 4.1), we only found 44 (43%) to be dependent using the modified Rankin scale. This is almost certainly the result of different interpretation of the measures, with the modified Rankin score providing a more 'global' assessment by the clinician than the individual items scored on the Barthel Index (used in our definition of 'needing help with at least one activity of daily living'). It was not surprising, given the screening questions used to ascertain cases, that motor weakness was very common.

## Table 4.6 The proportion (percentage) of stroke survivors with various measures of impairment and disability

| Scale / Impairment | n | Percentage of all stroke survivors |
|---|---|---|
| Barthel Index <20 | 75 | 73 |
| Barthel Index <15 | 38 | 37 |
| Barthel Index <10 | 19 | 19 |
| mRankin scale 0-2 | 59 | 57 |
| mRankin scale 3-5 | 44 | 43 |
| Decreased level of consciousness | 1 | 1 |
| Motor weakness | 96 | 93 |
| Unable to lift arm against gravity | 13 | 13 |
| Sensory deficit | 65 | 63 |
| Cerebellar signs | 5 | 5 |
| Dysarthria | 24 | 23 |
| Dysphasia | 13 | 13 |
| Dysphagia | 4 | 4 |
| Neglect | 9 | 9 |
| Visual field defect | 28 | 27 |
| Disorder of eye movement | 3 | 3 |
| Facial palsy | 70 | 68 |
| Urinary incontinence | 10 | 10 |

mRankin – modified Rankin score

The small proportion of patients with cerebellar signs and disorders of eye movement, in contrast to the large proportion with motor and sensory deficit, as well as facial palsy, is probably in keeping with the low frequency of posterior circulation syndromes we found. This may be a true reflection of the pattern of stroke in the region, but may also reflect insensitivity in our screening questions or perhaps some difference in outcome in patients in our area with posterior circulation strokes compared to other stroke subtypes.

Dysarthria was present in about a quarter of stroke survivors, but was only severe i.e. interfered with intelligibility of speech, in 6 (6%). Dysphasia was less common and was mild in half of those diagnosed with dysphasia i.e. only word finding difficulty, paraphasia or grammatical errors. Dysphagia was uncommon. This is probably not surprising given the remote nature of the area and limited medical facilities. It is unlikely that anyone with marked swallowing difficulty would survive very long both because of inadequate nutrition and the risk of aspiration pneumonia.

Visual field deficit occurred in almost a third of individuals which is just slightly less than the number of partial and total anterior circulation strokes identified i.e. the stroke subtypes in whom this finding would be most likely. Urinary incontinence was found in 10 individuals. This is somewhat surprising as we recorded 17 who complained of loss of continence using the Barthel Index. This difference is likely the result of the Barthel Index inclusion of ‘occasional accident’ as a form of ‘loss of continence’ while on our direct assessment of incontinence we only recorded complete loss of bladder continence.

We did not make any effort to formally assess the stroke survivors' cognition. None of the screening tools such as the Mini-Mental Status Examination (Folstein, Folstein, & McHugh, 1975) or Hodkinson Abbreviated Mental Test (Hodkinson, 1972) have been validated for use in Africa. Furthermore, by the start of the stroke prevalence study we already had experience in using the Hodkinson Abbreviated Mental Test in the pilot phase of the Johannesburg Hospital Stroke Register (chapter 5) and had found it almost impossible to use in our population.

### 4.1.5 Stroke related complications in prevalent stroke survivors

It is extremely difficult to be sure that associated findings in prevalent stroke cases are indeed complications of the stroke and not co-existent or new conditions that developed subsequent to the stroke. Despite this, we felt that four individuals had conditions that might be related to the stroke. These included: painful shoulder syndrome (2), thalamic pain syndrome (1), and dementia (1). The diagnosis of dementia was made after detailed discussion with relatives and assessment of the patient, as the currently available screening tools for dementia are not useful in rural South Africa (see section 4.1.4 above). In one individual who had Parkinsonism we were unable to tell whether this was related to vascular disease or some other cause.

### 4.1.6 Recurrent stroke

When assessing stroke survivors we focused on the history related to any first-ever stroke event. It is often difficult to decide whether a deterioration in weakness or other neurological symptom is indeed a recurrent stroke, or rather precipitated by another condition such as infection or seizure. For this reason it is best to concentrate on the first-ever-in-a-lifetime stroke events, both when 'counting' strokes for epidemiological studies, and when assessing the nature of strokes. Interestingly though, the pathological type of recurrent stroke is the same as the index stroke in most cases (Yamamoto & Bogousslavsky, 1997; Hankey, Jamrozik, Broadhurst et al, 1998).

We diagnosed 12 (12%) stroke survivors as having had recurrent strokes. In 7 this was a single recurrence and in 3 we thought the individuals had had more than one recurrence.

### 4.1.7 Use of medication for secondary prevention in stroke survivors

Eight of the 103 stroke survivors were taking blood pressure lowering medication when we assessed them, although a further 10 had been on treatment for hypertension at the time of the stroke. Thirty (29%) individuals had been on blood pressure lowering therapy at some point in their lives. One individual was taking daily aspirin, the only person taking antiplatelet therapy and no one was taking lipid lowering therapy. As mentioned in section 4.1.3, one stroke survivor with

valvular heart disease, who been admitted to an academic hospital in another province for their stroke, was taking warfarin.

### 4.1.8 Health seeking behaviour

Ninety-four stroke survivors (91%) had sought assistance from health care providers or healers following the stroke. Of these 10 (11%) said that they had only sought help from traditional healers, and 3 (3%) had only sought help from faith healers or church groups. Forty-two (45%) had only sought help from clinics or hospitals. The remainding 39 (41%) had sought help from both allopathic care and traditional or faith healers / church groups.

We asked where the stroke survivors or their care givers had sought help first. Unfortunately in retrospect this question was poorly worded. We received 78 responses: hospital or clinic first (49), traditional healer first (21), and church / faith healer first (8). It is thus not possible to assess whether these responses included all the individuals that had sought more than one source of assistance. It is clear from our findings, though, that 79% of stroke survivors had sought assistance from clinics or hospitals at some time following their stroke. This is valuable information in advising further health care planning and research in the area.

### 4.1.9 Home care

Fifty-seven (55%) of the 103 stroke survivors felt that they needed home care. Of these 53 (93%) had a carer available at home. In 17 cases (32%), the carer was the individual's partner.

## 4.2 Discussion

We based the assessment of pathological stroke type in our stroke survivors on our clinical assessment, as no CT scans were available. Using this approach we found cerebral haemorrhage to constitute almost a third of the pathological stroke types, roughly three times the number seem in the UK and double the number in African-Americans with incident strokes. We also found about twice the percentage of lacunar strokes in our stroke survivors as has been found in the UK or African-Americans. Hypertension was by far the most important risk factor in our stroke survivors. There was much less coronary artery disease and large vessel atherosclerotic disease (carotid bruits and peripheral vascular disease) than one would find in high income countries (Sandercock et al., 1989; Rothwell et al., 2004). We did not find many cardioembolic strokes or much evidence for HIV infection; although admittedly our assessment was based on our examination findings and we did not investigate directly for either.

It is important to emphasise that we almost certainly underestimated strokes without motor weakness (as highlighted in section 2.7.1). Similarly it is probably wise to interpret our large proportion of lacunar strokes compared to other studies with caution. Contrary to popular belief hypertension increases the risk of all subtypes of ischaemic stroke (Jackson & Sudlow, 2005a), and certainly the high prevalence in our population would not explain our finding of double the lacunar strokes found in other studies. This finding probably reflects the ascertainment bias towards strokes that caused long-term motor weakness as well as the

difficulty inherent in characterising the ischaemic stroke subtype at a point long after the stroke event.

We did not measure blood glucose because of resource limitations, and based our diagnosis of diabetes mellitus on a history of the condition or use of insulin or oral glucose-lowering agents. We did not assess body mass index (BMI), waist circumference, weight or height in stroke survivors. The relationship between obesity and stroke is likely to be confounded by several variables including hypertension, physical activity, smoking and indeed diabetes (Hankey, 2002). Since our study, however, abdominal obesity has been increasingly recognised as an independent risk factor for stroke (Hankey, 2006). At the time of our study we had several practical concerns related to the measurement of weight, height and waist circumference which we felt would impact on the stroke prevalence study as well as on other components of the SASPI (Southern African Stroke Prevention Initiative) study. Preliminary work in the Agincourt demographic surveillance site had suggested that individuals may not respond well to being measured. An earlier study in the site had run into difficulty when rumour spread that the researchers were providing undertakers with the measurements in order to prepare coffins, raising the concern that being measured implied imminent death. We planned to start the SASPI study of cardiovascular risk factors six months after the stroke prevalence study and these measurements were an integral part of the former study. SASPI anthropologists had not yet started their work on understanding local beliefs related to stroke and vascular risk factors at the time of the stroke prevalence study. We therefore decided not to include measures of weight, height and waist circumference in thes troke prevalence study.

As described in Chapter 1 (table 1.1), the health or epidemiologic transition theory provides a model for describing the shifts in disease patterns that occur in populations as they undergo industrialisation (Pearson, 1999; Bonita, 2001; Yusuf et al., 2001). It not only explains the shift from infectious to non-communicable disease, but also the changes in vascular disease patterns and the nature of stroke as the population moves through the transition. This may be an oversimplification, particularly given the rising burden of HIV infection in Sub-Saharan Africa, but it is useful to explain the development and evolution of vascular disease due to traditional vascular risk factors within a population. The profile of stroke in our population, with a high proportion of haemorrhagic stroke and lacunar stroke due to hypertension, the high prevalence of hypertension as a risk factor, the relative absence of extracranial atherosclerotic disease, and the young age of stroke occurrence would place the population in stage 2 of the health transition (table 1.1).

The levels of alcohol use amongst women and of cigarette smoking in men and women were particularly low and are likely to change. Twenty-six percent of African-American stroke patients smoke cigarettes (table 4.4). In a study of the prevalence of risk factors in the Agincourt community, we found the prevalence of cigarette smoking amongst males over the age of 35 years to be 31% (Thorogood, Connor, Tollman et al, 2005), and in a recent predominantly urban general practice study the prevalence of smoking in South African adult blacks was 59% (Connor, Rheeder, Bryer et al, 2005).

It was difficult to compare risk factors in our population with an African-American stroke population because of methodological differences and the limited available data on stroke risk factors in African-Americans (Gorelick, 1998). However, African-Americans have a much higher incidence of stroke than their white counterparts (Broderick et al., 1998; Sacco et al., 1998; Kissela et al., 2004). In terms of risk factors, African-American ischaemic stroke patients have a higher prevalence of hypertension and diabetes mellitus, a similar or slightly lower prevalence of coronary artery disease and a lower prevalence of atrial fibrillation (Sacco, Boden-Albala, Abel et al, 2001; Schneider et al., 2004) compared to whites. The proportions of various stroke risk factors in non-institutionalised African-American stroke survivors found in the National Health Interview Survey 1999 to 2001 (McGruder et al., 2004) are similar to those found in the GCNKSS. Hypertension was the most prevalent occurring in 79% of the approximately 800 stroke survivors. Diabetes mellitus was found in 32%, coronary heart disease (an affirmative answer to questions on myocardial infarction and coronary heart disease) in 29% and 26% were current smokers (all risk factors were self reported). Thus the risk factor profile found in African-Americans is in keeping with Gillum's (1996) modified health transition stage 4 and 5 (section 2.1.1). It is possible, or indeed likely, that without appropriate intervention, our population will end up with a similar vascular profile and high burden of stroke.

It remains surprising that we found so little rheumatic heart disease and dilated cardiomyopathy. We were only convinced of a potential cardioembolic source in five ischaemic stroke survivors. From the literature review (section 2.3.1.6) we expected to find cardioembolic stroke in around one fifth (much the same as in

high income regions) (Warlow et al., 2001), though not as a result of ischaemic heart disease but rather from rheumatic valvular heart disease and dilated cardiomyopathy (Gaziano, 2005; Sliwa, Damasceno, & Mayosi, 2005; Essop & Nkomo, 2005). Our findings may be the result of the lack of detailed investigation, and the fact that we saw patients often years after their stroke, or it may reflect inadequate access to health care services adversely affecting survival. In this remote area anticoagulation is seldom prescribed because of the difficulty monitoring blood levels. Indeed, only one of our stroke survivors was on warfarin and this had been initiated in another province.

South Africa has one of the highest HIV prevalence rates in the world. However, we found little evidence of HIV in our stroke survivors. This may be because we did not test HIV serology, but it may also be because the prevalence of HIV in the Limpopo Province (Agincourt was until recently a part of this province, now part of Mpumalanga) is known to be lower than the national average (Connolly, Shisana, Colvin et al, 2004; UNAIDS/WHO Working Group on global HIV/AIDS and STI surveillance, 2004).

We found a high prevalence of impairment and disability, whether we measured this using the 'needed help with at least one activity of daily living' definition, the closely related Barthel Index or by loss of independence using the modified Rankin score. A similar proportion of stroke survivors were dependent in Tanzania (60% compared to our 66%) (Walker et al., 2000b) using the 'needed help with at least one ADL' definition, compared to 22% of all prevalent strokes or one third of those who had made an incomplete recovery in New Zealand (Bonita et al., 1997). The

median score on the Barthel was the same in both our study and the study from Tanzania.

A stroke prevalence study in Newcastle, UK, that used a screening questionnaire and then door-to-door follow up of 76 stroke patients, found 71% were dependent using the Barthel Index (score < 20) compared to 73% in our study (O'Mahony et al., 1999). When they used the modified Rankin score of 3 – 5, 70% were dependent though in our study using this score only 43% were dependent. This difference may be methodological (Bamford et al., 1989).

While it is tempting to say that the high proportion of disabled strokes in our population is the result of poor health service delivery or more severe strokes in the population, it may well be that this is just the result of our methodology. Indeed, prevalence studies often tend to overestimate disability because they miss strokes in people that have made a good recovery or recovered completely and so over-emphasise the severe strokes (Bonita et al., 1997). As prevalence is influenced by incidence, case fatality (or duration that the person remains alive), and changes within age and sex strata of the population, the best estimates of prevalence come from an actuarial approach as used in the New Zealand study which was based on two stroke incidence studies with long term follow-up of survivors.

Twelve (12%) of our stroke survivors had had a recurrent stroke. Recurrent stroke usually constitutes about 25 to 30% of all stroke occurring in a population (Dennis, 2001; Hankey, 2005) so our finding seems a little low. This may reflect the nature

of stroke in the population. For example lacunar strokes, which were very prevalent in our population, have the lowest recurrence rate of ischaemic strokes, and large artery disease which was not common in our stroke survivors the highest, at least up to 30 days post-stroke (Lovett, Coull, & Rothwell, 2004). However, two stroke prevalence studies from India have commented on the proportion of recurrent stroke in their stroke survivors. They found a similar low proportion of recurrent stroke: 14 of 118 cases (12%) in Bombay (Bharucha, Bharucha, Bharucha et al, 1988) and 6 of 91 cases (7%) in rural Kashmir (Razdan, Koul, Motta et al, 1989). Possibly recurrent stroke is not as easy to diagnose in stroke prevalence studies were it is difficult enough to be sure of the first stroke diagnosis, and of course those with recurrent stroke are less likely to survive (Hankey et al., 1998), so influencing their prevalence in the community.

We found that alarmingly few stroke survivors were taking aspirin or blood pressure lowering medication following their stroke. Despite 79% having sought help from clinics or hospitals at some time for their stroke, only one person was taking daily aspirin, a medication which is theoretically available at all clinics as it is available on the South African primary health care essential drug list (National Department of Health (South Africa), 2003). Aspirin is also recommended by the South African Stroke Guidelines for the secondary prevention of stroke (Bothwell, Gatter, Van Rooyen et al, 2000). The study took place before the results of the PROGRESS study (PROGRESS collaborative group, 2001) could be put into practice in rural South Africa and we would not have expected many stroke survivors to be on blood pressure lowering therapy. However, this does not explain the high proportion of people with untreated hypertension. Indeed, although only

eight individuals were on antihypertensives, 30 had been on antihypertensives at some time in their life.

In another SASPI study, a team led by social anthropologist Professor Gillian Hundt saw a sample of our stroke survivors. The team found that there were several barriers to accessing care in the community. These barriers included: side effects of medication, inconsistent drug supply to clinics, costs of transport getting to clinics or hospitals (though health care itself is free at clinics), poor blood pressure monitoring equipment in clinics, and a perception that prolonged therapy for hypertension was not necessary (SASPI Project Team, 2004). Negative views about allopathic care were not a barrier to care.

We were not surprised that none of the stroke survivors were on cholesterol lowering medication. The BHF/MRC Heart Protection Study (Heart Protection Study Collaborative Group, 2002) had not yet been published and routine use of statin therapy as secondary prevention for stroke was unlikely to have been used at the time. Furthermore, given the generally low levels of cholesterol in this population, cholesterol lowering medication is seldom if ever used.

Anticoagulation with warfarin was also seldom used. We only found five stroke survivors with evidence of cardioembolic stroke and of these only one was on anticoagulation. It is possible that difficulty with controlling levels of anticoagulation results in under-prescribing of warfarin in the area, and may lead to an increase in cardioembolic stroke and even in stroke related death.

Prior to commencing the study we thought that people presenting with stroke in rural South Africa were likely to present to traditional healers. Our findings from this study, as well as related work done by the social anthropology team mentioned above, showed that individuals who developed stroke symptoms were likely to present to both allopathic medicine and either traditional medicine or faith healers and church groups, as people believed that the disease required 'double therapy' (SASPI Project Team, 2004; Hundt et al., 2004). This has important implications for future studies of stroke in the area as well as for the management of stroke patients. Given the poor level of blood pressure control and secondary prevention, there is an opportunity to educate health care providers about blood pressure and stroke management, including secondary prevention.

Finally, just over half our stroke survivors felt they needed a carer at home and in almost all cases this was available. We did not probe any deeper and cannot answer at what cost this care was provided. There are no social services in the area that would be able to provide care for anyone who has had a stroke. As such, families are forced to cope with their stroke survivors regardless of cost.

## 4.3 Conclusion

We found a pattern of stroke risk factors, types, subtypes, and causes that suggest that the rural South African population is in stage 2 of the health transition with a high proportion of probable cerebral haemorrhage and lacunar infarction and little clinical evidence of large vessel atherosclerotic disease. We did not find that HIV / AIDS played a major role in prevalent stroke, possibly reflecting the low prevalence in this area at the time of our study. Prevalent stroke resulted in a significant burden of disability. Despite the majority of stroke survivors having attended clinics and hospitals at some time following their stroke, blood pressure control was poor and use of secondary prevention for stroke almost non-existent.

### 4.3.1 What this study adds to the literature

This is the first data on the nature of prevalent stroke in South Africa and Sub-Saharan Africa. The study also provides: detailed information on the burden and nature of stroke related disability and impairment in rural South Africa; the first data on secondary prevention in rural South African stroke survivors; and data on the health seeking behaviour of individuals with stroke in rural South Africa. The findings provide evidence to support the theory of the health transition, and suggest that the nature of stroke does indeed change as a population progresses through the health transition. However, a more detailed community-based

assessment of incident strokes with imaging is required to clarify this, as well as to accurately document the nature of stroke in the region.

# CHAPTER 5 THE JOHANNESBURG HOSPITAL STROKE REGISTER (JHSR) – URBAN STROKE

## 5.0 Introduction

Hospital-based stroke registers do not accurately reflect stroke occurring in a community because there are many reasons why someone who has suffered a stroke may not be admitted to hospital. These include: early death before hospital admission, limited resources influencing the person's ability to get to hospital, and the pressures on the hospital service influencing admission criteria e.g. those with mild stroke being referred to outpatient clinics rather than admitted for investigation. Various other factors may influence the perceived advantage to hospital admission e.g. the elderly and disabled who are already in a nursing home or have care, someone with a very severe stroke who is unlikely to survive despite hospital care, and someone with a very mild stroke may not feel they need to seek medical help, or it may be perceived by their general practitioner, clinic or family that hospital admission is not required (Sudlow et al., 1996). As a result hospital-based stroke studies are more likely to include severe strokes and cerebral haemorrhages which have a more dramatic clinical presentation, than mild ischaemic strokes (section 2.3.1.1) (Bamford et al., 1986; Dennis et al., 1994).

However, despite these limitations, hospital-based registers are much cheaper and more practical to perform than community-based studies, provide useful

clinical and demographic data on the sort of patients being admitted, and give at least some idea of the current state of a local stroke service (Dennis, 2001). In countries such as South Africa, without community-based stroke incidence studies, hospital-based studies also provide the most detailed information on the nature of stroke (pathological stroke type, subtype, cause and risk factors) in the population; imperfect but at least a start.

Although I discussed the literature, including prospective hospital-based stroke registers from Sub-Saharan Africa in chapter 2, I will highlight more recent literature in the discussion section of this chapter.

### 5.0.1 South Africa – population demographics and socioeconomic factors

South Africa has a multiethnic population comprising: 37 205 700 (79%) black Africans (after this referred to as blacks), 4 379 800 (9%) whites, 4 148 800 (9%) coloureds (mixed race), and 1 153 900 (3%) Indian or Asians (Lehohla, 2005). The country's political history, in particular the apartheid regime between 1948 and 1994, has resulted in vast differences in the socioeconomic status, profile of disease, and access to health care between these population groups. The socioeconomic impact on the population has influenced the health and demographic transition in particularly the black and coloured population groups. The white population exhibits a disease profile typical of high-income regions elsewhere in the world, while the black population, particularly in rural areas, exhibits many characteristics of a population affected by infectious, perinatal and other disease typical of low-income regions (Kahn et al., 1999b; Bradshaw,

Groenewald, Laubscher et al, 2003). There are little data available on the impact of the demographic and health transition on South African blacks, although the low level of atherosclerotic disease, particularly ischaemic heart disease, in the black population has been well documented (Rossouw, Weich, Steyn et al, 1984; Walker et al., 1997; Walker, Walker, & Adam, 2002; Steyn, Sliwa, Hawken et al, 2005), and was confirmed in our prevalent stroke cases (chapter 4). These differences in the country's population groups are likely to impact on the nature of stroke, but none of the stroke registers previously performed in South Africa, or indeed in Sub-Saharan Africa, have compared stroke in different ethnic groups.

### 5.0.2 Aim of the Johannesburg Hospital Stroke Register (JHSR)

The aim of the JHSR was to audit the profile of stroke patients admitted to Johannesburg Hospital, including demographic and clinical characteristics, to provide data on the stroke types, subtypes, causes and risk factors seen in an urban South African population, and to compare the nature of stroke amongst the country's population groups. A further aim was to assess the stroke service at Johannesburg Hospital. We did not have much funding for this study and could not therefore influence the investigations performed or treatment of stroke patients, although of course they were all assessed by the stroke team which may have influenced their care. Largely the findings therefore represent and are to some extent limited by the routine care available at the Johannesburg Hospital during the study.

We hypothesised that there would be differences in the nature of stroke between population groups, and that these differences would be most marked between the black and white population groups given the available data on the prevalence of risk factors and based on the theory of the health transition.

Finally, we also thought the Johannesburg Hospital Stroke Register would provide us with experience in data collection form design and analysis, with a view to developing a stroke incidence study in South Africa.

## 5.1 Methods

### 5.1.1 Setting and population

The Johannesburg Hospital is a 1088 bed academic referral hospital (Gauteng Department of Health, 2005) that provides health care to predominantly indigent patients. Although it is a referral hospital, it also provides both primary and secondary level acute care to much of the population in Johannesburg (population 3.25 million) who do not have access to private health care (Gauteng Department of Health, 2005; Lehohla, 2005).

### 5.1.2 Case ascertainment and assessment

The Johannesburg Hospital Stroke Register (JHSR) included all cases of stroke admitted to Johannesburg Hospital, or which occurred while in hospital, over 23 months during two periods: from 1st July 2000 till 31st December 2000 and from 1st August 2001 till 31st December 2002.

The JHSR was well advertised around the hospital using posters in emergency wards, general wards and the casualty area, as well as at academic meetings. We identified all patients likely to have had a stroke using multiple overlapping sources. These included: referrals to the JHSR from both medical and nursing staff using a dedicated stroke team phone line with answering machine if the dedicated stroke assistant was not available; direct questioning of doctors and nurses in the emergency department, admission wards and medical wards about

admissions over the previous 24 hours; by reviewing ward admission books daily, and by daily reviewing of the files of patients who had died during the previous 24 hours.

After finding likely stroke patients, the stroke assistant informed the patient and / or their carers about the stroke register and asked for verbal permission for a doctor from the stroke team to assess them. The assistant also provided them with an information sheet about the stroke register in their language of choice (English, IsiXhosa, IsiZulu, Shangaan, Sesotho and Afrikaans available).

Clinicians from the University of the Witwatersrand, Division of Neurology, then assessed all patients in detail (the stroke team). Patients were included on the register if they had had a stroke within the last 3 months or if the stroke was the main reason for seeking medical assistance. Patients who had had their stroke more than six months previously were excluded even if the stroke was the main reason for their admission. Only individuals with first-ever-in-a-lifetime strokes were included.

The stroke team doctor on call for the day then took a full history, examined the individual and reviewed the medical notes and investigations. After confirming the stroke diagnosis, they then completed the JHSR questionnaire (Appendix D). I saw a large proportion of the cases entirely on my own, reviewed the majority of the remainder with the team member who had assessed the patient first, and reviewed the notes on all cases before we entered them onto the JHSR database.

I assigned a final diagnosis, stroke type and subtype. (See section 1.3 for a detailed account of my role in this study).

We documented the stroke patient's demographic details, a number of socioeconomic indicators such as education level and housing, their symptoms at onset of the stroke, known risk factors prior to the stroke (based on history from the patient or their carers), medication use and functional state prior to the stroke. Our examination focused on blood pressure at the time of our examination, the presence of any vascular disease including evidence of hypertensive end-organ damage affecting the heart and fundal vessels and any potential sources of emboli. We assessed the major neurological signs and the person's level of consciousness as well as the severity of the stroke using the National Institutes of Health Stroke Scale (National Institute of Neurological Disorders and Stroke, 2005) and the Scandinavian Stroke Scale (Scandinavian Stroke Study Group, 1985). We assessed the person's modified Rankin score (Rankin, 1957; Bamford et al., 1989) and Barthel score (Mahoney et al., 1965) as measures of their level of functioning and handicap. We documented the results of any investigations performed, any treatment provided, and any complications resulting from the stroke. Where possible we documented the person's length of stay, where they were discharged to, and any in hospital deaths. Unfortunately, given the enormous service load, rapid turn-over of admissions to the medical wards and our lack of resources we were not able to accurately document case fatality and discharge data in all cases.

We assessed the following risk factors: age, sex, hypertension (see definition below), diabetes mellitus (see definition below), cigarette smoking (current smoker, former smoker for more than one year, never smoked), alcohol consumption (never / hardly ever, ex-drinker for more than a year, current alcohol use), snuff use, ischaemic heart disease (defined as typical angina, symptoms of myocardial infarction accompanied by any signs of ischaemic heart disease on ECG, or clear ECG evidence of ischaemic heart disease), previous stroke or transient ischaemic attack (although we only included first-ever-in-a-lifetime strokes in the register), atrial fibrillation (confirmed on ECG) and family history of a first degree relative with a stroke.

#### 5.1.2.1 Other definitions used

We defined **stroke** according to the World Health Organisation (WHO) criteria as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, leading to death or lasting longer than 24 hours, with no apparent cause other than vascular " (Hatano, 1976a).

**First-ever-in-a-lifetime stroke** was defined as the first symptoms of a stroke ever experienced by the individual based on the history obtained from the individual or their care givers and any available medical records. It did not take into account the brain scan findings, so someone without a history of previous stroke but brain scan evidence of previous stroke would still be considered to have had a 'first-ever-in-a-lifetime' or 'first-ever' stroke.

**Transient ischaemic attack:** We defined transient ischaemic attack (TIA) as 'a clinical syndrome characterised by an acute loss of focal cerebral or monocular function with symptoms lasting less than 24 hours and which is thought to be due to inadequate cerebral or ocular blood supply as a result of low blood flow, arterial thrombosis or embolism associated with disease of the arteries, heart or blood' (Hankey & Warlow, 1994).

**Pathological stroke type:** We assessed the pathological stroke type after we reviewed the CT or MRI brain scan and classified the type as ischaemic stroke, cerebral haemorrhage or subarachnoid haemorrhage (see specific subarachnoid haemorrhage definition below). If no scan was available then the stroke type was coded as 'uncertain type.'

In patients who did not have a CT brain scan, we assigned the pathological stroke type based on the patient's clinical presentation alone. We were more likely to diagnose cerebral haemorrhage than ischaemic stroke if the person gave a history of severe headache, seizure or loss of consciousness at the onset, as these presentations are unusual in ischaemic stroke (Warlow et al., 2001). We diagnosed subarachnoid haemorrhage if the patient had a typical presentation of sudden very severe headache, associated with neck stiffness and characteristic lumbar puncture findings (though we anticipated all patients with subarachnoid haemorrhage would have a CT brain scan prior to lumbar puncture). **In all cases, we have noted when we have used our clinical assessment of pathological stroke rather than the far more accurate CT scan diagnosis (above).**

**Subarachnoid haemorrhage:** We diagnosed subarachnoid haemorrhage in patients who had a characteristic sudden severe headache with a positive CT brain scan or cerebrospinal fluid findings to support the diagnosis; *or* in patients who were unable to give a history who had a positive CT brain scan or a normal CT brain scan but with supportive cerebrospinal fluid abnormalities (Warlow et al., 2001).

**Ischaemic stroke subtype**

We classified ischaemic stroke subtypes according to the **Oxfordshire Community Stroke Project (OCSP) classification** as: total anterior circulation infarction, partial anterior circulation infarction, posterior circulation infarction or lacunar infarction, using the accepted clinical criteria (Bamford et al., 1991). The OCSP classification was based on the clinical assessment and not altered by the findings on brain scan, although we did document instances when the clinical classification differed from the brain scan findings.

We also used the **Trial of Org 10172 in Acute Stroke Treatment** trial (TOAST) classification to classify the strokes into five causal subtypes atherothromboembolic, cardioembolic, small vessel thrombotic (lacunar), other determined aetiology and undetermined cause (Adams, Jr. et al., 1993). However, instead of classifying those patients with more than one cause as 'undetermined' we classified them as having 'multiple causes' (Goldstein, Jones, Matchar et al, 2001).

The TOAST classification is dependent on detailed investigation of patients and even after these diagnostic tests have been performed about 15% of patients remain unclassified (Warlow et al., 2001). In our relatively low resource setting, we anticipated an even larger proportion of 'undetermined' strokes using this classification system. We therefore decided to assign our own **'most likely cause'** based on all the clinical assessment, brain imaging findings and available investigations.

**Ethnicity:** We defined someone's ethnicity based on their self-identified ethnic group assigned at time of admission to the hospital.

**Risk factors**:

**Historical risk factors:** We used this term to describe risk factors defined on a self-reported history from the patient or their carers.

**Hypertension:** We defined hypertension as current use of antihypertensive medication, a history of having been diagnosed as hypertensive by a doctor or nurse prior to the stroke, documented blood pressure of greater than or equal to 140 mmHg systolic or 90 mmHg diastolic prior to the stroke or more than one week following the stroke, or evidence of hypertensive heart disease on ECG (left ventricular hypertrophy as assessed using the Sokolow-Lyon index)(Sokolow & Lyon, 1949) or echocardiography.

**Diabetes mellitus:** We defined diabetes mellitus as current use of anti-diabetic drugs, a history of being diagnosed as diabetic by a doctor or clinic nurse prior to the stroke, documented non-fasting blood glucose of greater than 11.1 mmol/L or fasting blood glucose of greater than or equal to 7.0 mmol/L (both blood glucose values measured on admission).

**Peripheral vascular disease (PVD):** We defined peripheral vascular disease as intermittent calf claudication or absence of both foot pulses or presence of femoral bruits or having had peripheral vascular disease surgery.

### 5.1.3 Data analysis

We entered all questionnaires onto Microsoft Access 2002 SP3 and then analysed the data using STATA software (StataCorp, 2001). In some instances we calculated confidence intervals using Confidence Interval Analysis software (Bryant, 2000) as well as STATA (StataCorp, 2001). We assessed differences in patient characteristics, risk factors and investigations, between ethnic groups and by stroke pathological type and ischaemic stroke subtype, by $\chi^2$ test (for categorical variables) or analysis of variance (for continuous variables). We compared median values using the Wilcoxon test, and we used logistic regression to assess the influence of age on the risk of cerebral haemorrhage. We compared differences between all population groups and then between black and white patients in keeping with our *a priori* hypotheses. We considered a level of $p<0.05$ as statistically significant.

### 5.1.4 Ethics

Ethics approval for the study was granted by the University of the Witwatersrand Human Ethics Research Committee (M00/03/7).

## 5.2 Results

Five hundred and twenty-four patients were referred to the JHSR. We excluded 92 patients. Figure 5.1 shows the outline of the study and the reasons why we excluded the 92 patients. Very few patients referred had recurrent strokes or transient ischaemic attacks (TIA). These findings probably reflect admission practices and the pressure on acute medical beds. In other words, people with TIAs and recurrent stroke were less likely to be admitted than patients with a new (and probably more severe) stroke.

### 5.2.1 Characteristics of JHSR stroke patients

A total of 432 stroke patients were entered onto the JHSR; including 308 (71%) black, 76 (18%) white, 22 (5%) coloured and 26 (6%) Indian / Asian patients. Table 5.1 shows the main characteristics of JHSR stroke patients, categorised by population group and sex. Although there were slightly more females than males, the rounded male to female ratio was 1 for all but the coloured and Indian / Asian population groups which were the least represented. The difference may simply reflect the small numbers of patients included.

The mean age of stroke patients was 53 years (SD 16) (95% CI, 52 to 55). The ages ranged from 18 to 97 years, with a median age of 55 (95% CI, 52 to 56). Females were slightly older (mean 54 years) than men (53 years) but this difference was not significant (p=0.4). There was a significant difference in mean

age between population groups ($p<0.001$) but when we compared individual groups we only found a significant difference in age between whites (who were slightly older) and blacks ($p<0.001$) and whites and Indian / Asians ($p=0.04$).

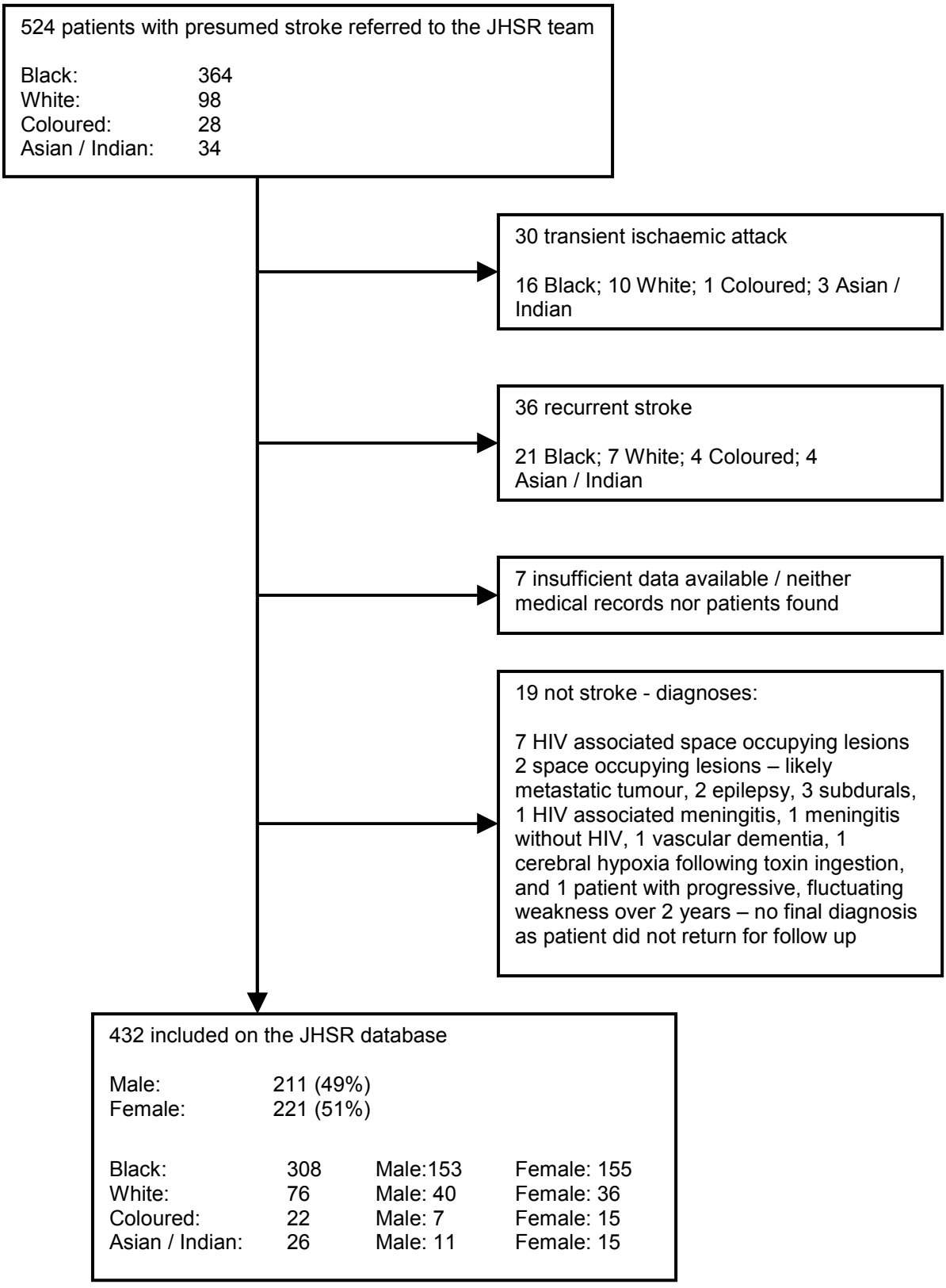



Figure 5.1 Study outline: cases included in the Johannesburg Hospital Stroke Register

**Table 5.1 Characteristics of the stroke patients in the Johannesburg Hospital Stroke Register, by population group**

| | Black | | White | | Coloured | | Indian / Asian | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | M | F |
| Strokes n | 153 | 155 | 40 | 36 | 7 | 15 | 11 | 15 | 211 | 221 |
| (ratio M:F) | 1.0 | | 1.0 | | 0.5 | | 0.7 | | 1.0 | |
| Age – mean (95% CI) | 51 (48 to 53) | 50 (49 to 54) | 58 (53 to 62) | 66 (61 to 71) | 64 (57 to 72) | 54 (41 to 66) | 55 (44 to 66) | 53 (43 to 64) | 52 (50 to 54) | 54 (52 to 56) |
| Age – mean (95% CI) both sexes | 51 (49 to 52) | | 61 (58 to 65) | | 58 (49 to 66) | | 54 (47 to 61) | | 53 (52 to 55) | |
| | p<0.001* | | | | | | | | | |
| Independent prior to stroke** (% of all with available data for population group) n = 315 | 213 (98%) | | 57 (95%) | | 17 (94%) | | 23 (100%) | | 310 (98%) | |
| | p=0.4 | | | | | | | | | |
| Mean time to presentation (days)(95% CI) n = 401 | 3.5 (2 to 5) | | 2 (1 to 3) | | 2 (1 to 4) | | 2 (0.5 to 3) | | 3 (2 to 4) | |
| | p=0.5* | | | | | | | | | |
| Median time to presentation (days) n=401 | 1 (1 to 1) | | 1 (0.5 to 1) | | 1 (0.5 to 2) | | 0.4 (0.25 to 1) | | 1 (1 to 1) | |
| Number who presented within 3 hours / total number with time to presentation data (%) n=401 | 32 / 285 (11%) | | 14 / 70 (20%) | | 1 / 21 (5%) | | 5 / 25 (20%) | | 53 / 401 (13%) | |
| | p=0.1 | | | | | | | | | |
| Number who presented within 6 hours / total number with time to presentation data (%) n=401 | 63 / 287 (22%) | | 19/ 70 (27%) | | 1 / 21 (5%) | | 9 / 25 (36%) | | 94 / 404 (23%) | |
| | p=0.06 | | | | | | | | | |
| Number scanned (% of all strokes in population group) | 207 (67%) | | 47 (62%) | | 16 (73%) | | 17 (65%) | | 287 (66%) | |
| | p=0.8 | | | | | | | | | |
| Number scanned within 24 hours of admission (% of those scanned) | 121 (59%) | | 29 (62%) | | 4 (25%) | | 13 (76%) | | 167 (58%) | |
| | p=0.02 | | | | | | | | | |
| Number scanned within 7 days of admission (% of those scanned) | 193 (92%) | | 41 (87%) | | 14 (88%) | | 14 (83%) | | 262 (91%) | |
| | p=0.3 | | | | | | | | | |

M-male F-female * Analysis of variance comparing mean age of population groups and mean time to presentation between population groups; ** Independent prior to stroke defined as a modified Rankin score of 0 to 2

We were unable to assess functional independence prior to stroke in all patients for the following reasons: in 5 cases the patient died before assessment, in 53 the history was not clear e.g. in aphasic patients and patients in whom we could not find reliable collateral information, and in a further 58 cases because these data were not recorded on our questionnaire. We assessed and recorded the level of functioning prior to stroke in 318 patients. The vast majority were independent (modified Rankin score of 0 to 2) prior to their stroke (98%) (table 5.1). We did not find any significant difference in the level of independence prior to stroke between population groups (p=0.4) or between male and female stroke patients (p=0.5).

We were able to assess the time from stroke onset to presentation to the emergency service at Johannesburg Hospital (or another hospital in patients who were later transferred to Johannesburg Hospital) in 401 patients. The range of time to presentation was wide. Although 13 strokes occurred in hospital, the time to presentation ranged from 1 hour to 120 days in those in whom the stroke did not occur in hospital. Figure 5.2 depicts the spread of times to presentation for each population group. Table 5.1 shows the mean time to presentation which was not significantly different between population groups (p=0.5) or between males and females (p=0.5). The median time from stroke onset to presentation was the same (1 day) for all population groups other than the Indian / Asian group in whom the median was 10 hours. The lower median in the Indian / Asian group compared to other groups may well be a reflection of the small number of strokes in this group.

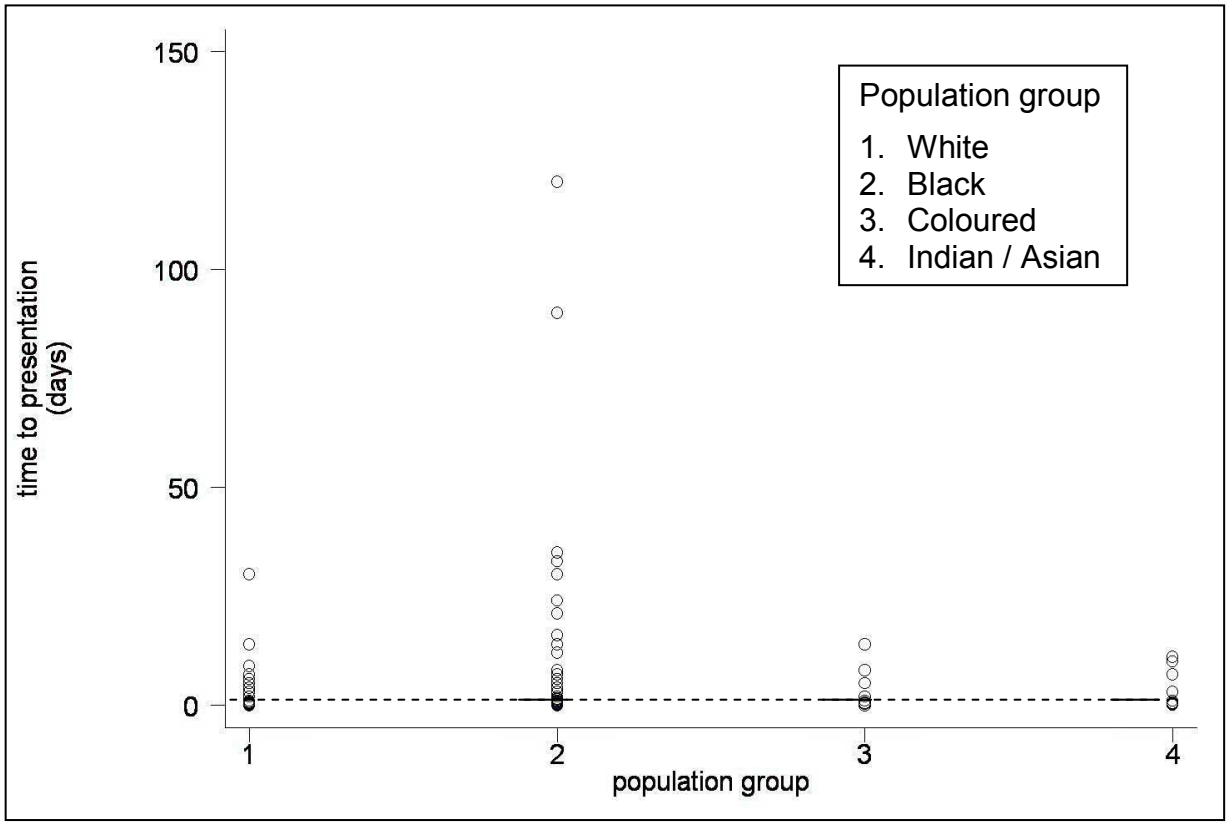



Figure 5.2 Distribution of time from stroke onset to presentation (days) by population group. Population group: 1 = white; 2 = black; 3= coloured; 4= Indian / Asian.
The median time from stroke onset to presentation for white, black, coloured and all patients combined (1 day) is indicated with a dashed horizontal line. The median was slightly lower for Asian / Indian patients (0.4 days)

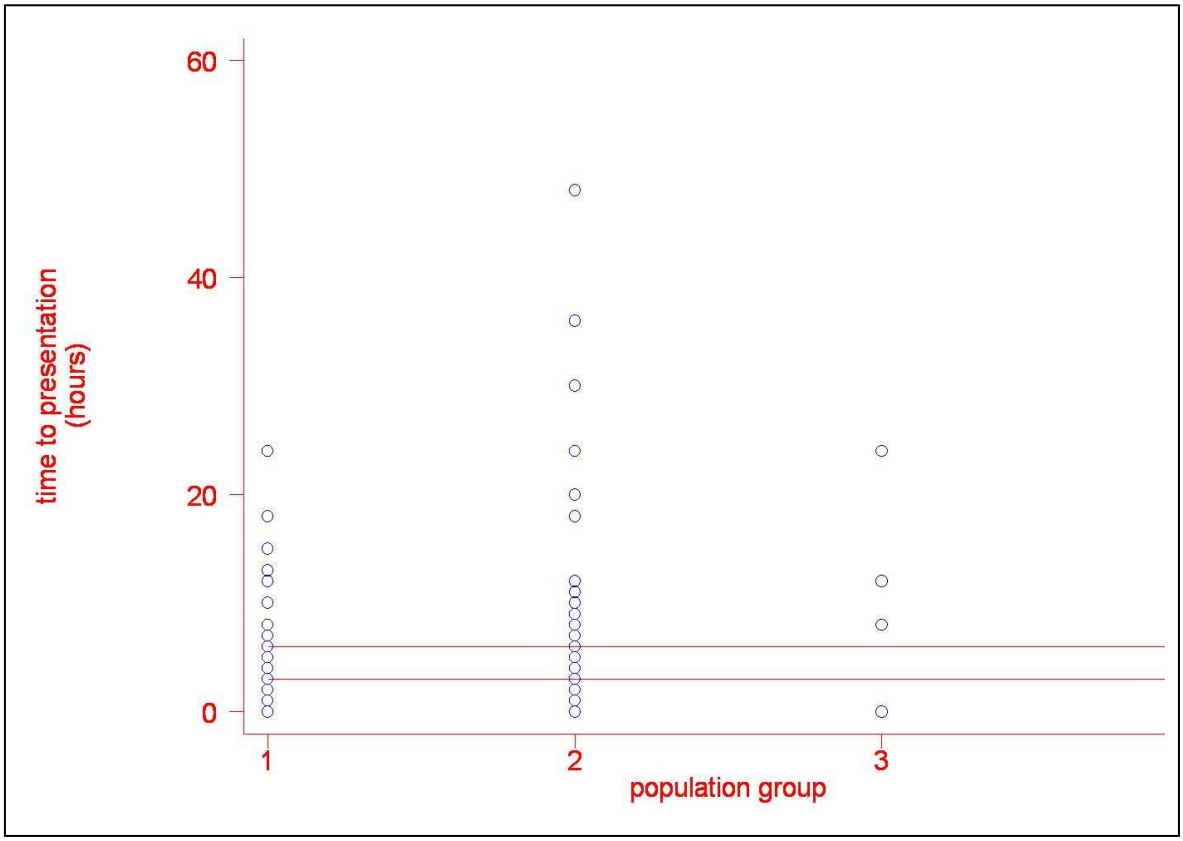



Figure 5.3 Distribution of time from stroke onset to presentation (hours) in those patients who presented to Johannesburg Hospital within 48 hours by population group. The 3 hour and 6 hour time lines are shown. Population group: 1 = white; 2 = black; 3= coloured; 4= Indian / Asian

As a number of stroke treatments are only available to patients who present within a narrow time-window, we have shown the proportion of patients who presented to the hospital within three and six hours of onset (table 5.1) (figure 5.3). Fifty-three (13%) of the 401 patients for whom we had accurate time to presentation data, presented within three hours of stroke onset. The proportion of patients who presented within three hours ranged between 5% in the coloured population (again possibly the result of the small number of strokes in this group) and 21% in the white population (table 5.1). However, there was no significant difference between population groups (p=0.9) or between males and females (p=0.5). The proportion of patients who presented within six hours of stroke onset increased to 23% with a range from 5% in the coloured population to 36% in the Indian / Asian population. There was no significant difference in the proportion who presented within six hours of stroke onset between population groups (p=0.06) or males and females (p=0.08).

Two hundred and eighty-seven patients (66%) had a CT brain scan. Only three patients had an MRI brain scan (<1%) which in all cases followed the CT brain scan. No population group (p=0.8) or sex (p=0.05) was more likely to have a CT brain scan, although more males (150, 71%) than females (137, 62%) had scans. In 167 (58%) of the patients scanned, the CT scan was done within 24 hours of presentation to hospital. Although blacks and whites, the two largest groups, had a similar percentage of scans performed within 24 hours, coloureds (25%) and Indian / Asians (72%) were at the extremes of likelihood to have a scan within 24 hours (p=0.02). The difference between males and females scanned within 24 hours was not significant (males: 89, 53%; females: 78, 47%) (p=0.7). Two-

hundred and sixty two (91%) of the 287 stroke patients scanned were scanned within 7 days of presentation to hospital. There was no significant difference in the number of patients scanned within 7 days and after 7 days between population groups (p=0.3) or males (137) and females (125) (p=0.6).

### 5.2.2 Pathological stroke types in the JHSR

Table 5.2 presents the proportion of pathological stroke types by population group and sex in those patients who had a CT brain scan. About a quarter of the strokes were cerebral haemorrhages. Cerebral haemorrhage was far more common in the black (27%) compared to the white (15%) and Indian / Asian (12%) population groups. The difference in pathological stroke type between all population groups (p=0.5) or between males and females (p=0.1) was not statistically significant. Surprisingly the difference between the black and white population groups was also not significant (p=0.2). Cerebral haemorrhage tends to be more common in younger rather than older stroke patients in community-based stroke studies (Marini et al., 2001) and we therefore repeated the comparison between white and black stroke patients adjusting for age. This did not alter the significance (p=0.62). However, when we included only those stroke patients known to be negative for HIV the difference was significant both with adjustment for age (p=0.03) and without (p=0.03). (See section 5.3.5.4 for further discussion on the impact of HIV on pathological stroke type). Ischaemic stroke constituted just under three-quarters of all strokes and was least common in the black population (68%); while subarachnoid haemorrhage (SAH) was not common in any group (6%).

