TRENDS AND ETHNIC DISPARITIES IN THE INCIDENCE AND OUTCOME OF STROKE IN AUCKLAND, NEW ZEALAND OVER 20 YEARS.

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ABSTRACT

Aims: The aims of this thesis were to investigate trends and ethnic disparities in the incidence and outcome of stroke in Auckland, New Zealand between 1981 and 2003.

Methods: Trends were assessed using information from the three Auckland Regional Community Stroke (ARCOS) studies, conducted in people (aged ≥15 years) in Auckland, during 12-month calendar periods in 1981-1982, 1991-1992, and 2001-2002. These studies used comparable definitions and case finding methods and have been shown to meet the stringent criteria for a population-based "ideal" stroke incidence study. Rates were calculated using Poisson distribution and are presented with 95% confidence intervals. Trends in survival were assessed using Cox Proportional hazards regression modelling.

Results: Overall trends in the incidence and event rates of stroke declined across the study period. These declines were significant in males and for the ages 65 to 74 years only. However, growing disparities in the rates of stroke between the major ethnic groups in New Zealand were found, with significant declines in New Zealand Europeans and increases in Māori and Pacific populations.

Dramatic improvements in survival over the study period were also found, with the greatest improvement in the acute period, within the first 28-days after stroke. Adjustments for patient or disease severity factors strengthened the survival model. However, adjustments for care/service factors nullified the survival model, thus explaining most of the improving trend.

Conclusions: The small declines in the incidence of stroke, improvements in survival and the ageing of the New Zealand population will lead to data dramatic increases in the number of people living with the effects of stroke. To maintain stable numbers of strokes occurring, more intensive prevention strategies need to target high-risk populations and population-wide health education strategies are needed to improve the health of the general population, hence reducing the risk of stroke.

To my parents

Phil and Judy Carter,

for their continued support and encouragement.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACE Inhibitor	Angiotensin Converting Enzyme Inhibitor
AF	Atrial Fibrillation
AIC	Akaikes Information Criterion
ANOVA	Analysis of Variance
ARCOS	Auckland Regional Community Stroke studies
BMI	Body Mass Index
C	Community Case Ascertainment
CF	Case Fatality
CHD	Coronary Heart Disease
CI	Confidence Interval
CT	Computed Tomography
CTRU	Clinical Trials Research Unit
CVA	Cerebrovascular Disease
D	Death Certificate Case Ascertainment
DALY	Disability Adjusted Life Years
DRG	Diagnostic Related Grouping
FDA	Federal Drug Administration
FSP	Framingham Stroke Profile
GCNKS	Greater Cincinnati Northern Kentucky Stroke study
GCS	Glasgow Coma Score
GP	General Practitioner
H	Hospital Case Ascertainment
HR	Hazard Ratio
ICD	International Classification of Diseases
ICH	Intracerebral Haemorrhage
IPA	Independent Practitioners Associations
IQR	Inter-quartile Range
ISC	Ischaemic Stroke
ISEI	International Socioeconomic Index
LR	Likelihood Ratio
MONICA	Monitoring of Trends and Determinants in Cardiovascular Disease
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging

N	Number of strokes
NHANES	National Health and Nutrition Examination Surveys
NIHSS	National Institute of Health Stroke Scale
NOMAS	Northern Manhattan Stroke study
NZ	New Zealand
NZ/European	New Zealand European
NZHIS	New Zealand Health Information System
NZSCO	New Zealand Occupational status
NZSEI	New Zealand Socioeconomic Index
OCSP	Oxford Community Stroke Project
OR	Odds Ratio
OXVASC	Oxford Vascular Study
PH	Proportional Hazards
PICH	Primary Intracerebral Haemorrhage
rFVIIa	recombinant activated factor VIIa
RR	Rate Ratio
rtPA	recombinant tissue plasminogen activator
SAH	Subarachnoid Haemorrhage
SD	Standard Deviation
SER	Standardised Event Ratio
SES	Socioeconomic Status
SF	Stroke Foundation
SLSR	South London Stroke Register
SMR	Standardised Mortality Ratio
TIA	Transient Ischaemic Attack
TOAST	Trial of Org 10172 in Acute Stroke Treatment
UK	United Kingdom
UND	Undetermined Stroke Type
US	United States
WHO	World Health Organization

STATEMENT OF PARTICIPATION

The research presented in this thesis was based in part on data obtained from the third Auckland Regional Community Stroke (ARCOS) study conducted in Auckland between 2002 and 2003 by investigators of the University of Auckland. Professor Craig Anderson, formerly the co-director of the Clinical Trials Research Unit (CTRU) was the primary investigator of this study and the main supervisor of this PhD. Associate Professor Anthony Rodgers was maintained as the University of Auckland based supervisor after Professor Anderson moved to The George Institute for International Health in Sydney. Professor Ruth Bonita was responsible for the development, conduct and data from the two previous ARCOS studies conducted in 1981-1982 and 1991-1992.

Initially, I was brought into the study team to advise on statistical methodology and provide projections of potential sample size calculations. I was part of the Operations Committee that met weekly for the study, the Steering Committee that met monthly and the Qualitative and socio-economic analysis group that met bi-monthly to develop and conduct qualitative interviews of stroke victims and their informal caregivers of four ethnic groups. At these meetings I would provide updates of the notification and registration of cases to the study. I was involved in developing the Manual of Procedures for the study and the development of face to face and telephone questionnaires. It was through this process that Professor Anderson and I developed the proposal for this PhD.

As part of this study I was responsible for all statistical analyses and the supervision of a junior statistician who checked the results. I was also responsible for liaising with the New Zealand Health Information Service to sort through the notifications of all hospital discharges for stroke, match the names with the current ARCOS database and provide the study manager, Faith Mahoney, with a list of names of patients to be followed up in each hospital in the Auckland region. I worked closely with the data management and information technology teams at the CTRU to develop and validate the

data base with which the data would be entered by the data entry team of the data management team and the permanent Oracle 8i database. All data was then extracted into SAS 8.1 from the Oracle database.

As part of this thesis I spent a considerable amount of time sorting through a mass of SAS datasets from the previous studies conducted in 1981-1982 and 1991-1992. All of these data were reviewed and organised and copied into a permanent Oracle 8i database with the help of the data management and information technology teams at the CTRU. The data was organised into datasets by forms and follow up studies. As part of the continuation of the 1981-1982 and 1991-1992 ARCOS studies I developed a 21 year and 11 year follow up of all of the survivors, respectively. Ethical approval for this study was provided by the Auckland Ethics committee. Through this study I supervised third year medical student, who contacted all those cases who were not known to have died from these studies and completed a short telephone questionnaire about their current residence and health status and their health related quality of life using the Short Form 36 questionnaire (SF36).

PUBLICATIONS AND PRESENTATIONS

To date the following publications have resulted from this PhD thesis:

1. Tobias M, Cheung J, **Carter K**, Feigin F. Stroke surveillance: Population-based estimates and projections. *Australia and New Zealand Journal of Public Health*. 2007 (In press).
2. **Carter KN**, Anderson CS, Hackett ML, Barber PA, Bonita R. Improved survival after stroke is admission to hospital the major explanation? Trends analyses of the Auckland Regional Community Stroke (ARCOS) studies. *Cerebrovascular Diseases.* 2007; 23: 162–168.
3. Dyall L, **Carter K**, Bonita R, Anderson C, Feigin V, Kerse N, Brown P. Incidence of Stroke in Women in Auckland, New Zealand. Ethnic Trends Over Two Decades. *NZ Med J*. 2006;19:1245
4. **Carter KN**, Anderson CS, Hackett ML, Feigin V, Barber PA, Broad JB, Bonita R, on behalf of the Auckland Regional Community Stroke (ARCOS) Study Group. Trends in Ethnic Disparities in Stroke Incidence in Auckland, New Zealand, During 1981 to 2003. *Stroke*. 2006;37:56-62.
5. Feigin V, **Carter K**, Hackett M, Barber PA, McNaughton H, Dyall L, Chen M-h, Anderson C. Ethnic disparities in incidence of stroke subtypes: Auckland Regional Community Stroke Study, 2002-2003. *The Lancet Neurology*. 2006;5:130-139
6. Anderson CS, **Carter KN**, Hackett ML, Feigin V, Barber PA, Broad JB, Bonita R, on behalf of the Auckland Regional Community Stroke (ARCOS) Study Group. Trends in Stroke Incidence in Auckland, New Zealand, During 1981 to 2003. *Stroke*. 2005;36:2087-2093
7. **Carter KN**, Hackett ML, Anderson CS. Disparities in the incidence of stroke in Asian populations in Auckland, New Zealand. Inaugural International Asian Health Conference. Conference Proceedings. 2004.
8. Feigin VL, **Carter K**. Editorial Comment--Stroke Incidence Studies One Step Closer to the Elusive Gold Standard? *Stroke.* 2004;35(9):2045-2047.
9. Anderson CS, **Carter KN**, Brownlee WJ, Hackett ML, Broad JB, Bonita R. Very Long-Term Outcome After Stroke in Auckland, New Zealand. *Stroke.* 2004;35(8):1920-1924.

To date the following presentations have resulted from this PhD thesis:

1. Stroke Society of Australasia. Adelaide, October 2006. Oral Presentation. How preventable is stroke? Projecting the future burden of stroke from the Auckland Regional Community Stroke (ARCOS) study data.
2. New Zealand Rehabilitation Association. Auckland, November 2005. Oral Presentation. Trends in ethnic disparities of stroke in Auckland New Zealand, 1981-2003.
3. School of Public Health seminar series, University of Sydney, October 2005. Invited lecture. Ethnic variation in Stroke.

4. Stroke Society of Australasia. Melbourne, September 2005. Oral Presentation. Can we explain any improvement in stroke survival?: Results from population-based incidence studies in Auckland, New Zealand over 20 years
5. European Stroke Conference. Bologna, Italy, May 2005. Oral Presentation. Continued improvements in short-term survival after stroke: Experience from population-based studies in Auckland, New Zealand.
6. Inaugural Asian health and Wellbeing Conference, Auckland, November 2004. Oral Presentation. Ethnic disparities and trends in stroke in Auckland over 20 years.
7. Stroke Society of Australasia. Hobart, October 2004. Key-note presentation. Ethnic variation in Stroke.
8. Stroke Society of Australasia. Hobart, October 2004. Oral Presentation. Complex trends in stroke incidence in Auckland, New Zealand during 1981-2003.
9. World Stroke Congress. Vancouver, Canada, June 2004. Poster presentation. Ethnic disparities in trends in stroke rates in Auckland, New Zealand during 1981-2003.

1. INTRODUCTION

> *"Almost 6 million people will die from stroke in 2005, and nearly 90% of these deaths will occur in less-affluent countries. Without urgent action, deaths from stroke will increase over the next decade by 12% globally – and by 20% in low-income countries." The Lancet Neurology (2005)*[1]

Stroke is a chronic, disabling, non-communicable disease of increasing global importance. Due to the ageing and adverse lifestyle changes in most populations around the world, the risk of stroke is mounting, especially in developing countries.[2] Currently, stroke is ranked the second single leading cause of death worldwide, a position that is expected to remain stable for at least the next few decades.[3, 4] It has been estimated that 15 million people worldwide suffer a stroke each year. Of these, one third will die and at least another third will be left with varying degrees of physical disability and mental ill-health, placing extra social and economic burden on families, health systems and societies.[5] As a result, stroke is the second leading cause of loss of healthy years of life due to death and disability, as quantified by the metric disability adjusted life years (DALYs).[4, 6] These data, along with others from the Global Burden of Disease study,[4, 7] have prompted the World Health Organization (WHO) to recognise the impending worldwide epidemic of chronic disease (including stroke) and call for action to prevent an increase in chronic disease worldwide.[8, 9]

Research on variations and disparities in health, be it between age groups, ethnic groups or socio-economic groups, provides information on the rate and outcome of disease. This assists the development of appropriate prevention and treatment strategies for the population as a whole and enables the targeting of high risk groups. A number of socio-demographic variables are well recognised to be associated with increased risk of having a stroke and

subsequent death from stroke. Essentially, stroke is a disease of the elderly, with over 80% of all events occurring in people over the age of 65.[10] Hence, age is the most important risk factor for stroke and this risk has been shown to increase exponentially with age.[11] Several studies conducted in developed countries have shown an increased risk of stroke among ethnic minority populations, with double the rate of stroke and higher risk of dying, in ethnic minority groups as compared to the majority (typically white) populations.[12-16] Ethnic minorities also tend to have their strokes at younger ages and these are more often more severe and of haemorrhagic form than white populations.[12, 13, 15-17] Possible explanations for these disparities are differences in the prevalence of potentially modifiable vascular risk factors such as hypertension, obesity and diabetes, as well as socio-economic and other factors including variation in access to health care.[18]

With the rapid ageing of populations in many countries, especially developing nations,[3, 19] the absolute numbers of strokes are likely to increase even if rates are stable or are declining over time.[20, 21] It has been estimated that there will be a doubling in the numbers of stroke deaths in the United States (US) over the next three decades, with the greatest increases in minority groups, which will outpace the overall growth of the population.[22] However, as stroke is essentially a preventable and to a certain extent, treatable disease, efforts can be made to reduce the burden of the disease and slow down or even halt the projected increases in the number of strokes. Therefore, untangling the puzzle of past and future trends in the burden of stroke is a matter of pressing importance because of its health impact on the community, especially the elderly, who constitute the fastest-growing segment of the population. If the incidence of stroke were to stabilise rather than fall, there would soon be an absolute increase in the numbers of disabled survivors of stroke, with major consequences for the health system and society. Population-specific data on trends in the incidence of stroke can provide important feedback on preventative strategies, while patterns of case fatality and disability bear a closer relationship to the management of acute stroke.

The understanding of the burden of, and trends in, stroke is reliant on the availability of high quality epidemiological data, investigating the risks and consequences of the disease. There is much variation in the surveillance of stroke in populations, providing varying degrees of bias in estimates of the rates and outcomes of stroke. Mortality data are most commonly used, as it is collected through routine registers in most countries. However, these registers capture only one third of all strokes,[5] and the data quality is variable in developing countries.[23] Hospital-based stroke registers are also used to survey stroke in a population, however, such registers may miss up to 40% of out-of-hospital cases.[24, 25] Ideally, the epidemiological study of stroke should be undertaken in a population-wide context, as a large proportion of the burden of stroke is borne by families and by health services outside the hospital sector.[26, 27] However, population-based studies are particularly challenging,[27, 28] so they are relatively rare when compared with studies using the convenience of mortality data, hospital-based stroke registers, or incidence studies in selected (younger) age groups. Even population-based studies may lead to biased estimates unless standard definitions, high quality methods of case ascertainment and analysis are used. Therefore, Malmgren et al. published a list of 12 methodological criteria in 1987 to standardise definitions and case ascertainment.[28] This involves a prospective study design, using multiple and overlapping sources of case notification, in order to identify all stroke events with a confirmed pathological diagnosis in a defined population. Such methods provide the least biased estimates of stroke and enable comparability between populations.[28] These criteria have evolved, being updated over the years, with changes in case-finding methods and improvements in stroke diagnosis and management. Such studies fulfilling all or most of the criteria have been termed “ideal” stroke incidence studies to identify them as unique, well designed studies with the least biased data, and serve as the gold standard for undertaking studies of the incidence of stroke.[26, 27, 29-31]

Much of the data on temporal and geographical trends in the rate of stroke has arisen from mortality studies. Trends in stroke mortality have been falling in many developed countries, including New Zealand, Australia and the United

States, since the early 1950s, although the rate of this decline appears to have decelerated recently.[32-34] However, there is still great variability in the rates of mortality from stroke around the world, with ongoing high rates in Eastern Europe and Asia.[35] Temporal trends in stroke mortality around the world are diverging with increasing rates in developing countries and decreasing rates in more affluent, industrialised countries.[35, 36] To what extent these trends relate to trends changes in the incidence or outcome from stroke is uncertain.

There have been varied reports of trends in event rates and outcome from stroke due to variability of study designs, methodology and in the quality of the studies. Declines in the incidence of stroke were found in the mostly homogeneous populations who participated in the WHO Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) collaboration, except for Eastern European populations where trends increased over time.[37] Most recently, a large decline in the rate of incident stroke was found over 20 years in Oxford, but short-term case fatality was stable.[38] Other studies have found no change or even increases in the incidence of stroke and variable changes in case fatality over time. Due to the variability across a number of populations, even in ideal stroke incidence studies, there is a need to investigate trends in the rate of stroke in a stable, multi-ethnic population, using reliable and consistent data.

Much of the data on temporal trends in stroke has been collected within homogeneous developed populations. The limited data on ethnic disparities in trends in the rate of stroke over time have shown diverging trends among ethnic groups within developed countries. Although, stroke mortality has declined in all ethnic groups in New Zealand, the gaps between ethnic minority groups and European New Zealanders have increased due to smaller declines in Māori and Pacific populations.[39, 40] Greater increases in the rates of hospitalised stroke have been shown for African Americans when compared to other ethnic groups in the US,[41] which in turn has been proposed as an explanation for the excess stroke related mortality in African

Americans.[42, 43] It has also been shown that the disparity in stroke rates between ethnic groups in the US is not changing over time.[43]

As the largest Polynesian city in the world, with a relatively large stable indigenous Māori population and high immigration from Pacific and Asian countries, Auckland, New Zealand, provides a unique opportunity to investigate trends in the incidence and outcome from stroke among a multi-ethnic population. Previous studies of stroke in Auckland have shown that Māori and Pacific people have higher rates of stroke, and on average these occur 10-15 years earlier than New Zealand Europeans.[13] Greater deaths and poorer functioning from stroke have also been shown to be worse for Māori and Pacific New Zealanders.[13, 44] The New Zealand population is ageing at an alarming rate, with the population aged 65 years and older which is expected to grow by 72%, between 2001 and 2021.[19] Māori and Pacific populations are also ageing at a quicker rate than New Zealand Europeans, leading to a larger group of people being at risk for stroke.[19] Ethnic disparities in health outcomes in New Zealand should be investigated to allow for more culturally-appropriate planning of strategies to improve the management of risk factors, acute hospital care, rehabilitation and continuing care for people affected by stroke.

The Auckland Regional Community Stroke (ARCOS) studies of 1981-1982,[45, 46] 1991-1992,[26] and 2002-2003 are among the few population-based stroke studies that are recognised as meeting the criteria for an ideal stroke incidence study. This is the first time that three large population-based ideal stroke incidence studies have been used to investigate trends in the rate of stroke and outcome from stroke across two decades enabling the investigation of the effects of socio-demographic changes on the rate of stroke over time. The results of this study may identify groups at high risk for stroke and may be used to inform future research and health care planning in stroke both in New Zealand and worldwide. This data is particularly applicable to other populations with ethnically disparate communities, where resources may be too limited to conduct such a large population-based study on stroke.

The aim of this thesis is to compare data from the third ARCOS study conducted during 2002-2003 with that from the two previous studies (1981-1982 and 1991-1992), to investigate the effects of socio-demographic changes on trends in stroke incidence and outcome after stroke. Explanations for any trends and disparities will be explored through associations with trends in patient demographics, vascular risk factors, hospital management, and stroke care in the community. These trends in stroke rates and outcome will be applied to the New Zealand population to estimate the number of stroke events and deaths occurring now and in the future, so informing health care planners and policy makers of the future burden of stroke in New Zealand.

The specific aims of this thesis are:

- to describe the current burden of stroke on the individual, the family and the community, and ways to reduce the burden through the control and modification of common risk factors for stroke and methods of treatment and prevention (Chapter 2);
- to evaluate the methods used to survey stroke in a population and review the literature on temporal trends of stroke mortality and incidence, providing a systematic review of trends in stroke rates in ideal stroke incidence studies, explanations for these trends and the future burden of stroke (Chapter 3);
- to outline the standardised methods and definitions used in the three ARCOS studies and the statistical methods used for analysis (Chapter 4);
- to describe trends in case ascertainment, case mix, and stroke incidence and event rates by age and sex across the three studies (Chapter 5);
- to describe ethnic disparities in trends in case mix, and stroke incidence and event rates by ethnicity across the three studies (Chapter 6);
- to describe and model trends in mortality and survival across the three studies (Chapter 7);
- to project the future burden of stroke in New Zealand (Chapter 8);
- to present conclusions on trends in stroke and its implications for health policy and practice in New Zealand (Chapter 9).

2. STROKE AND ITS EFFECTS

Annually, 15 million people worldwide will suffer a stroke and of these, a third will die and another third will be left severely disabled, placing extra burden on families and communities.[5] Nearly 90% of the worldwide burden of stroke occurs in developing (low and middle income) countries.[1] Stroke is also a heterogeneous disorder, with a greater burden falling among the elderly and ethnic minority groups. The surveillance of stroke involves the ongoing collection of information on the number of strokes and associated risk factors occurring in a well-defined population. The monitoring and analysis of the incidence and prevalence of stroke allows a better understanding of the aetiology of the disease and the impact of primary and secondary prevention strategies. It is essential to have high quality information for assessing healthcare needs and in the planning and implementation of health policies, but unfortunately this type of information is limited.

This chapter provides an overview of how stroke is measured in a number of populations and how it is related to lifestyle and risk factors. The first section provides a description of what a stroke is and how it is commonly defined in research. The second section describes the common non-modifiable and modifiable risk factors for stroke. The third section describes how the incidence of stroke can be reduced through the primary prevention of modifiable risk factors. The fourth section describes demographic and geographical variations in the rates of stroke mortality and incidence. The fifth section describes variations in different outcome measures of stroke. The final section describes common acute treatment and care for stroke patients and secondary prevention measures used to prevent recurrent stroke.

2.1. What is a Stroke?

The term “stroke” refers to a clinical syndrome of vascular origin, typified by rapidly developing signs of focal or global disturbance of cerebral functions lasting more than 24 hours, or leading to death.[47] In contrast, a transient ischaemic attack (TIA) is defined as a syndrome with rapidly developing signs

of focal or global disturbance of cerebral functions that subside within 24 hours of onset.[48] TIAs have been shown to be predictive of a more major stroke in the future.[49, 50]

A stroke occurs when the blood flow to the brain is impaired, resulting in a loss of oxygen and nutrients to the brain, thus causing damage to the brain tissue. Common signs and symptoms of having a stroke include hemiparesis, aphasia, dysphagia, dysarthria, hemianopia, ataxia, apraxia, severe headache and/or disturbed consciousness.[51] Signs and symptoms usually occur suddenly or are known upon waking.

There are two major pathological types of stroke: ischaemic and haemorrhagic.[52] An ischaemic stroke typically occurs when an artery bringing blood to the brain gets blocked by an embolus (blood clot) or through atherosclerosis (thickening of the artery walls). The neurons in the area of the blockage are deprived of blood and oxygen and hence die, causing part of the brain to stop working and body functions to be impaired. Ischaemic stroke can be further classified according to their pathophysiology, into large-vessel atherothrombosis, cardioembolism, lacunar (small-vessel), other determined cause (dissection, sickle cell disease) and undetermined ischaemic stroke (ischaemic stroke that cannot be attributed to a single cause).[53, 54] Ischaemic strokes are the most common form of stroke and typically represent over 80% of all strokes in developed populations. Haemorrhagic strokes are generally more severe than ischaemic strokes with two main subtypes: a primary intracerebral haemorrhage (PICH) and a subarachnoid haemorrhage (SAH). A PICH occurs when a small artery in the brain ruptures or leaks blood into brain tissue forming a haematoma and hence, damaging the cells. PICH occurs mostly in the setting of chronic hypertension and is the most frequent form of haemorrhagic stroke. A SAH most frequently occurs from an the rupture of a cerebral aneurysm, where a weakness in the wall of an artery forms a balloon and ruptures, leaking blood into the subarachnoid space and cerebrospinal fluid.[54] SAH is a severe form of stroke with over 50% of patients dying in the first three months and it is typically preceded by a sudden severe headache. Other secondary causes of haemorrhagic stroke are

arteriovenous malformations, anticoagulation therapy, bleeding disorders and trauma.

The diagnosis of stroke is typically based on the clinical assessment of the patient, which has been shown in epidemiological research to be a reliable indicator of the incidence of stroke.[55, 56] The WHO standard diagnostic criterion for defining a stroke is "the sudden onset of focal or global neurological deficit lasting 24 hours or longer or leading to death, of presumed vascular origin".[47] This definition includes PICH and SAH, but excludes cases of TIA or silent stroke detected by neuroimaging only. A popular approach used to further classify ischaemic strokes is according to the TOAST criteria (from the Trial of Org 10172 in Acute Stroke Treatment); large artery disease, cardioembolic, small artery disease or other ischaemic stroke.[53] An alternate classification of ischaemic stroke subtypes was introduced in the Oxfordshire Community Stroke Project: total anterior circulation infarction, partial anterior circulation infarction, posterior circulation infarction, and lacunar infarction.[57] Neuroimaging such as computed tomography (CT) or magnetic resonance imaging (MRI) is used to differentiate between stroke types and ischaemic stroke subtypes, to identify the location of the lesion and to direct the correct treatment of acute stroke. Lumbar puncture is sometimes used to identify patients with suspected SAH but with normal neuroimaging, where blood is found in the cerebrospinal fluid.

2.2. Risk Factors for Stroke

There are a number of risk factors that have consistently been shown to be associated with higher rate of stroke. Some of these are non-modifiable such as age, sex, ethnicity and being of lower socioeconomic status. However, some are potentially modifiable or controllable, such as hypertension, high cholesterol, having diabetes, a history of heart disease, being overweight or obese, smoking, and living a physically inactive lifestyle.

2.2.1. Non-Modifiable Risk Factors

Investigating the risk of stroke in non-modifiable risk factors such as age, sex and ethnicity enable the identification of high-risk groups and aiding the

development of health strategies and policies, targeting the reduction of stroke burden among these groups. People recognised as belonging to a high risk group may be identified for more intensive primary prevention of stroke through the control of modifiable risk factors.

Age and sex

Age is the most important risk factor for stroke and stroke is essentially a disease of the elderly, with over 80% of strokes occurring in people over the age of 65.[10] Stroke risk increases exponentially with age. The risk of stroke doubles with each successive decade of age after the age of 55 years.[11] Stroke is uncommon in children younger than 15 years of age and if it does occur, it is usually due to sickle cell disease. Males tend to have their strokes on average six years younger than females,[58] and at all ages, males have a higher risk of stroke than females.[11, 59] However, females are at higher risk of having a SAH than males in all age groups.[60-62] Stroke has also been shown to affect different ethnic groups at different ages, with minority groups tending to have their strokes at younger ages.[13, 15]

Ethnicity

It has been well established that ethnicity is associated with disparities in health and access to healthcare.[40, 63] In particular, ethnic minority groups are associated with an increased risk of non-communicable disease worldwide.[8] However, ethnicity is a complex and heterogeneous concept and is difficult to define as it encompasses a wide range of personal characteristics, such as biology, history, culture, language, and religion.[64] Ethnicity is also commonly confused with the term race which is used to describe genetic or biological differences between groups.[65, 66] Ethnicity is useful in epidemiological research as it highlights the social and cultural characteristics of people and not just their biology.[67] However, ethnicity is not a dichotomous variable. For example, most people identify with a range of different heritages, cultures and languages and typically do not want to be forced to identify with just one ethnic group.[64, 68] It has also been shown that people may change the ethnic group that they identify with through changes in definitions and politics.[69] Researching health in developing countries is difficult and costly, yet is highly

needed due to large projected increases in age in these countries.[3] So an advantage of researching health and ethnicity in developed countries is that the results may be extended to indigenous populations in developing countries. Researching migrant populations in developed countries may also highlight how the lifestyle adoption of the new country (acculturation) may be protective or detrimental to the health of that migrant population.[70]

It has been well documented that ethnicity, in particular ethnic minority groups, are associated with an increased risk of stroke and increased mortality.[12, 15-17] In the US, African Americans carry a disproportionate burden of strokes relative to their number in the population,[71] and have double the rate of stroke compared to white Americans.[72] Possible explanations for the increased risk of stroke in minority groups are lower levels of income and occupation and the increased prevalence of potentially modifiable vascular risk factors such as hypertension, obesity and diabetes in their populations.[73, 74] Ethnic disparities in stroke rates and outcomes will be explored in more detail in the following sections.

Socioeconomic Status

Socioeconomic status (SES) incorporates income, education, occupation and socio-cultural factors. Lower levels of SES are associated with ethnic minority groups and increased mortality.[75] SES is recognised as an important risk factor for stroke, with the incidence and poor outcome increasing as socioeconomic deprivation increases.[76-79] Stroke risk has been shown to be inversely related to income, with higher income associated with lower mortality.[77] Men in manual occupations have also been shown to be 60% more likely to die from stroke than professionals.[78] Patients with stroke from low SES backgrounds also tend to be younger, have worse outcomes, and require more care after their stroke.[80, 81] It has been shown in an international overview of socioeconomic inequalities in stroke mortality that countries such as the Nordic welfare states which have adopted an egalitarian healthcare system, have small differences in mortality between upper and lower SES groups.[76]

The relationship between ethnicity and SES is varied. SES may explain most of the association between ethnicity and stroke, however, ethnicity does not explain the association between SES and stroke.[82] In New Zealand, even after controlling for age and ethnicity, stroke mortality rates in the lowest SES group were approximately twice that of the highest group.[83]

Family History

Having a positive family history of stroke has also been associated with increased risk.[84] However, recent reports provide conflicting results and data is limited due to the complexities of genetic studies. In a recent meta-analysis, family history of stroke was found to be only a moderate risk factor for future stroke.[85] It is difficult to determine whether a positive family history is the result of shared genes, shared environment, or both. However, having a positive family history of stroke may be a marker for the presence of other more established vascular risk factors.[86]

2.2.2. Modifiable Risk Factors

There are a number of well known risk factors for stroke that are potentially modifiable or controllable through drug treatment or simple lifestyle changes, thereby reducing the risk of having a new or recurrent stroke. Up to 76% of stroke burden, worldwide, may be prevented by controlling modifiable risk factors, such as reducing or controlling hypertension, hyperlipidaemia, body mass index, and tobacco use, and by increasing fruit and vegetable intake and physical activity.[87]

Hypertension

Hypertension (high blood pressure) continues to be the most important modifiable risk factor for both ischaemic and haemorrhagic strokes. There is a log-linear relationship between increasing levels of blood pressure and the risk of both ischaemic and haemorrhagic stroke,[88, 89] with a steeper relationship in haemorrhagic than ischaemic strokes. Up to 62% of strokes worldwide are attributable to systolic blood pressure levels >115 mmHg.[90] Hypertension has been shown to be more prevalent in ethnic minority groups

in a number of developed countries,[74, 91-93] and Mexican Americans have the lowest rates of controlled hypertension in the US.[94]

Hyperlipidaemia

Hyperlipidaemia (high blood cholesterol) is an important risk factor for cardiovascular disease, particularly heart disease but also ischaemic stroke. The relationship between cholesterol and stroke is complex as the association varies by age and between stroke subtypes. A higher association with ischaemic strokes has been shown with a negative or null association with haemorrhagic strokes.[95] There has been much debate about the association between cholesterol levels and the risk of stroke, with no definitive study finding a consistent relationship between the reduction of cholesterol and the reduction of the risk of stroke.[96-98] However, high cholesterol has been estimated to cause 15% of stroke worldwide,[99] with 32% of ischaemic stroke attributable to a total cholesterol level >3.8mmol/l.

Heart Disease

Various cardiac diseases are associated with an increased risk of stroke as they share many common risk factors. Myocardial infarction has long been recognized as a risk factor for stroke, with the risk of stroke highest in the first five days after myocardial infarction.[100] The risk of stroke has been shown to increase twofold with a history of coronary heart disease, and three to fourfold with a history of cardiac failure.[101] Therefore, the primary prevention of stroke through the control of modifiable risk factors is particularly important in patients with a history of heart disease.[102] In studies of ethnic disparities in cardiovascular risk factors, it has been shown that white (majority) populations have a higher prevalence of cardiac diseases (coronary heart disease, atrial fibrillation) than ethnic minority groups.[92, 93] Stroke is also a major complication following coronary operations (coronary artery bypass, carotid endarterectomy), with postoperative strokes contributing significantly to increased perioperative mortality.[103, 104]

Atrial fibrillation (AF) is the most common cardiac arrhythmia and treatable cardiac precursor of stroke. Among patients with AF, there is a fivefold

increase in the risk of stroke and up to a quarter of all strokes occurring in the elderly can be directly attributed to AF.[101, 105] Strokes associated with AF are especially large and disabling, and occur due to cardioembolism.[106] The risk of stroke in patients with AF, can be greatly reduced with anticoagulation treatment (Wafarin).[107] However, many patients with AF still do not receive anticoagulation therapy,[108] due to concerns regarding an increased risk of haemorrhagic stroke.[109]

Diabetes

The presence of diabetes mellitus (typically Type II diabetes) is a well known risk factor for stroke. There is a two to sixfold increase in the risk of having a stroke for diabetic compared to non-diabetic patients.[110-112] Diabetes has also been shown to be more prevalent in ethnic minority groups, explaining part of the increased risk of stroke among these groups.[74, 93, 111, 113] However, the true incidence and prevalence of diabetes in the population is under-estimated as many patients with diabetes are asymptomatic and go undiagnosed.[114] Hypertension is also strongly related to the presence of diabetes, thus the combination of these risk factors increases the risk of stroke dramatically.[115]

Body Mass Index

Being overweight (body mass index [BMI] ≥ 25) or obese (BMI ≥ 30) increases the risk of stroke through the increase of other vascular risk factors such as hypertension, hyperlipidemia or diabetes. Overweight and obesity are more prevalent in ethnic minority groups in developed countries.[74, 93, 111] There is a continuous relationship between BMI and non-fatal stroke, with a stronger relationship between BMI and ischaemic stroke.[116] A reduction in BMI has been shown to reduce the risk of both ischaemic and haemorrhagic stroke.[117]

Smoking

It has been estimated that tobacco smoking accounts for 9% of the total deaths worldwide,[99] and as the rates of smoking have increased dramatically in developing countries over the past decade, deaths attributed to smoking are expected to rise even more.[118] Active smoking is well recognised as a risk

factor for stroke and is associated with a doubling of the risk of ischaemic stroke.[119] Smoking is associated with increased blood pressure and the development of atherosclerosis, leading to increased risk of ischaemic stroke.[110] Cigarette smoking has been shown to be the most important modifiable risk factor for SAH.[120, 121] Former smokers are also at increased risk for stroke, however, research has shown that this risk decreases with increased periods of cessation.[122-124] Passive smoking, working or living in a smoky environment, also increases the risk of stroke.[125]

Physical Activity

There is an inverse relationship between physical activity (energy expenditure) and stroke risk. There is a dose response relationship between increased levels of physical activity and decreased risk of ischaemic stroke.[126] Even moderate levels of physical activity are reported to have a protective effect on stroke risk.[127] Globally, physical inactivity has been shown to account for 3.3% deaths worldwide and 11% of ischaemic stroke.[128] The association between physical activity and ischaemic stroke is thought to be through the reduction of atherosclerotic plaques, hypertension and BMI.[126]

Other Risk Factors

There are a number of other potentially modifiable risk factors for stroke. Carotid stenosis is reported to occur in over 50% of the population aged ≥ 65 years, which is related to an annual risk of stroke of about 2%.[107, 129] Sickle cell disease is associated with a higher risk of stroke in children.[130] Increased alcohol intake has been associated with an increased risk of stroke, whereas light or moderate drinking may have a protective effect on the risk of ischaemic stroke.[131] There is evidence of an increased risk of stroke due to increased levels of homocysteine, as well as use of hormone replacement therapy in women, however the evidence is limited.[107] There is also a weak relationship between nutrition and the risk of stroke, with increased fruit and vegetable intake associated with a lower risk.[132]

Multiple Risk Factors

As most of the factors described above are interrelated, it has become common to investigate the effects of multiple risk factors on the risk of stroke. It has been shown that multiple risk factors (two or more) are more common in ethnic minority and lower socioeconomic.[133] Up to 76% of stroke incidence can be attributed to the joint effects of common vascular risk factors. A reduction in high blood pressure is attributed to up to 62% of the population attributable risk for stroke, with 18% associated with a reduction in high cholesterol, 13% with a reduction in BMI, 11% with an increase in fruit and vegetable intake, 7% with an increase in physical activity and 12% with a reduction in numbers smoking.[134] One of the important facts about these vascular risk factors for stroke is that they are potentially modifiable and relatively easy to treat with the appropriate medications (once identified) and lifestyle behaviour modifications, such as smoking cessation, losing weight, consuming less salt and fat and increasing levels of physical activity.

2.3. Primary Prevention of Stroke

Reversing the consequences of stroke is difficult, thus primary prevention is of utmost importance. The effective prevention of first-ever stroke, especially in high risk groups, is the best method for reducing the burden, as over 70% of all strokes are first-ever in a lifetime (incident).[106] Increasing public knowledge about stroke risk factors is important in enhancing the success of primary and secondary stroke prevention activities.[135] However, knowledge of common stroke risk factors is still limited among the general population, with even poorer knowledge in high risk groups.[136]

It is important for healthcare providers and the general public to be able to estimate a person's risk of first-ever stroke. However, risk assessment tools, which investigate the independent effects of risk factors for stroke, as well as interactions between risk factors, are difficult to develop and validate across many age, sex, and ethnic groups worldwide. The Framingham Stroke Profile (FSP) used 36 years of follow-up data and identified that age, systolic blood pressure, hypertension, diabetes mellitus, current smoking, and established cardiovascular disease were independent predictors of stroke.[137] This risk

profile provides a quantitative determination of the probability of stroke, relative to what is average for a person of this age. However, despite its widespread use, the validity of the FSP among different populations or ethnic groups is limited.[138]

The total numbers of strokes are expected to rise due to the ageing of the world's population,[20, 21] so efforts to reduce the number of new strokes occurring need to be focussed on the primary prevention of stroke, through the control and modification of common vascular risk factors. As described earlier, there are several potentially modifiable risk factors that have consistently been shown to be associated with higher risk of stroke. Applying simple lifestyle modifications such as improving diet (less saturated fats and salt, more fruits and vegetables) and increasing levels of physical activity have been shown to help control normal blood pressure levels and decrease elevated blood pressure, cholesterol, diabetes and body weight.[106, 139]

Drug treatments are also commonly used to control risk factors such as hypertension and hyperlipidemia. There has been compelling evidence that the control of hypertension contributes to the prevention of stroke. In a review of randomised controlled trials of antihypertensive drug treatment, a 10 mmHg decrease in blood pressure was associated with a 30% decrease in the risk of stroke.[140] Therefore, much of the excess risk of stroke due to high blood pressure is potentially reversible with the treatment and control of hypertension. Research has shown that as long as blood pressure was decreased, there were no significant differences between blood pressure lowering regimens based on ACE inhibitors, calcium antagonists, diuretics or beta blockers in the prevention of stroke or other cardiovascular disease.[141] However, African Americans are generally more responsive to diuretics and calcium channel blockers than to ACE inhibitors or beta-blockers.[142] Tight control of hypertension in diabetic patients has been shown to reduce the risk of stroke considerably.[143]

Aspirin has been shown to reduce the risk of stroke in women at high risk of cardiovascular disease, however, the results are non-conclusive in men.[106] Lipid-lowering drugs (statins), used to control high cholesterol, have been

shown to reduce the risk of stroke, although the evidence is mixed.[110, 144] Anticoagulation treatment has also been shown to reduce of the risk of stroke by at least 60% in patients with AF, with a lower reduction, of ~20%, when AF patients were treated with Aspirin.[110] Carotid endarterectomy, the most-commonly used surgical procedure to prevent stroke, is recommended for patients with more than 70% of carotid stenosis.[145, 146] However, there are operative risks of stroke or death associated with carotid endarterectomy and many patients go untreated.[145] Ethnic disparities in the surgical treatment of carotid stenosis have been shown in the US, with higher rates of surgery among white Americans.[147]

There has been much debate about the combination of lipid and blood pressure lowering drugs and antiplatelet treatments into a single drug treatment (termed a "poly-pill"), and targeting everyone at high risk of cardiovascular disease.[148] It has been hypothesised that this poly-pill will reduce the risk of stroke by 80% through simultaneous reduction of the four major cardiovascular risk factors: raised low-density lipoprotein, high blood pressure, platelet aggregability, and raised blood homocysteine levels. The pill would consist of a statin, an antihypertensive agent, Aspirin, and folic acid and would be targeted toward everyone aged >55 years and those with previous cardiovascular disease.[148]

It has been shown that 14% of all incident cardiovascular mortality can be attributed to the inadequate control of multiple risk factors in people without previous cardiovascular disease.[149] Therefore, guidelines for the primary prevention of ischaemic stroke recommend that regular screening for common vascular disorders and risk factors such as hypertension and diabetes, is needed and control of risk factors should be maintained through the appropriate drug treatments, and diet and lifestyle modifications.[110] Efforts to educate the public about common risk factors for stroke and the importance of lifestyle modification are also necessary.[150, 151] The New Zealand government has implemented a number of population-wide education and advertising campaigns encouraging people to increase their levels of physical activity and improve their nutrition.[152] Although this is still in the implementation phase, it

has lead to a number of joint action plans between the New Zealand Ministry of Health, industry and government organisations.

To reduce the risk of stroke in non-modifiable risk factors, such as ethnicity and SES, efforts need to be made to identify high risk groups and disparities between these groups. Changes to policy and practice are required to minimise these disparities, by targeting primary prevention strategies in high-risk groups. In New Zealand, and the US, public health policies have been developed to eliminate disparities in health and access to healthcare between different ethnic and socioeconomic groups.[150, 153]

2.4. Rates of Stroke

There is variation in the rates of stroke, by mortality and incidence, worldwide and within populations. Mortality data are commonly used to compare the risk of stroke between populations, as many countries routinely collect mortality information, although the reliability is variable, especially within developing countries.[4, 154] Even though stroke incidence data are becoming more common, the results are varied due to differences in the study designs and reliability of the data (differences in study designs are discussed in depth in Chapter 3). There needs to be more research into variation in the rates of stroke worldwide, as well as within populations, to identify disparities and high-risk groups, leading to the development of informed health policies aimed at reducing the burden of stroke.

2.4.1. Mortality

There is variation in stroke mortality rates worldwide, with higher rates of death due to stroke, in Eastern European countries (up to six-times higher) compared to more affluent developed countries in Europe and the US.[36, 155] In China, stroke is the most common cause of death, which may be related to high rates of hypertension leading to more haemorrhagic strokes in Asian populations.[115, 156-158] Within the Asia-Pacific region, stroke mortality rates are highest in Japan and Korea and lowest in Malaysia and Thailand.[159] Considerable geographical variation in stroke mortality also occurs within countries. A north-south gradient of stroke has been shown in China with

higher death rates in northern provinces than southern.[160] The opposite has been found in the US with higher rates of stroke in the South and South-Eastern states, which has been labelled the "stroke-belt" of the US.[161-163]

Increased mortality from stroke occurs in ethnic minority groups in many developed countries around the world: African Americans and Hispanics in the US[15, 17, 72], African Caribbean's in the United Kingdom (UK)[16] and Māori and Pacific populations in New Zealand.[12] Mortality from stroke in African Americans is higher than white Americans across all subtypes and age groups, except for the oldest age group.[72] Minority populations are also more likely to die in hospital rather than in a nursing home when compared to white Americans, which may be linked to socioeconomic circumstances.[164]

2.4.2. Incidence

It is important to measure the incidence of stroke (first-ever in a life-time stroke events), to estimate the number of new cases occurring per year and to advise the future planning of acute healthcare. As with stroke mortality, higher rates of incident stroke have also been found in Asian countries and Russia.[27, 28, 30, 165, 166] However, the differences between countries were smaller than found between mortality rates.[28] A recent review of population-based stroke incidence studies has shown the highest age specific rates in Japan, Russia and the Ukraine.[30] However, most of the reviews that have investigated geographical variation in the rate of stroke, have been confined to white populations in developed countries or limited through different study designs. The similarities between geographical variation in stroke mortality and incidence rates indicate that mortality rates are driven, in part, by the incidence of the disease.

The data on ethnic disparities in the incidence of stroke is limited, with only a small number of studies conducted in the US, UK and New Zealand being large enough to explore disparities in the rate of stroke within a defined population. As with stroke mortality, higher rates of stroke incidence have been found in ethnic minority groups. In New Zealand, it was shown that Māori and Pacific people had significantly higher risk of stroke compared with

New Zealand Europeans.[13] In the US, African Americans had double the rate of stroke compared to white Americans and these also tended to be more severe, with higher rates of haemorrhagic strokes (both ICH and SAH).[15] The excess burden of ischemic strokes among African Americans compared with whites is not uniformly spread across the different subtypes, with higher rates of large-vessel strokes among African Americans.[167] Similar results were found in a population-based stroke incidence study from London.[168] The excess in the incidence of stroke among ethnic minority groups compared to white (majority) groups may explain most of the excess shown in stroke mortality rates.

2.5. Outcome from Stroke

Stroke is a largely disabling disease with over one third of people who suffer a stroke living with lasting disability.[5] Variations in the outcome from stroke need to be identified in order to predict who is likely to survive from their stroke and if they do survive their risk of disability. This may be used to prioritise post stroke healthcare and rehabilitation.

2.5.1. Survival

The chance of surviving the acute phase of stroke is a complex function of the extent of neurological damage, the complications of disability, and the presence of associated co-morbid vascular disease. Patients who survive the first year of their stroke typically, live on average 6 years after their stroke, with males surviving on average one and a half years longer than females.[169] Survival is highly dependent on age, with case fatality increasing with increasing age.[30] There are several simple clinical parameters that have been shown to be strongly predictive of survival after stroke: the level of consciousness, age and history of pre-morbid dependency.[170-172] Many of these factors are not modifiable at the time of the stroke, therefore, it is important, that any assessment of the impact of medical care on trends in survival should take these factors into account.

Ethnic minority populations (Māori and Pacific in New Zealand, African Americans in the US) have been shown to have worse case fatality than the

majority (white) populations.[13, 14] However, it has recently been shown in South London that African Caribbean stroke patients are more likely to survive longer after their strokes than whites.[173]

2.5.2. Disability

The burden of disability from stroke to the individual is substantial, as it encompasses impairment of body structure or function, limitation in daily activities and restriction of participation in normal activities. Over one half of stroke survivors will make a full recovery from their stroke, however at least 20% will remain dependent on others for activities of daily living.[169] In Auckland, it was previously found that, among stroke survivors, more women (27%) reported being dependent on others for activities of daily living (such as bathing, washing, cooking) than men (16%).[169] Rates of disability after stroke are higher in African and Asian countries, which may be due to the higher frequency of more severe and disabling haemorrhagic strokes in these regions.[10] Common predictors of outcome after stroke are age, disability pre-stroke, history of diabetes, recurrent stroke and the National Institutes of Health Stroke Scale (NIHSS) score, a widely used rating instrument to measure neurological deficits.[174-176]

A large proportion of stroke survivors report poor health-related quality of life after stroke. This is related to the level of handicap, disability or impairment, age and anxiety or depression after stroke.[177, 178] Mood is commonly affected after stroke, with the most common disturbance being depression, where approximately 33% of stroke survivors experience depressive symptoms after their stroke.[179] Having a stroke is also reported to double the risk of developing dementia post-stroke, which is predicted by pre-stroke dependency and a history of various vascular risk factors (hypertension, AF, diabetes).[180]

2.5.3. Caregiver Burden

As stroke is a largely disabling disease, considerable burden is placed on families and caregivers of stroke sufferers. Among 3-month stroke survivors, over 70% require some sort of assistance with activities of daily living and

receive informal care from family or friends, with two thirds of the primary caregivers being women, typically wives and daughters.[169] However, although most stroke survivors receive some form of informal care from relatives and friends, this care was generally provided during either leisure or family time, or by using existing leave entitlements for those in the paid workforce.[181] It has been shown that informal caregivers of stroke victims have an increased risk of developing depressive symptoms.[182-184]

2.6. Treatment and Secondary Prevention of Stroke

The outcome of acute stroke is highly dependent on the interval from onset of symptoms until treatment, as the restoration of blood flow to the brain needs to be achieved as quickly as possible. Many of the new acute treatments for stroke have been shown to be most beneficial within the first three hours after stroke onset.[185, 186] Despite the availability of these new acute therapies, many patients remain ineligible mainly because of late hospital arrival.[187]

Population-wide educational programs and stroke campaigns should not only teach typical and less common stroke symptoms and signs, but also that emergency medical services provide the fastest means of transportation to the stroke unit and the best chances of getting early treatment.[188] However, attempts to increase public awareness of the need to respond quickly to stroke symptoms through educational programs have had only limited success.[187, 189] The inability of patients and bystanders to recognize stroke symptoms and to quickly access the emergency medical system are the largest barriers to effective early acute stroke therapies.[136, 189] This is reported to be worst in high risk groups, such as the elderly, African Americans, and men.[136]

The next section describes the advancements in the acute treatment of stroke, with a focus on the more common forms of ischaemic and haemorrhagic strokes. Evidence of the importance of complete care, provided in a stroke unit setting is provided, and the need for appropriate rehabilitation in reducing disability and burden from stroke. The importance of secondary prevention of recurrent stroke in reducing the overall burden is also discussed.