Cerebral haemorrhage may be underestimated in stroke populations if imaging is done more than a few days after stroke (Sudlow et al., 1996; Keir, Wardlaw, & Warlow, 2002). Signs of cerebral haemorrhage may disappear on CT brain scan within 14 days or less if the haemorrhage is small (Dennis et al., 1987; Keir et al., 2002). We did not have data on how long the CT scan was performed from *stroke*

*onset*, but we did have data on the time to scan after admission. We recorded the time to scan after admission as: less than 24 hours, 24 to 48 hours, 48 to 72 hours, 3 to 7 days, and more than 7 days. Considering the median time to admission was 1 day following the stroke onset, and given the potential disappearance of cerebral haemorrhage on CT brain scan with increasing time from stroke onset, we analysed the pathological stroke types when the time to

## Table 5.2 Pathological stroke type in the JHSR by population group and sex (percentage of all scanned patients in the population and sex group shown in brackets)

| | Black | | | White | | | Coloured | | | Indian / Asian | | | Combined | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | T | M | F | T | M | F | T | M | F | T | M | F | T |
| Total number of patients scanned | 109 | 98 | **207** | 27 | 20 | **47** | 6 | 10 | **16** | 8 | 9 | **17** | 211 | 221 | **287** |
| **Pathological Stroke Type:** | | | | | | | | | | | | | | | |
| Cerebral Haemorrhage | 35 (32) | 20 (20) | **55 (27)** | 6 (22) | 1 (5) | **7 (15)** | 1 (17) | 3 (30) | **4 (25)** | 1 (13) | 1 (11) | **2 (12)** | 43 (29) | 25 (18) | **68 (24)** |
| Ischaemic stroke | 68 (62) | 73 (75) | **141 (68)** | 20 (74) | 16 (80) | **36 (77)** | 5 (83) | 7 (70) | **12 (75)** | 7 (88) | 7 (78) | **14 (82)** | 100 (67) | 103 (75) | **203 (71)** |
| Subarachnoid haemorrhage | 6 (6) | 5 (5) | **11 (5)** | 1 (4) | 3 (15) | **4 (9)** | 0 | 0 | **0** | 0 | 1 (11) | **1 (6)** | 7 (5) | 9 (7) | **16 (6)** |

M- male; F - female; T- total
We did not find a significant difference in stroke type between population groups (p=0.5) or males and females (p=0.1)

**Table 5.3 Pathological stroke type in the JHSR by population group, comparing patients who were scanned within 7 days of presentation to hospital (percentage of all scanned patients in the population group shown in brackets)**

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of patients scanned within 7 days | 195 | 43 | 14 | 14 | 266 |
| **Pathological Stroke Type:** | | | | | |
| Cerebral Haemorrhage n (%) | 54 (28) | 7 (16) | 3 (21) | 2 (14) | 66 (25) |
| Ischaemic stroke n (%) | 130 (67) | 32 (74) | 11 (79) | 11 (79) | 184 (69) |
| Subarachnoid haemorrhage n (%) | 11 (6) | 4 (9) | 0 | 1 (7) | 16 (6) |

No significant difference in pathological stroke type between population groups (p=0.5)

scan was within 7 days of admission to hospital (table 5.3). There was very little difference at all between the proportion of cerebral haemorrhage and other pathological stroke types in those patients scanned at any time and those scanned within 7 days of admission.

### 5.2.3 Ischaemic stroke subtypes in the JHSR

Table 5.4 presents the Oxfordshire Community Stroke Project (OCSP) classification of ischaemic stroke patients on the JHSR. The table only includes the 203 patients with ischaemic stroke confirmed on CT brain scan. The majority of these patients (36%) had partial anterior circulation infarcts (PACI) followed in frequency by lacunar infarction (LACI) (28%), total anterior circulation infarcts (TACI) (25%) and posterior circulation infarcts (POCI) (12%). Although there was no statistical difference in the ischaemic stroke subtypes found in the four population groups, the black population group had more LACIs (28%) and TACIs (28%) than their white counterparts who had 22% and 19% respectively (p=0.4). Both these groups had a similar proportion of POCIs (12% and 11%), while the white population had more PACIs (47% versus 32%). It is difficult to comment on the subtypes in the coloured and Indian / Asian population, as there were so few ischaemic strokes in each category.

There was a borderline statistically significant difference between the ischaemic stroke subtypes found in males (n=100) and females (n=103) (p=0.044). Women were more likely to have LACIs (32% vs 24%) and TACIs (27% vs 22%), and men

were more likely to have POCIs (18% vs 6%). A similar proportion had PACIs (36% vs 35%).

Table 5.5 shows the OCSP classification applied not only to the stroke patients with confirmed ischaemic stroke on CT, but also to those whom we presumed to have had an ischaemic stroke. Using these criteria we increased the number of eligible patients to 340. Again there was no statistically significant difference in the subtypes of ischaemic stroke between the population groups (p=0.98). Indeed in this comparison there was very little difference in the proportions of stroke subtypes seen in the four population groups, particularly the larger black and white groups. The difference between males (n=158) and females (n=182) remained (p=0.01). Both sexes now had similar proportions of LACIs (29% females and 30% males) and PACIs (36%), but as in the CT brain scan confirmed sample, females had far more TACIs (31% vs 20%) and males had more POCIs (13% vs 4%).

**Table 5.4 Ischaemic stroke subtypes (Oxfordshire Community Stroke Project classification) in patients with ischaemic stroke confirmed on CT brain scan by population group (percentage of all scanned strokes in the population group)***

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of ischaemic strokes** | 141 | 36 | 12 | 14 | 203 |
| **Pathological Stroke Type:** | | | | | |
| Total Anterior Circulation Infarction (TACI) n (%)* | 39 (28) | 7 (19) | 0 | 4 (29) | 50 (25) |
| Partial Anterior Circulation Infarction (PACI) n (%) | 45 (32) | 17 (47) | 5 (42) | 5 (36) | 72 (36) |
| Posterior Circulation Infarction (POCI) n (%) | 17 (12) | 4 (11) | 2 (17) | 1 (7) | 24 (12) |
| Lacunar Infarction (LACI) n (%) | 40 (28) | 8 (22) | 5 (42) | 4 (29) | 57 (28) |

** confirmed on CT brain scan
No significant difference in ischaemic stroke type between population groups (p=0.6)

**Table 5.5 Ischaemic stroke subtypes (Oxfordshire Community Stroke Project classification) in patients with presumed ischaemic stroke (CT confirmed or clinical diagnosis) by population group (percentage of all scanned strokes in the population group)***

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of ischaemic strokes by clinical assessment** | 235 | 65 | 18 | 22 | 340 |
| **Pathological Stroke Type:** | | | | | |
| Total Anterior Circulation Infarction (TACI) n (%)* | 62 (26) | 16 (25) | 5 (28) | 5 (23) | 88 (26) |
| Partial Anterior Circulation Infarction (PACI) n (%)* | 84 (36) | 23 (35) | 6 (33) | 9 (41) | 122 (36) |
| Posterior Circulation Infarction (POCI) n (%)* | 18 (8) | 8 (12) | 2 (11) | 1 (5) | 29 (9) |
| Lacunar Infarction (LACI) n (%)* | 71 (30) | 18 (28) | 5 (28) | 7 (32) | 101 (30) |

** confirmed on CT brain scan or presumed likely ischaemic
No significant difference in ischaemic stroke type between population groups (p=0.98)

### 5.2.4 Trial of ORG 10172 in Acute Stroke Therapy (TOAST) trial classification of stroke patients in the JHSR

Table 5.6 presents the findings by population group of the TOAST classification applied to our patients with CT brain scan confirmed ischaemic strokes. While there was no statistical difference between the clinical subtypes of ischaemic stroke when we compared all four population groups (section 5.2.3) most likely because of the small number of coloured and Asian / Indian patients, we did find a significant difference in the aetiopathological subtypes of ischaemic stroke using the TOAST classification. As we expected, many (36%) of the 203 eligible patients were not sufficiently investigated to allow us to determine the TOAST type and were therefore classified as 'undetermined.' Cardioembolic, lacunar and 'other' causes of stroke formed roughly the same proportion (17 to 19%), and a small proportion (4%) had atherothrombotic strokes.

## Table 5.6 TOAST Classification of ischaemic stroke by population group

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of patients with ischaemic stroke (confirmed with brain imaging) n | 141 | 36 | 12 | 14 | 203 |
| Atherothrombotic n (%)* | 0 | 5 (14) | 2 (17) | 1 (7) | 8 (4) |
| Cardioembolic n (%)* | 21 (15) | 11 (31) | 2 (17) | 5 (36) | 39 (19) |
| Lacunar n (%)* | 25 (18) | 6 (17) | 3 (25) | 2 (14) | 36 (18) |
| Other cause n (%)* | 24 (17) | 5 (14) | 2 (17) | 3 (21) | 34 (17) |
| Undetermined n (%)* | 61 (43) | 6 (17) | 3 (25) | 3 (21) | 73 (36) |
| Multiple possible causes n (%)* | 10 (7) | 3 (8) | 0 | 0 | 13 (6) |
| | Significance of difference between groups: p=0.002 | | | | |

* percentage of ischaemic strokes confirmed on CT brain scan

We distinguished 13 (6%) patients with multiple causes from the 'undetermined' group which is often used to categorise patients with more than one cause, to distinguish these patients who were investigated from the majority of the patients in the undetermined group who were not. Indeed only one of the patients in the undetermined group, a 44-year-old white female, had a complete workup and yet we could not find any determinable cause for her stroke.

Using the strict TOAST criteria, we classified far more black patients as 'undetermined' than any of the other population group. None of the black patients had an atherothrombotic stroke. Cardioembolic stroke was most frequent in the Indian / Asian and white populations. Lacunar stroke was most common in the coloured population and roughly equally as common in the white and black populations. We found other determined causes in roughly the same proportion of blacks, whites and coloureds, but slightly more often in Indian / Asian patients, although, as we have mentioned before the small numbers of strokes in the coloured and Indian / Asian groups make these comparisons inaccurate.

### 5.2.5 Causes of ischaemic strokes in the JHSR

#### 5.2.5.1 Analysis of ischaemic stroke using the 'most likely cause' approach

Using the TOAST classification criteria (Adams, Jr. et al., 1993) we were only able to assign an aetiopathological classification to 117 (27%) of all stroke patients. We therefore used a less rigid approach to assigning cause in an attempt to reduce the number of 'undetermined' and 'multiple cause' strokes. For this analysis we assigned patients a 'most likely cause' based on the clinical, CT scan and

investigation findings. In patients who did not have a CT brain scan, we assigned a cause if we thought the pathological stroke type was most likely ischaemic (as in table 5.5). In patients with multiple causes, we assigned the most likely primary cause.

Using this 'most likely cause' approach in the 340 eligible patients we reduced the number of undetermined causes to 67 (20%) of presumed ischaemic strokes (table 5.7). We could not agree on a primary cause in one patient classified as having multiple causes for their stroke. This was a 79-year-old white male who presented with a LACI clinically and on CT brain scan. He had a long history of hypertension, but also had atrial fibrillation, tight aortic stenosis and ischaemic heart disease.

Although the frequency of atherothrombotic stroke increased to 10% of the 340 patients with ischaemic stroke, it remained much lower in the black patients (6%) than the approximately 20% found in the other population groups. Cardioembolic stroke accounted for approximately 28% of strokes in whites, coloureds and Indian / Asian patients, and for slightly fewer black patients (24%). Lacunar strokes remained about as common in white and black patients (28% and 26%) using the 'most likely cause' approach, but 'other determined causes' were more common in the black and coloured population (23% and 22%) compared to the white and Indian / Asian population. The difference in subtype between population groups was significant (p=0.01), but we did not find a significant difference in 'most likely cause' subtypes between males (n=158) and females (n=182) (p=0.2).

**Table 5.7 Classification of ischaemic stroke using our 'most likely cause' approach in patients with presumed ischaemic stroke (CT confirmed or clinical diagnosis)* by population group**

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of patients with ischaemic stroke* n | 235 | 65 | 18 | 22 | 340 |
| Large vessel atherosclerosis n (%)** | 13 (6) | 13 (20) | 4 (22) | 5 (23) | 35 (10) |
| Cardioembolic n (%)** | 52 (21) | 18 (28) | 5 (28) | 6 (27) | 82 (24) |
| Small vessel (lacunar) (%)** | 60 (26) | 18 (28) | 3 (17) | 4 (18) | 85 (25) |
| Other cause n (%)** | 57 (24) | 6 (9) | 4 (22) | 3 (14) | 70 (21) |
| Undetermined n (%)** | 53 (23) | 9 (14) | 2 (11) | 4 (18) | 67 (20) |
| Multiple possible causes n (%)** | 0 | 1 (2) | 0 | 0 | 1 (<1) |
| | Significance of difference between groups: p=0.03 | | | | |

** percentage of ischaemic strokes

Although we were able to assign more patients to a likely cause using this analysis, our findings did not describe whether there were differences in the underlying cause for cardioembolic or lacunar strokes, and did not describe the 'other causes of stroke' in the four population groups. The nature and pattern of atherosclerotic disease in the patients assigned to the 'atherothrombotic cause' is also not clear. We will now describe each of these categories of ischaemic stroke in detail.

#### 5.2.5.2 Cardioembolic stroke

The proportion of patients with cardioembolic ischaemic stroke was similar in each of the population groups (table 5.7). However, the underlying cause of cardioembolic strokes differed between the groups (p=0.02). Table 5.8 presents the causes of cardioembolic strokes by population group.

Atrial fibrillation and cardiomyopathy together accounted for about two-thirds of cardioembolic causes of stroke, while ischaemic heart disease and valvular heart disease accounted for about 10% each. Notable differences between populations were the large proportion of whites with atrial fibrillation (65%) and ischaemic heart disease (30%) in contrast to the other groups. Indeed ischaemic heart disease was only found in 2 (4%) black patients with presumed cardioembolic stroke. Half of black and a quarter of coloured stroke patients had an underlying cardiomyopathy, while this cause was not found in the white and Indian / Asian populations. While dilated cardiomyopathy is a well accepted cause for

## Table 5.8 Cardioembolic strokes in the JHSR

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of patients with cardioembolic stroke (CT confirmed or clinical diagnosis) | 52* | 20* | 4* | 5* | 81* |
| Atrial fibrillation: Total (% of cardioembolic strokes) | 15 (29) | 13 (65) | 1 (25) | 2 (40) | 31(38) |
| - unknown cause | 6 | 7 | 0 | 2 | 15 |
| - with ischaemic heart disease | 1 | 4 | 0 | 0 | 5 |
| - with valvular heart disease | 2 | 1 | 0 | 0 | 3 |
| - with dilated cardiomyopathy | 0 | 1 | 0 | 0 | 1 |
| - with hypertensive heart disease | 6 | 0 | 1 | 0 | 7 |
| Ischaemic heart disease: Total (% of cardioembolic strokes) | 2 (4) | 6 (30) | 0 | 0 | 8 (10) |
| - following acute myocardial infarction | 1 | 1 | 0 | 0 | 3 |
| - IHD with atrial fibrillation | 1 | 4 | 0 | 0 | 5 |
| - IHD with dyskinetic segment on echocardiography | 0 | 1 | 0 | 0 | 0 |
| Valvular heart disease: Total (% of cardioembolic strokes) | 9 (17) | 2 (10) | 1 (25) | 2 (40) | 14 (17) |
| - unknown cause | 1 | 0 | 0 | 0 | 1 |
| - rheumatic valvular disease | 6 | 1 | 1 | 2 | 10 |
| - associated with dilated cardiomyopathy | 2 | 1 | 0 | 0 | 3 |
| Cardiomyopathy: Total (% of cardioembolic strokes) | 27 (52) | 0 | 1 (25) | 0 | 28 (35) |
| - dilated | 10 | 0 | 1 | 0 | 11 |
| - associated with hypertensive heart disease** | 17 | 0 | 0 | 0 | 17 |
| Infective endocarditis (% of cardioembolic strokes) | 0 | 1 | 1 | 1 | 3 (4) |
| Other (% of cardioembolic strokes) | 0 | 1† | 0 | 0 | 1(1) |
| Unknown** (% of cardioembolic strokes) | 0 | 1 | 0 | 0 | 1 (1) |
| Significance of difference between groups: p=0.02 | | | | | |

* NB subtotals and percentages do not add up to combined total as some causes are repeated
** See text for detail on this category (section 5.2.5.2)
† This cardioembolic event occurred intra-operatively during aortic valve replacement / aortic aneurysm repair

cardioembolic stroke, the role of hypertensive heart disease (HTHD) is controversial. Patients were only included in this category if they had evidence (clinical or echocardiographic) of heart failure associated with HTHD. However, 6 black patients and one coloured patient had HTHD and atrial fibrillation. Patients did not need to have evidence of heart failure for inclusion in this group. We will discuss the controversies regarding the role of hypertensive heart disease in causing stroke in section 5.3.4.

Three patients had strokes caused by infective endocarditis, and one had a stroke noted immediately following surgery for aortic valve replacement and repair of an aortic aneurysm. We included in the 'unknown' group a 73-year-old white male who presented with a first-ever-in-a-lifetime right PACI. He was a previous smoker and currently used alcohol excessively. He gave a history of a recent transient ischaemic attack. However, the CT brain scan showed recent cortical infarctions involving the left middle cerebral artery territory and left occipital cortex, as well as one infarct involving the right cerebellum. He was lost to follow up before investigations were completed. Given the multiple territories involved with large vessel strokes we felt that a cardiac cause was most likely, but we acknowledge that other causes such as aortic atherosclerosis are still possible.

#### 5.2.5.3 Large vessel atherosclerosis in the JHSR patients

Black patients were much less likely to have atherothrombotic / large vessel atherosclerotic causes of stroke than the other population groups. None of the black patients with CT confirmed ischaemic strokes had atherothrombotic strokes

when we used the strict TOAST classification definition. When we used our 'most likely' cause approach, 13 (6% of 235) black patients had large vessel atherosclerotic strokes. Whites, coloureds and Indian / Asian patients had a similar, higher, proportion (20 to 23%) using the latter approach.

Few of the 432 stroke patients in the JHSR underwent detailed investigation for atherosclerosis. In total 23 patients had carotid Dopplers, 21 angiograms and no one had an MR angiogram. It is thus difficult to describe the pattern of atherosclerosis in our study population. However, there were a few interesting findings which provided some insight into the differences in large vessel atherosclerosis between population groups.

Of the 35 patients classified as having atherothrombotic strokes: 3 had carotid bruits (2 Indian / Asian and 1 white); 8 had carotid artery stenosis on Doppler (6 white, 1 coloured and 1 Indian / Asian); and 3 had extracranial atherosclerosis on angiogram (2 whites and 1 coloured). Sixteen (5%) of 340 patients with likely ischaemic strokes had peripheral artery disease (9 blacks, 2 whites, 3 coloureds and 2 Indian / Asians) and 19 (6%) had ischaemic heart disease (6 blacks, 12 whites, 1 coloured and no Indian / Asian). Therefore, while the black stroke population did infrequently have evidence of ischaemic heart disease and peripheral vascular disease, none of them had evidence of extracranial atherosclerotic disease, although admittedly few patients were adequately investigated.

#### 5.2.5.4 Lacunar (small vessel) strokes

We found 85 lacunar strokes in 340 patients with presumed ischaemic stroke. Table 5.9 outlines the frequency of hypertension, diabetes mellitus and the combination in patients with lacunar strokes. We did not find a significant difference in the frequency of hypertension (p=0.8) or diabetes (p=0.3) between population groups in those who had lacunar strokes. Two white and four black patients had no significant risk factors or cause for their lacunar stroke.

#### 5.2.5.5 Other determined causes of ischaemic stroke in the JHSR

Sixty-five of the 340 patients with presumed ischaemic strokes had specific conditions which were likely to have caused their stroke. The vast majority occurred in black patients (52). Thirty-eight (73%) of the 52 black patients classified in this group were HIV positive. In these 38 patients, HIV seropositivity was the only identifiable disease in 26 patients. In the remaining 12 patients, HIV seropositivity was associated with: carotid artery dissection in 1, internal carotid artery occlusion of unknown cause in 2 (with no evidence of atherosclerosis in the remainder of the arteries), cerebrospinal fluid features compatible with tuberculous meningitis in 2, cryptococcal meningitis in 1, venous stroke during pregnancy in a patient with a CD 4 count of 92 x $10^6$/L in 1, elevated CSF protein and hypertensive heart disease in 1, elevated CSF protein and a tuberculous pleural effusion in 1, pulmonary tuberculosis in 1, and incomplete investigation as a result of early death in 2.

**Table 5.9 Frequency of hypertension and diabetes mellitus in patients presenting with lacunar stroke* (n followed by percentage of lacunar strokes in brackets)**

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Number of lacunar strokes* | 60 | 18 | 3 | 4 | 85 |
| Hypertension without diabetes mellitus | 47 (72) | 11 (61) | 2 (67) | 3 (75) | 63 (70) |
| Diabetes mellitus without hypertension | 2 (3) | 1 (6) | 0 | 1 (25) | 4 (4) |
| Both hypertension and diabetes mellitus | 7 (11) | 4 (22) | 1 (33) | 0 | 12 (13) |
| Neither hypertension or diabetes mellitus | 4 (10) | 2 (11) | 0 | 0 | 6(9) |

* diagnosed using combined CT brain and clinical 'most likely' diagnosis

Of the 6 white patients with an 'other determined' cause: 3 had an arterial dissection, 1 had temporal arteritis, and 1 was HIV seropositive without any other associated illness or abnormal findings. Of the 4 coloured patients in this category: 1 had a migrainous stroke, 1 had a post-partum cerebral venous thrombosis, 1 had a middle cerebral artery aneurysm in the appropriate site to explain her stroke, perhaps as a result of distal embolisation of thrombus, and 1 patient was HIV seropostive with no associated disease. Two Indian / Asian patients had cerebral venous thrombosis: one occurred post-partum, and the other had systemic lupus arthritis with associated vasculopathy.

### 5.2.6 Causes of cerebral haemorrhages in the JHSR

Sixty-eight (24%) of the 287 JHSR patients who had a CT brain scan had a cerebral haemorrhage. Table 5.10 shows cause of the cerebral haemorrhage for each population group. We assigned a cause based on the CT appearance and clinical findings e.g. of thrombocytopenia. Hypertension was by far the most likely cause for the stroke occurring in 79% of all cerebral haemorrhages and over 80% of cerebral haemorrhages in the black population. Thrombocytopenia occurred in a patient with leukaemia (platelet count 29 x $10^9$/Ll) and another patient with eclampsia who had a platelet count of 67 x $10^9$/L. A presumptive diagnosis of amyloid angiopathy was made in two coloured women one aged 76 and the other 56 based on CT brain appearance of lobar haemorrhage and the lack of any other likely cause (although one had evidence of left ventricular hypertrophy on echocardiogram). We accept that this is far from ideal, particularly in the younger patient. The 'other' category (table 5.10) included a 65-year-old patient who was

## Table 5.10 Causes of cerebral haemorrhage and subarachnoid haemorrhage by population group (only CT confirmed cases of cerebral haemorrhage and subarachnoid included)

| | Black | White | Coloured | Indian / Asian | Combined |
|---|---|---|---|---|---|
| Total number of patients with cerebral haemorrhage | 55 | 7 | 4 | 2 | 68 |
| – Hypertension | 45 | 6 | 1 | 2 | 54 (79)* |
| – Aneurysm | 2 | 0 | 0 | 0 | 2 (3)* |
| – Amyloid | 0 | 0 | 2 | 0 | 2 (3)* |
| – Thrombocytopenia | 2 | 0 | 0 | 0 | 2 (3)* |
| – Other | 2 | 1 | 0 | 0 | 3 (4)* |
| – Unknown | 4 | 0 | 1 | 0 | 5 (7)* |
| | Significance of difference between groups: p<0.001 | | | | |
| Total number of patients with SAH* | 11 | 4 | 0 | 1 | 16 |
| – Aneurysm | 4 | 3 | 0 | 0 | 7 (44)* |
| – Suspected aneurysm | 3 | 1 | 0 | 0 | 4 (25)* |
| – Unknown | 3 | 0 | 0 | 1 | 4 (25)* |
| – Thrombocytopenia | 1 | 0 | 0 | 0 | 1 (6)* |
| | Significance of difference between groups: p=0.3 | | | | |

* percentage of all cerebral haemorrhages or subarachnoid haemorrhages

overwarfarinised for deep venous thrombosis, a 67 year old black patient with a ruptured mycotic aneurysm and 44 year old black patient with a history of hypertension, well controlled at the time of the stroke, who had a cerebral haemorrhage following an alcohol binge.

### 5.2.7 Causes of subarachnoid haemorrhage in the JHSR

We have also outlined the causes of subarachnoid haemorrhage (SAH) in the JHSR in table 5.10. Aneurysms diagnosed on angiography accounted for 7 (44%), and in a further 4 patients we suspected aneurysms based on the clinical presentation and CT brain findings, but angiograms were not available. One SAH was associated with thrombocytopenia (platelet count 24 x $10^9$/L) in a patient with aplastic anaemia and in 4 cases we could not identify a cause for the SAH. The number of patients with SAH was too small for us to comment confidently on any differences between population groups.

### 5.2.8 Risk factors in the JHSR

Table 5.11 shows the frequency of risk factors in the JHSR and compares the frequency of risk factors between the four population groups. Hypertension (defined as a history of hypertension from the patient or their previous medical notes, if the patient was on treatment for hypertension or if there was evidence of hypertensive end organ damage) was the most frequent risk factor in our stroke patients, present in 73% of the 406 for whom we had sufficient data.

## Table 5.11 Risk factors in the JHSR by population group (n = number assessed)
## Percentage of all patients assessed in each population group shown in brackets, unless otherwise stated

| | Black | White | Coloured | Indian / Asian | Total | |
|---|---|---|---|---|---|---|
| Total number of strokes (n) | 308 | 76 | 22 | 26 | 432 | |
| Age – mean (95% CI) both sexes | 51 (49 to 52) | 61 (58 to 65) | 58 (49 to 66) | 54 (47 to 61) | 53 (52 to 55) | *p<0.001 |
| Male sex n=432 | 155 (50) | 40 (53) | 7 (32) | 11 (42) | 211 (49) | p=0.3 |
| Hypertension n=406 | 214 (74) | 50 (69) | 15 (79) | 17 (74) | 296 (73) | p=0.4 |
| Mean total cholesterol level at time of presentation (95% CI) n=174 | 4.6 (4.3 to 4.9) | 5.3 (4.8 to 5.7) | 5.3 (3.9 to 6.6) | 5.6 (4.9 to 6.4) | 4.9 (4.6 to 5.0) | p=0.02 |
| Proportion with total cholesterol ≥ 6 mmol/L n=174 | 14 (12) | 9 (22) | 2 (22) | 5 (45) | 30 (17) | p=0.03 |
| Cigarette smoking n=350 | | | | | | |
| - Current | 57 (23) | 34 (54) | 6 (32) | 8 (35) | 105 (30) | p<0.001 |
| - Ex | 28 (11) | 15 (24) | 4 (21) | 2 (9) | 49 (14) | |
| - Never | 160 (65) | 14 (22) | 9 (47) | 13 (57) | 196 (56) | |
| Alcohol use n=339 | | | | | | |
| - Current | 63 (27) | 14 (23) | 2 (3) | 1 (4) | 80 (24) | p=0.14 |
| - Ex | 16 (7) | 7 (12) | 1 (5) | 2 (9) | 26 (8) | |
| - Never | 158 (67) | 39 (65) | 16 (84) | 20 (87) | 233 (69) | |
| Diabetes mellitus n=378 | 42 (16) | 11 (16) | 6 (30) | 6 (24) | 65 (17) | p=0.3 |
| Previous transient ischaemic attack n=343 | 4 (1) | 4 (7) | 1 (6) | 3 (14) | 12 (4) | p=0.01 |
| Ischaemic heart disease n=256 | 8 (4) | 12 (25) | 1 (10) | 0 | 21 (8) | p<0.001 |
| Known previous atrial fibrillation n=424 | 10 (3) | 7 (10) | 1 (5) | 2 (8) | 20 (5) | p=0.14 |
| Peripheral vascular disease n=424 | 9 (3) | 4 (5) | 3 (14) | 2 (8) | 18 (4) | p=0.2 |
| Family history of stroke n=423 | 27 (9) | 11 (15) | 6 (29) | 3 (12) | 47 (11) | p=0.2 |

*p: significance of difference

The mean total cholesterol level measured on admission was relatively low (4.9 mmol/L) and only 17% of the 174 patients with cholesterol results available had a total cholesterol level of 6 mmol/L or greater. Current cigarette smoking was common (105 of 350), as was current alcohol use (80 of 339). Diabetes mellitus (defined as a history of diabetes mellitus, on treatment for diabetes mellitus, or an admission random blood glucose of ≥ 11.1 mmol/L) was also common (65 of 378; 17%). In contrast, known previous atrial fibrillation (20 of 424; 5%) and peripheral vascular disease (18 of 424; 4%) were uncommon.

We found a significant difference ($p<0.05$) in age, mean total cholesterol, the proportion with a total cholesterol greater than or equal to 6 mmol/L, frequency of cigarette smoking, ischaemic heart disease and prior transient ischaemic attack (TIA) between population groups. Comparing the two larger population groups represented, black patients were more likely to be younger, have a lower total cholesterol (with fewer cholesterol values greater than or equal to 6 mmol/L), and never have smoked, than white patients. They were less likely to be current smokers, to have reported a prior TIA, or to have ischaemic heart disease. However, the low percentage of TIAs may be the result of under-reporting.

Indian / Asian patients were notable in having the highest mean total cholesterol level, highest proportion with a total cholesterol level greater than or equal to 6 mmol/L, and least likely to be current users of alcohol or ever to have used alcohol. Coloured patients were most likely to have a history of hypertension, to be diabetic, and have PVD and a family history of stroke. The small numbers of patients in these groups make these findings unreliable, however, and the

absence of ischaemic heart disease in the Indian / Asian patients most likely results from this limitation.

In Table 5.12, we have compared risk factors by pathological stroke type (CT brain scan confirmed) for ischaemic stroke and cerebral haemorrhage. The only significant differences in the frequency of risk factors found in these two pathological types were in male sex, hypertension and ischaemic heart disease. There was a marginally significant sex difference and males were more likely to have cerebral haemorrhages than ischaemic strokes (p=0.046). We found a history of hypertension or clinical features of previous hypertension more often in patients with cerebral haemorrhage than in ischaemic stroke. We found ischaemic heart disease more often in ischaemic stroke than in cerebral haemorrhage. Surprisingly, there was no significant difference in total cholesterol levels, diabetes mellitus, prior TIA, the frequency of PVD, or known atrial fibrillation between the two pathological stroke types.

We found differences in the frequency and proportions of risk factors between population groups (table 5.11). To enable us to compare other components of this work which focus only on black stroke patients (chapters 3, 4, 6 and 7), and as the black population group was the largest population group in the JHSR, we compared the risk factors between ischaemic stroke and cerebral haemorrhage in black stroke patients (table 5.13). A history of hypertension (or clinical evidence of prior hypertension) was the only risk factor that differed significantly between the two pathological stroke types in black patients. Ischaemic heart disease was more frequently associated with ischaemic stroke than with cerebral haemorrhage (8%

**Table 5.12 Risk factors in the JHSR by pathological stroke type (only ischaemic stroke and cerebral haemorrhage compared) (n = number assessed); Percentage with the risk factor shown in brackets unless otherwise stated**

| | Cerebral Haemorrhage | Ischaemic Stroke | |
|---|---|---|---|
| Total number of strokes confirmed by CT brain scan n=271 | 68 | 203 | |
| Age – mean (SD) (95% CI) both sexes | 53 (13) (49 to 56) | 50 (17) (47 to 52) | *p=0.2 |
| Male sex n=271 | 43 (63) | 100 (49) | p=0.046 |
| Hypertension n=251 | 58 (88) | 114 (62) | p<0.001 |
| Mean total cholesterol level at time of presentation (95% CI) n=173 | 5.1 (4.2 to 6) | 4.7 (4.4 to 5) | p=0.2 |
| Proportion with total cholesterol ≥ 6 mmol/L n=173 | 4 (19) | 15 (16) | p=0.8 |
| Cigarette smoking n=211 | | | |
| - Current | 11 (24) | 43 (26) | p=0.6 |
| - Ex | 9 (20) | 23 (14) | |
| - Never | 26 (57) | 99 (60) | |
| Alcohol use n=207 | | | |
| - Current | 10 (23) | 35 (22) | p=0.9 |
| - Ex | 5 (11) | 16 (10) | |
| - Never | 29 (66) | 112 (69) | |
| Diabetes mellitus n=237 | 8 (14) | 30 (17) | p=0.6 |
| Previous transient ischaemic attack n=318 | 1 (2) | 9 (5) | p=0.3 |
| Ischaemic heart disease n=131 | 1 (2) | 15 (13) | p=0.04 |
| Known previous atrial fibrillation n=265 | 3 (5) | 8 (4) | p=0.8 |
| Peripheral vascular disease n=365 | 2 (3) | 10 (5) | p=0.5 |
| Family history of stroke n=423 | 6 (9) | 28 (14) | p=0.4 |

*p: significance of difference

**Table 5.13 Risk factors in Black stroke patients in the JHSR by pathological stroke type (only ischaemic stroke and cerebral haemorrhage compared)**
**(n = total number assessed for the risk factor; percentage shown in brackets unless otherwise stated)**

| | Cerebral Haemorrhage | Ischaemic Stroke | |
|---|---|---|---|
| Total number of strokes confirmed by CT brain scan n=196 | 55 | 141 | |
| Age – mean (SE) (95% CI) both sexes | 51 (1.7) (47 to 54) | 47 (1.4) (44 to 50) | *p=0.1 |
| Male sex n=196 | 35 (64) | 68 (48) | p=0.052 |
| Hypertension n=182 | 48 (89) | 77 (60) | p=<0.001 |
| Mean total cholesterol level at time of presentation (95% CI) n=75 | 4.8 (3.7 to 5.8) | 4.4 (4.1 to 4.7) | p=0.3 |
| Proportion with total cholesterol ≥ 6 mmol/L n=75 | 2 (12) | 7 (12) | p=0.97 |
| Cigarette smoking n=150 | | | |
| - Current | 7 (19) | 22 (20) | p=0.6 |
| - Ex | 7 (19) | 14 (12) | |
| - Never | 23 (62) | 77 (68) | |
| Alcohol use n=147 | | | |
| - Current | 10 (29) | 27 (24) | p=0.7 |
| - Ex | 4 (11) | 9 (8) | |
| - Never | 21 (60) | 76 (68) | |
| Diabetes mellitus n=167 | 5 (11) | 18 (15) | p=0.6 |
| Previous transient ischaemic attack n=192 | 1 (2) | 3 (2) | p=0.3 |
| Ischaemic heart disease n=111 | 1 (3) | 6 (8) | p=0.4 |
| Known previous atrial fibrillation n=192 | 2 (4) | 3 (2) | p=0.5 |
| Peripheral vascular disease n=365 | 1 (2) | 4 (3) | p=0.5 |
| Family history of stroke n=192 | 5 (9) | 15 (11) | p=0.6 |

*p: significance of difference

compared to 3%) but this difference was not significant. This finding is influenced by the low prevalence of IHD in the black population and therefore the small numbers in all stroke types.

#### 5.2.8.1 Socioeconomic status of patients in the JHSR

Socioeconomic status, particularly social deprivation, is said to be associated with stroke, specifically stroke mortality and incidence, though the effect on specific pathological stroke types and subtypes is not clear (Warlow et al., 2001; Cox, McKevitt, Rudd et al, 2006). It has been suggested that the increase in stroke is effected via an increase in risk factor prevalence, but this has not been investigated sufficiently (Cox et al., 2006).

There were no generally accepted socioeconomic scores for South Africa when we first developed the questionnaire for the JHSR. Despite this we included several measures that possibly have a bearing on the socioeconomic status of an individual living in South Africa (see appendix D). While scoring systems are still being developed, one measure based on housing, household commodity index (ownership of items such as a telephone, oven, microwave oven) and education level is gaining popularity (Professor Paul Rheeder, Professor of Clinical Epidemiology, University of Pretoria – personal communication 7 April 2006)(Westaway & Gumede, 2000). While we did not use the same scoring system and did not measure household commodities, we did assess employment and housing, as well as marital status. We also asked whether the stroke patient was the sole breadwinner for the household. In table 5.14 we compare the proportion of each of these measures in the four population groups studied.

## Table 5.14 Possible socioeconomic measures / factors in stroke patients in the JHSR (percentage of those in the population group assessed)

| Socioeconomic measure n=number assessed | Black | White | Coloured | Indian / Asian | Total | |
|---|---|---|---|---|---|---|
| Marital status n=314 | | | | | | |
| - Married | 126 (58) | 25 (45) | 8 (49) | 16 (73) | 175 (56) | *p<0.001 |
| - Single | 60 (27) | 7 (13) | 2 (12) | 2 (9) | 71 (23) | |
| - Widowed | 28 (13) | 14 (25) | 6 (35) | 4 (18) | 52 (17) | |
| - Divorced | 5 (2) | 10 (18) | 1 (6) | 0 (0) | 16 (5) | |
| Sole breadwinner for the household n=284 | 100 (57) | 28 (57) | 7 (44) | 8 (40) | 143 (50) | p=0.6 |
| Housing n=278 | | | | | | |
| - live in house / flat | 131 (69) | 47 (89) | 13 (93) | 18 (90) | 209 (75) | p=0.04 |
| - dormitory / hostel / single room | 12 (6) | 1 (2) | 0 | 0 | 13 (5) | |
| - retirement home | 1 (1) | 2 (4) | 1 (7) | 2 (10) | 6 (2) | |
| - live with employer | 27 (14) | 3 (6) | 0 | 0 | 30 (11) | |
| - live in serviced shack | 13 (7) | 0 | 0 | 0 | 13 (5) | |
| - live in un-serviced shack | 7 (4) | 0 | 0 | 0 | 7 (3) | |
| Years of schooling passed n=223 | | | | | | |
| - mean (SD) (95% CI) | 8 (3) (7 to 8) | 11(2) (10 to 11) | 10 (2) (8 to 11) | 8 (3) (6 to 10) | 9 (3) (8 to 9) | p<0.001 |
| - median | 8 (8 to 9) | 11 (10 to 12) | 10 (7 to 12) | 9 (6 to 10) | 9 (8 to 10) | p<0.001** |
| - none | 8 | 0 | 0 | 1 | 9 | |
| - less than 7 years | 44 | 2 | 1 | 4 | 51 | |
| - 7 years | 19 | 0 | 1 | 2 | 22 | |
| - less than 12 years | 128 | 26 | 8 | 13 | 175 | |
| - 12 years | 26 | 18 | 2 | 2 | 48 | |
| - any in-service or post-school formal training | 53 | 28 | 4 | 7 | 92 | |
| Employed n=314 | | | | | | |
| - unemployed and looking for work | 36 (17) | 8 (13) | 2 (13) | 3 (13) | 49 (16) | p=0.046† |
| - any pension | 50 (23) | 29 (48) | 9 (56) | 6 (26) | 94 (30) | |

* significance of difference
* Wilcoxon test: only significant for difference between black and white and Indian / Asian and white;
† Comparison of employed, unemployed and those on social pension or unemployed by choice

About half the stroke patients who were asked whether they considered themselves the sole breadwinner for their household said “yes,” and there was no significant difference between the population groups for this measure (p=0.6). We included social pensioners as ‘bread-winners’ as pensions (state, disability or private) are so often the major sources of income in households in South Africa (Case, 2001). This figure does appear high, particularly in the black and white population groups. In the black population it is feasible because of the young mean age of the stroke patients. This possibly results in an increased proportion that is economically active. However, it may also be the result of HIV infection causing loss of young economically active lives and resulting in more families dependening on the elderly. It is more difficult to explain the high proportion of sole-breadwinners in the white population group.

There was a significant difference in housing between population groups (p=0.004). Far fewer black patients lived in a house or flat (131 of 191 assessed; 69%) compared to white patients (47 of 53 assessed; 89%) and other population groups (table 5.14). Black patients were more likely to live with their employer or in a shack than other population groups.

The mean and median number of years of schooling was significantly higher for whites than any other population group (table 5.14). This probably reflects the apartheid regime’s educational policy which favoured the white population. Current employment was more common in black stroke patients, possibly because of their younger age than other groups, though this was of borderline significance. Indeed when we only assessed patients aged less than 65 years the difference was no

longer significant (p=0.6). There was a significant difference in marital status between groups with black patients more likely to be single, Indian / Asian patients more likely than other groups to be married, coloured to be widowed, and whites more likely to be divorced than other groups. This is unlikely to have any role to play in stroke risk or even socioeconomic status; though the likelihood of home care following stroke seems good for Indian / Asian patients and perhaps black patients.

#### 5.2.8.2 Snuff use in the JHSR

Whether snuff (smokeless tobacco) results in an increased risk of stroke or not is not clear (Asplund, 2001; Asplund, 2003; Asplund et al., 2003; Henley et al., 2005). Twenty stroke patients in the JHSR used snuff (18 black, 1 coloured and 1 Indian / Asian patient), predominantly women (15 women and 5 men) (p=0.04).

### 5.2.9 Human immunodeficiency virus (HIV) in the JHSR

As mentioned in section 5.0.2 we did not have the resources to carry out additional investigations on patients entered onto the JHSR. Our results were dependent on the investigations available as part of the routine management of patients in the medical wards at Johannesburg Hospital. Although HIV infection is an important consideration in medical patients admitted to Johannesburg Hospital, elderly patients and particularly older stroke patients are not as likely to be tested for HIV as younger patients. This practice is based on the lower prevalence found in older population groups (Directorate: Health Systems Research, 2001). Our finding of

HIV frequency in the JHSR must therefore be considered to be a minimum frequency.

One hundred and seventy-four (40%) of the 432 stroke patients were tested for HIV. There was a significant difference in the likelihood of being tested in the four population groups assessed ($p<0.001$): 148 (48%) black, 12 (16%) white, 7 (32%) coloured and 7 (26%) Indian / Asian patients. Sixty-five (15%) of the JHSR patients tested for HIV were positive: 61 (41%) black patients, 2 (17%) white, and 2 (29%) coloured patients. None of the Indian / Asian patients tested were positive. This difference was not statistically significant ($p=0.06$) comparing all groups, but was significantly different between blacks and whites ($p<0.001$). There was no significant difference between males and females, either in the likelihood of having a positive HIV test result (29 males and 36 females, $p=0.06$) or of being tested ($p=0.02$).

The mean age of patients who tested positive was 38 years (SD 10) (95% CI, 35 to 40 years) with a range of 18 to 65 years. Of the 65 HIV positive patients, 6 (9%) had a cerebral haemorrhage, 1 had a subarachnoid haemorrhage and the remainder (58; 89%) had ischaemic strokes. The likelihood of a person being tested for HIV was not increased with any particular pathological stroke type ($p=0.5$) or OCSP subtype ($p=0.9$).

We found no difference in the likelihood of patients with HIV having a particular OCSP ischaemic stroke subtype ($p=0.6$). Of the 58 patients with ischaemic stroke who tested positive for HIV, 14 (24%) had total anterior circulation infarcts (TACI),

25 (43%) had partial anterior circulation infarcts (PACI), 1 (2%) had a posterior circulation infarct (POCI) and 18 (31%) had lacunar infarct (LACI).

There was, however, an increased likelihood for black patients of certain aetiological stroke types to be tested for HIV (p=<0.001). Using our ‘’most likely cause’’ classification, not surprisingly strokes in the ‘’other’’ ischaemic stroke category were most likely to be tested (51 of 112 ischaemic stroke tested; 51%), but then patients were more likely to be allocated to this category if they were HIV positive and had no other cause for their stroke. However, black patients with atherothrombotic strokes were least likely to be tested (3 of 112 ischaemic stroke tested; 3%).

Twenty-two HIV positive patients had their CD4 count measured. The mean count was 218 (SD 268)(95% CI, 99 to 336) with a range of 2 to 1047. Twenty of these were measured in black stroke patients, and one each in a white and coloured individual. The investigation of HIV positive stroke patients was not extensive enough for us to comment on the likely causes of stroke in these patients.

#### 5.2.9.1 HIV in young stroke patients

Young stroke patients are often considered separately because they are less likely to have stroke caused by atherosclerotic disease or complex small vessel disease than patients over the age of 60 years (Warlow et al., 2001). In South Africa as elsewhere, HIV is more prevalent in young people than in the older population, probably because of its sexual transmission and early deaths in people not using

antiretroviral therapy. For this reason it is worth considering the impact of HIV infection in young patients. The definition of young varies from study to study. Usually patients up to the age of somewhere between 30 and 50 years of age are considered young. We will consider all patients less than 50 years of age to be young patients to allow us to compare our findings with those of the Durban Stroke Data Bank (Hoffmann, 2000).

There were 171 young stroke patients in the JHSR: 139 black, 15 white, 8 coloured and 9 Indian / Asian. HIV infection was significantly different across population groups (p=0.04). Young black stroke patients had the highest frequency with HIV infection in 49 of 94 tested patients (52%). Coloured patients followed with 2 of 6 tested infected (33%) and then whites with 1 of 6 tested (17%). None of the 5 Indian / Asian patients tested were positive. As the numbers are so small in all but the young black population we will only discuss HIV infection in young black stroke patients in more detail.

The difference in the frequency of HIV infection between young male and female stroke patients was not significant with 21 of 47 tested males positive for HIV (45%) and 28 of 47 tested females positive (60%) (p=0.2). Mean age of the HIV positive young black patients was 35 years (SD 7; 95% CI 33 to 37) with a range of 22 to 49 years. One young black male gave a history of substance misuse (cannabis) but we did not test him for HIV infection.

### 5.2.10 Syphilis in the JHSR

We did not systematically test for syphilis in our patients. Indeed, we only tested for syphilis in 78 patients: 59 black, 9 white, 6 coloured and 4 Indian / Asian patients. Syphilis serology (VDRL) was positive in 9 patients (6 males and 3 females) all of whom were black. Of those 9, we tested 6 patients for HIV infection and found one patient positive. One patient with a positive VDRL had a cerebral haemorrhage and the rest had ischaemic strokes. The ischaemic strokes were: cardioembolic (total anterior circulation infarct) in 1, lacunar in 4, associated with HIV in 1 (partial anterior circulation infarct) and undetermined in 2 patients (total anterior circulation infarct in one and partial anterior circulation infarct in the other).

Only two of the patients with a positive VDRL result had CSF results available. In both the CSF was abnormal. In the first patient, a 58 year old white female who did not have an HIV test, the CSF protein was raised at 1,02 without any other abnormality, but syphilis FTA antibodies were not present thereby excluding a diagnosis of neurosyphilis (Timmermans et al., 2004).

The other patient, a 35-year-old HIV negative male with a cerebral haemorrhage had an active CSF with 1 polymorphonuclear cell, 25 lymphocytes, 25 erythrocytes, glucose of 3.5 mmol/L and a raised protein of 0.73 g/L. The India ink test and cryptococcal antigen were negative, the adenosine deaminase (ADA) level was normal, and the CSF VDRL was negative. He was previously well and did not have any symptoms of meningitis prior to the stroke. While it is possible to have neurosyphilis in the presence of a negative CSF VDRL (Timmermans et al.,

2004), this is unlikely and so we cannot confidently diagnose neurosyphilis in either of these two patients.

### 5.2.11 Stroke severity and related disability

#### 5.2.11.1 Stroke severity

We used the National Institutes of Health stroke score (NIHSS) as well as the Scandanavian Stroke Score (SSS) to determine stroke severity. Table 5.15 presents our findings categorised by population group. We did not find any significant difference in the mean or median scores between population groups or male and female sex. The mean and median scores for all groups and using both scoring systems suggested that the strokes overall were of moderate severity (comparison with other populations will be discussed in section 5.3.6.1).

#### 5.2.11.2 Barthel Index and modified Rankin score

We assessed the Barthel Index and modified Rankin score at the time we first assessed the patient, i.e. within one to two days of admission. Table 5.15 shows the proportion of patients who scored below a Barthel Index (BI) of 20, 15 and 10 to compare the proportions of patients across population groups who had varying levels of functional difficulty. We also compared the proportion of each population group with a modified Rankin score (mRs) of 0 to 2 representing those who were independent, and a score of 3 to 5 representing those stroke patients who were not independent. We found no significant difference between population groups

## Table 5.15 Severity of stroke and stroke related functional impairment and disability in the JHSR, by population group (percentage of population group assessed)

| **Scale / Impairment**<br>n = total number assessed in JHSR | **Black** | **White** | **Coloured** | **Indian / Asian** | **Total** | **Significance of difference** |
|---|---|---|---|---|---|---|
| NIH stroke scale | | | | | | |
| - Mean (SD) | 12(9) | 12(10) | 12(11) | 12(9) | 12(10) | 0.9 |
| - Median (95%) CI) | 10<br>(8 to 12) | 7<br>(5 to 12) | 7<br>(3 to 17) | 9<br>(5 to 15) | 10<br>(8 to 11) | 0.4* |
| Scandinavian SS | | | | | | |
| - Mean (SD) | 29 (20) | 30 (22) | 30 (23) | 36 (19) | 30 (21) | 0.5 |
| - Median (95% CI) | 30<br>(26 to 36) | 33<br>(20 to 47) | 30<br>(10 to 52) | 43<br>(25 to 50) | 31<br>(26 to 36) | 0.5* |
| Barthel Index* <20 n=432 | 259<br>(84) | 56<br>(74) | 16<br>(73) | 22<br>(85) | 353<br>(82) | p=0.1 |
| Barthel Index <15<br>n=432 | 214<br>(69) | 45<br>(59) | 12<br>(55) | 19<br>(73) | 290<br>(67) | p=0.2 |
| Barthel Index <10<br>n=432 | 174<br>(55) | 42<br>(57) | 11<br>(50) | 14<br>(46) | 241<br>(56) | p=0.9 |
| Barthel Index median<br>(95% CI)<br>n=432 | 7<br>(6 to 9) | 7<br>(4 to 17) | 10<br>(2 to 18) | 9<br>(4 to 14) | 7<br>(6 to 9) | |
| mRankin scale 0-2<br>n=416 | 100<br>(34) | 30<br>(41) | 7<br>(33) | 9<br>(35) | 146<br>(35) | p=0.7 |
| MRankin scale 3-5 | 196<br>(66) | 43<br>(59) | 14<br>(67) | 17<br>(35) | 270<br>(65) | |

* for black / white population comparison but no significant difference in the median between any two population groups
NIH: National Institute of Health; SS: stroke scale

(p=0.1) or males and females (p=0.4) in the proportion of people who scored below 20 on the BI. However, when we compared black and white stroke patients alone, we found a significant difference (p=0.03). White stroke patients were more likely than black stroke patients to have retained normal functioning and independence i.e. to have a score of 20 on the BI. There was no significant difference when we compared the proportion of patients with moderate and severe or severe loss of functioning and increasing dependence (scores below 15 and 10 on the BI) between the four population groups, black and white patients alone (p=0.09 and 0.9 respectively), or sexes (p=0.08 and 0.3 respectively).

We were able to assess the modified Rankin score in 416 of 432 patients. This figure is lower than the BI assessment probably because it requires a more subjective assessment of the patient's level of independence. As such, we could not assess the modified Rankins score retrospectively in patients who had died or left the hospital before we examined them. Although a larger proportion of white patients (30 of 73 white patients assessed; 41%) were independent than the approximately 35% found in other population groups, this difference was not statistically significant (p=0.7) (table 5.15). We did not find any statistically significant difference when we did a direct comparison between whites and blacks (p=0.2) or between males and females (p=0.4).

Thus, using both the Barthel Index, which includes a measure of disability and dependence in activities of daily living (Warlow et al., 2001), and the modified Rankin score, which does not just measure handicap but rather dependency and change in lifestyle (Warlow et al., 2001), we found no statistical difference between

patients in the four population groups other than in the proportion of whites and blacks with a normal BI. However, there we did find a non-significant increase in the proportion of white patients who were fully independent and functional compared to other population groups.

#### 5.2.11.3 Other measures of impairment

We assessed the neurological findings as well as urinary incontinence (Appendix D) for the calculation of the Barthel Index, NIHSS and Scandinavian Stroke Scale, and to ensure that stroke patients were thoroughly assessed. We did not find a significant difference in any of these measures between population groups.

### 5.2.12 Stroke related complications in the JHSR

Pneumonia was the commonest complication in our stroke patients. It occurred in 22 patients, 17 black, 2 white, and 2 coloured, although this difference was not significant (p=0.5). This was followed in frequency by early post-stroke seizures which occurred in 21 patients (19 black, 1 white, and 1 coloured patient) (p=0.3). Other complications included: post-stroke depression which occurred in 6 patients (1 white, 5 black), painful shoulder syndrome in 5 (3 black, 1 coloured and 1 Indian / Asian), urinary tract infection in 1 black patient, deep venous thrombosis in 1 white patient, and surprisingly myocardial infarction in 1 black patient in whom the myocardial infarction occurred following his admission for stroke. In the latter patient it is possible that he embolised to the heart and the brain.

Five patients had recurrent strokes while in hospital: 3 black, 1 coloured and 1 Indian / Asian patient (p=0.1).

Thirty-five patients died in hospital following their stroke: 23 black, 9 white, 1 coloured and 2 Indian / Asian patients (p=0.2). Twenty males and 15 females died (p=0.4).The pathological stroke types in those patients who had a CT brain scan prior to death were: ischaemic stroke 14, cerebral haemorrhage 13, and subarachanoid 2. The NIH stroke score was ≥ 14 (severe) for 33 of the 35 patients who died (p<0.001). In two it was ≤ 5 (mild) on admission. One, a 64-year-old white male with a partial anterior circulation infarct died from aspiration, and the other a 35-year-old HIV positive black male died of unknown causes. No autopsies were done on patients in the JHSR who died, but the following were noted as cause of death: 2 metabolic (diabetes and renal failure), 1 aspiration, 1 pulmonary embolus, 1 pulmonary infection, 26 irreversible coma following stroke or progressive raised intracranial pressure following the stroke, and in 4 the cause of death was not known.

## 5.3 Discussion

In this section we will initially summarise the key findings of the JHSR and then go on to compare our findings with other stroke registers in South Africa, recent stroke registers from the rest of sub-Saharan Africa, and with populations in the rest of the world. The latter will focus on comparing our black stroke patients with Africans living in the United States of America and in the United Kingdom and on briefly comparing the findings in white patients with other typical high-income white populations.

### 5.3.1 Summary of the JHSR findings

The JHSR included 432 first-ever-in-a-lifetime stroke patients admitted to the urban Johannesburg Hospital over 23 months. The ethnic profile of patients (71% black, 18% white, 5% coloured and 6% Indian / Asian) mirrored the demographic profile of South Africa as a whole, although we had twice as many white and Indian / Asian patients and about half as many coloured in the register (Lehohla, 2005). However, this profile closely mirrors the population group mix found in the city of Johannesburg. In 2000 the population of Johannesburg consisted of: 72% black, 17% white, 7% coloured and 4% Indian / Asian inhabitants (City of Johannesburg Local Government, 2001). We found a sex ratio of 1:1.