2.6.1. Acute treatment

The acute treatment for stroke has changed considerably over time as new treatments have become available. The clinical diagnosis of stroke is made purely on clinical grounds, using information about the suddenness of the illness and the acute signs and symptoms, to determine if a stroke has occurred or not and to prioritise treatments and imaging.[190] However, it is important to differentiate between ischaemic, or haemorrhagic stroke, because of the marked difference in the management of these conditions. Brain imaging is used to guide the selection of acute interventions to treat patients with stroke, through identification of the size, location, and vascular distribution of the infarction, as well as the presence of bleeding. For most cases and at most institutions, CT scans are the most important and common brain imaging test. However, MRI and magnetic resonance angiography (MRA) are useful in determining malformations or aneurysms, and the time course of haemorrhage in acute ICH.[191, 192] Examination of the cerebrospinal fluid is indicated if the patient has symptoms suggestive of SAH and a CT does not demonstrate any blood.[62]

2.6.1.1. Treatment for Acute Ischaemic Stroke

The evaluation of patients with acute ischemic stroke should be performed as soon as possible. Early clinical evaluation and neuroimaging provides information about the cause of the neurological symptoms, identifies regions of salvageable brain tissue, and assesses the risk for haemorrhagic transformation and potential contraindications for treatment with thrombolytic agents.[191] Intravenous administration of recombinant tissue plasminogen activator (rtPA) is currently the only FDA-approved therapy for treatment of patients with acute ischaemic stroke.[185] It has been shown to be associated with improved outcomes for a spectrum of carefully selected patients who can be treated within 3 hours of onset of stroke. Earlier treatment (within 90 minutes) is more likely to result in a more favourable outcome, but later treatment, at 90 to 180 minutes, has recently been shown to be beneficial.[191] However, typically only 50% of patients arrive at the hospital within three hours of the stroke event and an additional 25% within three to six hours,

leading to only a limited number of patients being eligible for this treatment.[188] There is, however, concern with the administration of intravenous rtPA, with symptomatic haemorrhagic transformation occurring in 6% of patients, leading to caution in treatment.[185] It has been argued that rtPA should be used in patients who have been shown through imaging, to have a large penumbra, functionally impaired yet still viable tissue surrounding the ischaemic core.[193] However, there is mixed evidence as to how to measure the penumbra and the estimated threshold for treatment.[194]

The appropriate treatment of blood pressure in the setting of acute ischaemic stroke also remains controversial,[195] with little scientific basis and no clinically proven benefit for lowering blood pressure among patients with acute ischaemic stroke. However, it is recommended that most patients with ischaemic stroke should receive antiplatelet drugs such as Aspirin within 48 hours of stroke, unless contraindicated, to prevent early recurrent ischaemic stroke and reduce the risk of death or dependency.[190, 191, 196]

Anticoagulants such as heparin and heparinoids are often prescribed to patients with AF and recent ischaemic stroke, in an effort to prevent early recurrent stroke and to improve neurological outcomes. However, the evidence for this is inconclusive and these medications also increase the risk of symptomatic haemorrhagic transformation of ischaemic strokes, especially among patients with more severe strokes.[191, 196]

2.6.1.2. Treatment for Acute Haemorrhagic Stroke

ICH is the least treatable form of stroke. It is associated with the worst outcome and high mortality, and treatment is varied by hospital.[192] Surgical evacuation of the haematoma is used in <20% of patients, even though there is no clear evidence of the benefit of surgery and there are increased risks which may lead to further brain damage.[192, 197]

A new therapy, still in the trial stage, recombinant activated factor VIIa (rFVIIa) is under study to coagulate the blood and decrease the early enlargement of the haematoma in the acute treatment of ICH.[197] As with rtPA in ischaemic stroke, the benefit of rFVIIa is most significant when it is initiated within 3

hours of stroke onset.[186] However, patients are at increased risk for thromboembolic events.[197] Increased intracranial pressure has been shown to increase the risk of mortality after ICH, and recommendations have been made to treat elevated blood pressure in patients with ICH more aggressively than for patients with ischaemic stroke.[192] Findings suggest that elevated blood pressure increases the risk of haematoma enlargement and efforts should be made to lower systolic blood pressure to <150 mmHg to prevent this risk.[192, 198]

2.6.1.3. Stroke Units

Specialised care for stroke patients has been shown to be the most effective management of stroke patients in the acute setting.[199] Many institutions have developed clinical care pathways which provide structured care plans for patients with stroke, which are used by different members in a multidisciplinary team [200, 201] These pathways aim to assist in clinical decision-making and promote organised and efficient patient care and are commonly used in the context of stroke units. [202]

Organised inpatient stroke unit care is a form of care provided in hospital by nurses, doctors and therapists and is characterised by i) coordinated multidisciplinary rehabilitation team, meeting regularly ii) staff with a specialist interest in stroke or rehabilitation, iii) routine involvement of carers in the rehabilitation process, and iv) regular programs of education and training. The Stroke Unit Trialists' Collaboration systematically pooled randomised trials of organised inpatient stroke unit care to investigate the effects on patient outcomes.[199, 203, 204] It was found that patients who received organised in-patient (stroke unit) care were more likely to survive, regain independence and return home than those receiving a less organised service.[204] Stroke unit care has also been associated with better long-term quality of life.[205] Therefore, it is recommended in many health policies related to stroke that if it is available, patients should receive treatment and care in a stroke unit, or as close to an equivalent as possible.[206, 207]

2.6.1.4. Rehabilitation

Rehabilitation is also an important aspect in the treatment of stroke. This should begin the day after the stroke (where possible), and it is an integral aspect of stroke unit care.[199] The key aspects of rehabilitation, physiotherapy and occupational therapy, not only aim to improve physical functioning but also to help reintegrate the stroke person back into the community.[208] However, it has been shown in practice that the organisation and type of rehabilitation services available for people with stroke are not consistent with best practice or accepted guidelines.[209, 210] Early supported discharge linking inpatient care with community services has been shown to reduce the length of stay in hospital and readmission rates, as well as increasing the likelihood of independence and living at home for the stroke person.[211]

2.6.2. Secondary Prevention

Secondary prevention of recurrent strokes is a primary objective for all stroke survivors, as patients with previous stroke or TIA are at increased risk of serious vascular events (death from all vascular causes, non-fatal stroke, or non-fatal myocardial infarction).[50, 146] The risk of first recurrent stroke is six times greater than the risk of first-ever stroke in the general population.[212] The rate of stroke recurrence is approximately 5% per annum, but tends to be higher in the first few weeks and months after stroke.[213] The risk of having a secondary or recurrent stroke is up to 10% within 1 week of a previous stroke or TIA and 18% within 3 months.[50] Patients in high risk groups, or those having more than one risk factor, are at an increased risk of recurrent stroke and appropriate management of any risk factors need to be addressed soon after the event.[146] However it has been shown that both physiological and behavioural risk factors still go untreated or unchanged after stroke.[214, 215]

It has been recommended that all patients suffering a stroke should be put on Aspirin or an alternate antiplatelet drug, reducing the risk of a further serious vascular event by 25%.[191, 216] Blood pressure reduction, or the treatment of hypertension, reduces the risk of having a secondary stroke as well as other vascular events.[146, 217] Recently it has been suggested that all patients with a history of stroke will benefit from blood pressure lowering to reduce the risk of

recurrent stroke, whether they are hypertensive or not.[218] Blood pressure-lowering in patients with a history of stroke, has also been reported to reduce the risk of associated long-term disability and dependency.[219] It has also been recently recommended that patients with a recent stroke or TIA be placed on statin therapy to reduce the recurrence of secondary stroke.[220]

2.7. The Cost of Stroke

Stroke is a very costly disorder and healthcare costs are expected to rise with increasing numbers of stroke patients, due to the ageing of the world's population and improvements in survival. It was estimated that the total cost of stroke in Australia in 1997, was A$917 million, which was ~2% of the total health expenditure for that year.[221] This data was adapted to the New Zealand population in 2002 and the mean cost for a person who suffered a stroke was estimated to be ~NZ$23,000 per year, with a lifetime cost of ~NZ$50,000.[206] The majority of the cost of stroke is still borne through inpatient acute care and rehabilitation, although this is decreasing with the shift from inpatient to outpatient treatment and rehabilitation.[222, 223]

The average cost of hospitalisation and rehabilitation varies greatly between different stroke subtypes with substantially greater costs for stroke patients who suffered an ICH, rather than an ischaemic stroke.[224] It is difficult to estimate the true cost of stroke because of the large proportion of burden that is cared for outside the hospital arena. Informal carer costs and out of pocket costs to the patient account for up to 8% of the total cost for stroke during the first year after stroke, with indirect costs (loss of employment activity in cases with stroke up to age 65) accounting for up to 6% of the total cost.[221]

2.8. Summary

Stroke is essentially a preventable and treatable disease. Reducing the growing burden of stroke requires the primary prevention of new stroke cases, through the control of modifiable risk factors, the early evaluation and treatment of acute stroke, and the effective secondary prevention of recurrent stroke. There is a large financial cost incurred by inadequate primary and secondary prevention of cardiovascular disease risk factors, which justifies

major efforts directed towards the detection and treatment of such risk factors. The main modifiable risk factors for stroke can be improved through appropriate drug treatment and through simple lifestyle modifications, which have been shown to help control high blood pressure, cholesterol, diabetes and body weight. Simple lifestyle modifications such as a better diet (less saturated fats and salt, more fruits and vegetables) and increasing levels of physical activity can be aimed at a population-wide level through intensive education and advertising campaigns.

It is important that disparities in the risk of stroke among different populations are identified, to enable targeted stroke prevention and treatment strategies. There is a gap in the knowledge of ethnic variations in risk factors and the associated mechanisms that lead to disparities in the rates of stroke. This should be investigated in well-designed population-based stroke incidence studies, in populations where there is significant ethnic variation. This will provide accurate measures of where ethnic disparities in stroke lie in the whole population and how they are related to disparities in common risk factors.

Past trends in the rate of disease among different populations need to be investigated, to estimate future changes in the burden of stroke and in which populations the greatest burden is likely to lie. This research can be used to inform clinical practice of the success of primary and secondary prevention programs on reducing the burden of stroke, and to influence health policies related to stroke prevention, treatment, rehabilitation and care, within the general population, as well as within high-risk groups.

3. TEMPORAL TRENDS IN STROKE

There is a good deal of variability in temporal trends in the rate of stroke, due to varying study designs and the availability of data. The continuous surveillance of stroke in a population allows any changes in rates to be detected, with respect to changes in risk factor or health care initiatives. With the changing socio-demographic profile of populations in many countries, especially in the developing world,[3, 19] the absolute numbers of strokes are expected to increase even if the rates of stroke are declining over time.[20] So current and future trends in the rates of stroke need to be investigated, in order to inform health care planners and policy makers of what populations are at increased risk and where the future burden may lie.

There are several approaches to the surveillance of disease in a population-wide setting. Comparing rates of stroke across time and place increases our understanding of the determinants, risk of disease, and populations at high risk of stroke. To be comparable, though, studies must use consistent methods, definitions and mode of data presentation, which is particularly pertinent in the epidemiological study of stroke. This chapter will provide a review of the literature on and methods used to investigate temporal trends in the occurrence of stroke in a population. The first section investigates the complexities of surveying stroke in different populations and across time, and provides a detailed description of the methodologically "ideal" stroke incidence study. The second section investigates trends in stroke mortality and ethnic disparities in trends in mortality. The third section reviews trends in the incidence of stroke from cohort and population-based studies, with a systematic review of trends in the incidence of stroke in ideal stroke incidence studies. The fourth section reviews trends in short- and long-term survival after stroke. The fifth section, explores explanations for trends in the rate of stroke through trends in incidence and survival. The final section, investigates future projections of the rate of stroke due to historical trends in rates and future changes in the socio-demographic profile of populations.

3.1. Stroke Surveillance

There are many different methods used to survey stroke in a population. Information can be collected prospectively using "hot" pursuit methods of case ascertainment (active screening of patients) or retrospectively using "cold" pursuit methods (passive screening), anytime after a stroke has occurred. Hot pursuit (active) screening of patients involves prospectively collecting patients as soon after the onset of symptoms as possible. This is typically conducted within the hospital setting but can be done in the community by having general practitioners and other specialists involved in the study and notifying the register of all stroke patients. An advantage of using a prospectively designed study is identifying patients as soon as they occur and collecting the information as soon after the event as possible, thereby minimising recall and observer biases. Cold pursuit (passive) screening of patients involves the retrospective collection of information, typically checking hospital discharge registers and death certificates during and at the end of the study. Cold pursuit methods have the advantage of consuming considerably less time and resources than hot pursuit ones. However, the information collected is more prone to bias as it is collected retrospectively (sometimes several months after the event), relies on the verification and coding of stroke by a person external to the study and the patient may not be interviewed in person.[27] A combination of both approaches to case ascertainment should ideally be used in stroke incidence studies.[225]

There are varying levels in the quality of stroke surveillance data. Stroke mortality data are useful for investigating changes in the rates of death from stroke in a population, and typically involves the retrospective ascertainment of cases. By their very nature, mortality studies do not provide an accurate measure of the burden of stroke in a population, as only one third of strokes are fatal.[5] Hospital-based studies are useful for examining trends in acute stroke but may miss the many patients with stroke who are diagnosed and treated out of hospital.[24, 25] In order to obtain accurate estimates of the total disease burden, information needs to be collected on all fatal and non-fatal strokes (both incident and recurrent) occurring in hospital, as well as in the

community. A number of population-based studies have collected information on both fatal and non-fatal patients, however, many of these are limited in study design, to younger age groups or hospitalised patients only. It is important that information is collected on all patients of stroke, including those in the oldest age group (≥ 85 years), as stroke is still largely a disease of the elderly. A set of criteria have been developed to provide the most reliable and comparable data, using both hot and cold pursuit methods of case ascertainment to collect information on all fatal and non-fatal patients occurring within hospital the and community.[27, 28] Studies fulfilling these criteria have been termed ideal population-based stroke incidence studies.

3.1.1. Mortality Studies

One of the most easiest and common methods for measuring the occurrence of stroke death in a population is to use routinely collected mortality data. This typically involves the retrospective checking of all death certification in a defined region. Mortality data are useful for investigating trends in stroke death within a population over time because any biases within the population surveillance are likely to be consistent over time.[36] Mortality data are also useful for measuring the implications of political unrest or disease outbreaks on changes in death rates within a population.[36] However, there are limited mortality data from developing countries, especially Sub-Saharan Africa, which has had to be estimated from data from other countries, in global burden of disease studies.[4, 154] One of the main limitations of mortality studies is that they do not provide accurate estimates of the burden of stroke in a community as they only focus on fatal patients of stroke, thereby excluding two-thirds of stroke patients who survive the acute phase. It is also challenging to obtain information on mortality from incident strokes only, as hospital records are not typically checked.

Mortality studies are invaluable in providing comparable information from countries around the world as retrospective data collection is used and patients do not need to be contacted, leading to less resource use than other types of surveillance studies.[155] However, the reliability of mortality data from developing countries is questionable.[23, 226, 227] Mortality studies have identified

disparities in stroke mortality in the developed world with the highest rates occurring in Eastern European countries, and the lowest rates in Switzerland, Canada, the United States and Australia.[35, 36, 155] Mortality studies have also been invaluable in highlighting high risk populations and identifying ethnic disparities[12, 18, 228] and socioeconomic variation[76, 229, 230] in the risk of stroke death in many countries.

There are many potential sources of error in using mortality data alone, with questionable internal validity, errors and variation in the diagnosis or coding of stroke, and variation in case fatality between countries.[231] In early years, it was shown that there were problems with the accuracy of causes of death on death certificates, with up to 40% of certified fatal strokes in the Framingham Heart Study having no mention of stroke on the death certificate.[232] Changes in the coding of stroke subtypes in mortality data have also been found due to changes in the diagnostic coding of strokes. Since the introduction of neuroimaging, there has been a decline in the proportion of strokes coded as haemorrhagic and an increase in the proportion of ill-defined strokes.[233] This is supported by data from the Framingham study where the over-reporting of haemorrhagic strokes in death certificates was found in early years.[232] It has been shown in the WHO Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) project that the rates of stroke in Eastern European populations identified through routine mortality data were lower than those found in the population-based study, indicating underestimation of stroke deaths in mortality data in developing countries.[165] In addition to the problems with the diagnostic coding of strokes on death certificates, there are problems with the recording of demographic data on death certificates, especially with ethnicity in the US[234] and in New Zealand.[235, 236] This may lead to an under (or over) estimation of the burden of stroke in ethnic groups creating difficulties in assessing the health care needs of different ethnic groups. Researchers from New Zealand attempted to quantify the amount of error in the recording of ethnicity data on the death certificate data and adjusted the mortality estimates by ethnicity.[235, 236]

There is an important place for mortality studies in stroke surveillance, with their low cost and easy accessibility of data. They are useful for projecting the number of stroke deaths in a community and advising health care planning. However, only a small proportion of the total burden of stroke is examined and comparisons of stroke mortality between countries or over time, should be interpreted with caution due to variability in data collection and quality.

3.1.2. Hospital- and Population-Based Studies

There a number of different methods used to survey stroke in a population. Hospital-series studies measure the number of stroke occurring within a hospital but there is uncertainty about the base population in these studies. A population-based study measures the burden of stroke within a defined population. There are many types of population-based studies such as hospital-based series, cohort studies, or limited population-based studies. However, they are often restricted through only using retrospective case ascertainment, collecting only a subset of cases (hospitalised patients only) or registering only limited age ranges (MONICA). As different methods of case ascertainment are used, it is difficult to compare rates between studies, and even over time within populations.

Hospital-based Studies

Hospital-series studies, using only hospital morbidity or separations data, are useful for estimating the number of stroke patients treated by a hospital and for the projection and planning of future stroke burden within that hospital. However, estimates from hospital-series do not give a complete estimate of the burden of stroke in a population, as they fail to recognise the proportion, up to 40%, of fatal and non-fatal strokes that occur outside the hospital.[25, 237] Problems may also occur in comparing hospital-series studies across place or time, as hospitalisation rates for stroke may vary between, and even within, populations.[164, 238, 239] Rates are also likely to vary with time as management strategies change and new treatments for stroke emerge.[27] As mentioned earlier, there are a number of problems with the coding of stroke subtypes with inaccurate coding of ischaemic stroke subtypes,[240, 241] and changes in the coding of stroke subtypes over the years.[242] Hospital-series studies may also

overestimate the risk of stroke, as younger patients with increased severity of stroke are more likely to be admitted to hospital.[25, 225, 237] Use of hospital series data alone may also overestimate stroke mortality in African and Hispanic Americans in the US, as these groups are more likely to die in hospital when compared to white Americans.[164]

Cohort Studies

A number of unique cohort studies have been conducted in the US, the Framingham Study,[137, 243] and the Rochester Epidemiology Project (conducted through the Mayo Clinic),[244] which have monitored chronic diseases for over half a decade. These studies were not specific to stroke but have provided reliable estimates of stroke within the populations and over time.[137, 245, 246] However, there are only a small number of strokes occurring annually in these studies, and are conducted on mainly white populations, thereby limiting their comparability with other populations. Also, their results may not be comparable with prospective stroke incidence studies as they use different methods for case ascertainment, or are comprised of a healthy set of volunteers by excluding certain disease states at the start of the study. Even so, it has been shown that the retrospective medical record linkage of the Mayo Clinic in Rochester, Minnesota, is as reliable as prospective methods of case ascertainment through complete record documentation for the whole community.[247]

The WHO MONICA Project

The first study attempting to use standard methods and definitions to monitor trends in the incidence of stroke across a number of different populations was the WHO MONICA project, which was initiated in the early 1980s.[248] This involved a detailed protocol for stroke registers in 41 collaborating centres, which provided instructions for stroke event registrations, guidelines for case ascertainment, validation procedures, and coding rules for diagnosis of events and case fatality rates.[47] The MONICA project has been instrumental in enabling the comparison of rates of stroke between a number of European and Chinese populations, as well as investigating trends in the rates of stroke within and between these populations.[249] Over the past 20 years, the

MONICA project has produced in excess of 1000 publications from 21 countries, investigating the epidemiology of stroke.[249] However, there are a number of limitations inherent in the MONICA studies. A limited age range was covered in most studies, with many centres only monitoring stroke up to the age of 65 years, thereby excluding up to 80% of strokes occurring in the elderly. Although a defined protocol was used in the MONICA studies, there was variation in the methods of case ascertainment between the studies, with some studies using hot pursuit methods of case ascertainment only, some using cold pursuit only and others using a mixture, limiting the comparability of rates between studies.[226]

The WHO STEPwise Approach to Stroke Surveillance

In 2000, the 53rd World Health Assembly passed a resolution on the prevention and control of non-communicable diseases. In response to this the WHO has developed a STEPwise approach to the surveillance of non-communicable disease that can be used in a variety of settings.[250] The goal is to achieve data comparability over time and between countries, especially low and middle income countries. The WHO STEPS-Stroke approach to stroke surveillance provides a flexible system and an opportunity for all countries to contribute to data and information on stroke, to help improve global information about trends in key measures of stroke.

There are three basic additive steps that countries can build upon to provide information on the burden of stroke.[251] Step 1 involves collecting hospital-based data on all hospitalised strokes including demographic data and information on treatments received in hospital and type of stroke. Step 2 collects information on community-based fatal events using death certificates and autopsy reports. Step 3 identifies all non-fatal non-hospitalised strokes through liaison with local health facilities. This flexible technique aims to provide vital basic epidemiological estimates of the burden of stroke worldwide. Information on incidence rates and case fatality are the most valuable epidemiological measures and the best guide to public health initiatives for the prevention of stroke. Therefore, it is recommended that

every country should aim to advance their surveillance to include all three steps.

Limitations of Hospital- and Population-Based Studies

The main limitation of hospital-based studies is that they do not include an easily defined population and it is difficult to estimate an appropriate denominator for rates. There are a number of problems that have been identified with using diagnostic coding of the primary cause of hospitalisation in discharge or hospital separations lists,[252] leading to an under- or over-estimation of stroke numbers, depending on the population.[241, 253] The sensitivity in identifying stroke cases increases as the number of discharge codes used increases i.e. from primary to the first three diagnoses.[241, 254, 255] However, limiting discharge codes to primary diagnosis allows the identification of incident rather than prevalent cases, with a greater accuracy of coding stroke.[240, 241, 253, 256] There are also problems with the coding of ischaemic stroke subtypes using the International Coding of Diseases, 9th Edition (ICD-9) codes (430 to 436, [Appendix 1]), overestimating ischaemic stroke subtypes and TIAs.[240] Hospital discharge lists may overestimate the prevalence of stroke as sequelae from the stroke tend to be coded using acute stroke ICD codes.[257] Trends in the incidence of stroke are also affected by changes in the coding of stroke subtypes between ICD-9 and ICD-10, with more specific diagnoses for ischaemic stroke decreasing the number of ill-defined subtypes.[242] The introduction of diagnosis-related groupings (DRGs) in allocating hospital resources have been shown to also influence trends in the diagnostic coding for stroke. In the US, it was found that the proportion of ischaemic strokes increased between 1980 and 1991 and the proportion of ill-defined strokes decreased, due to higher costing allocated for defined strokes.[252] Increases in the number of haemorrhagic strokes have been found due to the increased use of CT scanning, which detect smaller, less fatal haemorrhages, which would have previously been coded as ill-defined ischaemic strokes.[258]

Population-based studies of the burden of stroke are useful in estimating high-risk populations and advising health care planning. However, as there is great

variability in the methods of case ascertainment, it can be difficult to compare rates between studies and any comparisons should be interpreted with caution. Therefore, similar definitions and methodologies should be maintained where possible, to enable comparability across and between populations.

3.1.3. The "Ideal" Stroke Incidence Study

The best quality information on the incidence of stroke in a population comes from population-based ideal stroke incidence studies, which prospectively collect information on all cases of stroke from hospitals, death certificates and from community sources within a defined population. In 1987, Malmgren and her colleagues published a list of 12 core criteria recommended for an ideal stroke incidence study by which the quality of population-based studies of stroke could be judged (Table 3.1).[28] These criteria involved the use of a prospective, population-based study design, with standard definitions for stroke and multiple and overlapping sources of case notification in order to identify all stroke events in a defined region. The criteria have been updated over the years by Bonita (1995),[26] Sudlow and Warlow (1996),[27] and by Feigin et al. (2003, 2004),[29-31] to enable greater comparability of studies and to reflect changes in the management of stroke. Ideal stroke incidence studies provide the most accurate and reliable data on the occurrence of stroke and outcome in a population, enabling comparability between geographical regions and trends over time.[27, 28] However, such studies are complex, large, expensive and difficult to accomplish, especially when monitoring all sources of case ascertainment on a regular basis. The following criteria may be used as a guideline for such studies.

Definitions

The WHO definition for stroke (described in Section 2.1) has been broadly accepted as the standard definition used in ideal stroke incidence studies. This definition allows for a clinical diagnosis of stroke and characterises stroke as a cerebral deficit with symptoms lasting longer than 24 hours. This time duration cut-off is useful in epidemiological studies as it can be used irrespective of neuroimaging, across different populations and differentiates

strokes from TIAs. This definition also includes SAH, but as SAH is aetiologically different from ischaemic stroke and ICH, researchers should state clearly whether SAH is included in the definition used or not. The WHO also recommends that any new stroke that develops more than 28 days after a previous stroke is classified as a recurrent event.[248] However, recently it has been suggested that this definition for a recurrent event underestimates the risk of stroke and a definition of any stroke occurring ≥ 24 hours after the initial stroke be defined as a recurrent event. [259] It is important that standard definitions are used to define strokes, recurrent and incident strokes, to enable comparability between similar studies.

First-ever-in-a-lifetime Strokes

It is important that information on first-ever-in-a-lifetime (incident) strokes are collected, as data on incident strokes offer a more reliable outcome for the investigation into the aetiology of the disease. Collecting information on incident strokes requires a careful review of the history of stroke for each patient, through the checking of previous medical records.[27] This can be resource intensive. It is important to distinguish between first-ever-in-a-lifetime strokes and first-in-the-study-period strokes, as the latter could include patients with previous stroke, leading to confusion and non-comparability between studies.

Defined Study Population

Most studies use populations that are clearly defined by geographical, statistical or census boundaries and assume a degree of stability with limited in- and out-immigration. A population may also be defined using particular health districts or regions,[38, 260] but the key requirement for the calculation of rates is a reliably identifiable base population. If possible, the study population should not be limited by age and should be large enough to provide accurate estimates of age specific rates (i.e. more than 250 cases per year).[27] However, the larger the study population, the more resources that are required to ascertain all cases of stroke. Therefore, the reliability of the study is dependent on the appropriate balance between the amount of available resources and the size of the study population.

Official census statistics are typically used as the denominator (base population) in the calculation of stroke rates. However, estimates may become unreliable if the study is not conducted in the same year as a census and estimated population data are used, with bias increasing as the time since the last census increases.[27] Finally, errors in ethnic specific census data may lead to biases in population data, due to the undercounting of ethnic minority groups in developed countries.[69, 261]

Case Ascertainment

One of the most important aspects of an ideal stroke incidence study is that patients are collected "prospectively", as soon after the onset of symptoms as possible. This minimises recall bias (error due to the accuracy of recall of past events or experiences) and observer bias (the influence of knowledge and experience on the responses of physicians or researchers).[262] Misclassification bias may occur in the verification of strokes with increasing time from the initial event and sequelae of the event.[27] Prospective case ascertainment is typically conducted within the hospital setting, but can also be conducted in the community, by having general practitioners and other specialists notify a central register of all patients with stroke as soon as they occur. Within the hospital setting a range of diagnostic codes with similar symptoms to stroke (vertigo, dizziness, confusion, seizures, headaches and transient ischaemic attacks) should be screened in the hospital admission and discharge lists, to identify any potential strokes, with alternative stroke-like diagnoses.

Cold pursuit (or passive screening) typically involves retrospectively checking hospital discharge registers and death certificates at various intervals during and at the end of the study.[27] Once a patient is identified to the register, it is recommended that all patients are independently assessed by a study investigator (preferably a stroke physician or neurologist) to verify and classify the patient as a stroke, which lowers the error rate of incorrect stroke diagnosis.[27, 263]

Table 3.1 The gold standard criteria for an "ideal" stroke incidence study.

Domains	Core criteria	Supplementary criteria
Standard definitions	• WHO definition of stroke • At least 80% CT/MRI verification of the diagnosis of ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage* • First-ever-in-a-lifetime stroke (incident)	• Classification of ischaemic stroke into subtypes (e.g. large artery disease, cardioembolic, small artery disease, other)* • Recurrent stroke*
Standard methods	• Complete, population-based case ascertainment, based on multiple overlapping sources of information (hospitals, outpatient clinics, GP's, death certificates)† • Prospective study design • Large, well-defined and stable population, allowing at least 100,000 person-years of observation† • Follow-up of patients' vital status for at least 1 month* • Reliable method for estimating denominator (not more than 5 years old census data)†	• Ascertainment of patients with TIA, recurrent strokes and those referred for brain, carotid or cerebral vascular imaging* • "Hot pursuit" of cases • Checks for completeness of case ascertainment† • Direct assessment of under-ascertainment* by regular checking of GP databases and hospital admissions for acute vascular problems and imaging studies and/or interventions
Standard data presentation	• Complete calendar years of data; not more than 5 years of data averaged together† • Men and women presented separately • Mid-decade age bands (e.g., 55 to 64 years) used in publications, including oldest age group (≥85 years)† • 95% confidence interval around rates	• Unpublished 5-year age bands available for comparison with other studies

*New criteria; †Updated, modified from Sudlow and Warlow[27]

Taken from Feigin and Carter (2004)[31]

It is important that the stroke registers cover whole calendar years to avoid the confounding effects of seasonal variation in stroke, as higher rates of stroke may occur in the winter months.[264, 265] Where studies have collected data on consecutive years, rates should not be averaged over time intervals longer than 5 years, as it has been shown that rates tend to vary over 5 year periods.[266] Data also need to be collected, analysed and presented in 5-year age bands to allow comparisons with more studies and to reduce the effect of different age structures in different populations. It is important that data from ideal studies are similarly presented in publications and it is recommended that data be presented in mid-decade age bands (e.g. 55 to 64 years) to enable comparability between published studies.[27]

Multiple Sources of Case Ascertainment

Cases of stroke can be identified through a number of different sources including acute and rehabilitation (public and private) hospitals, GPs, aged-care facilities and death certificates. Ideal stroke incidence studies use as many sources of notification as possible to ensure that no cases are missed.[27] The use of multiple sources of notification in studies of trends over time can identify any modification in case management through changes in first notification of patients to the study. Multiple sources are also used as a check for the completeness of case ascertainment, as overlaps between sources of notification are indicative of good case finding methods.[27, 267]

The majority of patients in stroke incidence studies are identified through sources within hospitals, with up to 95% of all patients admitted to hospital in some European studies.[268] Inpatient case ascertainment is typically conducted using trained staff, actively checking admissions and discharge lists for all departments in the hospital, with special effort around medical or neurological wards, emergency departments, and neuro-radiology lists. These regular checks also identify patients who were admitted to hospital for other reasons and subsequently had a stroke. Hospitals outside the study region also need to be monitored regularly, to identify any patients (usually resident in the study region) who had their stroke outside the study region, controlling for “cross boundary effects”.[27] In countries with a two-tiered health

system, such as New Zealand, all public and private hospitals of the study region should be checked regularly.

Other sources of case notification are useful for ascertaining up to 6% of patients.[26] These sources include regular checking of patient lists for outpatient stroke clinics, day wards, rehabilitation, physiotherapy, occupational and speech therapy clinics or emergency service (ambulance) lists. The ascertainment of all stroke patients in the community is facilitated through the setting up of networks with all aged-care facilities (i.e. private hospitals and rest homes or hostels), specialists and GPs in the region. These sources are more likely to identify patients of mild stroke or TIA that were not admitted to hospital,[237] cases of sudden death at home and severely disabled patients who have a stroke remaining in rest homes or private hospitals. However, some European studies have shown that the majority of stroke patients are admitted to hospital, especially in Scandinavian countries, with an egalitarian health systems.[76, 268, 269]

Routinely collected mortality data are useful for identifying non-hospitalised fatal cases of stroke. Fatal patients of stroke are less likely to be hospitalised and therefore less likely to receive a primary diagnosis of stroke on the death certificate.[254] It is also recommended that all autopsy or coroner's records be checked for possible patients of stroke, due to the sudden attack rate of stroke and to assess the accuracy of diagnosis in fatal patients.[226] In many countries, there are delays in the coding and entering of mortality data into routine mortality statistics, so it is recommended that mortality data should be checked up to one year after the end of the register, to capture any delayed cases of stroke. Fatal strokes identified only by death certificate or autopsy should be verified with the registering doctor or family.[27]

Assessment of the Completeness of Case Ascertainment

Checks for the completeness of case ascertainment in an ideal stroke incidence study are recommended,[27] to measure the quality of the data and estimate if any group of cases are being missed by the register. Completeness of case ascertainment can be assessed either directly, through additional checks of GP and hospital databases, or indirectly through

statistical checks such as the capture-recapture technique. Ideally a stroke incidence study should be shown to be either 100% complete or provide an estimate of the proportion of missing cases.[270]

Two measures that directly assess the completeness of case ascertainment have recently been proposed.[25] Firstly, anonymised electronic primary care records are accessed to identify any patients who received medical attention for stroke but had not been notified to the study. Secondly, a "high risk" (if they had an acute coronary or peripheral vascular event or a related investigation or intervention during the study period) subset of the study population, may be interviewed and followed up to see if they had a stroke. In the recent Oxford Vascular Study (OXVASC) study, the first method identified only an additional two patients, whereas the second method did not identify any additional patients.[25]

An indirect method to assess the data quality of a stroke incidence study was developed for the MONICA project.[226] This can be used as an indirect measure of the quality of the data and hence the comparability between studies. This method uses five criteria:

1. the ratio between the number of deaths in the register and the number of deaths from routine statistics;

2. the proportion of fatal cases occurring outside the hospital in relation to all stroke deaths which is used to estimate the completeness of data on fatal out-of-hospital events; (a fatal event is defined as death within the first 28 days after onset);

3. the 28-day case fatality ratio is used as an indicator of the completeness of registration of non-fatal stroke patients;

4. the proportion of surviving stroke patients cared for outside the hospital is used to estimate the completeness of non-fatal, non-hospitalised stroke events; and

5. the proportion of fatal patients examined by a physician before the death or subjected to autopsy is used to estimate the accuracy of the assignment of diagnostic category in fatal patients.

These criteria are useful for identifying problems in the data which may require further validation, such as differences in the diagnosis of stroke in the stroke register as compared to routine statistics. They may also measure internal consistency in case-finding efficiency, in studies that collect patients over a number of years, identifying changes in case ascertainment due to variations in the management of patients or in the collection of routine statistics.

The capture-recapture method also provides an indirect measure of the completeness of case ascertainment. These were originally developed to estimate the number of animals in a population,[271] but more recently have been applied to human populations in public health and used in epidemiological methodology.[270, 272-274] The technique assesses the overlap of case notification between multiple sources of notification, to estimate and quantify the number of cases missing in the survey.[273] It can also be used in cost effectiveness analysis to identify sources of notification which were not useful in ascertaining new cases of stroke, indicating that such sources may not be required in future studies.[270, 272] However, these methods remain controversial in their application in epidemiological studies of chronic disease,[270, 275-278] mainly because of the number of assumptions (discussed in Chapter 4, Methods, Section 4.5.2.1) that are required.[275] Consequently, the results of capture-recapture analyses should be interpreted with caution, as they are subjective and depend on the method of analysis used. However in stroke research, capture-recapture techniques are becoming more common in estimating the completeness of stroke registers and adjusting rates, through modelling of the overlap in the sources of notification.[270, 279]

Pathological Stroke Subtypes

Stroke is a heterogeneous pathological condition encompassed by the WHO definition. Data on stroke subtypes are less common in studies conducted before the 1990s due to the limited use of neuroimaging. However, with the

greater availability of neuroimaging in most developed countries over the past decade, it is now possible to define strokes into specific pathological subtypes, including ischaemic stroke, PICH and SAH. Therefore, it has been recommended that the subtyping of strokes is dependent on over 80% of patients receiving some form of neuroimaging (CT or MRI) within 30 days of the stroke, or an autopsy, or in the case of SAH with evidence of blood in a lumber puncture.[29] Definitions for stroke subtypes must be standardised and made clear in publications, to enable comparability of rates between studies.

Supplementary Criteria

The original criteria for an ideal stroke incidence study were developed almost two decades ago, but they have been updated to encompass changes in case ascertainment, rates of hospitalisation and neuroimaging, to improve the comparability between studies.[25-27, 29-31] In 2004, the updated criteria were combined and a new gold standard for an ideal stroke incidence study was proposed (Table 3.1).[31] These supplementary criteria include the classification of ischaemic subtypes of stroke, and recommend the collection of all recurrent strokes and TIAs. The checking of all TIAs patients may provide an extra 15% of incident cases.[25] Studies that use all of the core and most of the supplementary criteria for an ideal stroke incidence (Table 3.1) have been shown to have near complete case ascertainment.[25]

Complexities in Ideal Studies

In 1987, Malmgren et al. reviewed 65 stroke incidence studies worldwide, using the core ideal criteria, of which only nine studies met the criteria.[28] In 1997, Sudlow and Warlow conducted a review of stroke incidence studies carried out between 1984 and 1994 and found that only 11 out of the 35 studies, fulfilled the criteria for an ideal study.[166] The limited number of studies that fulfil the criteria for an ideal stroke incidence study is a reflection of the difficulties involved in undertaking such studies. Although it is important that incidence studies fulfil most of the criteria to enable comparability within populations over time and between studies, the criteria are difficult to apply in developing countries due to variation in the organisation of health care. Stroke incidence studies need to be clear and concise about the definitions

and methods used in case ascertainment and data analysis and in the presentation of data in publications, to enable comparability between similar studies.

3.1.4. Summary

There is variation in the methods used to survey stroke. The gold standard is to use a prospective population-based study design utilising both hot and cold pursuit methods of case ascertainment, to collect all fatal and non-fatal strokes occurring in hospital and the community, hence fulfilling the criteria for an ideal stroke incidence study. Ideal studies provide the most reliable estimates of stroke in a population because of these standard methodologies and definitions and provide data that are typically comparable across populations. However, as these studies are resource intensive and expensive to conduct, they are traditionally confined to developed countries that have already identified non-communicable disease as a major health problem. With the growing burden of stroke in developing countries, it is important to develop stroke awareness and surveillance systems in these regions, which has been made possible through the development of the WHO STEPS-Stroke program.

3.2. Trends in Stroke Mortality

Many studies have used mortality data to review trends, and geographical variation in trends, in stroke mortality worldwide, as it is easily accessible and can be reviewed retrospectively. Trends in stroke mortality may also be used to project the number of stroke deaths to estimate future burden on health care services. However, as mentioned earlier, stroke mortality data only focuses on a small proportion of the actual burden of stroke on health care services, as only approximately 30% of stroke patients die as a direct consequence of their stroke. In this section, due to the large number of trends in the mortality of stroke studies in developed countries, the focus is on international review papers that have compared trends worldwide. Trends in low to middle-income countries and ethnic disparities in trends in stroke mortality in developed countries are also explored.

Stroke mortality declined dramatically over the past four decades in many countries worldwide.[35, 155, 280] In the US, stroke mortality rates began to decline in the 1920s, the decline accelerating in the 1970s.[18, 281] In many industrialised countries, the average decline from 1970 to 1990 was around 50%, with declines up to 75% in Japan.[35] However, more recently, there have been suggestions of a reduction in the decline in stroke mortality in many countries.[33, 36] There is great variability in trends across the world, with diverging trends, due to increasing rates in Eastern Europe and decreasing or stable rates in affluent industrialised countries.[36, 282]

A recent review of international trends, compared mortality data from 51 industrialised and developing countries worldwide, from 1968 to 1994, using mortality data from the WHO data bank.[36] This review was one of the first to investigate trends in mortality in the elderly (people aged over 75 years). In general, the highest rates of stroke mortality were found in Eastern European countries, Mauritius and Trinidad and Tobago, with the lowest rates in Switzerland, Canada, the United States and Australia. The largest declines in stroke mortality were observed in Japan, Australia, France, Switzerland and the United States, as well as in Israeli women. Increasing trends were found in Eastern European countries, especially the former republics of the Soviet Union, since the 1990s. Temporal trends were more favourable for women than men, with steeper declines in mortality and if there was an increase in rates, the increase was smaller for women than men. The countries with low mortality rates, or showing steep declines in stroke mortality, were typically affluent industrialised countries.[36]

These results are comparable to other international comparisons of trends in stroke mortality rates, where countries with higher rates tended to experience less favourable secular trends than countries with low rates.[35, 36, 155] Japan had the largest declines in stroke mortality, [35, 36, 283-285] with an average annual decline of 7%, from the 1970's onwards.[36] However, as with other developed countries this decline has been reduced since the 1990s.[283] Recently, there have been consistent declines in stroke mortality in Brazil over the past three decades, with the greatest decline in more recent years between 1990 and

2000.[286] Less decline in the poorer regions of Brazil, led to the assumption that improved general health and economic conditions are partially responsible for the decline in stroke mortality.[286]

New Zealand was ranked within the top 10 countries with the largest declines in stroke mortality from the 1970s.[36, 155] However, greater declines in stroke mortality have been found in Australia compared to New Zealand.[287, 288] In a review of cardiovascular mortality in New Zealand and Australia from 1968-1983, New Zealand had lower rates of stroke in the beginning period. However, due to larger declines in Australian populations stroke mortality rates became lower in Australia over time.[288] The reasons for the differences are not known but may be due to a slower uptake of primary prevention strategies for cardiovascular risk factors in New Zealand.

Most mortality studies do not provide information on trends in stroke subtypes due to problems with the coding of stroke subtypes on death certificates, which may mask different patterns of change among subtypes. A study from the UK, reviewing autopsy studies, found steep declines in mortality from cerebral haemorrhage with an increase then decline in ischaemic stroke subtypes.[233] The ratio of ischaemic stroke to haemorrhage increased from 0.5 in the 1930s to 2.0 in the 1970s, which may be due to increasing diagnostic capabilities and declines in the proportion of uncertainty about stroke diagnosis.[233] Similar trends of larger declines in haemorrhagic compared with ischaemic stroke have been shown in several countries worldwide.[258, 284, 289] The decrease in mortality for haemorrhagic stroke occurred after CT scanning was first introduced, which may be due to the identification of smaller haemorrhages which would have been previously classified as ischaemic strokes.[258] Whereas, trends in mortality from ischaemic stroke were found to mirror those in coronary heart disease, suggesting changes in common causes such as atherosclerosis.[290]

3.2.1. Ethnic Disparities in Trends in Stroke Mortality

As discussed in Chapter 2, disparities in the rates of stroke among ethnic groups in developed countries have been shown, with the highest rates in

ethnic minority groups. Ethnic disparities in trends in the rate of stroke mortality over time have also been shown. In the US, African Americans had consistently higher rates of stroke mortality than white Americans over time, with no change in the ratio of stroke mortality rates between African Americans and whites.[18, 291, 292] Declines, up to the year 1996 were largest in white men and smallest in African American men,[293] whereas, in the UK, the largest declines in stroke mortality were found in Caribbean and African immigrants.[294] More recently, the decline has dropped off, particularly in US white populations.[281] It has been hypothesised that the reduction in the decline in stroke mortality rates in white Americans was due to a plateau being reached and rates are not expected to decline much more.[293] However, mortality rates in African Americans have not yet reached this plateau and are expected to keep declining.

Variability in trends in stroke mortality has also been shown in New Zealand. Significant declines were found from 1953-1979 in non-Māori men and women and Māori women, with stable rates among Māori men.[39] Recently, it was shown that in New Zealand, all cause mortality declined across all ethnic groups from 1980 to 1999.[12] However, the gaps in mortality between Māori and Pacific and non-Māori non-Pacific New Zealanders actually widened across the 20 years, due to steeper declines in the latter group. For stroke, it was found that Pacific populations had the highest rates of stroke mortality, and again although rates declined in all ethnic groups, the decline was slower in Māori and Pacific populations, leading to widening of the disparities over time.[40]

3.2.2. Summary

Mortality data are invaluable in investigating changes in the rates of disease over time, for comparing rates between populations and identifying high-risk groups, due to the low cost, easy accessibility of the data. Significant geographical variations in trends in stroke mortality have been shown over time, with declines in most developed countries and increases in Eastern European countries. Mortality data has also been important in identifying ethnic disparities in the rates and trends in stroke death in developed

countries, leading to the development of health policies aimed at eliminating these disparities, particularly in the US and New Zealand.[150, 153]

Comparisons of trends in stroke mortality between populations or over time should be interpreted with caution, due to the variability in the access to, and quality of, mortality data. Mortality data also only provides information on fatal patients of stroke, which is only 30% of the burden of stroke and trends in stroke mortality may be influenced by changes in diagnostic coding of stroke.[233] Inferences can be made about what has influenced trends in stroke mortality over time, with associations with changes in the incidence of the disease or improvements in treatment and survival over time. However, these associations need to be made in a population-wide setting, to ensure that all patients of stroke are captured, not just deaths, and the causal relationship between incidence, survival and mortality can be explored.

3.3. Trends in Stroke Incidence

It is important to investigate trends in the incidence of stroke to identify the number of new patients occurring and highlight the effectiveness of primary prevention strategies. However, the results of trends in the incidence of stroke in population-based studies are varied, due to differences in study design and methodology and different study populations. The first section focuses on trends in stroke incidence from large cohort studies from the US. The second section focuses on trends in hospitalised stroke incidence from hospital-based studies. The third section reviews, integral publications from the MONICA collaboration, comparing trends in the incidence of stroke across countries in Europe and China. The fourth section reviews the limited studies that have investigated ethnic disparities in trends in the rate of stroke. The final section provides a systematic review of trends in the incidence of stroke from ideal population-based studies, as these studies provide the most reliable and comparable data on trends in the rate of stroke over time. A detailed review of how these studies were collected and analysed is provided with a summary of the results in the context of other, less robust population-based studies.

3.3.1. Trends in Cohort Studies

The incidence of stroke declined from the 1950s to the 1970s in the US.[258, 266] In a large cohort study conducted in Rochester, Minnesota, a decline of 45% in the average annual incidence of stroke between 1945 and 1979 (an annual decline of 1.3%) was found.[258, 295] In the Framingham cohort it was found that incidence rates rose non-significantly from 1953 to 1973, though these results are hampered by the small numbers of strokes.[243, 296] However, these cohort studies were limited to unique white populations in the US and were based on retrospective data analysis. As with trends in stroke mortality, the incidence of stroke stabilised in the 1970s and started to increase in the early 1980s.[11, 258] This appears to have coincided with the introduction of CT scanning, possibly increasing the detection of less severe strokes.[258] Similar trends have been found in cohort studies across Europe and Asia, with declines in the rates of stroke in the 1970s and stabilising in the 1980s.[297, 298]

3.3.2. Trends in Hospital-Based Studies

Hospital-based studies have been used to investigate trends in the incidence of stroke in many developed countries, using admission and discharge lists, due to the easy accessibility of electronic medical records. It has been shown that the incidence of stroke stabilised in the 1970s and 1980s, and then started to increase in many countries.[239, 292, 299-302] However, in Finland, continuous declines in the incidence of stroke up to 2002 have been shown.[303, 304] Declines in the incidence of stroke were typically influenced through large declines in ischaemic stroke subtypes, as ischaemic stroke contributes the largest proportion of overall stroke burden.[304, 305] However, declines were found in rates of ICH and rates in ischaemic stroke were stable or increasing in China,[156] and Japan,[284] which may be due to the high initial rates of haemorrhagic stroke in Asian countries.

Dramatic increases in the hospitalisation rates for stroke have been found, even in the light of declining or stable trends in event rates.[238, 306, 307] This may be due to improvements in the general public's knowledge about the risks and signs of stroke, and the importance of going to hospital if they have

a stroke.[189] However, this also highlights one of the problems with using only hospitalisation data, as this is influenced by changes in hospital admission and clinical care practices.