Although we have compared all four population groups in the results section, the small number of patients in both the coloured and Indian / Asian groups makes the findings somewhat imprecise. Therefore, we will focus on the findings in the black

and white stroke patients and any differences between these two groups in the discussion section.

#### 5.3.1.1 Key findings of the JHSR

*Characteristics of stroke patients*

- We found that the mean age of black stroke patients was 10 years younger than the mean for white stroke patients
- 98% of patients were independent prior to their stroke with no significant difference between population groups
- 13 strokes occurred in hospital
- The mean time from stroke onset to presentation was long (3 days) with a wide range of 1 hour to 120 days, but the median was the same (1 day) for both white and black patients as well as the register as a whole
- 23% of stroke patients presented to hospital within 6 hours of the onset of their stroke and the difference between black (22%) and white (27%) patients was not significant
- 287 patients (66%) had a CT brain scan; 58% within 24 hours of presentation and 91% within 7 days of presentation to hospital. There was no significant difference between population groups or sex in the CT scan rate or time to scan

*Pathological stroke type and ischaemic stroke subtype*

- 24% of scanned patients had a cerebral haemorrhage. More black (27%) than white patients (15%) had cerebral haemorrhage (p=0.2)
- Ischaemic stroke occurred in 71% of patients and subarachnoid haemorrhage in 6%; again without a significant difference between population groups
- The majority of ischaemic strokes were partial anterior circulation events (PACI) (36%), followed by total anterior circulation events (TACI) (25%), lacunar infarcts (LACI) (28%) and posterior circulation infarcts (POCI) (12%)
- Black and white stroke patients had almost the same proportion of POCIs (12% vs 11%), but black patients had more LACIs (28% vs 22%) and TACIs (28% vs 19%) than white patients
- We found a difference in ischaemic stroke subtypes between men and women (p=0.01). Women had more TACIs (31% vs 20%), and men had more POCIs (13% vs 4%)

*Cause of stroke*

- The TOAST classification did not perform well in our population and 36% of patients who had undergone brain imaging (43% of black patients) were classified as being of “undertermined” cause
- There was a statistically significant difference in the TOAST categories between population groups. Atherothrombosis caused 14% of strokes in

white patients, but none of the strokes in black patients. Cardioembolic stroke occurred twice as often in white patients, lacunar stroke occurred in a similar number of white and black patients, and other determined causes of stroke occurred slightly more often in black patients (17% vs 14% of whites)

- Using our 'most likely cause' approach in ischaemic strokes:
    - Very few (6%) black stroke patients had **atherothrombotic** strokes, and none of these patients had evidence of extracranial carotid artery disease
    - **Cardioembolic** stroke occurred in about a quarter of strokes in all population groups, but the underlying cause for the cardioembolic event differed. Atrial fibrillation and ischaemic heart disease occurred commonly in white stroke patients. In contrast ischaemic heart disease was rare in black stroke patients, but cardiomyopathy was common. Dilated cardiomyopathy accounted for about a third and hypertensive heart disease for two-thirds of the cardiomyopathies in black patients. In black patients atrial fibrillation was caused by hypertensive and valvular heart disease and rarely if ever by ischaemic heart disease. Rheumatic valvular disease accounted for about 10% of all cardioembolic stroke
    - Hypertension and diabetes accounted for 90 - 100% of **lacunar strokes** in all population groups
- **HIV infection** was found in 17% of presumed ischaemic strokes and 15% of all strokes, although we cannot comment on the mechanism of stroke in

most patients. 80% of HIV infected patients were black. HIV infection did not result in an increase in any particular stroke subtype

- None of our patients had a confirmed diagnosis of **neurosyphilis,** although we admit that this may well reflect inadequate investigation for syphilis rather than a low prevalence of positive syphilis serology and neurosyphilis
- Hypertension was the single most important likely cause of **cerebral haemorrhage** (around 80%) in all patients. Amyloid was rare, though again this may reflect an inadequate level of investigation for the condition
- The majority of **subarachnoid haemorrhages** were the result of cerebral artery aneurysm

*Risk factors*

- **Hypertension** was the commonest risk factor in all population groups and was found in just under three-quarters of patients. Although black patients had a history of hypertension more often than white patients, the difference was not significant
- **Cholesterol** levels were significantly lower in black patients compared to all other groups
- Twice as many white patients were current **cigarette smokers** as black patients
- **Diabetes mellitus** occurred in a similar proportion of black and white stroke patients

- **Peripheral vascular disease** occurred about as often in black and white stroke patients, but **ischaemic heart disease** occurred about five times more often in white than in black patients
- **Previous TIA** was uncommon in all population groups but rare in black patients
- In terms of **socioeconomic** measures between population groups; whites had received more years of schooling, black patients were less likely than other groups to live in a house or flat and more likely to live with their employer or in a shack

*Stroke severity and the impact of stroke on the stroke survivor*

- **Stroke severity** and the resulting impact on patients level of **functioning**, as well as stroke related **impairments** and **complications** were remarkably similar between population groups

*Comparison of population groups*

Thus, black stroke patients compared to white stroke patients: were younger, had lower cholesterol levels, were less likely to smoke cigarettes, had less atherosclerosis in the extracranial carotid and coronary arteries, but were more likely to have strokes associated with HIV. While the proportions of pathological stroke types and subtypes, and even aetiopathological categories did not differ enormously between the two groups other than in atherothrombosis, the underlying cause of cardioembolic stroke and other specific causes of stroke did

differ. The nature of stroke in whites was dominated by atherosclerotic disease and in blacks by hypertension and infectious disease, particularly HIV.

Apart from the differences in the nature of stroke between black and white stroke patients, the characteristics of stroke patients including time to presentation, severity of stroke and impact on level of functioning, did not differ significantly between population groups.

### 5.3.2 Limitations of the JHSR

There are several limitations of the JHSR which fall into four main categories. Firstly the limited number of stroke patients in the coloured and Indian / Asian population groups result in wide, but probably insignificant, variations in findings. As a result, we are not able to draw conclusions from our findings in these two groups with any confidence. We decided against combining these groups or even comparing patients in the black population and other population groups because we do not know if the nature of stroke is comparable across these groups. Therefore, we have limited many of our comparisons to the two larger groups i.e. white and black patients.

The second major limitation results from our lack of funding to investigate all patients in detail, as well as the limited resources available for all forms of imaging at Johannesburg Hospital at the time of the register. The enormous burden on the hospital also forces very rapid turnover of patients and many patients are discharged early and asked to return for further investigation as outpatients. In our

experience this seldom happens in stroke patients. As a result we have a relatively low CT scan rate, and the investigation of the cause of strokes was not as detailed as we would have liked. This influences our ability to comment accurately on the cause of stroke in some patients, particularly those with HIV. It also influences our ability to comment on the influence of diseases such as syphilis in our population. A further limitation related to resource limitations relates to the register running on two occasions between July and December. There is some evidence to support a seasonal variation in stroke incidence (Rothwell, Wroe, Slattery et al, 1996; Connor, 2002), and ideally studies of stroke, particularly incidence studies, should include full years of ascertainment (Sudlow et al., 1996).

Thirdly, the high service load placed on our clinicians meant that we could not follow up all stroke patients to the day of discharge. Our in-hospital case fatality assessment is therefore likely to be very inaccurate and we do not have assessments at the time of discharge.

Finally, the study was hospital-based and took place in a hospital with severe pressure on acute medical beds. Hospital-based bias as well as admission bias may have influenced the characteristics of stroke patients in the JHSR, although the hospital did not have an official stroke admission policy. The younger age of both white and black stroke patients may be the result of admission bias, though the difference in mean age between the two groups is not. Rather the age difference is likely a reflection of a younger black population (demographic factors), possibly a higher stroke incidence in young age groups in the black

population, and perhaps the impact of HIV infection (these are explored further later).

It is extremely difficult to know whether more young white patients tended to seek private medical care, therefore avoiding admission to the Johannesburg Hospital. Given the surprisingly low age of our white stroke patients compared to white populations elsewhere in the world, this is not likely to have been a major source of bias. The high proportion of patients who were previously independent may well reflect admission bias. It may also reflect a high stroke case fatality rate, but it is difficult to know if this is relevant given the lack of stroke case fatality data for the population.

Despite these limitations, however, we feel that our case ascertainment was excellent over the 23 months, that we assessed patients in detail as often as was possible (allowing for those patients who were discharged or died before we could see them), and that we have provided useful information comparing stroke across a representative population of South Africa in an urban setting, during the HIV era. This is the first study in Sub-Saharan Africa to do this.

We will now compare our findings first with other stroke registers from South Africa, and then with other populations in the world.

### 5.3.3 Comparison of JHSR with other South African stroke registers

Three stroke registers have investigated stroke in South Africa previously (Rosman, 1986; Joubert, 1991; Hoffmann, 2001). The Kalafong (Rosman, 1986) and Medunsa (Joubert, 1991) studies included predominantly urban and semi-urban black patients, while the urban-based Durban Stroke Data Bank (DSDB) included all population groups (Hoffmann, 2001). Although both the DSDB and our JHSR included all population groups and were urban-based, there are a number of differences between the JHSR and the DSDB. The DSDB included consecutive stroke patients referred to a single neurologist in private practice, although he did include some stroke patients seen at the state King Edward Hospital in Durban. The DSDB therefore predominantly included higher socioeconomic patients who had medical insurance. This influenced the population group profile of the 1000 patients in the DSDB: 781 (78%) white, 103 (10%) Indian, 100 (10% black – all young patients), 14 mixed race / coloured (1%), 1 Asian patient and 1 patient of uncertain ethnicity. All patients underwent extensive investigation according to a defined protocol. The JHSR on the other hand included indigent patients, better reflected the population group profile of South Africa, but did not investigate patients to nearly the same extent. It is therefore difficult to compare our findings in black patients with those of the DSDB other than for young patients, and the best comparison is probably between white and Indian / Asian patients in the two studies. Unfortunately, the published data from the DSDB seldom provides population specific information for older stroke patients.

#### 5.3.3.1 Comparison of black patients in South African stroke registers

Table 5.16 compares the nature of stroke in black patients in the JHSR, with that in the Kalafong and Medunsa studies. It is important to note that the original publication of the Kalafong study (n=116) did not include all the data used for comparison (Rosman, 1986). The complete data set is available in the original dissertation and we have used this when necessary for comparison (Rosman, 1989). There are several publications related to the Medunsa study (Joubert, 1991) and the number of patients included varies from publication to publication (Joubert et al., 1989; Joubert, Lemmer, Fourie et al, 1990; Joubert, Pilloy, Van Reenen et al, 1990; Joubert et al., 2000). We have noted when we have compared our findings with data from secondary or later publications.

##### 5.3.3.1.1 Comparison of black patients in South African stroke registers – age and sex

Our patients were younger than those included in the Medunsa study (table 5.16). This may be the play of chance but it is surprising that our study conducted twenty years after the Medunsa study in a similar population has found a lower age. If the health transition was influencing age, even over this short period, one might expect a similar or slightly older mean age. The lower mean age in black patients in our study may be the result of an increased prevalence of HIV in our population, which is more likely to have an effect on young patients.

## Table 5.16 Comparison of findings in the black population group in the JHSR with previous stroke registers in black stroke patients from South Africa (only first-ever-in-a-lifetime strokes compared)

| | JHSR (n=342) | Kalafong (n=116)* | Medunsa (n=304) |
|---|---|---|---|
| Age | | | |
| - males (mean years) | 51 | n/a | 55 |
| - females (mean years) | 51 | n/a | 62 |
| Sex ratio (M:F) | 1:1 | 1:1 | 1:1.2 |
| Employed at time of stroke n (%) | 110 (32) | 97 (37)* | Only percentage available (29) |
| Proportion with 10 or more years of schooling (%) | 59 (48) (total assessed n=223) | 7 (7) (total assessed n=101) | n/a |
| Brain scan rate n (%) | 207 (67) | 92 (79) | 250 (82) |
| **Pathological stroke type (only CT confirmed cases):** | | | |
| - Cerebral haemorrhage (%) | 55 (27) | 38 (33)** | 65 (26) |
| - Ischaemic stroke (%) | 141 (68) | 77 (66)** | 178 (71) |
| - Subarachnoid haemorrhage (%) | 11 (5) | Excluded from study | 7 (3) |
| - Unspecified (%) | 0 | 1 (1)** | 0 |
| **Ischaemic stroke subtype (all strokes included not only those with brain imaging):** | | | |
| - Small vessel disease (% of all stroke) | - 86 (20) | - 24 (21) | - 4 (1) |
| - Cardioembolic (% of all stroke) | - 82 (19) | - 16 (14)† | - 47 (16) |
| **Cause of cardioembolic stroke (percentage of all stroke):** | | | |
| Atrial fibrillation: total | 15 (4) | 14 (7)* | 5 (5) ‡ |
| - unknown cause | 6 | n/a | 1 |
| - with ischaemic heart disease | 1 | n/a | 0 |
| - with rheumatic valvular heart disease | 2 | n/a | 2 |
| - with dilated cardiomyopathy | 0 | n/a | 0 |
| - with hypertensive heart disease | 6 | n/a | 1 |
| - with non-obstructive hypertrophic cardiomyopathy | 0 | n/a | 1 |
| Ischaemic heart disease | 4 (<1) | 0 * | 7(7)‡ |
| Cardiomyopathy: total | 27 (6) | 5 (2)* | 7 (7)‡ |
| - dilated cardiomyopathy | 10 | n/a | 3 |
| - associated with hypertensive heart disease | 17 | n/a | 4 |
| Rheumatic valvular heart disease | 6 (1) | 27 (13)* | 16 (16)‡ |
| Infective endocarditis | 0 | 5 (2) | 5 (2) |
| Hypertensive heart disease without cardiac failure (this is not an accepted cause of cardioembolic events – see section 5.2.5) | 17 (4) | n/a | 20 (20) ‡ |

* n=212 for complete register findings reported in dissertation (Rosman, 1989)
**all patients not only patients with CT brain scan
† embolic causes not separated into cardioembolic and artery to artery emboli; total number of embolic strokes used here
‡ separate publication of 102 consecutive stroke patients who had more extensive cardiac investigation (see section 2.3.1.6) (Joubert et al., 1989) n/a: data not available

The mean age of the 61 HIV positive black stroke patients in the JHSR was 38 years (SD 10; 95% CI 35 to 40) compared to the mean age of 54 years (SD 15, 95% CI 52 to 56) in HIV negative black stroke patients.

All three studies in table 5.16 found a similar proportion of males and females and a sex ratio of about one. A similar proportion of patients were employed in the three studies (range 29 to 37%), but far more had 10 or more years of education in the JHSR (48%) than in the Kalafong study (7%). We cannot exclude the possibility that variations in admission bias in the three studies resulted in these differences.

#### 5.3.3.1.2 Comparison of black patients in South African stroke registers – pathological stroke types and ischaemic stroke subtypes

The scan rate was lower in our study than in the Kalafong or Medunsa studies for the reasons we have discussed in section 5.3.2. Despite this limitation the proportions of pathological stroke types was remarkably similar in the three studies shown in table 5.16. Cerebral haemorrhage occurred in 26% in the Medunsa study, 33% in the Kalafong study and 27% in the JHSR. Ischaemic stroke also occurred in a very similar proportion of patients (68 to 71%) in the three studies, while subarachnoid haemorrhage occurred in 3% in the Medunsa study and 5% in the JHSR. Subarachnoid haemorrhage was not assessed in the Kalafong study. The high proportion of cerebral haemorrhage in these three studies is typical of hospital-based stroke studies in Africa (section 2.4.1.2) and may be the influence of the health transition but equally may simply reflect a hospital-based stroke study

bias because cerebral haemorrhages are more dramatic in presentation and more likely to result in admission than small ischaemic strokes (Bamford et al., 1986; Dennis et al., 1994).

We found almost exactly the same proportion of lacunar (small vessel) ischaemic strokes as were found in the Kalafong study (table 5.16). This suggests that the low frequency of lacunar stroke in the Medunsa study (1%) is likely the result of lacunar strokes not being admitted to hospital, or of the different definition of and criteria for the diagnosis of lacunar stroke used in the Medunsa study (section 2.3.1.7).

We found roughly the same proportion of cardioembolic stroke in our study and the two previous South African studies in black patients (14 to 19%) (table 5.16). The underlying cause of the cardioembolic stroke was also similar in the three studes. Atrial fibrillation accounted for 4% of strokes in the JHSR and 5 to 7% of strokes in the other two studies. It was only associated with ischaemic heart disease (IHD) in one patient in the JHSR and not associated with IHD in the other two studies. As in the Medunsa study, atrial fibrillation in the remainder of patients with a known cause was caused by rheumatic valvular heart disease and hypertensive heart disease.

Ischaemic heart disease was found in 7 (7) of 102 patients investigated in detail for a cardiac cause in the Medunsa study (Joubert et al., 1989), in 4 (<1%) of 342 black patients in the JHSR and in none of the patients in the Kalafong study. The patients in the Medunsa study were diagnosed with ischaemic heart disease on

the basis of ECG evidence of old myocardial infarction in 4 patients, echocardiogram (hypokinetic segment) changes alone in 2 and in the final patient solely on the basis of ischaemic T wave changes on the ECG. None of the patients had symptoms of IHD. We diagnosed IHD in our four patients based on ECG changes of previous myocardial infarction in two patients, one of whom gave a history of supportive symptoms, and acute ischaemic changes on history and ECG in two patients. Thus, the slightly lower frequency in our series compared to the Medunsa study may be the result of less intensive cardiac investigation in the JHSR or our requirement of definite ECG changes or clear symptoms with supportive evidence on ECG for diagnosing IHD, or both.

Cardiomyopathy (both dilated and secondary to hypertensive heart disease with myopathic ventricles i.e. secondary systolic failure) was present in similar proportions in our study (6%) and the Medunsa study (7%), and in a somewhat smaller proportion (2%) in the Kalafong study. We found much less rheumatic valvular heart disease than the other two studies though. In the Kalafong study rheumatic valvular heart disease occurred in 13% of stroke patients and in the Medunsa study it occurred in 16%. In the JHSR we only found it in 6 patients (1%). This may reflect the anecdotal decrease in the prevalence of rheumatic fever in the urban South African black population (Essop et al., 2005) but we cannot be sure of this without community-based evidence of a decreasing prevalence of the disease.

We did not find any cases of infective endocarditis in black stroke patients in the JHSR, although we did find three cases in other population groups (table 5.8).

While this too may reflect a decline in rheumatic heart disease the number of patients with infective endocarditis in both the Kalafong and Medunsa study is so small that it may simply be the play of chance that we did not find any patients.

Hypertensive heart disease although listed in table 5.16 is not an accepted source of cardiac emboli, particularly in the absence of heart failure. We will discuss this further in section 5.3.4.

#### 5.3.3.1.3 Comparison of black patients in South African stroke registers – risk factors

We found **hypertension** (70%) in a similar proportion to that found in the Kalafong study (74%), but in substantially more than in the Medunsa study (42%) (table 5.17). It is not clear how hypertension was defined in the Medunsa study, but our definition (section 5.1.2.1) was similar to that used in the Kalafong study in which the diagnosis of hypertension was based on previous treatment for hypertension or confirmation in the hospital records of hypertension, or on the basis of end-organ hypertensive damage. However, the limits of blood pressure differed between our study and the Kalafong study. We diagnosed hypertension if the systolic blood pressure was greater than or equal to 140 mmHg, or a diastolic blood pressure of greater than or equal to 90 mmHg, whereas the respective figures used in the Kalafong study were 160 mmHg and 95 mmHg. The lower prevalence in the Medunsa study may reflect a lower frequency of hypertension in their stroke patients or different criteria for the diagnosis. As the Kalafong study was performed at a similar time and in a population very close geographically to the Medunsa population, the latter is more likely.

The **mean cholesterol** level in the JHSR and Kalafong study were remarkably similar and the 0.2 mmol/L difference between the two means is unlikely to represent a real difference between the two populations. Mean cholesterol levels were lower in the 14 HIV positive black patients for whom we had cholesterol levels: 3.7 mmol/L (SD 1; 95% CI 3.2 to 4.3) compared to the 4.7 mmol/L (SD 1, 95% CI 4.1 to 5.2) in the 20 HIV negative black patients for whom we had

## Table 5.17 Comparison of risk factors in the black population group in the JHSR with previous stroke registers of black stroke patients from South Africa (only first-ever-in-a-lifetime strokes compared)

| | JHSR (n=342) | Kalafong (n=116)* | Medunsa (n=304) |
|---|---|---|---|
| **Risk factors:** | | | |
| Hypertension (%) | 214 of 291 assessed (74) | ** (70) | ** (42) |
| Cholesterol (mean) mmol/L | n=113<br>mean=4.6 | n=128<br>mean 4.8 | n/a |
| Diabetes (%) | 42 of 264 assessed<br>(16) | 22 of 211 assessed<br>(10) | n/a |
| Current cigarette smokers (%) | 57 of 245<br>(23) | 32 of 115<br>(28) | ** (28) |
| Current alcohol use (%) | 63 of 237 (27) | 43 of 119 (36) | n/a |
| Peripheral vascular disease (%) | 9 of 303<br>(3) | n=n/a (15) | 3 (1) |
| Previous TIA (%) | 4 of 303<br>(1) | n=n/a<br>(7) | 5 of 267<br>(2) |
| **Other:** | | | |
| HIV (%) | 61 of 148 (41) | Not tested | Not tested |
| Syphilis – positive serology only (%) | 9 of 59 (15) | 41 of 147 (28) | n/a |

* n=212 for complete register findings reported in dissertation (Rosman, 1989)
** only percentage available

cholesterol levels. However, this difference may be the result of other factors such as the younger mean age of HIV positive patients.

**Diabetes mellitus** was slightly more common in the JHSR than in the Kalafong study. Our definitions were similar. We diagnosed diabetes if the patient had a prior diagnosis or was on treatment for diabetes but differed in the requirements for blood glucose levels. The definition of diabetes in the Kalafong study required a fasting glucose of greater than 7.8 mmol/L, or a two-hour value of greater than or equal to 11.1 mmol/L following a glucose tolerance test. We required a random blood glucose of over 11.1 mmol/L or a fasting blood glucose of greater than or equal to 7.0 mol/L. This may account for our increased frequency of diabetes mellitus, but we cannot exclude the possibility that the prevalence of diabetes mellitus is increasing in South Africa in the black population, as it is elsewhere in sub-Saharan Africa (Unwin, Setel, Rashid et al, 2001; Aspray & Unwin, 2001; Walker et al., 2002).

Cigarette smoking was slightly less frequent in our patients (23%) compared to the Kalafong patients (28%). The difference is small but it may reflect the decreasing prevalence of cigarette smoking in adults that has occurred in South Africa following tighter government legislation against cigarette advertising and smoking in public places and associated increased cigarette prices (van Walbeek, 2002). Current use of alcohol was also lower in our patients (27%) than in the Kalafong patients (36%). However, the current use of alcohol in our black patients in the JHSR was similar to the prevalence of current alcohol use in South Africa found in 1998 in the Demographic and Health Survey (DHSA). The prevalence of current

alcohol use in urban black males in the DHSA was 44% and in urban black females it was 13% (Parry, Pluddemann, Steyn et al, 2005). The frequency of current alcohol use in JHSR black males was 41% and in black females it was significantly lower at 12% ($p<0.001$).

Peripheral vascular disease (PVD) was far more common (15%) in the Kalafong study than in our study (3%) or the Medunsa study (1%) (table 5.17). The diagnosis of peripheral vascular disease in the Kalafong study included 'diminished' as well as absent pulses in the dorsalis pedis or femoral pulses (Rosman, 1989). Our definition was different and required a history of intermittent calf claudication, both foot pulses *absent* or the presence of femoral bruits. This may explain the discrepancy between the two studies. The definition of PVD in the Medunsa study is not clear (Joubert, 1991).

A history of previous transient ischaemic attack (TIA) was present in 1% of our black stroke patients, in a similar 2% of the Medunsa study patients and in slightly more (7%) of the Kalafong patients. This difference may be related to the accuracy of our histories of previous TIA compared to those in the Kalafong study or to the interpretation of symptoms, or may simply be the play of chance as the numbers are small in all three studies compared in table 5.17.

As discussed in section 5.2.8.1 socioeconomic status is difficult to assess in South Africa and we used a few surrogate measures (table 5.16) in an attempt to assess and compare socioeconomic status between population groups. We certainly cannot readily compare our findings with any study done outside South Africa.

However, we can compare the same measures with other South African studies. The Kalafong study assessed employment and level of education (Rosman, 1989). One hundred and fifteen (63%) of the 212 patients were not economically active compared to 103 (48%) of the 213 black stroke patients assessed in the JHSR. Unfortunately we cannot compare the proportion of patients who were unemployed and actively looking for work (17% in the JHSR) with those who were unemployed by choice e.g. students, unemployed partners living at home, between the two studies because these data are not available for the Kalafong study. Ninety-one (90%) of 101 patients received 8 or less years of schooling in Kalafong. In the JHSR the median years at school was 8 years. Based on these measures it would appear as though our stroke patients are better off than those in the Kalafong study. This may represent an element of economic improvement since the end of the apartheid regime, but it may also reflect a difference in case mix, or in the case of unemployment a difference in the definitions used. We cannot compare the mean age of our patients with the Kalafong study, as the data are not available for the latter. Perhaps our black stroke patients were younger, possibly the result of HIV infection (section 5.2.6.4) and so more likely to be employed. However, this does not explain the higher proportion of patients that had more than 8 years of schooling in our study. This may be geographically determined i.e. people in the greater Johannesburg area are more likely to have received more schooling than in areas away from the main economic centre of the country.

#### 5.3.3.1.4 Comparison of black patients in South African stroke registers – HIV and syphilis

Human immunodeficiency virus was far less of a problem in the mid-1980s in South Africa than it was by the late 1990s. Indeed in sexually transmitted disease clinics in Johannesburg in 1988, HIV seropositivity was found in less than 2% of males and females (Martin, Schoub, Padayachee et al, 1990). So, it is not surprising that the Kalafong and Medunsa studies did not include any assessment of their patients' HIV status. Thus, we cannot compare our findings with other South African stroke studies that included black patients of all ages.

The Durban Stroke Data Bank (DSDB) assessed HIV status in young (less than 50 years of age) black patients. They found 20 of 100 (20%) young black stroke patients to be HIV positive, however the prevalence of HIV infection in pregnant black females at the time was 31%. They therefore considered their prevalence of HIV positive stroke patients to reflect the background population prevalence. We found HIV infection in 49 of 94 tested young black patients (52%) a frequency much higher than the prevalence of HIV infection in young people in Gauteng Province around that time. The prevalence of HIV infection in women attending antenatal clinics in Gauteng Province in 1996 was 16% (Swanevelder, Kustner, & van Middelkoop, 1998). This rapidly rose to around 30% by 2001 with the highest prevalence found in the 25 to 29 year old age group of women attending antenatal clinics, who had a prevalence of 31% (95% CI, 30 -33%) (Directorate: Health Systems Research, 2001). Even if we had found that all the young black stroke patients who were not tested for HIV were negative, the proportion of HIV infected

patients would still have been higher than the population prevalence (49 of 139; 35%). This possibly supports recent studies that suggest that HIV infection is an independent risk factor for stroke (Cole et al., 2004; Patel et al., 2005).

#### 5.3.3.2 Comparison of white patients in South African stroke series

The Durban Stroke Data Bank (DSDB) is the only stroke register that prospectively assessed consecutive white patients admitted to a hospital in South Africa (Hoffmann, 1998). The DSDB included 781 (78% of 1000 patients) with a mean age of 61 years (SD 14). The mean age of the 76 white patients in the JHSR was the same as that in the DSDB (JHSR: 61 years SD 15). This is surprisingly low compared to studies in white patients from western (usually high-income) populations (Rothwell et al., 2004) and probably reflects admission and referral bias. Unfortunately neither the publications related to the DSDB (Hoffmann, 2000; Hoffmann et al., 2000a; Hoffmann, 2001), nor the dissertation associated (Hoffmann, 1998) with the DSDB, provide data that are comparable with the JHSR by population group, with the exception of the findings in young stroke patients (Hoffmann, 2000). We only included 15 white patients under the age of 50 years in the JHSR, so direct comparison with the 260 young white patients in the DSDB is not likely to be accurate or informative.

Other series of stroke patients have included selected patient populations referred to the Johannesburg Hospital TIA Clinic and have dealt with important management problems such as the role of carotid endarterectomy, rather than defining the nature of stroke patients in detail (Levien, Fritz, & Lithgow-Jolly, 1984;

Fritz, Voll, & Levien, 1985; Fritz & Levien, 1988). Others have studied patients with transient ischaemic attack, an exclusion criteria for entry into the JHSR (Giovannoni & Fritz, 1993). One study from the Johannesburg Hospital TIA Clinic compared the proportions of TIA and minor stroke patients who had diabetes mellitus as a risk factor (Fritz, Bilchik, & Levien, 1987). In this study 28 (20%) of the 137 patients with minor stroke referred to the clinic had diabetes mellitus. This was higher than the 11 (16%) of 69 white patients in the JHSR, but this difference may be explained by the referral pattern to the clinic or, given the small numbers in the JHSR, by the play of chance.

### 5.3.4 Hypertensive heart disease and stroke in the JHSR

We diagnosed hypertensive heart disease without any clinical or echocardiogram evidence of heart failure in 17 patients (4% of all stroke patients) on the basis of isolated left ventricular hypertrophy on echocardiogram, although 2 patients had diastolic dysfunction without systolic dysfunction. Three patients had cerebral haemorrhages. In two of these, both black patients, the cerebral haemorrhage was the result of hypertension, but in the third, a coloured patient, we considered amyloid angiopathy more likely.

Fourteen patients with ischaemic stroke had hypertensive heart disease, 9 black, 3 white, 1 coloured and 1 Indian / Asian patient. We considered the cause of the stroke in these patients to be: lacunar on the basis of hypertension in 6, cardioembolic in 2 (1 with atrial fibrillation and the other who was described in

section 5.2.5.2 had an ‘unknown’ cardiac source), atherosclerotic in 4, arterial dissection in 1 and complicated migraine in 1.

Hypertensive heart disease (HTHD) is the term given to the structural and resulting functional damage which occurs in the heart secondary to prolonged hypertension. A full discussion of HTHD is beyond the scope of this work, but the role of HTHD in stroke is worth consideration. HTHD may be associated with systolic or diastolic dysfunction, concomitant or related ischaemic heart disease, increased arrhythmias, sudden death and in extreme cases overt heart failure (Lip et al., 2000; Ramakrishnan, Kothari, & Bahl, 2003), which in some cases results from an end-stage dilated cardiomyopathy (Iriarte, Olea, Sagastagoitia et al, 1995).

HTHD has been associated with increased stroke risk for all stroke (ischaemic and cerebral haemorrhage) (Verdecchia, Porcellati, Reboldi et al, 2001) but particularly ischaemic stroke in case control studies (Di Tullio, Zwas, Sacco et al, 2003). It is not at all clear whether this is simply because of an association with hypertension and other risk factors, or whether HTHD itself predisposes to cardioembolic stroke. The latter is possible if there is associated atrial fibrillation as there was in seven of our patients, or if the patient develops systolic failure and particularly a dilated cardiomyopathy with left ventricular mural thrombus. We included seventeen (black) patients with evidence of left ventricular hypertrophy in our cardioembolic stroke group because they had echocardiographic evidence of systolic heart failure as well as symptoms of heart failure. We accept this is controversial as hypertrophic cardiomyopathy is seldom if ever associated with embolic events

(Warlow et al., 2001), but we feel that cardioembolic events are more likely in the presence of systolic heart failure. HTHD is particularly common in black stroke patients (table 5.8) and the mechanism for cardioembolic stroke (if there is one) requires further study.

### 5.3.5 Comparison of stroke in black and white patients in the JHSR with other studies from Sub-Saharan Africa and the rest of the world

We have compared the black and white population groups in the JHSR with stroke patients in prospective stroke registers of consecutive stroke admissions to hospital from other regions in Sub-Saharan Africa (Zimbabwe and Gambia)(Matenga et al., 1986). The Zimbabwean study used brain imaging, but the two studies from the Gambia did not have access to brain scanning. We also compared our findings to those in African-Americans in the Northern Manhattan Stroke Study (NMSS) (Sacco et al., 1998) or where comparisons were not possible with the NMSS then with the Greater Cincinnati / Northern Kentucky Stroke Study (GCNKSS) (Broderick et al., 1998). Finally we compared our findings to those from two community-based studies in Oxfordshire, United Kingdom, the recent OXVASC study (Rothwell et al., 2004), and when we had insufficient data for comparison from this study, from the earlier Oxfordshire Community Stroke Project (OCSP) (Bamford et al., 1991).

#### 5.3.5.1 Comparison of pathological stroke type and ischaemic stroke subtype

Table 5.18 compares the pathological stroke types and ischaemic stroke subtypes in black and white patients from the JHSR, who had had brain imaging, in patients from Zimbabwe, the Gambia, African-American patients and community-based stroke patients from the United Kingdom.

Although there are two stroke studies from the Royal Victoria Hospital in the Gambia (Walker et al., 2003; Garbusinski, van der Sande, Bartholome et al, 2005), we have only used one (Garbusinski et al., 2005) for comparison in table 5.18, as the other (Walker et al., 2003) did not distinguish between pathological stroke types. Pathological stroke type in JHSR black patients was very similar to that found in Zimbabwe in a sub-study of 93 patients, all of whom had had CT brain scans (Matenga et al., 1986). This is in keeping with the similar proportions of pathological stroke types found in other South African stroke registers (table 5.16). Cerebral haemorrhage was far more frequent in the study from the Gambia (Garbusinski et al., 2005). However, this study did not have brain imaging available and used the Siriraj Stroke Score to assess pathological stroke type. This score has not been validated for use in Sub-Saharan Africa and it is possible that it overestimated cerebral haemorrhage (see chapter 6 for further discussion on the Siriraj Stroke Score).

**Table 5.18 Comparison of pathological stroke type and ischaemic stroke subtype found in black and white patients in the JHSR, with African-American stroke patients in the NMSS and with the community-based OXVASC / OCSP studies (all figures are number of participants with percentages in brackets)**

| | JHSR – black stroke patients* n=207 | Zimbabwe* n=93 (Matenga, 1986) | Gambia† n=138 (Garbusinski, 2005) | NMSS** (1993 - 1996) (n=148) (Sacco, 1998) | JHSR – white stroke patients* n=47 | OXVASC (n=262 ) (Rothwell, 2004) |
|---|---|---|---|---|---|---|
| **Pathological stroke type:** | | | | | | |
| Cerebral haemorrhage | 55 (27) | 29 (31) | 63 (46) | 21 (15) | 7 (15) | 17 (7 ) |
| Ischaemic stroke | 141 (68) | 62 (67) | 42 (30) | 120 (81) | 36 (77) | 223 (85) |
| Subarachnoid haemorrhage | 11 (3) | 2 (2) | Not assessed | 6 (4) | 4 (9) | 16 (6) |
| Unsure | 0 | 0 | 17 (24) | 0 (0) | 0 | 6 (2) |
| | **JHSR n=235 (clinical assessment of ischaemic stroke)** | **Zimbabwe* n=93** | **Gambia† n=105 (all pathological stroke types)** | **NMSS* (1993 - 1997) n=155 (White, et al, 2005)** | **JHSR n=65 (clinical assessment of ischaemic stroke)** | **OCSP n=543 (Bamford, 1991)** |
| **OCSP classification of ischaemic stroke subtype:** | | | | | | |
| Total anterior circulation syndrome | 62 (26) | n/a | 46 (35) | - | 16 (25) | 92 (17) |
| Partial anterior circulation syndrome | 84 (36) | n/a | 35 (27) | - | 23 (35) | 185 (34) |
| Lacunar syndrome | 71 (30) | n/a | 18 (14) | 33 (21) | 18 (28) | 137 (25) |
| Posterior circulation syndrome | 18 (8) | n/a | 6 (5) | - | 8 (12) | 129 (24) |

OXVASC - Oxford Vascular Study ; NMSS – Northern Manhattan Stroke Study
* only CT brain scan confirmed cases included for pathological stroke type
** Data for the NMSS are only for African-Americans. The NMSS did not classify stroke cases using the OCSP classification and only lacunar strokes overlap the with the classification used.
† Siriraj score used to diagnose pathological stroke type into cerebral haemorrhage, ischaemic stroke or undetermined

Our white JHSR patients had more than double the number of cerebral haemorrhages compared to patients in the OXVASC study from the UK (Rothwell et al., 2004). This may well be the influence of hospital bias resulting in more patients with cerebral haemorrhage and fewer with mild ischaemic stroke admitted to hospital. Interestingly, African-Americans had a pathological stroke type profile very similar to the white patients in the JHSR. Although the NMSS attempted to include community-based strokes it is not considered a truly community-based stroke study (Feigin et al., 2003b). The higher frequency of cerebral haemorrhage in our white stroke patients compared to that in the OXVASC study may reflect a slight hospital-based bias, when compared to the OXVASC study that was truly community-based. However, if one considers that the percentage of cerebral haemorrhage in our black patients was almost double that found in NMSS, then perhaps the NMSS findings support the view that African-Americans represent a population that has progressed through the health transition (Gillum, 1996a) (section 1.6 and table 1.1). In contrast black South African and Zimbabwean stroke patients are at a point much earlier in the transition. It is probably unwise to interpret the high proportion of cerebral haemorrhage in the Gambian stroke patients as a sign of them being at an even earlier stage of the transition, because of the potential for overestimation of cerebral haemorrhage in that study.

Only four of the studies in table 5.18 used the OCSP classification. It is a clinical classification and so less likely to be influenced by the lack of brain imaging in the Gambia, although the inclusion of some cerebral haemorrhages in the patient group assessed may have caused an increase in the number of total and partial anterior circulation events and a decrease in milder lacunar strokes. There were

more total anterior circulation infarcts in the Gambia study than in any other study, and the smallest number of lacunar infarcts. This suggests that this study included more severe strokes and fewer mild ischaemic strokes. An even larger proportion of total anterior circulation syndrome strokes (51%) were found in another study of 106 patients from the Gambia undertaken 10 years previously (Walker et al., 2003).

In a similar vein, there were far more total anterior circulation infarcts in the JHSR white patients compared to the OCSP patients, likely at least in part the result of hospital-based study bias. The proportion of partial anterior circulation infarcts and lacunar infarcts were very similar between the two groups, but the proportion of posterior circulation events (POCIs) in the JHSR patients was about half that in the OXVASC patients. This may reflect a true difference in proportions of POCIs in the community, a difference in likelihood of diagnosing POCIs i.e. a different diagnostic approach, or perhaps there was some reason why POCIs, which sometimes have unusual presentations, did not present to Johannesburg Hospital. However, even in the group of patients with CT brain scan confirmed infarction, there were only 4 POCIs (11%) in the white population group and 24 (12%) if we included all population groups.

Interestingly, the white and black JHSR patients compared most closely with one another rather than any other study population. However, as discussed in section 5.2.5.2., the underlying causes for the clinical subtypes differed. Hypertension was more frequent in JHSR black patients, yet lacunar stroke was only slightly more common in black than in white patients. Of course it has recently been shown that

hypertension is equally associated with lacunar stroke and other ischaemic stroke subtypes (Landau & Nassief, 2005; Jackson & Sudlow, 2005b), and previous studies using risk factor based classifications have probably overestimated the association of hypertension (and diabetes mellitus) and lacunar infarction.

#### 5.3.5.2 Comparison of TOAST classification subtypes

Both the NMSS and GCNKSS classified ischaemic according to the TOAST classification, but only the GCNKSS has provided the number of patients in each category. In 362 ischaemic strokes in black patients in the GCNKSS, cardioembolic stroke occurred in 54 (15%), a similar finding to the 21 of 141 (15%) black patients in the JHSR. In white patients in the GCNKSS, cardioembolic stroke occurred in 344 of 1594 (22%) ischaemic stroke patients. Our white patients also had a larger proportion (11 of 36; 31%) than our black patients (21 of 141; 15%), although the numbers were so small that this finding may be inaccurate. The similarity in proportion of cardioembolic stroke in JHSR black patients and those in the GCNKSS is striking. However, the underlying cause of the cardiac embolus may differ as it did between our white and black patients. We do not have sufficient data from the GCNKSS to assess this possibility.

Small vessel disease occurred in 64 (18%) black patients in the GCNKSS and in 25 (18%) of our black patients. Again there is a clear similarity, given the need for brain imaging and the strict criteria for the TOAST classification. In JHSR white patients small vessel disease accounted for 6 (17%) stroke patients, and in the GCNKSS for 244 (15%), again a fairly similar finding. One possible explanation for

this similarity across all four groups is that small vessel disease is equally common in all groups despite the very high levels of hypertension in JHSR black patients. Of course, we could classify fewer than half our patients using the TOAST classification and it is likely that the OCSP classification which shows a high proportion of lacunar infarcts, is more accurate.

Large-vessel atherosclerotic disease occurred in a similar proportion of white patients in the two studies: 194 (12%) in the GCNKSS and 5 (14%) in the JHSR. However, the findings in black patients were quite different: 37 (10%) in the GCNKSS, and nil in the JHSR. This may again reflect a difference in stage of the health transition between South African black stroke patients and African-American stroke patients, with more atherosclerotic disease in the African-American patients as shown in autopsy studies previously (compare section 2.3.3).

Other identified causes of stroke were found in 11 (3%) blacks and 37 (2%) whites in the GCNKSS, and in 24 (17%) blacks and 5 (14%) whites in the JHSR. The much higher proportion of other causes in the JHSR may reflect the younger population in our study compared to both whites and blacks in the GCNKSS. The mean age of black patients in the JHSR was 51 years (SD 16) and of white patients 61 years (SD 15), compared to blacks in the GCNKSS who had a mean age of 68 years (SD 15) and whites who had a mean age of 73 years (SD 14).

We had enormous difficulty in classifying a large proportion of patients using the TOAST classification: 61 (43%) black patients and 6 (17%) white patients. Yet it

appears as though this is a common problem. In the GCNKSS 196 (54%) black and 775 (49%) white patients were unclassified. The proportion of undetermined strokes in our series would increase if we included the 130 patients who did not have a CT brain scan to 162 (53%) blacks and 35 (46%) whites. However, the imaging rate for the GCNKSS is likely to be 100% (not stated in the manuscript) (Schneider et al., 2004) and so the large proportion of undetermined cause in all groups represents a shortcoming of the TOAST classification which has been noted previously (Warlow et al., 2001).

In summary, there was great similarity in the proportion of cardioembolic and small vessel strokes between the JHSR black population and the GCNKSS black population using the TOAST classification, although the underlying mechanism of cardiac embolism may differ. However, the JHSR black patients had no large vessel atherosclerotic strokes and more ‘other determined’ causes, reflecting a younger population in earlier transition than the African-American population. The JHSR white patients had a similar proportion of large-vessel atherosclerotic and small vessel strokes to the GCNKSS white patients, more cardioembolic and other determined causes. The latter likely reflects the 12 year difference in mean age between the two populations.

#### 5.3.5.3 Comparison of risk factors

Table 5.19 compares various accepted risk factors for stroke as well as the frequency of HIV and syphilis infection found in the JHSR black and white population groups, with findings from stroke registers in Zimbabwe (Matenga et al., 1986), Gambia (Garbusinski et al., 2005), the United States of America (African-American patients only) (Kissela, Broderick, Woo et al, 2001), the United Kingdom (patients of African descent only) (Lawrence, Coshall, Dundas et al, 2001) and the mostly white OXVASC study (Rothwell et al., 2004). All studies prospectively included first-ever-in-a-lifetime strokes and brain imaging except the study from the Gambia in which 12% of patients had recurrent stroke and none had brain imaging (Garbusinski et al., 2005). Other recent stroke studies from Sub-Saharan Africa were excluded because they ascertained stroke cases retrospectively (Zabsonre, Yameogo, Millogo et al, 1997; Talabi, 2003; Ogunrin, Unuigbe, Eregie et al, 2004; Osalusi, Ogun, Ojini et al, 2004; Ogun, Ojini, Ogungbo et al, 2005; Zenebe, Alemayehu, & Asmera, 2005a). Where appropriate we have included the prevalence of risk factors in the general South African population from the Demographic and Health Survey (Medical Research Council, 1998).

**Table 5.19 Comparison of the risk factors found in black and white patients in the JHSR, with African-American stroke patients in the GCNKSS and with the community-based OXVASC study (all figures refer to the number of participants and percentages of the total number assessed for that risk factor group are shown in brackets)**

| | JHSR – Black stroke patients n=308* | Zimbabwe n=93 (Matenga, 1986) | Gambia** n=148 (Garbusinski, 2005) | GCNKSS (n=705) (Kissela, 2004) | SLSR - Black stroke patients n=204 (Lawrence, 2001) | JHSR – White stroke patients n=76* | OXVASC (n=262 ) (Rothwell, 2004) |
|---|---|---|---|---|---|---|---|
| **Risk factor:** | | | | | | | |
| Age – mean (SD) | 51 (16) | 52 (n/a) | n/a | n/a | 63 (15) | 61 (15) | 74 (12) |
| Sex ratio (M:F) | 1:1 | 1:1.7 | 1:1 | n/a | 1:1.2 | 1:1 | 1:1 |
| Hypertension (%)† | 214 (74) | 49 (53) | 71 (65) | 456 (65) | 134 (66) | 50 (69) | 118 (46) |
| Cholesterol – mean (95% CI) mmol/L | 4.6 (4.2 to 5.0) | n/a | n/a | n/a | n/a | 5.4 (4.9 to 5.8) | 5.4 (5.3 to 5.5) |
| Diabetes mellitus (%) | 42 (16) | (3) | 7 (5) | 212 (30) | 60 (29) | 11 (16) | 25 (10) |
| Atrial fibrillation (%) | 10 (3) | n/a | 6 (4) | 51 (7) | n/a | 7 (10) | 44 (17) |
| Current cigarette smoking (%) | 57 (23) | (14) | n/a | 195 (28) | 47 (23) | 34 (54) | 47 (18) |
| Peripheral vascular disease | 9 (3) | n/a | n/a | n/a | n/a | 4 (5) | 22 (9) |
| Previous myocardial infarction | 0 | n/a | n/a | n/a | n/a | 3 (4) | 33 (13) |
| Previous TIA | 4 (1) | n/a | n/a | n/a | n/a | 4 (7) | 41 (16) |
| **Other:** | | | | | | | |
| HIV seropositive (%) | 61 of 148 (41) | n/a | n/a | n/a | n/a | 2 of 12 (17%) | n/a |
| Syphilis serology positive (%) | 9 of 59 (15) | 10 of 62 (16) | n/a | n/a | n/a | 0 of 9 (0%) | n/a |

JHSR – Johannesburg Hospital Stroke Register; OXVASC - Oxford Vascular Study ; GCNKSS – Greater Cincinnati / Northern Kentucky Stroke Study; SLSR – South London Stroke Register; * n will vary for each risk factor in study; ** not all first-ever-in-a-lifetime strokes – 18 (12)% recurrent stroke; † See text for definition of hypertension in each study; n/a not available

Black patients in the JHSR were young with a mean age of 51 years, similar to the mean age of 52 years found in the Zimbabwean study (table 5.19), but much younger (median age 51 years) than stroke patients in the Gambia (median age 64 years). In the South of London study, the mean age of black patients was closer to the mean of 61 years in our JHSR white patients than to our black patients. Patients in the community-based OXVASC study were noticeably older than any hospital-based population. This may reflect an older population, but may also at least in part reflect the possibility that institutionalised elderly patients or elderly patients with good home care are not readily admitted to hospital (Sudlow et al., 1996).

The sex ratio of males to females was about 1 in the JHSR for both population groups compared in table 5.19 and for the study population as a whole. It was also 1 in the Gambia and OXVASC but there were slightly more females in the Zimbabwean and South London studies. Without community-based studies in the latter two areas, it is difficult to comment on whether this reflects case mix or a true increase of females with stroke in the population.

Hypertension was found most often in our black stroke population (74%), closely followed by our white population (69%). African-Americans (65%), Africans living in London (66%), and Africans from the Gambia also had a high frequency of hypertension. We defined hypertension as the current use of antihypertensive medication, a history of having been diagnosed as hypertensive by a doctor or nurse prior to the stroke, a documented blood pressure of greater than or equal to

140 mmHg systolic or 90 mmHg diastolic prior to the stroke or more than one week following the stroke, or evidence of hypertensive heart disease on ECG or echocardiography. In the Greater Cincinnati / Northern Kentucky Stroke Study (GCNKSS) hypertension was diagnosed on review of the patient's medical notes but the exact definition used is not clear. The definition is also not clear from the South London study. In the Gambia hypertension was diagnosed if patients were on treatment for hypertension on admission, or if their blood pressure was >140 mmHg systolic and / or > 90 mmHg diastolic twice, more than one week after the stroke onset. It is possible that we were more likely to diagnose hypertension than investigators in the other three studies, though the difference in definition particularly in the Gambian study must only have accounted for a small proportion of patients.

Hypertension was least common in stroke patients in the OXVASC study (46%) when we defined it as a blood pressure of ≥ 150 mmHg systolic or ≥ 85mmHg diastolic using the data provided. Blood pressures were the most recent blood pressure reading prior to stroke taken from the general practitioner's notes (Rothwell et al., 2004). Again, differences in the definition of hypertension may account for some but not all of the inter-study differences in the proportion of patients with hypertension. It is likely that hypertension is more common in our stroke population than in others compared in table 5.19.

Cholesterol levels were only available for stroke patients in the JHSR and the OXVASC study in table 5.19. The mean cholesterol levels of JHSR whites and the OXVASC population were the same (5.4 mmol/L) and much higher than the mean

level (4.6 mmol/L) found in black stroke patients. In the THUSA study from the North-Western province of South Africa, cholesterol levels were measured in a community sample of 1854 people over the age of 15 years. Mean total cholesterol in black South Africans living in an urban area were found to be 4.0 mmol/L (95% CI, 4.5 to 5.0) in 171 HIV negative individuals and 3.85 mmol/L (95% CI 3.6 to 4.0) in 50 HIV positive individuals (Oosthuizen, Vorster, Kruger et al, 2002). When we analysed mean cholesterol levels in our black stroke patients with and without HIV we found a mean of 4.7 mmol/L (95% CI 4.1 to 5.2) in HIV negative patients and a mean of 3.7 mmol/L (95% CI 3.2 to 4.3) in HIV positive individuals. One hypothesis may be that in HIV negative individuals elevated cholesterol levels carry an increased level of risk for stroke or vascular disease in general, but in HIV positive individuals the risk of stroke is independent of accepted vascular risk factors. Of course, HIV positive patients in our study were younger than HIV negative patients and we did not systematically test everyone for HIV. It is possible that clinicians were more likely to test younger patients, who may have lower cholesterol levels, for HIV than to test older patients who may have higher cholesterol levels.

Diabetes mellitus was present about half as frequently in our black and white stroke patients as in African-American patients and African stroke patients living in London, and it was slightly more common than in OXVASC. Blood glucose was not measured in the Gambian study and so the lower proportion with diabetes mellitus may be an under-representation. However, diabetes mellitus certainly increases as populations progress through the health transition, and African-Americans have a disproportionately high prevalence of diabetes mellitus (Egede

& Dagogo-Jack, 2005; Graham, Leath, Payne et al, 2006). In the South London Stroke Register, black stroke patients had almost three times the frequency of diabetes mellitus as their white counterparts (Lawrence et al., 2001). So the progression in the proportion of patients with diabetes from the Gambia (5%), through South African patients in the JHSR (16%) to African-American and African-UK patients may represent a transitional change.

Atrial fibrillation was far more common (17%) in the OXVASC population than in any other stroke population in table 5.19, though we found the next highest proportion JHSR white patients (10%). While atrial fibrillation was far less common in black patients in the JHSR (3%) and in the Gambia (4%), it was slightly more common in African-American stroke patients (10%). Atrial fibrillation in JHSR black patients is seldom if ever caused by ischaemic heart disease which is not common in this population group, but rather by hypertensive heart disease, valvular or cardiomyopathic disease (table 5.8). It is possible that the frequency of atrial fibrillation increases as the prevalence of ischaemic heart disease increases in the population, resulting in the progressive increase in the frequency of atrial fibrillation from Africans to Africans living outside Africa and then Caucasians. Equally, however, the low frequency of atrial fibrillation in our black stroke patients and even our white stroke patients compared to those in the OXVASC study, may be because they were younger.

In the JHSR stroke patients a history of current smoking was found in 48 (31%) black males and significantly fewer (9 of 155, 7%) black females ($p<0.001$). In white JHSR patients smoking occurred in higher proportions of males (68%) and

females (41%) (p=0.09). In both this was higher than the national prevalence of 39% of 500 males and 27% of 600 females (Steyn, Bradshaw, Norman et al, 2002) in the community over the age of 15 years. Indeed smoking in white JHSR stroke patients was more common than in any other stroke population, while current smoking was least common in the OXVASC study. This finding of increased current smoking in white stroke patients compared to black stroke patients was found in the South London Stroke Register (whites 31%; blacks 23%) but not in the GCNKSS study in the USA (whites 19%, blacks 28%). One has to be cautious comparing these studies as cigarette smoking decreases with increasing age, and both our white and black stroke patients were younger than other populations. Thus, current smoking is currently less frequent in our black stroke patients. Smoking should not increase if new government anti-smoking policies work (van Walbeek, 2002).

It is not clear whether snuff (smokeless tobacco) is a risk factor for stroke, and there are conflicting results of two case-control studies in the literature (Asplund et al., 2003; Henley et al., 2005). The situation is further confused by the fact that some snuffers chew the tobacco (the predominant method in Sweden) (Asplund et al., 2003) and others (the predominant method in South Africa) (Steyn et al., 2002) sniff or inhale the tobacco nasally. Of the almost 14 000 people over the age of 15 years in the South African Demographic and Health Survey (SADHS), 1% of males and 10% of females used snuff. However, snuff use was very limited in all but the black population where 1% of males and 13% of females used snuff (Steyn et al., 2002). Snuff use gradually increased with age in black females in the SADHS ranging from 3% of 15 to 24 year olds to 29% of over 65 year-olds. Our

finding that 18 (12%) of 155 females stroke patients used snuff is probably in keeping with the general population prevalence, though of course a large prospective case-control study is needed to assess the relationship between snuff and stroke in our population.

Peripheral vascular disease and ischaemic heart disease are both markers of large vessel, extracranial atherosclerosis. Although myocardial infarction was more common in the OXVASC study and white JHSR patients than in JHSR black patients, the proportion of patients with peripheral vascular disease did not differ markedly between groups though we are likely to have overestimated it compared to the OXVASC study. In the OXVASC study baseline peripheral vascular disease was diagnosed on the basis of symptoms (good history of claudication) or a confirmed (by medical records) history of a diagnoisis of chronic / acute on chronic arterial disease in the legs, irrespective of whether treated and now symptomatic (e.g. previous critical ischaemia, amputation, angioplasty, bypass surgery). OXVASC did not include asymptomatic previously undiagnosed disease, such as absent pulses or femoral bruits (personal communication Professor Peter Rothwell, Professor of Neurology, University Department of Clinical Neurology, Radcliffe Infirmary, Oxford, United Kingdom), but we did include these patients.

There are no community-based surveys of peripheral vascular disease in urban South Africans, though there is one small survey of ankle-brachial pressure indices in rural South Africans which found the prevalence of sub-clinical peripheral vascular disease to be similar to that found in high-income populations (Fowkes, Thorogood, Connor et al, 2006). Ischaemic heart disease in general was

more prevalent in the South London Stroke Register black patients (14%) than in black JHSR patients (6%), but less common than in white JHSR patients (27%). Extracranial artery atherosclerosis increases as a population moves through the health transition (section 1.6). It is not surprising, therefore that IHD increases in frequency from South African black patients to Africans living outside Africa and white populations. Whether peripheral vascular disease increases before IHD in low and middle-income stroke populations requires further investigation.

A history of prior transient ischaemic attack (TIA) was seldom found in black JHSR patients (1%) and only found about half as often in white JHSR patients (7%) as in the OXVASC population (16%). This may reflect a real difference in the likelihood of prior TIAs, perhaps reflecting the prevalence of extracranial carotid artery disease in part, but it is more likely we did not identify previous TIAs that accurately on history. The much higher proportion of patients in the Kalafong study with previous TIAs suggests that this is possible (Rosman, 1989).

#### 5.3.5.4 HIV infection in stroke patients

Two of twelve (17%) white JHSR patients tested positive for HIV, though HIV testing was done so infrequently in white JHSR patients that the pre-test probability of a positive test was probably high in those tested (table 5.19). A much higher proportion of black patients were HIV positive (40%), and while only 48% of patients were tested, this proportion probably more accurately reflects the true prevalence of HIV infection in our black patients than our findings in white JHSR

patients. The population prevalence of HIV infection was discussed in section 5.3.3.1.4.

None of the other studies in table 5.19 assessed HIV infection in their stroke patients. However, a recent study from Malawi included 100 consecutive adult patients with a stroke-like presentation i.e. a sudden onset of focal neurological deficit which had been present for less than 7 days (Kumwenda et al., 2005). All patients were antiretroviral therapy naïve (as were all patients on the JHSR). Ninety-two patients received a CT brain scan with and without contrast within one week of admission. They then compared the presence of non-stroke lesions, any differences in pathological stroke type, and outcome in HIV positive and negative patients. To compare their findings to the JHSR we have assessed our experience with non-stroke lesions from the original 524 patients referred to the JHSR, and compared HIV positive and negative stroke and non-stroke black patients in the JHSR with those in the study from Malawi (table 5.20). Three HIV positive and 4 HIV negative patients were excluded from the JHSR because of ring enhancing lesions noted on CT brain scan, and two HIV negative patients because of subdural haematoma noted on CT brain scan. We did not therefore find, as the Queen Elizabeth Central Hospital (QECH) study did, that HIV positive patients were more likely to present with stroke-like presentation than HIV negative patients. In both studies there was a slight increase in the number of females who were HIV positive compared to males, yet in the HIV negative group males predominated. The mean age of HIV positive black patients was lower than HIV negative patients, though this difference was less marked in the JHSR than in the QECH study. The mean age of the patients excluded from the JHSR is distinctly

different between the HIV positive group who were younger and the HIV negative group who were older. It is possible that there is a difference in the underlying aetiology of the ring-enhancing lesions between the young HIV positive and older HIV negative patients, with more infective causes in the young patients and more neoplastic / metastatic lesions in the older patients, but this requires further investigation.

## Table 5.20 Comparison of stroke and non-stroke lesions in the black population group referred to the JHSR and to QECH in Malawi (Kumwenda, 2005), by HIV status

| | JHSR | | QECH | |
|---|---|---|---|---|
| | HIV positive | HIV negative | HIV positive | HIV negative |
| Total number | 157 | | 98 | |
| Male | 28 | 60 | 19 | 30 |
| Female | 36 | 33 | 28 | 21 |
| Mean age (SD) in years** | 38 (10) | 48 (15) | 38 (13) | 59 (17) |
| Mean age of excluded patients (SD) | 32 (8) | 60 (14) | n/a | n/a |
| **Stroke (CT confirmed) (% of all strokes scanned):** | n=117 | | n=81 | |
| Cerebral haemorrhage (%) | 5 (10) | 23 (34) | 1 (3) | 15 (32) |
| Ischaemic stroke* (%) | 43 (88) | 41 (60) | 33 (97) | 32 (68) |
| Subarachnoid haemorrhage (%) | 1 (2) | 4 (6) | n/a | n/a |
| Other lesion: | 3 | 6 | 7 | 2 |
| - brain tumour | 0 | 0 | 1 | 0 |
| - subdural | 0 | 2 | 0 | 1 |
| - white matter disease (not PML) | 0 | 0 | 0 | 1 |
| - PML | 0 | 0 | 2 | 0 |
| - ring enhancing lesion | 3 | 4 | 4 | 0 |

JHSR: Johannesburg Hospital Stroke Register;
QECH: Queen Elizabeth Central Hospital, Blantyre, Malawi;
* includes CT normal stroke;
** mean age for JHSR is only for those patients with confirmed stroke

## Table 5.21 Comparison of risk factors in HIV-positive and HIV-negative black stroke patients in the JHSR (percentage in brackets unless otherwise stated)

| | HIV positive | HIV negative | Significance of difference |
|---|---|---|---|
| **Risk factor:** | | | |
| Mean age (SD) years<br>n=148 | 38 (10) | 48 (15) | p<0.001 |
| Hypertension<br>n=134* | 25 (49) | 62 (75) | p=0.002 |
| Diabetes<br>n=125* | 1 (2) | 10 (14) | p=0.03 |
| Cholesterol – mean (95% CI)<br>n=64* | 3.7 (3.2 to 4.3) | 4.7 (4.1 to 5.2) | p=0.02 |
| Current cigarette smoking<br>n=110* | 14 (29) | 18 (29) | p=0.4 |
| Current alcohol use<br>n=109* | 17 (35) | 15 (25) | p=0.5 |
| Atrial fibrillation<br>n=145* | 0 | 2 (2) | p=0.2 |
| Cardiomyopathy<br>n=148 | 5 (6) | 7 (8) | p=0.8 |

JHSR: Johannesburg Hospital Stroke Register;
*n refers to total number of patients with HIV status and risk factor assessed

We found a similar influence of HIV status on pathological stroke type diagnosed on CT brain scan as was found in the QECH study (Kumwenda et al., 2005)(table 5.20). In HIV negative patients, cerebral haemorrhage accounted for about 30% of strokes in both the JHSR and the QECH study, a similar finding to most hospital-based stroke series from Sub-Saharan Africa (tables 5.16 and 5.18). In HIV positive patients, however, haemorrhage is not common (10% in the JHSR and 3%) in the QECH study. We found this difference to be statistically significant (p=0.005).

HIV may cause a dilated cardiomyopathy (Magula & Mayosi, 2003) and so cause embolic stroke. We did not find any significant difference in the frequency of atrial fibrillation in HIV positive black stroke patients (table 5.21) or in cardiomyopathy although the small numbers of patients make this assessment inaccurate. Of the 148 patients tested for HIV infection, 5 HIV positive patients had a cardiomyopathy and 7 patients without HIV infection had a cardiomyopathy (p=0.8).

The QECH study did not find a significant difference in risk factors between HIV positive and negative patients, although not surprisingly it found an increase in stroke risk factor prevalence in people over the age of 40 years. We found significantly less hypertension, diabetes mellitus, as well as lower mean cholesterol in HIV positive patients, but no difference in current cigarette smoking, alcohol use, or atrial fibrillation between the two groups (table 5.21).

Although we did not find the same preponderance of space-occupying lesions in HIV positive patients presenting with a stroke-like onset, as was found in the QECH study (Kumwenda et al., 2005), we did find space occupying lesions mimicking stroke. It is possible that the clinicians who assessed patients before referring them to us excluded some patients with space occupying lesions.

The rest of our findings are very similar to those found by the QECH study. In summary HIV positive stroke patients are younger, less likely to have cerebral haemorrhage than ischaemic stroke, have a lower cholesterol level, and are less likely to have hypertension and diabetes than HIV negative patients. In a setting with a high prevalence of HIV, when a patient presents with clinical features of a stroke, it is probably prudent to assess their HIV status. If found to be HIV positive, patients should have a brain scan if possible and a lumbar puncture to exclude infective or other HIV related causes of the stroke (Connor et al., 2000; Mochan et al., 2003; Kumwenda et al., 2005).

#### 5.3.5.5 Syphilis infection in stroke patients

Most studies from SSA and outside SSA have not provided data on syphilis serology in stroke patients (table 5.19). Syphilis was positive in almost the same proportion of stroke patients in the stroke study from Zimbabwe as in black patients in the JHSR (16% versus 15%), though syphilis serology was only assessed in 62 of 93 patients in Zimbabwe and in 59 of 308 patients in the JHSR. The mean age of patients with positive blood serology for syphilis in the JHSR was 52 years (SD 13) (range 30 to 70). In the JHSR none of the patients tested were

found to have neurosyphilis (although again investigation was incomplete in almost all patients), and in the Zimbabwean study, 8 patients were found to have neurosyphilis. The prevalence of syphilis infection in South Africa appears to be declining, and in 2001 2.7% of women attending antenatal clinics in Gauteng province had the infection, with the highest prevalence in the 20 to 34 year-old age group (Directorate: Health Systems Research, 2001). Despite this decline the association between HIV infection and syphilis infection is well documented (Lynn et al., 2004) and the search for neurosyphilis should be more detailed than in the JHSR.

### 5.3.6 Stroke severity, impairment and related disability

#### 5.3.6.1 Stroke severity

Stroke severity as measured on the Scandinavian Stroke Scale (SSS) (Scandinavian Stroke Study Group, 1985) and the National Institutes of Health Stroke Scale (NIHSS) (National Institute of Neurological Disorders and Stroke, 2005) was not significantly different in any population group (table 5.14). It was not possible to compare the severity of acute stroke in our patients with other studies in South Africa because, although the Durban Stroke Data Bank assessed acute stroke, they used the Canadian Neurological Scale (Hoffmann, 1998).

Prospective hospital-based studies from the rest of Sub-Saharan Africa have also not used the NIHSS or SSS frequently. However, the recent study from the Gambia (Garbusinski et al., 2005) (tables 5.18 and 5.19) did assess initial stroke severity using a modified NIHSS. The modification (mNIHSS) consisted of two substitutions: “what is the season” and “who is the head of your compound” replaced asking a patient his/her age and the current month (Garbusinski et al., 2005). We did not modify the NIHSS in the JHSR. Most patients (no exact data provided) in study from the Gambia were admitted within 48 hours, so possibly slightly later than in the JHSR where the median time to admission was 1 day (table 5.1). In the study from the Gambia, 18 (12%) of the 148 patients were admitted with a recurrent stroke, while all patients in the JHSR had first-ever-in-a-lifetime stroke.

The Gambian study assessed the mean mNIHSS in 146 patients on admission and found it to be 16 (SD 7) (higher figures correspond to higher severity). They did not provide a median value for the scale. In the JHSR the mean NIHSS score at our first assessment was 12 (SD 10) in the 431 patients assessed. The mean in black stroke patients was 12 (SD 9). Strokes appear to be more severe in the Gambia study than in the JHSR, perhaps in keeping with the greater proportion of total anterior circulation syndrome strokes and cerebral haemorrhages (as assessed by the Siriraj Score) in the Gambian study compared to the JHSR (table 5.18).

Very few publications gave separate data on the NIHSS at time of admission for African-Americans (Sheinart, Tuhrim, Horowitz et al, 1998; Rundek, Mast, Hartmann et al, 2000) and we could not find any studies that assessed the SSS in African populations. One study, which included 958 patients with first ischaemic stroke, 30% African Americans, 51% Hispanics and 19% whites Americans, from the Northern Manhattan Stroke Study group, did assess the NIHSS though data were not provided separately for each population group (Rundek et al., 2000). The NIHSS score was categorised as: mild (NIHSS ≤ 5), moderate (NIHSS 6 to 13), and severe (NIHSS ≥ 14). We categorised our ischaemic stroke patients (n= 339, all population groups included) similarly, and compared the two studies (Northern Manhattan Study / JHSR). We found fewer mild (56% / 39%) and moderate (35% / 26%), and more severe (9% / 35%) strokes in the JHSR than was found in the NMSS.

We could not find studies including African-Americans or Africans living in Africa, or in countries outside Sub-Saharan Africa that used the Scandinavian Stroke Scale. We have therefore compared our findings to the Copenhagen stroke study which used the Scandinavian Stroke Scale (Jorgensen, Nakayama, Raaschou et al, 1995). In contrast to the NIHSS the SSS scores decrease with increasing severity and patients are usually categorised as: very severe (0 to 14 points), severe (15 to 29 points), moderate (30 to 44 points), and mild (45 to 58 points) (Jorgensen et al., 1995; Reith, Jorgensen, Nakayama et al, 1997). We compared our patients to those in the Copenhagen Stroke Study, but excluded all subarachnoid haemorrhages for the comparison (included n=416), as the Copenhagen study did not include this pathological stroke type. The Copenhagen study included 1197 patients and 82% had a CT brain scan. Comparing the two studies we found the following proportions of patients in each category of the SSS (Copenhagen Stroke Study / JHSR): very severe (19% / 31%), severe (14% / 17%), moderate (26% / 17%), and mild (41% / 35%). Thus, we found far more severe strokes and fewer mild strokes in the JHSR than were found in the Copenhagen Stroke Study (Jorgensen et al., 1995). Strokes presenting to hospital may be more severe in urban Johannesburg than in high-income regions.

Of course, this does not suggest that stroke is more severe in the urban South African community, because the likelihood of someone presenting to hospital, or being admitted once they present to the emergency service, is probably very different in Johannesburg compared to the many high-income regions. Indeed, with the pressure of HIV infected medical patients on local health services and resulting long waiting times for assessment, people are likely to avoid presenting

to the emergency services and once there doctors are only likely to admit more severe patients. To assess stroke severity in the community, we need a community-based incidence study.

#### 5.3.6.2 Stroke related acute impairment and disability

Independence following stroke, whether assessed using the Barthel Index (BI) or the modified Rankin score was not significantly different between population groups, although slightly more white than black patients were fully independent (BI score of 20) (table 5.15). Disability was also not significantly different between groups.

It is not possible to compare functional impairment in the JHSR with other hospital-based stroke studies from South Africa. The Kalafong study (Rosman, 1989) did not assess the Barthel Index or modified Rankin score, and it is not clear from published results whether these scores were assessed in the Medunsa study (Joubert et al., 1989; Joubert, 1991; Joubert et al., 2000). Both scores were assessed in the Durban Stroke Data Bank (Hoffmann, 1998), but the results were not reported in sufficient detail to allow us to compare our findings. The DSDB did not report the results of the Barthel Index in black patients because they found it difficult to assess functions such as combing hair and bathing, wheelchair skills, and stair use. We did not find an enormous difference between the assessment of the Barthel Index in black stroke patients and other population groups.

In the study from the Gambia, a modified Barthel Index was used (Garbusinski et al., 2005), but this was assessed at discharge and we assessed the BI in our patients on admission. It is therefore not appropriate to compare the two assessments. Similarly, the BI was assessed one week following stroke onset in the South London Stroke Register, and it is therefore not appropriate to compare our patients with theirs.

#### 5.3.6.3 Stroke related complications, recurrent stroke in hospital and death

Our follow-up of stroke patients until discharge was not complete for logistical reasons. The high service load, frequent transfer of patients around the hospital because of the ongoing bed shortage, and high turnover of patients admitted and discharged, made it almost impossible to follow up patients effectively or note complications accurately. We regard the frequency of complications in the JHSR as a minimum likely value. Our findings of recurrent stroke in hospital and death are likely to be more accurate because the medical units invariably drew our attention to patients who suffered recurrent stroke or died. We did not follow up patients following their discharge and did not establish the 30-day case fatality.

Despite these limitations, major complications in the Durban Stroke Data Bank (DSDB) occurred with a very similar frequency to those in the JHSR. In the DSDB and JHSR specific post-stroke complications occurred in the following proportion respectively (n=1000 for the DSDB / n=432 for the JHSR): pneumonia in 23 / 22 (2% / 5%), seizures in 53 / 21 (5% in both), depression in 44 / 6 (4% / 1%), recurrent stroke in 30 / 11 (3% / 3%), and death in 53 / 35 (5% / 8%). We did not

distinguish between onset seizures (occurring in the first 24 hours following stroke) and post stroke seizures (occurring after a stable deficit is present) (Burn et al., 1997).

The DSDB placed a focus on the impact of stroke on higher cortical function and so not surprisingly found behavioural abnormality in 166 (17%) of patients. We did not assess higher function at all. In the trial period leading up to the development of the JHSR (data not included in the JHSR), we attempted to modify the Hodkinson Abbreviated Mental Test (Hodkinson, 1972) (10 items) to suit South African patients, by replacing the address to be repeated with a local Johannesburg address, and the question 'present monarch' with 'previous president.' Despite this adaptation, we found the test very unreliable in our local population and decided against using any cognitive score in the JHSR.

Post-stroke lung infections occurred more frequently (18%), and epilepsy less frequently (2%) in the 148 patients in the Gambian stroke study (Garbusinski et al., 2005) than in the JHSR. Death occurred far more frequently during hospitalisation (61 of 148 patients; 41%) than in our study, most likely in keeping with the high proportion of severe strokes in the Gambian study. Our lack of long term follow up of patients prevented comparison with data from the second study from the Gambia undertaken in 1990, which provided 4 years of community follow up (Walker, 1963).

Post stroke epilepsy occurred in 48 (7%; 95% CI 6 to 9) of 675 stroke patients in the community-based Oxfordshire Community Stroke Project (OCSP) compared to

our similar finding of 21 of 432 (5%; 95% CI 3 to 7) (Burn et al., 1997). We also found an increased proportion with total anterior circulation infarcts (28%) compared to other OCSP ischaemic stroke subtypes (4 with partial anterior circulation events and 1 with a lacunar infarct) (p=0.004).

### 5.3.7 Evidence of the health transition based on the JHSR

Our comparison of the nature of stroke in black JHSR patients, white JHSR stroke patients and African-American stroke patients supports the notion of a health transition taking place in black South Africans. As we discussed in chapter 1 (section 1.6) (table 1.1), it is postulated that the nature of stroke should change with a population's transition from stroke initially caused predominantly by cardioembolic events resulting from cardiomyopathy and rheumatic heart disease, to stroke associated with hypertension and hypertensive heart disease and a high proportion of cerebral haemorrhage; and finally the emergence of atherosclerotic stroke and ischaemic heart disease.

We found a high proportion of cerebral haemorrhage (almost all hypertension related) and hypertension related small vessel disease in black stroke patients. While the ischaemic stroke subtypes were remarkably similar between our black and white stroke patients, the underlying cause of large artery strokes differed. Cardioembolic strokes were seldom if ever caused by ischaemic heart disease (IHD), though we found IHD in a small number of black stroke patients. Instead the major causes of cardioembolic stroke were cardiomyopathies, often caused by end-stage hypertensive heart disease, rheumatic valvular heart disease and atrial fibrillation unrelated to IHD.

Although we found the emergence of symptomatic IHD in black stroke patients, and a similar frequency of peripheral vascular disease, we did not find significant atherosclerosis of the extracranial carotid arteries in black patients. Hypertension

was the major risk factor in black stroke patients, cholesterol levels were low and cigarette smoking was less frequent than in white stroke patients. Diabetes mellitus was about as common in black and white stroke patients. The mean age of black stroke patients (excluding HIV positive patients) was significantly younger than white stroke patients and African-Americans.

This profile of risk factors, pathological stroke types, ischaemic stroke subtypes and causes of stroke is, we think, in keeping with a population in transition. Black stroke patients are probably in stage 2 of the postulated transition (table 1.1), but there are distinct features compatible with stage 3 i.e. the emergence of IHD, the presence of peripheral vascular disease and a similar frequency of diabetes mellitus to that found in white stroke patients. However, compared to African-American stroke patients and African's with stroke living in London, South African urban black stroke patients have strokes at a younger age, have more cerebral haemorrhage, more small vessel disease, and are more frequently hypertensive. They have less diabetes mellitus and ischaemic heart disease, but a similar proportion smoke cigarettes. If African-Americans (and other African populations living permanently in high-income regions) represent the final stages of the African vascular transition, then South African black stroke patients are in a much earlier stage of the transition. We anticipate a change in stroke types, subtypes and vascular risk factors over future decades as our population advances towards this final stage, unless effective primary prevention in the population alters this course.

## 5.4 Conclusion

In an urban stroke hospitalised population that was representative of the diverse population of South Africa, we found distinct differences in the nature of stroke in different population groups, particularly between blacks and whites. Black stroke patients were younger, had lower cholesterol levels, were less likely to smoke cigarettes, had features of lower socioeconomic status, had less atherosclerosis in the extracranial carotid arteries and coronary arteries and had distinctly different causes of cardioembolic strokes, compared to white stroke patients. In black stroke patients cardioembolic stroke was caused by cardiomyopathy, atrial fibrillation and rheumatic valvular disease. The most important underlying mechanism of cardioembolic events was not ischaemic heart disease as in the whites, but hypertension and hypertensive heart disease. The exact mechanism causing stroke in hypertensive heart disease, and the cardioembolic risk at various stages of hypertensive heart disease, require further investigation.

When we compared the nature of stroke in South African black patients with that in African Americans, in Africans living in high-income regions, and in white stroke populations, we found distinct differences that suggest that black stroke patients are in an earlier stage of the vascular health transition. However, they are developing stroke types, subtypes and the associated risk factor profile compatible with later stages of the transition.

We found HIV infection predominantly in black stroke patients. This subgroup was younger and had fewer traditional risk factors than HIV negative stroke patients

had. Although cerebral haemorrhage occurred less frequently in HIV positive stroke patients, ischaemic stroke subtypes occurred about as often as in HIV negative stroke patients. We cannot comment on the likely underlying cause of the stroke in these patients, however.

Despite the difference we found in the nature of stroke between population groups in the JHSR, the other characteristics of stroke patients in the various groups were very similar. In particular, the time taken to presentation, stroke severity, clinical impairment, complications arising from stroke, and the impact of stroke on the individual's level of functioning and independence did not differ markedly between population groups.

Our findings suggest that there is still time to improve primary prevention in the black South African population to prevent an otherwise inevitable increase in atherosclerosis related stroke and heart disease. Hypertension is currently the single most important risk factor for, and underlying cause of stroke in the South African population. Simply lowering the population's blood pressure would likely decrease stroke incidence significantly. HIV infection has clearly altered the profile and nature of stroke, particularly in black South Africans, and more research is needed to clarify the underlying cause and risk of stroke related to HIV infection.

### 5.4.1 What this study adds to the literature

The JHSR is the first stroke register that is reasonably representative of the whole South African population and therefore able to compare the nature of stroke in the various populations (though this is most accurate for the larger black and white populations). It is also the first stroke register in Sub-Saharan Africa to provide a direct comparison between population groups. The comparison of the nature of stroke in black and white stroke patients, in particular the differences in cardioembolic stroke and emergence of ischaemic heart disease, provide evidence for a vascular health transition occurring in the South African black population. The JHSR is also the first stroke register in Sub-Saharan Africa to show the impact of HIV on the nature of stroke across the full age spectrum of black South African stroke patients. Finally, it is the first Sub-Saharan African stroke register to highlight the impact of hypertensive heart disease on the cause of stroke in black patients.

# CHAPTER 6 VALIDATION OF THE ALLEN (GUY'S HOSPITAL) AND SIRIRAJ STROKE SCORES IN URBAN SOUTH AFRICAN BLACK STROKE PATIENTS

## 6.0 Introduction

The assessment of pathological stroke type (cerebral haemorrhage, ischaemic stroke and subarachnoid haemorrhage) is essential for understanding the nature of stroke in a population, and for comparing the nature of stroke across populations. We have described the nature of urban hospital-based strokes in the Johannesburg Hospital Stroke Register (JHSR) in chapter 5, and in chapter 7 we will describe the nature of strokes presenting to the rural Tintswalo Hospital.

Ideally, a CT or MRI brain scan is necessary to distinguish pathological stroke type, but unfortunately Tintswalo Hospital did not have a scanner. The nearest CT scanner available for patients admitted to Tintswalo Hospital was 300 km away (about 4 hours drive). With scarce resources and very often only one ambulance servicing the entire hospital and region, few if any stroke patients ever have a brain scan. Indeed, CT and MRI scanners are not readily available throughout Sub-Saharan Africa, and few stroke patients are scanned (El Khamlichi, 2001; Bower & Zenebe, 2005). In hospitals without access to CT or MRI scanners, clinicians attempt to assess pathological stroke type at the bedside.

However, previous studies in high-income populations have shown that the bedside assessment of pathological stroke type by clinicians is inaccurate (von

Arbin, Britton, de Faire et al, 1981; Allen, 1983). Prior to the widespread availability of CT scanners in high-income regions of the world, clinical scores were developed in an attempt to improve the clinician's bedside assessment of pathological stroke type. Some of these, such as the Siriraj Stroke Score, have been used in Sub-Saharan Africa to distinguish pathological stroke type in epidemiological studies e.g. in one study from the Gambia (discussed in chapter 5) (Garbusinski et al., 2005).

However, none of these stroke scores have been developed or prospectively validated for use in Sub-Saharan Africa. Indeed, many of the scores rely on measures of atherosclerosis to distinguish pathological stroke type. Thus, while they may perform relatively well in stroke populations with a high prevalence of atherosclerosis, it is not at all certain how well they perform in the Sub-Saharan African black stroke population which has a low prevalence of atherosclerosis.

We decided to prospectively validate two of the most frequently used stroke scores, the Siriraj Score and the Allen (Guy's Hospital) score, in the South African black population using the Johannesburg Hospital Stroke Register in the hope that we could use one or the other in the Tintswalo Hospital Stroke Register (chapter 7). Although several scores have been developed (Hatano, 1976b; Allen, 1983; Poungvarin, Viriyavejakul, & Komontri, 1991; Besson, Robert, Hommel et al, 1995; Talavera, Wacher, Laredo et al, 2000), we chose the Siriraj Stroke Score (SSS) (Poungvarin et al., 1991) and the Allen (Guy's Hospital) Stroke score (hereafter referred to as the Guy's Hospital Stroke Score or GHSS) (Allen, 1983), because they required the least ancillary testing and investigation, and were the simplest to

use in our low resourced setting. The SSS only requires a clinical history and examination, and the GHSS only requires a chest x-ray and ECG in addition to a clinical history and examination.

During the second period of the 23 months that we ascertained stroke patients for the JHSR (chapter 5), we also decided to evaluate the stroke team members' ability to assess the pathological stroke type based on a patient's clinical presentation. We did not specifically instruct to use specific criteria in the hope that their assessment would be as generalisable as possible to doctors elsewhere. We added instructions to the team members to assign each patient a pathological stroke type prior to finding out the CT scan result (Appendix D), and assured them that we would not assess the accuracy of any individual clinician. We therefore have limited data to compare the stroke team clinicians' assessment of pathological stroke type, compared to the assessment using the two scoring systems, and the CT scan "gold-standard" result.

We assessed the accuracy of the scores in black patients with first-ever-in-a-lifetime stroke (the JHSR patients described in chapter 5), and in black patients with recurrent stroke separately. We included recurrent stroke, as have other studies (Hawkins, Bonita, Broad et al, 1995), because the diagnosis of pathological stroke type is not only important for epidemiological studies assessing first-ever strokes, but also in the management of all stroke patients in settings where a CT or MRI scan is not available.

The literature related to clinical assessment of pathological stroke type as well as to the performance of the SSS and GHSS in other populations will be outlined and compared to our findings in the discussion (section 6.3).

### 6.0.1 Aim of the study

Our aim was to assess the accuracy of the Siriraj Stroke Score (SSS) and the Guy's Hospital Stroke Score (GHSS) in distinguishing between intracranial haemorrhage (see section 6.1.3 for the definition and reason we used this assessment) and ischaemic stroke in both first-ever-in-a-lifetime and all (recurrent and first-ever-in-a-lifetime) black stroke patients in the Johannesburg Hospital Stroke Register (JHSR). A secondary aim was to assess whether the scores were more accurate than our stroke team clinicians were in diagnosing cerebral haemorrhage.

## 6.1 Methods

### 6.1.1 Setting and population, and methods used in the JHSR

We described the population, setting and methods for the JHSR in section 5.1. In the JHSR we only included patients with first-ever-in-a-lifetime stroke, however we also assessed the Siriraj and Guy's Hospital Stroke Scores in black patients who presented with recurrent stroke. We considered a stroke recurrent if the patient had a sudden onset of a new focal neurological deficit at least 28 days following their initial stroke.

### 6.1.2 Assessment of Siriraj and Guy's Hospital Score

The stroke team clinician documented all the information required for assessing the SSS and GHSS as part of the JHSR questionnaire (Appendix D), but they did not calculate the scores. Instead, the variables were combined on the stroke questionnaire in a format similar to that used on the Department of Clinical Neuroscience, University of Edinburgh, online prediction model website (Perry, 1998). From the 1st August 2001 till 31st December 2002 (the second time period of case ascertainment for the JHSR), the clinicians also documented what they thought the likely pathological stroke type was and whether this assessment was made without knowledge of the brain imaging result.

The stroke team clinicians included neurology registrars (predominantly), medical registrars rotating through neurology, and psychiatry registrars rotating through neurology. I was the only consultant neurologist assessing the JHSR patients. Apart from the patients I assessed on my own, I often re-examined those stroke patients who the registrars had initially examined. However, we only analysed the assessment of pathological stroke type made by the first stroke team clinician to see the patient.

Stroke patients were entered into this sub-study if they were black South Africans, had sufficient data available to calculate the SSS and GHSS, and had had a CT brain scan within 15 days of admission (to exclude the misdiagnosis of possible resolving haemorrhage – see section 5.2.2).

### 6.1.3 Data analysis

We calculated both the SSS and GHSS using the technique provided in the original descriptions (Allen, 1983; Poungvarin et al., 1991), and used the same cut-off points for diagnosing intracranial haemorrhage and ischaemic stroke (infarction) used in these publications (Appendix F). From a clinical perspective it is useful to distinguish all sources of intracranial haemorrhage (subarachnoid haemorrhage and cerebral haemorrhage) and we followed previous studies that have validated the SSS and GHSS and combined subarachnoid haemorrhage and cerebral haemorrhage as 'intracranial haemorrhage' for the purposes of analysis (Sandercock, Allen, Corston et al, 1985; Hawkins et al., 1995).

We calculated the scores using STATA (StataCorp, 2001), and analysed the distribution of the scores using SSC-stat (Statistical Services Centre, 2004). We compared the population with and without CT brain scans using a $\chi^2$ test for homogeneity using STATA. We calculated the sensitivity, specificity, positive predictive values, likelihood ratios and kappa scores (comparing each score and the clinicians with the CT scan result), as well as confidence intervals with Confidence Interval Analysis software (Bryant, 2000) using the 'uncertain' results i.e. the results that did not yield a definite answer of haemorrhage or infarction in the analysis (see section 6.3 for discussion of the effect of including or excluding 'uncertain' results in the calculation). We only used the clinicians' evaluation of pathological stroke type if they were not aware of the brain scan result at the time of the assessment.

We analysed the sensitivity, specificity, positive predictive value and kappa scores separately for first-ever-in-a-lifetime strokes and all strokes. The remainder of the analyses included all strokes.

### 6.1.4 Ethics

The assessment of the SSS and GHSS was an integral part of the original methodology of the JHSR and we requested and were granted ethics approval as part of the JHSR: University of the Witwatersrand Human Ethics Research Committee (M00/03/7).

## 6.2 Results

The JHSR included 432 first-ever-in-a-lifetime stroke patients. Of these 308 were black stroke patients. Two-hundred and seven (67%) of these patients had a CT brain scan within 15 days of admission and sufficient information available for calculation of the Siriraj and Guy's Hospital scores. One hundred and twenty-one scans (59%) were done within 24 hours. A further 15 black patients presented with recurrent stroke, had a scan within 15 days of onset and complete score data. Sixty-six (32%) first-ever stroke patients and 70 (32%) of all stroke patients (including recurrent strokes) had an intracranial haemorrhage (59 cerebral haemorrhages and 11 subarachnoid haemorrhages).

We described the demographic details of first-ever black stroke patients in chapter 5. There were 9 male and 6 female recurrent stroke patients with a mean age of 51 years (SD 16; 95% CI 42 to 60; range 28 to 74). The mean age of the recurrent stroke and first-ever stroke patients was the same.

### 6.2.1 Stroke score findings

Figure 6.1 shows the distribution of scores in each pathological stroke type (ischaemic stroke and combined intracranial haemorrhages) using the Siriraj Stroke Score (SSS), and figure 6.2 shows the equivalent distribution of the scores using the Guy's Hospital Stroke Score (GHSS).

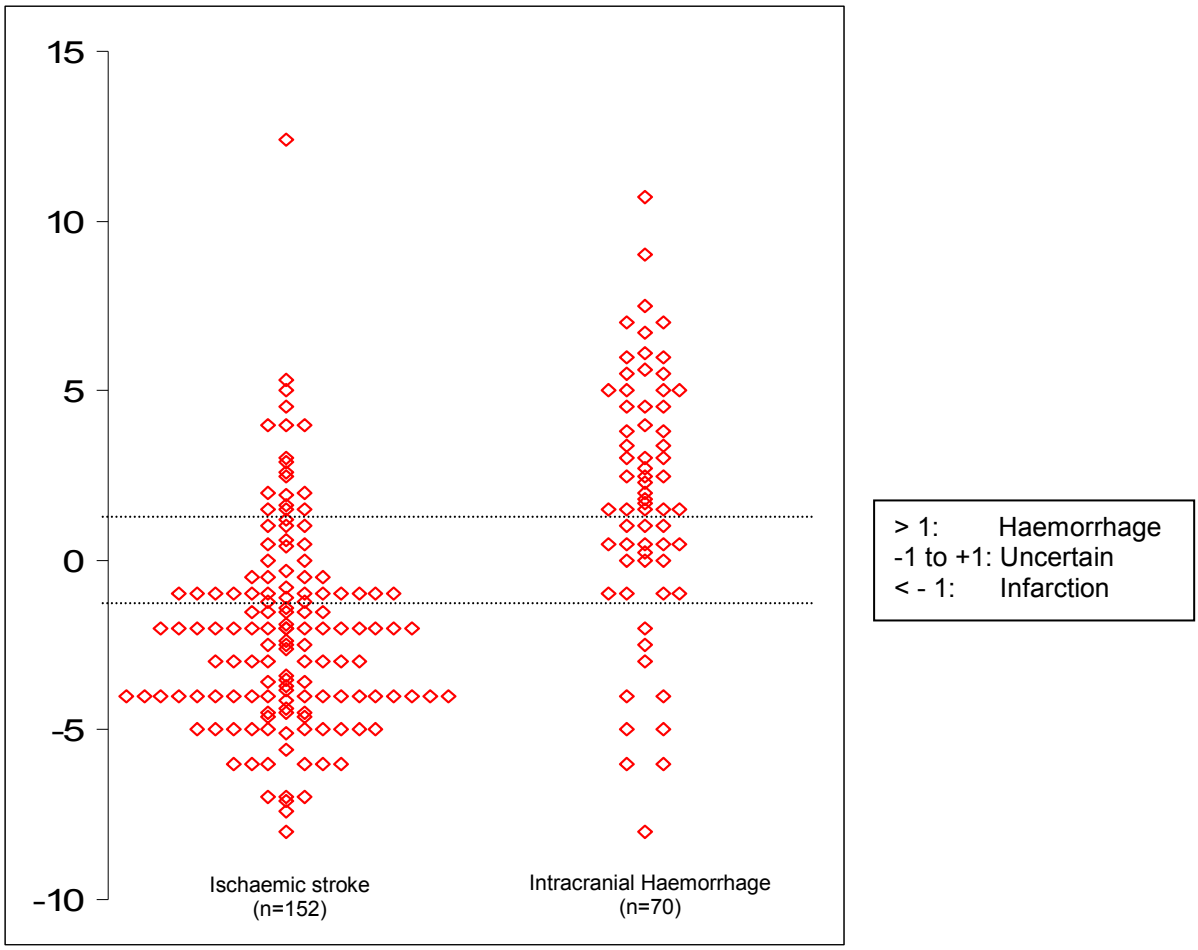



**Figure 6.1 Distribution of diagnostic scores for the Siriraj Stroke Score**

The dotted horizontal lines refer to the cutoff level at which the score predicted the pathological stroke type with around 90% certainty (see Appendix F)

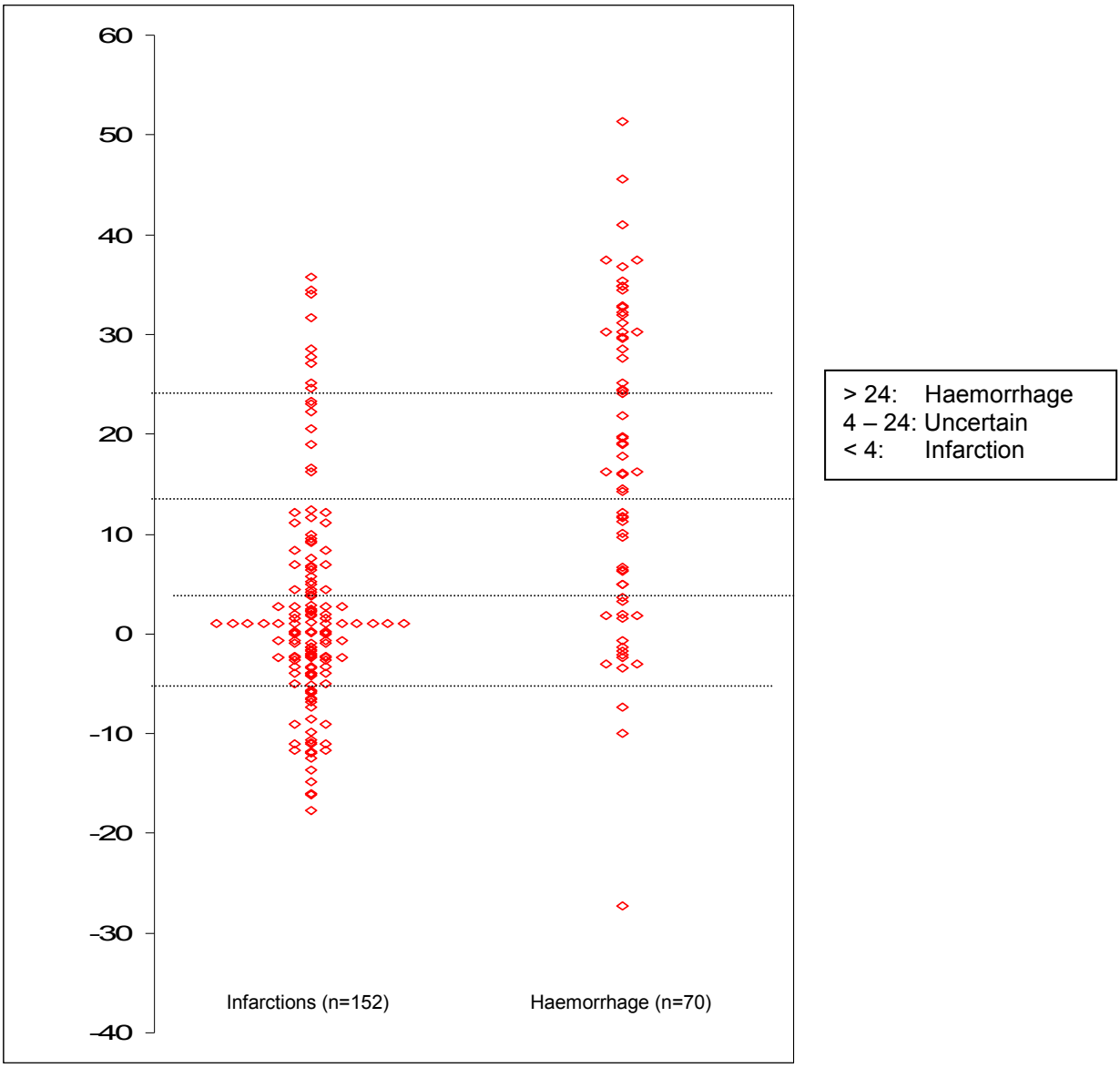



**Figure 6.2 Distribution of diagnostic scores for the Guy's Hospital Stroke Score**

The dotted horizontal lines refer to the cutoff level at which the score predicted the pathological stroke type with around 90% certainty (see Appendix F)

Each figure demonstrates the threshold values above and below which there was about 90% certainty of the stroke type diagnosis (see Appendix F) in the original validation studies for each score (Allen, 1983; Poungvarin et al., 1991). Between these thresholds, the scores return an uncertain result.

Applying the optimum threshold values described in Appendix F, the SSS produced an uncertain result in 44 (20%) and the GHSS in 65 (29%) of 222 stroke patients. The SSS score diagnosed intracranial haemorrhage in 60 (27%) and the GHSS in 31 (14%) stroke patients. The scores diagnosed ischaemic stroke in 118 (53%) and 126 (57%) of the stroke patients respectively. The SSS identified intracranial haemorrhage reasonably well with a score over 5, but did not accurately identify ischaemic stroke at any cut-off point. The GHSS diagnosed ischaemic stroke reasonably well below a score of 10 but did not identify intracranial haemorrhage well. However, using these new cut-off points the scores would only identify pathological stroke type in very few patients, for example 57 (81%) of the intracranial haemorrhages would not be scored as such with the SSS and 135 (89%) of the true infarcts with the GHSS.

We assessed whether the population studied in the validation of the SSS and GHSS, which therefore had CT brain scans, differed from the population that did not have CT brain scans in terms of score diagnosis or pathological stroke type. Sixty-nine black stroke patients had complete SSS and GHSS scores but did not have a CT brain scan. A smaller proportion of patients without a CT scan had intracranial bleeds according to the SSS and GHSS than those that did not have a scan (15% versus 29% for the SSS; and 4% versus 14% for the GHSS), possibly

because intracranial haemorrhage has a more dramatic presentation than ischaemic stroke or may have an atypical stroke presentation and so patients with cerebral haemorrhage were more likely to have a CT brain scan. When we compared the results of the scores for definite intracranial haemorrhage, definite ischaemic stroke and uncertain results across the two populations, we did not find a significant difference (p=0.07 for the SSS and p=0.06 for the GHSS). Thus, patients with and without a CT brain scan did not differ significantly in terms of score result.

Clinicians from the stroke team assessed stroke type in 199 consecutive black stroke patients. We excluded their assessment in 80 patients, who did not have a CT brain scan and in a further 43 because they admitted to having some idea of the CT brain scan result prior to assessing the pathological stroke type. Despite making every attempt to blind themselves to the CT scan result, and reminders on the questionnaire (appendix D), stroke team clinicians were often inadvertently informed of the scan result by the referring physician, the patient or some other source, prior to making their own assessment. The clinicians finally assessed the pathological stroke type in 76 black stroke patients who also had a CT brain scan available. They assessed the pathological stroke type as ischaemic stroke in 52 (68%) patients, intracranial haemorrhage in 16 (21%), and ‘uncertain’ in 8 patients who had an ischaemic stroke on CT scan. They diagnosed two patients who had subarachnoid haemorrhage on CT brain scan with secondary ischaemic stroke, as having had cerebral haemorrhages, though for the purposes of the following analysis we combined cerebral haemorrhage and subarachnoid haemorrhage as

‘intracranial haemorrhage.’ The clinicians accurately assessed the pathological stroke type in 56 (74%) of the 76 patients.

Table 6.1 shows the sensitivity, specificity, positive predictive value, likelihood ratios and kappa score for the SSS, the GHSS and the clinicians’ assessment of intracranial haemorrhage in all (first-ever-in-a-lifetime and recurrent) stroke patients.

**Table 6.1 Comparison of the Siriraj Stroke Score, Guy's Hospital Stroke Score and clinician assessment of *intracranial haemorrhage* with CT brain scan diagnosis of *intracranial haemorrhage* in all* stroke patients (Note: an uncertain result was included as an incorrect assessment in the analysis of the Siriraj Stroke Score and Guy's Hospital Stroke Score)**

| | | CT scan result | | |
|---|---|---|---|---|
| | **Diagnosis** | **ICH** | **Not ICH** | **Total** |
| **Siriraj Stroke Score** | ICH (score >1) | 42 | 18 | 60 |
| | Not ICH (score ≤1) | 28 | 134 | 162 |
| | **Total** | **70** | **152** | **222** |
| **Guy's Hospital Score** | ICH (score >24) | 24 | 7 | 31 |
| | Not ICH (score ≤ 24) | 46 | 145 | 191 |
| | **Total** | **70** | **152** | **222** |
| **Clinicians Assessment** | ICH | 12 | 4 | 16 |
| | Not ICH | 8 | 52 | 60 |
| | **Total** | **20** | **56** | **76** |

| | **Results (95% CI)** | | |
|---|---|---|---|
| | **Siriraj Stroke Score** | **Guy's Hospital Stroke Score** | **Clinician assessment** |
| **Sensitivity** | 0.60 (0.48 to 0.71) | 0.34 (0.24 to 0.46) | 0.60 (0.39 to 0.78) |
| **Specificity** | 0.88 (0.82 to 0.92) | 0.95 (0.90 to 0.98) | 0.93 (0.83 to 0.97) |
| **Positive predictive value** | 0.70 (0.58 to 0.80) | 0.77 (0.60 to 0.89) | 0.75 (0.51 to 0.90) |
| **Likelihood ratio:** | | | |
| - **for a positive score** | 5.1 (3.2 to 8.1) | 7.5 (3.4 to 16.5) | 8.4 (3.0 to 23) |
| - **for a negative score** | 0.5 (0.3 to 0.6) | 0.7 (0.6 to 0.8) | 0.4 (0.3 to 0.7) |
| **Kappa statistic** | 0.5 (0.4 to 0.6) | 0.4 (0.2 to 0.5) | 0.6 (0.3 to 0.8) |

* All stroke patients = first-ever-in-a-lifetime and recurrent stroke patients
ICH – intracranial haemorrhage

**Table 6.2 Comparison of the Siriraj Stroke Score, Guy's Hospital Stroke Score and clinician assessment of *intracranial haemorrhage* with CT brain scan diagnosis of *intracranial haemorrhage* in *first-ever-in-a-lifetime* stroke patients (Note: an uncertain result was included as an incorrect assessment in the analysis of the Siriraj Stroke Score and Guy's Hospital Stroke Score)**

| | | CT scan result | | |
|---|---|---|---|---|
| | **Diagnosis** | **ICH** | **Not ICH** | **Total** |
| **Siriraj Stroke Score** | ICH (score >1) | 42 | 17 | 59 |
| | Not ICH (score ≤1) | 24 | 124 | 148 |
| | **Total** | **66** | **141** | **207** |
| **Guy's Hospital Score** | ICH (score >24) | 23 | 5 | 28 |
| | Not ICH (score ≤ 24) | 43 | 136 | 179 |
| | **Total** | **66** | **141** | **207** |
| **Clinicians Assessment** | ICH | 11 | 4 | 15 |
| | Not ICH | 7 | 49 | 56 |
| | **Total** | **18** | **53** | **71** |

| | **Results (95% CI)** | | |
|---|---|---|---|
| | **Siriraj Stroke Score** | **Guy's Hospital Stroke Score** | **Clinician assessment** |
| **Sensitivity** | 0.64 (0.52 to 0.74) | 0.35 (0.25 to 0.47) | 0.61 (0.39 to 0.80) |
| **Specificity** | 0.88 (0.82 to 0.92) | 0.97 (0.92 to 0.99) | 0.93 (0.82 to 0.97) |
| **Positive predictive value** | 0.71 (0.59 to 0.81) | 0.82 (0.64 to 0.92) | 0.73 (0.48 to 0.89) |
| **Likelihood ratio:** | | | |
| - **for a positive score** | 5.3 (3.3 to 8.5) | 9.8 (3.9 to 24.7) | 8.1 (2.9 to 22.3) |
| - **for a negative score** | 0.4 (0.3 to 0.6) | 0.7 (0.6 to 0.8) | 0.4 (0.2 to 0.8) |
| **Kappa statistic** | 0.5 (0.4 to 0.7) | 0.4 (0.2 to 0.5) | 0.6 (0.3 to 0.8) |

ICH – intracranial haemorrhage

Table 6.2 provides the same analyses but only in black patients with first-ever-in-a-lifetime stroke. The findings were not markedly different when applied to first-ever-in-a-lifetime stroke patients or all stroke patients. The GHSS had a slightly better sensitivity (probability of a positive test in people with the disease), specificity (probability of a negative result in people without the disease) and positive predictive value (probability of the person having the disease when the test is positive) when only first-ever strokes were assessed, although this did not change the ranking of the scores. The likelihood ratio for a positive score using the GHSS was better when only first-ever strokes were considered, but the Kappa statistic was the same for both all stroke and first-ever stroke patients.

In general, the SSS had about the same sensitivity for detecting intracranial haemorrhage as the clinicians, and both had a higher sensitivity than the GHSS. The GHSS was, however, more specific than the SSS or clinicians, and had the highest positive predictive value. The likelihood ratio incorporates both the sensitivity and specificity of the test and provides a direct estimate of how much a positive test will change the odds of having a disease or in this case an intracranial haemorrhage (Sackett, Haynes, Guyatt et al, 1991; Altman, Machin, Bryant et al, 2000; Simon, 2006). The likelihood ratio for a positive score tells one how much the odds of the disease increase when a score (for intracranial haemorrhage in this case) is positive, and the likelihood ratio for a negative score tells one how much the odds of the disease decrease with a negative score. Both the GHSS and the clinicians had a higher likelihood ratio with a positive diagnosis of intracranial haemorrhage than the SSS, and the GHSS performed best in the patients with first-ever stroke.

We used the Kappa statistic, which in this case is a measure of agreement between the scores and the CT findings, or clinician assessment and the CT findings. The Kappa statistic assesses agreement beyond the level of agreement expected by chance alone (Altman et al., 2000). Using this statistic, the GHSS had fair agreement, the SSS moderate and the clinicians good agreement with the CT result (0.0 to 0.2: slight agreement; 0.2 to 0.4: fair agreement; 0.4 to 0.6: moderate agreement; 0.6 to 0.8: good / substantial agreement; 0.8 to 1.0: almost perfect agreement) (Sackett et al., 1991; Simon, 2006).

Thus, the SSS and clinicians were more likely to detect intracranial haemorrhage and had moderate to good agreement with the CT findings, but if the GHSS gave a definite diagnosis of intracranial haemorrhage the odds of patient indeed having intracranial haemorrhage were higher than with the SSS or clinician assessment.

Table 6.3 (all stroke) and 6.4 (first-ever-in-a-lifetime stroke) show the same analyses of sensitivity, specificity, positive predictive value, likelihood ratio and Kappa statistic for the SSS, GHSS and clinician assessment of ischaemic stroke. The findings in all stroke and first-ever-in-a-lifetime stroke patients were almost identical for the diagnosis of ischaemic stroke. The SSS and GHSS were equally sensitive, but the SSS was more specific than the GHSS in the diagnosis of ischaemic stroke, when compared to the CT brain scan diagnosis. Clinicians were more likely to detect ischaemic stroke than the scores, but less specific.