3.3.3. Trends in Stroke in MONICA

The MONICA project was the first large population-based study initiated to investigate trends in the rate of stroke over time, using standard definitions and methods of case ascertainment. As with trends in the incidence of stroke from cohort and hospital-based studies, the rates of stroke declined in the 1970s and stabilised in the 1980s, across most individual MONICA studies.[308-310] However, trends between countries diverged, with increasing rates in Eastern European countries and decreasing or stable rates in more affluent European countries.[36, 282]

In a review of 17 MONICA studies, annual stroke attack rates (all stroke) decreased from 1985 to 1990, among men in 13 studies (ranging from -6.5% to 6.8%) and among women in 15 studies (ranging from -13.8% to 4.5%),[37] producing an average annual change of -1.2% and -3.5%, respectively. However, only a few of the trends were statistically significant, with significant declines in men in Denmark and Northern Sweden and in females in Finland and Moscow and significant increases in Warsaw, Poland. Similar results of ten-year trends (between 1982 and 1995) in stroke rates using 14 of the MONICA studies, showed declines in attacks rates in men in Finland becoming significant.[311] However, most of the MONICA results are based on all stroke attack rates (not incidence strokes) and only limited age ranges were registered in the studies, thereby excluding the large proportion of strokes occurring in the elderly, and limiting the comparability of the results with other population-based studies.

3.3.4. Ethnic Disparities in Trends in Stroke Incidence

Few studies have investigated ethnic disparities in trends in the incidence of stroke, due to the limited number of populations with a large enough ethnic minority population. In the US, trends in the incidence of hospitalised stroke in African Americans were stable between 1985 and 1991, with continuous

declines in US white populations.[239] However more recently, increases in hospital discharge rates for stroke in African Americans have been shown, with declines in white Americans, suggesting a widening of the ethnic gap in the risk of stroke in the US.[41] Moreover, in-hospital mortality rates were stable over time in both African American and white American populations, suggesting that the ethnic disparities shown in stroke mortality rates are likely to be due to differences in the incidence of stroke rather than case fatality.[41] In the only large population-based study that has investigated trends in the incidence of stroke in an ethnic disparate population, it was found that trends in hospitalised stroke incidence rates were stable across all ethnic and demographic groups from 1993 to 1999, in the US.[43] However, when all hospitalised and non-hospitalised patients were included in the analyses, there was a significant increase in the incidence rates of stroke which was primarily due to increases in the rate of ischaemic stroke in the white population. In the older age groups, the ratio between African American stroke rates and whites declined slightly, which may indicate a decline in the disparity between the populations, however, this was not significant.[43]

3.3.5. Trends in Ideal Stroke Incidence Studies

This section provides a systematic review of trends in stroke incidence in ideal stroke incidence studies, explaining the methods used to select, analyse and pool the results from the studies. This review aims to provide reliable information on the direction of trends in the incidence of stroke worldwide and quantify the size of the annual change in incidence and case fatality. To date there has been no systematic review of trends in stroke incidence and outcome using data from ideal studies.

3.3.5.1. Methods

Data for this review were identified from the following databases: MEDLINE, EMBASE, CINAHL, and BIO ABSTRACTS using similar search strategies. The search strategy (Appendix 2) identified all publications with "cerebrovascular disorders" (based on the Cochrane Stroke Group methodology) and any mention of "ethnicity", "incidence", "prevalence", "case fatality", "mortality", "morbidity" or "epidemiology" and "trend" or "decline" in

the title, keywords or abstract of the publication. Reference lists and conference proceedings were also checked for relevant studies. Studies were included in this review if they met the following criteria for an ideal stroke incidence study (described previously):

- prospective population-based study
- standard definitions of stroke
- no upper age limit
- hot pursuit of patients, hospitalised and fatal
- inclusion of non-hospitalised non-fatal patients by regularly checking with GPs, rest homes and private hospitals
- temporal trends in the incidence of stroke
- similar protocols and definitions used across the studies
- published between 1990 and 2005.

The studies from the searches were grouped into four categories: population-based ideal stroke incidence trends (if they met the inclusion criteria), population-based (not ideal) stroke incidence trends, stroke mortality trends, and not stroke or temporal trend. If a study met the inclusion criteria, but had not published data on trends in the incidence of stroke, the authors were contacted for any information on the study. If no information was provided, this study was labelled as a "drop out" study and not included in the review.

Data Extraction

Data on the incidence and case fatality from stroke were extracted from the published papers, using a standardised form and excel spreadsheet. A second reviewer did not check the data extraction, it was however, checked on multiple occasions. If data from the same cohort, using the same study design and geographical region but covering different study periods, were published in multiple publications, these were maintained in the review as

separate studies or the most recent publication was used. The results from the study periods across were combined to give an overall result for that study cohort.

Statistical Analysis

A study was defined as data from a publication meeting the inclusion criteria for this review. Study periods were defined as the continuous measurement of stroke data, usually over whole calendar years. Sequential study periods were studies conducted using the same methodology and geographical region at different time points. The percentage change in rates was calculated between sequential study periods for each study, by taking the rate of sequential study period away from the prior rate:[312]

$$\%change = \frac{R_2 - R_1}{R_1},$$

where R_i is the published standardised rate of the sequential study periods. The annual percentage change was calculated by summing the changes between sequential study periods and dividing this by the total number of years the study covered. The overall percentage change was calculated by taking the rate of the last study period away from the rate from the first study period. 95% confidence intervals were calculated by using a Poisson Distribution, using $\alpha = 0.05$. See Appendix 3 for a detailed description of these calculations. All of the analyses were conducted on published standardised rates. Therefore, the rates were not re-analysed or re-standardised to a common standard population, as not all of the papers presented crude incidence rates by age and sex.

Pooled estimates

Where appropriate the overall and annual percentage changes were pooled to give an overall effect of trend for the study cohort. For each endpoint, the inverse variance method was used to calculate a fixed effects estimate of the pooled effect size of the studies.[313] See Appendix 4 for a detailed description of these analyses. The Q-statistic was used to test for heterogeneity between the studies. If significant heterogeneity was found (p-value <0.05), the

DerSimonian and Laird random effects model was used to pool the data.[313] Both the fixed and random effects are presented here to show the difference between the fixed and random effects models. A number of sensitivity analyses were conducted by grouping studies into similar geographic regions (Australasia, Western Europe and Eastern Europe) and study decades 1970 to 1990 and 1990 to 2000. Studies with extreme results were removed from the pooled estimates to check the reliability of the pooled results. Only data on total incident stroke were pooled, if the published data were only presented by sex then the studies were not included in the pooled analysis.

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology • Age groups • Standardisation • Rate denominator • Analysis	Presented Data	Strengths and Limitations
Bonita et al. 1993 [314] Auckland, New Zealand	1981-1982, 1991-1992	Patients admitted to 4 hospitals checked daily. Death certificates and necropsy reports checked monthly. Monthly contact with sampled GPs, rest homes, private hospitals, stroke groups. Out of region hospitals checked. Sampling of out of hospital strokes. Extra checks in 1991 study, electronic discharge list, neuro-radiology lists.	• 15+ years, 10 year age groups • Direct, to Segi world population, per 100,000 • National census 1981 and 1991 for the Auckland region • 95% CI adjusted for sampling procedures. Mantel-Haenszel chi-square test, Breslow-Day test for heterogeneity	• Crude incidence rates by age and sex • Standardised rates by sex • Rate ratio of standardised rates by age (<75,≥75) and sex • 28 day case fatality (%) with rate ratio	**Strengths** • Similar protocols and quality-control measures • Same length of study periods • Crude and standardised rates • Extra checks for case ascertainment in latter study **Limitations** • Trends across only 2 study periods • Sampling procedures of non-hospitalised patients • Unadjusted numbers for sampling presented for 1981 study • No subtypes due to low CT rates

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology •Age groups •Standardisation •Rate denominator •Analysis	Presented Data	Strengths and Limitations
D'Alessandro et al. 2000 [315] Valle d'Aosta, Italy	1989, 1996-1997	Collected all strokes and TIAs Daily checks of hospital admission records, neurology and geriatric departments. GPs, first-aid and hospital doctors asked to refer cases. Death certificates checked weekly. Out of region hospitals checked.	•All ages, 10 year age groups •Direct, to 1991 Italian population, per 1000 •ISTAT census 1988 and 1996 for Valle d'Aosta •Chi-square test for comparisons between the two periods	•Crude incidence rates by stroke subtype, and sex •Crude and standardised incidence rates by age and sex •Age and sex distribution of Valle d'Aosta and Italy •30 day fatality (%) by stroke subtype	**Strengths** •Similar protocols •All strokes and TIAs registered •Same length of study periods •High CT rate for subtypes **Limitations** •Small population size •Small number of annual strokes •Trends across only 2 study periods
Feigin et al. 1995 [316] Novosibirsk, Russia	1982-1992	Notification from 2 hospitals, GPs, neurologists, in- and out-patient clinics, pathologists and forensic experts. Daily review of death certificates and ambulance registrations, weekly review of hospital registrations, outpatient clinics and autopsy's.	•All ages, 10 year age groups •Direct, 1970 US white population, per 100,000 •All-Union census, 1979 to 1989 •Poisson regression adjusting for sex, age, and period	•Annual crude and standardised incidence rates, overall, by age and sex •Plots of 3-year running average incidence rates, by sex and age •Crude and adjusted 30 day case fatality rates by sex, overall	**Strengths** •Constant methodology •Provides annual crude and standardised age*sex rates •97% of patients seen by a study neurologist •Comparisons with Rochester study **Limitations** •No subtypes, no CT until 1992 •Used US population as standard

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology •Age groups •Standardisation •Rate denominator •Analysis	Presented Data	Strengths and Limitations
Jamrozik et al. 1999 [317] Perth, Australia	1989-1990, 1995-1996	Collected all strokes and TIAs Neuro-radiology lists, inpatient admissions to 2 hospitals, and death registrations. Nursing homes and GPs contacted regularly. Electronic records of all inpatient separations and death registrations for Western Australia.	•All ages, 10 year age groups •Direct, Segi world population, per 100,000 •Census estimate, 1989 and 1995 •Poisson regression adjusting for age, period	•Plots of age-specific incidence and attack rates by period by sex •Standardised incidence and attack rates by sex, and subtype •Measures of severity of strokes by time •28 day case fatality (%) by subtype	**Strengths** •Similar protocols •Registered all stroke and TIA •Stroke subtypes **Limitations** •Uneven periods of registration •Small study population •Trends across only 2 study periods
Jorgensen et al. 1992 [318] Frederiksberg, Denmark	1972-1974, 1989-1990	All hospital cases evaluated. GPs and nursing institutions regularly asked to send non-hospitalised patients to out-patient clinic. Checked death certificates regularly.	•All ages, 10 year age groups •Indirect, to 1990 study population and 1990 Danish population, per 1000 •Frederiksberg official statistics, 1973 and 1990 •Chi-square test	•Sex and age distribution of the 2 periods •% Incident and recurrent cases •Tables of crude and standardised incidence rates overall, male and female •Incidence rates by stroke subtype for 1989-1990	**Strengths** •Similar protocols •Provide the age-sex distribution of the area for the two study periods •Crude and standardised rates **Limitations** •Different time lengths of the studies •Trends across only 2 study periods •Decrease in population over time •GP notification in 1972 study, only if not already registered

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology • Age groups • Standardisation • Rate denominator • Analysis	Presented Data	Strengths and Limitations
Korv et al. 1996 [319] Tartu 1, Estonia	1970-1973, 1991-1993	Collected all strokes and TIAs in 1970 study. DNN University hospital, 5 hospitals, one outpatient clinic. Home call registers, death certificates and autopsy records checked. Discharge lists of other departments and hospitals checked monthly. All neurologists and GPs asked to send patients to outpatient clinic.	• All ages, 10 year age groups • Direct method to average pop 1991-1993 and 1990 Estonia pop, per 100,000 • Tartu census, 1970 and 1989 • Chi-square test	• Crude incidence rates, overall by age, and sex • Standardised incidence rates overall and by sex • 30 day (%) case fatality	**Strengths** • Similar protocols • Registered all strokes and TIAs only in the 1970 study • Crude and standardised rates **Limitations** • Different lengths of study periods • Different rates of patients admitted to DNN, with patients aged <60 years only admitted in 1970 • Trends across only 2 study periods • Did not use mid-year age bands • Small population • Only incident cases registered • Low use of CT in 1970 study

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology • Age groups • Standardisation • Rate denominator • Analysis	Presented Data	Strengths and Limitations
Lemesle et al. 1999 [320] Dijon, France	1985-1994	Collected all first ever strokes and TIAs. University hospital, 4 private hospitals, 3 radiological centres, neurologists and vascular specialists, GPs, death certificates checked regularly.	• All ages, (<55, 55-74, 75+ years) • Direct, Segi world population, per 100,000 • Annual census estimates for Dijon • Mean annual change in incidence rate=a*exp(bt)	• Standardised incidence rates by subtype by sex, year • Mean annual change in crude rates by sex, age by subtype • Plots of crude rates by subtype, by sex, by age	**Strengths** • Constant methodology • Registered all strokes and TIAs • Annual rates for 10 years • Ischaemic stroke subtypes • Low rates of undetermined strokes **Limitations** • Only ischaemic rates presented • Overall rates not presented • Rates not presented by age • Small population • Low numbers of strokes • Only incident strokes collected

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology •Age groups •Standardisation •Rate denominator •Analysis	Presented Data	Strengths and Limitations
Morikawa et al. 2000 [260] Oyabe, Japan	1977-1981, 1982-1986, 1987-1999	All admissions from 3 general hospitals, all GPs in the area (25 in 1977 and 31 in 1991). Also public health nurses, local associations, and stroke support groups were checked. Death certificates, social insurance records and ambulance registers were regularly checked.	•Ages 25+ yrs, 10 year age groups •Indirect, mean population of the Oyabe Health centre 1977-1991, per 100,000 •Population of the Oyabe Health centre •Chi-square test for trend for pairwise tests	•Proportion of stroke subtype by sex, and period •Crude incidence rates by age and sex, by period •Standardised rates by age (<75, >75) and sex, by period •28 day case fatality (%) by age, sex	**Strengths** •Similar protocols •Crude and standardised rates •Presented stroke subtypes •Annual collection of cases **Limitations** •Only incident strokes collected •Overall rates not presented •Low number of reports from GPs, high from death certificates •Small number of annual strokes •Not all hospitals and GPs included •Change in CT use

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology •Age groups •Standardisation •Rate denominator •Analysis	Presented Data	Strengths and Limitations
Rothwell et al. 2004 [38] Oxford, UK	1981-1984, 1986, 2002-2004	Collected all strokes and TIAs Computerised hospital diagnostic codes, hospital admission and emergency department registers, coroners office and death certificates, checked regularly. Regular visits and newsletters to 9 general practices, 63 GPs. Extra checks in 2002 study, daily visits hospital units and wards. List of patients having brain imaging or Doppler.	•All ages, 10 year age groups •Direct, 2001 England and Wales population, per 1000 •Age-sex register of GP practices •CIs calculated with Poisson distribution. Poisson regression models adjusted for age and sex	•Age-sex structure of two populations with crude incidence rates •Standardised incidence rates by three periods, sex, age, overall, subtype, disability •Plots of rates by age for TIA, minor and non-minor stroke •Crude and standardised incidence TIA's •Plots and tables of premorbid risk factors and medication	**Strengths** •Similar protocols •Registered all strokes and TIAs •All cases in both studies were reviewed by the same neurologist •Crude and standardised rates •Presented stroke subtypes •Extra methods of case ascertainment in 2002 study •Checks for complete case ascertainment **Limitations** •Different lengths of study periods •Small population, not defined by geographical boundaries •Small number of annual strokes •Not all GP practices in region included. •Census not used for denominator

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology • Age groups • Standardisation • Rate denominator • Analysis	Presented Data	Strengths and Limitations
Terent 2003 [268] Soderhamn, Sweden	1975-1978, 1983-1987, 1987-1990	Collected all strokes and TIAs One Hospital checked daily, GPs, nursing institutions in the area checked weekly. Asked all doctors to send all strokes and TIAs to hospital. Death certificates were checked from the National Bureau of statistics.	• Ages 15+ years, 10 year age groups • Direct, age and sex to 1990 Swedish pop, per 100,000. Direct, age to Euro pop of 1999 • Census population of Soderham 1974, 1983, 1987. • CIs calculated using Poisson distribution. Linear regression for trends. Survival analysis, logistic regression and Kaplan Meier	• Crude and adjusted incidence rates, by sex, overall • Plots of correlation between rates and year, by subtype • Case fatality (%), 7 days, 28 days, and 3 months • Survival 1, 5 and 10 years, by age and overall	**Strengths** • Similar protocols • Collected all stroke and TIAs • Crude and standardised rates • Survival analysis **Limitations** • Different lengths of study period s • Different length of times between study periods • Small population, small number of annual strokes • Low use of CT scanning • Large proportion of industrial workers • Only incident cases in first period

Table 3.2 Summary table of methods used for case ascertainment, analysis and data presentation, and the strengths and limitations for population-based ideal stroke incidence studies.

Study/Region	Years	Case Ascertainment	Methodology •Age groups •Standardisation •Rate denominator •Analysis	Presented Data	Strengths and Limitations
Vibo et al. 2005 [321] Tartu 2, Estonia	1991-1993, 2001-2003	Similar to Korv (1996) DNN University hospital. Death certificates and autopsy records checked. Discharge lists of other departments and hospitals checked. All GPs contacted monthly.	• All ages, 10 year age groups • Direct, European pop • Mean Tartu census population 1991-1993 and 2001-2003 • CIs calculated using binomial distribution. Trend in rates per year. Chi-square for test	• Crude incidence rates, overall by age, and sex • Standardised incidence rates overall and by sex • 28 day case fatality by sex	**Strengths** • Similar protocols • Crude and standardised rates • Annual trend presented **Limitations** • Uneven periods of registration • Trends across only 2 time points • Did not use the first study period 1970-1973

CI = Confidence Interval, CT = Computed Tomography Scan, DNN = Department of Neurology and Neurosurgery (Tartu), GP = General Practitioner, TIA = Transient Ischaemic Attack

3.3.5.2. Results

The search strategy produced a large number of publications (over 3000 publications). Only 11 ideal studies investigating trends in stroke incidence met the inclusion criteria (Table 3.2).[38, 260, 268, 314-321] Six out of the eleven studies used only two time points to investigate trends,[314, 315, 317-319, 321] and two studies used annual incidence data to investigate trends.[316, 320] One study published data on ischaemic strokes only, although information on all strokes was collected.[320]

There were three publications investigating trends in stroke from Soderhamn, Sweden: two investigating trends from 1975 to 1986[322, 323] and one investigating trends from 1975 to 2001.[268] The latter publication was used in this review as it encompassed the data from the previous papers and provided updated data.[268] Two separate publications investigating trends in the incidence of stroke from Tartu, Estonia were published.[319, 321] Three studies were conducted using similar definitions and methodology, with the first publication investigating trends in stroke between 1970-1973 and 1991-1993 (Tartu 1)[319] and the second investigating trends between the 1991-1993 and 2001-2003 studies (Tartu 2).[321] The individual published papers were included in this review.

Drop-out studies

In 2005, data on trends in stroke incidence and case fatality rates in Southern Greece, were presented at the European Stroke Conference in Bologna.[324] The original study in Athens, Greece fulfilled the criteria for an ideal stroke incidence study.[325] However, to date the trend data has not been published. The authors of the conference abstract were contacted for information about the trends analysis, but no information was heard back from them, so the study was not included in the review.

Study Methods

Even though all of the studies fulfilled the criteria for an ideal study, there was still variation in the methods of case ascertainment, standardisation and

analysis in each study. This section describes the variation in study methodology between the studies.

Case Ascertainment. Most studies used a defined geographic region involving all hospitals in the region. However, the study population of the Oxfordshire Community Stroke Project (OCSP) and the OXVASC studies were based on a selection of GP practices in Oxfordshire, if they had an age-sex register of patients, and were willing to notify all stroke patients to the register. Therefore not all GPs in the Oxfordshire area were included in the study and the rates calculated are only valid for those practices used in the analysis.[24] Whole calendar years of data (12 months) were used in all studies to eliminate any bias due to seasonal variation in the disease. However, different lengths of data collection were used in three publications, Frederiksberg (3 years and 1 year),[318] Tartu 1 (4 years and 3 years),[319] and Oxford (3 years, 1 year, 2 years).[38] It has been assumed that this was adjusted for in the original calculation of the rates.

All studies received immediate or daily notifications of all hospitalised patients of stroke, and death certificates and autopsy records were checked regularly. All studies used GPs as the main source of notification of non-hospitalised patients, with nursing homes and private hospitals also checked regularly throughout the study periods. Extra checks for community patients involved inspection of first-aid and ambulance registers[260, 314-316], social insurance records[260], neuro-radiology lists,[38, 314, 317] and stroke support groups[260, 314]. Five studies collected all strokes and TIAs occurring in the population.[38, 268, 315, 317, 320] Five studies also checked for hospitalisations and deaths of residents in the study region due to stroke in hospitals in surrounding regions.[314, 315, 317, 319, 321] Sampling methods in the collection of community case ascertainment were used in the Auckland studies.[26, 45] The Auckland studies were used in the trends analysis for this thesis and will be explained in more detail in Chapter 4.

*Methodolo*gy. Most studies included all age groups in their registration, with the exception of Auckland[314] and Soderhamn[268] registering patients over the

age of 15 years, and Oyabe[260] registering patients over the age of 25 years. Most studies presented incidence rates in 10 year age groups.

In all of the studies, the method of standardisation used in the analysis of rates and the standard population, were clearly stated in the publication. Most studies used the direct method of standardisation to age-standardise rates to a relevant population. However, the standard population used to standardise rates varied across the studies, with only two studies using a standard world population.[314, 317] This makes comparisons between studies more difficult as different standard populations were used. The indirect method of standardisation was used in two studies, which is a useful method of standardisation when comparing rates within a population and when there are small numbers in the age and sex categories.[260, 318]

It is important that official standard data were used for the calculation of rates, which typically involves using census data for the given region. Most studies used official national census data for the study region on, or around the time of the study period as the denominator in the calculation of rates,[268, 314, 315, 318-320]. However, the age-sex register of the GP practices included in the Oxford study were used as the denominator for the calculation of rates[38] and annual data from the Oyabe health centre was used in the Oyabe study.[260]

Poisson regression was used in five studies to test for a temporal trend, adjusting for age, sex and study period.[38, 268, 316, 317, 320] In studies, spanning two periods a chi-square test was typically used to test for differences in rates between the periods. Confidence intervals around the rates were typically calculated using Poisson distribution, with the exception of one study, which used the Binomial distribution to calculate confidence intervals.[321] Trends in long-term survival, up to 10 years after stroke, was conducted in Soderhamn, Sweden.[268]

Presented Data. All studies presented information on first-ever in a life-time (incident) strokes, with only one study presenting data on all stroke events.[317] Incident cases of stroke only were registered in five studies, so total event rates could not be investigated.[260, 268, 319-321] Incidence rates were presented

using mid-decade age-bands including the oldest age groups (85+ years), with the exception of Tartu 1.[319] Most studies published both crude and standardised rates of strokes by age and sex for the study populations, by period of study. Nine studies presented information on 28 or 30 day case fatality.[38, 260, 268, 314-317, 319, 321] Although information on all strokes were collected in Dijon, France, only the data for ischaemic stroke subtypes were presented in the publication, limiting the comparability to other studies.[320]

Strengths and Limitations. The main strength of these studies is that they all used similar methodologies across the study periods. Additional checks for case ascertainment were added in subsequent study periods in two studies.[38, 314] Five studies actively registered TIA's as well as strokes, thereby increasing the sensitivity of capturing mild patients of stroke.[38, 268, 315, 317, 320] Five studies presented rates by stroke subtypes, allowing investigations of changes in the aetiology of the disease over time.[38, 260, 315, 317, 320] Two studies presented annual stroke rates across the study period.[316, 320]

One of the main limitations in these studies is that they all have small base populations, with less than 250 patients of stroke occurring per annum, with the exception of Auckland.[314] Only five studies used more than two time points to investigate trends.[38, 260, 268, 316, 320] Due to the time periods of these studies, CT imaging was limited in early studies, thereby limiting the presentation of results by stroke subtype.

Table 3.3 Summary table of overall percentage change in incidence and annual percentage change in incidence and case fatality for ideal studies.

Study/Region	Years	Incidence Overall % change		Incidence Annual % change		28 day CF Annual % change
Bonita et al. 1993 [314] Auckland, New Zealand	1981-1982, 1991-1992	Incident 0.74 •Male -9* •Female 9		Incident 0.07 •Male -0.9 •Female 0.9		28 day CF -2.5* •Male -1.9 •Female -3.1*
D'Alessandro et al. 2000 [315] Valle d'Aosta, Italy	1989, 1996-1997	Incident 10.4* •Male 14.0 •Female -2.3	Subtype •ISC 58.7 •PICH 0 •SAH 140 •UND -80	Incident 1.3 •Male 1.8 •Female -0.3	Subtype •ISC 7.3 •PICH 0 •SAH 17.5 •UND -10	30 day CF 0.06 •ISC 1.9* •PICH -1.7 •SAH -5.3 •UND 1.9
Feigin et al. 1995 [316] Novosibirsk, Russia	1982-1992	Incident -13.8 •Male -16.0 •Female -11.1		Incident -0.7 •Male -0.5 •Female -0.1		30 day CF -0.5 (age adjusted rate)
Jamrozik et al. 1999 [317] Perth, Australia	1989, 1995	Incident -26.9* •Male -29.9* •Female -24.4	Subtype •ISC -19.4 •PICH -40.7 •SAH -48.4 •UND -50.0	Incident -3.8 •Male -5.0 •Female -4.1	Subtype •ISC -2.8 •PICH -5.8 •SAH -6.9 •UND -7.1	28 day CF 0.4
Jorgensen et al. 1992 [318] Frederiksberg, Denmark	1972-1974, 1989-1990	Incident 18.1* •Male 41.5* •Female 3.3		Incident 1.0 •Male 2.3 •Female 0.2		
Korv et al 1996. [319] Tartu 1, Estonia	1970-1973, 1991-1993	Incident 13.1 •Male 14.2 •Female 10.1		Incident 1.0 •Male 1.1 •Female 0.8		28 day CF -3.8
Lemesle et al 1999. [320] Dijon, France	1985-1994		Subtype ISC •Male -5.6 •Female 4.4		Subtype ISC •Male 0.9 •Female 5.6	

Table 3.3 Summary table of overall percentage change in incidence and annual percentage change in incidence and case fatality for ideal studies.

Study/Region	Years	Incidence Overall % change		Incidence Annual % change		28 day CF Annual % change
Morikawa et al. 2000 [260] Oyabe, Japan	1977-1981, 1982-1986, 1987-1991	Incident •Male -39.5* •Female -30.9*		Incident •Male -2.9 •Female -2.0		28 day CF •Male -1.5 •Female -2.0
Rothwell et al. 2004 [38] Oxford, UK	1981-1984, 1986, 2002-2004	Incident -28.6* •Male -33.6* •Female -23.7*	Subtype •ISC -26.4* •PICH -54.5* •SAH -27.3	Incident -1.3 •Male -1.6 •Female -1.1	Subtype •ISC -1.2 •PICH -2.4 •SAH -0.2	30 day CF -0.15
Terent 2003 [268] Soderhamn, Sweden	1975-1978, 1983-1987, 1987-1990	Incident 3.1 Crude 1.8 Crude male 0.2 Crude female 3.7		Incident 0.36 Crude 1.8 Crude male 0.2 Crude female 3.7		28 day CF -1.2
Vibo et al. 2005 [321] Tartu 2, Estonia	1991-1993 2001-2003	Incident -18.3* •Male -14.5 •Female -19.6*		Incident -1.8 •Male 1.5 •Female -2.0		28 day CF -1.3 •Male 0.4 •Female -2.0*

* Significant change, stated in publication

ISC = Ischaemic Stroke, PICH = Primary Intracerebral haemorrhage, SAH = Subarachnoid Haemorrhage, UND = Undetermined

CF = Case Fatality

Overall percentage change

Table 3.3 presents the overall percentage change in incidence rates for the 11 studies included in this review. This was calculated to show the magnitude and direction of the change in incidence rates between the first and last time points in the studies. There were significant declines in overall incident stroke in Valle d'Aosta,[315], Perth,[317], Oxford,[38] and Tartu 2,[321]. However significant increases in the incidence of stroke were found in Frederiksberg,[318] and Tartu 1.[319] The trends between the sexes were variable across studies with significant declines in both males and females in Oxford,[38] and Oyabe.[260] Declines were found in males only in Auckland,[314] and Perth,[317] with declines in females in Tartu 2,[321] and large increases in males only in Frederiksberg.[318] However, the pooled overall percentage change was -7.0% (95% CI -3.5% to 10.6%). Significant heterogeneity in the overall percentage change was found between the studies (p-value for heterogeneity <0.0001). Therefore, the random effects model was used to pool the results, giving a non-significant overall absolute change across these studies, -4.9% (95% CI, -16.6% to 6.8%).

Annual Percentage Change

Annual percentage change in incidence is a better measure of change as it takes into account information from all periods/registers used in the study and over how many years the data were collected (Table 3.3, Figure 3.1). There is still much heterogeneity between the results of the studies (p-value for heterogeneity <0.0001), with many of the confidence intervals crossing zero indicating a non-significant annual change in rates. A large decline in annual percentage change in Perth was still evident,[317] as well as a significant annual decline in Oxford,[38] and Tartu 2.[321] There was also a trend towards increasing annual change in Frederiksberg,[318] and Tartu 1.[319] Significant heterogeneity in the annual percentage change estimates was found between the studies, so the random effects method was used to calculate the pooled estimate of annual change. A non-significant decline, -0.6% (95% CI, -2.0% to 0.7%), in the annual change in the incidence of stroke was found across the studies.

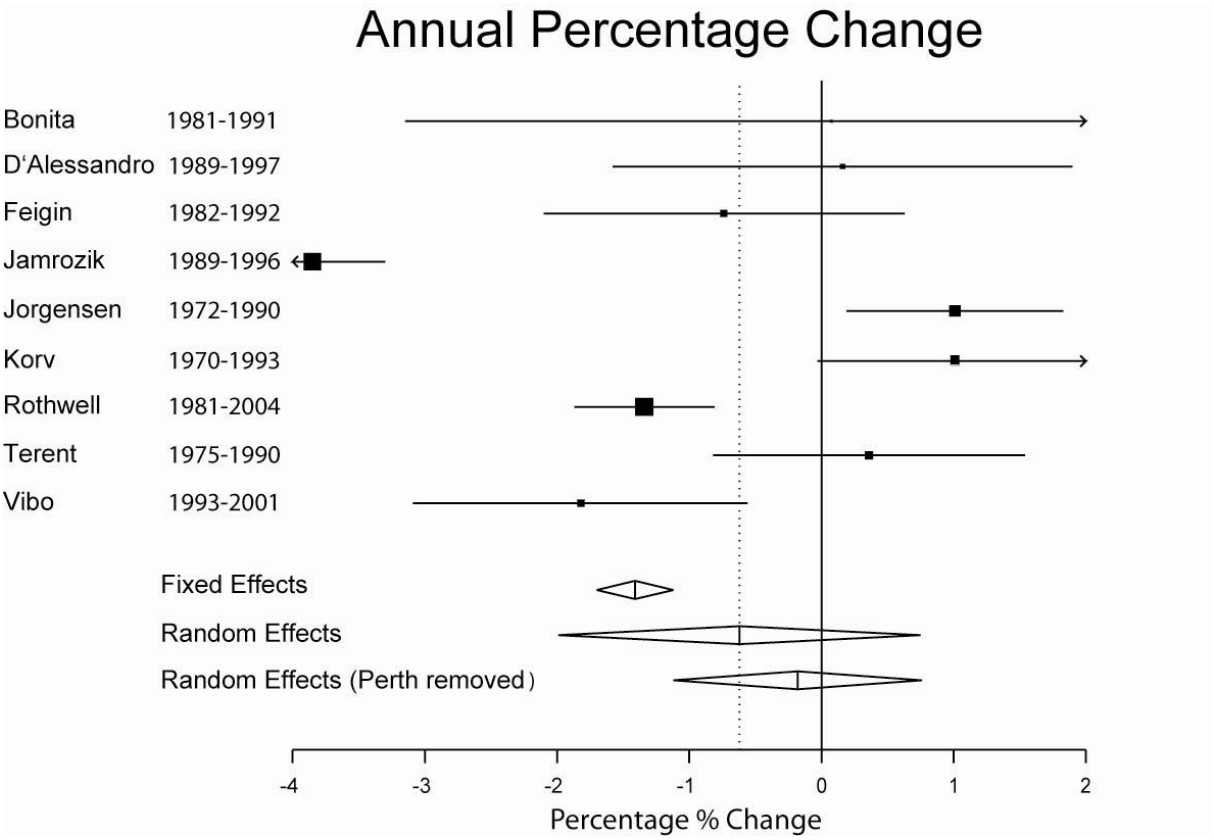

Figure 3.1 Forrest plot of annual percentage change in incidence of stroke, from ideal stroke incidence studies.

The trends across stroke subtypes were variable, with declines in all subtypes in two studies,[38, 317] and increases in Valle d'Aosta.[315] Declines in undetermined (UND) stroke subtypes were found due to the increased use of CT imaging over the years, leading to better classification of stroke subtypes.[315, 317] Two separate publications from Tartu, Estonia were published using different time points. In the first study, there was an increase in the annual change between 1970 and 1993[319] and in the second study there was a significant decline from 1993 to 2001.[321] After combining the results from these two studies a significant decline in the annual change in incidence from 1970 to 2001, -0.7 (95% CI -1.3 to -0.1) was found.

A number of sensitivity analyses were conducted to control for the heterogeneity in the results. Firstly, the outlying Perth study (with the largest annual decline in rates as compared to other studies) was removed, this moved the pooled random effects estimate towards the null (-0.2% [95% CI -1.1% to 0.7%]). The studies were grouped by similar time periods: 1970-1990[268, 314, 316, 318, 319] and 1990-2000.[315, 317, 321] Significant heterogeneity in the estimate between the studies was still evident using these sub-groupings, so the random effects model was used to pool the results. A non-significant increase in the annual change was found between 1970 and 1990, 0.5% (95% CI -0.1% to 1.2%), which was influenced by the large increases in Frederiksberg[318] and Tartu 1.[319] A non-significant decline was found between 1990 and 2000, -1.9% (95% CI -4.2% to 0.3%). Finally, the studies were grouped by region, Australasia,[314, 317] Western Europe,[38, 268, 315, 318] and Eastern Europe.[316, 319, 321] Using the random effects model, a non-significant annual decline was found in Australasia, -2.2% (95% CI -6.0% to 1.6%) as well as Eastern Europe, -0.5% (95% CI -2.1% to 1.2%). No change was found in Western Europe, 0.01% (95% CI -1.4% to 1.4%).

3.3.5.3. Limitations of review

There were a number of problems in the comparability of the data in this review. Firstly, published data only were used in the analyses and rates were standardised using different methods and standard populations across the studies. However, the calculation of annual percentage change in rates controls for differences in standardisation by using standard methodology. Secondly, the studies spanned three decades (1970 to 2004) and previous literature suggested that only studies covering similar periods should be combined.[27] The heterogeneity between the studies could not be explained by geographical or periodical differences. However, the large annual decline in incidence found in the Perth study influenced the decline in the pooled estimate considerably. Thirdly, all studies, except Auckland, had small base populations with less than 250 patients of stroke occurring per annum, leading to less precise estimates of stroke with wide confidence intervals.[27] Lastly, less than half of the studies used more than two time points to investigate trends.[38, 260, 268, 316, 320] It is important that trends are investigated over more

than two time points, as this provides more reliable estimates of trends over time.

3.3.5.4. Summary

The 11 studies included in the systematic review were of high quality as they all fulfilled the stringent criteria for an ideal stroke incidence study. This review showed that there was a non-significant decline in the annual incidence of stroke from 1970 to 2004 across studies covering Europe and Australasia. The results also reflect the geographical differences in the rates of stroke found in other studies,[37] with no change or increases in rates in Eastern European populations[268, 316, 318, 319] and the largest declines found in affluent white populations.[38, 317] This review suggests that even when registers are population-based and otherwise of high quality, fulfilling most of the criteria for an ideal stroke incidence study, care is still needed in comparing the results.

3.3.6. Summary

There is much variation in trends in the incidence of stroke, which may be due to variation in the study methodologies or true geographical differences in the rates of stroke. In general, trends in the incidence of stroke declined up to the 1970s then began to stabilise, with declines occurring again in the late 1990s. The results of hospital-based and cohort studies are consistent (in the same direction or fall within the limits of the confidence intervals) with the findings in the review of trends in ideal studies, where non-significant declines or increases were found in rates between the 1970s and 1990s and larger declines occurring after the 1990s.

Although, consistent ethnic disparities in the rates of incident stroke have been shown in a number of developing countries, exploration of ethnic disparities in trends in the rate of stroke are limited to data from the US. Disparities in trends in the rates of stroke have not yet been explored within the setting of an ideal stroke incidence study. More studies over similar periods, from large, ethnically disparate, populations are needed to provide

more reliable estimates of the trends in stroke incidence over time and how these trends vary by population groups.

3.4. Trends in Survival from Stroke

Investigating trends in survival after stroke is useful as it is the most fundamental measure of stroke outcome. The majority of deaths that occur within one week after stroke are a direct consequence of the stroke, with case fatality after the first week indicating more secondary complications or co-morbidity. There is conflicting data regarding trends in short- and long-term survival, leading to uncertainty regarding the impact of improved stroke care and declines in stroke severity in populations. This section provides a review of studies that have investigated temporal trends in survival within the first month after stroke, with a pooled analysis of short-term case fatality in ideal studies. Also reviewed are studies that have investigated trends in long-term survival, up to ten years post-stroke.

3.4.1. Short-term survival

Many studies have shown significant declines in short-term case fatality (death within one month after stroke) from the US[258, 326-328] and Europe.[310, 329-332] In the MONICA project, the annual change in case fatality between 1985 and 1990 declined by -0.08 in males (ranging from -3.9 to 2.5) and -1.01 in females (ranging from -4.3 to 1.6).[37] Similar results were found over ten years, between 1982 and 1995.[311] Increasing trends in case fatality, particularly in Russian populations reflect increases in stroke mortality.[311] A number of other European studies have shown little or no change in short-term case fatality over time.[333-336]

It has been hypothesized that improvements in short-term survival may be different for ischaemic or haemorrhagic strokes, with a number of studies reporting larger improvements in survival over time among haemorrhagic strokes, indicating that declines in short-term case fatality were greater among more severe strokes.[11, 258, 297, 329, 337-339] However, this may be a reflection of increased hospitalisation of stroke and more mild patients of ICH being identified due to increases in neuroimaging.[258] Greater improvements in

survival among African Americans may be related to improvements in survival from ICH.[338]

Among 30-day survivors of first-ever stroke, about half survive five years and of those survivors, one third remain disabled, and 1 in 7 live in permanent institutional care.[174] It has been hypothesised that if survival is improving over time, then the prevalence of stroke will increase, as more people are living with the effects of stroke which in turn will lead to more patients who are disabled or dependent after their stroke.[20] However, recently it has been shown that there was no change in the number of stroke patients admitted to rehabilitation and disability scores on admission and discharge decreased over time.[340] Three independent studies found no change in disability or functional outcome upon discharge from hospital or rehabilitation after stroke.[334, 341, 342] It was also found in the National Health and Nutrition Examination Surveys (NHANES) that although the prevalence of non-institutionalised stroke survivors increased over time, there was no change in the average "health in general" among stroke survivors.[343] However, increases in the number of patients with a history of stroke will lead to increases in the proportion of people at risk of, and suffering from, post-stroke dementia.[328]

Trends in Case Fatality in Ideal Studies

Table 3.3 and Figure 3.2 show that 9 of the 11 studies in the systematic review of trends in ideal studies presented information on changes in one month, 28 or 30 day, case fatality. Five studies found significant declines in one month case fatality,[268, 314, 315, 319, 321] and four found no change in case fatality over time.[38, 260, 316, 317] The largest declines were found in females.[260, 314, 321] Of the studies that found large declines in one month case fatality, most had high initial case fatality (over 30%) and studies that found no change in case fatality had lower ratios of around 20% across all time periods, with the exception of Novosibirsk where rates were consistently around 30%.[316] The random effects model was used to pool the results due to significant heterogeneity between the studies, producing a significant decline in annual case fatality, from 1970 to 2004, -1.7% (95% CI -2.9 to -0.6). Most

of the results of trends in short-term case fatality, from other studies, fall within these confidence limits.

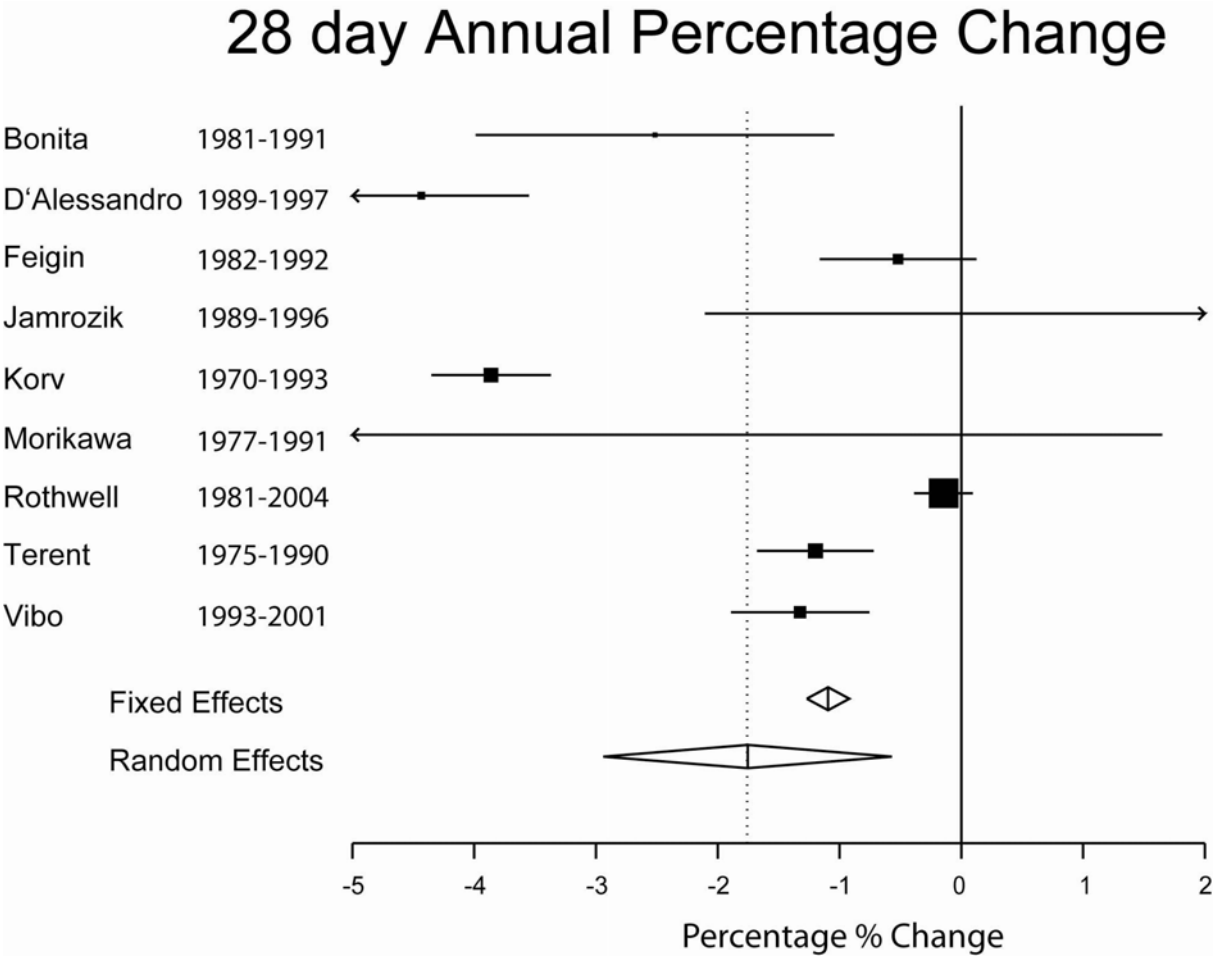

Figure 3.2 Forrest plot of the annual percentage change of 28 day case fatality, in ideal stroke incidence studies.

3.4.2. Long-term survival

Long-term survival after stroke has been shown to have improved over time in a number of studies, 1 year survival[11, 268, 296, 332, 335] and 2-5 year survival.[268, 297, 326, 332, 335, 344] Median survival times have been shown to increase four- to five-fold over the 1970s and 1980s.[345] There were only two ideal stroke incidence studies that investigated trends in long-term survival after stroke. Significant improvements in long-term survival up to 10 years after stroke

were found in Soderhamn, Sweden,[268, 323] whereas, no change in survival up to five-years post-stroke in Perth, Australia was found.[346]

Improvements in long-term survival are typically influenced by improvements in short-term survival.[326, 332, 344] However in two recent studies, no change in short-term survival was found with a significant improvement in long-term survival, which was attributed to improvements in long-term care of the elderly.[268, 335]

There is variation in the methods used to examine trends in short- and long-term survival. If modelling of survival over time was conducted, typically logistic regression was used, comparing the odds of death in one period to the next.[268, 326, 332, 344, 347] Only a few studies used the more rigorous Cox proportional hazards survival analysis, taking into account time to death and the censoring of patients (patients lost to follow up).[258, 335, 338, 345, 348]

3.4.3. Summary

Significant improvements in survival (declines in case fatality) were found in many studies across the US and Europe. Significant declines in annual one-month case fatality were also found when the results from nine ideal stroke incidence studies were pooled. There are a number of explanations for these improvements in survival, with associations with improvements in the care and management of stroke patients, changes in the severity of the disease and improvements in case ascertainment leading to the registration of milder patients of stroke.

3.5. Explanations for Trends in Rates

Trends in mortality, incidence and survival are all inter-related, so explanations for these trends are explored in this section, in order to investigate what is driving changes in the burden of stroke over time. There have been a number of explanations given for the declining trend in mortality over time, these being associated with trends in the incidence of stroke and changes in survival over time. However, most studies have only been able to investigate relationships with trends in risk factors and treatments with trends

in the rate of disease. It is important to find out whether the decline in mortality has resulted in an increase in stroke morbidity, due to improvements in survival rather than a reduction in the patients of stroke.[20]

It is difficult to untangle the puzzle of trends in the rates of stroke over time, as explanations for trends in mortality are reliant on trends in incidence and survival. Therefore, the first section will explore explanations for trends in mortality, with reference to trends in incidence, through improvements in primary prevention of stroke and trends in survival, through improved care and management of patients. The next section explores reasons for trends in incidence in more depth and the final section examines explanations for trends in survival.

3.5.1. Explanations for Trends in Stroke Mortality

A number of hypotheses have been given to explain the decline in mortality over time and why this decline has subsequently dropped off in the past decade. The decline in stroke mortality, likely reflects both declines in stroke attack rates, through preventing new strokes, and improved survival after stroke, through developments in hospital care and management.

Declining incidence of stroke may explain the declines in stroke mortality through primary prevention strategies and the effective management of vascular risk factors. A number of population-based studies have reported that declines in stroke mortality rates were due to reductions in the incidence of stroke rather than improvements in survival.[38, 258, 303, 317, 349, 350] Continuing disparities in stroke mortality among ethnic groups are more likely to reflect changes in incidence, rather than survival.[16, 41]

One main explanation for the decline in incidence has been that declines in the rate of stroke have paralleled improvements in the treatment of hypertension. There has been much research investigating the effects of anti-hypertensive treatment on declines in stroke mortality. However, most of this has only investigated the association of stroke mortality trends and trends in the use of anti-hypertensive medication in the community, so cause and effect relationships could not be established.[351-354] It has been estimated that the

treatment of hypertension accounts for only 10% of the decline in mortality from stroke.[351, 355] However, trends in the detection and control of hypertension have been shown to mirror those in stroke mortality. Rapid declines in stroke mortality occurring after 1970, may be associated with the increased treatment of hypertension,[352, 353, 356] and the off of levelling of blood pressure control in the 1980s, was followed by a marked increase in stroke mortality from 1995.[357] However, this does not explain the decline in stroke mortality that occurred before the 1970s, and the increased treatment of hypertension.[353, 358, 359]

Declines in stroke mortality have also been shown to parallel population-wide reductions in blood pressure and cholesterol levels.[360] A population-wide program aimed at reducing cardiovascular risk factors was introduced in Finland in the 1970s, producing a reduction in stroke mortality.[360] Using this data it has been argued that two thirds of the decline in stroke mortality in Finland can be explained by changes in diastolic blood pressure, total serum cholesterol and smoking, with about half of the decline explained by falls in blood pressure alone.[361]

Changes in stroke mortality over time may also be influenced by changes in the natural history of the disease or changes in diagnostic coding. It has been shown that mortality rates declined at a steeper rate in haemorrhagic strokes compared to ischaemic strokes.[233, 258, 284, 289, 356] This may be due to less haemorrhagic strokes occurring through the treatment of hypertension,[353] or due to changes in diagnostic coding and improvements in neuroimaging.[258, 290] It has been shown that the decrease in mortality from haemorrhagic stroke occurred after the introduction of CT scanning, which may have led to the identification of smaller (less severe) haemorrhages which would have been previously classified as ischaemic strokes.[258, 337]

Another potential explanation for the decline in mortality is corresponding declines in case fatality or improvements in survival over time.[238, 292, 310, 311, 328] Recently, it has been argued that over two thirds of the change in stroke mortality can be attributed to changes in case fatality.[311] If stroke mortality increased, it was found that this was almost entirely due to increases in case

fatality.[311] Other studies have also found direct relationships between declines in stroke mortality and declines in case fatality.[238, 326, 331, 362]

3.5.2. Explanations for Trends in Stroke Incidence

A number of explanations have been provided for the decline in the incidence of stroke and the levelling off of trends seen in the 1980s and 1990s. The main explanation is through changes in risk factors, and risk factor management over time. Associations have been made with changes in lifestyle factors, due to improvements in the treatment and control of hypertension and other risk cardiovascular risk factors. However, this has been shown to explain only small amounts of the variation seen in the trends of stroke rates over time.

As hypertension is the most important modifiable risk factor for stroke, many arguments have been made linking the treatment of hypertension to trends in the incidence of stroke. The appropriate treatment of hypertension has been shown to reduce the risk of first-ever stroke by at least 30%.[140, 363] Therefore, it is likely that improvements in the treatment of hypertension have led to declines in the rates of first-ever stroke.[349, 364] Recently, it has been shown that up to 40% of the variation in trends in stroke event rates, can be explained by changes in systolic blood pressure.[365] As with trends in stroke mortality, trends in stroke event rates, mirrored the trends in the treatment of hypertension, with a levelling off of the detection and control of hypertension in the 1990s.[94, 258, 349, 357, 366] However, the rate and pattern of the decline in ischaemic stroke incidence rates in hypertensive and non-hypertensive individuals were similar, showing no demonstrable population effect of anti-hypertensive medication.[367] Ischaemic stroke incidence in AF patients decreased significantly from 1980 to 2000, during which time a substantial increase in the use of antithrombotic therapy and reduction of systolic blood pressure was evident.[368]

The MONICA project has provided a unique opportunity to investigate the extent to which trends in stroke event rates can be attributed to changes in classic risk factors. It was found that combining trends in systolic blood

pressure, daily cigarette smoking, serum cholesterol, and body mass index into a risk score, only part of the variation in trends in stroke event rates could be explained.[365, 369] The decrease in the prevalence of hypertension and smoking accounted for about 29% of the decline in event rates.[370] Similar relationships were found between trends in smoking, blood pressure and cholesterol levels and BMI with trends in coronary heart disease in the MONICA project.[371]

Declines in common cardiovascular risk factors, such as smoking, cholesterol levels and hypertension have also been shown in a number of other populations.[369, 372-374] However, increases in the prevalence of obesity and diabetes may attenuate the influence of these declining risk factors on trends in stroke event rates, leading to stabilising incidence rates.[375-377] Coronary heart disease (CHD) is an important risk factor for stroke.[101] It has been shown that trends in CHD mortality are continuing to decline, even in the light of stabilising trends in stroke.[372] The incidence of CHD has been shown to have increased in Japan.[378] Therefore, if more people are living after CHD, then more people are at higher risk of having a stroke.[367] As both stroke and CHD share key risk factors, such as high blood pressure, tobacco use, and BMI, primary prevention of stroke is important in patients with a history of heart disease.[102]

3.5.3. Explanations for Trends in Stroke Survival

There are three possible explanations for improvements in survival after stroke, over time. The first correlates improvements in survival with improved medical care or treatment, leading to earlier and more appropriate management of patients with stroke. This is related to improvements in diagnostic testing through the increased availability and use of neuroimaging and increases in the rates of hospital admission for stroke. Specialised stroke teams and stroke units have been shown to significantly improve long-term survival after stroke.[203, 204] The increased use of aspirin in patients of ischaemic stroke to prevent early recurrent strokes and decreased use of aspirin and heparin in haemorrhagic strokes introduced in the 1990s, was mainly due to the results of large clinical trials[146, 379] and the introduction of

neuroimaging.[258] Also blood pressure lowering drugs help to prevent recurrent stroke, hence reducing the risk of death or major vascular event after stroke.[146, 217, 219]

The second explanation, relates improvements in survival after stroke with decreased severity of stroke over time. This could be reflected through changes in the natural history of the disease, where stroke is becoming less severe due to changes in population-wide risk factor levels.[360, 365] It has been argued that changes in the severity of stroke are a significant contributor to changes in case fatality,[345, 347] with up to 80% of the decline in case fatality in a US study explained by declines in the severity of stroke.[327] Many studies that found significant improvements in survival over time also found greater improvements in less severe patients of stroke.[326, 329] In early years, modest improvements in survival up to 5 days after ischaemic stroke were found with large improvements in patients with ICH.[337] The large improvement in survival following ICH may have been influenced by the introduction of CT scanning and the identification of smaller, less severe, haemorrhages.[258] However, in a more recent study declines in case fatality following stroke were restricted to 28 days to one year, reflecting improvements in secondary care rather than declines in the severity of stroke.[332]

The third and final explanation refers to increased registration of milder strokes due to improvements in case ascertainment or improvements in the diagnosis of stroke through neuroimaging techniques. In Allengheny County, the advent of CT scanning was accompanied by a twofold increase in survival.[327] A marked improvement in survival following ICH is due to the introduction of CT scanning, identifying smaller and less severe haemorrhages.[258, 337] However, improvements in survival up to 10 years post stroke, were found in a series of ideal studies, which provides the most reliable data over time through consistent case finding and diagnostic techniques.[268]

3.5.4. Summary

There is conflicting data as to the explanations for trends in mortality rates over time, with some studies finding large improvements in incidence and no change in survival and other studies attributing declines in mortality to large improvements in survival. Improvements in anti-hypertensive therapy only play a limited role in explaining declines in stroke mortality through declines in the incidence of stroke. However, as hypertension is still the most important modifiable risk factor for stroke, efforts still need to be made ensure that hypertension is prevented in adults or controlled well with medications. There has been limited data from ideal stroke incidence studies investigating explanations for trends in the rates of stroke over time.

3.6. The Future Burden of Stroke

It is important to estimate the future burden of stroke within population demographic groups as the rates of stroke and rates of population growth within these groups differ, and prioritised healthcare planning and prevention efforts are needed for groups suffering the highest burden of the disease. The future burden of stroke can be estimated by identifying current trends in the rate of stroke and explanations for these trends through changes in population demographics, hospital management and care of stroke patients. Another way to estimate the future burden of stroke is to apply the current rates of stroke to the future population, controlling for assumed changes in the demographic structure of the population.

It is expected that the future burden of stroke is going to grow with the ageing of populations around the world,[2] even if declines in stroke mortality continue. With the majority of stroke deaths worldwide occurring in developing countries, the number of deaths from stroke is projected to increase by 12% in 2015, if no action is taken to reduce the risk of having a stroke in the developing world.[1] However, in the US it was predicted that the number of stroke deaths will increase by 98% from the year 2002 to 2032, with the largest increases in minority groups.[22] The US population is projected to

increase by only 27% over the same time period, so increases in stroke deaths will outpace the overall population growth.

The absolute numbers of incident stroke patients were projected to decline for the period 1985 to 2005, in the Netherlands.[20] This model assumed an annual decline of 2% in stroke incidence rates, based on trends from the Rochester study, 1950 to 1979.[20, 295] However, the study ignored the more recent increase in the incidence rates found in Rochester after 1980, thereby using old trend data on a more recent population. In contrast, a more recent study conducted on the same population, assumed no change in the incidence rate of stroke and found a dramatic increase in the number of new stroke patients.[21] Changes in the size and composition of the population, alone, resulted in an increase of stroke incidence of 28% for men and 12% for women, from 2000 to 2020.[21] Changes in hypertension and smoking prevalence were also modelled in the projected stroke burden, however, these changes only increased the burden of stroke by 4%.[21]

The prevalence of stroke has also increased over many years in the US.[243, 342, 343] Age, race and sex adjusted prevalence of stroke among the US population increased by 30% between 1973 and 1991.[343] Similar findings have been found in Denmark, where even though the rates of stroke have been declining, the occurrence of stroke in the population remains stable due to increases in the elderly population over time.[308] It is expected that the prevalence rates for stroke will decline in the younger age groups but increase amongst the older age groups due to the ageing of the population and improvements in survival after stroke.[20, 21] This increase in prevalence will be associated with an increase of >30% in the potential years of life lost due to stroke.[21]

Increases in the number of people having a stroke will result in an increased burden on acute healthcare.[380] Improvements in survival will result in the increasing burden of care of long-term disabled survivors of stroke. However the number of newly dependent stroke patients, disabled as a result of their stroke, is not expected to increase over time, as patients disabled before their stroke are more likely to die as a results of their stroke.[380, 381]

The absolute numbers of people having a stroke worldwide are expected to grow, even if the rate of stroke continues to decline.[32, 382] A large proportion of this burden of care for stroke is borne by health services outside the hospital sector and by families of affected patients. This out of hospital burden is increasing as the length of acute stay in hospital is declining, with the increased use of early supported discharge care after stroke.[211, 222]

3.7. Summary

There is variability in the methods used to survey stroke over time. Mortality data are useful for estimating the burden of stroke death in populations worldwide as it is routinely collected in many countries. However, mortality data only include death from stroke, thereby, excluding two thirds of the stroke burden. Hospital-based studies provide estimates of the acute burden of stroke within a region, however, many do not include fatal and non-fatal non-hospitalised patients of stroke. Many other population-based studies are limited to restricted populations or ages, such as the MONICA project. The gold standard is an ideal stroke incidence study, which uses a prospective population-based study design, collecting all fatal and non-fatal strokes occurring in a defined region. Ideal studies provide the most reliable estimates of stroke that are comparable across populations, as standard methodologies and definitions are used. However, these studies are resource intensive and expensive to conduct and are traditionally confined to developed countries.

Due to the variability in study design and methodology, there is variation in trends for stroke incidence and outcome. However, much of the data on trends in incidence and case fatality are in the same direction of, or fall within the limits of the confidence intervals found in the review of trends in ideal studies. Trends in stroke mortality and incidence rates followed a similar pattern in many countries, with declines up to the 1970s, stabilisation in the 1980s, and the beginning of decline occurring in the late 1990s. This indicates that trends in stroke mortality are related, in part, to trends in incidence. However, other studies have found stable trends in incidence with large declines in case fatality (improvements in survival). Therefore,

improvements in survival have been strongly associated with trends in mortality. There has been limited data from ideal stroke incidence studies investigating explanations for trends in the rates of stroke over time.

It is important to explore current trends in the rate of stroke in order to be able to estimate the future burden in the community. Exploring explanations for these trends, through changes in population demographics, hospital management and care of stroke patients, will enable the identification of successful treatment and prevention strategies, and highlight high-risk groups. Trends in the rate of stroke need to be determined within population demographic groups, as the rates of stroke and rates of population growth within these groups tend to differ. This will enable prioritised healthcare planning for groups suffering the highest burden of the disease.

More studies over similar periods, from large populations are needed to provide more reliable estimates of the trends in stroke incidence and survival over time. There is a need for ethnic disparities in trends to be investigated in large well-defined studies, to enable comparisons and inferences about disparities occurring in other populations.

4. METHODS

Three large population-based prospective stroke incidence studies have been conducted in the Auckland region during 1981-1982[45] and 1991-1992[13, 26], with a more recent study conducted in 2002-2003. For the purposes of this document these will be called the Auckland Regional Community Stroke (ARCOS) studies. Similar protocols, definitions and methods for case-ascertainment were used across the three studies to enable comparability of the data and to meet the stringent criteria for an ideal stroke incidence study as described earlier in Chapter 3. The ARCOS studies used hot and cold pursuit case finding methods within the main hospitals in the region, as well as in the community, to identify cases of stroke in the "usually resident" population, aged 15 years or older, of Auckland, New Zealand. Sampling procedures were used in the two earlier studies due to limited resources, with the third study aiming to identify all people who had a stroke in the Auckland region.

This is the first time three population-based ideal stroke incidence studies have been used to investigate trends in the incidence and demographics of a stroke in a large multi-ethnic population. Therefore, this work provides a unique look into trends in stroke at a population wide level. The first section describes the study population of the Auckland region and how it has changed over the past 20 years. The second section provides a detailed description of the similarities and differences in case finding methods used across the three studies. The third section describes the consistent definitions and variables used across the three studies. The final section provides a detailed description of the statistical methods used to evaluate trends in demographics, trends and survival across the three studies.

4.1. Study Aims

The aim of this thesis was to compare data from the third ARCOS study conducted during 2002-2003, with that from the two previous ARCOS studies (1981-1982 and 1991-1992), to:

1. investigate trends in stroke incidence and event rates;
2. identify ethnic disparities in trends in stroke incidence and event rates;
3. investigate trends in outcome after stroke;
4. investigate explanations for trends and disparities through associations with trends in patient demographics, vascular risk factors, hospital management, and stroke care in the community;
5. estimate the future burden of stroke in New Zealand.

4.2. The Auckland population

Auckland is the largest city in New Zealand and includes both urban and semi-rural areas. The target population of the metropolitan region of Auckland had a usually resident population (all people who had lived in the Auckland region for the past year or intending to live there permanently), of approximately 940,000, aged 15 years and over, in 2002. The geographical region of Auckland is based on the statistical census boundaries and extends from Mercer and the Waikato River in the south, to Mangawhai Heads, north of Wellsford to Oruawharo Heads, including Waiheke and other islands in the Hauraki Gulf (see Figure 4.1). Auckland is the largest Polynesian city in the world with a diverse ethnic mix of Pacific and Asian ethnic groups providing a unique opportunity to investigate disparities in the trends in stroke incidence and outcome among Māori, Pacific and Asian peoples.

Figure 4.1 Map of the study population, the greater Auckland region.

4.2.1. Changes in the Population

In line with the ageing of the world's population, the number of New Zealanders aged 65 years and older continues to grow over the years, with an increase of 17% between 1993 and 2003.[383] It was the older people within this group who recorded the most significant growth rate. The number of people aged 65 to 74 years rose by 6%, while those aged 75 to 84 years and 85 years and over, increased by 29% and 53%, respectively. Females also significantly outnumbered males in these older age groups. Improvements in mortality, which resulted in increased life expectancy, have been an important element in this growth.[383]

In 2001, the Auckland population made up 31% of the New Zealand population. This is projected to increase to 37% by 2021 due to increasing immigration to the Auckland region from external countries as well as within New Zealand.[384] Over the past 20 years, from 1981 to 2001, the Auckland population also aged. The number of people in older age groups increased by 76% in the 75 years and over age group, and by 120% in the 85 years or older age group. Figure 4.2 shows the changes in the age and sex structure

of the Auckland population across the 1981, 1991, and 2001 censuses.[385-387] The largest increases occurred in the proportion of people aged 35 years to 65 years, which may be due to increasing immigration from younger Asian populations. The greatest increase in older populations occurred in Māori and Pacific groups, as these populations are ageing at a greater rate than New Zealand European (NZ/European).[388]

The ethnic diversity within the Auckland population has also grown, over the past 20 years, due to increasing immigration from and the ageing of Pacific and Asian populations.[388] Table 4.1 shows the change in ethnic share of the Auckland population aged 15 years or older, taken from the 1981, 1991 and 2001 censuses, for NZ/European, Māori, Pacific and Asian & Other populations.[385-387] The proportion of the population identifying as "Pacific" doubled over the 20 years from 1981 to 2001 and the Asian & Other ethnic population increased 10-fold over the 20 years. The decline in the proportion of NZ/European reflected the slower growth rate of this population when compared to Pacific and Asian populations.[389]

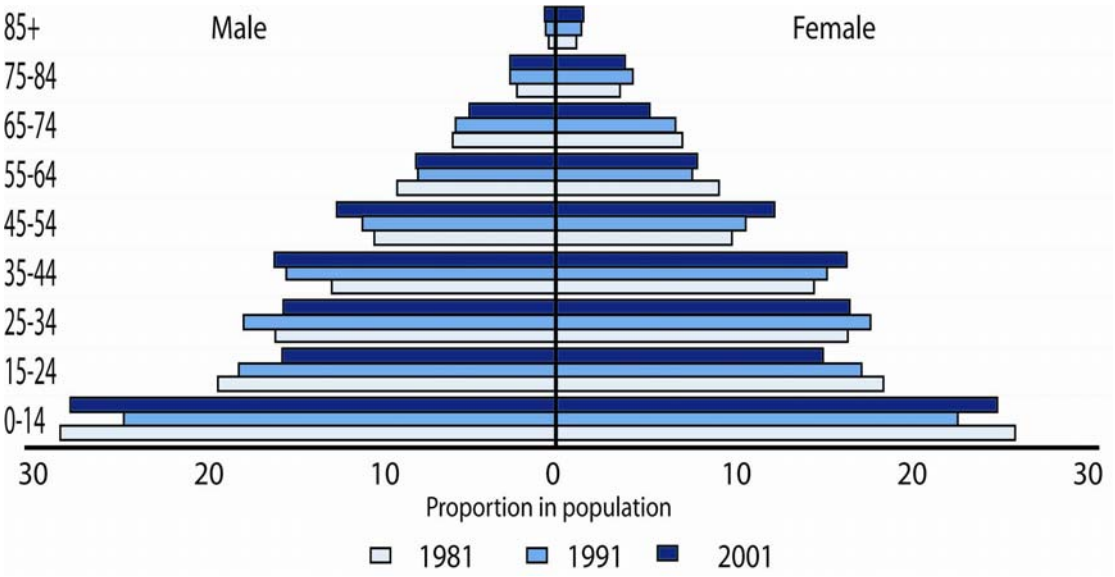

Figure 4.2 Age structure of the Auckland population from the 1981, 1991 and 2001 censuses.[385-387]

Table 4.1 Ethnic share of the Auckland population aged 15 years or older, from the 1981, 1991 and 2001 census.

	Auckland Census (%)		
Ethnic group	**1981**	**1991**	**2001**
NZ/European	83.4	76.2	66.4
Māori	9.0	9.1	9.0
Pacific	5.8	9.3	10.6
Asian & Other	1.8	5.4	14.0

4.3. The Auckland Regional Community Stroke (ARCOS) Studies

The three ARCOS studies used similar methodologies and definitions to allow for comparability between the studies. There were, however, some differences in methodological issues and case finding methods, which were typically due to limited resources and funding in the two earlier studies, changes in the record keeping in the hospitals and changes in the *Privacy Act* in New Zealand.[390] This section describes the common inclusion criteria and case ascertainment that were used across the three studies, then describes in detail the unique methodology used in each study. More specific details of the case ascertainment used in the 2002-2003 study are provided, as the candidate was involved in the design, development and conduct of the study.

4.3.1. Inclusion Criteria

- Patients must have had a stroke according to standard definitions.
- Stroke episode must have occurred between 1 March 1981 and 28 February 1982, 1 March 1991 and 29 February 1992, or 1 March 2002 and 28 February 2003.
- Patients must have been usually resident in the Auckland Statistical Area at the time of the stroke.
- Patients must have been aged 15 years or older.

4.3.2. Case Ascertainment

The ascertainment of cases used in the three ARCOS studies employed multiple-overlapping sources of notification, using both hot and cold pursuit methods. Hot pursuit screening involved prospectively collecting cases as soon after the onset of stroke symptoms as possible in the hospital setting, as well as in the community, by having general practitioners and other specialists inform the study investigators of any new cases. Cold pursuit screening involved checking all death certificates and electronic hospital discharge lists (when available).

New Zealand has a two-tiered health system with parallel public and private health care, with approximately 30% of the population paying for extra private health cover. The Auckland region has been consistently served by five public hospitals (Auckland, Middlemore, Greenlane, North Shore and Waitakere hospitals) and a number of private hospitals over the past 20 years.

Screening for cases within the hospital setting involved checking admission and discharge lists for a range of diagnostic codes for stroke, as well as similar symptoms to stroke (vertigo, dizziness, confusion, seizures, headaches and transient ischaemic attacks). To ensure ascertainment of the large proportion of patients with stroke who are not admitted to hospital, good liaison and collaboration with GPs, residential care facilities (rest homes and private hospitals) and all other community services (speech therapists, social workers and district nurses) in Auckland was essential. All GPs, rest homes and community service workers included in the studies were informed of the study and contacted regularly to ensure timely screening and follow up of all stroke patients as early as possible. All death certificates in Auckland were checked regularly for strokes and hospital pathologists' and coroner's offices were also asked to refer any potential cases. As an extra check for completeness of case ascertainment medical records officers of all public hospitals in New Zealand were asked to identify any Auckland residents who had been admitted for suspected stroke to hospitals outside the Auckland region. Table 4.2 shows the list of sources of notification used in each study.

Table 4.2 Sources of notification for the three ARCOS studies.

	1981-1982	1991-1992	2002-2003
Public Hospital	Hospital admission lists, hospital discharges, Resus at Hospital Accident & Emergency depts	Hospital admission lists, hospital ward lists, hospital discharges (NZHIS). Neuro-radiology lists	Hospital admission lists, hospital discharges (NZHIS), outpatient clinics. Neuro-radiology lists
GP	50% sample of GPs	25% sample of GPs	All GPs contacted
Other Community	Extra mural hospitals (speech therapists, social workers, district nurses), Private hospitals and rest homes, St John Ambulance service, Stroke Clubs (SF)	Other community services (speech therapists, social workers, physio's, district nurses), private hospitals and rest homes, SF	Extra mural hospitals (speech therapists, social workers, physio's, rehab plus, district nurses), private hospitals and rest homes, SF, other NZHIS notifications (not hospital).
Death certificates **Coroners**	Death certificates (hand searched) and post-mortem/coroner's reports	Death certificates (hand searched) and post-mortem/coroner's reports	Death certificates (NZHIS) and post-mortem/coroner's reports

NZHIS = New Zealand health Information Service, SF = Stroke Foundation, GP = General Practitioner

All provisional patients were screened and reviewed by trained study nurses, and once it was established that the patient met the clinical criteria for stroke, residential criteria, age and GP sampling criteria (in the first two studies), an interview was set up with the patient, or a suitable proxy informant if the patient was unconscious or cognitively impaired. This interview was completed on pre-coded interview forms as soon after the event as possible and covered various medical and social aspects of the patient. All patients registered through death certificates were verified by discussing the case with the certifying doctor or by checking the medical records of the patient. Patients, not known to the study investigators to have died, were followed up at regular intervals, over the past 21 years, to investigate survival and functional outcome after stroke.

A cluster sampling method was used in the two earlier ARCOS studies to collect cases of stroke. This method was developed by Fraser in 1978 and involves surveying a representative sample of all GPs in the Auckland region and estimating the proportion of the population enrolled with the selected doctors.[391] It is dependent on the assumption that the majority of people in a population can identify a particular doctor as their usual GP. The proportion of replies to a survey of the Auckland population was used to formulate an estimate of the proportion of the community used in the sample.

4.3.2.1. ARCOS 1981-1982

Originally called The Auckland Region Coronary or Stroke study, the 1981-1982 ARCOS study was developed to provide baseline information on coronary and stroke events against which future changes in incidence or case fatality could be measured.[45] The stroke register was undertaken to represent half the stroke events occurring in the Auckland region for the year ending March 1, 1982. In this study, a random sample of 218 GPs was drawn (51% of all GPs in Auckland), using Fraser's sampling methodology.[391] Each selected practitioner was visited and invited to participate in the study, by referring all cases of coronary and stroke episodes, as well as any sudden deaths of patients in their practices.[45] Only patients who identified with a practitioner registered in the study, were included. Therefore, if the stroke

patient identified with a practitioner not included in the study sample, the patient was not interviewed.

In 1981-1982, the Auckland region was served by three main acute hospitals (Auckland, Middlemore, and Greenlane) and two other hospitals specialising in geriatric care (North Shore and Waitakere hospitals). All routinely available sources of notification such as hospital admissions and discharges were systematically searched daily by a research nurse. All death certificates registered in the 17 births, deaths and marriages registration centres in Auckland were hand searched monthly, and details of all deceased patients who had evidence of a stroke were reviewed. Additional case-finding methods included regular checking of community based services through an extra mural hospital (speech therapists, social workers and district nurses). The resuscitation books at the Accident and Emergency departments of the acute hospitals and St John Ambulance registers were also checked regularly, however these proved to be poor sources of case finding.[46]

4.3.2.2. ARCOS 1991-1992

In 1991, a second stroke register was developed to identify all new stroke cases in Auckland for the 12-month period ending March 1, 1992. Typical case-finding methods were used to collect all hospitalised and fatal cases of stroke, and a cluster sample of 25% of the GPs in the Auckland region was used to obtain a sample of non-hospitalised non-fatal cases.[26] A sample of 171 general practitioners were selected, using Fraser's method.[391] They were informed about the study and asked to refer any patients who were suspected of having a stroke and were managed outside a public hospital. A 24-hour telephone service was made available to selected GPs for notification about these patients and monthly telephone contact with the doctors was also made.

The 1991-1992 study implemented more intensive case finding methods than the 1981-1982 study, where the New Zealand Health Information Service (NZHIS) provided the investigators with computerised discharge lists of all discharge diagnoses with any mention of stroke (ICD-9 codes 430-436; see Appendix 1) occurring in Auckland residents. These were matched against

the patients already registered in the study and all discrepancies were reviewed by a study review team. Daily searches of hospital admission lists and neuro-radiology lists were also made in the three acute hospitals, with weekly searches conducted in the two other hospitals.

Checks for non-hospitalised, non-fatal patients were made though regular contact with GPs, residential care facilities, all community based physiotherapists and speech therapists, as well as the Auckland Stroke Foundation. Patients, not already registered in the study, who were referred from these sources only, were only included if their nominated GP was one of the 25% sample.

4.3.2.3. ARCOS 2002-2003

The most recent ARCOS study aimed to collect all cases of stroke in the Auckland region, for the period from March 2002 to February 2003. Daily systematic searches of presentations and admissions to the four general acute hospitals in Auckland (Auckland Public Hospital, North Shore Hospital, Waitakere Hospital and Middlemore Hospital) with any diagnoses suggestive of stroke were made. Regular checks of medical and neurological wards, day-wards, and rehabilitation services, in all of the hospitals were also made. Hospital discharges (separations lists), outpatient clinics and radiology department investigation lists were reviewed by each hospital research nurse weekly. Monthly visits were also made to the two large public specialised care hospitals (Green Lane and National Women's Hospitals), and two large private acute-care hospitals (Mercy and Ascot Hospitals).

Community Screening

Presentations about stroke and the study were given at the Independent Practitioner Association (IPA) meetings around the Auckland region before the study started. This provided the GPs with information kits about the study and to obtain details about their practices and preference for contact about the study. Each general practice surgery in the Auckland region was contacted by email or fax monthly, to ascertain any potential stroke patients, and all cases provided by the practitioners were followed up and checked

against other sources. All district nurses, physiotherapy specialists, speech therapy and occupational therapy services (including those in private hospitals and private physicians [neurologists, physiotherapists]) were also contacted monthly for referrals of patients with stroke as diagnosis. Direct liaison with all aged care facilities (i.e. private hospitals and rest homes or hostels) in the Auckland region, was also undertaken, to identify people with acute stroke, who were permanent residents of such facilities but were not transferred for care in hospital because of frailty. Monthly visits were made to the larger institutions with high dependency units. The Stroke Foundation of New Zealand was contacted every month and a list of all patients was checked against the existing register for completeness of case ascertainment and new patients were followed up by a research nurse.

New Zealand Health Information Service

The NZHIS sent quarterly lists of any hospital admission or separation with any diagnosis (up to 100 diagnoses) of stroke or TIA (ICD10 codes: I60.0-I60.9, I61.0-I61.9, I63.0-I63.9, I64, I67.0, I67.5-I67.9, I68.0-I68.8, I69.0-I69.8, G45.0-G45.9, G46.0-G46.8, Appendix 1) to the Clinical Trials Research Unit (CTRU). This data was linked to the existing stroke register to ensure complete case ascertainment. All patients who were not already included in the register were checked for stroke diagnoses through hospital databases and contacted by hospital staff for further information about their stroke. These patients were included in the study, if a true stroke diagnosis was found. The NZHIS also provided details of eligible Auckland residents who suffered a stroke in any hospital or residential care facility outside of the Auckland region. These patients were followed up by contacting the primary physician from the hospital where the patient had their stroke and questioning them about the event and obtaining notes to register the participant.

Due to changes in the privacy laws, death certificates could no longer be hand searched, so the NZHIS also provided regular lists of all deaths of Auckland residents with any mention of cerebrovascular disease (stroke, cerebrovascular accident (CVA), cerebral infarction, intracranial/intracerebral haemorrhage, subarachnoid haemorrhage). This information was checked

against the existing register and if there was suggestive evidence of a stroke, the patient was included in the register and the required record forms were completed retrospectively from medical records. Coroners' reports for the study area were also checked for any mention of cerebrovascular disease. Eligible patients were contacted by the nurse at the coroner's office, who informed the relatives of the deceased stroke patient about the study and asked them if a study research nurse could contact them. If the family agreed to participate in the study they were contacted by the study manager, if not they were entered into the study database as a "possible" case of stroke.

4.4. Definitions

This section describes the definitions for stroke and other variables that were consistent across the three studies. Due to changes and improvements in case ascertainment and study design, the data that could be used in the current analyses were limited and only questions and information that were consistent across the three studies were used.

Stroke was defined according to the WHO standard diagnostic criteria as "a sudden onset of focal or global neurological deficit lasting 24 hours or longer or leading to death, presumably of vascular origin",[248] including PICH and SAH. Each stroke was further classified as "first-ever in a lifetime stroke" (first-ever, incident) or recurrent stroke. Any stroke that developed within 28 days after the onset of previous stroke was considered as progressing stroke illness and was not recorded as a new stroke. Any stroke that developed 28 days or more after the previous stroke were regarded as a recurrent stroke event. In each of the three studies, every case of stroke was adjudicated by a group of study researchers, including at least one neurologist and geriatrician, using the case record forms and information from hospital investigations and management. These strokes were adjudicated as a "definite", "probable", or "possible" stroke case, or not a stroke after all, and classified into stroke subtypes (where possible). Only definite and probable strokes were included in the current analyses. In the most recent study, 2002-2003, stroke was subdivided into pathological types (ischaemic, PICH, SAH) according to standard clinical and neuroimaging (CT/MRI/autopsy) findings. Patients

without imaging or pathological autopsy confirmation of stroke type were classified as stroke of undetermined type. All ischaemic strokes were classified into five aetiological subtypes based on the TOAST criteria; atherothrombotic (large artery disease), cardioembolic, lacunar (small artery disease), other determined and undetermined aetiology.[53, 392]

The definition of usually resident in the Auckland region, was consistent with the census definition of the time of the study and included all people who had lived in the Auckland region for the past year, people who were intending to live permanently in the area, and Auckland residents who had a stroke while outside the Auckland region. People who were in a rest home, hospital, prison or other institution, resided where they considered themselves to live. This definition excluded people who were visiting the study area before onset but stayed on after the stroke.

4.4.1. Variables

A number of variables were used to explore associations with trends in stroke over time and explanations for disparities between groups. Although efforts were made to keep questions and information consistent across the three studies, this was difficult due to changes in case ascertainment methods, hospital management and varying aims within the three studies. Therefore, only certain variables could be used in the analysis of trends and these were grouped into patient factors (socio-demographic and pre-morbid risk factors), disease factors (information about the stroke event), care and management factors (how the disease was managed) and outcome factors (death and disability from stroke).

Patient Factors

Patient factors include pre-stroke patient demographics and pre-morbid risk factors and disease. Basic demographic information was collected as soon after the stroke as possible from the patient, or next of kin, or medical records if the former two were unavailable. This included information on age (defined as age at the time of the stroke, calculated from date of stroke – date of birth), sex, residence at the time of stroke (defined as whether they lived in

institutional care or not), marital status (defined as whether a participant had ever been married or not, including people who were divorced or separated) and ethnicity. Age was grouped into four categories, in most analyses: 15 to 64 years, 65 to 74 years, 75 to 84 years and 85 years and older. Ethnicity was self-defined according to categories from the corresponding census year's question (see next section for detailed description). For the current analyses these were grouped according to "NZ/European" (New Zealand Europeans, British, American, Australian, etc), "Māori" (indigenous New Zealanders), "Pacific peoples" (Tongan, Samoan, Nuiean, Cook Island Māori, etc), and "Asian & Other" (mainly Chinese and Indian with other ethnic groups such as Pakistani, Iraqi, etc).

A measure of the stroke patients' socioeconomic status (SES) was defined using the New Zealand Occupational status (NZSCO) and was coded into a measure of socioeconomic status (6-levels), using the Elley-Irving index in the 1981-1982 study and the New Zealand Socio Economic Index (NZSEI) in the 1991-1992 and 2002-2003 studies. The Elley-Irving index was created using the NZSCO-68 and was classified into six-levels using an equal weighting of median income and education scores.[393] In contrast, the NZSEI was developed using the International Socioeconomic Index (ISEI) and the three-digit level of the NZSCO-90 as an occupationally-derived measure of socioeconomic status. The validation of the NZSEI and its relationship to the Elley-Irving index has been thoroughly tested.[394, 395] The NZSEI was divided into a six-level measure of SES, comparable to the six-levels of the Elley-Irving index: SES 1 = NZSEI 66-90; 2 = 56-65; 3 = 42-55; 4 = 32-41; 5 = 24-31; and 6 = 10-23.[395]

Medical history of common risk factors for stroke and any co-morbid disease was also recorded at the baseline interview. These questions were consistent across the three studies and asked if the patient had, or had ever been told by a doctor, that they had a risk factor or disease. This data included information on whether a patient had a history of high blood pressure, or if they were on blood pressure lowering drugs, or had a history of stroke (used to define incident and recurrent strokes), diabetes, or heart disease (defined by

whether the participant had ever had a heart attack or myocardial infarction prior to their stroke). BMI was calculated using self-reported weight and height, (weight kg)/(height m)^2 and was used as a measure of obesity. "Overweight" was defined by a BMI ≥ 25 and "obese" by a BMI of ≥ 30. Smoking status was defined by whether the participant was a current smoker at the time of their stroke or not. These variables were combined into a vascular risk factor index, quantifying the number of co-morbid diseases and vascular risk factors that a patient had at the time of the stroke, including a history of high blood pressure, heart disease, stroke, diabetes, being obese, and smoking at the time of stroke. This index was coded into 0, 1, or ≥ 2 risk factors present at the time of their stroke. Dependency before stroke was measured through a number of different questions asking the patient if they depended on someone else to fulfil simple tasks of everyday living, such as showering, washing, dressing and feeding.

Disease Factors

Disease factors were used as a proxy measure of stroke severity and were measured by loss of consciousness, or motor deficit or paresis at the time of stroke. Unfortunately a direct measure of the severity of stroke for the three studies could not be calculated as the 1981-1982 study did not collect much information about the acute stroke event and hospital information, due to limited recording keeping in the hospitals. Therefore, loss of consciousness was used as a surrogate measure of the severity of stroke and was defined as whether the patient lost consciousness at the time of their stroke, or if they had an acute Glasgow Coma Score (GCS) of ≤ 8. This has been commonly used as a proxy measure for stroke severity in other publications.[326, 396] If the patient had any motor deficit as a result of the stroke (weakness or paralysis of the limbs) was also used as a surrogate measure of the severity of stroke.

Care and Management Factors

There were a number of factors around the admission to hospital and services received that could be used to measure changes in the management of stroke over the three periods. However, these were limited across the three studies due to differences in the information collected between the three studies.

These care and management factors are the only possible factors that are potentially modifiable to influence changes in survival. Admission to hospital was defined as whether the participant was admitted to hospital within 28 days after their stroke. Rates of neuroimaging were defined as whether the participant received a CT or MRI scan for their acute stroke. Necropsy was defined as whether a patient had an autopsy on death or not, and was more common for sudden deaths occurring at home. The time to medical attention was sought after the stroke was defined as the time taken by the patient to seek medical attention after their stroke (calling a doctor or arriving at the hospital) minus the time of the stroke (if known), or the time of waking. The duration of stay in hospital was defined by the number of days between admission to hospital and discharge. This was used as a measure of access to health care.

Outcome Factors

There were a number of factors used to measure trends in outcome across the three studies. The primary outcome measure was survival up to one year after stroke. Using this data, case fatality within 28 days, six months and one year after the patients' initial stroke in the study period were calculated. Case fatality was defined as the number of patients who had died by the time point of interest, over the number of patients in the study. Mortality was defined as the number of patients who had died over the population at risk (the Auckland population).

In the most recent 2002-2003 study, answers to two simple questions were used to assess the functional outcome of patients after stroke,[397] for each patient alive at the six month interview after their stroke.

- Patient dependency was measured through: "Do you require help from another person for everyday activities?"
- Recovery after stroke was measured through: "Do you feel that you have made a complete recovery from your stroke?"

These questions have been validated in a number of studies.[398-400] Residential status at six months after stroke was also measured to investigate changes in institutionalisation pre- and post-stroke. Unfortunately trends in dependency or institutionalisation across the three studies could not be investigated due to inconsistencies in data recording and questions over time.

4.4.2. Population Data

The ARCOS studies were conducted in the year (or next year for the 2002 study) of the National Census of Populations and Dwellings, so the data from the corresponding census was used as the denominator in the calculation of rates in 1981, 1991, 2001.[385-387] Census data was available by age, sex, and ethnicity. In the New Zealand Census, ethnicity is classified as the ethnic group or groups that people identify with, or feel they belong to. Thus, ethnicity is self-perceived and people can belong to more than one ethnic group. In the 1981 Census, the ethnicity question reflected "'ethnic origin" and referred to the blood mixture of races within a person, calculated by adding fractional distributions of their origin.[385] Up to three races were recorded for each individual with an indication of what fraction each response represented. Half or more origin was the general classification for inclusion into an ethnic group and cases of half origins were assigned to one particular ethnic classification according to the following priority order: NZ Māori, Pacific Island Polynesian, Other Ethnic Groups (excluding European), and European. In contrast, the 1991 and 2001 census ethnicity questions were based on a measure of cultural affiliation, as opposed to race, ancestry, nationality or citizenship.[386, 387] Up to three possible responses were coded in the 1991 census, with a maximum of nine responses in the 2001 census.

A method of prioritisation of ethnicity was used in all census data, to group people into a single ethnic group ensuring that numerically small groups were identified from the majority.[69] The prioritisation method gives priority to non-European groups, with special priority to Māori and Pacific groups, when multiple responses are given. Therefore, in order of priority: the Māori ethnic group refers to those people who indicated Māori as any one of their ethnic groups; the Pacific Island ethnic group refers to those people that indicated a

Pacific Island ethnic group as at least one of their ethnic groups (excluding those people who identified also with Māori ethnic group); with the remaining population, people who specified other groups (excluding those who specified only European ethnicities) were then coded to "Other"; and the residual group were those who specified only one or more European ethnicities (European). At the highest aggregation this resulted in the following categories: European Only, Māori Ethnic Group, Pacific Island Group, Other, Not Specified, and Total. In the current analyses, the prioritised output of ethnic groups was used as it provided a single ethnic group comparable with the question used in the ARCOS study. This may provide slight overestimates of the population denominator for Māori and Pacific populations, producing underestimation of rates of stroke in these groups.

For the future projections of stroke rates in the New Zealand population, the estimated population from 2001 to 2051 was obtained from Statistics New Zealand.[401, 402] This most recent projection of the New Zealand population, by age and sex, was estimated using the 2004 resident population as the base and was projected out to 2051, in five-year census periods.[401] The data used in the current analyses (Series 5) assumes medium mortality (increases in life expectancy), fertility (a decrease in births up to 2016 then remaining constant) and migration (gains in net migration after 2009). Ethnic specific projections of future stroke rates used the Statistics New Zealand population projections based on the 2001 census populations and were estimated out to the year 2021, assuming medium fertility, mortality, net migration and inter-ethnic mobility (Series 6).[402]

4.5. Statistical Methods

This section provides a detailed description of the statistical analyses and procedures used to examine trends and changes in patient characteristics, rates of disease and outcome across the three studies. The first section describes how adjustments were made for the sampling procedure in each of the first two ARCOS studies. The second section describes the checks that were made for quality, consistency and completeness of case ascertainment across the three studies. The third section describes descriptive statistics

used to assess changes in the demographic characteristics of stroke patients. The fourth section provides a detailed description of the formulae used to calculate crude and standardise rates and their corresponding variance estimates. The fifth section describes methods used to investigate trends in outcome, mortality and survival over time. The final section describes the calculation of the prevalence and projections of the future burden of stroke.

All of the data from the two previous ARCOS studies were reviewed and reanalysed. The data were combined into datasets corresponding with the relevant forms used in the previous two studies, to aid future data management and analysis. This data was imported into a permanent Oracle8i[403] database so the data could be locked and permanently stored in an external database. All data was then re-extracted into SAS 8.2[404] for use in the current analyses.

4.5.1. Adjustment for Sampling Methods

As mentioned in Section 4.3.2, sampling procedures were used in the two earlier ARCOS studies. Although, appropriate methodology was used to sample cases, this has resulted in long-term complexities with analyses of the data sets, in particular calculating standard errors of estimates. Therefore, all current analyses of rates and outcome were adjusted for the sampling procedures to represent all patients with stroke in the region during the given period, and to adjust for the extra variability sampling brings to the variance around the estimates. For the 1981-1982 ARCOS study, where a 50% sample of all patients was registered, all patients were weighted by two in the current analysis. The 1991-1992 ARCOS study sampled 25% non-fatal, out-of-hospital cases, so these patients were weighted by four, to represent the total non-fatal, out-of-hospital treated population in the current analysis. All standard errors around rates were adjusted for the sampling procedure (see Section 4.5.4).

Over the twenty years since the first ARCOS 1981-1982 study was conducted, information on 23 extra events in the 680 patients was lost. Therefore, for the current analyses the numbers of extra events were imputed

using data from previously published publications, by age sex and ethnicity, where all information except age, sex and ethnicity was set to missing, to estimate the original 703 stroke events registered in the study.

4.5.2. Quality of Case Ascertainment

It was important to verify the completeness of case ascertainment in the registers, to provide evidence of consistency across the three studies, to justify the comparability of the data and to rule out any measurement bias in the estimation of rates in the population. Capture recapture techniques were used to assess changes in case ascertainment and to estimate the number or proportion of cases missing in the three studies. A number of procedures used in the MONICA project (described in Chapter 3) were used to assess the consistency and quality of the three ARCOS studies against international criteria.

4.5.2.1. Capture-Recapture

Capture-recapture methods have been advocated as a measure for estimating the completeness of a disease register and quantifying the number of cases estimated to be missing.[273] These methods have also been used to adjust incidence and prevalence rates by the proportion missing to give a complete estimate of the rate of disease.[270, 405] Therefore, capture-recapture techniques were used to evaluate the completeness of case ascertainment of the three ARCOS studies and to estimate the proportion of cases missing.

The simple example of a capture-recapture problem with two sources is illustrated in Table 4.3, where *X* is the unknown number of cases to be estimated, not identified by either Source 1 or Source 2. This approach can be extended to data that is obtained from more than two sources as well, however, it becomes more complex because further multiple estimates are produced.

Table 4.3 Example of capture-recapture for two sources of notification.

Source 1	**Source 2**		
	Yes	**No**	**Total**
Yes	N1	N2	N1+N2
No	N3	*X*	N3+*X*
Total	N1+N3	N2+*X*	N1+N2+N3+*X*

The main assumptions of the capture-recapture model are described with respect to the three Auckland stroke studies.

Assumption 1. The study population is closed. The Auckland region was well defined as per the census region at the time of the study. Strict residency criteria prevented new immigrants and visitors to New Zealand from being included in the stroke registers. Also efforts were made to check for cases of stroke in Auckland residents that occurred outside the study region, by checking with all major hospitals around New Zealand. Therefore, the study population was kept as closed as possible, however international emigration could not be controlled for.

Assumption 2. Independent sources of ascertainment. It is not clear that each of the sources of notification were independent from each other across the three studies. However, it has been shown that log-linear modelling adjusting for interactions between the sources of notification controls for the lack of independence.[270, 276]

Assumption 3. All cases have the same probability of being captured. This assumption was violated for the 1991 study as non-hospitalised non-fatal cases only had a 25% chance of being captured due to sampling methods. This was not adjusted for in the current analysis because of the small numbers in this group.[405]

Assumption 4. All cases can be matched on all lists using a common identifier. This was not a problem in the ARCOS studies, as patients were registered through internalised data entry systems and every patient was assigned an individual patient identifying number.

The first source of notification was defined as the source from which the patient was first notified and is important in identifying sources that were most useful in the "hot pursuit" of patients. The different sources of notification were combined into four independent sources that were consistent across the three studies. These were (described in Table 4.2; Section 4.3.2):

- hospital notifications;
- GP notifications;
- other community notifications (stroke foundation, rest homes, etc) and
- death certification.

Inpatient and hospital discharge lists were combined into one source, "hospital notification", as in the 1981-1982 study if a case was already notified by an inpatient list then they were not subsequently included on the hospital discharge list. This was different from the 1991-1992 and 2002-2003 studies, where independent lists of all hospital discharges in the Auckland region were sent to the study office by the NZHIS.

The numbers used in the capture recapture analyses were conducted separately for each study and were based on the first stroke registered in the ARCOS study (patients). Crude numbers, not adjusted for the sampling procedures, were used to reflect the true sources notifying the studies of patients, in order to estimate the usefulness of each source for future stroke incidence studies. Log-linear modelling assuming a Poisson distribution of the data, was used to estimate the number of patients missing in each study. This has been shown to control for dependencies between the sources of notification by adjusting for interactions between sources, overcoming problems with the assumption of dependence.[270, 276] In log-linear modelling, if

there are *k* sources of notification there can be at most *k-1* interactions between the sources. It has been shown that the capture-recapture assumptions hold best when three or four sources of notification are used, as more sources lead to greater complexity in the interpretation of the results.[267, 276] Therefore, *k* = 4 sources of notification were used in the analyses, with a maximum of 114 possible combinations of sources that could be modelled.

The first model assumed independence between the sources of notification and included just the main effects of the four sources. Next, two-way interactions between the various sources of notification were added to the model, to assess the dependence between the sources. Finally, three-way interactions between the sources of notification were added to the model, controlling for the fixed effects. The Akaike's Information Criterion (AIC) was used as a guide for the goodness of fit of a given model.[273, 406] This was calculated using the likelihood ratio statistic (LR):

$$AIC = LR - 2(df),$$

where df is the degrees of freedom in the model.[407] The AIC is preferable over the likelihood ratio statistic or the deviance of the model as it is dependent on the number of parameters included in the model and, hence, penalises the model for the addition of extra parameters (or interactions between sources).[276] The most suitable model was chosen as the model with the lowest AIC, as a small AIC value suggests that the covariates included in the model explain most of the variation in the counts. Implausible models with extremely large values for interaction terms were discarded.

4.5.2.2. Quality measures

As mentioned in the previous chapter, the MONICA collaboration used a series of quality measures to determine the quality of the stroke registers in the project and to ensure comparability of information between the registers.[226] These criteria were used as an indirect measure of the quality of data consistency across the three studies, and are as follows:

1. The proportion of fatal cases that occurred outside the hospital in relation to all stroke deaths was used to estimate the completeness of data on fatal out-of-hospital events;
2. The 28-day case fatality rate was used as an indicator of the completeness of registration of nonfatal stroke cases. Incomplete coverage of non-fatal events leads to an overestimation of case fatality;
3. The proportion of surviving stroke patients cared for outside the hospital was used to estimate the completeness of non-fatal, non-hospitalised stroke events; and
4. The proportion of fatal cases examined by a physician before the death or subjected to autopsy was used to estimate the accuracy of the assignment of diagnostic category in fatal cases.