**Table 6.3 Comparison of the Siriraj Stroke Score, Guy's Hospital Stroke Score and clinician assessment of *ischaemic stroke* with CT brain scan diagnosis of *ischaemic stroke* in all* stroke patients (Note: an uncertain result was included as an incorrect assessment in the analysis of the Siriraj Stroke Score and Guy's Hospital Stroke Score)**

| | | CT scan result | | |
|---|---|---|---|---|
| | **Diagnosis** | **IS** | **Not IS** | **Total** |
| **Siriraj Stroke Score** | IS (score < -1) | 107 | 11 | 118 |
| | Not IS (score ≥ -1) | 45 | 59 | 104 |
| | **Total** | 152 | 70 | 222 |
| **Allen (Guy's Hospital) Score** | IS (score < 4) | 108 | 18 | 126 |
| | Not IS (score ≥ 4) | 44 | 52 | 96 |
| | **Total** | 152 | 70 | 222 |
| **Clinicians Assessment** | IS | 44 | 8 | 52 |
| | Not IS | 12 | 12 | 24 |
| | **Total** | 56 | 20 | 76 |

| | **Results (95% CI)** | | |
|---|---|---|---|
| | **Siriraj Stroke Score** | **Allen (Guy's Hospital Score)** | **Clinician assessment** |
| **Sensitivity** | 0.70 (0.63 to 0.77) | 0.71 (0.63 to 0.78) | 0.79 (0.66 to 0.87) |
| **Specificity** | 0.84 (0.74 to 0.91) | 0.74 (0.63 to 0.83) | 0.60 (0.39 to 0.78) |
| **Positive predictive value** | 0.91 (0.84 to 0.95) | 0.86 (0.79 to 0.91) | 0.85 (0.73 to 0.92) |
| **Likelihood ratio:** | | | |
| - **for a positive score** | 4.5 (2.6 to 7.8) | 2.8 (1.8 to 4.2) | 2.0 (1.1 to 3.4) |
| - **for a negative score** | 0.4 (0.3 to 0.5) | 0.4 (0.3 to 0.5) | 0.4 (0.2 to 0.7) |
| **Kappa statistic** | 0.5 (0.4 to 0.6) | 0.4 (0.3 to 0.5) | 0.4 (0.1 to 0.6) |

* All stroke patients = first-ever-in-a-lifetime and recurrent stroke patients
IS – ischaemic stroke

**Table 6.4 Comparison of the Siriraj Stroke Score, Guy's Hospital Stroke Score and clinician assessment of *ischaemic stroke* with CT brain scan diagnosis of *ischaemic stroke* in *first-ever-in-a-lifetime* stroke patients (Note: an uncertain result was included as an incorrect assessment in the analysis of the Siriraj Stroke Score and Guy's Hospital Stroke Score)**

| | | CT scan result | | |
|---|---|---|---|---|
| | **Diagnosis** | **IS** | **Not IS** | **Total** |
| **Siriraj Stroke Score** | IS (score < -1) | 99 | 10 | 109 |
| | Not IS (score ≥ -1) | 42 | 56 | 98 |
| | **Total** | 141 | 66 | 207 |
| **Allen (Guys Hospital) Score** | IS (score < 4) | 100 | 17 | 117 |
| | Not IS (score ≥ 4) | 41 | 49 | 90 |
| | **Total** | 141 | 66 | 207 |
| **Clinicians Assessment** | IS | 42 | 7 | 49 |
| | Not IS | 11 | 11 | 22 |
| | **Total** | 53 | 18 | 71 |

| | **Results (95% CI)** | | |
|---|---|---|---|
| | **Siriraj Stroke Score** | **Allen (Guy's Hospital Score)** | **Clinician assessment** |
| **Sensitivity** | 0.70 (0.62 to 0.71) | 0.71 (0.63 to 0.78) | 0.79 (0.67 to 0.88) |
| **Specificity** | 0.85 (0.74 to 0.92) | 0.74 (0.63 to 0.83) | 0.61 (0.39 to 0.80) |
| **Positive predictive value** | 0.91 (0.84 to 0.95) | 0.86 (0.78 to 0.91) | 0.86 (0.73 to 0.93) |
| **Likelihood ratio:** | | | |
| - **for a positive score** | 4.6 (2.6 to 8.3) | 2.8 (1.8 to 4.2) | 2.0 (1.1 to 3.7) |
| - **for a negative score** | 0.4 (0.3 to 0.5) | 0.4 (0.3 to 0.5) | 0.3 (0.2 to 0.7) |
| **Kappa statistic** | 0.5 (0.4 to 0.6) | 0.4 (0.3 to 0.5) | 0.4 (0.1 to 0.6) |

IS – ischaemic stroke

The positive predictive value was similar for clinicians and the two scores, but the likelihood ratio of a positive score was almost double for the SSS compared to both the GHSS and clinicians. The Kappa statistic showed that the measure of agreement between the scores and the clinicians, and a definite CT scan diagnosis of ischaemic stroke, was moderate at best.

Thus, although there was not a great deal of difference between the accuracy in diagnosing ischaemic stroke using the SSS, the GHSS and clinician assessment, the SSS performed slightly better. The scores and clinician assessment were more sensitive in the diagnosis of ischaemic stroke than intracranial haemorrhage, but less specific. Agreement above that expected by chance (the Kappa statistic) with CT brain scan findings of pathological stroke type, was moderate for both scores and the clinician assessment.

While scores used in epidemiological studies should be accurate in diagnosing both intracranial haemorrhage and ischaemic stroke, in the day-to-day management of stroke patients in a setting without a CT scanner, a score's ability to identify patients with haemorrhage, who might be harmed by the use of antiplatelet agents or in certain circumstances antithrombotic agents, is very important. Thus, a good screening score with a high sensitivity for diagnosing intracranial haemorrhage would be useful clinically, particularly if it added to the clinician assessment. The SSS, although it did not perform particularly well, was the more sensitive of the two scoring systems in detecting intracranial haemorrhage. Given that the SSS only requires a history and examination, it is

more likely to be used in low resource settings like rural South Africa, and is therefore the more promising of the two scores.

## 6.3 Discussion

We found that the Siriraj Stroke Score (SSS) and the Guy's Hospital Stroke Score (GHSS) did not perform particularly well in diagnosing the pathological stroke type in black South African stroke patients. The SSS performed marginally better than the GHSS and had a much higher sensitivity for detecting intracranial haemorrhages. Neither score offered much advantage over our stroke team clinicans' assessments of pathological stroke type.

This study is the first prospective study of scores used to distinguish pathological stroke type in Sub-Saharan African stroke patients. There have, however, been retrospective assessments of the Siriraj Score and WHO score from elsewhere in Sub-Saharan Africa (Ogun, Oluwole, Oluremi et al, 2001; Ogun, Oluwole, Fatade et al, 2002; Zenebe, Asmera, & Alemayehu, 2005b). We have compared our findings with those found in Nigeria (Ogun et al., 2001; Ogun et al., 2002) and Ethiopia (Zenebe et al., 2005b), and in other regions of the world in tables 6.5 and 6.6. We separated prospective and retrospective studies, as incomplete records so often affect the latter. We also noted when studies included and excluded 'uncertain' results from their calculations. Both sensitivity and specificity may be increased by excluding 'uncertain' results. For example in our evaluation of the SSS, if we had excluded the 'uncertain' results, we would have increased the sensitivity for diagnosing intracranial haemorrhage from 0.60 to 0.79, although the specificity decreased marginally from 0.88 to 0.86 and the positive predictive value was unchanged. As a high sensitivity for detection of intracranial haemorrhage is essential in the clinical setting, and 'uncertain' results are part of the routine use of

a score, inclusion of the ‘uncertain’ results provides the more accurate assessment of the score.

**Table 6.5 Performance of the Siriraj Stroke Score and Guy's Hospital Stroke Score in diagnosing intracranial haemorrhage compared to gold standard (brain imaging or autopsy) in different populations**

| Study | Study size* | Design | Sensitivity | Specificity | PPV | Uncertain scores included / excluded |
|---|---|---|---|---|---|---|
| **Siriraj Stroke Score** | | | | | | |
| **Diagnosis of intracranial haemorrhage** | | | | | | |
| **Africa** | | | | | | |
| JHSR (South Africa) | 222 | prospective | 0.60 | 0.88 | 0.70 | included |
| Nigeria (Ogun et al) | 96 | retrospective | 0.50 | 0.63 | 0.55 | included |
| Ethiopia (Zenebe et al) | 41 | retrospective | 0.48 | 0.75 | 0.67 | included (re-calculated from data provided) |
| **Rest of the world** | | | | | | |
| Thailand (Poungvarin et al) | 165 | prospective | 0.89 | 0.93 | 0.97 | excluded |
| Italy (Celani et al) | 193 | prospective | 0.61 | 0.94 | 0.63 | excluded |
| India (Badam et al) | 134 | prospective | 0.79 | 0.71 | - | N/A |
| India (Kochar et al) | 159 | prospective | 0.85 | 0.73 | 0.71 | N/A |
| Pakistan (Shah et al) | 100 | prospective | 0.73 | 0.90 | 0.83 | N/A |
| Hong Kong, China (Hui et al) | 253 | prospective | 0.91 | 0.90 | 0.69 | N/A |
| Malaysia (Kan et al) | 160 | prospective | 0.50 | 0.91 | 0.66 | included |
| USA (Akpunonu et al) | 254 | retrospective | 0.36 | - | 0.77 | excluded |
| New Zealand (Hawkins et al) | 485 | retrospective | 0.48 | 0.85 | 0.59 | included |
| United Kingdom (Weir et al) | 482 | retrospective | 0.67 | 0.71 | 0.22 | N/A |
| **Guy's Hospital Stroke Score** | | | | | | |
| **Diagnosis of intracranial haemorrhage** | | | | | | |
| **Africa** | | | | | | |
| JHSR (South Africa) | 222 | prospective | 0.34 | 0.95 | 0.77 | included |
| **Rest of the world** | | | | | | |
| Italy (Celani et al) | 187 | prospective | 0.38 | 0.98 | 0.71 | excluded |
| Taiwan (Huang et al) | 180 | prospective | 0.67 | 1.00 | 1.00 | excluded |
| India (Badam et al) | 134 | prospective | 0.81 | 0.76 | - | N/A |
| India (Kochar et al) | 147 | prospective | 0.60 | 0.91 | 0.82 | N/A |
| New Zealand (Hawkins et al) | 472 | retrospective | 0.31 | 0.95 | 0.73 | included |
| United Kingdom (Sandercock et al)† | 228 | retrospective | 0.78 | 0.81 | 0.95 | N/A |
| United Kingdom (Weir et al) | 322 | retrospective | 0.79 | 0.66 | 0.21 | N/A |

JHSR – Johannesburg Hospital Stroke Register; *Study size refers to the number of cases used in the analysis and not the total number of stroke cases; †Figures refer to the results for the Oxfordshire Community Stroke Project assessment of the score; PPV – positive predictive value; N/A – not available

**Table 6.6 Performance of the Siriraj Stroke Score and Guy's Hospital Stroke Score in diagnosing ischaemic stroke compared to gold standard (brain imaging or autopsy) in different populations**

| Study | Study size* | Design | Sensitivity | Specificity | PPV | Comment on handling of cases with uncertain scores |
|---|---|---|---|---|---|---|
| **Siriraj Stroke Score** | | | | | | |
| **Diagnosis of ischaemic stroke** | | | | | | |
| **Africa** | | | | | | |
| JHSR (South Africa) | 222 | prospective | 0.70 | 0.84 | 0.91 | included |
| Nigeria (Ogun et al) | 96 | retrospective | 0.58 | 0.55 | 0.63 | included for sensitivity, excluded for specificity and PPV |
| Ethiopia (Zenebe) | 41 | retrospective | 0.40 | 0.86 | 0.73 | included (re-calculated from data provided) |
| **Rest of the world** | | | | | | |
| Thailand (Poungvarin et al) | 165 | prospective | 0.93 | 0.89 | 0.76 | excluded |
| Pakistan (Shah et al) | 100 | prospective | 0.71 | 0.85 | 0.87 | N/A |
| India (Kochar et al) | 159 | prospective | 0.73 | 0.85 | 0.85 | N/A |
| Hong Kong, China (Hui et al) | 253 | prospective | 0.78 | 0.80 | 0.93 | N/A |
| Malaysia (Kan et al) | 160 | prospective | 0.70 | 0.64 | 0.85 | included |
| New Zealand (Hawkins et al) | 485 | retrospective | 0.61 | 0.74 | 0.84 | included |
| USA (Akpunonu et al) | 254 | retrospective | 0.90 | - | 0.61 | excluded |
| **Allen (Guy's Hospital) Score** | | | | | | |
| **Diagnosis of ischaemic stroke** | | | | | | |
| **Africa** | | | | | | |
| JHSR (South Africa) | 222 | prospective | 0.71 | 0.74 | 0.86 | included |
| **Rest of the world** | | | | | | |
| India (Kochar et al) | 147 | prospective | 0.91 | 0.60 | 0.77 | N/A |
| New Zealand (Hawkins et al) | 472 | retrospective | 0.78 | 0.70 | 0.86 | included |
| United Kingdom (Sandercock et al) | 228 | retrospective | 0.78 | 0.81 | 0.95 | N/A |

JHSR – Johannesburg Hospital Stroke Register; *Study size refers to the number of cases used in the analysis and not the total number of stroke cases; †Figures refer to the results for the Oxfordshire Community Stroke Project assessment of the score; PPV – positive predictive value; N/A – not available

### 6.3.1 Comparison of our SSS and GHSS findings with other studies – intracranial haemorrhage

We found a higher sensitivity, specificity and positive predictive value for the SSS in detecting intracranial haemorrhage than was found in the two retrospective assessments of the score in Nigeria and Ethiopia. This was in spite of their higher proportions of intracranial haemorrhage (59% in Ethiopia and 47% in Nigeria) (Ogun et al., 2002; Zenebe et al., 2005b), compared to the 70 intracranial haemorrhages in our 222 (32%) stroke patients. This probably reflects patient selection or case mix and the limitations of a retrospective study design rather than a true difference in the performance of the SSS in other black populations in Sub-Saharan Africa. Our findings are well within the range of findings in populations with a varying prevalence of cerebral haemorrhage (table 6.5). The most appropriate study for comparison with our study is from Malaysia (Kan, Lee, Low et al, 2000). It too was a prospective study of 160 patients which included 'uncertain' results in the analyses. We found the SSS had a slightly higher sensitivity for detecting intracranial haemorrhage than in the Malaysian study (0.60 versus 0.50), but the specificity and positive predictive values were similar in the two studies.

Not surprisingly, the SSS did not fare nearly as well in our study as it did in the original validation study (Poungvarin et al., 1991), though only one study from Hong Kong (Hui, Wu, Tang et al, 2002) has ever replicated the promise of the original study. It has been suggested that the SSS has failed to impress in high-income white populations because it was developed in Thailand in a population

with a high prevalence of cerebral haemorrhage (Hawkins et al., 1995). However, the score did not do much better in our population despite a high prevalence of cerebral haemorrhage. The SSS, despite performing better than the GHSS, needs further refinement and adaptation to meet our population needs.

Although the GHSS has shown a high specificity in the diagnosis of intracranial haemorrhage and a fairly good positive predictive value, the sensitivity has been more variable (table 6.5). Together with studies from Italy (Celani, Righetti, Migliacci et al, 1994) and New Zealand (Hawkins et al., 1995) we found the lowest sensitivity (0.31 to 0.38) for detecting intracranial haemorrhage using the GHSS. Again it has been suggested that the GHSS was developed with relatively young stroke patients (under the age of 76 years), and therefore in a population with a higher prevalence of intracranial haemorrhage (Hawkins et al., 1995), yet the score failed to perform well in our very young stroke population.

### 6.3.2 Comparison of our SSS and GHSS findings with other studies – ischaemic stroke

The SSS performed better in our study than in the two retrospective studies from Nigeria and Ethiopia (table 6.6). We found the same sensitivity for diagnosing ischaemic stroke as was found in Malaysia in a study that also included 'uncertain' cases in the analyses (Kan et al., 2000). Our findings for sensitivity, specificity and positive predictive value are remarkably consistent with those found in prospective studies from Pakistan, India and Hong Kong (Kochar, Joshi, Agarwal et al, 2000; Hui et al., 2002; Shah, Salih, Saeed et al, 2003).

The GHSS performed better at diagnosing ischaemic stroke than intracranial haemorrhage in our study, yet this was still poor compared to the GHSS performance in other studies (table 6.6). The GHSS score places far more emphasis on measures of atherosclerosis than the SSS does. It is possible that it performs better in populations in which atherosclerosis is an important cause of ischaemic stroke, rather than in populations such as ours where atherosclerotic diseases such as ischaemic heart disease, extracranial carotid artery disease and symptomatic peripheral vascular disease are uncommon.

### 6.3.3 The accuracy of bedside clinical diagnosis of pathological stroke type

Previous studies have shown that the bedside assessment of pathological stroke type by clinicians is not accurate (von Arbin et al., 1981; Allen, 1983; Allen, 1984). In Stockholm (von Arbin et al., 1981), clinicians made an accurate bedside diagnosis in 69% of 206 stroke cases, a very similar finding to our clinicians who accurately diagnosed 56 (74%) of 76 stroke patients. Clinicians at Guy's Hospital were less accurate than the Guy's Hospital Stroke Score, but still diagnosed stroke type accurately in 84% of patients (detailed number of patients not available). In a recent study from Ethiopia, stroke type was accurately diagnosed in 37 (76%) of 49 stroke patients, far more often than by the SSS which only managed to accurately make the diagnosis in 18 (44%) of 41 patients (Zenebe et al., 2005a).

Thus, our clinicians performed about as well as other clinicians have around the world. However, clinicians in our study as in the other three studies were working

in major centres. In our study, neurologists or trainees in neurology assessed the majority of patients. Possibly clinicians without neurology training would not perform as well. This would limit the generalisation of our findings to hospitals and clinics in remote areas of South Africa, and it is in these settings that the stroke score may still have a role.

### 6.3.4 Limitations of this study

Apart from the difficulty with generalisation of our clinician assessments, this study has several further limitations. The number of patients assessed by clinicians was very small resulting in wide confidence intervals around our assessments of their accuracy in diagnosing stroke type. We added the clinician assessment about half-way through the study and were unable to assess many patients because the clinicians already knew the results of the CT brain scan. In any future studies, we would have to put a great deal of effort into alerting colleagues in the medical department to the need for withholding the pathological stroke type information.

Although we did not find a significant difference between the score results in those patients who had a CT brain scan and those that did not have a CT scan, our low scan rate may have influenced our findings. The ideal validation study would have an almost 100% scan rate, preferably in a community-based study in order to assess the stroke score in stroke patients with a wide range of severity, and to assess the score's potential performance in epidemiological studies.

We did not assess whether the intracranial haemorrhages missed were indeed clinically relevant. It is possible that many of the haemorrhages missed were small and from a management perspective in rural South Africa this might not be too important. The 800 patients with cerebral haemorrhages in the International Stroke Trial who were given aspirin did not show evidence of net hazard (Chen, Sandercock, Pan et al, 2000), and it would not be of great concern should a score miss this type of small cerebral haemorrhage, as long as it accurately detected larger haemorrhages.

We have not evaluated the sequential use of the two scores, nor what factors in the scores are most predictive of intracranial haemorrhage. This analysis and the further validation in a new population would be important in devising a stroke score that performs well in the local South African black population.

## 6.4 Conclusion

We agree with others who have suggested that stroke scores are not sufficiently accurate to replace CT brain imaging in either epidemiological studies or clinical management (Weir, Murray, Adams et al, 1994; Hawkins et al., 1995; Kan et al., 2000; Badam, Solao, Pai et al, 2003). The scores were only accurate when we used new cut-off points that resulted in a diagnosis of uncertain stroke type in the vast majority. Therefore, one could only possibly consider using the scores, as was done in the Oxfordshire Community Stroke Project, to supplement CT scan results.

Unfortunately, stroke incidence is likely to increase across Sub-Saharan Africa, a region with very limited access to CT or MRI scanners, and stroke scores may yet have a clinical role here. For great parts of Sub-Saharan Africa, thrombolytics and even anticoagulation for the few that need it, are not feasible therapeutic options given the limited access to imaging and laboratory facilities. However, a score that excluded significant cerebral haemorrhage would encourage doctors and nurses in remote areas to initate aspirin therapy. Only one of the 103 prevalent stroke patients in the SASPI study (chapter 3 and 4) were taking aspirin, and early initiation of aspirin in hospital may increase the number of patients who continue it as secondary prevention. We need further studies to adapt these scores for use in our population.

In the following chapter, we present the findings of the Tintswalo Hospital Stroke Register, a rural register established in a hospital without easy access to CT brain

scanning. We used the same methodology to calculate the SSS and GHSS in the Tintswalo Hospital Stroke Register as we used in the JHSR. Despite the poor performance of the SSS and GHSS, we will report the assessment of pathological stroke types using the stroke scores as well as using our clinical assessment.

### 6.4.1 What this study adds to the literature

This study provides the first prospective, and largest, validation study of stroke scores designed to distinguish pathological stroke type in Sub-Saharan Africa, and is the only stroke score validation study from South Africa. Apart from being prospective, our study also had a higher CT scan rate than the Nigerian and Ethiopian studies in tables 6.5 and 6.6, and is the first to assess the performance of the Guy's Hospital Stroke Score in Sub-Saharan Africa. Furthermore, this study provides the only prospective assessment of the accuracy of clinician bedside diagnosis of pathological stroke type in Sub-Saharan Africa.

# CHAPTER 7 THE TINTSWALO HOSPITAL STROKE REGISTER (THSR) – RURAL STROKE

## 7.0 Introduction

Most stroke case series and all previous prospective stroke registers from Sub-Saharan Africa (SSA) have been urban based (chapter 2), and included urban or a mixture of both urban and rural stroke patients (Kwasa et al., 1990; Walker et al., 2003; Garbusinski et al., 2005). Several studies have found a higher prevalence of vascular risk factors in urban than in rural populations in SSA (Edwards, Unwin, Mugusi et al; Aspray, Mugusi, Rashid et al; van Rooyen, Kruger, Huisman et al, 2000; Kruger, Venter, & Vorster, 2001; Vorster, 2002; Oosthuizen et al., 2002), most likely the result of urbanisation of the population. The increase in vascular risk drives the emergence of vascular disease in populations undergoing health transition (chapter 1). As discussed in section 1.6, the nature of stroke is likely to change during a population's transition. It is probable, though not well documented, that the nature of stroke differs between rural and urban populations as it does between high and low income regions of the world (chapter 1 and 2).

We established a rural stroke register, based at Tintswalo Hospital, to compare the nature of rural stroke with urban stroke in blacks (Johannesburg Hospital Stroke Register). Furthermore, although we had assessed the prevalence and nature of prevalent stroke cases in the Bohlabela region (chapters 3 and 4), it is likely that our assessment of pathological stroke type, ischaemic stroke subtype, and underlying cause in the prevalent cases was influenced by the sometimes lengthy

time delay between stroke onset and our assessment of the stroke survivors. The Tinswalo Hospital Stroke Register (THSR) provided the opportunity to assess acute stroke patients in the same rural population and to document their pattern of presentation to hospitals in this under-resourced area, where simply getting to hospital provides a major challenge to most patients.

### 7.0.1 Aim of the THSR

Our aim was to assess the profile of stroke patients admitted to Tintswalo Hospital, including their demographic characteristics, pathological stroke type as far as possible, ischaemic stroke subtype, risk factors, cause, severity, and in-hospital outcome, and to compare this with black stroke patients in the Johannesburg Hospital Stroke Register (JHSR).

## 7.1 Methods of the THSR

### 7.1.1 Population and setting

Tintswalo Hospital is a 400 bed hospital, based in Acornhoek in the Bohlabela region of Limpopo Province, in the north-east of South Africa (Acornhoek is shown on the map in figure 3.1). The population served is almost exclusively black South African. Although the region is considered rural (Tollman, Mkhabela, & Pienaar, 1993; Tollman, Herbst, Garenne et al, 1999), some parts of the region are probably semi-urban. Tintswalo Hospital is one of the three hospitals that provide

secondary level care to people living in the Agincourt Health and Population Unit demographic surveillance site, where we assessed the prevalence of rural stroke (chapter 3). Although the hospital has 400 beds, a large proportion are for psychiatric patients, as the hospital is the regional psychiatric referral hospital. Most doctors are either interns (house officers) or doing their community-service, and the number of doctors varies from year to year. There were between four and eight permanent doctors at the time we ran the THSR, with a couple of general practitioners in the area providing emergency cover from time to time.

Tintswalo Hospital, and the Bohlabela region, did not have access to a CT scanner at the time of the THSR. Indeed the province only had one CT scanner servicing patients without medical insurance, based in the provincial capital, Polokwane, some 300 km away. The hospital only had access to three ambulances, but in our experience, only one was operational at any given time. X-ray facilities were limited and although basic chest x-rays were theoretically available, we were only able to obtain them erratically if at all during the THSR. The medical wards had an electrocardiograph machine, but this too seldom functioned. The hospital laboratory provided a limited and erratic service but about halfway through the register, as part of the SASPI study, we received funding to courier blood samples to the University of the Witwatersrand Contract Lab Services.

### 7.1.2 Case ascertainment and assessment

The Tintswalo Hospital Stroke Register (THSR) included all consecutive cases of stroke admitted to Tintswalo Hospital, or which occurred while in hospital, over 20

months during two periods: from 1st June 2001 till 31st December 2001 and from 1st April 2002 till 30th June 2003. Initially a nurse trainer from the primary health care nursing group based at Tintswalo Hospital ascertained stroke cases. During the second longer period, we had a trained senior nurse dedicated to the THSR. The THSR nurse ascertained cases on a daily basis from the casualty (emergency room) register, the hospital admission book, the medical wards and by checking the death register. All the hospital doctors met every morning to hand over the patients admitted overnight and to discuss clinical 'problem cases.' The THSR nurse used this opportunity to ask the doctors whether they had admitted any patients with stroke or transient ischaemic attack, or if any in-patients had had a stroke or transient ischaemic attack. We assessed patients with transient ischaemic attack (TIA) but did not include them on the register, as so often patients assumed to have had a TIA turn out to have had a stroke.

Once the THSR nurse had located a potential stroke patient, she informed the patient or their carers (if the patient could not communicate), about the THSR. She provided them with an information sheet in Shangaan (the most frequently spoken local language), and asked for verbal consent to assess them. She also asked for consent to take blood (from the 1st July 2002 when we had funding for blood investigations to be sent to Johannesburg), and for me to assess the patient with her on my approximately weekly to fortnightly visits to the hospital. She obtained consent for HIV testing separately, and if the patient agreed she counselled the patient prior to venesecting them. (Figures 7.1 and 7.2 show scenes of Tintswalo Hospital and the staff who ran the THSR).



Figure 7.1 Tintswalo Hospital male surgical (above) and female medical ward (below)



Figure 7.2 Entrance and outpatient waiting area – Tintswalo Hospital (above); below (left to right) Myles Connor, Andrina Sambo (THSR nurse) and Bulelwa Ngoma SASPI research fellow and co-ordinator

I assessed all possible patients in detail when I visited the hospital, i.e. unless the patient had died, or rarely been discharged prior to my visit. I also reviewed each questionnaire in detail before entering the patient's data onto the THSR database.

Unlike in the JHSR where we excluded patients who had had a stroke more than 6 months prior to admission, patients were included in the register if the stroke was the main reason for seeking medical assistance. We took this approach because we wanted to obtain a full picture of the health seeking behaviour of rural stroke patients.

We assessed and documented the patients' demographic details, history and examination findings, as well as the results of investigations on the THSR questionnaire (Appendix G), which was adapted from the basic questionnaire used for the JHSR and stroke prevalence study. The methodology of the JHSR and THSR therefore overlapped in the following areas of assessment: socioeconomic indicators, symptoms at stroke onset, known stroke risk factors (based on the history from the patient and their carers), medication use, assessment of functional state both at the time of our assessment and prior to the stroke, findings of the neurological, cardiac, vascular and general medical examination, stroke severity (National Institutes of Neurological Disorders and Stroke Scale and Scandinavian Stroke Scale), modified Rankin score and Barthel score (see section 5.1.2 for more detail). We also documented any complications arising from the stroke and any in-hospital deaths in the THSR.

We used the same definitions of stroke, first-ever-in-a-lifetime stroke, and transient ischaemic attack as we used in the JHSR (section 5.1.2.1). However, in view of the lack of CT brain scanning, we assessed pathological stroke type (cerebral haemorrhage or ischaemic stroke) based on our clinical judgement and the Siriraj and Guy's Hospital stroke scores (chapter 6). We were more likely to diagnose cerebral haemorrhage if the patient presented with sudden onset of neck stiffness, severe headache, and seizures, accompanied by new focal neurological signs and symptoms. We diagnosed subarachnoid haemorrhage based on the characteristic sudden severe headache without new focal neurological signs. We considered appropriate cerebrospinal fluid abnormalities and neck stiffness supportive of the diagnosis.

We assessed ischaemic stroke subtypes using the Oxfordshire Community Stroke Project (OCSP) classification, and used the Trial of Org 101 in Acute Stroke Treatment (TOAST) classification as in the JHSR (section 5.1.2.1). However, in the absence of CT brain imaging we did not anticipate that the TOAST classification would be helpful, and as in the JHSR we also assigned a 'most likely' cause to all first-ever-in-a-lifetime stroke patients, based on their history, risk factors, examination findings and investigations.

The risk factors assessed and the definitions we used for: diabetes mellitus, cigarette smoking, alcohol use, ischaemic heart disease, peripheral vascular disease, first-ever-in-a-lifetime stroke, transient ischaemic attack, ethnicity, and historical risk factors were the same as those used in the JHSR (see section 5.1.2). We used the same definition for hypertension as we used in the JHSR, but

we did not have access to echocardiography for the diagnosis of left ventricular hypertrophy. Therefore, we diagnosed hypertensive heart disease on the basis of a history of hypertension, marked clinical evidence of left ventricular hypertrophy, ECG findings of left ventricular hypertrophy or a blood pressure of greater than or equal to 140 mmHg systolic or 90 mmHg diastolic if this was recorded prior to the stroke or more than one week following the stroke. We seldom had access to ECGs for the diagnosis of atrial fibrillation, so unlike in the JHSR where our definition of atrial fibrillation included ECG evidence of atrial fibrillation, in the THSR, we accepted the clinical finding of an irregularly irregular heart rate without a better explanation, as atrial fibrillation. We considered recurrent stroke to be a stroke (new focal neurological signs in a different territory to the index stroke) that occurred following our index stroke, and prior stroke to be a history of stroke prior to the current admission. We assessed patients with prior stroke in detail, but did not include them in the analysis and results of the first-ever-in-a-lifetime stroke cases.

Blood investigations requested included: full blood count, erythrocyte sedimentation rate, urea and electrolytes, blood glucose (random), serum total and high denity lipid (HDL) cholesterol (random), syphilis serology and if the patient had given consent, HIV serology (ELISA). Cerebrospinal fluid was sent for routine testing when appropriate.

### 7.1.3 Data analysis

We entered all questionnaires onto Microsoft Access 2002 SP3 and analysed the data using STATA software (StataCorp, 2001) using exactly the same methodology as used in the JHSR (section 5.1.3). We used Confidence Interval Analysis software (Bryant, 2000) and STATA to assess confidence intervals.

### 7.1.4 Ethics approval

The University of the Witwatersrand Human Ethics Research Committee provided us with approval for the Tintswalo Hospital Stroke Register as an extension to the approval for the Johannesburg Hospital Stroke Register (M00/03/7) (March 2001 full meeting) (Appendix H).

## 7.2 Results

### 7.2.1 Characteristics of the THSR stroke patients

One hundred and seventy-two patients with presumed stroke were referred to the THSR team over a 20-month period. We diagnosed 138 patients with first-ever-in-a-lifetime stroke. Figure 7.3 shows the reasons why we excluded 34 patients. Three patients with a history of prior stroke were dead on arrival at the hospital, and 11 patients did not have a stroke. Twenty patients had a history of prior stroke, and now presented with new focal neurological signs rather than simply deterioration in their old symptoms. We assessed these patients but did not include them in our analyses of the 138 first-ever-in-a-lifetime stroke patients. None of the patients had a transient ischaemic attack.

All the stroke patients were black South Africans from the local Bohlabela area. Table 7.1 shows the main characteristics of the stroke patients by sex. We found that females predominated, with a male to female ratio of 1:1.7. We could assess age in 133 of 138 patients. In five patients, we could not assess age because the patient and their relatives did not know their age and they did not have any official record of their age. The mean age was 64 years with a wide range of 19 to 94 years and a median age of 68 years (95% CI, 65 to 71 years). We did not find a significant difference in the mean (p=0.8) or median (p=0.7) age of males and females. All but one of the 129 patients we could assess for prior independence, were independent (modified Rankin score of 0 to 2) prior to the stroke.

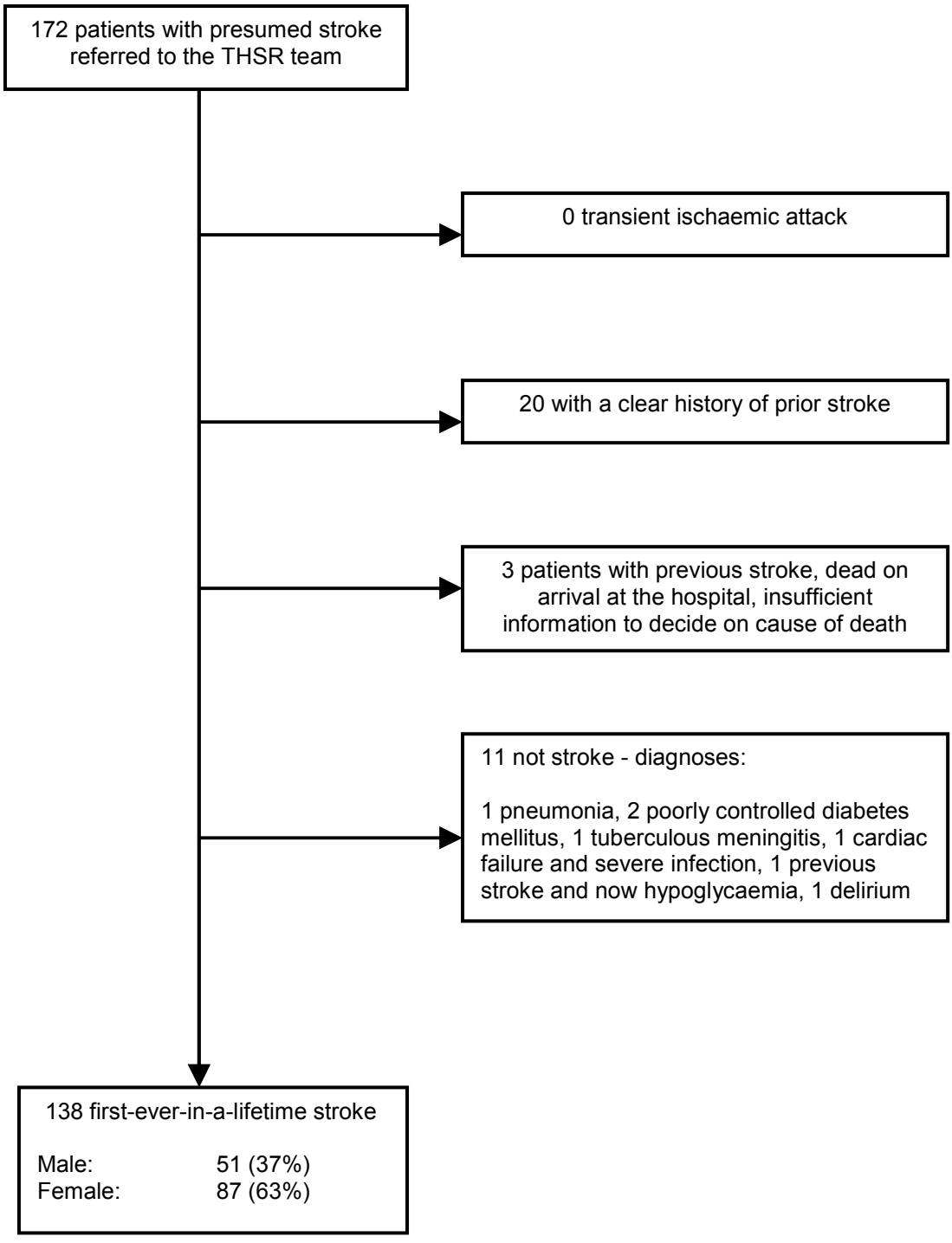



**Figure 7.3 Study outline: cases included in the Tintswalo Hospital Stroke Register**

## Table 7.1 Characteristics of the stroke patients in the Tintswalo Hospital Stroke Register, by sex (n is the number of patients with sufficient data to assess the characteristic; number with characteristic / total number assessed shown where relevant)

| | Male | Female | Total | |
|---|---|---|---|---|
| Strokes n | 51 (37%) | 87 (63) | 138 | |
| (ratio M:F) | 1:1.7 | | | |
| Age years – mean (SD) (95% CI) (range) n=133 | 65 (14) (61 to 69) (range 25 to 94) | 64 (18) (60 to 68) (range 19 to 93) | 64 (17) (61 to 67) (range 19 to 94) | *p=0.8** |
| Independent prior to stroke** (%) n=129 | 47 / 47 (100) | 81 / 82 (99) | 128 / 129 (99) | p=0.9 |
| Mean time to presentation (days)(95% CI) n=120 ‡ | 2 (1 to 3 days) | 11 (1 to 22) | 8 (1 to 15) | p<0.001 |
| Median time to presentation (days) (95% CI) n=120 ‡ | 0.5 (8 hours to 1 day) | 1 day (1 to 1) | 1 (1 to 1) | p=0.06† |
| Number who presented within 3 hours / total number with time to presentation data (%) n=125 | 10 / 46 (22) | 15 / 79 (19) | 25 / 125 (20) | p=0.6 |
| Number who presented within 6 hours / total number with time to presentation data (%) n=125 | 23 / 46 (50) | 26 / 79 (33) | 49 / 125 (39) | p=0.7 |
| Number scanned (%) n=138 | 3 / 51(6) | 6 / 87 (7) | 9 / 138 (7) | p=0.8 |

* p: significance of difference
** Analysis of variance comparing mean age and mean time to presentation by sex; ** Independent prior to stroke defined as a modified Rankin score of 0 to 2; ‡ excluding 5 patients who had strokes in hospital; † Wilcoxon test for comparison of medians

Five patients had a stroke in hospital. When we excluded these five patients, the mean time to presentation was long (8 days), but this was heavily influenced by the wide range of time to presentation (2 hours to 365 days). The median time to presentation was thus much shorter (1 day). Although there was a significant difference between the mean time to presentation for males (2 days) and females (11 days), the median time was not significantly different. The range of time to presentation for males was 2 hours to 21 days, and for females was 2 hours to 365 days. Three female patients presented more than three months following their stroke; two within 4 months and one a year after their stroke. All three patients had attended traditional healers for assistance prior to seeking help from allopathic health care. Twenty-five (20%) of patients presented within 3 hours of stroke onset, and 49 patients (39%) within 6 hours of stroke onset. Neither of these figures was significantly different for males and females.

The Tintswalo Hospital doctors referred nine patients (7%) to the provincial capital, Polokwane, for a CT brain scan. Although both males and females were as likely to have a CT brain scan (p=0.8), the mean (47years, SD 19; 95% CI 33 to 62) and median (42 years; 95% CI 30 to 72) age for those nine patients was lower than for the stroke population as a whole (p=0.06). All nine patients had their brain scans done within 7 days of admission to Tintswalo Hospital.

### 7.2.2 Pathological stroke types in the THSR

Of the nine patients who had a CT brain scan, the pathological stroke type was cerebral haemorrhage in three patients and ischaemic stroke in six patients. In the remaining patients, we assessed pathological stroke type using our clinical judgement and the Siriraj Stroke Score (SSS). We also attempted to assess the Guy's Hospital Stroke Score (GHSS), but failed in the majority of patients. Accurate assessment of the GHSS requires a chest x-ray and electrocardiogram (ECG) to assess cardiomegaly and atrial fibrillation respectively (Allen, 1983) (appendix F). Given the difficulties with access to both at Tintswalo Hospital, only 36 patients had a chest x-ray and 32 patients had an ECG. As such, we could only reliably assess the GHSS in the 32 patients who had both a chest x-ray and an ECG, and have therefore not considered the GHSS findings further.

Table 7.2 compares pathological stroke types using our assessment and the SSS in males and females. No stroke patient presented with subarachnoid haemorrhage during the time we ran the THSR and so for simplicity we coded any SSS diagnosis of 'intracranial haemorrhage' as cerebral haemorrhage. The SSS did not perform very well in the THSR. While the SSS produced an uncertain diagnosis in 20% of the JHSR stroke patients assessed, in the THSR it provided an 'uncertain' diagnosis in 35 (37%) of the 128 patients with sufficient data available for assessment.

## Table 7.2 Comparison of pathological stroke types (cerebral haemorrhage and ischaemic stroke)* in the Tintswalo Hospital Stroke Register as assessed by clinician and the Siriraj Stroke Score, by sex (percentage in brackets)

| | Clinician assessment | | | Siriraj Stroke Score | | |
|---|---|---|---|---|---|---|
| **Pathological stroke type:** | **Male** | **Female** | **Total** | **Male** | **Female** | **Total** |
| Total number of stroke patients assessed | 51 | 87 | 138 | 47 | 81 | 128 |
| Cerebral haemorrhage* | 16 (31) | 16 (18) | 32 (23) | 16 (34) | 23 (28) | 39 (31) |
| Ischaemic stroke | 32 (63) | 66 (76) | 98 (71) | 16 (34) | 38 (47) | 54 (42) |
| Uncertain | 3 (6) | 5 (6) | 8 (6) | 15 (32) | 20 (25) | 35 (37) |
| Significance of difference between sexes | p=0.5 | | | p=0.4 | | |
| Significance of difference between our assessment and SSS | p=0.2 | | | | | |

* The SSS does not distinguish between subarachnoid haemorrhage and cerebral haemorrhage (chapter 6). However as none of the THSR patients had a subarachnoid haemorrhage-like presentation, we coded all 'intracranial haemorrhage' as cerebral haemorrhage

The large number of ‘uncertain’ diagnoses rendered the SSS almost useless in the THSR. When we excluded patients with an ‘uncertain’ score, 42% of patients had a cerebral haemorrhage and 58% had an ischaemic stroke. In males, the proportion with cerebral haemorrhage increased to 50% when we excluded the ‘uncertain’ scores, in comparison to 33% if we excluded ‘uncertain’ scores from the clinician assessment (table 7.2). When we compared the SSS diagnosis of pathological stroke type with the CT findings in the nine patients who had CT brain scans, one patient with a cerebral haemorrhage had an ‘uncertain’ SSS result, the SSS score correctly diagnosed two patients with ischaemic stroke and one patient with cerebral haemorrhage. In the remaining 5 patients, the SSS diagnosis was wrong in 3 and in 2 the score had not been completed, presumably because the patient already had a CT brain scan diagnosis. We could not compare clinician diagnoses with CT brain findings as the clinician assessments already incorporated the CT findings.

Despite the high proportion of ‘uncertain’ and cerebral haemorrhage results found using the SSS, we did not find a significant difference between the clinician and SSS diagnoses ($p=0.4$). There was no statistical difference in the proportions of pathological stroke type found in males and females with either method of diagnosing pathological stroke type (table 7.2), although males we thought had more cerebral haemorrhages than females, particularly in our clinician assessment.

In summary, we found cerebral haemorrhage occurred in somewhere between a quarter and a third of stroke patients, and was more common in males than in

females though this difference was not significant statistically. We did not find any subarachnoid haemorrhages during the study, despite our careful case ascertainment and the generally higher awareness of stroke that occurred at Tintswalo Hospital as a result of the THSR. However, we acknowledge that without a CT scan diagnosis our assessment of pathological stroke type using both clinician and Siriraj Stroke Score diagnosis was inaccurate.

#### 7.2.2.1 Ischaemic stroke subtypes in the THSR

Table 7.3 presents the Oxfordshire Community Stroke Project (OCSP) classification of ischaemic stroke patients as assessed by both clinician diagnosis and the Siriraj Stroke Score. Both assessments found a high proportion (36 to 37%) of the more severe total anterior circulation ischaemic strokes. About a third were partial anterior circulation strokes, a quarter were lacunar strokes and a small number (2 to 4%) were posterior circulation strokes. Lacunar strokes were less common in males than in females (table 7.3) and total anterior circulation strokes more common. Thus, males were more likely to have a severe stroke at presentation, although the difference in OCSP types between males and females was not statistically significant. Posterior circulation strokes were uncommon.

#### 7.2.2.2 The cause of ischaemic strokes in the THSR

Not surprisingly, the Trial of ORG 10172 in Acute Stroke Therapy (TOAST) trial classification was not at all useful in the THSR. Using the TOAST classification we classified all but one of the ischaemic stroke patients as having strokes of ‘undetermined cause’, because of the lack of investigation available at Tintswalo Hospital. This one patient, a 30-year-old woman with a total anterior circulation infarct confirmed on CT brain scan, had severe post-partum cardiomyopathy with intraventricular thrombus visible on echocardiogram.

## Table 7.3 Ischaemic stroke subtypes (Oxfordshire Community Stroke Project classification) in patients with presumed ischaemic stroke (using clinical assessment or SSS) by sex (percentage in brackets)

| | Clinical assessment | | | Siriraj Stroke Score | | |
|---|---|---|---|---|---|---|
| | **Males** | **Females** | **Total** | **Males** | **Females** | **Total** |
| Total number of ischaemic strokes | 32 | 66 | 98 | 16 | 38 | 54 |
| Total number of patients assessed using OCSP | 30 | 64 | 94 | 15 | 36 | 51 |
| **Pathological Stroke Type:** | | | | | | |
| Total Anterior Circulation Infarction (TACI) (%) | 14 (47) | 20 (31) | 34 (36) | 9 (60) | 10 (28) | 19 (37) |
| Partial Anterior Circulation Infarction (PACI) (%) | 10 (33) | 26 (41) | 36 (38) | 3 (20) | 13 (36) | 16 (31) |
| Posterior Circulation Infarction (POCI) (%) | 1 (3) | 3 (5) | 4 (4) | 0 | 1 (3) | 1 (2) |
| Lacunar Infarction (LACI) (%) | 5 (17) | 15 (23) | 20 (21) | 3 (20) | 12 (33) | 15 (29) |
| Significance of difference between males and females | p=0.5 | | | p=0.2 | | |

OCSP: Oxfordshire Community Stroke Project classification

Table 7.4 compares the possible cause of ischaemic stroke in the THSR using our 'most likely diagnosis' approach in males and females, and using our clinician diagnosis of ischaemic stroke. We were unable to make a diagnosis in 40 (41%) of the 98 patients with presumed ischaemic stroke. Cardioembolic stroke and lacunar stroke were the commonest assigned causes, with cardioembolic strokes accounting for just over a quarter and lacunar strokes for just under a quarter of all ischaemic strokes. Large vessel atherosclerosis almost never occurred.

We did not have carotid Doppler or angiography available, which made the accurate diagnosis of large vessel atherosclerosis almost impossible. However, given the absolute lack of ischaemic heart disease and relative lack of peripheral vascular disease (see section 7.2.9 below for further discussion) it is unlikely that we have grossly underestimated extracranial carotid atherosclerosis. We diagnosed large vessel atherosclerosis in one patient, a 94-year-old male who had an ischaemic stroke without any obvious cause other than a carotid bruit on the appropriate side.

The 22 small vessel lacunar strokes we diagnosed were associated with hypertension in 16 (73%) patients, diabetes mellitus in 1 (5%) patient, and both hypertension and diabetes mellitus in 4 (18%) patients. The remaining patient had neither hypertension nor diabetes mellitus and we did not find any other potential cause for their lacunar infarct.

**Table 7.4 Cause of ischaemic stroke using our 'most likely cause' approach in patients with presumed ischaemic stroke (clinician assessment)* by sex (percentages in brackets)**

| | Male | Female | Total | |
|---|---|---|---|---|
| Total number of patients with presumed ischaemic stroke* | 32 | 66 | 98 | |
| Large vessel atherosclerosis (%) | 1 (3) | 0 | 1 (1) | |
| Cardioembolic (%) | 8 (25) | 19 (29) | 27(28) | Significance of difference |
| Small vessel (lacunar) (%) | 7 (22) | 15 (23) | 22(23) | p=0.7 |
| Other cause (%) | 2 (6) | 6 (9) | 8 (8) | |
| Undetermined (%) | 14 (44) | 26 (39) | 40 (41) | |

The ‘other cause’ category of ischaemic strokes included one presumed arterial dissection in a patient with epilepsy since childhood, who had not suffered a head injury, and four patients who had HIV infection. However, in one of these four HIV infected patients, a 33-year-old woman, the stroke occurred immediately post-partum and the HIV infection may have been unrelated to her stroke. We were unable to establish an exact cause of the stroke in the HIV infected patients.

#### 7.2.2.3 Cardioembolic stroke in the THSR

We diagnosed 28 (29%) of the 98 ischaemic stroke patients as potentially cardioembolic in aetiology. Table 7.5 shows the likely underlying cause of the cardioembolic strokes in these patients. None of the patients had any signs or symptoms to suggest ischaemic heart disease, though few had ECGs. Atrial fibrillation, accounted for almost half of the cardioembolic strokes (13 patients). We thought that the atrial fibrillation had been caused by rheumatic valvular heart disease in three patients, dilated cardiomyopathy in three patients, hypertensive heart disease in 3 patients, and in the remaining 4 patients we could not find an underlying cause.

## Table 7.5 Cardioembolic strokes in the THSR

| | Male | Female | Total |
|---|---|---|---|
| Total number of patients with cardioembolic stroke (CT confirmed or clinical diagnosis) | 8 | 19 | 27 |
| Atrial fibrillation: Total (% of cardioembolic strokes) | 3 (38) | 10 (53) | 13 (48) |
| - unknown cause | 2 | 2 | 4 |
| - with ischaemic heart disease | 0 | 0 | 0 |
| - with valvular heart disease | 0 | 3 | 3 |
| - with dilated cardiomyopathy | 0 | 3 | 3 |
| - with hypertensive heart disease | 1 | 2 | 3 |
| Ischaemic heart disease: Total (% of cardioembolic strokes) | 0 | 0 | 0 |
| Valvular heart disease: Total (% of cardioembolic strokes) | 2 (25) | 6 (32) | 8 (30) |
| - unknown cause | 0 | 0 | 0 |
| - rheumatic valvular disease | 0 | 4 | 4 |
| - associated with dilated cardiomyopathy | 2 | 2 | 4 |
| Cardiomyopathy: Total (% of cardioembolic strokes) | 5 (63) | 7 (37) | 12 (44) |
| - dilated | 4 | 7 | 11 |
| - associated with hypertensive heart disease** | 1 | 0 | 1 |
| Infective endocarditis (% of cardioembolic strokes) | 0 | 0 | 0 |
| Significance of difference between sexes | p=0.4 | | |

* NB subtotals and percentages do not add up to combined total as some causes are repeated
** See chapter 5 text for detail on this category (section 5.2.5.2)

Twelve patients had a cardiomyopathy. In eleven patients, this was a dilated cardiomyopathy and in one, we suspected end-stage hypertensive cardiomyopathy. Only one patient (discussed in at the beginning of section 7.2.4) had an echocardiogram which confirmed a post-partum dilated cardiomyopathy with intraventricular thrombus. None of the patients had infective endocarditis. Eight patients had valvular heart disease, which we thought was the result of rheumatic heart disease in at least half the patients. We could not be sure whether the four patients we diagnosed with dilated cardiomyopathy were originally rheumatic in origin or not.

In summary, cardioembolic stroke in the THSR was almost always the result of atrial fibrillation, dilated cardiomyopathy and rheumatic heart disease. Ischaemic heart disease or at least symptomatic ischaemic heart disease did not occur in our patients. Our findings are limited by the lack of ECGs and echocardiograms and further detailed investigation would be needed to diagnose the underlying cause of cardioembolic ischaemic stroke in rural stroke patients.

### 7.2.3 Hypertensive heart disease in the THSR

We discussed the controversy surrounding the role of hypertensive heart disease in stroke in section 5.3.4. In the JHSR we diagnosed hypertensive heart disease in patients with isolated left ventricular hypertrophy (i.e. in the absence of cardiac failure or any other cardiac abnormality) seen on echocardiograms. Unfortunately, only one patient in the THSR had an echocardiogram. The diagnosis of hypertensive heart disease requires post-mortem, echocardiographic, MRI or ECG

evidence for left ventricular hypertrophy (Lip et al., 2000). Given the frequency of hypertension in our rural stroke population (see section 7.2.9) it is likely that there is a high prevalence of hypertensive heart disease, and we found clinical evidence of marked left ventricular hypertrophy in 45 (33%) of our 138 stroke patients. Ten of these 45 patients had an ECG, and 7 patients had features of left ventricular hypertrophy (Lip et al., 2000). Considering we only managed to obtain ECGs on 32 stroke patients, it is likely that we missed many cases of hypertensive heart disease.

### 7.2.4 Causes of cerebral haemorrhage in the THSR

Thirty-two of the 138 stroke patients had a presumed cerebral haemorrhage according to our clinician assessment. None had cerebral angiograms and only three had CT brain scans. We thought that the cerebral haemorrhage was caused by hypertension in two of the patients with a CT brain scan, and by a low platelet count (66 x $10^9$/l) in a 73-year-old HIV negative female. Twenty-five of the remaining patients who did not have a CT brain scan had hypertension, and in five patients, we could not find any likely cause for the cerebral haemorrhage. None of the patients with cerebral haemorrhage had positive HIV serology or appeared to have HIV on clinical examination.

### 7.2.5 HIV infection in the THSR

Testing for HIV infection in South Africa is fraught with difficulty. Given the lack of therapy available at the time of the THSR and the potential social stigma of a positive diagnosis, we were very cautious about requesting informed consent for HIV testing from our stroke patients. At the same time the THSR was running, we were conducting a survey of vascular risk factors in people over the age of 35 years in the Agincourt Health and Population Unit field site. We had to abandon our attempt to perform anonymous unlinked HIV testing as so many people refused HIV testing and then withdrew consent for other blood investigations (Thorogood et al., 2005). We also had great difficulty obtaining consent for HIV testing from stroke patients. Of the 47 patients who consented to our register blood investigations, only 14 consented to HIV testing. Five (36%) of the 14 were positive. A further patient had previously documented HIV infection. In three patients, we did not have HIV serology, but their clinical findings were highly suggestive of HIV infection. Thus, HIV infection was either definitely present or likely to be present in nine (6%) of all our stroke patients. While this is almost certainly an underestimation of the true HIV prevalence in our patients, the prevalence of HIV infection in Limpopo Province at that time was one of the two lowest recorded in the country (15% of antenatal clinic attendees) (Directorate: Health Systems Research, 2001).

The mean age of HIV infected stroke patients was 38 (SD 19; 95% CI, 23 to 53) with a median age of 33 years (95% CI, 23 to 65) (range 20 to 72 years). Of the

nine patients who had definite or suspected HIV infection, eight were females and one was male.

### 7.2.6 Syphilis in the THSR

We tested 49 of the 138 stroke patients for syphilis using a rapid plasma reagin (RPR) screening test. This test is 100% sensitive and 98% specific during secondary syphilis, but less sensitive (98% and 73% respectively) during primary and latent phases of the disease (Larsen, Steiner, & Rudolph, 1995). Only one patient (1% of all stroke patients and 2% of those tested) had a positive RPR. This was a 71-year-old female who presented with a total anterior circulation presumed ischaemic stroke. We thought that the cause of the stroke was likely to be cardioembolic, caused by atrial fibrillation and a dilated cardiomyopathy rather than related to her positive syphilis serology. She did not have any clinical evidence of aortic regurgitation to suggest aortic root disease caused by syphilis, and we did not examine her cerebrospinal fluid. About 2% of woman between 45 and 49 years of age attending antenatal clinics in South Africa were positive for syphilis in 2000, and 4% of antenatal clinic attendees in Limpopo Province had a positive RPR in 2000 (Directorate: Health Systems Research, 2001).

Doctors at Tintswalo Hospital had requested syphilis serology on eight of the 49 patients tested for syphilis, including the one positive patient before we started our THSR blood investigations. We tested 41 of the 47 patients with blood sent to Johannesburg for syphilis. None of these patients was positive. Frustratingly, although we should have tested all 47 patients, six were not tested because of

logistical errors such as laboratory error, difficulty with venesection resulting in insufficient blood arriving at the laboratory, and broken specimens during the courier process. We gained a great deal of experience in getting blood specimens couriered safely from rural Limpopo Province to Johannesburg and then tested during the running of the THSR and SASPI.

### 7.2.7 Risk factors for stroke in the THSR

Table 7.6 compares the frequency of stroke risk factors in males and females by clinician assigned pathological stroke type. None of the risk factors shown was significantly more frequent in presumed cerebral haemorrhage than in presumed ischaemic stroke. The mean age of the population as previously noted was 64 (95% CI, 61 to 67) years, and the median slightly higher at 68 (95%CI, 65 to 71) years, with a range of 19 to 94 years. Only 51 (37%) of the stroke patients were male. There were slightly more females than males in the general population. The Agincourt Health and Population Unit is representative of the local population, and in this population 47% of people were male (figure 3.1). In 1995, 44% of the population over the age of 35 years were male. Therefore, there must be some reason why males were less likely to be admitted to hospital. One factor might be the high labour migration out of the area to the larger towns for most of the year. Although both males and females were involved in labour migration, far more males (60%) than females (14%) in the 30 to 49 year old age group were absent from the area for a great deal of the year (Tollman et al., 1999).

## Table 7.6 Risk factors in the THSR by sex and clinician assessed pathological stroke type (n = number assessed) (percentage in brackets unless otherwise stated)

| | Cerebral haemorrhage | | Ischaemic stroke | | | |
|---|---|---|---|---|---|---|
| | **M** | **F** | **M** | **F** | **All strokes*** | |
| Total number of strokes n | 16 | 16 | 32 | 66 | **138** | |
| Age – mean (95% CI) n=133 | 65 (58 to 73) | 71 (65 to 78) | 66 (61 to 70) | 62 (57 to 67) | **64 (61 to 67)** | **p=0.06 |
| Age – median (95% CI) n=133 | 65 (57 to 76) | 73 (65 to 81) | 67 (60 to 73) | 68 (63 to 72) | **68 (65 to 71)** | p=0.2 |
| Male sex (% of stroke type) n=138 | 16 (50) | 16 (50) | 32 (33) | 66 (67) | **51 (37)** | p=0.08 |
| Hypertension (%) n=136 | 14 (88) | 11 (69) | 23 (72) | 41 (62) | **95 (70)** | p=0.07 |
| Mean total cholesterol level mmol/L (95% CI) n=44 | 4.9 (3.8 to 6.0) | 4.8 (1.6 to 8) | 4.3 (3.0 to 5.6) | 4.7 (4.2 to 5.1) | **4.7 (4.4 to 5.0)** | p=0.5 |
| Cigarette smoking n=123 | | | | | | |
| - Current | 1 (7) | 0 | 4 (14) | 0 | **6 (5)** | p=0.96 |
| - Ex | 2 (14) | 0 | 6 (21) | 0 | **8 (7)** | |
| - Never | 11 (79) | 15 (100) | 19 (66) | 59 (100) | **109 (89)** | |
| Alcohol use n=124 | | | | | | |
| - Current | 5 (36) | 2 (13) | 7 (24) | 4 (7) | **19 (15)** | p=0.2 |
| - Ex | 0 | 1 | 7 (24) | 4 (7) | **14 (11)** | |
| - Never | 9 64) | 12 (80) | 15 (52) | 52 (87) | **91 (73)** | |
| Diabetes mellitus n=138 | 5 (31) | 3 (19) | 8 (25) | 6 (9) | **24 (17)** | p=0.2 |
| Previous transient ischaemic attack n=133 | 0 | 0 | 2 (7) | 4 (6) | **6 (5)** | p=0.4 |
| Ischaemic heart disease n=133 | 0 | 0 | 0 | 0 | **0** | |
| Known previous atrial fibrillation n=136 | 1 (6) | 0 | 0 | 1 (2) | **2 (2)** | p=0.4 |
| Peripheral vascular disease n=134 | 0 | 2 (13) | 3 (10) | 0 | **5 (4)** | p=0.7 |
| Family history of stroke n=133 | 1 (6) | 0 | 0 | 3 (5) | **4 (3)** | p=0.9 |

* All strokes includes strokes of 'uncertain' pathological stroke type

** Significance of difference between stroke types

If these people were to have symptoms of a stroke, it is highly likely that they would present to the health service close to their employment rather than to Tintswalo Hospital. This may also explain the slightly older mean age of males (65 years) compared to females (64 years) (table 7.1). It remains possible, however, that other as yet unrecognised factors contributed to the low proportion of males in the THRS.

Hypertension was the commonest modifiable risk factor in the THSR. We did not find a significant difference between the frequency of hypertension in males and females (p=0.5). The frequency of hypertension in stroke patients was much higher than in the local community over the age of 35 years where we found 43% of people over the age of 35 years were hypertensive (Thorogood et al., 2005).

We diagnosed diabetes mellitus in 24 (17%) stroke patients. Significantly more males (14) were diabetic than females (10) (p=0.02). The prevalence of diabetes mellitus in our stroke patients (17%) was much higher than the 3% found in the local population over the age of 35 years (Thorogood et al., 2005), though we suspect this finding may be an underestimate because of difficulty getting specimens to the laboratory rapidly. The mean blood glucose within 72 hours of admission in stroke patients was 8.9 mmol/L (SD 5.5; 95% CI 7.5 to 10.4; range 2.5 to 31) and the median was 7 mmol/L (95% CI, 6.2 to 8.2). In contrast, the mean random blood glucose in 262 people over the age of 35 years in the community was 5.3 mmol/L.

We found a mean non-fasting total cholesterol taken within the first three days of admission of 4.7 mmol/L (95% CI, 4.4 to 5.0) in stroke patients, compared to the mean of 4.28 mmol/L in males and 4.53 mmol/L in females found in the same survey of risk factors previously mentioned in those aged over the age of 35 years (Thorogood et al., 2005). We did not find a significant difference in the mean random total cholesterol level in males and females (p=0.9).

Cigarette smoking was not common and none of the female stroke patients was a current smoker or had ever smoked cigarettes. Only 3% of males were current smokers. This was much lower than the percentage of the general population over the age of 35 years in the area who were current daily smokers (13% of females and 32% of males) (Thorogood et al., 2005). This finding is surprising and suggests perhaps, that we did not obtain an accurate smoking history from our stroke patients.

Significantly more males (13 of 45; 29%) drank alcohol than females (6 of 79; 8%) (p=0.002), but this mirrored the survey mentioned in the Agincourt population where 8% of females were current drinkers and 43% of males. In contrast, females used snuff more often than males (25 of 78 females; 32% and only 3 of 40 males; 8%). In the community 36% of females used snuff and 4% of males. Thus, the use of alcohol and snuff was similar in our stroke patients to that found in the general adult population (Thorogood et al., 2005). We did not find a family history of stroke in first-degree relatives in many patients (4 of 133 asked; 3%).

A history of previous transient ischaemic attack was uncommon and only occurred in presumed ischaemic stroke patients. A history of atrial fibrillation too was rare (2 patients), though on examination 17 of 138 (12%) stroke patients had atrial fibrillation. We found peripheral vascular disease in 5 patients, but we did not find any patients with ischaemic heart disease. Four patients had a carotid bruit, two of these patients had ischaemic strokes (1 lacunar and one large vessel), one had a presumed cerebral haemorrhage and in one, we could not assign a pathological stroke type. Thus, we did not find much evidence of large artery extracranial atherosclerosis in the Tintswalo Hospital Stroke Register patients.

### 7.2.8 Socioeconomic measures in the THSR patients

We discussed the association of socioeconomic measures and stroke risk, as well as the lack of an accepted measure of socioeconomic status in South Africa in section 5.2.8.1. We assessed the same socioeconomic measures in the THSR as we assessed in the JHSR. Two measures were significantly different between males and females, marital status and sole-breadwinner status. Males were more likely to be currently married than females who were far more likely to be widowed than men. This may simply reflect the fact that women live longer than men (World Health Organisation, 2006). A larger proportion of male (25 of 41; 61%) than female (25 of 76; 33%) stroke patients considered themselves as sole breadwinners for the household they lived in.

## Table 7.7 Possible socioeconomic measures / factors in stroke patients in the THSR (total number of patients assessed in bold with percentage of those assessed in brackets)

| Socioeconomic measure n=number assessed | Male | Female | Total | Significance of difference |
|---|---|---|---|---|
| Marital status n=117 | **41** | **76** | **117** | p<0.001 |
| - married | 35 | 19 | 54 (46) | |
| - single | 3 | 14 | 17 (15) | |
| - widowed | 2 | 41 | 43 (37) | |
| - divorced | 1 | 2 | 3 (3) | |
| Sole breadwinner for the household n=104 | 25 | 25 | 50 (48) | p=0.01 |
| Housing n=115 | **41** | **74** | **115** | p=0.5 |
| - live in house / flat | 40 | 69 | 109 (95) | |
| - dormitory / hostel / single room | 0 | 0 | 0 | |
| - retirement home | 0 | 0 | 0 | |
| - live with employer | 0 | 1 | 1 | |
| - live in serviced shack | 1 | 1 | 2 | |
| - live in un-serviced shack | 0 | 3 | 3 | |
| Years of schooling passed n=109 | **38** | **71** | **109** | |
| - mean (SD) (95% CI) | 4 (1) (3 to 5) | 3 (0.5) (2 to 4) | 3 (0.5) (2 to 4) | p=0.2 |
| - median (95% CI) | 4 (0to 6) | 0 (0 to 2) | 0 (0 to 4) | p=0.2 |
| - none | 17 | 41 | 58 (53) | p=0.7 |
| - less than 7 years | 29 | 57 | 86 (79) | |
| - less than 12 years | 36 | 69 | 105 (96) | |
| - 12 years | 2 | 2 | 4 (4) | |
| - any in-service or post-school formal training | 2 | 1 | 3 (3) | |
| Employment assessed n=120 | **42** | **78** | **120** | p=0.1 |
| - unemployed and looking for work | 1 | 9 | 10 (8) | |
| - any pension | 28 | 50 | 78 (65) | |

Almost all males and females said they lived in a house or flat (table 7.7). This is difficult to interpret knowing the low-resourced area surrounding Tintswalo Hospital. Perhaps stroke patients who are able to get to hospital tend to be of a higher socioeconomic status, or more likely the interpretation of ‘house’ by stroke patients and their families included informal dwellings that many, especially urban dwellers, might consider shacks.

The mean and median years of schooling were very low for both males and females. Seventy-nine percent of stroke patients had less than 7 years of schooling and only 4% had passed 12 years of schooling (table 7.7). Only ten (8%) stroke patients considered themselves ‘unemployed and looking for work.’ This likely reflects the age of the THSR stroke patients, as 78 (65%) patients were receiving some form of pension (social / disability).

In summary, the THSR stroke population had a very low level of education. The majority were receiving a state pension and almost half supported their household financially.

### 7.2.9 Stroke severity and related disability in the THSR

#### 7.2.9.1 Stroke severity

We assessed stroke severity in the THSR using the same two measures, the National Institutes of Health Stroke Scale (National Institute of Neurological Disorders and Stroke, 2005) and the Scandanavian Stroke Scale (Scandinavian Stroke Study Group, 1985), used in the Johannesburg Hospital Stroke Register (JHSR)(section 5.2.11.1). In table 7.8 we compare stroke severity in males and females in the THSR.

We did not find any significant difference in the severity of stroke between sexes. The mean and median scores were almost identical in the two groups (mean score of 16 in both sexes, median of 15 in females, 16 in males). The NIHSS score was categorised as: mild (NIHSS ≤ 5), moderate (NIHSS 6 to 13), and severe (NIHSS ≥ 14).

**Table 7.8 Severity of stroke and proportion of stroke survivors with various measures of disability in the THSR, by sex (percentage of males, females or total patients assessed in brackets unless otherwise stated)**

| **Scale / Impairment**<br>n = total number assessed | **Males** | **Females** | **Total** | **Significance of difference** |
|---|---|---|---|---|
| NIH stroke scale | 48 | 82 | 130 | |
| - Mean (SD) | 16 (9) (13 to 18) | 16 (8) (14 to 17) | 16 (8) (14 to 17) | p=0.95 |
| - Median (95%) CI) | 16 (12 to 19) | 15 (13 to 18) | 15 (13 to 18) | p=0.9 |
| Scandinavian SS | 46 | 84 | 130 | |
| - Mean (SD) | 23 (17) (18 to 28) | 23 (16) (20 to 27) | 23 (16) (20 to 26) | p=0.97 |
| - Median (95% CI) | 20 (15 to 26) | 19 (16 to 25) | 20 (17 to 23) | p=0.95 |
| Barthel Index <20<br>n=134 | 49 (100) | 80 (94) | 129 (96) | p=0.8 |
| Barthel Index <15<br>n=134 | 45 (92) | 66 (78) | 122 (91) | p=0.9 |
| Barthel Index <10<br>n=134 | 40 (82) | 66 (78) | 106 (79) | p=0.5 |
| Barthel Index median (95% CI)<br>n=134 | 3 (1 to 5) | 2 (1 to 3) | 2 (1 to 4) | p=0.4 |
| mRankin scale 0-2<br>n=135 | 6 (12) | 10 (12) | 16 (12) | p=0.4 |
| MRankin scale 3-5 | 44 (88) | 75 (88) | 119 (88) | |

NIH: National Institute of Health; SSS: Scandinavian Stroke Scale

#### 7.2.9.2 The Barthel and modified Rankin scores in the THSR

We discussed the use of the Barthel Index (BI) and modified Rankin scores in stroke patients in section 5.2.11.2, and presented the findings from the THSR in the same format (table 7.8). Only 5 of the 134 patients in whom we were able to assess the Barthel Index had a score of 20, i.e. no functional impairment. The majority of patients were severely functionally impaired, 79% (106 of 134) scored below 10 and the median score was very low (2). We did not find any difference in BI score between males and females.

We considered stroke patients independent if they had a modified Rankin score of between 0 and 2. Only 16 of 135 patients assessed (12%) were independent when we assessed them. There was no difference in the proportion of males and females who were independent (table 7.8).

### 7.2.10 Stroke related complications in the THSR

Pneumonia and post-stroke seizures were the commonest in-hospital complications in the THSR stroke patients. Pneumonia occurred in 9 patients (3 males and 6 females), and seizures in 9 (5 males and 4 females). Other complications included painful shoulder syndrome in three patients and bedsores in two patients. None of the patients developed symptoms of depression or deep venous thrombosis, though the frequencies of these and the other complications were probably underestimates given the limited potential for investigation and inadequate staffing levels at the hospital.

Two patients, both female, had a recurrent stroke during their in-hospital stay. Twenty-five of the 138 stroke patients died in-hospital. Males died significantly more frequently (15) than females (10) (p=0.008). It is not clear why males died more often. We did not find a significant difference in the mean (male: 21; female 25; p=0.2) or median (male 23; female 23.5; p=0.5) NIHSS score, or mean (male 68; female 65; p=0.8) and median (male 70; female 72; p=0.9) age in males and females who died, using analysis of covariance (ANOVA) to compare the means and the Wilcoxon ranksum test to compare the medians. Although none of the patients underwent autopsy, the cause of death in the 25 patients was assessed as: directly related to severe stroke with raised intracranial pressure in 11, infection (pneumonia, infected bed sores, tuberculosis) in 5, renal and liver failure in 1 patient, hypokalaemia (potassium of 2 mmol/l in one patient) and in 7 the cause of death was unknown. The hypokalaemia mentioned in one patient who died, a 71 year old female with a total anterior circulation infarction likely caused by dilated cardiomyopathy and atrial fibrillation, was not noted until the THSR blood investigations were performed in Johannesburg. Unfortunately, she had died by the time this result was available.

### 7.2.11 Length of hospital stay for stroke patients in THSR

We had accurate data on the length of hospital stay in 66 patients. The mean duration of hospitalisation was 8 days (95% CI, 7 to 9 days) with a median stay of

7 days (95% CI, 6 to 9 days). We did not find any difference in the mean or median duration of stay for males and females (p=0.8 and 0.4 respectively).

## 7.3 Discussion

### 7.3.0 Outline of the discussion

In this section we will outline the key findings of the THSR and discuss the limitations of the study. We will then discuss the findings generally and briefly compare the findings with black JHSR stroke patients and patients from the Gambia. In chapter 8 we will compare the nature of stroke in the prevalent stroke cases (chapter 3 and 4) and the nature of stroke patients at Johannesburg and Tintswalo Hospitals. Thus, to prevent too much repetition we will keep the discussion and comparison with other work brief.

### 7.3.1 Summary of the THSR findings

The THSR included 138 patients with first-ever-in-a-lifetime stroke admitted to the rural Tintswalo Hospital over 20 months. All patients were black Shangaan speaking South Africans from the local Bohlabelo region.

#### 7.3.1.1 Key findings of the THSR

*Characteristics of stroke patients*

- More females were admitted with stroke than males (ratio M:F 1:1.7)

- The stroke patients were elderly with a mean age of 64 years and median age of 68 years
- 99% of patients were independent prior to the stroke
- 5 patients had a stroke in hospital
- The mean time to presentation was very long (8 days) with a wide range of 2 hours to 365 days, but the median time to presentation was much shorter (1 day)
- 20% of patients presented within 3 hours of stroke onset, and 39% within 6 hours of stroke onset
- Only 7% of patients had a CT brain scan and these patients were significantly younger than the patients who did not have a brain scan

*Pathological stroke type and ischaemic stroke subtype*

- The Guy's Hospital Stroke Score required a chest x-ray and ECG and these were so seldom available that it could not be used in the THSR to differentiate pathological stroke type
- The Siriraj Stroke Score (SSS) performed poorly with 37% of patients diagnosed as 'uncertain' pathological stroke type, and a very poor correlation with the CT brain scan findings in the nine patients who had a scan
- Using our clinical assessment of pathological stroke type, about a quarter of patients were thought to have had a cerebral haemorrhage, none a subarachnoid haemorrhage, and three-quarters an ischaemic stroke

- We found about the same proportion of total anterior circulation (36%) and partial anterior circulation (38) ischaemic strokes, with slightly fewer lacunar infarcts (21%) and a small number of posterior circulation infarcts (2%)
- We did not find a statistically significant difference in pathological stroke type or ischaemic stroke subtype between males and females

*Cause of stroke*

- We found the TOAST classification impossible to use in this low-resource setting, as all but one ischaemic stroke patient were classified as 'undetermined' because of inadequate investigation
- Using our 'most likely diagnosis' approach, we still remained with an 'undetermined' cause in 41% of 'ischaemic stroke' patients, but in the remainder we found 28% to be cardioembolic, 23% to be caused by small vessel disease which was mainly the result of hypertension, and only 1 patient to likely have large vessel atherosclerotic disease
- Cardioembolic 'ischaemic' strokes were caused by atrial fibrillation, dilated cardiomyopathy and rheumatic valvular heart disease and we did not find any evidence of ischaemic heart disease in our 'ischaemic' stroke patients
- The commonest cause of 'cerebral haemorrhage' was hypertension (84%), but we did not adequately investigate patients to exclude vascular malformations or aneurysms
- Other determined causes of 'ischaemic' stroke included: arterial dissection and possible HIV related stroke in 6% of our stroke patients, though this is likely to be an underestimate as we only received consent from 14 patients

for HIV testing. The mean age of HIV infected stroke patients was much lower than the general stroke population (38 years; median 33 years), and HIV infected patients were predominantly female (8 female, 1 male)

- Only one stroke patient had positive syphilis serology, and none had evidence of neurosyphilis, although we did not actively exclude neurosyphilis in this patient and only tested syphilis blood serology in 36% of patients

*Risk factors*

- Hypertension was the commonest modifiable stroke risk factor in male and female stroke patients, found in 70% of all stroke patients
- Cholesterol levels were low with a mean of 4.7mmol/L
- We found diabetes mellitus in 17% of stroke patients, and significantly more males than females were diabetic (p=0.02)
- We found that cigarette smoking was uncommon and less frequent than in the local community, raising the possibility that we did not obtain an accurate history of cigarette smoking from our patients
- More males were current users of alcohol than females, and more females used snuff than males, in both cases this reflected the pattern of use in the local community
- Peripheral vascular disease was uncommon and ischaemic heart disease did not occur in our patients
- Previous TIA was uncommon

- Socioeconomic measures revealed that stroke patients had a low level of education, the majority were receiving a state pension and almost half supported their household financially

*Stroke severity and the impact of stroke on the stroke survivor*

- Strokes included in the THSR were severe, and over 80% were dependent and had significant loss of function at the time of our assessment
- The nature of impairments reflected the high proportion of severe total anterior circulation and partial anterior circulation strokes with cortical involvement
- Impairments and complications were similar in males and females, but more males died in hospital than females despite being of similar age and stroke severity
- In hospital case fatality was 18%

### 7.3.2 Limitations of the THSR

We aimed to establish the profile of stroke patients and nature of stroke in an under-resourced rural hospital. However, the lack of resources was limiting and we did not have sufficient research funding to adequately supplement the investigation of stroke patients. As a result we depended on our clinical assessment of pathological stroke type and cause of stroke, both of which were unlikely to be very accurate (see chapter 6 for clinician pathological stroke type assessment). We had planned to supplement our assessment of pathological stroke type with the Siriraj and Guy's Hospital Stroke Scores, but neither of these proved practical.

Even when we were able to supplement the blood investigations, very few patients gave consent for HIV testing, so limiting our assessment of the frequency of this prevalent condition. Lack of echocardiography limited our ability to assess the proportion of patients with hypertensive heart disease, a condition we found to be very prevalent in black stroke patients in the Johannesburg Hospital Stroke Register.

Despite these limitations, we were able to ascertain stroke patients admitted to Tintswalo Hospital over 20 months accurately and to assess the vast majority in detail clinically. We have therefore provided useful demographic and clinical data on the nature of stroke in a rural South African population. This is the first study in Sub-Saharan Africa to do this.

### 7.3.3 Comparison of the THSR stroke patients with black stroke patients from urban South Africa and from the Gambia

Tables 7.9 and 7.10 compare the main characteristics of stroke patients, pathological stroke types, Oxfordshire Community Stroke Project stroke subtypes, risk factors and measures of impairment, in stroke patients in the Tintswalo Hospital Stroke Register (THSR), black patients in the Johannesburg Hospital Stroke Register (JHSR), and stroke patients in two studies from the same hospital in the Gambia ten years apart (Walker et al., 2003; Garbusinski et al., 2005). The Gambian studies included first-ever-in-a-lifetime and recurrent stroke patients whereas the THSR and JHSR only included first-ever-in-a-lifetime stroke patients. Note that all comparisons made below are with black stroke patients from the JHSR unless otherwise stated.

Patients in the THSR were on average more than 10 years older than patients in the JHSR and more than five years older than patients in the Gambia. Females predominated in the THSR, whereas males and females were equally represented in the JHSR and the 2000 / 2001 study from the Gambia. Males predominated in the other study from the Gambia performed in 1990. As discussed in section 2.4.4.1 earlier stroke studies form Sub-Saharan Africa often found a male predominance, while later studies found little difference between sexes. This may be age related, as incidence studies in high-income populations have found a higher proportion of males than females in younger age groups and a similar proportion of males and females in older age groups.

**Table 7.9 Comparison of stroke patients in the Tintswalo Hospital Stroke Register, black patients in the Johannesburg Hospital Stroke Register, and stroke patients in two stroke studies from the same hospital in the Gambia (2000/1* and 1990**) (Garbusinski et al, 2005; Walker et al, 2003)**

| | **THSR (n=138)** | | **JHSR (n=308)** | | **Gambia, 1990 (n=106)** | **Gambia, 2000/1 (n=148)** |
|---|---|---|---|---|---|---|
| Age | | | | | | |
| - Mean (SD) | 64 (17) | | 51 (16) | | 58 (16) | n/a |
| - Median (95% CI) | 68 (65 to 71) | | 51 (49 to 55) | | 60 | n/a |
| Sex ratio (M:F) | 1:1.7 | | 1:1 | | 1.9:1 | 1:1 |
| Economically active (contribute to family income) n (%) | 106 (77) | | 117 (55)† | | n/a | n=? (53) |
| Brain scan rate (%) | 7% | | 67% | | 0 | 0 |
| Mean time to presentation (days) (95% CI) | 8 (1 to 15) | | 3.5 (2 to 5) | | n/a but mean of 29 hours for 80 admitted within 7 days | n/a |
| Median time to presentation (days) | 1 ( to 1) | | 1 (1 to 1) | | 8 hours for sample above | n/a |
| Proportion who presented within 3 hours (%) | 25 (20)† | | 32 (11)† | | n/a | n/a |
| NIHSS mean (SD) | 16 (8) | | 12 (9) | | n/a | 12 (6) |
| NIHSS median | 15 (13 to 18) | | 10 (8 to 12) | | n/a | n/a |
| Barthel Index <10 (%) | 106 (79)† | | 174 (55) | | n/a | n/a |
| Barthel Index median (95% CI) | 2 (1 to 4)† | | 7 (6 to 9) | | n/a | n/a |
| **Pathological stroke type:** | **n=138** | **n=138 SSS** | **n=207 CT scan** | **n=307 SSS** | **n=106** | **n=138 SSS** |
| Cerebral haemorrhage n (%) | 32 (23) | 39 (31) | 55 (27) | 71 (23) | n/a | 63 (46) |
| Ischaemic stroke n (%) | 98 (71) | 54 (42) | 141 (68) | 171 (56) | n/a | 42 (30) |
| Subarachnoid haemorrhage n (%) | 0 | 0 | 11 (3) | n/a | n/a | not assessed |
| Uncertain n (%) | 8 (6) | 35 (37) | 0 | 65 (21) | n/a | 17 (24) |
| **OCSP stroke subtype** | **n=98 IS stroke** | **n=131‡ all stroke** | **n=235 IS stroke** | **n=308 all stroke** | **n=106 all strokes** | **n=130 all stroke** |
| Total anterior circulation syndrome | 34 (36) | 60 (46) | 62 (26) | 92 (30) | 54 (51) | 46 (35) |
| Partial anterior circulation syndrome | 36 (38) | 41 (31) | 84 (36) | 105 (34) | 33 (31) | 35 (27) |
| Lacunar syndrome | 20 (21) | 23 (18) | 71 (30) | 76 (25) | 19 (18) | 18 (14) |
| Posterior circulation syndrome | 4 (4) | 7 (5) | 18 (8) | 21 (7) | 0 | 6 (5) |
| Undetermined | 0 | 0 | 0 | 14 (5) all CH / SAH | 0 | 25 (19) |

THSR: Tintswalo Hospital Stroke Register, JHSR: Johannesburg Hospital Stroke Register; NIH: National Institute of Health; SSS: using the Siriraj Stroke Score; † percentage of patients assessed ‡ all pathological stroke types assessed; CH: cerebral haemorrhage; SAH: subarachnoid haemorrhage; IS: ischaemic stroke

As discussed in 7.2.8 our finding of a significant female predominance in the THSR may be the result of a higher proportion of females in the local adult population and the result of labour migration which involves more males than females.

The older age of our patients suggests that stroke occurs less frequently in the young rural population of South Africa than in the young urban population. While this may be true and may even be the result of the rural population being at an earlier stage of the health transition, it is also likely that other factors such as labour migration, which results in many young patients working in urban areas for much of the week or even the year play a part. These young patients are more likely to present to the health service closer to their employment, and while in our experience many return home to the area, they are less likely to seek acute medical care in Bohlabelo.

Although the proportion of economically active stroke patients (defined as 'contributing to the family income') was higher in THSR than in the JHSR or in the Gambia, this is likely the result of a high proportion of THSR patients receiving state pensions. State pensions are an important source of income for families in the area (Case, 2001). Only 28 (20%) of the THSR patients were employed, compared to 110 (36%) of the black patients on the JHSR. This is probably the result of an older and therefore unemployed population in the THSR as well as higher unemployment in the rural areas around Tintswalo Hospital (Kahn, Tollman, Thorogood et al, 2005).

The mean time to presentation (8 days) for patients in the THSR was much longer than the mean of 3.5 days for patients in the JHSR.This was the result of a few patients who took months to present to hospital. The median time to presentation was the same in both registers, and the proportion of patients who presented within three hours, a time limit that influences management decisions such as the use of thrombolysis, was higher at Tintswalo Hospital than Johanneburg Hospital. It is difficult to compare our THSR and JHSR findings with the studies from the Gambia as the time to presentation is only reported for subgroups of the Gambian patients (Walker et al., 2003; Garbusinski et al., 2005).

The severity of stroke patients as measured using the mean and median NIH stroke scale (NIHSS) was higher in the THSR than the JHSR (table 7.9). Stroke severity in patients in the one Gambian study that reported NIH stroke scale findings was the same as in black JHSR patients. The median Barthel Index (BI) was lower (functioning worse) in THSR than JHSR, and the proportion of patients with a BI score less than 10 (severely functionally impaired) was higher in THSR than JHSR stroke patients, in keeping with the NIHSS finding that THSR strokes were more severe than JHSR strokes. This is also in keeping with the higher proportion of total anterior circulation syndrome strokes, lower proportion of lacunar syndrome strokes, and higher proportion of patients with a decreased level of consciousness in the THSR than in the JHSR and 2000 / 2001 Gambian study (tables 7.9 and 7.10).

There was a marked skew towards major stroke (as measured by NIHSS and mRS) in the THSR. This likely reflects hospital referral bias i.e. few people with

mild stroke present to hospital, and perhaps admission bias. It is likely that in a low resource area like Bohlabela there are many obstacles to hospital admission, such as the availability of transport and financial resources to pay for transport (SASPI Project Team, 2004). The elderly in Bohlabela also play an enormous role in supporting households by caring for children, particularly in the HIV era when many households have lost members in the 20 to 45 year old age group because of the disease. Thus, it is likely that people ignore minor stroke symptoms and only symptoms which result in a significant loss of function force people to hospital. No doubt, there is also a far higher awareness of stroke and stroke symptoms in Johannesburg than in Bohlabela, among health care workers and the public.

Pathological stroke type is difficult to assess in regions without access to brain imaging. One Gambian study used the Siriraj Stroke Score (SSS) to assess pathological stroke type (Garbusinski et al., 2005). Although the SSS performed relatively well in black JHSR stroke patients, with a moderately good sensitivity, specificity, likelihood ratio and Kappa statistic (chapter 6), it did not perform well in the THSR resulting in an 'uncertain' diagnosis in 37% of stroke patients as well as correlating poorly against the few available CT scan findings. The proportion of patients who had an 'uncertain' Siriraj Stroke Score was much lower in the JHSR (21%) and the Gambian study (24%). The SSS uses level of consciousness, vomiting and headache within two hours of stroke onset, diastolic blood pressure (multiplied by 0.1) and markers of atherosclerosis (diabetes history, peripheral artery disease, and angina) to derive a score (appendix F). Given the high proportion with a decreased level of consciousness (65%) in the THSH, a typical THSR patient might score 2.5 for level of consiousness, nil for vomiting and

headache, 9 for diastolic blood pressure (the mean and median diastolic blood pressure in both the THSR and JHSR was 90mmHg), and nil for atheroma markers. After subtracting the constant of -12, the result would be an uncertain score of -0.5. Although far more analysis and investigation are required to assess why the SSS does not perform well in rural patients, and to improve the SSS performance in all South African patients, it is likely that in patients with severe ischaemic stroke but without headache and vomiting associated, the score will return an 'uncertain' score. Given the low level of atherosclerosis in black South Africans, the score is likely to be driven by blood pressure (high blood pressure increasing a diagnosis of cerebral haemorrhage), and vomiting and headache after stroke. Given the high likelihood of elevated diastolic blood pressure in Sub-Saharan African populations, the score is likely to overestimate cerebral haemorrhage and underestimate ischaemic stroke.

In table 7.9 we compared the Gambian study with our CT based diagnosis of stroke type in the JHSR and clinician based assessment of stroke type in the THSR, as well as the SSS assessment of pathological stroke type in both our South African studies. Firstly comparing our clinician diagnosis in the THSR and the CT based diagnosis in the JHSR, both studies had similar proportions of ischaemic stroke (about 70%). There were slightly more cerebral haemorrhages in the JHSR (27% versus 23%). The proportion of ischaemic stroke was much lower when we used the SSS assessment, possibly for the reasons outlined above. In the Gambia, 46% of strokes were cerebral haemorrhages and only 30% ischaemic strokes. While it is tempting to implicate the health transition to explain a higher proportion of cerebral haemorrhage in the Gambia (indicative of the early phase of

the transition – chapter 1) than in South Africa, it is as likely that the high proportion of cerebral haemorrhages is the result of the SSS methodology. Community-based stroke incidence studies with early imaging are needed to clarify the pathological stroke types found in the Sub-Saharan African community. Hospital-based study bias and inaccuracies in clinical and stroke score diagnosis prevent an accurate assessment based on current data.

The two Gambian stroke studies applied the OCSP stroke classification to all strokes, not just ischaemic strokes. To compare our findings with these studies we have compared our assessment of stroke subtypes when applied to all strokes as well as ischaemic strokes (table 7.9). Posterior circulation syndrome strokes accounted for a similar proportion in all studies. Lacunar strokes were more frequent in the JHSR, whether applied to all or just ischaemic strokes (25% to 30%), than in the THSR or either of the two Gambian studies. Partial anterior circulation strokes accounted for somewhere between 27% and 38% of patients and were more frequent when applied to ischaemic strokes than to all strokes. This finding and the finding of a higher proportion of total anterior circulation strokes in 'all stroke' analyses than in ischaemic strokes, is probably the result of the inclusion of cerebral haemorrhages in the data. Cerebral haemorrhages are often more dramatic and severe in their presentation and more likely to be classified as partial or total anterior circulation events (Anderson, Taylor, Hankey et al, 1994). The lower proportion of lacunar strokes and higher proportion of total anterior circulation strokes in the THSR compared to the JHSR is probably the result of fewer mild strokes admitted in the THSR than in the JHSR as discussed previously.

### 7.3.4 Comparison of the THSR stroke patients with black stroke patients from urban South Africa and from the Gambia – risk factors and in-hospital deaths

In table 7.10 we compare the prevalence of risk factors found in the above studies. Unfortunately, the frequencies of most of the risk factors were not reported in the studies from the Gambia.

Hypertension was the commonest risk factor for stroke in both the THSR and the JHSR, present in similar proportions of stroke patients (70% to 74%). Only about half the patients in the Gambian study were hypertensive (48%). In the Gambian study hypertension was diagnosed when patients were on treatment for hypertension on admission, or when their blood pressure was greater than 140 mmHg or 90 mmHg diastolic more than one week after the stroke onset (Garbusinski et al., 2005). Our definition included a history of hypertension, or documented evidence of a blood pressure of more than 140 / 90 mmHg and evidence of left ventricular hypertrophy (clinically or on ECG in the THSR and on ECG or echocardiography in the JHSR). Thus, our wider-ranging definition may have increased the number of patients we diagnosed with hypertension. However, based on a history of hypertension alone we would have diagnosed hypertension in 51% of THSR stroke patients and 58% of JHSR black stroke patients. Given the high proportion of undiagnosed and untreated hypertensive patients in South Africa (Steyn, Gaziano, Bradshaw et al, 2001) and the inaccuracy of diagnosing hypertension in the acute stroke patient (Warlow et al., 2001), we consider it important to broaden the definition of hypertension as we have done.

**Table 7.10 Comparison of risk factors, prevalence of previous stroke and in-hospital death in the Tintswalo Hospital Stroke Register, black patients in the Johannesburg Hospital Stroke Register, and stroke patients in two stroke studies from the same hospital in the Gambia (2000/1* and 1990**)(Garbusinski et al, 2005; Walker et al, 2003) (percentage in brackets unless otherwise stated)**

| | THSR (n=138) | JHSR (n=308) | Gambia, 1990 (n=106) | Gambia, 2000/1 (n=148) |
|---|---|---|---|---|
| **Risk factors:** | | | | |
| - Hypertension n (%) | 95 / 136 (70) | 214 (74) | n/a | 71 (48) |
| - Diabetes n (%) | 24 / 138 (17) | 42 (16) | n/a | 7 (5) |
| - Mean total cholesterol mmol/l (95% CI) | 4.7 (4.4 to 5.0) | 4.6 (4.3 to 4.9) | n/a | n/a |
| - Ischaemic heart disease n (%) | 0 | 8 (4) | n/a | n/a |
| - Atrial fibrillation | 15 (11) | 20 (7) | n/a | 6 (4) |
| - Current cigarette smoking | 5 (5) | 57 (23) | n/a | 48 (32) |
| - Current alcohol use | 19 (15) | 63 (27) | n/a | n/a |
| - Peripheral vascular disease | 5 (4) | 9 (3) | n/a | n/a |
| - Previous transient ischaemic attack | 6 (5) | 4 (1) | n/a | n/a |
| - Carotid bruit | 4 (3) | 1 (<1) | n/a | n/a |
| **History of a previous stroke (NB n for THSR =172 )** | 23 (13) | 36 / 524 (7%) n/a by population group | 10 (9) | 18 (12) |
| **Death during initial admission** | 25 (18) | 23 (8) | 25 (19) of patients who presented within 7 days | 61 (41) |

THSR: Tintswalo Hospital Stroke Register, JHSR: Johannesburg Hospital Stroke Register NIH: National Institute of Health; SSS: Scandinavian Stroke Scale † percentage of patients assessed ‡ all pathological stroke types assessed

Diabetes was about as prevalent in THSR and JHSR stroke patients, but about a third as common in the Gambia (table 7.10). As discussed in section 5.3.5.3 diabetes mellitus increases in populations undergoing health transition. However, we cannot ignore the possibility that the lower prevalence in the Gambian study occurred because the diagnosis in these patients did not include the measurement of blood glucose.

The mean total cholesterol levels in THSR and JHSR patients were almost identical. This is interesting as one might expect that urban stroke patients would have higher blood total cholesterol than rural patients. As discussed in section 7.2.8 total cholesterol levels were lower (4.3 mmol/L in males and 4.5 mmol/L in females) in the local Bohlabela community and perhaps the higher level in THSR stroke patients simply reflects a high-risk group of people. Cholesterol levels were still much lower than has been found in populations with a high prevalence of large artery atherosclerosis (section 5.3.3.1.3).

In keeping with our finding that large artery atherosclerosis (ischaemic heart disease, peripheral vascular disease and carotid bruits as a marker of extracranial carotid artery disease) was uncommon in JHSR black patients, we did not find any patients with ischaemic heart disease in the THSR. We found a low prevalence of peripheral vascular disease and found carotid bruits infrequently (table 7.10). Previous transient ischaemic attack occurred slightly more frequently in the THSR patients than in the JHSR. Secondary prevention of stroke is poor in the Bohlabela region (Thorogood, Connor, Lewando-Hundt et al, 2004) and it is possible that detection and management of transient ischaemic attack is equally poor. Obtaining

accurate histories of a previous cerebral ischaemic event is not easy at Tintswalo Hospital. People are often not specific about weakness or sensory symptoms as we found in the SASPI stroke prevalence study (chapter 3 and 4)(Hundt et al., 2004). Although we were very cautious about recording a previous transient ischaemic attack, it is possible that we overestimated the frequency. History of previous stroke was a similar problem, but a history of prolonged focal neurological deficit was easier to establish than a history of transient deficit. Roughly a similar proportion of people with previous strokes were referred to the THSR and JHSR as were included in the Gambian studies, although we did not include these patients in our analyses.

Atrial fibrillation was slightly more common in the THSR than in the JHSR. This may be because cardiac disease is not well managed in Bohlabela, because more severe stroke patients tended to be admitted and cardioembolic strokes are often severe, because THSR patients were older than patients in the JHSR, or a combination of these factors. Current cigarette smoking and alcohol use were far less frequent in the THSR patients than in either JHSR or in the case of cigarette smoking, in the Gambia. This may reflect the older population admitted with stroke, or may suggest that we did not obtain accurate histories of cigarette smoking and alcohol use.

Far more stroke patients died during their initial admission in the THSR than in the JHSR (18% versus 8%). This may be the result of strokes being more severe in the THSR, and possibly explains why a similar proportion of the 1990 Gambian study patients died during hospital admission. The 2000 / 2001 Gambian study,

however, found a much higher in-hospital case fatality (41%) despite less severe stroke patients than in the THSR. Management differences or some other factors related to case mix differences not detected by the NIH Stroke Scale may account for this difference.

### 7.3.5 Comparison of cardioembolic stroke in the JHSR and THSR

In table 7.11 we compare the causes of cardioembolic stroke in the THSR and in black stroke patients in the JHSR. Cardioembolic stroke accounted for 27 of 98 (28%) of the ischaemic strokes in the THSR and a similar proportion, 53 of 235 (23%) of ischaemic strokes, in the JHSR. Atrial fibrillation, valvular heart disease and dilated cardiomyopathy were more common in the THSR than in the JHSR.

## Table 7.11 Comparison of cardioembolic stroke in the THSR and black stroke patients in the JHSR

| | THSR | JHSR |
|---|---|---|
| Total number of patients with cardioembolic stroke | 27 | 52 |
| Atrial fibrillation: Total (% of cardioembolic strokes) | 13 (48) | 15 (29) |
| - unknown cause | 4 | 6 |
| - with ischaemic heart disease | 0 | 1 |
| - with valvular heart disease | 3 | 2 |
| - with dilated cardiomyopathy | 3 | 0 |
| - with hypertensive heart disease | 3 | 6 |
| Ischaemic heart disease: Total (% of cardioembolic strokes) | 0 | 2 (4) |
| Valvular heart disease: Total (% of cardioembolic strokes) | 8 (30) | 9 (17) |
| - unknown cause | 0 | 1 |
| - rheumatic valvular disease | 4 | 6 |
| - associated with dilated cardiomyopathy | 4 | 2 |
| Cardiomyopathy: Total (% of cardioembolic strokes) | 12 (44) | 27 (52) |
| - dilated | 11 | 10 |
| - associated with hypertensive heart disease** | 1 | 17 |
| Infective endocarditis (% of cardioembolic strokes) | 0 | 0 |

THSR: Tintswalo Hospital Stroke Register, JHSR: Johannesburg Hospital Stroke Register
* NB subtotals and percentages do not add up to combined total as some causes are repeated
** See chapter 5 text for detail on this category (section 5.2.5.2)

Ischaemic heart disease though not common did occur in the JHSR, but did not occur at all in the THSR. No patient in either register had infective endocarditis.

The lower proportion of patients with hypertensive cardiomyopathy in the THSR, while possibly the result of less hypertensive heart disease in the community, is far more likely the result of the unavailability of echocardiography in the THSR. It is unlikely that we would have missed a cardiomyopathy, but it is quite possible that we would have diagnosed a patient with end-stage hypertensive heart disease in cardiac failure as having dilated cardiomyopathy (see section 5.2.5.2 for further discussion on hypertensive heart disease).

Thirteen patients (48% of cardioembolic stroke patients) had atrial fibrillation in the THSR. None of these patients had ischaemic heart disease and the cause of the atrial fibrillation was roughly equally distributed between valvular heart disease, dilated cardiomyopathy, hypertensive heart disease and atrial fibrillation of unknown cause. Possibly atrial fibrillation is common in Bohlabela because care of cardiac patients is poor. There are no specialist physicians and no cardiologists in the area and people are seldom referred to specialist centres because of limited resources. Follow up care for cardiac patients and specialist cardiac medication is not readily available in the area (National Department of Health (South Africa), 2003).

Valvular heart disease was more common in the THSR. This may reflect a higher prevalence of rheumatic heart disease and associated valvular disease in the rural

areas of South Africa, but this is simply speculation. A community-based study of rheumatic heart disease and indeed of all heart disease in South Africa is needed.

Thus, cardioembolic stroke is common in rural and urban South Africa, and the causes are very similar. We will, with due caution, highlight the possible role of the health transition in the subtle differences in causes of cardioembolic stroke in chapter 8.

### 7.3.6 Comparison of HIV and syphilis infection in the THSR and the JHSR

We tested very few (14) of the THSR stroke patients for HIV infection as most of the 47 patients who had blood investigations refused testing. We had similar experience in the SASPI risk factor survey in adults over 35 years of age conducted at the same time as the THSR (Thorogood et al., 2005). This possibly occurred because patients were concerned about a positive diagnosis with the associated social stigma, particularly at a time when antiretroviral therapy was not available (Sidley, 2001).

We found that 5 stroke patients were HIV positive in the THSR i.e. 36% of the 14 tested and 6% of all stroke patients. In contrast in the JHSR 61 of 148 black stroke patients tested for HIV were positive (41% of those tested and 20% of all black stroke patients). While the proportion of the patients tested who were positive is similar in the two registers, the findings from the THSR are unlikely to be accurate given the small number of patients tested, and all we can assume is that a

minimum of 6% of all stroke patients at Tintswalo Hospital were HIV positive at the time of the register.

We tested far more patients for syphilis (49 of 138; 36%) and only found one patient with the infection (2%). In the JHSR we tested 59 of 308 (19%) black patients and found 15% had the infection. It is likely that syphilis is not as prevalent in the rural South African elderly population as in the younger urban population of Johannesburg. In 2000 in Gauteng Province the prevalence of syphilis in antenatal clinic attendees was about 10% compared to the Limpopo Province prevalence of 4% (Directorate: Health Systems Research, 2001) and the prevalence decreased with age in all populations. Syphilis was far less common in our study than in other stroke studies that have assessed syphilis serology in Sub-Saharan Africa (section 5.3.5.5).

## 7.4 Conclusion

We found distinct differences between rural and urban South African hospital-based stroke patients. Patients admitted to the rural Tintswalo Hospital were older, more likely to be pensioners and to be female than in Johannesburg. Rural stroke patients had more severe strokes than in the urban stroke register and were more functionally impaired. The majority of patients took the same time to get to hospital as in Johannesburg. Pathological stroke types were not markedly different in the two sites as far as we could tell, but there were more large artery and fewer lacunar ischaemic strokes in rural patients than urban patients. This suggests that rural stroke patients were less likely to present to hospital than urban stroke patients.

Other than cigarette smoking and current alcohol use which were more common in urban stroke patients (possibly because patients were younger), the risk factors in rural stroke patients were remarkably similar to those in urban patients, including their cholesterol levels. Large artery atherosclerotic disease was about as common in rural and urban stroke patients but ischaemic heart disease did not occur. Cardiac causes of stroke were similar in rural and urban stroke patients, though rheumatic valvular heart disease was more common in rural stroke than urban patients.

HIV and syphilis infection were not common in rural stroke patients, possibly reflecting a lower community prevalence of HIV especially in the elderly. However,

we were not able to investigate enough patients for these conditions to be confident about this conclusion.

Hypertension was the most significant risk factor in rural and urban stroke patients, and is in our opinion the most important target for both primary and secondary prevention. More stroke patients died in the rural than the urban stroke register. This may well be the result of case mix differences i.e. rural hospital-based stroke patients had more severe strokes. However, seen together with the need for risk factor reduction and the need to detect and manage milder strokes in the community, what we really need is increased stroke awareness amongst both the general public and health care workers in the region, and a better package of care including improved acute and chronic management.

The nature of stroke in rural South Africa was similar to that found in two recent stroke studies from an urban referral hospital in the Gambia. Our rural stroke patients were older and had more severe strokes, likely the result of limited financial and household resources in the community discouraging hospital admission. Hypertension and diabetes mellitus appeared to be more common in rural South African patients, but this difference may in be the result of methodological differences between the Gambian studies and ours.

The lack of access to CT or MRI brain imaging in the Tintswalo Hospital Stroke Register and the Gambian stroke studies made it difficult to compare pathological stroke types. We found that the Siriraj Stroke Score did not perform as well in the rural stroke register as it did in the urban register. More than a third of patients did

not have a pathological stroke type assigned using the score, and the score appeared to underestimate ischaemic stroke and yet miss CT documented cerebral haemorrhages. The Siriraj Stroke Score may have underestimated ischaemic stroke in other studies from Sub-Saharan Africa including the Gambian stroke study. We could not use the Guy's Hospital Stroke Score in our study because it required ECGs and chest x-rays which were seldom available in our low-resourced rural hospital. We do not feel that either of these scores in their current form is useful to distinguish pathological stroke type in Sub-Saharan African populations.

Hospital-based studies present a biased view of stroke in any community, but when comparing our rural and urban stroke studies it appears that this bias is greatest in the rural population. To understand stroke in rural South African and indeed in Sub-Saharan Africa more clearly, we need community-based stroke incidence studies with good case ascertainment and early brain imaging.

### 7.4.1 What this study adds to the literature

This is the first prospective rural stroke register from South Africa and the first prospective stroke register from Sub-Saharan Africa to focus entirely on rural stroke patients. The overlap in timing and design between the rural THSR and urban JHSR gives us the opportunity to compare the nature of rural and urban stroke patients in the same country during the same period, and provides insight into the influence of urbanisation on the nature of stroke. This study is also useful from the health service perspective as it highlights deficiencies in our rural stroke care at present. Only severe stroke patients appear to be admitted to hospital, and it is likely that milder stroke patients in the community are missed, together with the opportunity to prevent them from having a subsequent major stroke. This study has also highlighted the inadequacies of both the clinical and stroke score assessment of stroke patients, and the need for brain imaging in epidemiological studies in Sub-Saharan Africa.

# CHAPTER 8 IS THERE EVIDENCE OF A HEALTH TRANSITION IN SOUTH AFRICA?

## 8.0 Introduction

In section 1.6 we described the postulated influence of the health and demographic transition on disease (Omran, 1971; Yusuf et al., 2001). For ease of reference we have repeated a table summarising the stages of the health transition (table 8.1). In summary, populations undergoing economic development undergo a gradual shift from infectious, perinatal and poverty related disease to non-communicable disease. Vascular risk factors emerge in a population in transition, with hypertension the predominant risk factor initially. Gradually diabetes mellitus and later elevated cholesterol levels add to the vascular risk factors as does increasing cigarette use. During the phase dominated by hypertension, stroke is the major vascular disease. Then later as the population moves into stage 3 of the transition (table 8.1), ischaemic heart disease takes the lead. During the transition, stroke is not only thought to increase in incidence but the nature of stroke also changes (Bonita, 2001). Pathological stroke type changes with an initial increase in the proportion of cerebral haemorrhage due to hypertension in stage 2, to a gradual decline in cerebral haemorrhage in stage 3 and 4. Other causes of cerebral haemorrhage such as amyloid angiopathy are likely to increase in the later stages of the transition.