The ratio between the numbers of deaths in the studies measured against routine mortality statistics were not created in the current analyses, as this data was not available for the Auckland region at the time of the publication of this thesis. However, the NZHIS was able to provide annual data for all deaths with any ICD cerebrovascular disease code (I60-I69, including TIAs G45- G46) between 1980 and 2001 for the whole of New Zealand. Crude annual mortality rates, overall and by sex, were calculated and plotted against the trends in mortality in the ARCOS studies to compare the direction and magnitude of change across the years. Linear regression models were applied to the mortality rates to estimate the slope of the trend lines in overall New Zealand stroke mortality and compared to the trend in one year mortality rates across the ARCOS studies.

4.5.3. Trends in Demographics

The significance of trends in the distribution of categorical demographic variables across the three studies was tested using the Cochrane-Armitage method. The Kruskal-Wallis non-parametric analysis of variance was used to test for a temporal trend in continuous variables. The Brown Mood test was

used to check for differences between median scores when the continuous distributions were skewed.

4.5.4. Trends in Event and Incidence Rates

All rates and standardisation of rates were calculated using Microsoft Excel,[408] and checked using SAS.[404] All rates were calculated by age, sex, and main ethnic grouping (NZ/European, Māori, Pacific, and Asian/Other). The population denominator used for the calculation of all rates was taken from the National census survey conducted around the time of the study (1981, 1991, 2001) for the Auckland region, provided by Statistics New Zealand.[385-387] For the most recent study the 2001 census data were used rather than the estimated 2002 population data, as it has been shown that census year data is more robust. Estimated population data increases the bias, (overestimation of the population) in the calculation of rates.[27]

Attack rates were calculated by including every stroke event, adjudicated as a definite or probable stroke that occurred during each study period. Incident rates were calculated by taking all patients who had a first-ever in a life-time stroke event, that occurred during the study periods. Recurrent rates were calculated by including anyone who had a previous history of stroke and all recurrent strokes that occurred during the study periods. The following sections describe in detail how the crude rates and their corresponding standard errors were calculated, and the methods used to standardise the rates of stroke.

4.5.4.1. Crude Rates

All crude rates and variance estimates were calculated using Poisson distribution, by:

$$R_i = \frac{N_i}{P_i} \ , \ \mathrm{var}(R_i) = \frac{N_i}{P_i^2} \, ,$$

where i represents the subgroup (by age, sex and ethnicity), R represents the rates, N is the number of patients and P is the population taken from the census.[262, 409] The Poisson model arises as a distribution for the number of

cases occurring in a stationary population of size N followed for a fixed period of time. The standard error that gives the best approximation to the log likelihood ratio is:

$$se(R_i) = \frac{\sqrt{N_i}}{P_i}.$$

The formulae used for calculating the standard error for the 1981-1982 and 1991-1992 studies, taking into account the sampling procedures used were:

$$se(R_{81}) = \frac{\sqrt{(N1)}}{(P/2)}, \quad se(R_{91}) = \frac{\sqrt{(N1 + (N4/0.25^2)}}{P}$$

where $N1$ in the 1981-1982 study represent the crude numbers of cases (50% of all cases) and $N1$ in the 1991-1992 study represents non-sampled cases and $N4$ represents the crude numbers of non-hospitalised non-fatal (25%) cases. An approximate 95% confidence interval was calculated by:

$$R_i \pm Z_{\alpha/2} stddev(R_i),$$

where $Z_{\alpha/2}$ is the $\alpha/2^{th}$ quartile of the standard normal distribution. In the current analysis, α = 0.05 was used to calculate a 95% confidence interval.

4.5.4.2. Direct Standardisation

Age standardised rates were used to compare rates across time and different populations, as this removes the distortion of crude rates by relating the data to a standard population with fixed age structure. However, age standardisation can also mask real effects as depending on the standard population used it tends to place more weight on younger populations and less on older. There is no conceptual justification for choosing one standard population over another, thus the choice is arbitrary, but it should be relevant to the study population and consistent across the populations being compared.[312] Therefore, if a world standard population is used, when investigating a disease of the elderly, populations that have the affliction at younger ages will have more weighting and higher rates than older populations. This occurs in the New Zealand stroke population when

investigating differences in ethnicity, as Māori and Pacific populations tend to have their strokes 10 years younger than NZ/European populations and hence will have more weight placed on the younger strokes providing higher overall rates.

With the increasing availability of age-specific rates, the use of direct age standardisation has become the predominant technique in most applications of demography and epidemiology. Direct standardisation yields a standardised rate which is a weighted average of the age-specific rates, for each of the populations being compared. The WHO world population was chosen as the reference group as this is the most recent published world data (Table 4.4).[410] This new grouping represents an updated world population adjusting for the older age distribution of the world compared to the previous "Segi" world population of 1967.[411]

The age groups, 15-64, 65-74, 75-84, and 85 years or older were used to calculate direct standardised rates because of the small numbers of events in the younger age groups, especially when stratified by sex or ethnicity.

Table 4.4 Weights used in direct age standardization of rates, taken from the WHO World population (2003).[410]

Age	Population Distribution (%)	Weight (w_i)
15-24	16.69	0.2259
25-34	15.54	0.2103
35-44	13.74	0.1860
45-54	11.41	0.1544
55-64	8.27	0.1119
65-74	5.17	0.0700
75-84	2.43	0.0329
85+	0.64	0.0086
Total	73.90	1.0000

The formulae used to calculate direct standardised rates were:

$$R_s = \frac{\sum(R_i \times w_i)}{\sum w_i}, \quad \text{var}(R_s) = \frac{\sum \text{var}(R_i)^2 \times w_i^2}{\left(\sum w_i\right)^2},$$

where R_s represents the standardised rate, R_i is the crude rate of subgroup i and w_i is the weight of the subgroup of the standard population.[262] The corresponding variance and standard error were calculated using the crude variance, $var(R_i)$, (adjusted for the sampling procedure):

$$\text{var}(\log(R_s) = \frac{1}{R_s^2} \times \frac{\sum\left(\text{var}(R_i) \times w_i^2\right)}{\left(\sum w_i\right)^2},$$

$$se(\log(R_s) = \frac{\sqrt{\sum\left(se(R_i)^2 \times w_i^2\right)}}{R_s \times \sum w_i}.$$

The 95% confidence intervals around the standardised rates were calculated by:

$$95\%CI(R_s) = R_{s\div}^{\times} \exp(Z_{\alpha/2} se(\log(R_s)))$$

Rate Ratios

Rate ratios (RR) between two standardised rates were used to compare two rates over time.[312] RRs of direct standardised rates were used to compare the rates of the two earlier studies with that of the 2002 study, to estimate the magnitude of change in the rates over time. RR's were also used to compare standardised rates of stroke between ethnic groups using the NZ/European ethnicity as the reference group to investigate disparities in the rates of stroke, within each study. The RR and the corresponding variance were calculated by:[262]

$$RR = \frac{Rs_1}{Rs_2}, \text{ , } \text{var}\{\log_e(RR)\} = \left\{\text{var}(Rs_1)^2 + \text{var}(Rs_2)^2\right\}$$

where R_{S1} is the rate being compared to the reference rate, R_{S2}. An approximate method of the Poisson model and the logarithm of the RR were used to calculate confidence intervals around the rate ratio:[409]

$$se\{\log(RR)\} \approx \sqrt{\frac{N_1}{P_1^2} + \frac{N_2}{P_2^2}} = \sqrt{se(R_1)^2 + se(R_2)^2} .$$

4.5.4.3. Indirect Standardisation

Indirect standardisation enables better comparisons of time trends within the Auckland population, as it adjusts for changes in the distribution of age, sex and ethnicity in the calculation of age, sex and ethnic specific rates. Indirect standardisation assumes the age-specific rates in the study group are the same as in the standard population and is useful when person-years are not available, or if there are small numbers in the groups.[412] Indirect standardisation is useful for assessing temporal trends in stroke rates within ethnic groups due to the variation in the age structure of the ethnic groups in New Zealand, and also because there were small numbers in minority ethnic groups in the earlier studies.

The 2002-2003 ARCOS study was the most recent and least biased, as no sampling procedures were used in the collection of cases. Therefore, in the current analysis, the rates of the 2002-2003 ARCOS study, using the 2001 Auckland census, were used as the standard population against which the expected values in the 1981-1982 and 1991-1992 studies were calculated. Rates in the earlier ARCOS studies were thus weighted by the population in each age, sex and ethnic group of the study population (ARCOS 2002-2003) to estimate the “expected number” of cases.

Standardised Event Ratios

The result from indirect standardisation is the standardised event ratio (SER) which calculates a measure of change in rates as compared to the reference group. The SER is a ratio of the observed to the expected number of events, or cases. When the events are deaths this ratio is often referred to as the standardized mortality ratio (SMR).[413] These ratios are equivalent to the RR

described earlier, allowing comparisons of each population under study to the standard or current population.

The formulae used to calculate the SER and the indirect standardised rate are shown below. The age-specific stroke rate in the standard population (s), for the *kth* age-group is equivalent to the crude rate,

$$R_{sk} = \frac{N_{sk}}{P_{sk}},$$

and the overall crude rate for the standard population is

$$R_s = \sum R_{sk}.$$

The expected number of events in the cohort is defined as

$$E_r = \sum R_{sk} \times P_k,$$

where P_k is the population of the *kth* age group in the cohort of interest and E_r is the expected number of strokes that would have been observed in the cohort if the age-specific rates were equal to the age-specific rates in the standard population.[413]

$$SER = \frac{observedrate}{\exp ectedrate} = \frac{\sum O_k}{\sum R_{sk} \times P_k} = \frac{O_r}{E_r}, \quad se(SER) = \frac{\sqrt{O_r}}{E_r}$$

All standard errors were adjusted for the sampling procedures in the 1981 and 1991 studies, as described earlier. Indirect standardised rates adjust the standard rate up or down to the SER accordingly and were calculated by

$$ISR = SER \times R_s, \quad se(ISR) = 100000 \times R_s \times se(SER)$$

with the corresponding confidence intervals being calculated by

$$95\%CI = SER \pm Z_{\alpha/2} se(SER), \quad 95\%CI = ISR \pm Z_{\alpha/2} se(ISR).$$

In the current analysis the inverse of the SER (1/SER) are presented, so the direction of the ratio is interpreted in the same way as the rate ratio of direct standardised rates. A 1/SER lower than one indicates that the rate is higher in the observed population compared to the standard population (the 2002-2003 study), indicating a declining trend in rates. On the other hand, a 1/SER higher than one indicates that the rate is lower than the standard population. SERs are useful in that they provide an estimate of the relative risk between the standard population and the population under study.[413] Discrepancies in SERs may be due to differences in the age structure of the populations.

4.5.4.4. Testing for Heterogeneity between rates and rate ratios

The Wald statistic was used to test for heterogeneity between standardised rates and rate ratios across age and ethnic subgroups:[262]

$$\chi^2_{wald}(Q) = \frac{\sum (RR_i - RR)^2}{Var(RR_i)}$$

where RR_i is the stratum specific rate or rate ratio and RR is the overall rate or rate ratio. The Wald statistic has a χ^2 distribution with degrees of freedom one less than the number of strata *(df = k-1)* to test for the significance of heterogeneity. If the p-value was <0.05 then there was significant heterogeneity among the rates, indicating differences between the groups.

4.5.5. Trends in Outcome

All three studies interviewed survivors at 28 days and 6 months after their first stroke in the study period, as well as conducting checks for all deaths up to one year after stroke. Therefore, trends in mortality and survival up to one year were investigated. In all mortality and survival analyses, only first-ever in a lifetime (incident) strokes were used to control for the confounding effects of recurrent stroke on survival. Case fatality at 28 days, 6 months and 1 year were calculated and defined as the number who had died at the time point over the number of cases. The significance of trends in the distribution of case fatality across the three studies was tested using the Cochrane-Armitage test for trends.

4.5.5.1. Trends in Mortality

Mortality was defined as the number of cases who had died up to one year after their first-ever stroke over the population at risk. Crude and age standardised mortality rates were calculated for the three studies. Age standardised rates were calculated using the direct method of standardisation with the WHO world population as the standard.[410] RRs were calculated to investigate the magnitude of change in rates across the studies.

4.5.5.2. Trends in Survival

Kaplan Meier estimators were used to estimate the survivor functions at 28 days and 1 year after stroke for the three studies. All cases not known to have died within 1 year after their stroke were right censored at 365 days. The log-rank test was used to test for differences in crude survivor functions between the three studies as well as looking for differences between combinations of two studies (1981/1991, 1981/2002, 1991/2002). This non-parametric method tests the null hypothesis assuming that there is no difference in the survivor functions of the groups being compared.[413]

Predictive Modelling

Cox proportional hazards regression was used to model the time to death up to one year after stroke. This is a useful semi-parametric approach to modelling time to death, which hypothesises that the relationship between survival times in two groups can be described in terms of the relationship of the hazards and also makes no assumption on the distribution of the survival times. When the proportional hazards assumption holds, the cumulative log(-log(survival)) survival curves should differ by a constant amount over time and be approximately parallel for the groups of interest.[413] The proportionality assumptions of constant hazards between subgroups in the three ARCOS studies were tested using SAS.

The variables used in the predictive modelling were categorised into three factors which could potentially influence survival:

Patient factors were pre-stroke patient demographics and pre-morbid risk factors and disease, which included: age (continuous); sex; ethnicity (European/non-European); history of hypertension; history of diabetes; history of heart disease; history of previous heart disease medication; overweight or obese (BMI ≥ 25); smoking (current, at the time of stroke or not); pre-morbid dependency. Patient factors were assumed to be fixed at the time of stroke and therefore could not be changed once the patient had a stroke.

Disease factors were used as a proxy measure of stroke severity and were measured by loss of consciousness at the time of stroke or a symptom of the stroke including motor deficit or paresis. Disease factors occurred at the time of the stroke and were assumed to be unchangeable as well.

Hospital management and care factors were the only possible factor that could potentially be modified to influence changes in survival. However, there were only three possible variables that were consistent across the three studies and could be used to investigate changes in the management or care of the stroke patient. These were: neuroimaging (CT or MRI scanning) received by the patient, admission to hospital; and the time to first seeking medical attention for the stroke (time from stroke to ringing GP, or getting to the hospital).

Missing Data Imputation

There were large proportions of missing values across the three studies for BMI and time to seeking medical attention. To account for possible missing value bias multiple imputation was performed.[414, 415] The main assumption of imputing missing data is that the data are missing at random. The probability of a value being missing does not therefore, depend on the unobserved data (which could not be verified) but may depend on observed data.[416]

The most common and direct way of dealing with missing data is to exclude observations with missing data. However, this method may give biased results by wasting data and reducing power, especially when dealing with large databases where many variables are captured. There are a number of methods that have been used to impute missing values in research data, such

as the unconditional and conditional mean methods, multiple hot deck methods and single and multiple imputation methods. The method of multiple imputation has been shown to be useful in the case of estimating epidemiological data, even when more than 60% of the data is missing.[417]

Multiple imputation was preferred over other methods of imputing missing data, as a joint probability distribution for the variable to be imputed can be specified and it yields estimates with good statistical properties. It takes into account the variability that occurs when imputing missing data and adjusts the standard errors accordingly. In multiple imputation of missing data, for each missing value *m* values are imputed using information from other (non-missing) parameters. Standard complete-data methods are then used to estimate the parameters of interest and their associated variances for each complete-data with imputed values. The results of those *m* analyses are then combined to provide a single inference about the parameter of interest that included uncertainty due to missing data.[418] Multiple imputation requires advanced statistical software which typically implement the algorithms of Rubin and Shafer.[415] Two new procedures were available in SAS Version 8.2, the MI procedure which conducts multiple imputation of missing data and the MIANALYZE procedure which combines the results of the analyses of imputations and generates valid statistical inferences.[404]

In the current analysis all variables that were used in the predictive analysis were utilised in the implementation of multiple imputation. Age, the logarithm of time to seeking medical attention, BMI and time to death or being censored were kept as continuous and were assumed to follow a normal distribution. The categorical variables sex, European ethnicity, pre-stroke dependency, history of heart disease, history of diabetes, history of hypertension, history of taking blood pressure lowering medication, smoking status, loss of consciousness at the time of stroke, motor deficit or paresis from the stroke, admission to hospital and neuroimaging (CT or MRI), were included in the model. Five imputations of the data were generated to impute missing values. Trends in descriptor variables were computed on the imputed data and the results were aggregated into summary measures. Forward stepwise Cox

proportional hazards regression was also conducted on all five generated datasets to develop a predictive model of survival up to one year after first-ever stroke, adjusting for the study periods 1991-1992 and 2002-2003 (using the 1981-1982 study as the reference period). The results from the final models were then combined to provide aggregated estimates of the hazard ratio and variance, using the MIANALYZE procedure in SAS.

Change in Survival

To determine what factors influenced changes in survival, the percentage change in the hazard ratio (HR) between study periods, from the Cox proportional hazards modelling, after controlling for the factors found to be significant in the stepwise regression analysis, was estimated by (HR_{adj}-HR_{unadj})/HR_{unadj}*100%. Three additive models were developed: Model 1 adjusted for patient factors; Model 2 adjusted for patient + disease factors; and Model 3 adjusted for patient + disease + hospital management and care factors. Sensitivity analyses were also conducted controlling for cases who survived the acute phase of the stroke (2 day survivors) and cases who were admitted to hospital.

4.5.6. Prevalence

As stroke is a chronic disease, with approximately 30% of sufferers dying from their stroke in the acute period and approximately 50% of all survivors living with some sort of lasting disability from their stroke, it is important to estimate the burden on the community by estimating the number of people living with the effects of a stroke. The prevalence of a disease is the estimated number of people living with the effects of the disease at a specified point in time, providing a measure of the burden of the disease in the population. Prevalence rates are influenced by the incidence of disease, and the duration of the disease which is influenced by survival (Figure 4.3).[419, 420] If the number of new incident strokes is stable over time or even increasing, as shown in the literature, the number of prevalent cases of stroke will increase. However, if survival continues to improve, as shown previously,[326] the number of prevalent cases of stroke will also increase. Therefore, in order to reduce

the burden of prevalent stroke cases in the population, the number of new stroke cases needs to be reduced though the primary prevention of stroke.

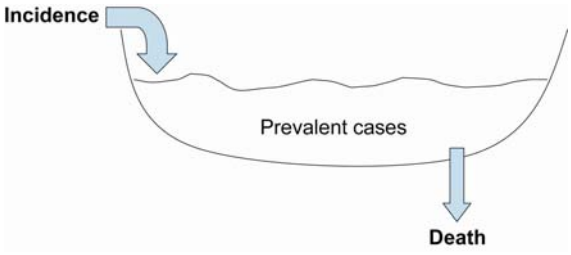

Figure 4.3 Diagram of the flow of prevalent cases in and out of the population (adapted from Beaglehole et al, 1993).[419]

First-ever prevalence rates were calculated, using incidence and survival information from the most recent ARCOS study (2002-2003), to estimate the burden of prevalent stroke in the New Zealand population. The age and sex adjusted number of first-ever prevalent stroke cases in New Zealand was calculated by:

$$P_{nz} = \sum IR_{ar\cos,ij} * \bar{x}_{surv,ar\cos,ij} * pop_{nz,ij}$$

where

IR_{arcos} = incidence rate in ARCOS 2002-2003

$\bar{x}_{surv,arcos}$ = mean survival within one year post-stroke in ARCOS 2002-2003

pop_{nz} = estimated census year population from Statistics New Zealand.[401]

i = age group (15-64, 65-74, 75-84, 85+)

j = sex (male, female).

Note, this measures of prevalence does not take into account people already living with the effects of stroke, so is an estimate of non-fatal stroke burden.

4.5.6.1. Dependency

To estimate the proportion of the prevalent stroke population who were living with lasting disability, three measures from the 2002-2003 study were used. Patient dependency was measured through the question "Do you require help from another person for everyday activities?". Recovery after stroke was measured through "Do you feel that you have made a complete recovery from your stroke?".[397] Institutionalisation after stroke was measured through residential status at six months. This information was combined to create a variable of recovery and disability in patients alive six months after their stroke: 1. fully recovered; 2. partially recovered (some dependency); 3. not recovered and dependent on others for activities of daily living; and 4. living in institutional care six months after stroke. Changes in pre- and post-stroke dependency and institutionalisation were calculated to estimate the net proportion of new patients dependent or institutionalised as a result of their stroke, taking into account death at six months. This was calculated by subtracting the proportion who were dependent (or institutionalised) before their stroke from the proportion dependent (or institutionalised) at six months after their stroke.

4.5.7. Projections of Future Burden

It is important to estimate the future burden of stroke and areas or groups that are most affected, to inform health care workers and policy makers of the estimated usage of health services. The future burden of stroke mortality was projected to estimate the number of deaths attributable to stroke occurring in the population, providing comparable numbers with other projected estimates around the world. The incidence rate of stroke was projected to estimate the number of new strokes occurring. The first-ever prevalence rate of stroke was projected to estimate the total stroke burden occurring in New Zealand. The age and sex specific mortality, incidence and prevalence rates of stroke from the most recent ARCOS study (2002-2003) were multiplied by the corresponding estimated population from 2001 to 2051 obtained from Statistics New Zealand.[401, 402] Ethnic specific incidence rates were multiplied

by the ethnic specific projected population of New Zealand from 2001 to 2021.[402]

A number of different scenarios were developed to investigate hypothesised changes in population demographics, the rate of disease and outcome after stroke. All rates and projections were adjusted for the estimated changes in the age and sex distribution of the New Zealand population.

Scenario 1 – demographic change. This scenario assumes the basic demographic changes in the age and sex structure of the population assuming medium mortality, fertility and migration[401] and no change in the annual rate of stroke (or stroke death) over time.

Scenario 2a – mortality change. This scenario assumes the basic demographic changes in the structure of the population with a conservative estimate of a decline in mortality from stroke of 1% per annum.

Scenario 2b – mortality change. This scenario assumes the basic demographic changes in the structure of the population with an annual decrease in the mortality rate from stroke of 2%, as found in other studies[36, 155] and is within the confidence interval of the annual percentage change in case fatality in ideal studies.

Scenario 2c – mortality change. This scenario assumes the basic demographic changes in the structure of the population and the annual percentage change in the age and sex adjusted mortality rates found in the three ARCOS studies.

Scenario 3a – incidence change. This scenario assumes the basic demographic changes in the structure of the population, and a decrease in the annual incidence rate of stroke of approximately 1%, as found in other epidemiological trend studies[421] and in the pooled estimates of the annual percentage change in the incidence of stroke in ideal studies (Chapter 3).

Scenario 3b – incidence change. This scenario assumes the basic demographic changes in the structure of the population, with a conservative estimate of the change in incidence, an increase of 1% per annum.

Scenario 3c – incidence change. This scenario assumes the basic demographic changes in the structure of the population, and the annual percentage change in the age and sex adjusted incidence rates across the three ARCOS studies.

Scenario 4 – survival change. This scenario assumes the basic demographic changes in the structure of the population as well as an annual percentage change in mean survival up to one year after incident stroke, found across the three ARCOS studies, of a 2.5 day improvement in survival.

Different combinations of these scenarios were used to investigate various changes in the demography of the population and epidemiology of the disease, as reflected in the projected number of new cases occurring (incidence), dying (mortality), or living with the effects of the disease (prevalence). The optimistic and pessimistic scenarios provide an estimate of the lower and upper bounds of the numbers of cases, within which the real number of cases will fall.

4.6. Ethical Approval

The University of Auckland Human Subjects Ethics Committee, Auckland Ethics (previously known as North Health Ethics) committee provided ethical approval for the three studies. Ethical approval to conduct research in and obtain medical records from each public hospital in Auckland was also obtained. Written informed consent was obtained for all patients, or their proxy informant, registered in the study.

5. TRENDS IN CASE ASCERTAINMENT AND RATES

Data on trends in stroke are varied due to variability in study design and in the reliability of the data. Trends in the rate of stroke from ideal stroke incidence studies, using standard definitions and case ascertainment, are limited and varied. When trends in stroke incidence from otherwise comparable ideal studies were pooled in Chapter 3, the results showed a modest decline in incidence over a number of studies worldwide.

This chapter presents results from the pooling from all three ARCOS studies to determine trends in the rate of stroke in Auckland over 20 years. In order to ensure that these trends were true and not biased through changes in case ascertainment, checks of the quality and reliability of the data over time were undertaken. The first section summarises trends in case ascertainment across the three studies, with measures of data quality and completeness of case ascertainment. The second section summarises changes in the characteristics of the patients with stroke included in each of the three studies. The third section presents trends in stroke incidence and attack rates, overall and by age and sex. The final section discusses the implications of these results in the context of other literature.

5.1. Trends in Data Quality

It is important to investigate how case ascertainment has changed over time, to provide evidence that the trends found are real trends and not an artefact of improvements in the identification of stroke patients. There are a number of methods that can be used to check the quality of the data. The data quality criteria, used in the WHO MONICA project to assess the quality of the studies, was used to measure of consistency of data collection over time. The capture recapture method was used to estimate the proportion of patients missing (not collected) in each study, as a measure of the completeness of case ascertainment.

A total of 3006 notifications of potential stroke patients were reviewed in the 1981-1982 study leading to 703 (23%) stroke events registered in 680 patients (unadjusted for sampling). Many of the ineligible patients were not included in the study because they were not registered with one of the sampled GPs. In the 1991-1992 study a total of 4780 notifications were made leading to 1803 (38%) stroke events registered in 1761 patients. In the 2002-2003 study approximately 6870 notifications were made from all sources of case ascertainment, leading to 2117 events registered in the study. 116 events were adjudicated as "possible" or not stroke by the specialised adjudication committee, leaving the final total of 2001 (29%) definite or probable stroke events in 1938 patients. Increases in the number of stroke patients across the three studies reflect increases in the ageing of the Auckland population.

Table 5.1 presents data on case ascertainment and assessment across the three ARCOS studies. The first source of notification identified the initial source of notification used to ascertain cases. In the 1981-1982 study over 79% of patients were first notified to the study through hospital admission and discharge lists, with only 2% initially identified through GPs. The community based extramural hospital services provided a unique contribution to the register being a useful source of notification of non-hospitalised patients. In the 1991-1992 study 62% of patients were first identified through daily hospital admission lists, 9% from death certificates or coroners reports and 21% from general practitioners and other community-based sources. The high proportion of first notifications from GPs in the 1991-1992 study reflects the sampling procedure used to identify 25% of non-hospitalised non-fatal patients. In the 2002-2003 study most patients were initially identified through the hospital system which is in line with increasing numbers of patients being admitted to hospital. The increase in hospitals as primary source of notification, most likely reflects changes in the patterns of health care delivery and associated complexities to surveillance research over time.

Table 5.1 Case ascertainment and assessment procedures for each study.

	1981-1982* (n=1360)		1991-1992 (n=1761)		2002-2003 (n=1938)		Test for trend
	n	%	n	%	n	%	P value†
First source of notification							
Hospital lists	1082	79.9	1092	62.0	1361	70.2	<0.001
GP	30	2.2	368	20.9	117	6.0	
Other community	138	10.1	140	8.0	365	18.8	
Death certificate/coroner	104	7.7	161	9.1	95	4.9	
Two or more sources	626	46.2	743	42.2	1229	67.0	<0.001
Assessment procedures							
Stroke onset to notification, Median (IQR), days	1	(12)	5	(20)	6	(32)	<0.001‡
Stroke onset to assessment, Median (IQR), days	20	(32)	16	(58)	8	(66)	<0.001‡
Notification to assessment, Median (IQR), days	7	(25)	5	(20)	0	(4)	<0.001‡
Main source of information							
Patient	466	34.3	816	46.3	853	44.0	<0.001
Proxy	488	35.9	742	42.2	502	25.9	<0.001
Medical records or staff	406	29.9	202	11.5	583	30.1	0.09

IQR = Inter-quartile range, GP = General Practitioner

* 6 patients with missing source of notification in the 1981-1982 study

† p-value calculated using Chi-squared test

‡ p-value calculated using Brown Mood test for median scores

Table 5.1 shows that 46% of patients registered in the 1981-1982 study were notified by more than one source of notification, which increased to 67% in the 2002-2003 study reflecting changes in case ascertainment procedures. The increase in the proportion of patients being notified to the study by more than one source is a reflection of improvements in case ascertainment across the three studies and easier access to electronic hospital morbidity and death data.

The time from stroke onset to first notification and assessment of the stroke in the studies were right skewed, with some extreme patients followed up or assessed many months after the initial stroke. There were significant differences in the median value of these variables across the three studies, with increases in the median number of days between the stroke onset and notification of the patient to the study register and declines in the time to assessment across the three studies. Once the stroke patient was notified to the study, the first assessment and interview was held soon after. The spread of the data (the inter-quartile range, IQR) also increased over time, reflecting changes in case ascertainment and increased use of cold pursuit methods such as notifications from the Stroke Foundation and NZHIS.

There was an increase in the proportion of interviews conducted directly with the patient across the three studies, leading to declines in the proportion of interviews being conducted with a spouse or close relative of the patient. However, over one third of interviews used medical records or medical staff as the main source of information in the 1981-1982 and 2002-2003 studies. Obtaining patient information from medical records may have influenced the amount of missing data in some of the demographic variables of interest.

5.1.1. MONICA Criteria

The WHO MONICA project measures of data quality were used as an indirect method of determining the quality and consistency of the data across the three studies. Table 5.2 presents four of the measures.

Table 5.2 Measures of data quality using the WHO MONICA quality criteria for each study.

	1981-1982 (n=1360)		1991-1992 (n=1761)		2002-2003 (n=1938)		Test for trend
MONICA quality criteria	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**P value***
Case fatality, 28 days	450/1360	33.1	421/1761	23.9	407/1938	21.0	<0.001
Fatal cases occurring outside hospital	156/450	34.7	112/421	26.6	81/407	20.0	<0.001
Non-fatal cases cared for outside hospital	354/910	38.9	373/1340	27.8	91/1531	5.9	<0.001
Fatal cases examined by physician or autopsy	306/450	68.0	334/421	79.3	339/407	83.3	<0.001

*p-value calculated using Cochran-Armitage trend test

n/N = Data shown are number of deaths/patients divided by number at risk and %

28-day case fatality was used as an indicator of the completeness of the registration of non-fatal stroke patients, where incomplete coverage of non-fatal events may lead to overestimates of case fatality. Case fatality decreased over the three study periods indicating improvements in short-term survival and possibly better ascertainment of non-fatal events and milder cases of stroke over time (discussed in depth in Chapter 7). The proportion of fatal stroke patients that occurred outside the hospital in relation to all stroke deaths in the three studies was used to estimate the completeness of data on fatal out-of-hospital events, since not all fatal cases reach the hospital alive. This was well over 10% in all of the studies indicating that checks of death certificates and autopsy reports were near complete. The proportion of surviving stroke patients cared for outside the hospital was used to estimate the completeness of non-fatal, non-hospitalised stroke events. This declined significantly over the three study periods reflecting increases in the number of patients admitted to hospital over time. The proportion of fatal cases examined by a physician before death or on autopsy was used to estimate the accuracy of stroke diagnosis of fatal patients. These rates were high and slightly increasing over time providing evidence of the high accuracy of diagnosis of stroke in fatal patients.

The ratio between the number of deaths identified in the register and the number of deaths according to routine statistics as 2002 death data for the Auckland region were unavailable at the time of publication of this thesis. Therefore, one year mortality rates in the ARCOS studies were plotted against annual stroke mortality for New Zealand to determine if the trends are in the same direction and compare the amount of change in mortality. Simple linear regression lines were fit to the data shown in Figure 5.1. The declining trend in stroke mortality was similar between the ARCOS studies and the New Zealand mortality data, with similar slopes (-1.5 across the ARCOS studies, -1.4 across the New Zealand data) and annual percentage change in rates (1.9% decline in ARCOS, 1.5% decline in New Zealand). Using these standard criteria it has been shown that the quality and comparability of these studies are of a high standard and this quality improved over the three study periods.

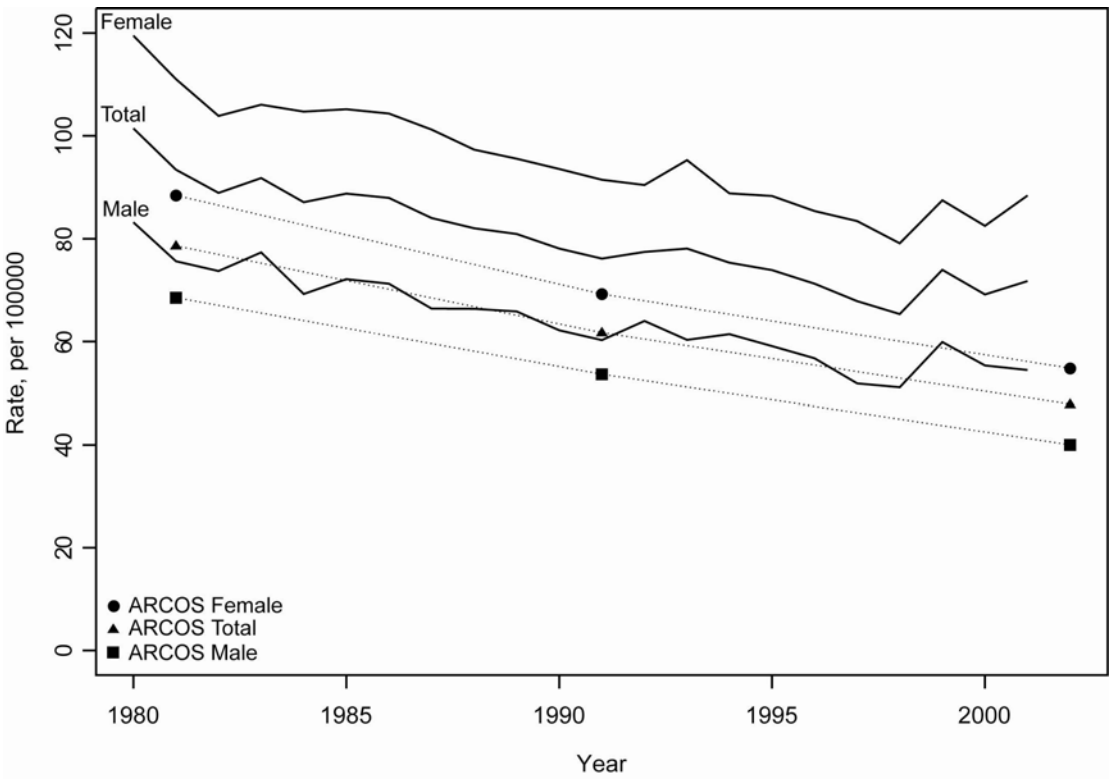

Figure 5.1 Trends in one year stroke mortality in the three ARCOS studies compared with trends in New Zealand.

5.1.2. Capture Recapture

The capture recapture technique was used to measure the completeness of case ascertainment in each of the three ARCOS studies and to estimate the number of cases that were missing from the studies. The sources of notification for the three studies were combined into four lists (described in Chapter 4, Table 4.2): hospital notifications, GP notifications, other community notifications (stroke foundation, rest homes, and allied health professionals) and death certification. The capture histories of the case ascertainment were aggregated into categorical combinations of the multiple notifications of patients in the three studies and are presented in the contingency table in Table 5.3. Only 15 distinct capture histories were observed out of a possible 114 different combinations.

Table 5.3 shows that there were more patients in the 2002-2003 study that were notified by three or more sources of notification (11%), compared to 5% in the 1981-1982 study and 3% in the 1991-1992 study, reflecting changes in case ascertainment and electronic data-base systems. In all three studies, the majority of cases were notified through the hospital system only or a combination of hospital and another source of notification. However, there were declines in the number of patients that were notified only through routinely available sources, such as hospital admission and discharge lists and death certificates and autopsies, 53%, 46% and 34%, across the three studies respectively. This reflects the increases in overlapping multiple sources of notification over time.

Table 5.3 Contingency table of the four sources of notification used in capture-recapture analysis.

History	Hospital	GP	Death	Other community	1981-1982*		1991-1992*		2002-2003	
					n	%	n	%	n	%
1	1	1	1	1	0	0.0	0	0.0	16	0.8
2	1	1	0	1	4	0.6	1	0.1	95	4.9
3	1	1	1	0	2	0.3	5	0.4	12	0.6
4	1	1	0	0	3	0.4	2	0.1	60	3.1
5	1	0	1	1	27	4.0	16	1.1	86	4.4
6	1	0	0	1	135	19.9	290	20.0	539	27.8
7	1	0	1	0	73	10.8	274	18.9	227	11.7
8	1	0	0	0	324	47.9	520	35.9	605	31.2
9	0	1	1	1	0	0.0	1	0.1	12	0.6
10	0	1	0	1	4	0.6	23	1.6	37	1.9
11	0	1	1	0	1	0.2	4	0.3	5	0.3
12	0	1	0	0	8	1.2	72	5.0	69	3.6
13	0	0	1	1	7	1.0	20	1.4	34	1.8
14	0	0	0	1	54	8.0	63	4.4	92	4.8
15	0	0	1	0	35	5.2	158	10.9	49	2.5
Total Patients					677†		1449		1938	

*1981-1982 and 1991-1992 numbers were not adjusted for the sampling procedures

† 3 patients had missing source of notification from the 1981-1982 study

Table 5.4 presents results from the capture-recapture log-linear modelling using different combinations of the sources of notification. The independent model included the main effects of the four sources of notification only and estimated that there was 18%, 22% and 9% cases missing from the three studies respectively. Two-way interactions between sources were added to the model adding complexity and inflating the proportion of cases estimated to be missing. Additional two-way interactions did not add any extra information on top of the single two-way interactions. Next, the three way interactions which included all two-way interactions between the sources of interest were added to the model. The most parsimonious model included all two-way and three-way interactions between hospital, GP, and death certification. This was selected as the final model as it was the most robust, with a small AIC estimate and it estimated the least number of patients missing in all three studies. It was estimated that there were 16%, 11% and 6% cases missing from the three studies, respectively. All models suggested that the estimated number of missing cases decreased across the three studies, reflecting improvement in case ascertainment and the use of multiple sources of notification.

Table 5.4 Capture-recapture log-linear modelling, estimating the number missing in each study.

	1981-1982				1991-1992				2002-2003			
Model	**AIC**	**#miss**	**95% CI**	**%miss**	**AIC**	**#miss**	**95% CI**	**%miss**	**AIC**	**#miss**	**95% CI**	**%miss**
Independent	-0.9	146	(115-186)	17.7	331.6	397	(342-460)	21.5	127.4	189	(164-217)	8.9
H*D	1.0	151	(112-204)	18.2	332.0	432	(354-526)	23.0	129.4	190	(161-224)	8.9
H*C	-1.9	186	(131-266)	21.6	267.0	620	(519-741)	30.0	108.4	274	(224-334)	12.5
H*GP	-6.9	134	(104-172)	16.5	189.5	300	(255-352)	17.1	67.5	139	(117-164)	6.7
D*C	-0.3	141	(109-180)	17.2	239.5	320	(274-374)	18.1	108.8	173	(150-200)	8.2
D*GP	1.1	146	(115-186)	17.7	318.2	385	(332-446)	21.0	120.8	184	(160-212)	8.7
C*GP	-0.5	148	(116-189)	17.9	332.8	399	(344-463)	21.6	116.2	200	(173-231)	9.3
H*D*C	-0.3	355	(148-849)	34.4	87.4	2650	(1770-3968)	64.7	46.2	475	(362-624)	19.7
H*D*GP	**-1.9**	**131**	**(95-181)**	**16.2**	**136.1**	**185**	**(140-243)**	**11.3**	**58.2**	**115**	**(92-144)**	**5.6**
D*C*GP	2.2	143	(111-184)	17.4	222.4	301	(257-352)	17.2	85.6	174	(150-203)	8.3

H=Hospital, D=Death, C=Community, GP=General Practitioner; AIC = Akaike's Information Criterion; CI = Confidence Interval

%miss = estimated percentage missing, (# missing)/(# missing + # in study)

5.2. Trends in Patient Characteristics

It is important to examine changes in case mix and demographic characteristics of patients across the three studies to identify changes in the baseline risk of stroke in the population. Table 5.5 shows the demographic characteristics of the patients at the time of their stroke, in each of the studies. There were similar proportions of male patients (under 50%) across the three studies. The mean age increased significantly, with the proportion of patients aged over 85 years increasing significantly over the three studies, mirroring trends in the ageing of the Auckland population. Female stroke patients were on average 5 years older than males across the three studies. There was a decline in the proportion of patients who identified as NZ/European ethnicity, with stable proportions of Māori. However, there were increasing proportions of patients identifying with other ethnic origins, in particular Pacific and Other populations, where the proportions increased nearly 4- and 5-fold, respectively, over the study periods. This reflects changes in the ethnic distribution of the Auckland population, with increasing immigration from the Pacific and Asia. Declines in the proportion of patients in high socioeconomic groups may also reflect increases in immigrant populations to Auckland.

Table 5.5 Patient demographics, socioeconomic status and medical history of stroke patients in the three ARCOS studies.

	1981-1982 (n=1360)		1991-1992 (n=1761)		2002-2003 (n=1938)		Test for trend
	n	%	n	%	n	%	P value*
Demographics							
Male	662	49.0	817	46.4	892	46.0	0.15
Age, mean (±SD)	71.2	(13.3)	71.6	(13.5)	73.0	(13.8)	<0.001†
Male, Age, mean	68.9	(13.4)	68.3	(12.5)	69.6	(13.3)	0.11†
Female, Age, mean	74.3	(12.9)	74.3	(13.6)	75.8	(13.5)	0.02†
Age, 15-64 years	344	25.3	425	24.1	472	24.4	0.57
Age, 65-74 years	366	26.9	499	28.3	445	23.0	0.005
Age, 75-84 years	476	35.0	592	33.6	637	32.9	0.21
Age, 85+ years	174	12.8	245	13.9	384	19.8	<0.001
Ethnicity							
NZ/European	1248	91.8	1532	87.0	1431	73.8	<0.001
Māori	60	4.4	82	4.7	102	5.3	0.25
Pacific Island	32	2.4	111	6.3	197	10.2	<0.001
Asian/Other	20	1.5	36	2.0	162	8.4	<0.001
Married/partnered	680	50.0	857	48.7	963	49.7	0.28
Institutionalised	300	22.1	218	12.5	421	26.1	0.001
Pre-stroke Dependency	414	30.4	423	24.1	431	23.3	<0.001
Socio-economic status‡							
High, 1-2	394	31.7	417	29.5	340	24.0	<0.001
Medium, 3-4	604	48.6	755	53.4	826	58.4	0.33
Low, 5-6	244	19.7	243	17.2	249	17.6	<0.001
Medical history							
High blood pressure	700	51.5	910	51.7	1079	55.7	<0.001
Blood Pressure Medication	640	47.5	763	53.4	943	52.1	0.02
Myocardial infarction	156	11.5	288	16.4	240	12.4	0.55
Stroke	330	24.3	456	25.9	477	24.6	0.91
Diabetes mellitus	134	9.9	236	13.4	329	17.0	<0.001
Current smoker	374	27.5	411	23.3	241	12.4	<0.001
BMI, mean (±SD)	23.7	(4.6)	24.1	(4.9)	25.6	(5.9)	<0.001†
Normal (BMI <25)	864	67.1	918	62.0	635	53.0	<0.001
Overweight (BMI 25-30)	330	25.6	417	28.2	344	28.7	0.08
Obese (BMI >30)	94	7.3	145	9.8	219	18.3	<0.001
Vascular Risk Index							
0	306	22.5	340	19.3	438	22.6	0.73
1	524	38.5	684	38.8	699	36.1	0.12
≥ 2	530	39.0	737	41.9	801	41.3	0.21

* p-value calculated using Cochran-Armitage trend test

† p-value calculated using ANOVA

‡ Socioeconomic status measured using Elley-Irving for 1981-1982[393] and NZSEI for 1991-1992 and 2002-2003.[395]

A non-linear increase in the proportion of patients who lived in institutional care was found over time. However, the proportion of patients dependent on others for performing activities of daily living before their stroke declined, indicating that the overall health of the population before their strokes was relatively stable over time. There were significant increases in the proportion of patients reporting that they had a history of hypertension, over 50% of patients. This is likely to be an underestimate as it does not take into account newly diagnosed hypertension at the time of the stroke. It was found that the proportion of patients with uncontrolled hypertension, patients reporting a history of high blood pressure but were not taking anti-hypertensive medication at the time of stroke, was relatively low across the studies (1981-1982: 4.9%; 1991-1992:9.7%; and 2002-2003:6.4%). There were significant increases in mean BMI across the studies with increases in the proportion of patients with diabetes from 10% to 17%. The proportion of patients with a BMI of <25 declined significantly, where the proportion of obese patients (BMI ≥ 30) increased across the three studies. There were significant declines in the proportion of current smokers (from 28% in 1981-1982 to 14% in 2002-2003), with a halving of the proportion of smokers between 1991 and 2002. The proportion of patients with a history of heart disease or stroke were relatively stable across the three studies, as was the proportion of patients reporting one or more vascular risk factors at the time of their stroke.

5.2.1. Trends in Acute Management

Data on the acute management of stroke patients were limited across the three studies due to differences in data collection over the three time points. Table 5.6 shows changes in the acute management and care of stroke patients across the three studies. There were improvements in the time that people took to first seeking medical attention after their stroke (ringing their GP or ambulance service or admission to hospital), with a trend towards increasing numbers of patients seeking medical attention within three hours after their stroke. However, there were large proportions of missing data for this variable in the 1991 and 2002 studies, as data on the time of stroke onset was missing. The increasing proportions of patients seeking medical attention within three hours after their stroke, and increases in the proportion of patients

admitted to hospital across the three studies, may reflect improvements in the knowledge of the general population about stroke and the importance of getting to the hospital as soon after the event as possible, enabling them to receive such treatments as the new thrombolytic therapies.

The proportion of patients having a stroke as a direct consequence of recent surgery increased over time, however, it was not possible to check what type of surgery the stroke followed across the three studies. In the 2002-2003 study, 17% of the strokes following surgery occurred within 4 weeks after coronary bypass surgery. The increases in the proportion of patients receiving neuroimaging through CT or MRI scans, from 21% in 1981-1982 to 88% in 2002-2003, reflect the increased availability of these scans in hospitals. Declines in the number of deaths being autopsied reflects increased diagnostic accuracy for death. Therefore, trends in acute management appear to have improved over time, with patients seeking medical attention earlier and increases in the proportion of patients being admitted to hospital and receiving some form of neuroimaging.

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Table 5.6 Trends in acute management of stroke patients in the three ARCOS studies.

	1981-1982 (n=1360)		1991-1992 (n=1761)		2002-2003 (n=1938)		Test for trend
	n	%	n	%	n	%	P value*
Time to Medical Attention, hrs							
Median (IQR)	3.0	(8)	1.0	(7)	1.5	(6)	<0.001†
0 – 3 hours	444	51.3	691	62.9	598	61.3	<0.001
3 – 6 hours	138	15.9	117	10.7	105	11.3	0.003
6 – 12 hours	118	13.6	59	5.4	80	8.6	<0.001
12 – 24 hours	72	8.3	71	6.5	82	8.8	0.66
> 24 hours	94	10.9	161	14.7	65	7.0	0.006
Hospital admission	878	64.6	1276	72.5	1757	90.7	<0.001
Stroke after surgery	38	2.8	45	3.5	114	6.0	<0.001
Management							
Neuroimaging, CT/ MRI	162	21.0	541	30.7	1694	87.6	<0.001
Lumber Puncture	60	7.8	56	4.4	20	1.0	<0.001
Autopsy	142	24.2	41	6.5	24	1.2	<0.001

* p-value calculated using Cochran-Armitage trend test

† p-value calculated using Brown Mood test for median scores

% does not include missing values

5.3. Trends in Attack Rates

Event and incidence rates of stroke were calculated overall, and by age group (15-64, 65-74, 75-84 and 85 years or older) and sex. Crude event and incidence rates by age and sex are presented in Table 5.7 and Figure 5.2 (detailed 10-year age- and sex-specific crude rates are presented in the Appendix 5 and 6, respectively). Crude rates of stroke increased with age increasing within all three studies (Figure 5.2, bottom), and for both male and female stroke patients. Generally, rates of stroke in males were higher than females at most ages, with the exception of the older age groups in the 1991-1992 and 2002-2003 studies. Age specific rates were typically highest in the 1981-1982 study and declining over time. However, significant downward trends were observed across the three studies in event and incidence rates for patients aged between 75 and 84 years. The crude rates for females and overall strokes increased slightly from 1981-1982 to 1991-1992, then declined in 2002-2003 (Table 5.7 and Figure 5.2, top). This may be attributed to either over sampling/registration of females or under registration/sampling of males in the 1991-1992 study, however the proportion of males did not change over the study periods. An increase in the proportion of females in the 85 years and older age group in the 1991-1992 study compared to males (1981-1982, 75% females aged ≥ 85 years; 1991-1992, 83%, 2002-2003, 76%) was found, which may explain part of the increase in rates in the 1991-1992 study. Overall crude incidence and event rates declined significantly across the three studies, however, the trend was not linear, due to the increases in female rates in the 1991-1992 study. Significant, linear declines were found in males over time and not females.