## Table 8.1 Stages of the health transition based on the original theory devised by Omran (adapted from Howson *et al.*, 1998; Bonita, 2001; Omran, 1971 and Yusuf, 2001)

| Stage of Transition | Percentage of all deaths caused by cardiac and vascular disease | Predominant cardiac and vascular diseases | Predominant nature of stroke | Likely regional examples |
|---|---|---|---|---|
| Age of pestilence and famine | 5-10 | Rheumatic heart disease, infections, and nutritional cardiomyopathies | Cardioembolic | Sub-Saharan Africa, rural India, and South America |
| Age of receding pandemics | 10-35 | 7As above, plus hypertension, hypertensive heart disease; stroke more common than ischaemic heart disease. High rheumatic heart disease to atherosclerotic heart disease ratio | As above, plus haemorrhagic stroke due to hypertension. Stroke occurring at relatively young age. Emergence of atherothrombotic stroke | China |
| Age of degenerative and man-made diseases | 35-55 | Ischaemic heart disease at relatively young ages. Heart disease more common than stroke. Very low rheumatic heart disease to atherosclerotic heart disease ratio | Proportion of strokes due to haemorrhage decreases and atherothrombotic stroke increases | Urban India, former socialist economies |
| Age of delayed degenerative diseases | <50 | Stroke and ischaemic heart disease at older ages | Atherothrombotic stroke; cardioembolic stroke often secondary to effects of ischaemic heart disease (atrial fibrillation, mural thrombi, cardiomyopathy) | Western Europe, North America, Australia, New Zealand |

The cause of ischaemic stroke is also thought to change from an initial predominance of cardioembolic strokes, with cardiac disease the result of rheumatic heart disease, infectious and nutritional cardiomyopathies, to a predominance of atherothrombotic disease (table 8.1) (Bonita, 2001). The cause of cardioembolic stroke too changes as ischaemic heart disease emerges in the population. Ischaemic heart disease results in atrial fibrillation, mural thrombi and ischaemic cardiomyopathy.

Early in the transition when hypertension is very prevalent, stroke tends to occur at a younger age than in later stages. However, the theory of the health transition, particularly as applied to stroke, is merely a framework. There are virtually no studies from Sub-Saharan Africa to support the theory, show changes in the nature of stroke occurring in a population, or that have assessed the impact of the HIV epidemic on the transition of vascular disease, as the continent develops economically.

Gillum has suggested that the health or epidemiologic transition in people of Sub-Saharan African origin is better explained in six stages spanning pre-colonial populations living in Africa to rural, inner city poor, and affluent urban African-American populations (Gillum, 1996a) (table 8.2). We described these phases in section 1.6. Figure 8.1 depicts the influence of salt intake, fat consumption and cigarette smoking on the prevalence of hypertension and atherosclerotic disease (Cappuccio, 2004) with reference to Gillum's six postulated stages of the health transition.

**Table 8.2 Gillum's adapted stages of the health / epidemiologic transition among person's of Sub-Saharan African origin (Gillum, 1996)**

| Stage | Example population | Acculturation | Urbanisation | Affluence | Saturated fat intake | Salt intake | Smoking | Cardiovascular Disease | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Hypertensive | Atherosclerotic |
| 1 | pre-colonial SSA | 0 | 0 | 0 | + | + | 0 | 0 | 0 |
| 2 | modern urban SSA | + | ++ | + | ++ | ++ | + | ++ | 0 |
| 3 | modern blacks living in the West Indies | ++ | ++ | ++ | ++ | +++ | ++ | ++++ | + |
| 4 | rural African-Americans | +++ | + | ++ | +++ | ++++ | +++ | ++++ | ++ |
| 5 | inner city, poor African-Americans | +++ | ++++ | +++ | ++++ | ++++ | ++++ | ++++ | ++++ |
| 6 | Affluent urban African-Americans | ++++ | ++++ | ++++ | +++ | +++ | +++ | ++ | +++ |

SSA: Sub-Saharan Africa

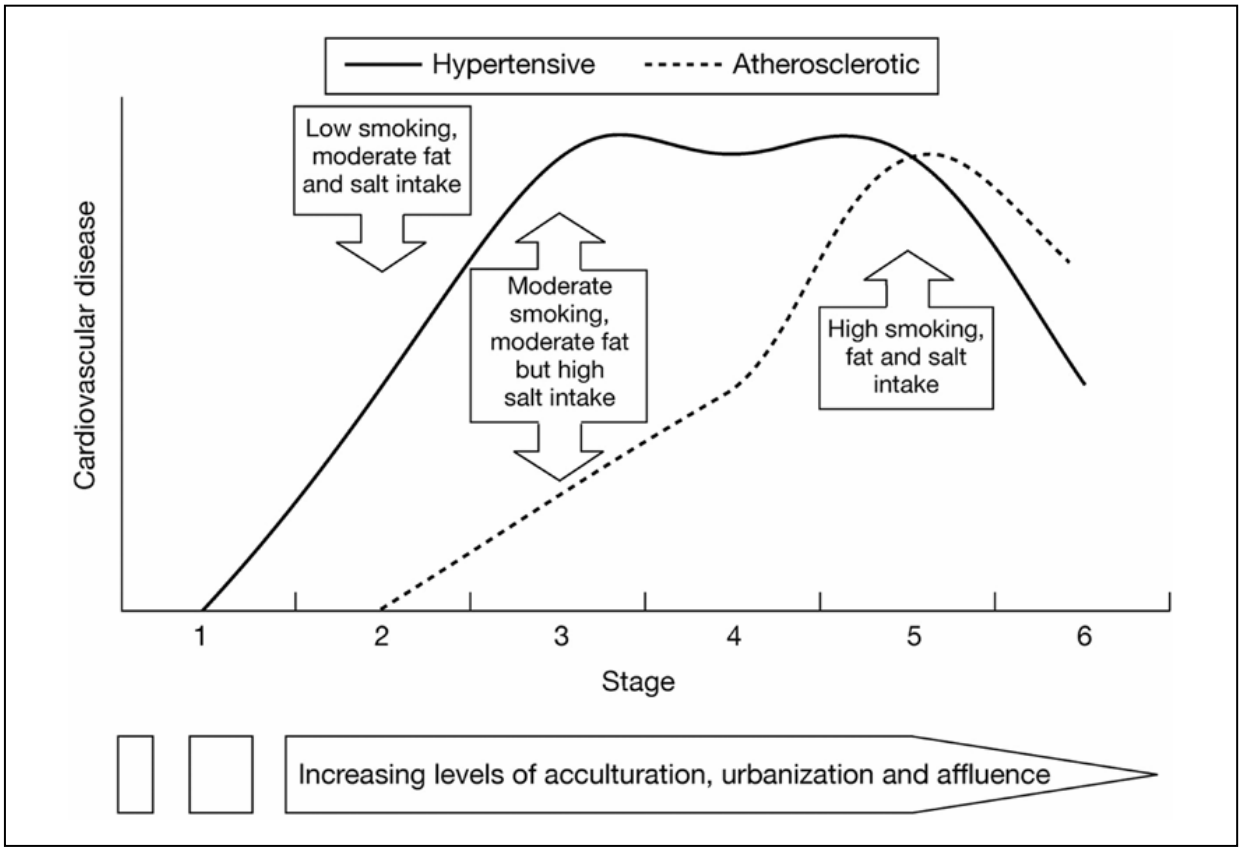



Figure 8.1 Gillum's stages of the epidemiological or health transition in populations of Sub-Saharan African origin (from Cappuccio, 2004)

**Key to Gillum's stages:**

Stage 1: Pre-colonial Africa and remaining traditional African populations

Stage 2: Modern urban Sub-Saharan Africans

Stage 3: Modern black populations of the West Indies

Stage 4: Rural African-Americans

Stage 5: Poor inner city African-Americans

Stage 6: Affluent urban African-Americans

To explore the health transition further, as it applies to SSA and in particular South Africa, we will in this chapter compare the pathological stroke types, ischaemic stroke subtypes, risk factors for stroke and where possible causes of cardioembolic stroke in our prevalent stroke, and rural and urban hospital-based stroke patients. We will focus on comparing black and white stroke patients from the JHSR as the small number of stroke patients in other population groups renders our findings inaccurate.

We acknowledge that our assessment of pathological stroke type was limited in the prevalent stroke cases because patients did not have a brain scan and we assessed them a long time after their stroke. In the Tintswalo Hospital Stroke Register (THSR) our assessment of pathological stroke type was also limited because patients were not scanned. Despite this, we feel that the comparison will provide some useful insight into the impact, if any, of the health transition on the nature of stroke in South Africa.

We will compare study populations in terms of: age, pathological stroke type, ischaemic stroke subtype, major causes of stroke, and when available causes of cardioembolic stroke, prevalence of hypertension, diabetes mellitus, total cholesterol levels, and cigarette smoking. Finally, we will review the influence, if any, of HIV infection on the health transition in our studies.

## 8.1 Comparison of studies

In table 8.3 we compare the age, stroke risk factors, pathological stroke types, ischaemic stroke subtypes and cause of cardioembolic strokes in black and white urban stroke patients in the JHSR (chapter 5), black patients in the rural THSR (chapter 7) and in prevalent black stroke patients (chapters 3 and 4). The case mix of patients in these studies is likely to have influenced our findings. Prevalence studies tend to exclude more severe stroke patients who are likely to die soon after their stroke. This probably accounts for the large proportion of small vessel / lacunar strokes and small proportion of large vessel strokes. Hospital-based patients are more likely to have severe strokes. Although black and white patients in the JHSR had strokes of similar severity (chapter 5), rural THSR patients had more severe strokes and were older (chapter 7). This may account for some of the differences seen in table 8.3 such as the large proportion of total anterior circulation ischaemic strokes.

The comparison of our studies is fraught with hospital-bias and the shortcomings of stroke prevalence studies. Only community-based incidence studies with early CT scanning (as we originally proposed but could not fund) would be able to assess the situation adequately.

**Table 8.3 Comparison of the nature of stroke in the black and white population group in the Johannesburg Hospital Stroke Register with prevalent stroke patients and patients from the Tintswalo Hospital Stroke Register (n for each assessment shown with percentages in brackets unless otherwise stated)**

| | JHSR | | THSR | SASPI Prevalence study |
|---|---|---|---|---|
| | Black | White | | |
| **Number** | 308 | 76 | 138 | 103 |
| **Mean age (SD) years** | 51 (16) | 61 (15) | 64 (17) | 61 (17) |
| **Pathological stroke type** | **207*** | **47*** | **138** | **103** |
| - Cerebral haemorrhage | 55 (27) | 7 (15) | 32 (23) | 31 (30) |
| - Ischaemic stroke | 141 (68) | 36 (77) | 98 (71) | 63 (61) |
| - Subarachnoid haemorrhage | 11 (5) | 4 (9) | 0 | 0 |
| - Unspecified | 0 | 0 | 8 (6) | 9 (9) |
| **OCSP ischaemic stroke subtype** | **141** | **36** | **98** | **63** |
| - Total anterior circulation infarct | 39 (28) | 7 (19) | 34 (36) | 4 (6) |
| - Partial anterior circulation infarct | 45 (32) | 17 (47) | 36 (38) | 22 (35) |
| - Lacunar infarct | 17 (12) | 4 (11) | 20 (21) | 30 (48) |
| - Posterior circulation infarct | 40 (28) | 8 (22) | 4 (4) | 7 (11) |
| **Ischaemic stroke subtype** | **235**** | **65**** | **98** | **63** |
| - Small vessel disease (% of all stroke) | 60 (26) | 18 (28) | 11 (23) | 30 (48) |
| - Cardioembolic (% of all stroke) | 53 (23) | 18 (28) | 27 (28) | 5 (8) |
| - Atherothrombotic stroke | 13 (6) | 13 (20) | 1 (1) | 0 |
| **Cause of cardioembolic stroke (percentage of cardioembolic stroke)** | **53**** | **20**** | **27** | **5** |
| Atrial fibrillation: total | 15 (28) | 13 (65) | 13 (48) | 1 (20) |
| - unknown cause | 6 | 7 | 4 | 1 |
| - with ischaemic heart disease | 1 | 4 | 0 | 0 |
| - with rheumatic valvular heart disease | 2 | 1 | 3 | 0 |
| - with dilated cardiomyopathy | 0 | 1 | 3 | 0 |
| - with hypertensive heart disease | 6 | 0 | 3 | 0 |
| Ischaemic heart disease | 3 (6) | 6 (30) | 0 | 0 |
| Cardiomyopathy: total | 27 (51) | 0 | 12 (44) | 2 (40) |
| - dilated cardiomyopathy | 10 | 0 | 11 | 2 |
| - associated with hypertensive heart disease | 17 | 0 | 1 | 0 |
| Rheumatic valvular heart disease | 6 (11) | 1 (5) | 4 (15)† | 2 (40) |
| Infective endocarditis | 0 | 1 | 0 | 0 |
| **Risk factors ( n / total assessed)** | | | | |
| Hypertension | 214/306 (74) | 50/74 (69) | 95/136 (70) | 73 / 103 (71) |
| Diabetes mellitus | 42/264 (16) | 11/74 (15) | 24/138 (17) | 12 / 103 (12) |
| Total cholesterol mean (95% CI) | 4.6 (4.3 to 4.9) | 5.3 (4.8 to 5.7) | 4.7 (4.4 to 5.0) | n/a |
| Current cigarette smoking | 57/ 245 (23) | 34/63 (54) | 6/123 (5) | 9 / 103 (9) |

*patients with brain imaging; ** all ischaemic stroke not only those with CT included OCSP: Oxfordshire Community Stroke Project
† this is likely to be an underestimate given the lack of echocardiography and may be as high as 8 (30%) ‡ history or ECG evidence

### 8.1.1 Comparison of age

Patients from Bohlabela (THSR and prevalent strokes) were older than black patients in the JHSR and about as old as white patients. While people develop stroke at a younger age as they progress through the early phases of the transition, and it is tempting to suggest that the JHSR stroke patients were younger because they were further along the transition, this is unlikely to be true. We are very likely to have missed young stroke patients in the prevalence and THSR studies because of labour migration and hospital-bias.

### 8.1.2 Comparison of pathological stroke type and ischaemic stroke subtype

In the JHSR 30% of black patients had cerebral haemorrhages, far more than we found in white JHSR stroke patients (15%). Our finding in white stroke patients was similar to the 12% found in 997 white stroke patients in the South London Stroke Register (Lawrence et al., 2001). The assessment of pathological stroke type in the THSR was probably too inaccurate for comparison here.

The proportion of stroke caused by cerebral haemorrhage is thought to increase in the early phases of the health transition (original Omran stage 1 to 2) and then decrease later in the transition (stage 3 to 4) (table 8.1). Therefore, the JHSR findings support the notion that urban black stroke patients are at an earlier phase of the health transition than white stroke patients in South Africa and the United Kingdom.

We did not find any patients in rural South Africa with subarachnoid haemorrhage, although the numbers of patients with subarachnoid haemorrhage were small in the JHSR and it is possible that we missed patients in the prevalence study of stroke survivors. Subarachnoid haemorrhage is not usually considered in the theory of the health transition which is probably sensible since typical vascular risk factors do not influence the incidence of subarachnoid haemorrhage as they do cerebral haemorrhage and ischaemic stroke (Warlow et al., 2001).

While ischaemic stroke subtypes differed between the studies, this was as likely to be the result of case mix differences as discussed above, as anything to do with the health transition. In the JHSR stroke severity was very similar in black and white stroke patients as was the proportion of large artery, small vessel and cardioembolic strokes (table 8.3).

However, we did find significant differences between the causes of cardioembolic strokes in the four groups (table 8.3). In white stroke patients, atrial fibrillation and ischaemic heart disease accounted for 95% of cardioembolic strokes. In urban black stroke patients, atrial fibrillation, cardiomyopathy and rheumatic valvular heart disease caused 96% of cardioembolic strokes. Ischaemic heart disease occurred but was uncommon. None of the rural stroke patients, whether hospital or community based, had cardioembolic strokes associated with ischaemic heart disease, but rheumatic heart disease was relatively common.

Thus, the rheumatic heart disease to ischaemic heart disease ratio (table 8.1) was very high in rural stroke patients and low in urban white stroke patients. Though uncommon, ischaemic heart disease did occur and decreased this ratio in urban black stroke patients.

### 8.1.3 Comparison of risk factors

The prevalence of hypertension and diabetes mellitus was similar across all four groups (table 8.3). The mean total cholesterol levels were no different in urban and rural black stroke patients, and both values were lower than in white stroke patients. However, current cigarette smoking was commonest in urban white stroke patients despite them being older, less common in urban black stroke patients and uncommon in rural black patients. Cigarrette smoking may have been more common in urban black patients because they were younger than rural black patients. This risk factor profile suggests that black stroke patients are at an earlier phase of the health transition than urban white patients (figure 8.1 and table 8.2).

### 8.1.4 Comparison with African-American stroke patients

Gillum suggests that African-Americans are representative of the final stages of the health transition in populations of Sub-Saharan African origin. In African-American stroke studies such as the Northern Manhattan Stroke Study and Greater Cincinnati / Kentucky Stroke Study (GCNKSS) hypertension was found in 65 to 68% of stroke patients, diabetes mellitus in 33%, and current cigarette

smoking in 26% (Woo, Gebel, Miller et al, 1999; White et al., 2005) as previously discussed in chapter 5. Cerebral haemorrhage accounted for 15% of strokes in the GCNKSS, a similar proportion to our white stroke patients. Unfortunately we could not find data from these studies on the causes of cardioembolic stroke to compare with our patients, other than atrial fibrillation which was more common in African-Americans (10% of all stroke) than in our urban black patients (3% of all patients) (section 5.3.5.3), though the African-American patients were much older. However, ischaemic heart disease is as common or almost as common in African populations living in America or the United Kingdom and far more common than in black Sub-Saharan African populations (Lawrence et al., 2001; Ferdinand, 2006).

## 8.2 Discussion

There is evidence from our hospital-based stroke studies and community-based stroke prevalence study to give some support to the theory of the health transition. As vascular risk factors increased with urbanisation in our black stroke patients, so ischaemic heart disease emerged and the ratio of rheumatic valvular heart disease to ischaemic heart disease decreased. In comparison with urban white South Africans and African-Americans who represent the final stages of the health transition, black South Africans probably have more cerebral haemorrhages and less atherosclerosis.

Rural South African stroke patients appear to be emerging from stage 1 into stage 2 of the original health transition proposed by Omran (table 8.1). Urban South African stroke patients are firmly in stage 2. When we apply Gillum's suggested six stage adaptation of the transition (table 8.2), it is more difficult to differentiate between our rural and urban stroke patients. Gillum stage 2 best describes our rural stroke patients, yet hypertension is at least as common in our rural stroke patients as it is in African-Americans. Atherosclerotic disease emerges in Gillum stage 3, which probably best describes the features exhibited by our urban stroke population. Gillum suggests that black populations of the West Indies are typical of stage 3. Urban black South African stroke patients may represent the vanguard or so called 'early-adopter' population (Yusuf et al., 2001) within Sub-Saharan Africa.

Gillum's suggested stages do not adequately describe our rural stroke patients. Furthermore, it is likely (as shown in autopsy studies investigating atherosclerosis

in chapter 2, section 2.3.3) that asymptomatic atherosclerosis emerges before symptomatic atherosclerotic disease in populations undergoing transition. We therefore suggest an adaptation of Gillum's six-staged transition for use in Sub-Saharan Africans (table 8.4).

Black Sub-Saharan Africans are currently at most at stage 3a of the modified Gillum classification (table 8.4). Their advance through the transition will depend on whether adequate preventative strategies are set in place to reduce vascular risk factors and subsequent vascular disease. If these measures fail or are not set in place then inevitably they will advance through the transition to an epidemic of stroke and ischaemic heart disease.

As we discussed in chapter 5, HIV-infected stroke patients were younger and less likely to have traditional vascular risk factors. However, our study was too small to investigate differences in the cause of stroke adequately. In section 5.3.5.4 we discussed our finding of similar frequencies of atrial fibrillation and cardiomyopathy in HIV positive and negative stroke patients. It is likely, that HIV positive stroke patients form a distinct group and will not follow the described transition unless they are treated. Antiretroviral therapy is associated with a marked elevation in blood lipids and the full impact of this on vascular disease in treated HIV infected patients will only become clear in time (Sekhar, Jahoor, Pownall et al, 2004). Meanwhile, the elderly in Sub-Saharan Africa, who are at highest risk of stroke, maintain households that have lost younger adults to HIV infection.

It is essential that these people and those who avoid HIV infection are not lost to an impending epidemic of vascular disease.

## Table 8.4 Adaptation of Gillum's stages of health / epidemiologic transition for use in Sub-Saharan Africa

| Stage | African populations outside of SSA | SSA population | Affluence | Saturated fat intake | Salt intake | Smoking | Vascular Disease | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Hypertensive | Atherosclerosis | |
| | | | | | | | | Asymptomatic | Symptomatic* |
| 1 | pre-colonial SSA | traditional SSA populations | 0 | + | + | 0 | 0 | 0 | 0 |
| 2a | - | rural SSA | + | ++ | ++ | + | ++ | 0/+ | 0 |
| 2b | - | rural / semi-urban SSA ** | + | ++ | +++ | + | ++++ | + | 0 |
| 3a | - | urban SSA | ++ | ++ | +++ | ++ | ++++ | +/++ | 0/+ |
| 3b | modern blacks living in the West Indies | The future, pending preventative strategies | ++ | ++ | +++ | ++ | ++++ | ++ | + |
| 4 | rural African-Americans | | ++ | +++ | ++++ | +++ | ++++ | ++ | ++ |
| 5 | inner city, poor African-Americans | | +++ | ++++ | ++++ | ++++ | ++++ | ++++ | ++++ |
| 6 | affluent urban African-Americans | | ++++ | +++ | +++ | +++ | ++ | +++ | +++ |

The degree to which each factor or disease is present in each stage is shown, with 0 denoting virtually absent and ++++ denoting present at the highest reported level
SSA: Sub-Saharan Africa *symptomatic here refers to symptomatic ischaemic heart disease or symptomatic extracranial carotid artery disease; ** early adopter populations within SSA

# CHAPTER 9 CONCLUSIONS

Using an urban and a rural hospital-based stroke register, and the first community-based South African stroke prevalence study, we found that:

- the prevalence of stroke in rural South Africa is about half that found in high-income countries and twice that found in rural Tanzania, but the prevalence of *disabling* stroke is already at least as high as that found in high-income countries;
- there is evidence that both urban and rural black South Africans are well into the health transition and that this transition is impacting on the nature of stroke in black stroke patients in South Africa;
- the cause of cardioembolic stroke, in particular the rheumatic valvular heart disease to ischaemic heart disease ratio, provides a useful marker of the evolution of the health transition in our population;
- HIV infection alters the nature of stroke and the profile of patients who suffer a stroke;
- Guy's Hospital and Siriraj Stroke Scores require further adaptation and refinement for use in black South African stroke patients. At present they are not helpful in clinical or epidemiological studies; and
- there is a dire need for community-based stroke incidence studies with complete case ascertainment, early brain imaging and detailed investigation of incident stroke cases, to clarify the nature of stroke, the role of the health transition in Sub-Saharan Africa, and the role of HIV infection in stroke.

Thus, from our findings it appears as though there is already a heavy burden of stroke in rural and urban South Africa. Comparing our rural and urban stroke populations, we found evidence to suggest that the South African black population is advancing into the early stages of the health transition. If stroke risk factors continue to increase as predicted by the health transition, then we can anticipate an increasing burden of stroke as well as increasing ischaemic heart and peripheral artery disease in the future. This vascular disease epidemic will place a further burden on our population, which already carries a large burden of infectious disease, specifically HIV infection, perinatal disease and trauma. To prevent this inevitable progression of vascular disease, we need to reduce whole population risk and identify and treat high-risk individuals. We also need to adjust our health service which is accustomed to providing acute medical care particularly for infections and trauma, to deal better with the management of chronic disease.

However, we need further research to fully understand the burden and nature of stroke in both South Africa, and the rest of Sub-Saharan Africa. Only high-quality community-based stroke incidence studies that adhere to ‘ideal’ incidence study criteria will provide accurate answers. We have shown the difficulties that arise in interpreting data from hospital-based stroke studies in rural and urban areas, and the failure of stroke scores designed to assess pathological stroke types. Until we have community-based studies with brain imaging we will never know the precise burden and nature of stroke, the effect of the health transition, the influence of HIV on stroke or the optimal approach to preventing a stroke epidemic in our population.

By comparing not only rural and urban stroke in South Africa, but also our findings compared to the limited data available from the rest of Sub-Saharan Africa, we have shown that stroke is not homogenous across the continent. Community-based incidence studies, while expensive, should be conducted in different populations across Sub-Saharan Africa, perhaps in well-defined populations that form part of established demographic surveillance sites.

Stroke, the forerunner of vascular disease in populations in transition, has been underestimated, poorly researched and poorly managed in Sub-Saharan Africa for decades. The difficulties that researchers experience in the region are often used as an excuse not to fund high quality research. It is now clear from this study, and many others, that stroke is increasing across the continent. We, the clinicians and researchers, together with research funders, face the challenge of accurately documenting the burden and nature of stroke, of providing adequate and appropriate stroke prevention, and care when prevention fails.

# APPENDIX A: SEARCH CRITERIA FOR THE SYSTEMATIC REVIEW (CHAPTER 2)

Comprehensive textword and MeSH-based search criteria for EMBASE designed to retrieve articles with data on stroke in Sub-Saharan Africa. We used a similar, appropriately adapted search strategy to retrieve articles from MEDLINE.

1. exp cerebrovascular disease/
2. stroke$.tw.
3. cerebrovascular$.tw.
4. (cerebral or cerebellar or brainstem or vertebrobasilar).tw.
5. (infarct$ or isch?emi$ or thrombo$ or emboli$).tw.
6. 4 and 5
7. carotid$.tw.
8. (cerebral or intracerebral or intracranial or parenchymal or brain or intraventricular or brainstem or cerebellar or infratentorial or supratentorial or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleeding or aneurysm).tw.
10. 8 and 9
11. transient isch?emic attack$.tw.
12. exp aphasia/
13. dysphasia/
14. hemianopia/
15. hemiplegia/
16. hemiparesis/

17. (aphasi$ or dysphasi$ or hemianop$ or hemipleg$ or hemipar$ or migraine$).tw.
18. exp carotid artery surgery/
19. 1 or 2 or 3 or 6 or 7 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. negro/
21. ethnic group/
22. race/
23. ethnic difference/
24. “ethnic and racial groups”/
25. “ethnic or racial aspects”/
26. ethnology/
27. (black$ or negro$ or African?).tw.
28. africa/
29. exp africa south of the sahara/
30. developing country/
31. underdeveloped country/
32. africa.tw.
33. sub?saharan.tw.
34. (“Ethiopia” or “Ghana” or “Kenya” or “Mozambique” or “Nigeria” or “Senegal” or “South Africa” or “Sudan” or “United Republic of Cameroon” or “Zaire” or “Zambia” or “Zimbabwe”).cp.
35. 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
36. 19 and 35

**APPENDIX B PREVALENCE STUDY QUESTIONNAIRE**

# South African Stroke Prevention Initiative – Prevalence Study

| Office use | Prevalent Patient number: | | Form complete | |
|---|---|---|---|---|

- **Doctor completing the form:**
- **Date of visit:** ☐☐.☐☐.2002
- **Name:**
- **Agincourt DSS ID Number:** ☐☐☐☐☐☐
- **Village and Household Number:** ☐☐ ☐☐☐☐
- **Village Name:**
- **Date of Census Screening Visit:** ☐☐.☐☐.2002
- **Individual: Alive** ☐ **Deceased** ☐ ……. **Date of Death:** ☐☐.☐☐.2002
- **Sex:** **Male** ☐ **Female** ☐
- **Refugee:** **Yes** ☐ **No** ☐
- **Age:** ☐☐☐ **years**
- **Is this an estimate:** **Yes** ☐ **No** ☐
- **Date of Birth:** ☐☐.☐☐.☐☐☐☐
- **Census Questions:** **'Yes' to weakness** ☐ **'Yes' to stroke** ☐
- **Date of onset of the symptoms (first event):** ☐☐.☐☐.☐☐☐☐
- **Age at time of first event:** ☐☐☐

- **History:**

- **Possibly a stroke or TIA?**
  - Yes ☐ - continue with form / interview
  - No ☐ - complete the examination to document as far as possible the likely cause of weakness or reason for 'yes' answer; and skip the rest of the form

**Specific questions on history (if more than one stroke or TIA then questions refer to the first event):**

- Symptoms present on waking?
  - Yes ☐ No ☐
- Blood pressure ever checked prior to the stroke?
  - Yes ☐ No ☐
    - ☐ Within the 3 months prior to stroke / TIA?
    - ☐ Between 3 and 12 months prior
    - ☐ More than a year before the stroke
- Ever told that they have high blood pressure before the stroke / TIA?
  - Yes ☐ No ☐
- On treatment for high blood pressure at the time of the stroke?
  - Yes ☐ No ☐
- After the stroke / TIA were they on antihypertensive treatment at any time?
  - Yes ☐ No ☐

**Activities of Daily Living (ADL):**

- Was the patient independent prior to admission? Yes ☐ No ☐ Unknown ☐
- Rankin modified before this event? * 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

*** Modified Rankin score**

**0** = no symptoms.
**1** = minor symptoms which do not interfere with lifestyle.
**2** = some restriction to lifestyle, but look after themselves.
**3** = significant restriction to llifestyle, preventing total independence.
**4** = severe handicap preventing independent existence but not requiring constant attention.
**5** = severe handicap, totally dependent, requiring attention night and day.

*RISK FACTORS*

- Hypertension YES ☐ NO ☐ UNKNOWN ☐
- Diabetes: YES ☐ NO ☐ UNKNOWN ☐
- Periph. vasc. disease: YES ☐ NO ☐ UNKNOWN ☐
- Atrial fibrillation: YES ☐ NO ☐ UNKNOWN ☐
- Hyperlipidaemia: YES ☐ NO ☐ UNKNOWN ☐
- Coagulopathy: YES ☐ NO ☐ UNKNOWN ☐
- Collagen vasc. disease: YES ☐ NO ☐ UNKNOWN ☐
- Migraine with aura: YES ☐ NO ☐ UNKNOWN ☐
- Pregnancy: YES ☐ NO ☐ UNKNOWN ☐
- Trauma: YES ☐ NO ☐ UNKNOWN ☐
- Previous TIA: YES ☐ NO ☐ UNKNOWN ☐
- Previous Stroke: YES ☐ NO ☐ UNKNOWN ☐
- Oral contraception: YES ☐ NO ☐ UNKNOWN ☐
- Family history: YES ☐ NO ☐ UNKNOWN ☐

- Any symptoms of angina? YES ☐ NO ☐ IMPOSSIBLE TO ASSESS ☐

- Substance abuse: YES ☐ NO ☐
  DAGGA ☐ MANDRAX ☐ OTHER: ☐
- Smoking: NEVER ☐ EX-SMOKER (> 1 YEAR) ☐
  CURRENT SMOKER ☐
  NUMBER SMOKED PER DAY ☐☐☐
- Snuff (current): YES ☐ NO ☐
- Alcohol: NEVER / HARDLY EVER ☐ EX-DRINKER (> 1 YEAR) ☐ DRINKS ☐
  AMOUNT OF ALCOHOL PER DAY * ☐☐☐ g
  - (100 ml wine (1 glass) or 30 ml spirits (1 tot) or 250 ml beer all = 10 g alcohol)

## General Examination

- Irregular pulse: Yes ☐ No ☐
- Is this Atrial Fibrillation clinically? Yes ☐ No ☐ Not sure ☐
- BP at first assessment (supine, average of 3 readings ):

  1. ☐☐☐/☐☐☐ 2. ☐☐☐/☐☐☐ 3. ☐☐☐/☐☐☐

  AVERAGE: ☐☐☐/☐☐☐

- Evidence of hypertensive end organ damage? YES ☐ NO ☐

  CARDIAC ☐ FUNDI ☐ RENAL (RENAL DYSFUNCTION) ☐

- Carotid bruits: RIGHT ☐ LEFT ☐
- Clinical heart failure:
  (i.e.: signs of LVF/RVF, not just on treatment) YES ☐ NO ☐
- Clinical valvular heart disease:
  (not a simple low murmur < 2/6) YES ☐ NO ☐
- Peripheral vascular disease:
  (both foot pulses absent or femoral bruits) YES ☐ NO ☐
- Cardiac disease: YES ☐ NO ☐

  ISCHAEMIC ☐ VALVULAR ☐ ATRIAL FIBRILLATION ☐

  CARDIOMYOPTHY ☐ HYPERTENSIVE HEART DISEASE WITHOUT CARDIOMYOPATHY ☐

- Other arteriopathy: ☐

**NEUROLOGIC DEFICIT:**

- Indicate whether the following signs and symptoms are present:

| | | |
|---|---|---|
| Coma: | Yes ☐ | No ☐ |
| Decreased LOC: | Yes ☐ | No ☐ |
| Motor weakness: | Yes ☐ | No ☐ |
| Sensory deficit: | Yes ☐ | No ☐ |
| Cerebellar signs: | Yes ☐ | No ☐ |
| Dysphasia: | Yes ☐ | No ☐ |
| Dysphagia: | Yes ☐ | No ☐ |
| Other cortical signs:<br>(apraxia, visual deficit, cortical sensory) | Yes ☐ | No ☐ |
| Urinary incontinence: | Yes ☐ | No ☐ |
| Can lift arm against gravity: | Yes ☐ | No ☐ |

**Modified Rankin Score**

- Circle your choice of score from the following list of options:

| DESCRIPTION: | SCORE: |
|---|---|
| No symptoms | 0 |
| Minor symptoms which do not interfere with lifestyle | 1 |
| Some restriction to lifestyle, but look after themselves | 2 |
| Significant restriction to lifestyle, preventing total independence | 3 |
| Severe handicap preventing independent existence but not requiring constant attention | 4 |
| Severe handicap, totally dependent, requiring attention night and day | 5 |

**Barthel Score**

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCOR |
|---|---|---|
| Bowels | Incontinent or needs enemas | 0 |
| | Occasional incontinence (< once per week) | 1 |
| | Continent | 2 |
| Bladder | Incontinent/unable to manage catheter | 0 |
| | Occasional accident ( < once per day) | 1 |
| | Continent | 2 |
| Grooming | Needs help with shaving, washing, hair or teeth | 0 |
| | Independent | 1 |
| Toilet use | Dependent | 0 |
| | Needs some help | 1 |
| | Independent on, off dressing and cleaning | 2 |
| Feeding | Dependent | 0 |
| | Needs some help (e.g. with cutting, spreading) | 1 |
| | Independent if food provided within reach | 2 |
| Transfer (e.g. bed or chair) | Unable and no sitting balance | 0 |
| | Needs major help | 1 |
| | Needs minor help | 2 |
| | Independent | 3 |
| Mobility | Unable | 0 |
| | Wheelchair independent indoors | 1 |
| | Walks with help or supervision | 2 |
| | Independent (but may use aid) | 3 |
| Dressing | Dependent | 0 |
| | Needs some help | 1 |
| | Independent including fasteners | 2 |
| Stairs | Unable | 0 |
| | Needs some help or supervision | 1 |
| | Independent up and down | 2 |
| Bathing | Dependent | 0 |
| | Independent in bath or shower | 1 |

**NIH Scale**

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION | *SCORE* |
|---|---|---|
| Conscious level | Awake | 0 |
| | Drowsy, somnolent | 1 |
| | Stupor (rousable to correct localization of painful stimulus) | 2 |
| | No reaction or extensor or flexor spastic response | 3 |
| Response to questions (month, age) | Both answers correct | 0 |
| | One answer correct | 1 |
| | Both answers wrong or no response | 2 |
| Eye movement | Normal | 0 |
| | Partial gaze palsy | 1 |
| | Complete gaze palsy (also to oculocephalic maneuver) | 2 |
| Facial palsy | Normal | 0 |
| | Slight | 1 |
| | Moderate | 2 |
| | Complete | 3 |
| Limb ataxia (affected side) | Normal | 0 |
| | One limb ataxic | 1 |
| | Both limbs ataxic | 2 |
| Neglect | Normal | 0 |
| | Partial neglect (inattention) on side | 1 |
| | Complete hemi-neglect (several sensory modalities) | 2 |
| Aphasia | Normal | 0 |
| | Mild dysphasia (word finding difficulty, paraphasia, grammatical errors) | 1 |
| | Motor (Broca) or sensory (Wernickle) aphasia or variants | 2 |
| | Complete aphasia, muteness | 3 |
| Attempted Posture (affected lower limb) | Unremarkable (5s) | 0 |
| | Droops | 1 |
| | Lower limb flops (5s) | 2 |
| | Postural attempt impossible | 3 |
| Reaction to Verbal Order (open or shut eyes, hand grip) | Both correct | 0 |
| | One correct | 1 |
| | No reaction or incorrect action | 2 |
| Visual fields | Full | 0 |
| | Incomplete hemianopia | 1 |
| | Complete hemianopia | 2 |
| Attempted posture (affected arm) | Unremarkable (10s) | 0 |
| | Pronation | 1 |
| | 90° posture fails <10s, rapid droop | 2 |
| | Postural attempt fails | 3 |
| Sensation | Normal | 0 |
| | Hypesthesia | 1 |
| | Anaesthesia | 2 |
| Dysarthria | Normal | 0 |
| | Dysarthric but easily understood | 1 |
| | Severe dysarthria, barely intelligible | 2 |

**Scandinavian Stroke scale**

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCORE: |
|---|---|---|
| Consciousness | Fully conscious | 6 |
| | Somnolent, can be awaked to full conscience | 4 |
| | Reacts to verbal command, but is not fully conscious | 2 |
| Eye movement | No gaze palsy | 4 |
| | Gaze palsy present | 2 |
| | Conjugate eye deviation | 0 |
| Arm motor, power * | Raises arm with normal strength | 6 |
| | Raises arm with reduced strength | 5 |
| | Raises arm with flexion in elbow | 4 |
| | Can move, but not against gravity | 2 |
| | Paralysis | 0 |
| Hand motor, power * | Normal strength | 6 |
| | Reduced strength in full range | 4 |
| | Some movement, fingertips do not reach palm | 2 |
| | Paralysis | 0 |
| Leg motor power * | Normal strength | 6 |
| | Raises straight leg with reduced strength | 5 |
| | Raises leg with flexion of knee | 4 |
| | Can move, but not against gravity | 2 |
| | Paralysis | 0 |
| Orientation | Correct for time, place and person | 6 |
| | 2 of these | 4 |
| | 1 of these | 2 |
| | Completely disorientated | 0 |
| Speech | No aphasia | 10 |
| | Limited vocabulary or incoherent speech | 6 |
| | More than yes/no, but not longer sentences | 3 |
| | Only yes/no or less | 0 |
| Facial palsy | None/dubious | 2 |
| | Present | 0 |
| Gait | Walks 5 in without aids | 12 |
| | Walks with aids | 9 |
| | Walks with help of another person | 6 |
| | Sits without support | 3 |
| | Bedridden/wheelchair | 0 |

- Motor power is assessed only on the affected side

**Glasgow Coma Scale**

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCORE: |
|---|---|---|
| Eye opening | None | E1 |
| | To painful stimulus | E2 |
| | To command/voices | E3 |
| | Spontaneously with blinking | E4 |
| Motor response | None | M1 |
| | Arm extension to painful stimulus | M2 |
| | Arm flexion to painful stimulus | M3 |
| | Arm withdraws from painful stimulus | M4 |
| | Hand localizes painful stimulus | M5 |
| | Obeys commands | M6 |
| Verbal response | None | V1 |
| | Sounds but no recognizable words | V2 |
| | Inappropriate words/expletives | V3 |
| | Confused speech | V4 |
| | Normal | V5 |

**Other relevant findings on examination:**

YES ☐ NO ☐

**CLINICAL OPINION OF LIKELY PATHOLOGICAL STROKE TYPE :**

HAEMORRHAGE ☐ INFARCT ☐ SAH ☐ NOT SURE ☐

Answer known on history e.g. patient told that it was a haemorrhage on CT scan: YES ☐ NO☐

**LOCALISATION AND SUBTYPE OF STROKE OR TIA (Clinically – include all information known about deficit at time of event and current findings to localize and subtype)**

➢ Select one

COMPLETE ANTERIOR CIRCULATION (TACS/I) ☐

PARTIAL ANTERIOR (PACS/I) ☐

POSTERIOR CIRCULATION (POCS/I) ☐

LACUNAR (LACS/I) ☐

**MEDICATION** (names only - no dosages necessary)

➢ At time of assessment

| | | |
|---|---|---|
| | | |
| | | |
| | | |

**Complications** since event that are likely directly related to the stroke:

➢ Select all relevant boxes:

PAINFUL SHOULDER SYNDROME ☐

RECURRENT STROKE ☐

PNEUMONIA ☐

DVT ☐

MYOCARDIAL INFARCT ☐

SEIZURES ☐

DEPRESSION ☐

BEDSORES ☐

PROGRESSING STROKE (SYMPTOMS AND SIGNS EVOLVE OVER HOURS) ☐

OTHER ☐

Specify:

➢ Home carer needed? YES ☐ NO☐

➢ Home carer available YES ☐ NO ☐

Is the patient's partner the carer? YES ☐ NO ☐

Specify: ☐

- *Aspirin:*
  - Should Aspirin be prescribed? YES ☐ NO ☐
  - Was Aspirin prescribed? YES ☐ NO ☐

**FINAL DIAGNOSIS (insert a number from the codes)**

- Stroke ☐
- TIA ☐
- Other ☐

If other then what?

- **First-ever-in-a-lifetime stroke:** YES ☐ NO ☐ UNABLE TO ASSESS ☐
  DEFINITE ☐ PROBABLE ☐ POSSIBLE ☐

- Was there more than one stroke or TIA?
  - Yes ☐ No ☐
- How many? ☐☐
- Date of most recent event: ☐☐.☐☐.☐☐☐☐
- Did the patient seek assistance from health care providers / healers following the stroke?
  - Yes ☐ No ☐
  - ☐ Clinic
  - ☐ Hospital: ☐ Tintswalo ☐ Mapulaneng ☐ Matikwane ☐ Other….. ☐
  - ☐ Traditional Healer
  - ☐ ZCC or other Church group
    - Which health service attended first? ☐Hospital/clinic ☐Traditional healer ☐Church
- Do you have any reason to believe that the patient may have retroviral disease?
  - Yes ☐ No ☐

## APPENDIX C: ETHICS APPROVAL FOR PREVALENCE STUDY

**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**

Division of the Deputy Registrar (Research)

**COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)**
Ref: R14/49 Tollman

**CLEARANCE CERTIFICATE** **PROTOCOL NUMBER** M02-04-63

**PROJECT** Southern Africa Stroke Prevention Initiative (SASPI): Survey of Clinical Risk Factors

**INVESTIGATORS** Prof S Tollman

**DEPARTMENT** School of Public Health, Wits Medical School

**DATE CONSIDERED** 02-04-26

**DECISION OF THE COMMITTEE** *

Approved unconditionally

**DATE** 02-06-04 **CHAIRMAN** .....(Professor P E Cleaton-Jones)

* Guidelines for written "informed consent" attached where applicable.

c c Supervisor: Prof S Tollman
Dept of School of Public Health, Wits Medical School

Werks2\sln0018\HumEth97.wdb\M 02-04-63

**DECLARATION OF INVESTIGATOR(S)**

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee.

DATE .....SIGNATURE .....

**PROTOCOL NO.**: M 02-04-63

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

# NORTHERN PROVINCE
## DEPARTMENT OF HEALTH AND WELFARE

TEL.: (015) 290 9000
(015) 290 9001
FAX.: (015) 291 5961
(015) 291 5146

PRIVATE BAG X9302
PIETERSBURG
0700

Enquiries: Sinah Mahlangu

Reference: Research & Quality Improvement

11 December 2001

University of the Witwatersrand
Private Bag 2600
Houghton
JOHANESBURG
2041

Dr Thorogood, M

PROTOCOL: PHASE A: M960720, PHASE B: MOO/037

**ENTITLED:"SOUTHERN AFRICA STROKE PREVENTION INITIATIVE: THE PILOT STAGE"**

1. Permission is hereby granted to Dr Margaret Thorogood and Professor Steven Meir Tollman to conduct research on above topic In Eastern District (previous Bushbuckridge region) Agincourt Health Centre and Tintswalo hospital, Northern Province, South Africa.

2. The following documents were reviewed and accepted by the Provincial Research Committee.

   2.1 Final protocol dated 13/02/01

      2.2.1 All the area shaded yellow, phase A-reference M960720

DR JAN MOOLMAN BUILDING
34 HANS VAN RENSBURG STREET
PIETERSBURG 0700

2.2.2 The area shaded orange, phase B- reference MOO/037

2.2 . University of the Witwatersrand Clearance certificate on human subjects-Ref R14/49 dated 07/08/1996.

2.3 The Department of Health & Welfare needs a copy of the research findings for its own resource centre.

4 The researcher should be prepared to assist in interpretation and implementation of the recommendations where possible.

5 **Implications**: Permission should be requested from regional and institutional management to do research.

Sincerely,

Acting SUPERINTENDENT GENERAL
DEPARTMENT OF HEALTH & WELFARE
NORTHERN PROVINCE

**LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE**

**ETHICS COMMITTEE**

**APPROVAL FORM**
**Application number:** **755**

| | |
|---|---|
| Name of Principal Investigator | **Dr Margaret Thorogood** |
| Department | **Public Health & Policy** |
| Head of Department | **Professor Nick Black** |

Title **Southern African stroke prevention initiative: Pilot stage**

Approval of this study is granted by the Committee.

Chair .....

(Professor Andrew Haines, Dean)

Date 5-4-10.

Comments from the Committee:

**Approval is dependent on local ethical approval having been received.**

**Any subsequent changes to the consent form must be re-submitted to the Committee.**

## APPENDIX D JOHANNESBURG HOSPITAL STROKE REGISTER QUESTIONNAIRE

**> > > > > > > > > > DO NOT LOOK AT THE CT SCAN BEFORE COMPLETING THIS FORM < < < < < < < < < <**

**Office use** Form completed ☐ Regist ☐

**NOTES:**

Each individual question is marked ' **>** '

Some responses require expansion most often facilitated by shading. Illustrated in the following example:

- Is it the weekend? YES ☐ NO ☐
  What day is it? SATURDAY ☐ SUNDAY ☐

Here, the second question only needs to be considered if the response to the first question is 'YES'

---

- Doctor completing this form: ☐
- Patient hospital number: ☐☐☐☐☐☐☐
- Ward: ☐☐☐
- Date of birth: ☐☐ . ☐☐ . 19 ☐☐
- Age: ☐☐
- Contact telephone number: (friend / relative) ☐☐☐☐☐☐☐☐☐☐☐☐
- Sex: MALE ☐ FEMALE ☐
- Ethnic group: WHITE ☐ BLACK ☐ COLOURED ☐ INDIAN-ASIAN ☐
- Date of stroke: ☐☐ . ☐☐ . 20 ☐☐
- Date of admission: ☐☐ . ☐☐ . 20 ☐☐
- Date of assessment by stroke team: ☐☐ . ☐☐ . 20 ☐☐
- Time between onset of stroke and hospital medical attention: ☐☐ HOURS ☐☐ DAYS

***HISTORY OF EVENT***

- Symptoms present on waking: YES ☐ NO ☐ UNKNOWN ☐
- Headache within 2 hours of onset: YES ☐ NO ☐ UNKNOWN ☐
- Vomited since symptom onset: YES ☐ NO ☐ UNKNOWN ☐
- Loss of consciousness at onset: YES ☐ NO ☐ UNKNOWN ☐
- Drowsiness since symptom onset: YES ☐ NO ☐ UNKNOWN ☐
- Seizure since symptom onset: YES ☐ NO ☐ UNKNOWN ☐
- If symptoms have resolved by the time of examination, how long were they present? ☐☐ HOURS ☐☐ DAYS

***ADL** (**A**ctivities of **D**aily **L**iving)*

- Was the patient independent prior to admission? YES ☐ NO ☐ UNKNOWN ☐
- Rankin modified before this event? * 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

*** Modified Rankin score**

**0** = no symptoms.
**1** = minor symptoms which do not interfere with lifestyle.
**2** = some restriction to lifestyle, but look after themselves.
**3** = significant restriction to llifestyle, preventing total independence.
**4** = severe handicap preventing independent existence but not requiring constant attention.
**5** = severe handicap, totally dependent, requiring attention night and day.