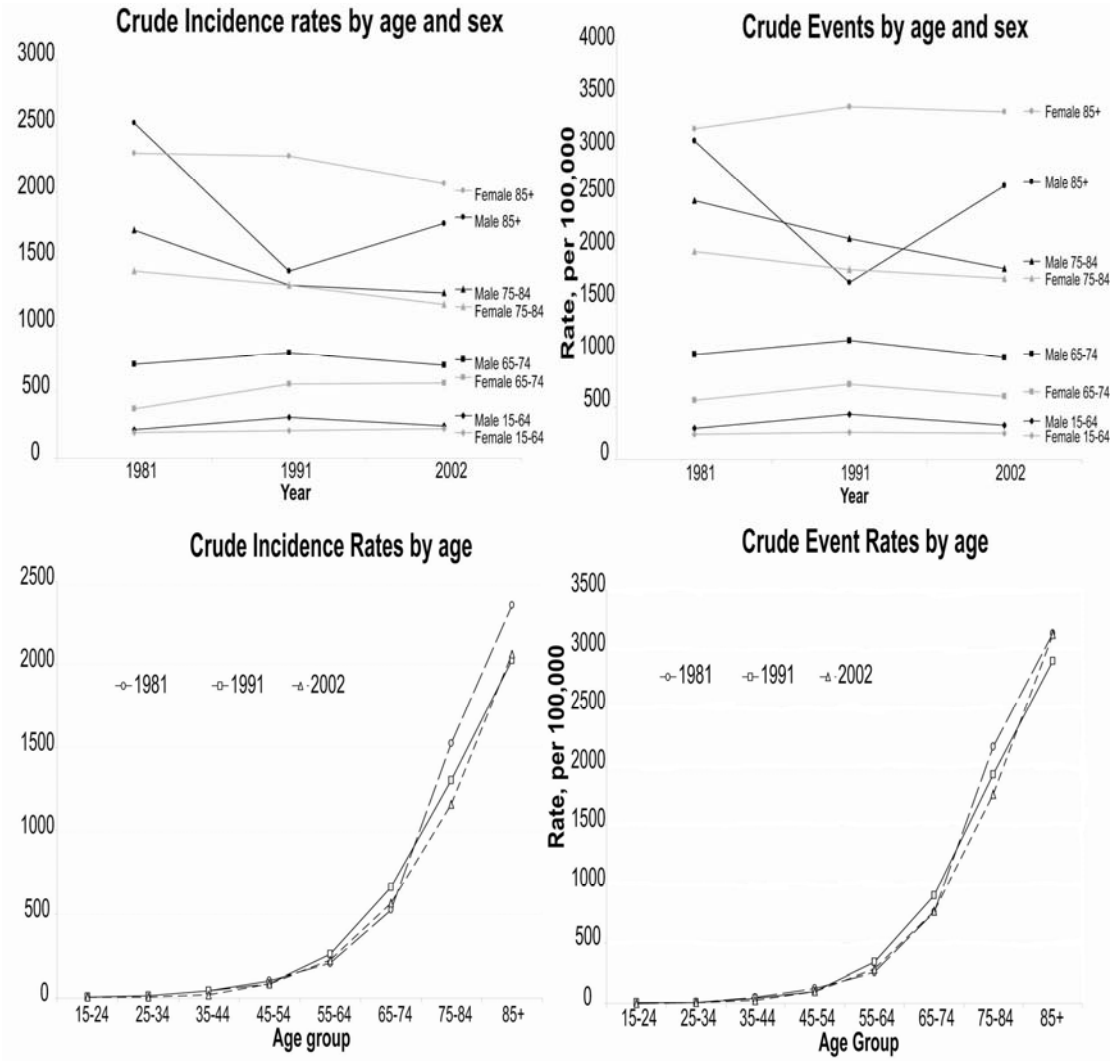


Figure 5.2 Plots of crude incidence and event rates by age and sex across the three studies (top), and age specific rates by study (bottom).

Table 5.7 Age-, sex- and overall crude stroke incidence and event rates per 100,000 population in Auckland, New Zealand, 1981-2003.

	1981-1982				1991-1992				2002-2003				Test for trend
	N	n	Rate	(95% CI)	N	n	Rate	(95% CI)	N	n	Rate	(95% CI)	P value
Incidence													
Age group													
15-64	518112	286	55	(46-64)	624828	347	56	(48-63)	788106	391	50	(45-55)	0.14
65-74	49812	260	522	(432-612)	56388	373	661	(564-759)	59454	336	565	(508-629)	0.44
75-84	22965	350	1524	(1298-1750)	31701	412	1300	(1139-1460)	37815	438	1158	(1055-1272)	<0.001
85+	5691	134	2355	(1791-2918)	8541	173	2026	(1684-2367)	12507	258	2063	(1826-2331)	0.28
Male	289002	510	176	(155-198)	348816	587	168	(150-186)	427155	667	156	(145-168)	0.03
Female	307578	520	169	(149-190)	372642	718	193	(179-207)	470727	756	161	(150-172)	0.20
Overall	596580	1030	173	(158-188)	721458	1305	181	(168-194)	897882	1423	158	(150-167)	0.02
Events													
Age group													
15-64	518112	350	68	(58-78)	624828	433	69	(61-77)	788106	484	61	(56-67)	0.13
65-74	49812	380	763	(654-871)	56388	512	908	(795-1021)	59454	460	774	(703-844)	0.97
75-84	22965	498	2169	(1899-2438)	31701	611	1927	(1730-2125)	37815	667	1764	(1630-1898)	<0.001
85+	5691	178	3128	(2478-3778)	8541	247	2892	(2460-3324)	12507	390	3118	(2809-3428)	0.85
Male	289002	690	239	(214-264)	348816	835	239	(218-261)	427155	918	215	(201-229)	0.03
Female	307578	716	233	(209-257)	372642	968	260	(239-281)	470727	1083	230	(216-244)	0.55
Overall	596580	1406	236	(218-253)	721458	1803	250	(235-265)	897882	2001	223	(213-233)	0.05

N=Auckland census population denominator, n=number of stroke patients, CI=confidence interval

Table 5.8 presents overall and age- and sex-specific stroke incidence and event rates for the three studies, age-standardised, using the direct method, to the WHO world population. As shown in the crude rates, age standardised rates were higher in males compared with females. The ratio of rates in males to females did not change significantly across the three study periods (incidence, male/female: 1981, 1.38 [95% CI 1.16-1.65]; 1991, 1.16 [95% CI 1.01-1.34]; 2002, 1.26 [95% CI 1.13-1.40]). This ratio was highest in males for all ages, except the oldest age group. Sex-specific differences in temporal trends in rates were found. A decline in stroke incidence of 16% (95% CI, 2% to 27%) was found for males between 1981-1982 and 2002-2003, with a decline of 14% (95% CI, 2% to 24%) in event rates (Figure 5.3). For females, rates increased from 1981-1982 to 1991-1992 and then declined in 2002-2003, producing a non-significant change in rates between the beginning and end of the study period. There were, however, significant changes in standardised incidence rates for females from 1991-1992 to 2002-2003 14% (95% CI, 2% to 24%), indicating a decline over the last decade, which may be influenced by the over-representation of females in the 1991-1992 study shown in the crude rates. As shown in crude rates there were significant declines in age standardised rates from 1981-1982 to 2002-2003 for the age group 75 to 84, which was influenced by significant changes in males in this age group. However, no significant difference was found when testing for heterogeneity between the age groups (p=0.96), so this difference in the 75 to 84 year age group may be due to chance.

Table 5.8 Age- and sex-specific annual stroke rates (per 100,000 age-standardised to the WHO world population) in Auckland, New Zealand, 1981-2003.

	1981-1982		1991-1992		2002-2003		Rate Ratio		Annual
Incidence	**n**	**Rate (95% CI)**	**n**	**Rate (95% CI)**	**n**	**Rate (95% CI)**	**1991-92:1981-82**	**2002-03:1991-92**	**% change**
Age group									
15-64	286	49 (42-58)	347	49 (43-56)	391	44 (40-49)	1.01 (0.82-1.24)	0.89 (0.76-1.05)	-0.48
65-74	260	37 (31-43)	373	46 (40-54)	336	40 (36-44)	1.27 (1.01-1.59)	0.85 (0.71-1.03)	0.58
75-84	350	50 (43-58)	412	43 (38-48)	438	38 (35-42)	0.85 (0.70-1.03)	0.89 (0.76-1.04)	-1.22*
85+	134	20 (16-26)	173	17 (15-20)	258	18 (16-20)	0.86 (0.64-1.15)	1.02 (0.83-1.25)	-0.58
Male	510	184 (163-209)	587	167 (150-185)	667	156 (144-168)	0.90 (0.77-1.06)	0.93 (0.82-1.06)	-0.78*
Female	520	133 (118-151)	718	143 (130-158)	756	124 (115-134)	1.08 (0.92-1.26)	0.86 (0.76-0.98)	-0.28
Overall	1030	156 (143-170)	1305	156 (145-167)	1423	139 (132-147)	1.00 (0.89-1.12)	0.90 (0.82-0.98)	-0.50*
Events									
Age group									
15-64	350	60 (52-70)	433	62 (55-69)	484	55 (50-60)	1.03 (0.85-1.24)	0.89 (0.77-1.03)	-0.42
65-74	380	53 (46-62)	512	64 (56-72)	460	54 (49-59)	1.19 (0.99-1.44)	0.85 (0.73-0.99)	0.20
75-84	498	71 (63-81)	611	63. (57-70)	667	58 (54-63)	0.89 (0.76-1.04)	0.92 (0.81-1.04)	-0.93*
85+	178	27 (22-33)	247	25 (21-29)	390	27 (24-29)	0.92 (0.72-1.19)	1.08 (0.90-1.29)	0.01
Male	690	248 (223-276)	835	236 (216-258)	918	214 (200-228)	0.95 (0.83-1.09)	0.91 (0.81-1.01)	-0.68*
Female	716	181 (163-202)	968	190 (175-206)	1083	173 (162-184)	1.05 (0.91-1.20)	0.91 (0.82-1.01)	-0.20
Overall	1406	211 (196-228)	1803	213 (201-227)	2001	193 (185-202)	1.01 (0.92-1.11)	0.91 (0.84-0.98)	-0.40*

* significant change between 1981-1982 and 2002-2003 studies

n=number of stroke patients, CI=confidence interval

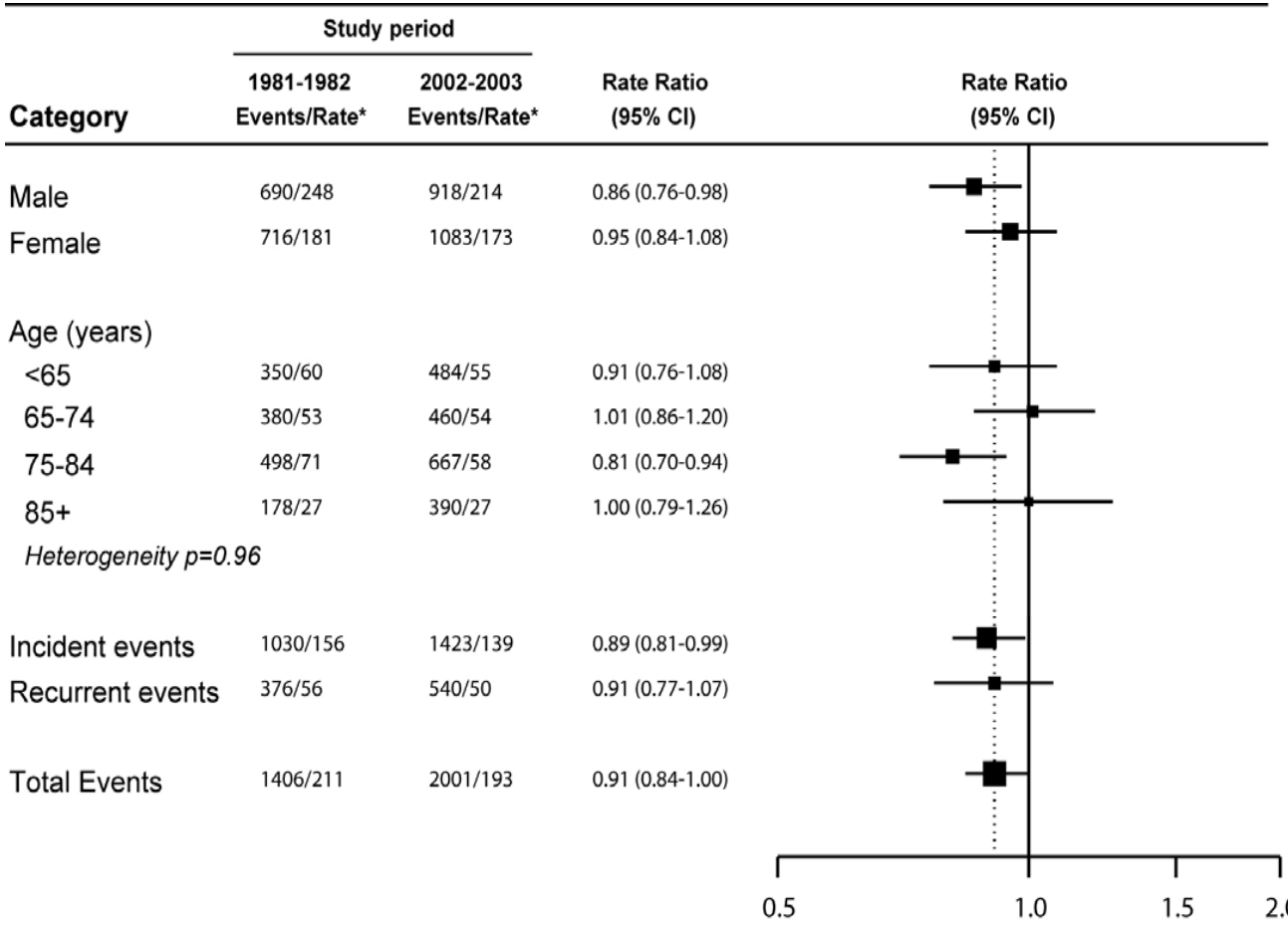


*Figure 5.3 Sex-, age- and sequence-specific stroke attack rate ratios (2002-2003 compared with 1981-1982). *Rates were age-standardised to the WHO world population and shown with 95% confidence intervals (CI).*

Figure 5.3 illustrates the overall change in rates, over the study period from 1981-1982 and 2002-2003, through rate ratios of age-standardised rates. There were modest declines in standardised incidence rates by 11% (95% CI, 1% to 19%) and event rates 9% (95% CI, 0% to 16%), over the study period. However, as shown in the crude rates, these changes were not linear over the 20 years with slight increases in rates in the 1991-1992 study and non-significant changes in rates between the 1981-1982 and 1991-1992 studies. The overall declines were influenced by significant changes from 1991-1992 to 2002-2003 in incidence 10% (95% CI, 2% to 18%) and attack rates 9% (95% CI, 2% to 16%). No significant changes the rates of recurrent stroke were found across the study period. Therefore, declines in event rates were influenced by changes in the incidence of stroke rather than changes in the recurrent rate of the disease.

The annual percentage change in standardised rates was calculated to enable comparisons with previously published data. There was a 0.5% annual decline in the rate of incident stroke across the study period, with large declines, up to 0.8% in males, compared 0.3% in females. This supports the results of a significant decline in rates in males over the 21 years. Similar trends were found across event rates. These results fall within the confidence intervals of the systematic literature review presented in Chapter 3, Section 3.3.5, -0.6% (95% CI, -2.0% to 0.7%).

5.4. Discussion

Overall declines in the incidence of stroke were found across three ideal stroke incidence studies conducted in Auckland, New Zealand, between 1981 and 2002. The largest declines were observed between the 1991-1992 and 2002-2003 studies. These results support previously reported trends in the incidence of stroke, with stable rates in the US and Europe in the 1980's[258, 330] and declining rates from 1990 onwards.[304, 321, 350] However, the magnitude of the decline in incidence in the current study was not nearly as large as that previously shown in two studies conducted in Oxford[38] and Perth[317] during similar time periods. This could be due to the differences in the higher socioeconomic status of the Oxford and Perth populations, and the increasing

ethnic share of the Auckland population. The annual declines in rates in Auckland over the 20 years were also found to be consistent with the declines found in the systematic review of trends in the incidence of stroke across ideal stroke incidence studies (Chapter 3).

The declines in the rates of stroke were found to be significant in males and not in females. These results were supported by the systematic review of trends in incidence across ideal stroke incidence studies (Chapter 3), where overall declines in rates were more likely due to steeper declines in males than females.[38, 260, 316, 317, 320] However, in the MONICA project, larger declines were found in females, across a number of studies.[37] The non-significant in females across the ARCOS studies, were due to increasing rates from 1981-1982 to 1991-1992 and then declining in 2002-2003. This may be attributed to either over-sampling or registration of female stroke patients, or under-sampling or registration of males in the older age groups in the 1991-1992 study. Although the proportion of males did not change over the study periods, there was a slight increase in the proportion of females in the older age group in the 1991-1992 study compared to males, which points to an over-registration of female stroke patients in this group.

To what extent can the trends in stroke rates be accounted for by changes in the prevalence of known risk factors in Auckland? On the basis of epidemiological data there is a strong, direct and near continuous association between stroke incidence and level of blood pressure.[88, 89] This can be reversed within a few years of blood pressure lowering treatment, so non-optimal control of blood pressure levels is considered the most important risk factor for stroke, accounting for almost two thirds of the global burden of stroke.[99] There were higher proportions of stroke patients with a history of high blood pressure in the ARCOS studies compared to the general population,[58] demonstrating the high risk of stroke associated with hypertension. Although there was an increase in the proportion of stroke patients with a history of high blood pressure across the three ARCOS studies, these data are confounded by changes in diagnostic criteria for hypertension and a lowering in the threshold to commence treatment over

time. There is some evidence of a decline in blood pressure levels, albeit within selected subsets of the New Zealand European population of Auckland.[422, 423] The Oxfordshire study showed that declines in stroke rates were associated with favourable trends in pre-morbid blood pressure levels and use of blood pressure lowering medication.[38] It was found that only a small proportion of patients who reported they had a history of high blood pressure were not on any anti-hypertensive medication before their stroke, indicating good control of blood pressure in the Auckland stroke population. However, many other studies have documented suboptimal levels of awareness and control of high blood pressure levels within communities,[366] and that control of blood pressure levels in high risk individuals explains only a small fraction of trends in stroke rates.[287, 365] It has been argued that changes in the prevalence of smoking and hypertension explain part of the variation in stroke rates between populations[424] and over time.[370]

Trends in the other risk factors in the ARCOS studies are more reliable, but they are also more complex. The halving in the proportion of stroke patients who were current smokers was offset by considerable increases in obesity and history of diabetes among stroke patients, from the 1981-1982 to 2002-2003. Large declines in the rates of smoking in this population occurred between 1991 and 2002, reflecting changes in the prevalence of smoking in the older population due to the success of anti-smoking campaigns run in New Zealand from 1985 onwards.[425] Increases in the prevalence of diabetes and obesity have also been shown in the New Zealand population.[113, 422, 426] These data reinforce the burgeoning global impact of obesity and diabetes on cardiovascular disease and other health problems.[427] It was also found that the proportion of patients with a history of myocardial infarction was stable over the study period, which supports other studies indicating that improvements in survival after acute myocardial infarction has not impacted adversely on stroke incidence.[428]

Several limitations to these analyses should be discussed. In order for these trends data to be reliable, it is crucial that there was consistency in the data acquisition methods across the three ARCOS studies, so that any variation in

the rates could not be attributed to artefacts of registration. To ensure comparability of the data, standard clinical diagnostic criteria and case ascertainment procedures, fulfilling the criteria for ideal stroke incidence studies were used across the three studies. The consistency of case ascertainment procedures across the three studies and the fulfilment of the MONICA criteria for high quality case ascertainment provide reassurance that the case ascertainment was high and reliable across the three studies. The proportion of patients missed in the three studies, as estimated through capture recapture analyses decreased over time, which may reflect improvements in case ascertainment methods and hospitalisation for stroke. There has been much debate as to whether capture recapture should be used in epidemiological studies of chronic disease,[275-278, 429] so the results should be interpreted with caution. However, capture recapture techniques are becoming more common in estimating the completeness of stroke registers and adjusting incidence rates in stroke research.[270, 279] A limitation of the capture recapture analysis is in the assumption of equal probability of a patient being captured, particularly in the 1991-1992 study, where a sampling procedure was used to identify non-hospitalised non-fatal strokes. These patients had only a 25% chance of being included in the study (if their GP had been sampled), where hospitalised and fatal patients had a 100% chance of being included in the study. However, the crude numbers (not adjusted for the sampling procedure) were used for these analyses, and it is likely that any error is likely to be small.

The sampling methods and case ascertainment procedures used in the first two studies may have lead to under-estimates of the number of patients in these study periods. Conversely, the increased availability of CT and other diagnostic techniques, higher rates of hospitalisation, and possibly greater awareness of stroke symptoms among the medical profession and general public, may have improved the detection of milder strokes in the most recent study. It has been argued that the increased use of neuroimaging may be associated with the identification of smaller, less severe, haemorrhagic strokes.[258] In the current analysis it was not possible to investigate trends among stroke subtypes, due to the low rates of imaging in the earlier studies.

However, consistent clinical diagnostic criteria, based on stroke signs and symptoms lasting for longer than 24 hours, were used to identify stroke patients across the three studies. Therefore, it is unlikely that variations in the rate of stroke were due to the increased used of neuroimaging.

It was shown in the current analysis that the trends in mortality across the ARCOS studies were similar to those from standard death data in New Zealand from the NZHIS. This provides confidence in the consistency and accuracy in the recording of death data in New Zealand over time. However, to measure the burden of stroke in a population, hospital and community based strokes, as well as information on all deaths need to be collected. It is important that stroke is studied in a population-wide context using multiple-overlapping sources of notification because many patients survive the acute phase with residual disability and a large proportion of the burden of care occurs outside of the hospital sector. Moreover, changes in diagnostic coding practices and referral patterns can significantly distort trends derived solely from death and hospital-based data. Yet, there are still few ideal population-based stroke incidence studies that have investigated trends in the rate of stroke over time, when compared with the number of studies that use mortality or hospital-based register data.

In showing modest declines in overall stroke incidence and attack rates in Auckland over two decades, this unique population-based series of stroke studies provides some feedback on the success of strategies to modify the risk of primary and secondary stroke on a background of structural and other changes in the population. However, some positive changes in the profile of risk factors, such as fewer smokers at the time of stroke, were counterbalanced by increases in the frequency of patients with diabetes and obesity. Efforts are needed to control the growing epidemic of stroke through the modification of risk factors such as blood pressure levels, smoking, obesity and diabetes. It is important to identify high risk groups, where a disproportionate amount of the burden occurs, in order to target primary and secondary prevention strategies.

6. TRENDS IN ETHNIC DISPARITIES IN RATES

Worldwide there is evidence that people from ethnic minority groups have poorer health status than White or European majority populations, including increased incidence and higher mortality rates for cardiovascular disease and stroke.[13, 15, 16, 42, 59, 430, 431] The excess burden of stroke in African Americans in the US has been well documented.[15] However, there has been limited data investigating at trends in stroke among ethnic minority groups. Data from the US has shown declining stroke mortality trends in both African and white American's over the past three decades, with no change in the ratio between ethnic groups.[18] Recently, stroke trends have stabilised, with no difference in case fatality between the groups.[43] Therefore, it has been argued that the excess stroke mortality in ethnic minority groups is due to excess incidence and not survival.[41, 43] However, there is no data on ethnic disparities in stroke trends from ideal stroke incidence studies to support or refute these arguments.

This chapter describes ethnic disparities in trends in stroke attack rates across the three ARCOS studies. The first section examines ethnic disparities in baseline demographics and risk factor trends across the three studies. The second section investigates ethnic disparities in trends in incidence and overall stroke event rates. The third section explores ethnic disparities in stroke subtypes within the most recent ARCOS study (2002-2003), which are discussed in the context of other population-based studies with ethnic disparate populations. Finally, these results, and the strengths and weaknesses of these analyses are discussed within the context of current literature.

6.1. Trends in Baseline Characteristics

Investigating changes in demographic characteristics by ethnic group provides detailed information on how these groups have changed over the past 20 years, and how these changes may have influenced temporal trends in the rate of stroke. As mentioned in Chapter 5, there was a significant

decline in the proportion of patients identifying as NZ/European ethnicity, with correspondingly increasing proportions of patients of other ethnic origins. In particular, the proportions of Pacific and Asian & Other ethnic groups increased nearly 4- and 5-fold, respectively, over the study period, reflecting increases in immigration of these populations to Auckland. Ethnic group or affiliation could not be identified in 46 patients in the 2002-2003 study, so these were set to missing.

Table 6.1 presents baseline demographic, medical history and hospital management for the four ethnic groups (NZ/European, Māori, Pacific, and Asian & Other) across the three studies. The majority of Pacific and Asian & Other ethnic groups were not born in New Zealand, reflecting the high immigration from these groups. It could not be estimated from the data how long these people had lived in New Zealand. Trends in demographic characteristics across the four ethnic groups were similar to those found in the overall population. The average age of stroke patients increased over time in the NZ/European, Māori and Pacific ethnic groups. However, Māori and Pacific populations had their strokes on average 10 years younger than NZ/European. This corresponds to lower average age in Māori and Pacific populations, with shorter life expectancy than NZ/Europeans.[383] NZ/European populations had higher social class than other ethnic groups, across the three studies. While there were no significant changes in social class in the ethnic groups, there was a trend towards an increasing proportion of patients in the higher social class groups among ethnic minority groups over time. The social class of the Asian & Other ethnic group grew to over 64% in the upper classes, reflecting the immigration of wealthier populations, however, there were small numbers in these groups, so the results should be interpreted with caution.

Table 6.1 Patient demographics, medical history and management by ethnic group, across the three studies.

NZ/European	**1981-1982 (n=1248)**		**1991-1992 (n=1532)**		**2002-2003 (n=1431)**		**Test for trend**
	n	**%**	**n**	**%**	**n**	**%**	**P value***
Born in New Zealand	868	69.6	1095	72.1	1018	73.6	0.0233
Demographics							
Male	608	48.7	692	45.2	652	45.6	0.1131
Age, mean (±SD)	72.8	(12.8)	73.5	(12.1)	75.6	(12.5)	<0.0001†
Married/partnered	624	50.0	727	47.5	696	48.6	0.5100
Social class, high (1-3)	680	59.4	700	57.3	651	59.1	0.8506
Medical history							
High blood pressure	632	50.6	802	52.7	783	57.7	0.0003
Myocardial infarction	146	11.7	273	17.9	190	13.5	0.2390
Stroke	314	25.2	404	26.4	361	25.2	0.9961
Diabetes mellitus	98	7.9	193	12.7	179	12.7	0.0001
Current smoker	330	26.7	330	21.7	162	12.7	<0.0001
BMI, mean (±SD)	23.3	(4.1)	23.7	(4.5)	24.7	(5.1)	<0.0001†
Management							
Admission to hospital	790	63.3	1088	71.0	1284	89.7	<0.0001
Neuroimaging, CT/MRI	134	18.9	851	69.5	1236	86.4	<0.0001
Māori	**1981-1982 (n=60)**		**1991-1992 (n=82)**		**2002-2003 (n=102)**		
	n	**%**	**n**	**%**	**n**	**%**	
Born in New Zealand	60	100	82	100	102	100	1.000
Demographics							
Male	28	46.7	40	48.8	43	42.2	0.5074
Age, mean (±SD)	56.7	(14.2)	55.0	(16.1)	60.7	(14.3)	0.0898†
Married/partnered	30	50.0	38	46.3	42	41.2	0.2600
Social class, high (1-3)	12	22.2	16	24.2	25	37.9	0.0519
Medical history							
High blood pressure	38	63.3	41	52.6	63	62.4	0.9163
Myocardial infarction	8	13.3	9	11.4	12	11.9	0.8134
Stroke	14	23.3	21	25.6	12	11.8	0.0397
Diabetes mellitus	20	33.3	19	24.7	35	34.7	0.6949
Current smoker	32	53.3	41	50.6	35	38.9	0.0675
BMI, mean (±SD)	28.6	(8.9)	28.3	(6.1)	29.8	(6.9)	0.4634†
Management							
Admission to hospital	48	80.0	73	89.0	99	97.1	0.0004
Neuroimaging, CT/MRI	18	50.0	65	83.3	99	97.1	<0.0001

Table 6.1 Patient demographics, medical history and management by ethnic group, across the three studies.

Pacific	**1981-1982 (n=32)**		**1991-1992 (n=111)**		**2002-2003 (n=197)**		**Test for trend**
	n	**%**	**n**	**%**	**n**	**%**	**P value***
Born in New Zealand	0	0.0	2	1.8	4	2.1	0.4782
Demographics							
Male	22	68.8	67	60.4	88	44.7	0.0011
Age, mean (±SD)	55.8	(9.0)	59.7	(15.0)	64.5	(13.6)	0.0007†
Married/partnered	18	56.3	68	61.3	103	52.3	0.2700
Social class, high (1-3)	6	21.4	34	34.0	47	36.4	0.1840
Medical history							
High blood pressure	22	68.8	49	45.0	124	65.6	0.1208
Myocardial infarction	2	6.3	3	2.7	15	7.9	0.2353
Stroke	2	6.3	25	22.5	54	27.4	0.0146
Diabetes mellitus	12	46.2	16	15.1	69	36.1	0.1584
Current smoker	12	37.5	31	28.7	23	13.1	<0.0001
BMI, mean (±SD)	30.2	(5.5)	29.1	(7.3)	30.8	(7.7)	0.3698†
Management							
Admission to hospital	26	81.3	87	78.4	189	95.9	<0.0001
Neuroimaging, CT/MRI	6	42.9	74	77.9	180	91.4	<0.0001
Asian & Other	**1981-1982 (n=20)**		**1991-1992 (n=36)**		**2002-2003 (n=162)**		
	n	**%**	**n**	**%**	**n**	**%**	
Born in New Zealand	4	20.0	0	0.0	4	2.6	0.0043
Demographics							
Male	4	20.0	18	50.0	87	53.7	0.0112
Age, mean (±SD)	72.9	(12.2)	65.6	(13.2)	65.9	(13.9)	0.3516†
Married/partnered	8	40.0	24	66.7	110	67.9	0.0400
Social class, high (1-3)	6	37.5	18	64.3	74	64.9	0.0739
Medical history							
High blood pressure	8	40.0	18	50.0	88	58.7	0.0839
Myocardial infarction	0	0.0	3	8.3	17	11.0	0.1248
Stroke	0	0.0	7	19.4	36	22.2	0.0205
Diabetes mellitus	4	20.0	8	22.9	40	26.1	0.4983
Current smoker	0	0.0	9	25.0	15	10.3	0.9803
BMI, mean (±SD)	22.9	(2.7)	22.5	(4.5)	25.6	(6.9)	0.0271†
Management							
Admission to hospital	14	70.0	28	77.8	157	97.5	<0.0001
Neuroimaging, CT/MRI	4	40.0	18	64.3	153	95.0	<0.0001

*p-value calculated using Cochran-Armitage trend test

†p-value calculated using ANOVA

Although, the proportion of current smokers declined in all ethnic groups, the proportional frequency remained high in Māori, as compared to the prevalence of smoking in the general New Zealand adult population (25%).[432] Rates of diabetes and BMI increased across all ethnic groups, with the highest rates continuing in Māori and Pacific populations. The proportions of patients with a history of high blood pressure or previous heart disease were generally stable over time, with the exception of NZ/Europeans where the number reporting a history of high blood pressure increased across the study period. There were declines in the proportion of patients with a history of stroke in Māori populations, with increases in Pacific and Asian & Other populations, which may reflect disparities in secondary prevention methods.

Significant changes in the patterns of stroke management were also evident among ethnic groups. Table 6.1 shows that the proportion of patients managed in hospital increased dramatically across the three studies, for all ethnic groups, with NZ/Europeans having the lowest and Māori the highest hospital admission rates, in each of the three studies. This may reflect the higher rates of pre-stroke institutionalisation in the NZ/European group. The proportion of patients receiving some form of neuroimaging (CT or MRI) also increased for all ethnic groups, from 19% in NZ/European (in 1981-1982) to 97% in Māori (2002-2003), reflecting increasing hospitalisation rates and the introduction of neuroimaging technology in all major hospitals in the region.

6.2. Trends in Attack Rates

Overall event and incidence rates of stroke were calculated by age group (15-64, 65-74, 75-84 and 85 years or older) and ethnicity. Table 6.2 presents crude incidence rates by age and ethnicity for the three studies. Crude event rates by age and ethnicity are presented in Appendix 7. Incidence rates generally increased with increasing age across the studies, for all ethnic groups. However, there were small numbers of patients in the older ethnic minority age groups in the earlier studies, producing wide confidence intervals, so the results should be interpreted with caution. As shown in the overall rates of stroke (Chapter 5), rates in males were generally higher than

females, at most ages and across all ethnic groups. In general, crude incidence rates were highest in NZ/European compared to other ethnic groups, which is counterintuitive since age-standardised rates are higher in ethnic minority groups. This is due to the fact that there are higher rates of stroke in the older age groups in NZ/European, which have less weighting when standardised to an external population.

There was an increase in crude rates from 1981-1982 to 1991-1992 in NZ/European stroke patients, which then declined to 2002-2003, reflecting the non-linear trend shown in Chapter 5. This is due to increases in the 65-74 age group in NZ/European and in the number of patients aged 75. There was an overall decline in crude incidence rates in NZ/Europeans, with an annual decline of 0.2%. Crude rates in Māori increased over the study period, with a change of 1.3% per annum. Whereas, rates in Pacific populations increased dramatically between 1981-1982 and 2002-2003, with an annual increase of 3%. Rates in the Asian & Other ethnic group were varied, with declines from 1981-1982 to 1991-1992, then increases to 2002-2003.

To compare rates between ethnic groups and over time changes in the age structure of the populations need to be controlled for. Therefore, the results are presented using two different methods of standardisation to enable comparisons of trends within ethnic groups over time and also between ethnic groups. Indirect standardisation of ethnic specific rates was used to adjust for the age and sex structure of the 2001 Auckland population within each ethnic group, to investigate trends in the rate of stroke within the NZ/European, Māori, Pacific, and Asian & Other ethnic groups. Whereas, direct age-standardisation, using the WHO World population[410] as the external reference population, was used to investigate disparities between ethnic groups and to enable comparisons with other published data.

Table 6.2 Age-specific crude first-ever (incident) stroke rates by ethnicity (per 100,000 population) in Auckland, New Zealand, 1981-2003.

	1981-1982				1991-1992				2002-2003			
Age group	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**
NZ/European												
15-64	422202	224	53	(43-63)	459267	233	51	(42-59)	501426	222	44	(38-50)
65-74	47481	238	501	(411-591)	52125	341	654	(552-756)	48633	219	450	(391-510)
75-84	22209	342	1540	(1309-1771)	30303	387	1277	(1114-1441)	34332	378	1101	(990-1212)
85+	5577	130	2331	(1764-2898)	8253	167	2024	(1675-2372)	11790	233	1976	(1723-2230)
Total	497469	934	188	(171-205)	549948	1128	205	(189-221)	596181	1052	176	(166-187)
Māori												
15-64	52179	36	69	(37-101)	63762	48	75	(49-101)	77742	53	68	(50-87)
65-74	1266	6	474	(-62-1010)	1344	3	223	(-29-476)	2292	22	960	(559-1361)
75-84	336	4	1190	(-459-2840)	429	8	1865	(573-3157)	654	10	1529	(581-2477)
85+	51	0	0	(0-0)	72	2	2778	(-1072-6628)	144	4	2778	(56-5500)
Total	53832	46	85	(51-120)	65607	61	93	(65-121)	80832	89	110	(87-133)

Table 6.2 Age-specific crude rates by ethnicity per 100,000 population of first-ever (incident) stroke events in Auckland, New Zealand, 1981-2003

	1981-1982				1991-1992				2002-2003			
Age group	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**
Pacific												
15-64	33672	20	59	(23-96)	64506	51	79	(55-103)	89724	66	74	(56-91)
65-74	741	10	1350	(167-2532)	2025	21	1037	(481-1593)	3840	47	1224	(874-1574)
75-84	213	0	0	(0-0)	597	12	2010	(402-3618)	1392	24	1724	(1034-2414)
85+	33	0	0	(0-0)	108	2	1852	(-715-4418)	246	3	1220	(-161-2599)
Total	34659	30	87	(43-130)	67236	86	128	(96-160)	95202	140	147	(123-171)
Asian & Other												
15-64	10059	6	60	(-8-127)	37293	15	40	(13-68)	119214	50	42	(30-54)
65-74	324	6	1852	(-244-3947)	894	8	895	(-86-1875)	4689	42	896	(625-1167)
75-84	207	4	1932	(-746-4611)	372	5	1344	(166-2522)	1437	21	1461	(836-2086)
85+	30	4	13333	(-5146-31812)	108	2	1852	(-715-4418)	327	7	2141	(555-3727)
Total	10620	20	188	(72-305)	38667	30	78	(40-115)	125667	120	95	(78-1123)

Table 6.3 and Figure 6.1 present trends in ethnic-specific indirect standardised rates and the corresponding inverse of the standardised event ratios (SERs), adjusting the 1981-1982 and 1991-1992 rates to the age, sex and ethnic structure of the 2001 census population. Rates declined by 19% among NZ/Europeans (incidence SER 0.81, 95% CI, 0.74 to 0.89; event SER 0.81 95% CI, 0.76 to 0.88) between 1981-1982 and 2002-2003. Most of this decline occurred between the 1991-1992 and 2002-2003 studies (incidence SER 0.83, 95% CI, 0.77 to 0.90; event SER 0.84, 95% CI, 0.78 to 0.89), mirroring the trends in overall rates shown in Chapter 5. However, as in the crude rates, increasing trends were found in the Pacific populations, with trends in event rates increasing a remarkable 66% (event SER 1.66, 95% CI, 1.11 to 3.25), over the study period from 1981-1982 to 2002-2003. This change was not significant in incidence rates, or between 1991-1992 to 2002-2003, indicating that this large increase in rates took place in the first decade of the three studies and in overall event rates. Non-significant trends towards increasing rates were also found in Māori and declining rates in Asian & Other ethnic groups, however, the numbers of patients in these groups were small reflected in the extremely wide confidence intervals. As shown in the crude rates the indirect standardised rates were highest in NZ/European patients, reflecting the older ethnic specific age structure of this population.

Table 6.3 Annual stroke attack rates (per 100,000) by ethnicity, indirect standardised to the Auckland 2001 population, adjusting for age, sex and ethnicity, in Auckland, New Zealand, 1981-2003.

	1981-1982			1991-1992			2002-2003			Standardised Event Ratio*			
	n	Rate	(95% CI)	n	Rate	(95% CI)	n	Rate	(95% CI)	2002-03:1981-82		2002-03:1991-92	
NZ/European													
Incidence	934	218	(198-238)	1128	213	(197-229)	1052	176	(166-187)	0.81	(0.74-0.89)	0.83	(0.77-0.90)
Event	1292	306	(282-329)	1572	298	(278-318)	1485	249	(237-262)	0.81	(0.76-0.88)	0.84	(0.78-0.89)
Māori													
Incidence	46	93	(55-131)	61	103	(73-134)	89	110	(89-136)	1.18	(0.84-2.00)	1.06	(0.82-1.51)
Event	62	127	(82-171)	82	140	(105-174)	104	129	(106-156)	1.02	(0.75-1.57)	0.92	(0.74-1.22)
Pacific													
Incidence	30	116	(57-175)	86	151	(113-189)	140	147	(125-173)	1.26	(0.84-2.56)	0.97	(0.78-1.30)
Event	32	128	(65-191)	113	202	(157-246)	202	212	(185-244)	1.66	(1.11-3.25)	1.05	(0.86-1.35)
Asian & Other													
Incidence	20	177	(67-287)	30	91	(47-135)	120	95	(80-114)	0.54	(0.33-1.42)	1.05	(0.71-2.01)
Event	20	173	(66-280)	36	110	(63-156)	163	130	(111-151)	0.75	(0.46-1.97)	1.18	(0.83-2.05)

* 1/SER – inverse of the standardised event ratio

n=number of stroke patients, CI=confidence interval

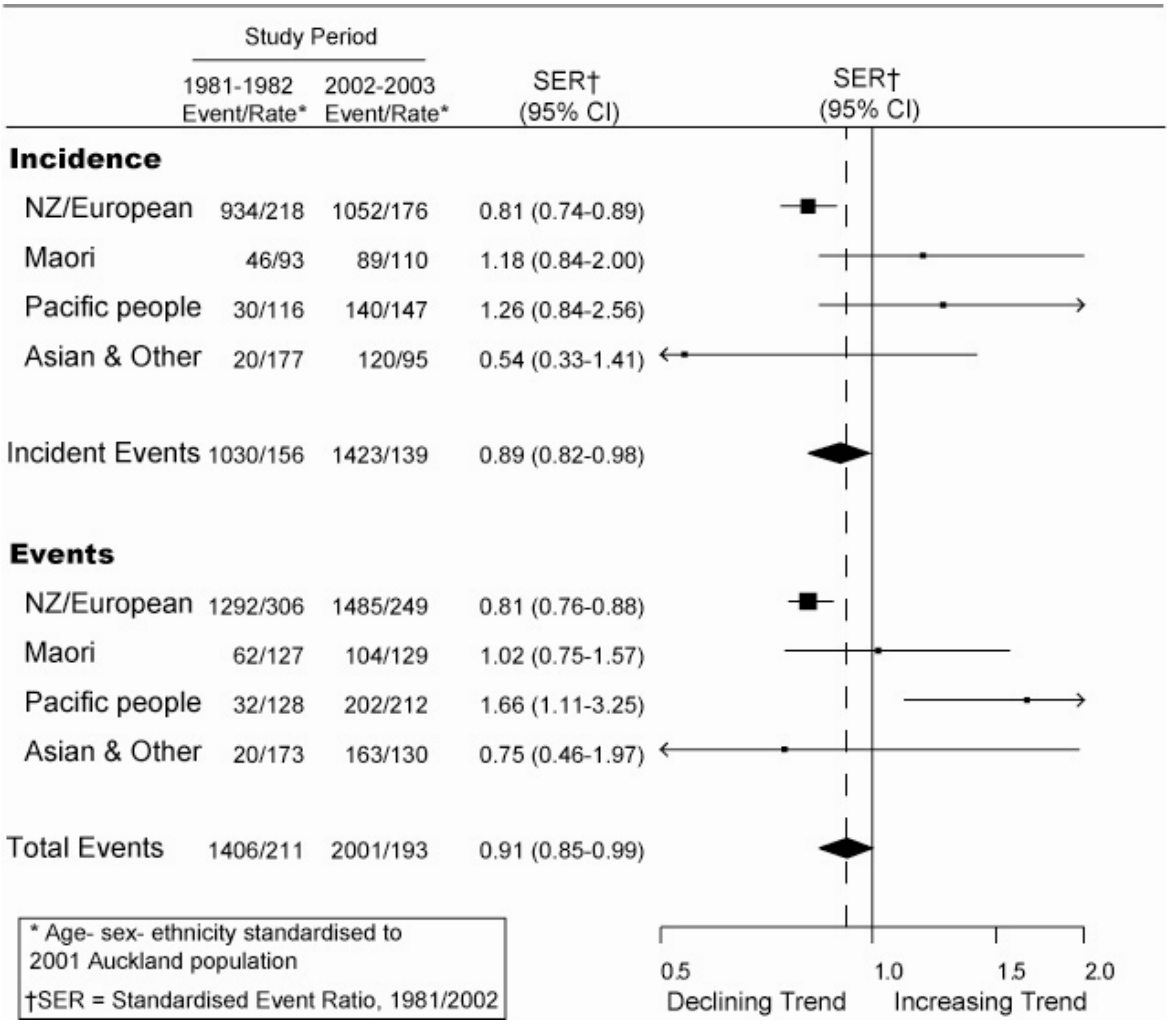


*Figure 6.1 Ethnic-specific stroke incidence and attack rates, and event ratios (SER). *Rates were age-, sex- and ethnicity- indirect standardised to the 2001 Auckland population and shown with 95% CI.*

Table 6.4 and Figure 6.2 present trends in direct age-standardised stroke rates for the ethnic groups. Trends in direct standardised rates mirror those found using indirect standardisation with non-linear declines in NZ/Europeans and increasing rates for both Māori and Pacific peoples. However, direct standardised event rates in Pacific patients increased over 100% (event RR 2.16, 95%CI 1.18 to 3.96) across the study periods. Rates in Pacific patients were the lowest in the 1981-1982 study, between the ethnic groups, growing to the highest in the 2002-2003 study. There were however, small numbers of patients in the 1981-1982 study reflecting the small population living in the Auckland region at that time. Direct standardised rates were typically higher in Māori and Pacific ethnic groups than NZ/Europeans and also compared to the crude and indirect standardised rates, which is due to the younger age structure of the WHO world population. As Māori and Pacific people have their strokes on average 10 years younger than NZ/European more weight is placed on the strokes at younger ages. In the 2002-2003 study, there were highly significant differences between all ethnic minority groups and NZ/European patients, with no overlap between confidence intervals (discussed further in Section 6.3).

Table 6.4 Annual stroke attack rates (per 100,000) by ethnicity, direct age-standardised to the WHO world population, in Auckland, New Zealand, 1981-2003.

	1981-1982			1991-1992			2002-2003			Rate Ratio			
	n	Rate	(95% CI)	n	Rate	(95% CI)	n	Rate	(95% CI)	2002-03:1981-82		2002-03:1991-92	
NZ/European													
Incidence	934	153	(139-167)	1128	150	(139-163)	1052	124	(116-132)	0.81	(0.69-0.95)	0.83	(0.71-0.96)
Event	1292	209	(193-226)	1571	206	(193-220)	1485	171	(162-180)	0.82	(0.71-0.94)	0.83	(0.72-0.95)
Māori													
Incidence	46	134	(78-229)	61	168	(116-241)	89	202	(157-259)	1.51	(0.83-2.73)	1.20	(0.77-1.87)
Event	62	192	(122-304)	82	254	(188-341)	104	247	(196-312)	1.28	(0.77-2.15)	0.97	(0.67-1.42)
Pacific													
Incidence	30	147	(80-270)	86	225	(163-310)	140	218	(183-261)	1.48	(0.79-2.78)	0.97	(0.67-1.40)
Event	32	153	(85-274)	113	291	(220-385)	202	329	(284-382)	2.16	(1.18-3.96)	1.13	(0.82-1.55)
Asian & Other													
Incidence	20	360	(185-702)	30	158	(92-271)	120	166	(137-203)	0.46	(0.23-0.93)	1.05	(0.59-1.86)
Event	20	360	(185-702)	36	194	(122-310)	163	234	(197-277)	0.65	(0.33-1.29)	1.20	(0.73-1.98)

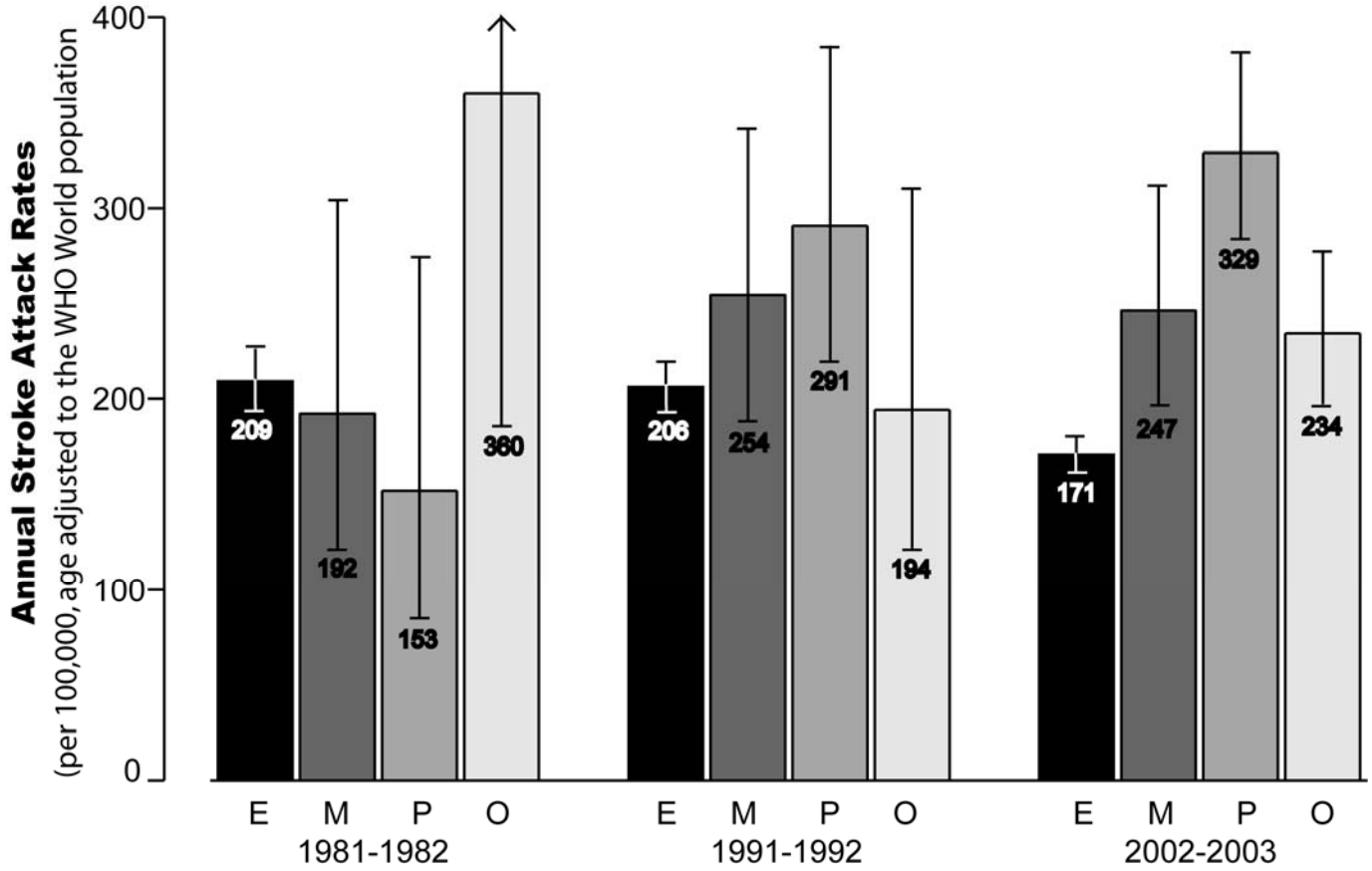


Figure 6.2 Trends in ethnic-specific stroke event rates, by period of ARCOS study. Rates were direct age-standardised to the WHO World population and shown with 95% CI.

The disparities in rates between the ethnic groups grew over time. Table 6.5 presents the ratio of direct standardised rates for the ethnic minority groups in comparison to the NZ/European population. This ratio increased over time as rates diverged, with declines in NZ/European populations and increasing rates in Māori and Pacific populations across the three studies. The difference between the NZ/European population and all ethnic minority groups were highly significant in the 2002-2003 study. The disparity was highest between Pacific and NZ/European event rates, with the ratio of rates in the Pacific group almost double that in NZ/European (1.93, 95%CI 1.65-2.26) in 2002-2003.

Table 6.5 The ratio of direct age-standardised rates (to the WHO World population) of ethnic minority groups compared to NZ/European, by study period.

	1981-1982		1991-1992		2002-2003	
	Ratio	**(95% CI)**	**Ratio**	**(95% CI)**	**Ratio**	**(95% CI)**
Incidence Rates						
Māori v NZ/E*	0.87	(0.51-1.51)	1.12	(0.77-1.62)	1.63	(1.26-2.11)
Pacific v NZ/E	0.96	(0.52-1.78)	1.50	(1.07-2.09)	1.76	(1.46-2.13)
Asian & Other v NZ/E	2.36	(1.20-4.62)	1.05	(0.61-1.82)	1.34	(1.09-1.65)
Event Rates						
Māori v NZ/E	0.92	(0.58-1.46)	1.23	(0.91-1.67)	1.45	(1.14-1.84)
Pacific v NZ/E	0.73	(0.40-1.32)	1.41	(1.06-1.88)	1.93	(1.65-2.26)
Asian & Other v NZ/E	1.72	(0.88-3.37)	0.94	(0.59-1.51)	1.37	(1.15-1.63)

* NZ/E – NZ/European

CI = confidence interval

6.3. Ethnic Disparities in Stroke Subtypes in 2002-2003

There is limited population-based data on ethnic disparities in the incidence of major pathological stroke types and ischaemic stroke subtypes. Unfortunately due to small numbers in ethnic minority groups and low rates of neuroimaging, temporal trends in stroke subtypes could not be investigated in this study. However, ethnic disparities in the pathological and ischaemic stroke subtypes could be explored within the most recent ARCOS study conducted in 2002-2003, as there were high rates of imaging and subtype classification of stroke. The Māori and Pacific ethnic groups were combined in this analysis, due to small numbers of patients per subgroup. A total of 1423 incident stroke patients were included in this analysis: 667 men (47%; mean age 68.7 years, standard deviation [SD] 13.7); and 756 women (mean age 74.6 years [SD 14.3]); 1052 (75%) NZ/European; 229 (16%) Māori & Pacific; and 120 (9%) Asian & Other ethnic groups. There were 22 incident stroke patients with missing ethnicity information. CT or MRI brain scans were typically conducted within the first week of stroke onset, with 1296 (91%) of the 1423 patients providing reliable diagnostic classification of stroke subtypes.

Significantly more Māori & Pacific (97%) and Asian & Other (98%) incident stroke patients were admitted to hospital for their stroke than NZ/European (92%). Of those patients admitted to hospital ethnic minority groups had longer lengths of stay in hospital than NZ/Europeans (Māori & Pacific [mean 10.7 days, SD 10.5]; Asian & Other [mean 11.1, SD 9.7]; NZ/European [mean 8.6, SD 8.7]). However, the frequency of investigations (CT, MRI, angiography, echocardiography, carotid artery ultrasound) did not differ significantly between the ethnic groups.

Table 6.6 Frequency of first-ever pathological stroke type and ischaemic stroke subtype, overall and by ethnic group, for the 2002-2003 ARCOS study.

	Overall		NZ/European		Māori & Pacific		Asian & Other		Chi-sq
	n	%	n	%	n	%	n	%	p-value*
Pathological type									
Ischaemic	1032	72.5	770	73.2	165	72.1	84	70.0	0.7341
PICH	177	12.4	111	10.6	39	17.0	26	21.7	0.0002
SAH	87	6.1	62	5.9	17	7.4	6	5.0	0.5961
Undetermined	127	8.9	109	10.4	8	3.5	4	3.3	0.0003
Ischaemic Subtype									
Atherothrombotic	59	5.7	49	6.4	7	4.2	2	2.4	0.2222
Cardioembolic	303	29.4	224	29.1	60	36.4	15	17.9	0.0096
Lacunar	116	11.2	85	11.0	16	9.7	13	15.5	0.3789
Other ischaemic	30	2.9	21	2.7	6	3.6	3	3.6	0.7714
Undetermined	524	50.8	391	50.8	76	46.1	51	60.7	0.0913

* Chi-square p-value for a difference between ethnic groups

n=number of stroke patients, PICH = Primary Intracerebral Haemorrhage, SAH = Subarachnoid Haemorrhage

6.3.1. Pathological types of stroke

Pathological type of stroke was documented by CT/MRI/autopsy or lumbar puncture (for SAH only) findings in 1296 patients. Table 6.6 shows that Ischaemic stroke occurred in 1032 patients (73%), PICH in 177 (12%), SAH in 87 (6%), and subtype was undetermined in 127 (9%). There was no difference in the proportion of ischaemic strokes between the ethnic groups, with over 70% in all groups. However, the proportions of PICH were significantly higher in ethnic minority groups compared to NZ/European, especially in the Asian & Other populations.

Table 6.7 presents crude and direct age-standardised rates of pathological type of stroke by ethnic group. Age-standardised rates for the Māori & Pacific and Asian & Other ethnic groups were inflated compared to the crude rates, due to the younger age structures of these populations. Figure 6.3 (top) shows RRs of age-standardised rates for stroke subtypes in the ethnic groups, using the NZ/European population as the reference group. Māori & Pacific and Asian & Other ethnic groups had higher rates of ischaemic stroke than NZ/European (Māori & Pacific RR 1.7; 95% CI 1.4 to 2.0; Asian & Other RR 1.3; 95% CI 1.0 to 1.7) as well as higher rates of PICH (Māori & Pacific RR 2.7; 95% CI 1.8 to 4.0; Asian & Other RR 2.3; 95% CI 1.4 to 3.7). There were no differences in the rates of SAH and undetermined stroke type between the ethnic minority groups and NZ/European. There were also no substantial differences in the rates of any stroke pathological type between the Māori & Pacific and Asian & Other ethnic groups.

Table 6.7 Stroke incidence rates (per 100,000) by pathological stroke type, overall and by ethnic group, in Auckland, New Zealand in 2002-2003.

	Ischaemic			PICH			SAH			Undetermined		
Ethnicity	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**
Overall												
Crude	1032	115	(108-122)	177	20	(17-23)	87	10	(8-12)	127	14	(12-17)
Standardised*		102	(96-108)		18	(15-21)		9	(8-12)		10	(9-12)
NZ/European												
Crude	770	129	(120-139)	111	19	(16-22)	62	10	(8-13)	109	18	(15-22)
Standardised*		92	(85-99)		13	(11-16)		10	(7-12)		10	(8-12)
Māori & Pacific												
Crude	165	94	(81-109)	39	22	(16-30)	17	10	(6-16)	8	5	(2-9)
Standardised*		155	(131-184)		35	(25-50)		10	(6-16)		12	(6-25)
Asian & Other												
Crude	84	67	(54-83)	26	21	(14-31)	6	5	(2-11)	4	3	(1-8)
Standardised*		122	(96-154)		30	(20-46)		6	(3-14)		9	(3-24)

n=number of stroke patients, CI = confidence interval

PICH = primary intracerebral haemorrhage, SAH = subarachnoid haemorrhage

*Age-standardised to the WHO world population

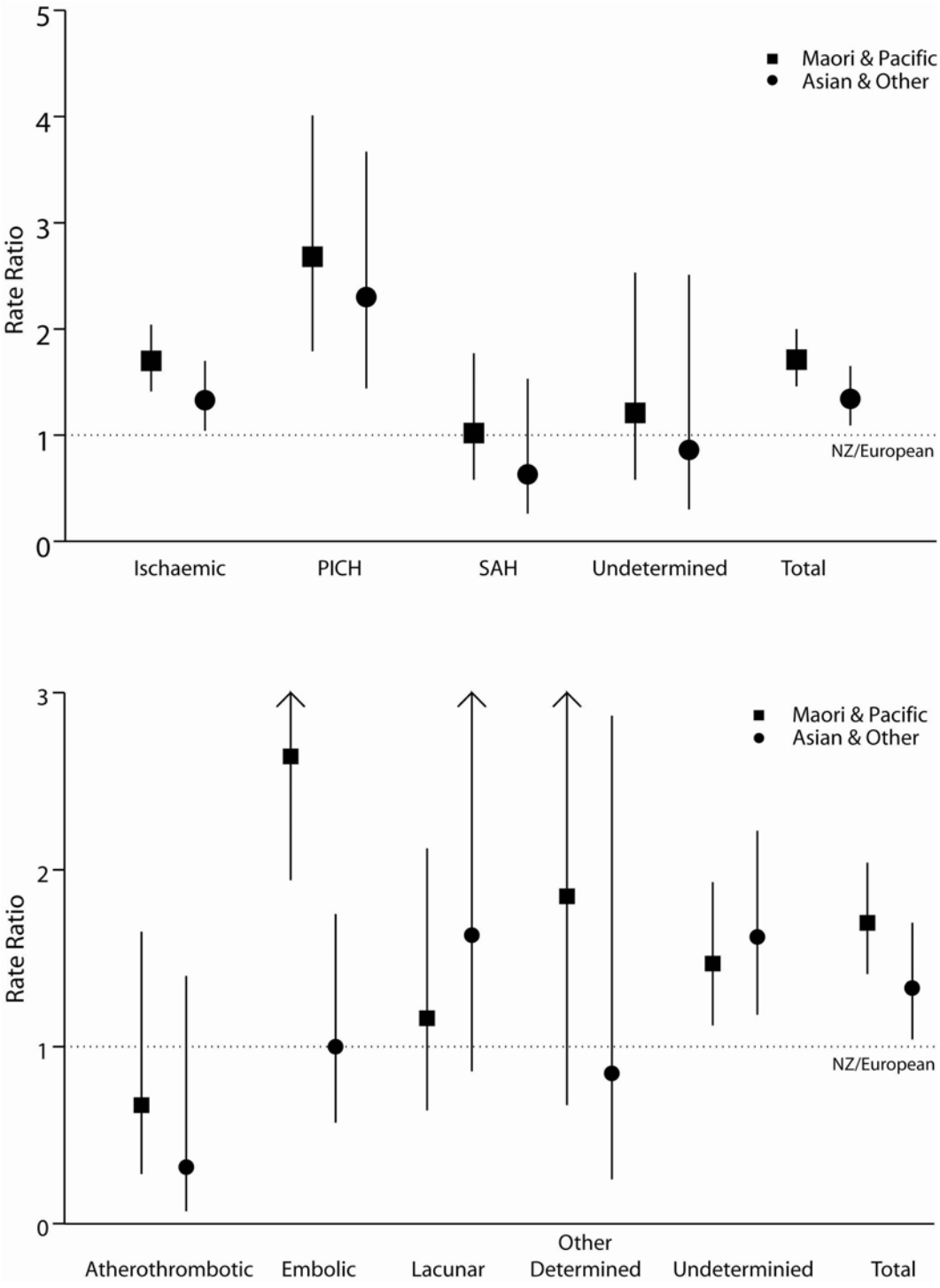


Figure 6.3 Rate ratios (RR) of age-standardised incidence rates of pathological stroke types (top) and ischaemic stroke subtypes (bottom) by ethnicity in Auckland, New Zealand 2002-2003.

6.3.2. Ischaemic stroke subtypes

Ninety-eight percent of ischaemic stroke patients were managed in hospital, and for determination of aetiological subtypes of ischaemic stroke, the following investigations were carried out: electrocardiography in 98% of patients, echocardiography in 13% (including transoesophageal echocardiography in 2%), carotid artery ultrasound examination in 13%, and MR angiography in 4%. The frequency of these investigations did not differ significantly between the ethnic groups. Of the 1032 patients with ischaemic stroke, 59 (6%) were atherothrombotic; 303 (29%) embolic, 116 (11%) lacunar; 30 (3%) were caused by other determined causes; and in 524 (51%) the exact cause of the ischaemic stroke remained unknown (or were of potential mixed aetiologies). There were high proportions of undetermined ischaemic stroke subtype, indicating that although an ischaemic stroke occurred, it could not be attributed to a single factor.

Table 6.6 presents the proportions of atherothrombotic, cardioembolic, lacunar, other determined cause or unknown aetiology of ischaemic stroke, by ethnic group. No substantial ethnic differences were found in the risk of atherothrombotic stroke and ischaemic stroke due to other determined causes. However, Māori & Pacific populations were particularly prone to cardioembolic strokes, with significantly higher prevalence than NZ/European and Asian & Other ethnic groups. Whereas, the risk of lacunar stroke was highest, though not statistically significantly, in the Asian & Other ethnic group. Table 6.7 and Figure 6.3 (bottom) show the age-standardised rates and RRs of ischaemic stroke subtypes by ethnicity. Compared to NZ/Europeans, Māori & Pacific patients had 116% higher risk of cardioembolic stroke (RR 2.6, 95% CI 1.9 to 3.6). Both Māori & Pacific and Asian & Other ethnic groups had significantly higher risk of ischaemic stroke due to undetermined causes compared to NZ/European, (Māori & Pacific RR 1.7, 95% CI 1.41 to 2.04; Asian & Other RR 1.33, 95% CI 1.04 to 1.70).

Table 6.8 Incidence rates for ischaemic stroke subtypes by ethnic group (per 100,000), in Auckland, New Zealand 2002-2003.

	Atherothrombotic			Embolic			Lacunar			Other			Undetermined		
Ethnicity	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**	**n**	**Rate**	**(95%CI)**
Overall															
Crude	59	7	(5-9)	303	34	(30-38)	116	13	(11-16)	30	3	(2-5)	524	58	(54-64)
Standardised*		6	(5-8)		29	(26-32)		12	(10-14)		3	(2-4)		52	(48-57)
NZ/European															
Crude	49	8	(6-11)	224	38	(33-43)	85	14	(12-18)	21	4	(2-5)	391	66	(59-72)
Standardised*		7	(5-10)		25	(21-28)		11	(9-13)		3	(2-4)		47	(42-52)
Māori & Pacific															
Crude	7	4	(2-8)	60	34	(27-44)	16	9	(6-15)	6	3	(2-8)	76	43	(35-54)
Standardised*		5	(2-11)		65	(49-85)		12	(7-22)		5	(2-12)		68	(53-88)
Asian & Other															
Crude	2	2	(0-6)	15	12	(7-20)	13	10	(6-18)	3	2	(1-7)	51	41	(31-53)
Standardised*		2	(1-10)		25	(14-42)		17	(10-32)		2	(1-7)		76	(56-102)

n=number of stroke patients, CI = confidence interval

*Age-standardised to the WHO world population

6.3.3. Comparison to Other Population-Based Studies

These results, from the most recent ARCOS study were compared to other population-based studies with a large ethnic minority population, which loosely fit the criteria for an 'ideal' stroke incidence study. To date there were only three comparable published population-based stroke incidence studies that have investigated ethnic disparities in a defined population. Two studies from the US, the Northern Manhattan Stroke (NOMAS) study and the Greater Cincinnati/Northern Kentucky Stroke (GCNKS) study, and one study from the United Kingdom, the South London Stroke Register (SLSR). The NOMAS study is unique in that it has a large Hispanic population and allows investigations into disparities in the three major ethnic groups in the US, whites (22%), African Americans (13%) and Hispanics (64%). The NOMAS study is an ongoing register of all strokes occurring in Northern Manhattan from 1993-1997, checking all hospitals, community centres, rest homes and deaths in the region.[59, 73, 433, 434] The GCNKS study was designed to investigate the differences in stroke incidence rates and case fatality in the biracial population of the greater Cincinnati metropolitan area which has a large African American population (29%).[42, 43, 167, 435, 436] Hospital discharge lists from 19 hospitals in the study region for any diagnosis of stroke (or similar), as well as coroners reports and death certificates were screened retrospectively and non-hospitalised non-fatal cases of stroke were identified through monitoring hospital emergency departments, private hospitals, public health clinics and sampling 6% of family physicians and 15% of nursing homes. A pilot phase of the GCNKS study collected information on all hospitalised and autopsied strokes in African Americans for six months before the main phase from 1 July 1993 to 30 June 1994.[42] The SLSR is a continuing register of all strokes in southern London using prospective data collection to collect cases from five hospitals, all GPs and community therapists within and around the study region, as well as from death certificates.[16, 93, 168, 437] Over the first two years of study, from 1995 to 1996, the SLSR registered 489 white (80%), 102 black (of which the majority were African-Caribbean) (17%), and 21 from other ethnic groups (3%).[168]

Information and data was extracted from published data for the three studies, and where possible incidence rates were recalculated using the age groups <25, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+ years and re-standardised using the age structure of the WHO world population.[410] The relative ratio of standardised rates for minority groups (African Caribbean and Other ethnicity in SLSR, African American and Hispanic in NOMAS, African American in GCNKS, and Māori and Pacific in ARCOS) compared to the majority, white or European populations were calculated to examine disparities between ethnic groups in the three studies compared to the ARCOS 2002-2003 study. This method removes the effect of the magnitude of the rates caused by different methods of standardisation. The prevalence of a number of vascular risk factors by ethnic groups was also extracted from published data.

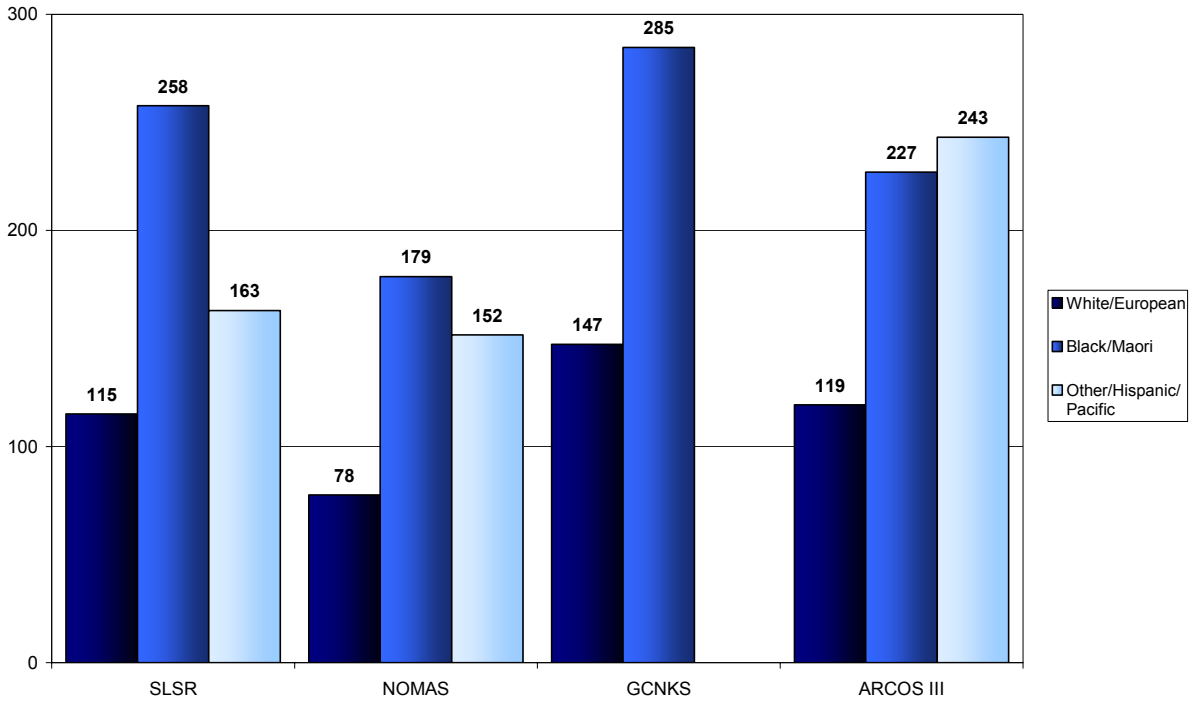


Figure 6.4 Ethnic disparities in age-standardised incidence rates of stroke, per 100,000 (standardised to the WHO world population) in four population-based stroke incidence studies.

Figure 6.4 shows the ethnic specific age-standardised incidence rates for the four studies. Minority groups, in all studies, had the highest rates of incident stroke, with the highest rates overall in the Cincinnati and Kentucky region. Rates in Hispanics in the NOMAS study were slightly less than in the African American group and, as shown previously, the standardised rates in Māori and Pacific population in Auckland were similar, but were higher than the NZ/European group. The high rates of stroke in African Americans in the GCNKS study could be an artefact of the published data, as the published incidence rates for this study were also adjusted for the sex distribution in the population, and the over-sampling of African Americans may have over-inflated the rates. Overall, the rates in the NOMAS study were lower compared to the other studies as they were originally standardised by age, sex and ethnicity and the age structure of the NOMAS study was slightly older than the other studies leading to a deflation of standardised rates. The standardised rates presented here were similar to the rates presented in the published papers of these studies. However, the rates in the GCNKS and ARCOS studies were slightly over-inflated compared to published results due to the different age-groups used for standardisation.

Figure 6.5 shows that stroke incidence rates in ethnic minority groups were approximately double that of the white/European ethnic group, across all four studies. The ratio between white and other ethnic groups in South London was much lower compared to the other studies, which may be due to small numbers in this ethnic group. Ethnic minority groups also had higher rates of ischaemic stroke and PICH than white/European populations, with around double the rate of stroke across the four studies. No differences between the ethnic groups in SAH were found, which may have been due to small numbers of this subtype across all ethnic groups. The NOMAS study reported that African Americans and Hispanics had 1.5 to 5 times higher rates of most ischaemic stroke subtypes compared with white Americans, who had a significantly greater proportion of cardioembolic stroke than Hispanics and African Americans.[434] Whereas, the GCNKS study found a trend towards more cardioembolic strokes in African Americans, which is in line with the findings from the current ARCOS study.[167, 436]

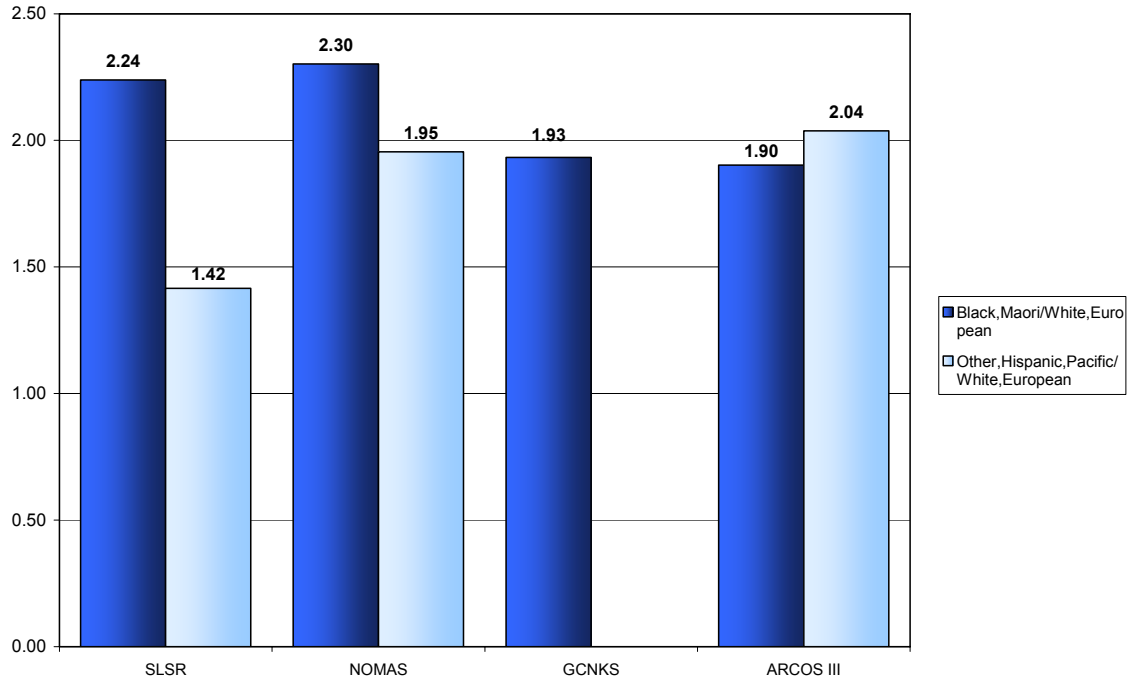


Figure 6.5 Ratio of age-standardised stroke incidence rates in ethnic minority groups (Black, Māori, Other, Hispanic, Pacific) compared to the majority white/European population, in four population-based stroke incidence studies.

The disparities in stroke subtypes between ethnic groups may be due to different risk factor profiles between ethnic groups. The distribution of vascular risk factors, hypertension, ischaemic heart disease, AF, diabetes and smoking were varied within the ethnic groups for the four studies. Higher rates of hypertension and diabetes were found in ethnic minority groups compared to white or European populations, which may be related to the higher rates of PICH in the ethnic minority groups. Higher rates of heart disease or AF in the white/European groups were typically found in the four studies. However, no large differences were found in the prevalence of major risk factors in the GCNKS study.[167] The results for smoking were varied across the four studies with higher rates of smoking in whites in South London, African Americans in Cincinnati and Māori smoking more in New Zealand.

6.4. Discussion

The current analysis has shown encouraging declines in both stroke event and incidence rates, as well as in some associated risk exposures, among NZ/Europeans in Auckland over 20 years. However, the doubling in event rates in Pacific peoples and ongoing high stroke rates in Māori, together with high frequencies of diabetes and obesity, indicate ongoing and increasing ethnic disparities in the burden of stroke in the Auckland population. Trends in the rates of disease provide feedback in relation to recent primary and secondary stroke prevention strategies on a background of structural and lifestyle changes. Therefore, these complex and divergent trends in ethnic-specific rates and exposures provide mixed views regarding the future burden of stroke, both locally and regionally.

The declines in rates among NZ/Europeans are consistent with trends found in the more homogeneous but older populations of Australia and Europe.[38, 317, 438] These results are also consistent with estimates of a decline in stroke incidence shown in the systematic review of trends in the incidence of stroke in ideal studies (Chapter 3). The previously recognised higher,[13] and now noted to be increasing rates among Māori and Pacific populations in Auckland supports published data of ethnic disparities in stroke risk.[42, 59, 168, 435] The near doubling of stroke rates in Māori and Pacific populations have lead to increased disparities between these groups and the NZ/European population, mirroring ethnic disparities shown in the US[42, 59] and the UK.[93, 168]

The increasing rates of stroke in Māori and Pacific populations are contrary to trends in national stroke deaths in New Zealand from 1980 to 1999, where declining rates of stroke mortality across all ethnic groups were found.[12, 40] However, diverging trends in ethnic specific mortality rates have also been shown in New Zealand, as mortality rates in NZ/European and other ethnic groups declined at a much steeper rate than rates in Māori and Pacific populations.[12, 40] These discrepancies highlight how trends in mortality data disguise trends in the event rate of the disease as it only focuses on one part of the disease, death.

The significant increase in stroke event rates as compared to the non-significant increase in incidence rates in Pacific populations, coupled with increasing proportions of Pacific stroke patients with a history of stroke suggests that secondary prevention of stroke is not working for this population. This may be due to worse follow up care after stroke as Pacific populations are least likely of any ethnic group to access primary health care, which may be reflected to lower socioeconomic status of Pacific populations.[439, 440] It is possible that the increase in the proportion of Pacific patients with a history of stroke is a result of the phenomenon called medical tourism, where patients seek healthcare in more developed countries. However, the strict eligibility criteria of residency should have controlled for this. It has been shown that Pacific populations in New Zealand are least likely to receive education about diabetes.[441, 442] A number of health plans have been developed by the Ministry of Health aimed at reducing disparities in health and access to health care, through providing more culturally appropriate care and services.[153, 439, 443]

A number of explanations for the changes in rates within ethnic groups can be made through associations with changes in the demographic characteristics of patients, or changes within the New Zealand population. Declines in rates of stroke in NZ/European populations mirror improvements in the treatment of hypertension in New Zealand and declines in blood pressure levels.[422, 423, 444, 445] This is also reflected in the increased proportions of NZ/European patients reporting a history of high blood pressure. However, it has been shown that trends in blood pressure control in high risk individuals explains only a small fraction of the trends in stroke rates.[355, 365] As previously mentioned, the uniform declines seen in the proportion of current smokers across ethnic groups has been shown in other populations[422, 444] and may be attributed to success from anti-smoking campaigns implemented in the mid-1980s in New Zealand.[425] However, the declines in the rates of smoking were less apparent in Māori populations, where the proportion remained disproportionately high in comparison to other ethnic groups and the general population of New Zealand.[425] The other notable trend of increasing BMI and history of diabetes in NZ/Europeans, together with the ongoing high frequencies of these

exposures in the other ethnic groups, reinforce the growing impact of these risks on cardiovascular disease and other health outcomes.[422, 427] Māori and Pacific populations have been consistently shown to have high rates of diabetes,[113] and higher prevalence of obesity in New Zealand, compared to NZ/Europeans.[440, 446] The dramatic increase in the prevalence of overweight and obesity in New Zealand over the past two decades,[422, 426] has lead to more people at risk of stroke, through increased risk of vascular risk factors associated with obesity.

Significant disparities were also found in the incidence of the major pathological stroke types and ischaemic stroke subtypes, with higher rates in Māori & Pacific, and Asian & Other people compared with NZ/Europeans. The ethnic-specific incidence of the major pathological stroke types were similar to those found in the South London Stroke Register[16, 168] the Northern Manhattan Stroke Study,[59] the Greater Cincinnati/Northern Kentucky Stroke Study,[42] and the Iquique Stroke Study in Chile.[447] These similarities suggest that Māori & Pacific populations, African Americans and Hispanics, and African Europeans, may share health conditions such as obesity, hypertension and diabetes or common socioeconomic traits that increase their susceptibility to ischaemic stroke and PICH. The high rates of PICH in the Asian & Other ethnic group were comparable to studies from Asia,[156] and may be related to higher levels of blood pressure in these populations. Compared to NZ/Europeans, Māori & Pacific people were at greater risk of cardioembolic stroke, Asian & Other people were at greater risk of lacunar stroke, which is in line with other population-based studies that have examined ethnic differences in ischaemic stroke subtypes.[167, 434, 436, 448] As is the relatively low incidence of atherothrombotic stroke and high incidence of lacunar stroke in minority groups in ARCOS compared with NZ/Europeans.[167, 448] The ethnic differences in the incidence and proportion of ischaemic stroke subtypes may in part be attributed to different risk factor profiles among the ethnic groups.

Given the large genetic variability within specific ethnic populations,[449] the most likely explanation for the risk factor differences observed is that ethnicity is a marker for socioeconomic and environmental factors (e.g. obesity,

hypertension and diabetes) that modify the risk of stroke and its subtypes.[73, 82, 431, 437, 450, 451] Previous studies have noted unfavourable cardiovascular risk profiles in Māori & Pacific populations with higher prevalence of obesity, physical inactivity, insulin resistance and metabolic syndrome compared to NZ/Europeans.[58, 113, 430, 452-454] These studies have also shown that ethnic minority groups also tend to have an earlier onset of risk factors such as diabetes, obesity and hypertension which may contribute to higher rates and earlier onset of the disease. Differences in the ethnic-specific risk factor profile are similar to those noted in other populations, with the highest prevalence of some risk factors (particularly hypertension and diabetes mellitus) found in ethnic minority or non-white populations compared with whites.[73, 93, 431, 437, 447, 450] Whereas, the higher rates of heart disease or AF in the NZ/European population, are consistent with other studies of risk factors profiles among different ethnic groups.[92, 455, 456]

The finding that Māori and Pacific populations had lower levels of socioeconomic status compared with other ethnic groups is in line with a report on New Zealand mortality trends from 1980 to 1999.[12, 457] Unfortunately, due to small numbers and the lack of population wide, age-specific data on socioeconomic status in New Zealand, the ethnic specific incidence rates were not adjusted for confounding by socioeconomic status, which may be have contributed to the observed ethnic differences in the incidence of stroke subtypes. However, given the high correlation between socioeconomic status and ethnicity, adjusting for socioeconomic status is unlikely to change the rates substantially. This is supported by data from the South London stroke register,[16, 168] where higher stroke rates in the African Caribbean population could not explained by differences in social classes, age, and sex. While other studies have shown that ethnic differences in the risk of stroke attenuate after adjustment for socioeconomic factors.[82, 458]

Ethnic differences in stroke risk factor profiles, however, cannot explain all of the increased stroke risk among ethnic minority groups.[294, 459] Current evidence suggests that stroke and vascular risk factors have similar relative effects across the world, with only modest interaction with ethnicity and

nationality.[449, 460, 461] The finding of higher proportions of hospitalisation and neuroimaging in Māori and Pacific populations are similar to those found in African Caribbean's in London.[462] This may reflect differences in access to health care and management or stroke severity between ethnic groups.[72] However, recently no race- or ethnic-based disparities were found in the utilisation of a variety of stroke-related procedures and services in the US and the UK.[462, 463] In a study of ethnic difference in diabetes care and outcomes in Auckland, it was found that Pacific populations were less likely to be receiving pharmacological therapies for cardiovascular risk factors, such as aspirin, hypertensive medication or statins.[464] Disparities in access to primary and secondary care are important to the management of risk factors.[465-467] These findings have important practical implications signifying insufficient stroke prevention measures in these high-risk populations.

Monitoring stroke in a population-wide context is challenging,[27, 30] but is needed to ensure that trends are not distorted by changes in diagnostic coding practices and referral patterns. In particular, consideration should be given to addressing confounding due to demographic changes, in particular age, for comparisons of rates between ethnic groups and over time. It has been shown here that there are differences in hospitalisation rates between ethnic groups with the lowest proportions in NZ/European populations, showing the importance of using a population-based method of case ascertainment to identify all strokes, even non-fatal non-hospitalised, through thorough checking of rest homes, private hospitals and GP registers. It is unlikely that the findings of this study can be explained by differences in the patterns of health care provision or health care seeking between NZ/European and ethnic minority populations.[468]

The comparison of rates of stroke between groups and over time needs to take into account confounding of differences and changes in demographic characteristics, in particular age, where comparisons of crude rates in different ethnic groups may lead to erroneous conclusions. Although the choice of a standard population for 'adjusting' for demographic differences in populations is arbitrary, it may change the interpretation of the results.[312, 447]

Indirect standardisation, which adjusted rates from the 1981-1982 and 1991-1992 studies to the age and sex structure of each ethnic group in the 2001 Auckland population, was used for assessing temporal trends in stroke rates within ethnic groups, also due to the sparse data in the Asian & Other group.[469] This method presents results more useful for the New Zealand population, health workers and policy makers as it takes into account changes in the age, sex and ethnic structure of the population. However, these rates were, like the crude rates for stroke, highest in NZ/Europeans, which may appear contrary to other studies which have shown higher stroke rates in African Americans or non-Europeans.[13, 18] However, most studies have commonly used the alternative method of direct standardisation, where rates are adjusted to an external standard population to enable comparisons between populations. Therefore, rates were also standardised using the WHO standard world population[410] to allow comparisons of stroke rates between ethnic groups in Auckland as well as to other populations around the world. This method produced higher rates of stroke in Māori and Pacific populations compared with NZ/Europeans as the world population is weighted towards younger ages and Māori and Pacific populations have their strokes at younger ages. By presenting both indirect and direct standardised rates it has been shown how the analysis (and interpretation) of rates is dependent on the method of standardisation and choice of reference population.[312]

Another issue to consider is that error in the estimation of rates may have occurred due to misclassification of ethnicity across the studies, due to changes in the self-perception of ethnicity, the census definition of ethnicity, or mode of collection of these data.[69] In the New Zealand Census of Populations and Dwellings, ethnicity was classified as the ethnic group or groups that people identify with or feel they belong to. Thus, ethnicity is self-perceived and people can belong to more than one ethnic group. There were changes in the census definition of ethnicity across the study period with the 1981 Census using the term “ethnic origin” which referred to the blood mixture of races within a person and the 1991 and 2001 census ethnicity questions measuring cultural affiliation, as opposed to race, ancestry, nationality or citizenship.[12, 69] The method of prioritisation of ethnicity was used in all

census data, which gives priority to non-European groups, with special priority to Māori and Pacific groups, when multiple responses are given. Therefore, there may be some bias in the measurement of the numerator and denominator for ethnicity, leading to underestimation of rates for Māori and Pacific peoples. It has also been shown that self-perception of ethnicity can change over time.[69] However, as all three ARCOS studies were undertaken in the same (or next in the most recent study) year of each Census, using similar questions of self-defined ethnicity as in the Census, any misclassification of ethnicity is likely to be non-differential. There may have been changes in the profile of the Asian & Other ethnic group over time, with more immigration from a variety of countries. However, the proportion of stroke patients in this group originating from the Asian continent was over 90% in all three studies. Therefore, it was assumed that this grouping is representative of Asian ethnicity across the three studies.

In summary, a decline in stroke rates in NZ/Europeans was offset by markedly increased rates in Māori and Pacific peoples, to produce only modest overall declines in stroke in Auckland. Some positive changes in the profile of risk factors, such as declines in the proportions of current smokers with stroke, were counterbalanced by increasing, or ongoing high, frequencies of diabetes and obesity in all ethnic groups. These divergent trends and increasing disparities in the rates of stroke between ethnic groups in New Zealand paints a disturbing picture for ethnic minority groups, in that primary and especially secondary prevention of stroke does not appear to be successful in these groups.

7. TRENDS IN OUTCOME AFTER STROKE

Stroke mortality rates have fallen substantially in many industrialised countries over recent decades.[36] These falls in stroke mortality may in part be due to reductions in stroke incidence[38, 317] or improvements in survival after stroke.[311] Explanations for trends in mortality include reduced rates of severe forms of stroke, which may have arisen from improved detection and control of elevated blood pressure levels, changes in the natural history of the disease, or improvements in the quality of stroke treatment and care.

This chapter describes the trends in mortality and survival after stroke from the three Auckland stroke registers and is divided into four sections. The first section presents trends in mortality up to 1 year after first-ever stroke across the ARCOS studies. The second section describes changes in 28 day and one year case fatality, by age, sex and ethnicity across the three studies. The third section describes trends in survival to one year after stroke in the three studies and provides explanations for these trends. The final section discusses these results in the context of other literature. All results presented are for first-ever in a life-time stroke, therefore outcome and survival can be attributed to the stroke as it is not confounded by previous vascular disease.

7.1. Trends in Mortality

Overall, 1030 incident strokes were registered in the 1981-1982 study, with 1305 in the 1991-1992 study, and 1423 in the 2002-2003 study. Table 7.1 presents age-standardised stroke mortality rates for the three ARCOS studies. Males had higher age standardised mortality rates than females. However, the disparity between males and females declined across the study period, leading to no difference in 2002-2003. There were consistent linear declines in stroke mortality by sex and in all but the oldest age group. Stroke mortality declined by 45% between 1981 and 2003 (RR 0.55, 95% CI 0.46 to 0.66), producing an annual decline of 2.5%. The biggest decline occurred in the 75 to 84 age group, with the majority of this decline occurring between 1981 and 1991. Whereas, in the younger age group (15 to 64) the greater

part of the decline in mortality occurred in the latter decade between 1991 and 2002. These differences in mortality may be due to differences in case fatality or survival over time. As shown in Section 5.1, Figure 5.1, the trends in one year mortality across the ARCOS studies were consistent with declines in annual stroke mortality in New Zealand over the same period.

Table 7.1 Annual stroke mortality rates, 1 year after first-ever stroke (per 100,000), direct age-standardised to the WHO world population, in Auckland, New Zealand, 1981-2003.

	1981-1982			1991-1992			2002-2003			Rate Ratio			
	n	Rate	(95% CI)	n	Rate	(95% CI)	n	Rate	(95% CI)	2002-03:1981-82		2002-03:1991-92	
Age group													
15-64	78	13	(10-18)	101	14	(11-18)	69	8	(6-10)	0.58	(0.39-0.86)	0.54	(0.40-0.74)
65-74	110	15	(12-20)	92	11	(9-14)	73	9	(7-11)	0.56	(0.39-0.79)	0.75	(0.54-1.04)
75-84	190	28	(23-34)	155	16	(14-19)	134	12	(10-14)	0.42	(0.33-0.55)	0.72	(0.57-0.92)
85+	90	13	(10-18)	97	10	(8-12)	153	10	(9-12)	0.77	(0.55-1.08)	1.08	(0.84-1.39)
Male	198	74	(60-90)	187	53	(38-75)	171	37	(32-42)	0.54	(0.43-0.68)	0.74	(0.60-0.92)
Female	272	66	(56-79)	258	49	(36-65)	258	37	(32-65)	0.55	(0.43-0.72)	0.75	(0.61-0.94)
Overall	470	70	(61-79)	445	52	(42-64)	429	38	(35-42)	0.55	(0.46-0.66)	0.75	(0.64-0.87)

7.2. Trends in Case Fatality

To investigate the reasons for the decline in mortality, trends in short- to medium-term survival were examined. Table 7.2 presents case fatality ratios at 28 days and one year after stroke, by patient demographic characteristics. Overall there were significant declines in 28 day case fatality from 32% in 1981-1982 to 19% in 2002-2003, leading to a relative decline of 40% over the study period. A relative decline of 34% was found in one year case fatality, from 46% in 1981-1982 to 30% in 2002-2003. These declines were consistent across age groups, with the exception of the oldest age group. Declines in case fatality were also consistent across ethnic groups, with the exception of 28 day case fatality in Māori where the decline was not significant. No differences in case fatality were found between the ethnic groups, within each of the three studies with all ethnic groups having case fatality at 28 days around or under 20% in 2002-2003.

Figure 7.1 presents unadjusted Kaplan Meier curves comparing survival up to one year in the three studies. The greatest improvement in survival occurred between the 1981-1982 and the 1991-1992 studies (log-rank p = <0.0001) and was most evident in the first few weeks following stroke. There was a significant improvement in 28-day case fatality between the 1991-1992 and 2002-2003 studies (log-rank p = 0.0112). However, no significant differences in one year survival between these two studies (log-rank p = 0.4697) were found, with an overlap between the curves for the 1991 and 2002 studies at around 330 days post-stroke. Therefore most of the improvement in survival occurred within the 28 days after first-ever stroke and between the 1981-1982 and 1991-1992 studies, producing an annual improvement in mean survival of approximately 2.5 days.

Table 7.2 28 day and 1 year case fatality after first-ever stroke, Auckland, New Zealand, 1981-2003.

	1981		1991		2002		Trend
Case Fatality	**n**	**%**	**n**	**%**	**n**	**%**	**p-value***
28 days	328	31.8	302	23.1	271	19.0	<.0001
Age < 65	72	25.2	72	20.8	56	14.3	0.0004
Age 65-74	78	30.0	63	16.9	47	14.0	<.0001
Age 75-84	122	34.9	95	23.1	71	16.2	<.0001
Age 85+	56	41.8	72	41.6	97	37.6	0.3701
Male	136	26.7	125	21.3	109	16.3	<.0001
Female	192	36.9	177	24.7	162	21.4	<.0001
European	292	31.3	253	22.4	205	19.5	<.0001
Māori	14	30.4	15	24.6	18	20.2	0.1871
Pacific	12	40.0	29	33.7	24	17.1	0.0010
Asian & Other	10	50.0	5	16.7	16	13.3	0.0004
1 year	470	45.6	445	34.1	429	30.2	<.0001
Age < 65	78	27.3	101	29.1	69	17.7	0.0018
Age 65-74	110	42.3	92	24.7	73	21.7	<.0001
Age 75-84	192	54.9	155	37.6	134	30.6	<.0001
Age 85+	90	67.2	97	56.1	153	59.3	0.2140
Male	198	38.8	187	31.9	171	25.6	<.0001
Female	272	52.3	258	35.9	258	31.1	<.0001
European	424	45.4	372	33.0	332	31.6	<.0001
Māori	20	43.5	23	37.7	22	24.7	0.0201
Pacific	14	46.7	41	47.7	39	27.9	0.0040
Asian & Other	12	60.0	9	30.0	24	20.0	0.0003

* p-value calculated using Cochran-Armitage trend test

n=number of deaths in stroke patients

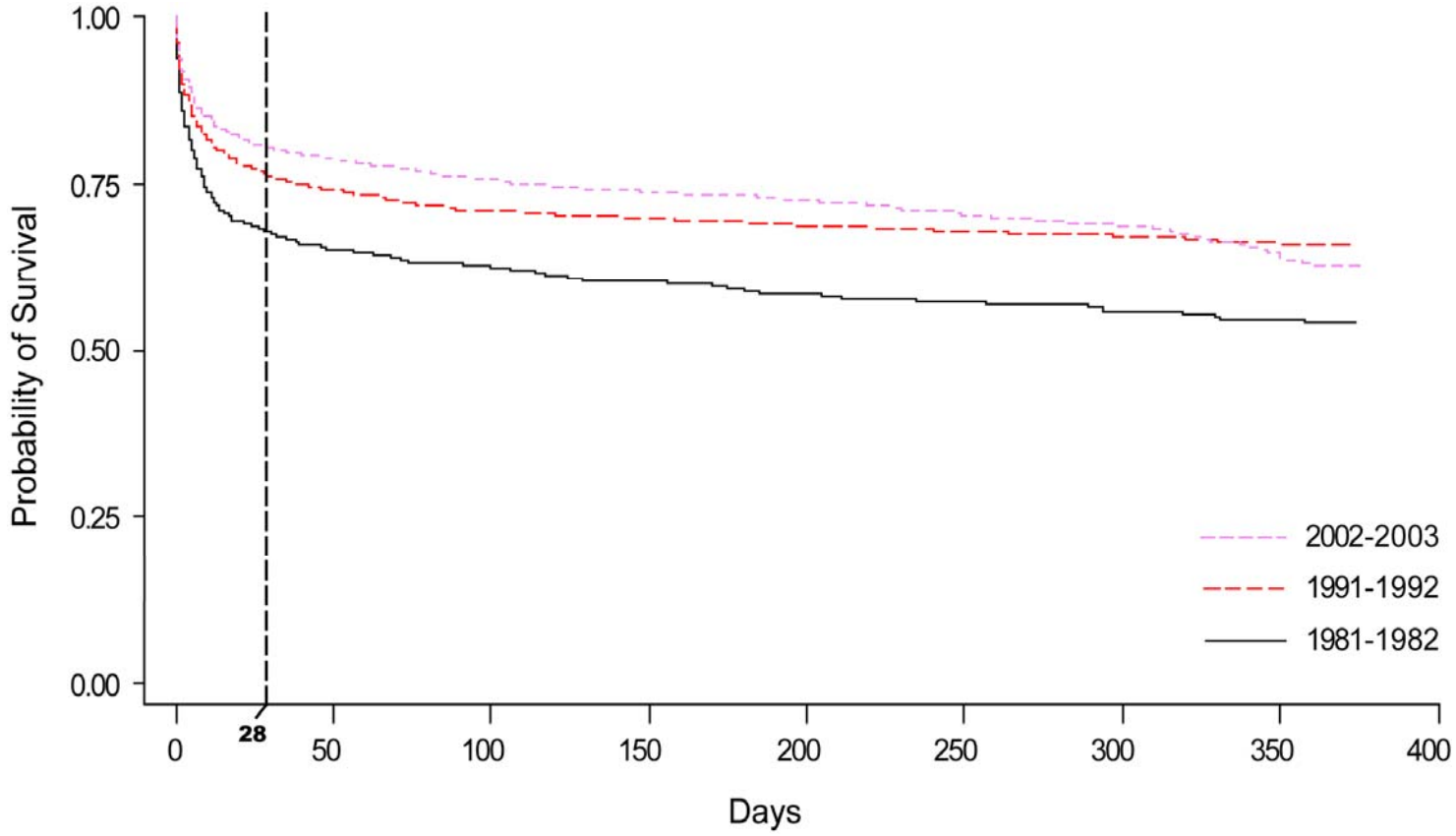


Figure 7.1 Unadjusted Kaplan Meier curves of survival up to one year post stroke, for the three ARCOS studies.