***RISK FACTORS***

- Hypertension: YES ☐ NO ☐ UNKNOWN ☐
- Diabetes: YES ☐ NO ☐ UNKNOWN ☐
- Periph. vasc. disease: YES ☐ NO ☐ UNKNOWN ☐
- Atrial fibrillation: YES ☐ NO ☐ UNKNOWN ☐
- Hyperlipidaemia: YES ☐ NO ☐ UNKNOWN ☐
- Recent infection: YES ☐ NO ☐ UNKNOWN ☐
- Coagulopathy: YES ☐ NO ☐ UNKNOWN ☐
- Collagen vasc. disease: YES ☐ NO ☐ UNKNOWN ☐
- Migraine with aura: YES ☐ NO ☐ UNKNOWN ☐
- Pregnancy: YES ☐ NO ☐ UNKNOWN ☐
- Trauma: YES ☐ NO ☐ UNKNOWN ☐
- Previous TIA: YES ☐ NO ☐ UNKNOWN ☐
- Previous Stroke: YES ☐ NO ☐ UNKNOWN ☐
- Oral contraception: YES ☐ NO ☐ UNKNOWN ☐
- Family history: YES ☐ NO ☐ UNKNOWN ☐

- Substance abuse: YES ☐ NO ☐
  DAGGA ☐ MANDRAX ☐ OTHER
- Smoking: NEVER ☐ EX-SMOKER (> 1 YEAR) ☐ CURRENT SMOKER ☐
  NUMBER SMOKED PER DAY ☐☐☐
- Snuff (current): YES ☐ NO ☐
- Alcohol: NEVER / HARDLY EVER ☐ EX-DRINKER (> 1 YEAR) ☐ DRINKS ☐
  AMOUNT OF ALCOHOL PER DAY * ☐☐☐ g

* (100 ml wine (1 glass) or 30 ml spirits (1 tot) or 250 ml beer all = 10 g alcohol)

***HANDEDNESS***

- Select one — LEFT HANDED ☐ RIGHT HANDED ☐ UNKNOWN ☐

***SOCIO-ECONOMIC***

- Marital Status: MARRIED/COMMON LAW * ☐ SINGLE ☐ WIDOWED ☐ DIVORCED ☐

* (includes partners where living together)

- Sole Bread Winner: YES ☐ NO ☐

NUMBER OF FINANCIAL DEPENDENTS INCLUDING PARTNER ☐

☐

Housing:

- Select one
  - OLD-AGE RETIREMENT FACILITY ☐
  - HOUSE/FLAT ☐
  - SERVICED SHACK (TOILET PLUS TAP) ☐
  - UNSERVICED SHACK ☐
  - DORMITORY/HOSTEL/SINGLE ROOM ☐
  - ACCOMMODATION WITH EMPLOYER E.G. DOMESTIC WORKER ☐
  - OTHER: ☐

- NUMBER OF PEOPLE LIVING IN DWELLING: ☐☐
  (if living with employer do not include employers family/house)
- NUMBER OF ROOMS USED FOR SLEEPING IN THE DWELLING: ☐☐
  (if living with employer do not include employers family/house)

Education:

- YEARS OF SCHOOLING PASSED: ☐☐
- YEARS OF TERTIARY EDUCATION PASSED: ☐☐

Employment:

- Select one

| Employed | Unemployed |
|---|---|
| ☐ PROFESSIONAL/MANAGERIAL | ☐ LOOKING FOR WORK |
| ☐ MIDDLE MANAGEMENT | ☐ UNEMPLOYED BY CHOICE E.G. HOMEMAKER |
| ☐ MANUAL FORMAN/SKILLED ARTISAN | ☐ FULL-TIME STUDENT |
| ☐ FARMER – LARGE FARM | ☐ SOCIAL PENSIONER – ON DISABILITY GRANT OR OLD AGE PENSIONER |
| ☐ SUBSISTENCE FARMER | |
| ☐ CLERICAL/SEMI-SKILLED | |
| ☐ UNSKILLED/ INFORMAL SECTOR TRADER | |

**GENERAL EXAMINATION**

- Irregular pulse: YES ☐ NO ☐

- BP at first assessment (supine, average of 3 readings ):

  1. ☐☐☐ / ☐☐☐ 2. ☐☐☐ / ☐☐☐ 3. ☐☐☐ / ☐☐

  AVERAGE: ☐☐☐ / ☐☐☐

- Evidence of hypertensive end organ damage? YES ☐ NO ☐

  CARDIAC ☐ FUNDI ☐ RENAL (RENAL DYSFUNCTION) ☐

- Carotid bruits: RIGHT ☐ LEFT ☐

- Clinical heart failure:
  (i.e.: signs of LVF/RVF, not just on treatment) YES ☐ NO ☐

- Clinical valvular heart disease:
  (not a simple low murmur < 2/6) YES ☐ NO ☐

- Peripheral vascular disease:
  (both foot pulses absent or femoral bruits) YES ☐ NO ☐

- Cardiac disease: YES ☐ NO ☐

  ISCHAEMIC ☐ VALVULAR ☐ ATRIAL FIBRILLATION ☐

  CARDIOMYOPTHY ☐ HYPERTENSIVE HEART DISEASE WITHOUT CARDIOMYOPATHY ☐

- Other arteriopathy: ☐

**NEUROLOGIC DEFICIT:**

- *Indicate whether the following signs and symptoms are present:*

| | | |
|---|---|---|
| *Coma:* | *YES* ☐ | *NO* ☐ |
| *Decreased LOC:* | *YES* ☐ | *NO* ☐ |
| Motor weakness: | YES ☐ | NO ☐ |
| *Sensory deficit:* | *YES* ☐ | *NO* ☐ |
| *Cerebellar signs:* | *YES* ☐ | *NO* ☐ |
| Dysphasia: | YES ☐ | NO ☐ |
| *Dysphagia:* | *YES* ☐ | *NO* ☐ |
| Other cortical signs:<br>(apraxia, visual deficit, cortical sensory) | YES ☐ | NO ☐ |
| Urinary incontinence: | YES ☐ | NO ☐ |
| Can lift arm against gravity: | YES ☐ | NO ☐ |

Glasgow Coma Scale

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCORE: |
|---|---|---|
| Eye opening | None | E1 |
| | To painful stimulus | E2 |
| | To command/voices | E3 |
| | Spontaneously with blinking | E4 |
| Motor response | None | M1 |
| | Arm extension to painful stimulus | M2 |
| | Arm flexion to painful stimulus | M3 |
| | Arm withdraws from painful stimulus | M4 |
| | Hand localizes painful stimulus | M5 |
| | Obeys commands | M6 |
| Verbal response | None | V1 |
| | Sounds but no recognizable words | V2 |
| | Inappropriate words/expletives | V3 |
| | Confused speech | V4 |
| | Normal | V5 |

*Barthel Score*

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCOR |
|---|---|---|
| Bowels | Incontinent or needs enemas | 0 |
| | Occasional incontinence (< once per week) | 1 |
| | Continent | 2 |
| Bladder | Incontinent/unable to manage catheter | 0 |
| | Occasional accident ( < once per day) | 1 |
| | Continent | 2 |
| Grooming | Needs help with shaving, washing, hair or teeth | 0 |
| | Independent | 1 |
| Toilet use | Dependent | 0 |
| | Needs some help | 1 |
| | Independent on, off dressing and cleaning | 2 |
| Feeding | Dependent | 0 |
| | Needs some help (e.g. with cutting, spreading) | 1 |
| | Independent if food provided within reach | 2 |
| Transfer (e.g. bed or chair) | Unable and no sitting balance | 0 |
| | Needs major help | 1 |
| | Needs minor help | 2 |
| | Independent | 3 |
| Mobility | Unable | 0 |
| | Wheelchair independent indoors | 1 |
| | Walks with help or supervision | 2 |
| | Independent (but may use aid) | 3 |
| Dressing | Dependent | 0 |
| | Needs some help | 1 |
| | Independent including fasteners | 2 |
| Stairs | Unable | 0 |
| | Needs some help or supervision | 1 |
| | Independent up and down | 2 |
| Bathing | Dependent | 0 |
| | Independent in bath or shower | 1 |

Modified Rankin Score

- Circle your choice of score from the following list of options:

| DESCRIPTION: | SCORE: |
|---|---|
| No symptoms | 0 |
| Minor symptoms which do not interfere with lifestyle | 1 |
| Some restriction to lifestyle, but look after themselves | 2 |
| Significant restriction to lifestyle, preventing total independence | 3 |
| Severe handicap preventing independent existence but not requiring constant attention | 4 |
| Severe handicap, totally dependent, requiring attention night and day | 5 |

NIH Scale

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION | *SCORE* |
|---|---|---|
| Conscious level | Awake | 0 |
| | Drowsy, somnolent | 1 |
| | Stupor (rousable to correct localization of painful stimulus) | 2 |
| | No reaction or extensor or flexor spastic response | 3 |
| Response to questions (month, age) | Both answers correct | 0 |
| | One answer correct | 1 |
| | Both answers wrong or no response | 2 |
| Eye movement | Normal | 0 |
| | Partial gaze palsy | 1 |
| | Complete gaze palsy (also to oculocephalic maneuver) | 2 |
| Facial palsy | Normal | 0 |
| | Slight | 1 |
| | Moderate | 2 |
| | Complete | 3 |
| Limb ataxia (affected side) | Normal | 0 |
| | One limb ataxic | 1 |
| | Both limbs ataxic | 2 |
| Neglect | Normal | 0 |
| | Partial neglect (inattention) on side | 1 |
| | Complete hemi-neglect (several sensory modalities) | 2 |
| Aphasia | Normal | 0 |
| | Mild dysphasia (word finding difficulty, paraphasia, grammatical errors) | 1 |
| | Motor (Broca) or sensory (Wernickle) aphasia or variants | 2 |
| | Complete aphasia, muteness | 3 |
| Attempted Posture (affected lower limb) | Unremarkable (5s) | 0 |
| | Droops | 1 |
| | Lower limb flops (5s) | 2 |
| | Postural attempt impossible | 3 |
| Reaction to Verbal Order (open or shut eyes, hand grip) | Both correct | 0 |
| | One correct | 1 |
| | No reaction or incorrect action | 2 |
| Visual fields | Full | 0 |
| | Incomplete hemianopia | 1 |
| | Complete hemianopia | 2 |
| Attempted posture (affected arm) | Unremarkable (10s) | 0 |
| | Pronation | 1 |
| | 90° posture fails <10s, rapid droop | 2 |
| | Postural attempt fails | 3 |
| Sensation | Normal | 0 |
| | Hypesthesia | 1 |
| | Anaesthesia | 2 |
| Dysarthria | Normal | 0 |
| | Dysarthric but easily understood | 1 |
| | Severe dysarthria, barely intelligible | 2 |

Scandinavian Stroke scale

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCORE: |
|---|---|---|
| Consciousness | Fully conscious | 6 |
| | Somnolent, can be awaked to full conscience | 4 |
| | Reacts to verbal command, but is not fully conscious | 2 |
| Eye movement | No gaze palsy | 4 |
| | Gaze palsy present | 2 |
| | Conjugate eye deviation | 0 |
| Arm motor, power * | Raises arm with normal strength | 6 |
| | Raises arm with reduced strength | 5 |
| | Raises arm with flexion in elbow | 4 |
| | Can move, but not against gravity | 2 |
| | Paralysis | 0 |
| Hand motor, power * | Normal strength | 6 |
| | Reduced strength in full range | 4 |
| | Some movement, fingertips do not reach palm | 2 |
| | Paralysis | 0 |
| Leg motor power * | Normal strength | 6 |
| | Raises straight leg with reduced strength | 5 |
| | Raises leg with flexion of knee | 4 |
| | Can move, but not against gravity | 2 |
| | Paralysis | 0 |
| Orientation | Correct for time, place and person | 6 |
| | 2 of these | 4 |
| | 1 of these | 2 |
| | Completely disorientated | 0 |
| Speech | No aphasia | 10 |
| | Limited vocabulary or incoherent speech | 6 |
| | More than yes/no, but not longer sentences | 3 |
| | Only yes/no or less | 0 |
| Facial palsy | None/dubious | 2 |
| | Present | 0 |
| Gait | Walks 5 in without aids | 12 |
| | Walks with aids | 9 |
| | Walks with help of another person | 6 |
| | Sits without support | 3 |
| | Bedridden/wheelchair | 0 |

* Motor power is assessed only on the affected side

***LOCALISATION OF STROKE OR TIA:*** *Clinically - before CT seen*

- Select one

COMPLETE ANTERIOR CIRCULATION (TACS/I) ☐

PARTIAL ANTERIOR (PACS/I) ☐

POSTERIOR CIRCULATION (POCS/I) ☐

LACUNAR (LACS/I) ☐

***FROM THE CHARTS OR RECORDS***

- Pyrexial (anytime since admission) YES ☐ NO ☐
- BP on admission: (cas or admission ward) ☐☐☐ / ☐☐☐
- BP 24 hours after admission: ☐☐☐ / ☐☐☐
- BP on discharge: ☐☐☐ / ☐☐☐

**MEDICATION** (names only - no dosages necessary)

- On admission:

| | | |
|---|---|---|
| | | |
| | | |
| | | |

- At time of assessment by stroke team:

| | | |
|---|---|---|
| | | |
| | | |
| | | |

**ECG**

- ECG: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Select all abnormalities: ☐

ATRIAL FIBRILLATION/FLUTTER ☐ LVH ☐
ST/T WAVE CHANGE ☐ ACUTE MI ☐
OLD MI ☐
LBBB/RBBB/LEFT AXIS ☐
OTHER ☐

Specify if other:

**RADIOLOGY**

- Chest x-ray: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

LUNG ☐ CARDIAC ☐

**> > > > > > > > > > > PLEASE FILL THIS IN BEFORE LOOKING AT THE CT SCAN < < < < < < < < < < <**

- What stroke type do you suspect the patient has had?

HAEMORRHAGE ☐ INFARCT ☐ SAH ☐ CAN'T SAY ☐

- *Do you already know the findings of the CT scan?* *YES* ☐ *NO* ☐

**ALLEN AND SIRIRAJ SCORES**

- ***Select/complete*** all relevant boxes:

**Onset:**

LOSS OF CONSCIOUSNESS ☐
HEADACHE WITHIN 2 HOURS ☐
VOMITING ☐
NECK STIFFNESS ☐

*Level of Consciousness:*

ALERT ☐
DROWSY ☐
UNCONSCIOUS ☐

*Plantar Response:*

BOTH FLEXOR/SINGLE EXTENSOR ☐
BOTH EXTENSOR ☐

**Diastolic BP 24 hours after admission:** ☐☐☐ mm Hg

*Atherama Markers:*

ANGINA ☐
CLAUDICATION ☐
DIABETES HISTORY ☐

**History of hypertension present:** YES ☐ NO ☐

**Previous event TIA or Stroke:** YES ☐ NO ☐

**Heart disease:**

AORTIC OR MITRAL MURMUR ☐ ATRIAL FIBRILLATION ☐

CARDIOMEGALY (CHEST X-RAY) ☐ MI WITHIN 6 MONTHS ☐

CARDIAC FAILURE ☐

CARDIOMYOPTHY ☐

END ALLEN AND SIRIRAJ SCORES

**CT scan - head**

- CT scan: DONE ☐ NOT DONE ☐

How many CT scans were done? 1 ☐ 2 ☐ > 2 ☐

Was contrast used? YES ☐ NO ☐

CT scan done: 0 – 24 HOURS ☐ 24 – 48 HOURS ☐ 48 - 72 HOURS ☐

3 – 7 DAYS ☐ > 7 DAYS ☐

CT scan: NORMAL ☐ ABNORMAL ☐

Specify:

**Cerebral angiogram**

- Angiogram: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Specify:

**MRI - head**

- MRI: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Specify:

**MRA - head**

- MRA: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Specify:

**SPECT**

- Spect: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Specify:

**Carotid duplex Dopplers**

- Dopplers: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Specify:

☐☐ % OCCLUSION LEFT ☐☐ % OCCLUSION RIGHT

Dissection YES ☐ NO ☐

**Transcranial Dopplers**

- Dopplers: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Specify:

**Cardiac Echo**

- Echo: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Transthoracic: INTRACAVITY CLOT ☐ DYSKINETIC SEGMENT ☐ VALVULAR LESION ☐

RIGHT TO LEFT SHUNT ☐ LV HYPERTROPHY ☐

Transoesophageal: INTRA-CAVITY CLOT ☐ DYSKINETIC SEGMENT ☐ R to L SHUNT ☐

VALVULAR LESION ☐ LV HYPERTROPHY ☐ AORTIC PLAQUE ☐

Other:

***OTHER RELEVANT INVESTIGATIONS***

| Bloods & CSF | | X | | X | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ***FBC*** | Normal | | Abnormal | | | Hb | | WCC | |
| | | | | | | Plts. | | | |
| **Blood glucose (on admission)** | Normal | | Abnormal | | | | mmol/l | | |
| **ESR** | Not done | | Done | | | | mm/hour | | |
| **Urea/Creat-inine/ Elecs.** | Normal | | Abnormal | | | Na | | $K^+$ | |
| | | | | | | Urea | | Creat. | |
| ***HIV*** | Not done | | Negative | | Positive | CD4 count | | | |
| **VDRL** | Not done | | Negative | | Positive | | | | |
| **INR/PTT** | Not done | | Normal | | Abnormal | INR | | PTT | |
| **Hypercoag-ulation screen** | Not done | | Negative | | Positive | Specify | | | |
| **Collagen screen** | Not done | | Negative | | Positive | Specify | | | |
| ***Lipids – non fasting*** | Not done | | Normal | | Abnormal | Cholesterol | | mmol/l | |
| **Lipids – fasting** | Not done | | Normal | | Abnormal | Cholesterol | | Tg | |
| | | | | | | HDL | | LDL | |
| ***CSF*** | Not done | | Normal | | Abnormal | Specify | | | |

***TREATMENT***

**Antiplatelet agents:**

- Select all relevant boxes:

ASPIRIN ☐
ASPIRIN + DIPYRIDAMOLE ☐
TICLOPIDINE ☐
CLOPIDOGREL ☐

**Anticoagulation:**

- Heparin: YES ☐ NO ☐

PROPHYLACTIC DOSE ☐ FULL DOSE ☐ IV ☐
SC ☐

- Warfarin: YES ☐ NO ☐

- **Oxygen:** YES ☐ NO ☐
- **Antibiotics:** YES ☐ NO ☐
- **Anti-pyretics:** YES ☐ NO ☐
- **Insulin:** YES ☐ NO ☐
- **Surgery:** YES ☐ NO ☐

Specify:

- **Thrombolysis:** YES ☐ NO ☐

Thrombolytic agent

Total dose:

Route of administration: INTRAVENOUS ☐ INTRA-ARTERIAL ☐

Time interval (stroke onset to infusion) : ☐☐ HOURS ☐☐ DAYS

Complications:

- Select all relevant boxes:
  - SYMPTOMATIC INTRACEREBRAL HAEMORRHAGE: ☐
  - ASYMPTOMATIC INTRACEREBRAL HAEMORRHAGE: ☐
  - EXTRACRANIAL HAEMORRHAGE: ☐
  - OTHER: ☐

Specify:

- **Neuroprotective agents:** YES ☐ NO ☐

Agent:

- **Steroids prescribed (for stroke):** YES ☐ NO ☐
- **Mannitol:** YES ☐ NO ☐
- **IV fluids:**

Up at time of assessment ? YES ☐ NO ☐

IV fluids contain glucose? YES ☐ NO ☐

- ***Anti-hypertensives:***

  Patient on anti-hypertensives prior to admission? YES ☐ NO ☐ UNKNOWN ☐

  Anti-hypersensitives continued during admission? YES ☐ NO ☐

  Is there evidence to suggest that the patient is a known hypertensive (history, end-organ damage, old notes)? YES ☐ NO ☐ UNKNOWN ☐

  - Patient hypertensive on admission? YES ☐ NO ☐ UNKNOWN ☐

    Anti-hypertensives given within the first week? YES ☐ NO ☐

    ANTI-HYPERTENSIVES GIVEN **OTHER THAN** B BLOCKER, DIURETICS, ICCB, ACE INHIBITOR:

    | |
    |---|
    | |

  - Anti-hypertensives started after 1st week? YES ☐ NO ☐ UNKNOWN ☐
  - Patient on anti-hypertensives at discharge? YES ☐ NO ☐ UNKNOWN ☐

*ASSESSMENT OF PROFESSIONALS ALLIED TO MEDICINE:*

- Select all relevant boxes:

  Physiotherapy ☐

  Within 24 Hours YES ☐ NO ☐

  Speech therapy ☐

  Within 24 hours YES ☐ NO ☐

  Occupational therapy ☐

  Within 24 hours YES ☐ NO ☐

  Community liaison ☐

  Within 24 hours YES ☐ NO ☐

  Social worker ☐

  Within 24 hours YES ☐ NO ☐

  Dietician ☐

  Within 24 hours YES ☐ NO ☐

  Psychologist ☐

  Within 24 hours YES ☐ NO ☐

**ASSESSMENT:**

**Stroke Type:** (only complete if CT scan available)

- Select one:

  TIA ☐ HAEMORRHAGE ☐

  ISCHAEMIC INFARCT ☐ UNCERTAIN (NO CT) ☐

  SAH ☐ RETINAL ARTERY OCCLUSION ☐

  MULTI-INFARCT PICTURE ☐

**Complications:**

- Select all relevant boxes:

| | |
|---|---|
| PAINFUL SHOULDER SYNDROME | ☐ |
| RECURRENT STROKE | ☐ |
| PNEUMONIA | ☐ |
| DVT | ☐ |
| MYOCARDIAL INFARCT | ☐ |
| SEIZURES | ☐ |
| DEPRESSION | ☐ |
| BEDSORES | ☐ |
| PROGRESSING STROKE (SYMPTOMS AND SIGNS EVOLVE OVER HOURS) | ☐ |
| OTHER | ☐ |

Specify:

**Aetiology of ischaemic stroke:**

- Large vessel atherothromboembolic: PROBABLE ☐ POSSIBLE ☐
- Cardioembolic: PROBABLE ☐ POSSIBLE ☐
- Small vessel (lacunar): PROBABLE ☐ POSSIBLE ☐
- Acute ischaemic stroke of other aetiology: YES ☐ NO ☐

Specify:

- Acute ischaemic stroke of unknown cause:
  (incomplete workup) YES ☐
  NO ☐
- Acute ischemic stroke of unknown cause:
  (no probable aetiology despite complete workup) YES ☐ NO ☐
- Acute ischaemic stroke of unknown aetiology:
  (more than one likely aetiology and a single likely aetiology cannot be determined) YES ☐ NO ☐

Specify:

- **Aetiology of intracerebral haemorrhage:**

- **Aetiology of SAH:**

**> > > > > > > COMPLETE BELOW ONLY IF YOU KNOW THE DETAILS OF THE FULL ADMISSION < < < < < < <**

**Duration of Hospitalisation:**

➢ Select all appropriate boxes:

| | | |
|---|---|---|
| ADMISSION WARD | ☐ ..... | DAYS ☐☐ |
| MEDICAL WARD | ☐ ..... | DAYS ☐☐ |
| STROKE UNIT | ☐ ..... | DAYS ☐☐ |
| OTHER WARD | ☐ ..... | DAYS ☐☐ |

➢ TOTAL ..... DAYS ☐☐

➢ **Death:** YES ☐ NO ☐

Cause:

➢ *Discharge:*

➢ Discharge to: HOME CARE ☐ REHABILITATION CENTER ☐ OTHER ☐

Specify:

➢ Home carer available YES ☐ NO ☐

Partner? YES ☐ NO ☐

Specify:

➢ Should Aspirin be prescribed? YES ☐ NO ☐

➢ Was Aspirin prescribed? YES ☐ NO ☐

**> > > > > > > > > > > > > > > > > > DO NOT COMPLETE THIS SECTION < < < < < < < < < < < < < < < < < < <**

➢ **Patient of interest?** YES ☐ NO ☐

Reason:

- **Final diagnosis:** STROKE ☐ TIA ☐ RAO ☐ OTHER ☐

Use the following codes:

Code **1** = possible (not for RAO)
Code **2** = probable (not for RAO)
Code **3** = definite
Code **9** = not applicable

(Include events within the last 6 months only.

Multiple diagnoses may be coded)

Reason:

- **First-ever-in-a-lifetime stoke:** YES ☐ NO ☐ UNABLE TO ASSESS ☐

DEFINITE ☐ PROBABLE ☐ POSSIBLE ☐

*SUMMARY OF ASSESSMENT BY STROKE TEAM*

Thank you for referring your patient to the Stroke Team!

---

- **Date seen:** ☐☐ . ☐☐ . 20☐☐ Patient hospital number: ☐☐☐☐☐☐☐

- **HISTORY** (key features that make this a vascular event, or not):

| |
|---|
| |
| |
| |
| |

**EXAMINATION:**

- Cortical signs present: YES ☐ NO ☐
  A/Dysphasia ☐ Parietal lobe signs ☐
  Other ☐

  Specify:

- Cranial nerves involved: YES ☐ NO ☐

  List:

- Motor signs: YES ☐ NO ☐
  LEFT ☐ RIGHT ☐ BILATERAL ☐
  ARM ☐ LEG ☐

- Sensory signs: YES ☐ NO ☐
  LEFT ☐ RIGHT ☐ BILATERAL ☐
  ARM ☐ LEG ☐

- Cerebellar signs: YES ☐ NO ☐
  LEFT ☐ RIGHT ☐ BILATERAL ☐ AXIAL ☐

- Other key features:

***ASSESSMENT:***

- TIA ☐ STROKE ☐ INFARCTION ☐ HAEMORRHAGE ☐ SAH ☐ NOT SURE ☐
- FIRST EVER IN A LIFETIME ☐ RECURRENT ☐
- ANTERIOR CIRCULATION: YES ☐ NO ☐
- PARTIAL ANTERIOR CIRCULATION: YES ☐ NO ☐
- LACUNAR YES ☐ NO ☐
- TOTAL ANTERIOR CIRCULATION: YES ☐ NO ☐
- POSTERIOR CIRCULATION: YES ☐ NO ☐

***SUGGESTION/S:***

- Further investigation/s:
- Treatment:
- Referral:

- **SIGN:**

APPENDIX E:

**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**

Division of the Deputy Registrar (Research)

**COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)**
Ref: R14/49 Connor

DIVISION OF THE DEPUTY REGISTRAR (RESEARCH)
RECEIVED 2000 -06- 22
FILE:
ACTION:

**CLEARANCE CERTIFICATE** **PROTOCOL NUMBER** M00/03/7

**PROJECT** Johannesburg Hospital Stroke Register

**INVESTIGATORS** Dr M Connor

**DEPARTMENT** Dept of Neurology/Medicine, Johannesburg Hospital

**DATE CONSIDERED** 00/03/31

**DECISION OF THE COMMITTEE** *

Approved unconditionally

**DATE** 00/05/29 **CHAIRMAN** .....(Professor P E Cleaton-Jones)

* Guidelines for written "informed consent" attached where applicable.

c c Supervisor: Prof VU Fritz
Dept of Dept of Neurology/Medicine, Johannesburg Hospital

Works2\lain0015\HumEth97.wdb\M 00/03/7

**DECLARATION OF INVESTIGATOR(S)**

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee.

DATE 20 : 6 : 2000 SIGNATURE .....

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

# APPENDIX F. THE SIRIRAJ STROKE SCORE AND GUY'S HOSPITAL STROKE SCORE

The scores are derived by assigning a value to various clinical features as indicated. A constant is then added to the sum of these indicators and the final value determines whether the patient has an ischaemic stroke, intracranial haemorrhage or falls into an 'uncertain' area according to cut-off points determined by the original validation studies (Allen, 1983; Poungvarin et al., 1991). These cut-off or threshold points for infarction (ischaemic stroke) or intracranial haemorrhage were validated at 90% certainty for the diagnosis. The threshold points are given below:

## Calculation of the Siriraj Stroke Score

1. Consciousness:
    a. Alert = 0
    b. Drowsy or stupor = 2.5
    c. Coma or semicoma = 5
2. Vomiting:
    a. No=0
    b. Yes=2
3. Headache (within 2 hours of stroke onset):
    a. No=0
    b. Yes=2
4. Diastolic blood pressure (in mmHg): diastolic BP multiplied by 0.1
5. Atheroma markers (history of diabetes mellitus, intermittent claudication, or angina):
    a. None=0
    b. One or more= -3
6. Constant: -12

**Threshold / cut-off points for the Siriraj Score:**

> 1: Haemorrhage; -1 to +1: Uncertain; < - 1: Infarction

**Calculation of the Allen (Guy's Hospital) Stroke Score**

1. Apoplectic onset (loss of consciousness, headache within 2 hours, vomiting, neck stiffness):
    a. One or none of these=0
    b. Two or more=+21.9
2. Level of consciousness (24 hours after admission):
    a. Alert=0
    b. Drowsy=+7.3
    c. Unconscious=+14.6
3. Plantar responses:
    a. Both flexor or single extensor=0
    b. Both extensor=+7.1
4. Diastolic blood pressure (24 hours after admission, in mmHg): diastolic BP multiplied by 0.17
5. Atheroma markers (angina, claudication, diabetes history):
    a. None=0
    b. One or more= -3.7
6. History of hypertension:
    a. Not present=0
    b. Present= -4.1
7. Previous event (transient ischaemic attack or stroke):
    a. None=0

b. Any number of events= -6.7

8. Heart disease:
    a. None=0
    b. Aortic or mitral murmur= -4.3
    c. Cardiac failure= -4.3
    d. Cardiomyopathy= -4.3
    e. Atrial fibrillation= -4.3
    f. Cardiomegaly (from x-ray) = -4.3
    g. Myocardial infarct (within 6 months) = -4.3
9. Constant= -12.6

**Threshold / cut-off points for the Allen Score:**

> 24: Haemorrhage; 4 – 24: Uncertain; < 4: Infarction

## APPENDIX G: TINTSWALO HOSPITAL STROKE REGISTER QUESTIONNAIRE

## UNIVERSITY OF THE WITWATERSRAND STROKE DATABASE – TINTSWALO HOSPITAL

**> > > > > > > > > > DO NOT LOOK AT THE CT SCAN BEFORE COMPLETING THIS FORM < < < < < < < < < <**

| **Office use** | Form completed ☐ | Regist ☐ |
|---|---|---|

**NOTES:**

Each individual question is marked ' **>** '

Some responses require expansion most often facilitated by shading. Illustrated in the following example:

- Is it the weekend? YES ☐ NO ☐
  What day is it? SATURDAY ☐ SUNDAY ☐

Here, the second question only needs to be considered if the response to the first question is 'YES'

---

- Doctor completing this form: ☐
- Patient hospital number: ☐☐☐☐☐☐☐
- Ward: MALE ☐ FEMALE ☐ OTHER ☐
- Date of birth: ☐☐ . ☐☐ . 19 ☐☐
- Age: ☐☐
- Contact telephone number: ☐☐☐☐☐☐☐☐☐☐☐☐
  (friend / relative)
- Sex: MALE ☐ FEMALE ☐
- Ethnic group: WHITE ☐ BLACK ☐ COLOURED ☐ INDIAN-ASIAN ☐
- Date of stroke: ☐☐ . ☐☐ . 20 ☐☐
- Date of admission: ☐☐ . ☐☐ . 20 ☐☐
- Date of assessment by stroke team: ☐☐ . ☐☐ . 20 ☐☐
- Time between onset of stroke
  and hospital medical attention: ☐☐ HOURS ☐☐ DAYS

***HISTORY OF EVENT***

- Symptoms present on waking: YES ☐ NO ☐ UNKNOWN ☐
- Headache within 2 hours of onset: YES ☐ NO ☐ UNKNOWN ☐
- Vomited since symptom onset: YES ☐ NO ☐ UNKNOWN ☐
- Loss of consciousness at onset: YES ☐ NO ☐ UNKNOWN ☐
- Drowsiness since symptom onset: YES ☐ NO ☐ UNKNOWN ☐
- Seizure since symptom onset: YES ☐ NO ☐ UNKNOWN ☐
- If symptoms have resolved by the time of
  examination, how long were they present? ☐☐ HOURS ☐☐ DAYS

***ADL** (**A**ctivities of **D**aily **L**iving)*

- Was the patient independent prior to admission? YES ☐ NO ☐ UNKNOWN ☐
- Rankin modified before this event? * 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

* **Modified Rankin score**

**0** = no symptoms.
**1** = minor symptoms which do not interfere with lifestyle.
**2** = some restriction to lifestyle, but look after themselves.
**3** = significant restriction to llifestyle, preventing total independence.
**4** = severe handicap preventing independent existence but not requiring constant attention.
**5** = severe handicap, totally dependent, requiring attention night and day.

***RISK FACTORS***

- Hypertension: YES ☐ NO ☐ UNKNOWN ☐
- Diabetes: YES ☐ NO ☐ UNKNOWN ☐
- Periph. vasc. disease: YES ☐ NO ☐ UNKNOWN ☐
- Atrial fibrillation: YES ☐ NO ☐ UNKNOWN ☐
- Hyperlipidaemia: YES ☐ NO ☐ UNKNOWN ☐
- Recent infection: YES ☐ NO ☐ UNKNOWN ☐
- Coagulopathy: YES ☐ NO ☐ UNKNOWN ☐
- Collagen vasc. disease: YES ☐ NO ☐ UNKNOWN ☐
- Migraine with aura: YES ☐ NO ☐ UNKNOWN ☐
- Pregnancy: YES ☐ NO ☐ UNKNOWN ☐
- Trauma: YES ☐ NO ☐ UNKNOWN ☐
- Previous TIA: YES ☐ NO ☐ UNKNOWN ☐
- Previous Stroke: YES ☐ NO ☐ UNKNOWN ☐
- Oral contraception: YES ☐ NO ☐ UNKNOWN ☐
- Family history: YES ☐ NO ☐ UNKNOWN ☐

- Substance abuse: YES ☐ NO ☐
  DAGGA ☐ MANDRAX ☐ OTHER ☐
- Smoking: NEVER ☐ EX-SMOKER (> 1 YEAR) ☐
  CURRENT SMOKER ☐
  NUMBER SMOKED PER DAY ☐☐☐
- Snuff (current): YES ☐ NO ☐
- Alcohol: NEVER / HARDLY EVER ☐ EX-DRINKER (> 1 YEAR) ☐ DRINKS ☐
  AMOUNT OF ALCOHOL PER DAY * ☐☐☐ g
  * (100 ml wine (1 glass) or 30 ml spirits (1 tot) or 250 ml beer all = 10 g alcohol)

***HANDEDNESS***

- Select one: LEFT HANDED ☐ RIGHT HANDED ☐ UNKNOWN ☐

***SOCIO-ECONOMIC***

- Marital Status: MARRIED/COMMON LAW * ☐ SINGLE ☐ WIDOWED ☐ DIVORCED ☐

  * (includes partners where living together)
- Sole Bread Winner: YES ☐ NO ☐
  NUMBER OF FINANCIAL DEPENDENTS INCLUDING PARTNER ☐

☐

Housing:

- Select one
  - OLD-AGE RETIREMENT FACILITY ☐
  - HOUSE/FLAT ☐
  - SERVICED SHACK (TOILET PLUS TAP) ☐
  - UNSERVICED SHACK ☐
  - DORMITORY/HOSTEL/SINGLE ROOM ☐
  - ACCOMMODATION WITH EMPLOYER E.G. DOMESTIC WORKER ☐
  - O[illegible] ☐

- NUMBER OF PEOPLE LIVING IN DWELLING: ☐☐
  (if living with employer do not include employers family/house)
- NUMBER OF ROOMS USED FOR SLEEPING IN THE DWELLING: ☐☐
  (if living with employer do not include employers family/house)

Education:

- YEARS OF SCHOOLING PASSED: ☐☐
- YEARS OF TERTIARY EDUCATION PASSED: ☐☐

Employment:

- Select one

| Employed | Unemployed |
| --- | --- |
| ☐ PROFESSIONAL/MANAGERIAL | ☐ LOOKING FOR WORK |
| ☐ MIDDLE MANAGEMENT | ☐ UNEMPLOYED BY CHOICE E.G. HOMEMAKER |
| ☐ MANUAL FORMAN/SKILLED ARTISAN | ☐ FULL-TIME STUDENT |
| ☐ FARMER – LARGE FARM | ☐ SOCIAL PENSIONER – ON DISABILITY GRANT OR OLD AGE PENSIONER |
| ☐ SUBSISTENCE FARMER | |
| ☐ CLERICAL/SEMI-SKILLED | |
| ☐ UNSKILLED/ INFORMAL SECTOR TRADER | |

**GENERAL EXAMINATION**

- Irregular pulse: YES ☐ NO ☐

- BP at first assessment (supine, average of 3 readings ):

  1. ☐☐☐ / ☐☐☐ 2. ☐☐☐ / ☐☐☐ 3. ☐☐☐ / ☐☐

  AVERAGE: ☐☐☐ / ☐☐☐

- Evidence of hypertensive end organ damage? YES ☐ NO ☐

  CARDIAC ☐ FUNDI ☐ RENAL (RENAL DYSFUNCTION) ☐

- Carotid bruits: RIGHT ☐ LEFT ☐

- Clinical heart failure:
  (i.e.: signs of LVF/RVF, not just on treatment) YES ☐ NO ☐

- Clinical valvular heart disease:
  (not a simple low murmur < 2/6) YES ☐ NO ☐

- Peripheral vascular disease:
  (both foot pulses absent or femoral bruits) YES ☐ NO ☐

- Cardiac disease: YES ☐ NO ☐

  ISCHAEMIC ☐ VALVULAR ☐ ATRIAL FIBRILLATION ☐

  CARDIOMYOPTHY ☐ HYPERTENSIVE HEART DISEASE WITHOUT CARDIOMYOPATHY ☐

- Other arteriopathy: ☐

**NEUROLOGIC DEFICIT:**

- *Indicate whether the following signs and symptoms are present:*

| | | |
|---|---|---|
| *Coma:* | *YES* ☐ | *NO* ☐ |
| *Decreased LOC:* | *YES* ☐ | *NO* ☐ |
| Motor weakness: | YES ☐ | NO ☐ |
| *Sensory deficit:* | *YES* ☐ | *NO* ☐ |
| *Cerebellar signs:* | *YES* ☐ | *NO* ☐ |
| Dysphasia: | YES ☐ | NO ☐ |
| *Dysphagia:* | *YES* ☐ | *NO* ☐ |
| Other cortical signs:<br>(apraxia, visual deficit, cortical sensory) | YES ☐ | NO ☐ |
| Urinary incontinence: | YES ☐ | NO ☐ |
| Can lift arm against gravity: | YES ☐ | NO ☐ |

Glasgow Coma Scale

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCORE: |
|---|---|---|
| Eye opening | None | E1 |
| | To painful stimulus | E2 |
| | To command/voices | E3 |
| | Spontaneously with blinking | E4 |
| Motor response | None | M1 |
| | Arm extension to painful stimulus | M2 |
| | Arm flexion to painful stimulus | M3 |
| | Arm withdraws from painful stimulus | M4 |
| | Hand localizes painful stimulus | M5 |
| | Obeys commands | M6 |
| Verbal response | None | V1 |
| | Sounds but no recognizable words | V2 |
| | Inappropriate words/expletives | V3 |
| | Confused speech | V4 |
| | Normal | V5 |

*Barthel Score*

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCOR |
|---|---|---|
| Bowels | Incontinent or needs enemas | 0 |
| | Occasional incontinence (< once per week) | 1 |
| | Continent | 2 |
| Bladder | Incontinent/unable to manage catheter | 0 |
| | Occasional accident ( < once per day) | 1 |
| | Continent | 2 |
| Grooming | Needs help with shaving, washing, hair or teeth | 0 |
| | Independent | 1 |
| Toilet use | Dependent | 0 |
| | Needs some help | 1 |
| | Independent on, off dressing and cleaning | 2 |
| Feeding | Dependent | 0 |
| | Needs some help (e.g. with cutting, spreading) | 1 |
| | Independent if food provided within reach | 2 |
| Transfer (e.g. bed or chair) | Unable and no sitting balance | 0 |
| | Needs major help | 1 |
| | Needs minor help | 2 |
| | Independent | 3 |
| Mobility | Unable | 0 |
| | Wheelchair independent indoors | 1 |
| | Walks with help or supervision | 2 |
| | Independent (but may use aid) | 3 |
| Dressing | Dependent | 0 |
| | Needs some help | 1 |
| | Independent including fasteners | 2 |
| Stairs | Unable | 0 |
| | Needs some help or supervision | 1 |
| | Independent up and down | 2 |
| Bathing | Dependent | 0 |
| | Independent in bath or shower | 1 |

Modified Rankin Score

- Circle your choice of score from the following list of options:

| DESCRIPTION: | SCORE: |
|---|---|
| No symptoms | 0 |
| Minor symptoms which do not interfere with lifestyle | 1 |
| Some restriction to lifestyle, but look after themselves | 2 |
| Significant restriction to lifestyle, preventing total independence | 3 |
| Severe handicap preventing independent existence but not requiring constant attention | 4 |
| Severe handicap, totally dependent, requiring attention night and day | 5 |

NIH Scale

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION | *SCORE* |
|---|---|---|
| Conscious level | Awake | 0 |
| | Drowsy, somnolent | 1 |
| | Stupor (rousable to correct localization of painful stimulus) | 2 |
| | No reaction or extensor or flexor spastic response | 3 |
| Response to questions (month, age) | Both answers correct | 0 |
| | One answer correct | 1 |
| | Both answers wrong or no response | 2 |
| Eye movement | Normal | 0 |
| | Partial gaze palsy | 1 |
| | Complete gaze palsy (also to oculocephalic maneuver) | 2 |
| Facial palsy | Normal | 0 |
| | Slight | 1 |
| | Moderate | 2 |
| | Complete | 3 |
| Limb ataxia (affected side) | Normal | 0 |
| | One limb ataxic | 1 |
| | Both limbs ataxic | 2 |
| Neglect | Normal | 0 |
| | Partial neglect (inattention) on side | 1 |
| | Complete hemi-neglect (several sensory modalities) | 2 |
| Aphasia | Normal | 0 |
| | Mild dysphasia (word finding difficulty, paraphasia, grammatical errors) | 1 |
| | Motor (Broca) or sensory (Wernickle) aphasia or variants | 2 |
| | Complete aphasia, muteness | 3 |
| Attempted Posture (affected lower limb) | Unremarkable (5s) | 0 |
| | Droops | 1 |
| | Lower limb flops (5s) | 2 |
| | Postural attempt impossible | 3 |
| Reaction to Verbal Order (open or shut eyes, hand grip) | Both correct | 0 |
| | One correct | 1 |
| | No reaction or incorrect action | 2 |
| Visual fields | Full | 0 |
| | Incomplete hemianopia | 1 |
| | Complete hemianopia | 2 |
| Attempted posture (affected arm) | Unremarkable (10s) | 0 |
| | Pronation | 1 |
| | 90° posture fails <10s, rapid droop | 2 |
| | Postural attempt fails | 3 |
| Sensation | Normal | 0 |
| | Hypesthesia | 1 |
| | Anaesthesia | 2 |
| Dysarthria | Normal | 0 |
| | Dysarthric but easily understood | 1 |
| | Severe dysarthria, barely intelligible | 2 |

Scandinavian Stroke scale

- Circle one score for each of the categories:

| CATEGORY: | DESCRIPTION: | SCORE: |
|---|---|---|
| Consciousness | Fully conscious | 6 |
| | Somnolent, can be awaked to full conscience | 4 |
| | Reacts to verbal command, but is not fully conscious | 2 |
| Eye movement | No gaze palsy | 4 |
| | Gaze palsy present | 2 |
| | Conjugate eye deviation | 0 |
| Arm motor, power * | Raises arm with normal strength | 6 |
| | Raises arm with reduced strength | 5 |
| | Raises arm with flexion in elbow | 4 |
| | Can move, but not against gravity | 2 |
| | Paralysis | 0 |
| Hand motor, power * | Normal strength | 6 |
| | Reduced strength in full range | 4 |
| | Some movement, fingertips do not reach palm | 2 |
| | Paralysis | 0 |
| Leg motor power * | Normal strength | 6 |
| | Raises straight leg with reduced strength | 5 |
| | Raises leg with flexion of knee | 4 |
| | Can move, but not against gravity | 2 |
| | Paralysis | 0 |
| Orientation | Correct for time, place and person | 6 |
| | 2 of these | 4 |
| | 1 of these | 2 |
| | Completely disorientated | 0 |
| Speech | No aphasia | 10 |
| | Limited vocabulary or incoherent speech | 6 |
| | More than yes/no, but not longer sentences | 3 |
| | Only yes/no or less | 0 |
| Facial palsy | None/dubious | 2 |
| | Present | 0 |
| Gait | Walks 5 in without aids | 12 |
| | Walks with aids | 9 |
| | Walks with help of another person | 6 |
| | Sits without support | 3 |
| | Bedridden/wheelchair | 0 |

* Motor power is assessed only on the affected side

***LOCALISATION OF STROKE OR TIA:*** *Clinically - before CT seen*

- Select one

COMPLETE ANTERIOR CIRCULATION (TACS/I) ☐

PARTIAL ANTERIOR (PACS/I) ☐

POSTERIOR CIRCULATION (POCS/I) ☐

LACUNAR (LACS/I) ☐

***FROM THE CHARTS OR RECORDS***

- Pyrexial (anytime since admission) YES ☐ NO ☐
- BP on admission: (cas or admission ward) ☐☐☐ / ☐☐☐
- BP 24 hours after admission: ☐☐☐ / ☐☐☐
- BP on discharge: ☐☐☐ / ☐☐☐

**MEDICATION** (names only - no dosages necessary)

- On admission:

| | | |
|---|---|---|
| | | |
| | | |
| | | |

- At time of assessment by stroke team:

| | | |
|---|---|---|
| | | |
| | | |
| | | |

**ECG**

- ECG: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

Select all abnormalities: ☐

ATRIAL FIBRILLATION/FLUTTER ☐ LVH

ST/T WAVE CHANGE ☐ ACUTE MI

OLD MI ☐

LBBB/RBBB/LEFT AXIS ☐

OTHER ☐

Specify if other:

**RADIOLOGY**

- Chest x-ray: NOT DONE ☐ NORMAL ☐ ABNORMAL ☐

LUNG ☐ CARDIAC ☐

**> > > > > > > > > > > PLEASE FILL THIS IN BEFORE LOOKING AT THE CT SCAN < < < < < < < < < < <**

- What stroke type do you suspect the patient has had?

HAEMORRHAGE ☐ INFARCT ☐ SAH ☐ CAN'T SAY ☐

- *Do you already know the findings of the CT scan?* *YES* ☐ *NO* ☐

**ALLEN AND SIRIRAJ SCORES**

- ***Select/complete*** all relevant boxes:

**Onset:**

LOSS OF CONSCIOUSNESS ☐
HEADACHE WITHIN 2 HOURS ☐
VOMITING ☐
NECK STIFFNESS ☐

*Level of Consciousness:*

ALERT ☐
DROWSY ☐
UNCONSCIOUS ☐

*Plantar Response:*

BOTH FLEXOR/SINGLE EXTENSOR ☐
BOTH EXTENSOR ☐

**Diastolic BP 24 hours after admission:** ☐☐☐ mm Hg

*Atherama Markers:*

ANGINA ☐
CLAUDICATION ☐
DIABETES HISTORY ☐

**History of hypertension present:** YES ☐ NO ☐

**Previous event TIA or Stroke:** YES ☐ NO ☐

**Heart disease:**

AORTIC OR MITRAL MURMUR ☐ ATRIAL FIBRILLATION ☐

CARDIOMEGALY (CHEST X-RAY) ☐ MI WITHIN 6 MONTHS ☐

CARDIAC FAILURE ☐

CARDIOMYOPTHY ☐

END ALLEN AND SIRIRAJ SCORES

**CT scan - head**

- CT scan: DONE ☐ NOT DONE ☐

How many CT scans were done? 1 ☐ 2 ☐ > 2 ☐

Was contrast used? YES ☐ NO ☐

CT scan done: 0 – 24 HOURS ☐ 24 – 48 HOURS ☐ 48 - 72 HOURS ☐

3 – 7 DAYS ☐ > 7 DAYS ☐

CT scan: NORMAL ☐ ABNORMAL ☐

Specify:

***OTHER RELEVANT INVESTIGATIONS***

Bloods & CSF **X** **X**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ***FBC*** | Normal | | Abnormal | | | Hb | | WCC | |
| | | | | | | Plts. | | | |
| **Blood glucose (on admission)** | Normal | | Abnormal | | | | mmol/l | | |
| **ESR** | Not done | | Done | | | | mm/hour | | |
| **Urea/Creat-inine/ Elecs.** | Normal | | Abnormal | | | Na | | $K^+$ | |
| | | | | | | Urea | | Creat. | |
| ***HIV*** | Not done | | Negative | | Positive | | CD4 count | | |
| **VDRL** | Not done | | Negative | | Positive | | | | |
| **INR/PTT** | Not done | | Normal | | Abnormal | | INR | | PTT |
| **Hypercoag-ulation screen** | Not done | | Negative | | Positive | | Specify | | |
| **Collagen screen** | Not done | | Negative | | Positive | | Specify | | |
| ***Lipids – non fasting*** | Not done | | Normal | | Abnormal | | Cholesterol | | mmol/l |
| **Lipids – fasting** | Not done | | Normal | | Abnormal | | Cholesterol | | Tg |
| | | | | | | | HDL | | LDL |
| ***CSF*** | Not done | | Normal | | Abnormal | | Specify | | |

***TREATMENT***

**Antiplatelet agents:**

- Select all relevant boxes:
  - ASPIRIN ☐
  - ASPIRIN + DIPYRIDAMOLE ☐
  - TICLOPIDINE ☐
  - CLOPIDOGREL ☐

**Anticoagulation:**

- Heparin: YES ☐ NO ☐
  PROPHYLACTIC DOSE ☐ FULL DOSE ☐ IV ☐
  SC ☐
- Warfarin: YES ☐ NO ☐
- **Oxygen:** YES ☐ NO ☐
- **Antibiotics:** YES ☐ NO ☐
- **Anti-pyretics:** YES ☐ NO ☐
- **Insulin:** YES ☐ NO ☐
- **Surgery:** YES ☐ NO ☐

Specify: ☐

- **Neuroprotective agents:** YES ☐ NO ☐

Agent: ☐

- **Steroids prescribed (for stroke):** YES ☐ NO ☐
- **Mannitol:** YES ☐ NO ☐
- **IV fluids:**

Up at time of assessment ? YES ☐ NO ☐

IV fluids contain glucose? YES ☐ NO ☐

- ***Anti-hypertensives:***

Patient on anti-hypertensives prior to admission? YES ☐ NO ☐ UNKNOWN ☐

Anti-hypersensitives continued during admission? YES ☐ NO ☐

→ Is there evidence to suggest that the patient is a known hypertensive (history, end-organ damage, old notes)? YES ☐ NO ☐

UNKNOWN ☐

- Patient hypertensive on admission? YES ☐ NO ☐ UNKNOWN ☐

Anti-hypertensives given within the first week? YES ☐ NO ☐

ANTI-HYPERTENSIVES GIVEN **OTHER THAN** B BLOCKER, DIURETICS, ICCB, ACE INHIBITOR:

| |
|---|
| |

- Anti-hypertensives started after 1st week? YES ☐ NO ☐ UNKNOWN ☐
- Patient on anti-hypertensives at discharge? YES ☐ NO ☐ UNKNOWN ☐

*ASSESSMENT OF PROFESSIONALS ALLIED TO MEDICINE:*

- Select all relevant boxes:
  - Physiotherapy ☐
    - Within 24 Hours YES ☐ NO ☐
  - Speech therapy ☐
    - Within 24 hours YES ☐ NO ☐
  - Occupational therapy ☐
    - Within 24 hours YES ☐ NO ☐
  - Dietician ☐
    - Within 24 hours YES ☐ NO ☐

**ASSESSMENT:**

**Stroke Type:** (only complete if CT scan available)

- Select one:
  - TIA ☐
  - HAEMORRHAGE ☐
  - ISCHAEMIC INFARCT ☐
  - UNCERTAIN (NO CT) ☐
  - SAH ☐
  - RETINAL ARTERY OCCLUSION ☐
  - MULTI-INFARCT PICTURE ☐

**Complications:**

- Select all relevant boxes:
  - PAINFUL SHOULDER SYNDROME ☐
  - RECURRENT STROKE ☐
  - PNEUMONIA ☐
  - DVT ☐
  - MYOCARDIAL INFARCT ☐
  - SEIZURES ☐
  - DEPRESSION ☐
  - BEDSORES ☐
  - PROGRESSING STROKE (SYMPTOMS AND SIGNS EVOLVE OVER HOURS) ☐
  - OTHER ☐

Specify:

| |
|---|
| |

**Aetiology of ischaemic stroke:**

- Large vessel atherothromboembolic: PROBABLE ☐ POSSIBLE ☐
- Cardioembolic: PROBABLE ☐ POSSIBLE ☐
- Small vessel (lacunar): PROBABLE ☐ POSSIBLE ☐
- Acute ischaemic stroke of other aetiology: YES ☐ NO ☐

Specify: ☐

- Acute ischaemic stroke of unknown cause:
(incomplete workup) YES ☐
NO ☐

- Acute ischemic stroke of unknown cause:
(no probable aetiology despite complete workup) YES ☐ NO ☐

- Acute ischaemic stroke of unknown aetiology:
(more than one likely aetiology and a single likely aetiology cannot be determined) YES ☐ NO ☐

Specify: ☐

- **Aetiology of intracerebral haemorrhage:**

☐

- **Aetiology of SAH:**

☐

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**> > > > > > > COMPLETE BELOW ONLY IF YOU KNOW THE DETAILS OF THE FULL ADMISSION < < < < < <**

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**Duration of Hospitalisation:**

- Select all appropriate boxes:

| | | |
|---|---|---|
| ADMISSION WARD | ☐ ..... | DAYS ☐☐ |
| MEDICAL WARD | ☐ ..... | DAYS ☐☐ |
| STROKE UNIT | ☐ ..... | DAYS ☐☐ |
| OTHER WARD | ☐ ..... | DAYS ☐☐ |

- TOTAL ..... DAYS ☐☐

- **Death:** YES ☐ NO ☐

Cause: ☐

- *Discharge:*
  - Discharge to: HOME CARE ☐ REHABILITATION CENTER ☐ OTHER ☐

    Specify:

  - Home carer available YES ☐ NO ☐

    Partner? YES ☐ NO ☐

    Specify:

*Aspirin:*

- Should Aspirin be prescribed? YES ☐ NO ☐
- Was Aspirin prescribed? YES ☐ NO ☐

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**> > > > > > > > > > > > > > > > > > DO NOT COMPLETE THIS SECTION < < < < < < < < < < < < < < < < < <**

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- **Patient of interest?** YES ☐ NO ☐

  Reason:

- **Final diagnosis:** STROKE ☐

  TIA ☐

  RAO ☐

  OTHER ☐

  Use the following codes:

  Code **1** = possible (not for RAO)
  Code **2** = probable (not for RAO)
  Code **3** = definite
  Code **9** = not applicable

  (Include events within the last 6 months only.

  Multiple diagnoses may be coded)

  Reason:

- **First-ever-in-a-lifetime stoke:** YES ☐ NO ☐ UNABLE TO ASSESS ☐

  DEFINITE ☐ PROBABLE ☐ POSSIBLE ☐

*SUMMARY OF ASSESSMENT BY STROKE TEAM*

Thank you for referring your patient to the Stroke Team!

---

- **Date seen:** ☐☐ . ☐☐ . 20☐☐ Patient hospital number: ☐☐☐☐☐☐☐

- **HISTORY** (key features that make this a vascular event, or not):

| |
|---|
| |
| |
| |
| |

**EXAMINATION:**

- Cortical signs present: YES ☐ NO ☐
  A/Dysphasia ☐ Parietal lobe signs ☐
  Other ☐

  Specify:

- Cranial nerves involved: YES ☐ NO ☐

  List:

- Motor signs: YES ☐ NO ☐
  LEFT ☐ RIGHT ☐ BILATERAL ☐
  ARM ☐ LEG ☐

- Sensory signs: YES ☐ NO ☐
  LEFT ☐ RIGHT ☐ BILATERAL ☐
  ARM ☐ LEG ☐

- Cerebellar signs: YES ☐ NO ☐
  LEFT ☐ RIGHT ☐ BILATERAL ☐ AXIAL ☐

- Other key features:

***ASSESSMENT:***

- TIA ☐ STROKE ☐ INFARCTION ☐ HAEMORRHAGE ☐ SAH ☐ NOT SURE ☐
- FIRST EVER IN A LIFETIME ☐ RECURRENT ☐
- ANTERIOR CIRCULATION: YES ☐ NO ☐
- PARTIAL ANTERIOR CIRCULATION: YES ☐ NO ☐
- LACUNAR YES ☐ NO ☐
- TOTAL ANTERIOR CIRCULATION: YES ☐ NO ☐
- POSTERIOR CIRCULATION: YES ☐ NO ☐

***SUGGESTION/S:***

- Further investigation/s:
- Treatment:
- Referral:

- **SIGN:**

# APPENDIX H: ETHICS APPROVAL FOR THE TINTSWALO HOSPITAL STROKE REGISTER

**Neurology Unit**
**Department of Medicine**

**Tel / Fax: 488 4430**
**Email: connorm@chiron.wits.ac.za**

**Professor P E Cleaton-Jones**
**Committee for Research on Human Subjects (Medical)**

12 March 2001

Dear Professor Cleaton-Jones

**RE: EXTENSION OF ETHICS APPROVAL – TINTSWALO HOSPITAL STROKE REGISTER**

I established the Johannesburg Hospital Stroke Register last year following unconditional ethics approval from the Committee for Research on Human Subjects (Medical) – Protocol number M00/03/7 considered on 00/03/31.

I now have funding to expand this urban-based register to Tintswalo Hospital in Acornhoek, Bushbuckridge, Northern Province in order to give a rural perspective. The register is to be established at Tintswalo Hospital using the same methodology, information sheets, questionnaires, and data will be handled in the same way as outlined for the Johannesburg Stroke Register. The day-to-day running of the register at Tintswalo will be managed by: a Primary Health Care Nurse Trainer, Mr. Freddy Sego; Dr. Thinus Coetzee a medical officer and the hospital superintendent; and Dr. Paul Pronyk, a specialist physician. I will personally assess stroke patients entered onto the register on a fortnightly basis.

As in the Johannesburg Stroke Register management of the stroke patients will follow usual practice in the area. Indeed the implementation of the register should improve general patient care following education of local staff in stroke care, increased awareness of the correct management of stroke, and exposure to physicians experienced in stroke management.

Please would you consider extending the Johanneburg Hospital Stroke Register ethics approval to the Tintswalo Hospital Stroke Register? If, however, you feel that a new application is necessary, I would be happy to submit one.

Yours sincerely

**DR. M D CONNOR: MBBCh, FCP(SA), FCP(Neurology)(SA)**
**Consultant Neurologist, University of the Witwatersrand**

**APPROVED**
20 APR 2001
**PROF. PE CLEATON-JONES**

please see Linn Anna.

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