7.3. Trends in Survival

Explanations for the improvements in case fatality over time, were assessed through changes in patient factors such as age, sex, ethnicity, BMI, smoking status and previous history of co-morbid disease. Changes in stroke severity factors were measured through loss of consciousness and/or some form of motor deficit/paresis at the time of the stroke, and changes in management and care factors were measured through time to seeking medical attention, admission to hospital and whether the patient received some form of neuroimaging. These variables were modelled to quantify how much of the improvement in survival could be explained by controlling for these factors.

7.3.1. Demographics

The distribution of several patient, disease and management or care factors changed significantly over time and are shown in Table 7.3. As seen in previous results (Chapters 5 and 6) the proportion of patients overweight or obese, or reported a history of diabetes and hypertension increased over time, and the proportion of smokers declined. There were also significant declines in the proportion of patients dependent on others for activities of daily living before their stroke. The significant increases in the proportion of patients who lost consciousness or who suffered from some form of motor deficit at the time of their stroke, may reflect changes in the severity or the natural history of the disease over time. The number of patients who were admitted to hospital for their stroke and received some form of neuroimaging also increased across the study periods. The number of stroke patients who sought medical attention (e.g. admission to hospital or calling a local GP) within three hours after their stroke also increased over time, indicating that more patients were eligible for early acute treatments of stroke. However, as mentioned in Chapter 4 (Methods) there were large proportions of missing data for the BMI and the time to seeking medical attention variables. As these variables could potentially influence survival after stroke multiple imputation was used to create a complete dataset in which to examine the reasons for

the improvements in survival. The proportion of data imputed for each variable is shown in Table 7.3.

7.3.2. Survival Modeling

Stepwise Cox proportional hazards regression analysis was used to develop a model of survival (time to death), up to one year after first-ever stroke. Table 7.4 presents the univariate and multivariate hazard ratios from the Cox proportional hazards modelling, using the imputed variables. Loss of consciousness at the time of stroke was the most important risk factor for one year mortality from stroke, with a sixfold increase in the risk of dying, even after adjusting for other significant factors. NZ/European ethnicity, history of heart disease, diabetes or previous blood pressure medication were not found to be associated with one-year survival. The patient factors, age and pre-stroke dependency were significantly associated with survival to one year after stroke and were kept in the final predictive model. Whereas, sex, being overweight or obese, having a history of diabetes or high blood pressure and smoking status were not associated with survival after adjusting for disease severity and hospital management and care factors in the model. The disease factors, loss of consciousness and motor deficit at the time of stroke and the hospital managements and care factors, being admitted to hospital within 28 days of the stroke and whether the patient received some form of neuroimaging were retained in the final predictive model. Being admitted to hospital was significantly associated with poorer survival, reflecting the fact that more severe strokes are admitted to hospital. Whereas, better survival was associated with whether a patient suffered from some form of motor deficit at the time of their stroke or if they received some form of neuroimaging (CT or MRI), which may also be related to being admitted to hospital. An interaction was found between loss of consciousness at the time of stroke and study period, so a sensitivity analysis was conducted, stratifying by loss of consciousness.

Table 7.3 Patient factors (demographics and medical history), stroke severity factors, and management and care of (first-ever) stroke patients in three ARCOS studies, using aggregated imputed data.

	1981 N=1030		1991 N=1305		2002 N=1423		Trend
	n	%	n	%	n	%	P-value*
Patient Factors							
Age, Mean (SD) †	71.0	(14.2)	70.6	(13.9)	71.8	(14.3)	0.1147
Male	510	49.5	587	45.0	667	46.9	0.2623
Ethnicity, NZ/European	934	90.7	1128	86.4	1052	73.9	<.0001
Overweight / Obese ‡	347	33.7	541	41.1	707	49.7	<.0001
% imputed		*4.7*		*15.7*		*35.9*	
Dependent pre-stroke	252	24.5	225	17.2	225	15.8	<.0001
% imputed		*0*		*0.2*		*3.8*	
History of heart disease	112	10.9	198	15.1	170	12.0	0.5853
% imputed		0		0.8		1.2	
History of diabetes	92	9.0	179	13.7	226	15.9	<.0001
% imputed	*14*	*1.4*	*22*	*1.7*	*14*	*1.0*	
History of high BP	492	47.8	648	49.7	797	56.0	<.0001
% imputed		*0.0*		*0.9*		*4.2*	
Previous BP medication	445	43.2	556	42.6	700	49.2	0.0012
% imputed		*1.0*		*18.9*		*4.9*	
Current smoker	304	29.5	322	24.7	218	15.3	<.0001
% imputed		*1.0*		*0.6*		*9.8*	

Table 7.3 Patient factors (demographics and medical history), stroke severity factors, and management and care of (first-ever) stroke patients in three ARCOS studies, using aggregated imputed data.

	1981 N=1030		1991 N=1305		2002 N=1423		Trend
	n	%	n	%	n	%	P-value*
Disease Severity factors							
Lost consciousness	340	33.0	369	28.3	579	40.7	<.0001
% imputed		*4.1*		*3.1*		*1.7*	
Motor Deficit	824	80.0	1092	83.7	1201	84.4	0.0057
% imputed		*0.2*		*1.5*		*2.2*	
Hospital management / Care Factors							
Admitted to hospital	664	64.5	939	71.9	1315	92.4	<.0001
Neuroimaging (CT/MRI)	142	13.8	452	34.6	1284	90.2	<.0001
Sought medical attention within 3 hrs	428	41.6	609	46.7	843	59.2	<.0001
% imputed		*15.9*		*15.8*		*34.7*	

* p-value calculated using Cochran-Armitage trend test

† p-value calculated using ANOVA

‡ Defined as BMI ≥ 25

n=number of stroke patients, SD=standard deviation, BP=Blood Pressure, CT=computed tomography, MRI=magnetic Resonance Imaging

Table 7.4 Univariate and multivariate Cox proportional hazards (PH) regression analysis of possible determinants of survival, with study forced into the model, using imputed data.

	Univariate (adjusting for study)			Stepwise Multivariate			
Variable	**Hazard Ratio**	**95% CI**	**Chi-sq p-value**	**Hazard Ratio**	**95% CI**	**Chi-sq p-value**	**Order†**
Study, 1991*	0.69	(0.65,0.73)	<.0001	0.81	(0.71,0.94)	0.0042	*1
Study, 2002*	0.65	(0.61,0.69)	<.0000	0.75	(0.61,0.91)	0.0038	*2
Patient Factors							
Age	1.03	(1.03-1.03)	<.0001	1.02	(1.01-1.02)	<.0001	4
Male	0.75	(0.71-0.78)	<.0001				
NZ/European	0.96	(0.90-1.03)	0.2360				
Overweight/Obese	0.74	(0.71-0.78)	<.0001				
Dependent pre-stroke	2.62	(2.49-2.76)	<.0001	1.60	(1.40-1.82)	<.0001	5
History of Heart Attack	1.07	(1.00-1.15)	0.0482				
History of Diabetes	0.99	(0.93-1.07)	0.8627				
History of High BP	0.87	(0.83-0.92)	<.0001				
Previous BP Medication	0.96	(0.92-1.01)	0.1014				
Current smoker	0.91	(0.86-0.97)	0.0021				
Disease severity factors							
Lost consciousness	6.29	(5.98-6.62)	<.0001	6.00	(5.24-6.86)	<.0001	3
Motor Deficit	0.85	(0.80-0.90)	<.0001	0.76	(0.66-0.87)	0.0001	8
Hospital Management/Care factors							
Admitted to Hospital	1.25	(1.17-1.33)	<.0001	1.48	(1.28-1.72)	<.0001	7
Neuroimaging (CT/MRI)	0.42	(0.39-0.45)	<.0001	0.49	(0.41-0.58)	<.0001	6
Sought medical attention within 3 hours	1.29	(1.23-1.36)	<.0001				

* Study 1991 and 2002 were forced into all models (using the 1981 study as the reference). † Order of the variable entered into model.

BP=Blood Pressure, CI=Confidence Interval, CT=Computed Tomography, MRI=Magnetic Resonance Imaging

7.3.3. Changes in Survival

The variables that were found to be significant in the predictive modelling were used to examine the influences on improved survival between the study periods. Table 7.5 shows the hazard ratios between the 1981-1982 and 1991-1992 studies and between the 1991-1992 and 2002-2003 studies for survival up to 28 days and one year after first-ever stroke after the factors that were found to be significant in the predictive modelling were sequentially added to the model. The percentage change in the hazard ratio quantified how much of the improvement in survival (HR) was attenuated, after adding the factors that were found to be significant in the predictive modelling. Hence, this estimates the amount of influence that factor had on the improvement in survival over time.

It can be seen in Table 7.5, that there were significant improvements in 28 day survival between 1981-1982 and 1991-1992 (HR 0.69, 95%CI 059-0.81), with a smaller improvement between 1991-1992 and 2002-2003 (HR 0.81, 95%CI 0.69-0.96). These results mirror the trends in case fatality and the Kaplan Meier curves in Figure 7.1. The results attenuated when patient factors (age and pre-stroke dependency) and disease severity factors (loss of consciousness and motor deficit) were added to the model, but the improvements in survival remained significant. However, once the hospital management and care factors (neuroimaging and admission to hospital) were added to the model most of the improvement in survival was explained. Up to 37% of the variation (change in HRs) in 28 day survival was explained by adding all factors to the model. Significant improvements in one year survival between the 1981-1982 and 1991-1992 studies were also found, however there was no improvement in one year survival between the 1991-1992 and 2002-2003 studies. Once all of the patient factors, disease severity factors and hospital management and care factors were added to the model the degree of improvement in one year survival attenuated but not all of the improvement in survival between the 1981-1982 and 1991-1992 studies could be explained.

Table 7.5 Hazard Ratios for change in 28 day and 1 year survival between studies, using imputed data, adjusting for patient, disease and care factors, sequentially.

	1991 v 1981				2002 v 1991			
	HR	**95% CI**	**p-value**	**% change**	**HR**	**95% CI**	**p-value**	**% change**
28 day survival								
Univariate, study	0.69	(0.59-0.81)	0.0002		0.81	(0.69-0.96)	0.0121	
+ Patient Factors*	0.74	(0.63-0.87)	0.0002	7.4	0.82	(0.69-0.96)	0.0166	0.9
+ Disease Factors†	0.78	(0.66-0.92)	0.0031	13.2	0.54	(0.46-0.64)	<.0001	-33.6
+ Management Factors‡	0.95	(0.80-1.12)	0.5129	37.2	0.96	(0.79-1.18)	0.7102	18.7
1 year survival								
Univariate, study	0.69	(0.60-0.78)	<.0001		0.94	(0.82-1.08)	0.3844	
+ Patient Factors*	0.73	(0.64-0.83)	<.0001	6.0	0.93	(0.82-1.07)	0.3164	-0.9
+ Disease Factors†	0.74	(0.65-0.85)	<.0001	8.5	0.64	(0.56-0.74)	<.0001	-32.0
+ Management Factors‡	0.81	(0.71-0.94)	0.0063	18.7	0.92	(0.78-1.09)	0.3326	-2.5

HR = Hazard Ratio, CI = confidence interval

% change = $(HR_{adj}-HR_{unadj})/HR_{unadj}*100\%$

* includes age and pre-stroke dependency

† includes loss of consciousness and motor deficit/paresis

‡ includes admission to hospital and neuroimaging (CT or MRI)

A significant interaction between the study period and loss of consciousness was found, which appears to have skewed the change in survival between the 1991-1992 and 2002-2003 studies. Therefore, a sensitivity analysis was conducted, stratifying by patients who lost consciousness at the time of their stroke and those who did not. Significant improvements in the survival of patients who did not lose consciousness at the time of their stroke between the 1981-1982 and 1991-1992 studies were found (univariate HR 0.63, 95%CI 0.51 to 0.78), with no improvement between the 1991-1992 and 2002-2003 studies (univariate HR 1.02, 95%CI 0.81 to 1.29). However, in patients that did lose consciousness at the time of their stroke, survival improved between both, the 1981-1982 and 1991-1992 studies (univariate HR 0.78, 95%CI 0.66 to 0.92) and the 1991-1992 and 2002-2003 studies (univariate HR 0.55, 95%CI 0.46 to 0.65). As in the non-stratified results once all of the patient, disease severity and hospital management and care factors were added to the model the improvements in survival attenuated and became no longer statistically significant. Other sensitivity analyses were conducted investigating changes in one year survival in patients who survived the acute period (two days) after their stroke, patients who survived to 28 days after their stroke and patients who were admitted to hospital. All produced similar results seen in Table 7.4.

7.4. Discussion

The current results show dramatic declines in stroke mortality and a striking improvement in survival after stroke over the 23 year period from 1981 to 2004. Most of this improvement occurred in the decade between 1981 and 1991, and for 28-day rather than 1-year outcomes. These improvements persisted even after adjusting for patient characteristics and stroke severity. However, after adjusting for hospital management and care factors with the increasing likelihood of being admitted to hospital and use of neuroimaging, the improvement in survival was no longer significant.

Declines in stroke mortality have been previously explained by changes in incidence[38, 258, 317, 349, 350] or improvements in case fatality.[238, 292, 310, 311, 328] It was previously shown in Chapter 5, that stroke incidence declined moderately

across the three ARCOS studies. However, the large improvements in survival, supports data from other ideal stroke incidence studies, where little or no change in incidence were found with large declines in case fatality.[268, 315, 319] It has previously been argued that up to two-thirds of the decline in stroke mortality can be attributed to improved case fatality.[311] Stroke mortality declined by 45% over the three studies, where stroke incidence declined by 10% and one year case fatality declines by 34%. Therefore, most of the decline in stroke mortality in Auckland between 1981 and 2004, can be explained by declines in case fatality rather than declines in the incidence of stroke over time.

The detection of a downwards trend in case fatality may be related to values in the reference (initial) study period. A recent review of stroke incidence studies showed that in general, declines in one-month case fatality were evident in those studies with initially high (over 30%) values as compared to studies with case fatality ratios of around 20% across time.[30] Broderick et al, for example, noted that the 30-day case fatality for stroke declined from 33% during 1945 to 1949, to 17% during 1980 to 1984 in Rochester, Minnesota.[258] This improvement in survival has been shown to have ended since the 1980s.[470] In the 1980s, the MONICA study found that the average case fatality was 30%,[165] and case fatality declined in most of these populations in the 1990s.[311] Whereas, studies with initially low case fatality ratios have shown little or no decline in case fatality over time.[38, 317] In the ARCOS 2002-2003 study case fatality was similar (around 20%) between the ethnic groups. These data, together with the decline in 28-day case fatality from 32% to 19% in the current analysis, support a “regression to the mean” effect in early case fatality, irrespective of advances in acute stroke management. It appears that the average early case fatality ratio is approximately 20%, so countries, or demographic groups, with initially high case fatality ratios will regress towards this mean.

In regard to long-term survival, several studies have shown improvement up to several years[11, 268, 297, 326, 332, 335, 344] and even 10 years[268] after the onset of stroke. The current data are consistent with previous research that have

shown that large improvements in short-term survival are translated into improvements in long-term survival.[326, 332, 344] There has, however, been two studies that have shown significant improvements in long-term survival with stable early case fatality have, which was attributed to improvements the care of older people rather than acute stroke care.[268, 335]

The chance of surviving the acute phase of stroke is generally a complex function of the extent of neurological damage, the complications of disability, and the presence of associated co-morbid vascular and other conditions that are more common in older people. As in other studies, it was found that several simple clinical parameters including level of consciousness, age and history of pre-morbid dependency, were strongly predictive of survival.[170-172] Many of these factors are not modifiable at the time of the stroke, therefore, it is important, that any assessment of the impact of medical care on trends in survival should take these factors into account. The assessments of the presence of reduced consciousness and of motor deficit (paresis/plegia) at the time of the stroke in this study were rather crude, and not standardised to time from the onset of stroke or validated against medical records, which may explain the variability in proportions of such impairments across the three studies. Motor deficit was found to be protective of survival which is contrary to an earlier analysis predicting three-year survival from the 1981-1982 study, where severe motor deficit was found to influence mortality.[171] However, trends in the severity of motor deficit could not be investigated due to differences in the questions across the three studies. Despite these problems, loss of consciousness, used as a surrogate measure of stroke severity, was by far the most important predictor of death after stroke, as shown in other studies.[171, 172, 326]

As discussed in Chapter 3, there are three possible explanations for improvements in survival after stroke, over time. The first correlates increases in survival with improved medical care or treatment of patients with stroke, leading to earlier and more appropriate management. This is related to improvements in diagnostic testing, through increased availability and use of neuroimaging, and increases in the rates of hospital admission for stroke,

as shown in the ARCOS studies. An increase in the availability and precision of diagnostic testing, allows the management of acute stroke to be better tailored towards specific pathological stroke types. In New Zealand and in particular Auckland, the most significant change in the hospital management of stroke from 1981-2002 was the introduction of a specialised mobile stroke team in the year 2000 in Auckland Public Hospital and stroke unit care in Middlemore hospital in the year 2001.[471] It has been shown specialised stroke teams and stroke units significantly improve long-term survival after stroke.[203] In 1996, the New Zealand Stroke Guidelines were published in an attempt to standardise stroke care across health facilities,[206] which has led to heightened awareness and the necessity of admitting possible cases of stroke to hospital to receive standard care. This may be reflected in the large increase in the proportion of patients admitted to hospital, and increases in the proportion of patients accessing health care within three hours of their stroke, across the three studies. The introduction of intravenous tissue plasminogen activator (rtPA) in carefully selected patients, use of aspirin within 48 hours of onset of ischaemic stroke, and the management of patients in well organised and coordinated stroke care unit facilities are key factors that may account for improvements in survival. However, the use of rtPA is still limited in Auckland, but the use of aspirin has increased since 1996.[472] Also, despite recommendations for standardised care in stroke units the organisation of stroke services are still varied across the country.[473] Therefore, while there has been an increase in the awareness of the importance of early assessment and management of stroke in hospital, the improved stroke outcomes appear to have arisen from other generic management changes and are independent of specific acute treatments.

The second explanation relates improvements in survival after stroke with decreased severity over time. This could be reflected through changes in the natural history of stroke i.e. changes in population-wide risk factor levels or changes in case ascertainment. It has been argued that changes in the severity of stroke significantly contribute to improvements in case fatality,[347] with up to 80% of the decline in case fatality in a US study could be explained by declines in the severity of stroke.[327] In the current study, however, the

proxy measure of stroke severity, the proportion of patients who lost consciousness at the time of their stroke, remained relatively stable across the three study periods, with a slight increase in the 2002-2003 study. Although significant improvements in some risk factors were found over time, such as declines in smoking and increases in the proportion of cases taking medication for high blood pressure, these factors did not explain any of the improvement in survival. In addition, even though the data presented here are incident strokes only, it was shown in Chapter 5, that there was no change in the rates of recurrent stroke over time, with the proportion of patient reporting a history of stroke at baseline around 25% across the three studies. In secondary analyses, it was found that the improvements in survival were limited to more severe cases of stroke, in patients who had altered consciousness at the time of their stroke. Unlike other studies where large improvements in survival in less severe cases of stroke were found.[326, 329]

The third and final explanation for improving survival after stroke refers to the increased registration of milder stroke patients, due to improvements in case ascertainment or improvements in the diagnosis of stroke through neuroimaging techniques. Increases in the number of patients being admitted to hospital, receiving some form of neuroimaging and possibly greater awareness of stroke symptoms among the medical profession and general public, may have increased the detection of milder stroke cases. However, consistent methodology and definitions were used across all three studies, fulfilling the criteria for an ideal stroke incidence study.[27, 28, 31] As presented in Chapter 5, the three ARCOS studies have been shown to fulfil a number of quality control criteria for the completeness of case ascertainment. Also improvements in case ascertainment were shown through the capture recapture technique, reflecting changes in changes in electronic data capture and the management of stroke in- and out-side the hospital. Therefore, any potential data acquisition bias was likely to be small due to the size of the study population and the consistency of definitions across the studies. The proportion of patients with altered consciousness remained relatively stable across the first two studies, and increased slightly in the 2002-2003 study and given the slight increase in the proportion of patients with a motor deficit at the

time of presentation, it seems unlikely that there was any increase in the registration of milder cases of stroke in the most recent ARCOS study.

While the ARCOS studies were not specifically designed to collect data on the process of care for patients, several factors may have accounted for the improvements in survival after stroke over time. Increases in the availability and precision of diagnostic testing would allow improved diagnosis of pathological stroke types. Previous studies found greater improvements in survival after ICH compared with ischaemic stroke over time.[258, 297, 329] Therefore, some of the improvements in short term survival may relate to differences in survival between cerebral infarction and ICH, however due to the low rate of neuroimaging in earlier studies changes in survival among the different stroke subtypes could not be investigated. However, the definition used to identify strokes in the three studies was based on clinical diagnosis of stroke, and not purely on neuroimaging, so the differential in diagnosis between the studies should be minimal.

Unfortunately there were large numbers of missing values for BMI and time to seeking medical attention, across the three studies. Therefore, multiple imputation of missing values was used, as there were few variables in hospital management and care that were consistent across the three studies. Multiple imputation has been shown to be useful in epidemiological studies with variables that have over 15% of the values missing.[417] One of the main assumptions of missing data imputation is that the data are missing at random i.e. that the probability of a value being missing does not depend on the unobserved data (which could not be verified) but may depend on observed data.[416] It was found that missing data were slightly more frequent for cases that were fatal or associated with loss of consciousness at onset. However, as neither BMI or time to seeking medical attention were found to be associated with survival after stroke, the potential problems associated with missing data and the technique used to correct for it are unlikely to have adversely influenced the overall findings.

In summary, large declines in stroke mortality over 23 years in Auckland were found which may be accredited to significant improvements in survival over

time. These improvements in survival are more likely to be attributed to advances in the quality of acute care in hospital. These positive trends commenced and continued without the introduction of any major advances in acute stroke treatments for the majority of patients, and prior to the introduction of specialist stroke services in the Auckland region. Therefore, it can only be inferred that a major contributing factor was widespread changes in the care of stroke patient's in general medical wards, through such factors as assessment, monitoring and management, care pathways, multidisciplinary team meetings, and early transfer to rehabilitation, in line with shortened stays in hospital.

8. THE FUTURE BURDEN OF STROKE

The future burden of stroke is expected to grow with the ageing of populations around the world even if declines in stroke mortality and incidence continue. Therefore, it is important to provide insight into the future trends of morbidity and mortality of stroke, to enable priority setting in health care. Estimations of the future numbers of stroke patients and the proportion of the population living with lasting disability from their stroke, are used to inform policy makers of the future burden, enabling them to establish rational decisions about related healthcare needs, and to plan healthcare facilities for stroke patients in the acute stage and in the medium- and long-term. The identification of groups that are high risk and have increased burden should lead to the development of more intensive preventive measures in such groups.

This chapter estimates the burden of stroke in Auckland and presents the projected burden in New Zealand. The first section combines information from the incidence and survival from stroke in the third ARCOS study to estimate the number of people living with the effects of stroke in Auckland. The second section describes the estimated changes in the New Zealand population up to the year 2051. The third section presents the censual number of stroke deaths in New Zealand up to 2051, using a number of scenarios assuming different trends in mortality over time. The fourth section presents the number of new cases of stroke in New Zealand up to 2051, using a number of scenarios assuming different trends in the incidence of stroke over time, and taking account of changes in demographic characteristics in the population. The fifth section projects the number of people living with the effects of stroke in New Zealand, up to 2051. The final section discusses these results in the context of other published literature.

8.1. First-Ever Prevalence

It is important to estimate the number of people living in the population with a history of stroke, as well as with lasting disability from stroke, to estimate the burden on healthcare facilities, and families and carers of stroke patients, in

the community. This section combines information on incidence and survival from the third ARCOS study (2002-2003) to calculate a crude estimate of first-ever stroke prevalence, the number of people who survive one year after incident stroke. The proportion of patients who were living in institutional care, were dependent or felt they had fully recovered within six months after their stroke were calculated to estimate the number of patients living with lasting disability from their stroke.

Prevalence rates of stroke were calculated by multiplying the age and sex specific crude incidence rates, from the most recent ARCOS study (2002-2003), by the mean duration of survival, by age and sex, within one year after stroke (mean survival across all three studies). Table 8.1 presents the estimated number of stroke patients surviving one year after their first-ever stroke in Auckland, as well as the crude and age-standardised prevalence rates by age, sex and overall. The total number of prevalent stroke cases does not equal the sum of males and females, as these were calculated using age stratified incidence rates and survival. Crude prevalence increased with increasing age and were higher in males than females, in all but the oldest age group. However, the rates in the oldest age groups may be unstable with wide confidence intervals because of small numbers in this group. The age standardised rate for females was also lower than males, which is comparable to the age-standardised incidence rates in Chapter 5, where males had significantly higher incidence of stroke than females.

Table 8.1 Crude and age-standardised (to the WHO world population) first-ever stroke prevalence rates (per 100,000) in Auckland, using data from the ARCOS 2002-2003 study.

	Male			Female			Total		
Age	**n**	**Rate**	**95% CI**	**n**	**Rate**	**95% CI**	**n**	**Rate**	**95% CI**
15-64	156	41	(35-48)	131	32	(27-38)	292	36	(32-41)
64-74	144	511	(428-595)	103	328	(265-392)	250	415	(363-467)
75-84	123	808	(665-951)	165	729	(618-840)	295	761	(673-849)
85+	28	784	(496-1072)	88	989	(782-1196)	120	930	(761-1099)
Total	452	106	(96-115)	486	103	(94-112)	958	104	(98-111)
Standardised		106	(96-116)		84	(76-92)		94	(88-101)

n=number of first-ever prevalent cases, CI=confidence interval

8.1.1. Disability

Stroke is a largely disabling disease, with over one third of people who suffer a stroke living with lasting disability. Lindley et al.'s two simple questions,[397] and residency status from the most recent ARCOS study (2002-2003), were used to estimate the level of disability in the stroke population alive six months after their first-ever stroke. For healthcare planning it is important to estimate the net increase in the number of newly disabled patients, as a result of their stroke, because patients who were already disabled before their stroke are already included in the existing healthcare burden.[380]

Table 8.2 presents information on the level of recovery, dependency and institutionalisation in patients alive, and interviewed, at six months after their incident stroke. Of the 898 patients alive at six months, approximately 26% felt they had made a full recovery from their stroke, with a higher proportion of males than females. Younger stroke patients were also more likely to have fully recovered from their stroke. Whereas, over one third of patients felt they had recovered from their stroke but still remained dependent on others for some activities of daily living. Over one third of patients remained dependent or were living in institutional care six months after their stroke, with higher rates of females than males. Dependency and institutionalisation was also associated with increasing age.

Table 8.2 The proportion of first-ever stroke patients alive at six months, recovered, dependent or living in institutional care at the six month follow up, from the ARCOS 2002-2003 study.

	Recovered		Partially Recovered		Dependent		Institutionalised	
	N	%	N	%	N	%	N	%
Male	122	29	189	44	69	16	48	11
Age 15-64	49	31	83	52	16	10	8	5
Age 65-74	36	26	59	43	25	18	11	8
Age 75-84	34	28	38	31	25	20	23	19
Age 85+	3	14	9	43	3	14	6	29
Female	108	25	143	33	98	22	89	20
Age 15-64	42	33	40	32	27	21	10	8
Age 65-74	24	26	35	37	24	26	7	7
Age 75-84	34	21	52	33	31	19	37	23
Age 85+	8	10	16	20	16	20	35	44
Overall*	230	26	332	37	167	19	137	15

* There were 32 patients alive at six months with missing residency and dependency information

n=number of patients

Table 8.3 presents the proportion of patients dependent or institutionalised pre-stroke compared to six months after stroke, taking into account death. The change in the pre- and post-stroke dependent and institutionalised population, estimates the net change in the burden of care due to stroke. Older patients were more likely to be dependent or institutionalised before their stroke, typically due to conditions not stroke related. The percentage of patients dependent or institutionalised after stroke increased with increasing age. Death at six months after stroke was also related to increasing age, with over a half of the patients aged 85 years and older dying within six months of their stroke. Therefore, many of the elderly patients who were dependent or institutionalised before their stroke, died within six months. This led to a negative change in the proportion of dependent patients from pre- to post-stroke in the oldest age group. The modelling of survival in Chapter 7 also showed that being dependent before stroke is highly associated with a greater risk of dying as a result of the stroke. Overall, there was a small increase (6%) in the net proportion of the stroke population dependent on others for activities of daily living. However, the net change in the proportion of patients living in institutionalised care before and after stroke was negative across most age groups, with a 9% decline overall. This also indicates that patients who were living in institutional care before their stroke were more likely to die as a result of their stroke. Therefore, it can be concluded that there was not a large change in the proportion of patients in the community requiring extra post-stroke care.

Table 8.3 Changes in dependency and living in institutional care before stroke and at the six month follow up, for first-ever stroke patients from the ARCOS 2002-2003 study.

	Dependent prestroke (%)*		Dependent 6 months (%)†		Dead 6 months (%)	Net change % dependency
Age	**Yes**	**No**	**Yes**	**No**	**Yes**	
15-64	13 (3)	365 (93)	62 (16)	215 (55)	63 (16)	13
65-74	20 (6)	299 (89)	73 (22)	151 (45)	61 (18)	16
75-84	83 (19)	345 (79)	123 (28)	150 (34)	111 (25)	9
85+	109 (42)	135 (52)	61 (23)	35 (14)	138 (53)	-19
Total	225 (16)	1144 (80)	319 (22)	551 (39)	373 (26)	6
	Institutionalised prestroke (%)‡		**Institutionalised 6 months (%)§**		**Dead 6 months (%)**	**Net change % institutionalised**
Age	**Yes**	**No**	**Yes**	**No**	**Yes**	
15-64	41 (10)	277 (71)	18 (5)	266 (68)	63 (16)	-5
65-74	49 (15)	224 (67)	18 (5)	212 (62)	61 (18)	-10
75-84	49 (11)	321 (73)	60 (14)	221 (50)	111 (25)	3
85+	112 (43)	111 (43)	39 (15)	57 (22)	138 (53)	-28
Total	251 (18)	933 (65)	135 (9)	756 (53)	373 (26)	-9

* 54 patients missing dependency information, pre-stroke,

† 195 patients missing dependency information at 6 months

‡ 239 patients with missing residency information, pre-stroke,

§ 164 patients with missing residency information at 6 months

8.2. New Zealand Population Projections

The New Zealand population, as in most developed nations, is going through a demographic transition, due to ageing of the population. This occurs as a results of the transition from high mortality and fertility rates, to lower rates of mortality and fertility.[388] The median age in New Zealand is expected to increase from 36 years in 2005 to 45+ years in 2045 and with a dramatic increase in the older population, aged over 65 years. The largest increase in the population aged 65 years and older will occur during 2021 and 2031 when the large birth cohorts of the 1950s and 1960s move into this age group.[388] Therefore, as the New Zealand population is ageing, and increased age is highly associated with increased risk of stroke, the population at risk of having a stroke is increasing.

The projected population data used in the current analyses were estimated from Statistics New Zealand, using the 2004 New Zealand population as the base population and were projected in five year censual intervals, assuming medium trends in mortality, fertility and migration (series 5 projections).[401] Table 8.4 shows the New Zealand census population (1981, 1991 and 2001) and the projected New Zealand population aged 15 years and older from 2004 to 2051, used in the current analyses. The projected population aged 15 years and older is estimated to increase by 47% between 2001 and 2051, an increase of approximately 1% per annum. The greatest increase will occur in the older age groups with the population aged 65 years and older increasing by 172% and with the population aged 85 years and older, increasing by 500% from 2001 to 2051. The estimated increase in the population was also greater in males than females reflecting a narrowing of the sex ratio due to larger increase in life expectancy in males.[388]

Table 8.4 The New Zealand census population (1981, 1991, 2001) and the estimated population projections in the New Zealand population aged 15 years and older (Series 5), from Statistics New Zealand.[401]

Year	Male	Female	Total	% change from 2001
1981	1,130,346	1,158,069	2,296,707	
1991	1,262,082	1,109,394	2,590,284	
2001	1,388,319	1,501,218	2,889,543	
2004	1,542,900	1,633,000	3,175,900	9.9%
2006	1,579,500	1,668,900	3,248,400	12.4%
2011	1,672,500	1,757,300	3,429,700	18.7%
2016	1,761,800	1,844,600	3,606,100	24.8%
2021	1,844,900	1,927,700	3,772,600	30.6%
2026	1,916,200	1,999,400	3,915,600	35.5%
2031	1,971,800	2,056,100	4,027,800	39.4%
2036	2,016,200	2,101,400	4,117,800	42.5%
2041	2,051,900	2,136,600	4,188,500	45.0%
2046	2,077,100	2,158,800	4,235,800	46.6%
2051	2,092,200	2,167,900	4,260,000	47.4%
% change 2001-2051	50.7%	44.4%	47.4%	

Ethnic specific projections were used to investigate changes within demographics groups. The Statistics New Zealand population projections were based on the 2001 census populations and were estimated out to the year 2021, assuming medium fertility, mortality, net migration and inter-ethnic mobility (Series 6). Increases in the New Zealand European population aged 15 years and older, were relatively stable over time, with and increase of 0.5% per annum. The Māori population was estimated to in crease by 2% per annum and an annual increase of 4% in the Pacific population. This was mainly due to increases in the older age groups. The Asian and Other ethnic group was estimated to increase by approximately 8% over the 20 years, which was a result of increases in older age groups as well as high immigration.

All projections presented in these analyses were adjusted for changes in the age and sex distribution of the population and were calculated for incident cases of stroke only. As described in Chapter 4 (Methods) a number of different scenarios were developed to investigate hypothesised changes in population demographics, the rate of disease and outcome after stroke. Table 8.5 presents the different combinations of the scenarios that were used to estimate how changes in the demography and epidemiology of the disease are reflected in the number of new deaths occurring from stroke (mortality), new cases with the disease (incidence) or living with the effects of the disease (prevalence). Published data on trends in mortality and incidence, as well as trends in the rates found across the three ARCOS studies, were used to estimate future changes in the number of stroke deaths and new stroke cases occurring in New Zealand over the next 50 years. A combination of these incidence and survival trends were used to estimate the future changes in the estimated burden of prevalent stroke cases in New Zealand.

Table 8.5 The combination of different scenarios used in the projection of stroke mortality, incidence and prevalence from 2001 to 2051 in New Zealand.

Scenario	Mortality				Incidence				Prevalence			
	1	**2a**	**2b**	**2c**	**1**	**3a**	**3b**	**3c**	**1**	**3a**	**4**	**3a+4**
1 Stable Rates	✓				✓				✓			
2a 1% ↓ mortality		✓										
2b 2% ↓ mortality			✓									
2c ARCOS mortality				✓								
3a 1% ↓ incidence						✓				✓		✓
3b 1% ↑ incidence							✓					
3c ARCOS incidence								✓			✓	
4 2.5day ↑ survival												✓

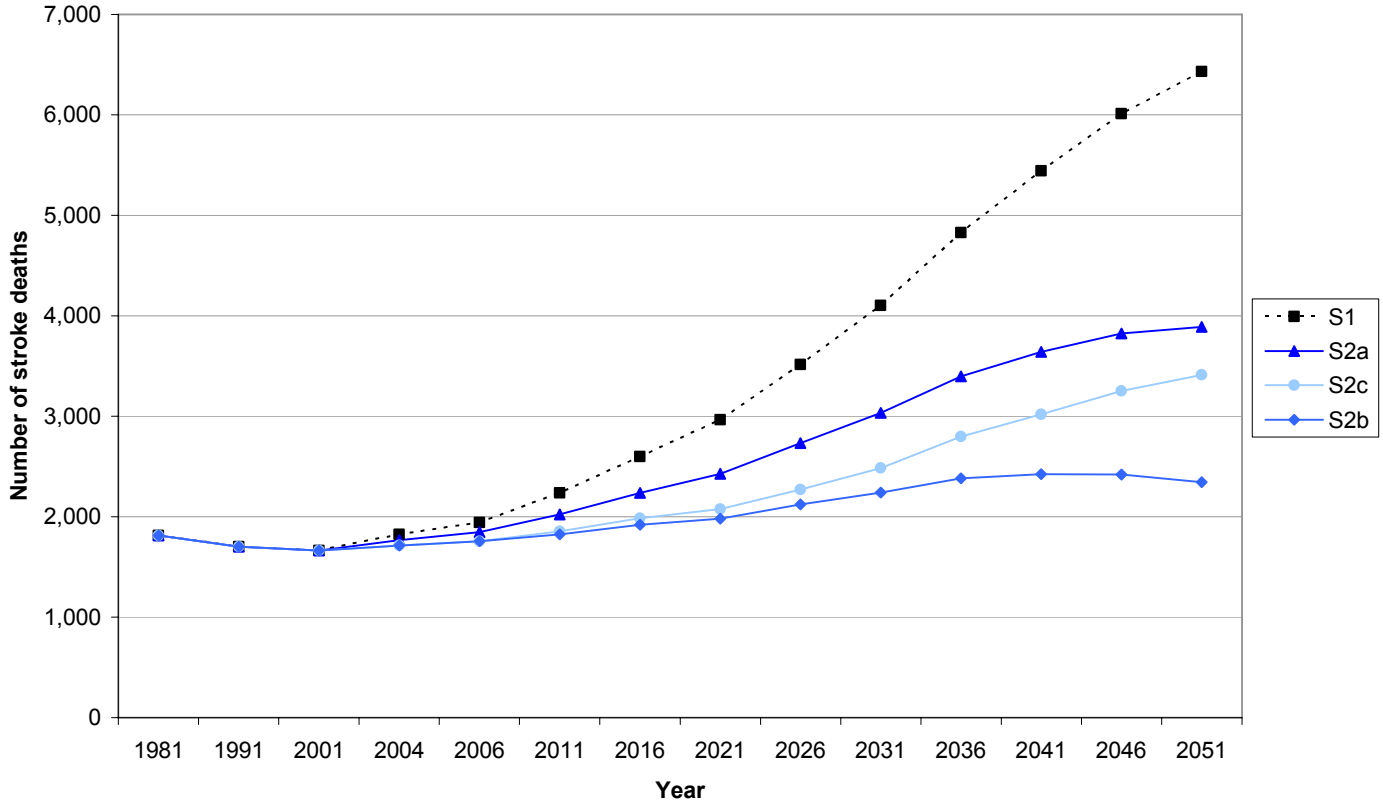
8.3. Projections of Stroke Deaths

In Chapter 7, it was shown that stroke mortality rates increased with increasing age and declined by 2.5% per annum across the three ARCOS studies. It is important to estimate the future number of stroke deaths occurring in New Zealand to determine whether these trends will continue over time and to assess the effect of changing mortality on public health and healthcare planning. To the estimate the projected number of stroke deaths in the New Zealand population, up to the year 2051 the age and sex specific stroke mortality rates from the 2002-2003 ARCOS study were multiplied by the projected age and sex population of New Zealand. The projected numbers of stroke deaths using different scenarios of changes in the annual rate of stroke mortality (Scenarios 1, 2a, 2b, 2c) are shown in Table 8.6 and Figure 8.1 presents them graphically.

Table 8.6 The projected number of stroke deaths from 2001 to 2051, using different scenario's of demographic and epidemiological change in mortality rates.

Year	S1 No change	S2a 1% ↓ mortality	S2b 2% ↓ mortality	S2c ARCOS*
2001	1,663	1,663	1,663	1,663
2004	1,823	1,769	1,715	1,714
2006	1,941	1,846	1,755	1,757
2011	2,235	2,021	1,826	1,854
2016	2,601	2,237	1,921	1,985
2021	2,966	2,426	1,980	2,075
2026	3,514	2,733	2,121	2,272
2031	4,104	3,036	2,239	2,483
2036	4,829	3,397	2,381	2,800
2041	5,442	3,640	2,425	3,019
2046	6,010	3,823	2,421	3,253
2051	6,430	3,890	2,342	3,411

* annual change in age and sex incidence rates found across the three ARCOS studies



S1 = Stable mortality, S2a = 1% annual decline in mortality, S2b = 2% annual decline in mortality, S2c = annual decline in mortality by age and sex, from the three ARCOS studies

Figure 8.1 Projections of new stroke deaths (adjusted for age and sex) in New Zealand, up to 2051.

In the published literature, it has been argued that stroke mortality rates have stabilised over recent years,[33, 36] so Scenario 1 assumed no change in mortality rates, controlling for the changes in the age and sex structure of the New Zealand population. Under Scenario 1 the number of stroke deaths will increase by 287%, between 2001 and 2051, producing an increase of 6% per annum. However, this is a very conservative estimate of the change in mortality over time. Therefore, a 1% decline in the annual rate of stroke mortality was assumed (Scenario 2a), which will produce a 134% increase in the number of stroke deaths from 1812 in 2001 to 3640 in 2051, an annual increase in stroke deaths of 3%. Whereas, assuming a more realistic decline in stroke mortality of 2% per annum (Scenario 2b), will produce a smaller (41%) increase in the number of stroke deaths, an annual increase of only 1%. The annual change in the age and sex stroke mortality rates found across the three ARCOS studies were applied in Scenario 2c, as it was shown in Chapter 7 that trends were varied by age and sex groups. This Scenario projects that the number of new stroke deaths will fall between the two previous estimates, with an increase of 105% from 2001 to 2051, an annual increase of 2%. Therefore, it can be concluded that even if the projected decline in stroke mortality continues, the number of stroke deaths will keep increasing, mainly due to the ageing of the population.

It is difficult to delineate whether the trends in stroke mortality are due to trends in the incidence of stroke or survival. If mortality continues to decline, prevalence rates will increase leading to more people living in the community with a history of or lasting disability from stroke. This will lead to increases in the burden on healthcare, in the medium- and long-term. Therefore, it is important to also investigate future trends in the number of new stroke patients as well as the number of patients living with the effects of stroke.

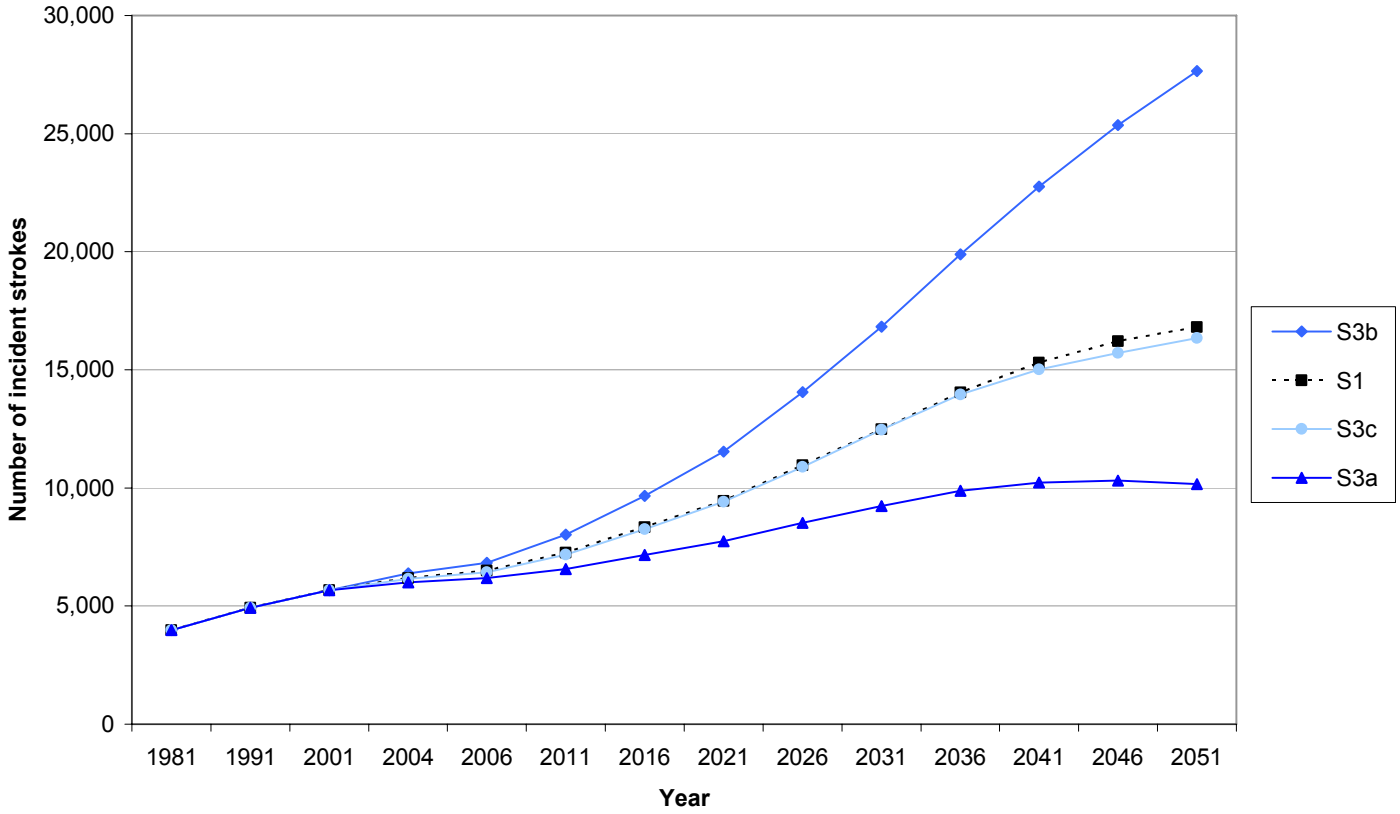
8.4. Projections of First-Ever Stroke Cases

To investigate changes in the future burden of stroke it is important to estimate the number of new strokes cases that are going to occur, to inform the appropriate planning of acute health care services in New Zealand. The projected numbers of new stroke cases in New Zealand were calculated by multiplying the age and sex specific incidence rates of stroke from the 2002-2003 ARCOS study by the estimated age and sex projected New Zealand population. As shown in Chapter 5, stroke incidence rates increased with increasing age and declined by 0.5% across the three ARCOS studies, 0.8% in males and 0.3% in females. The projected numbers of new stroke cases using different scenarios (Scenarios 1, 3a, 3b, 3c) of changes in the annual rate of stroke incidence are presented in Table 8.7 and plotted in Figure 8.2.

Table 8.7 Projected number of new stroke cases, using different scenarios of demographic and epidemiological changes in the incidence of stroke.

	S1	S3a	S3b	S3c
Year	**No change**	**1% ↓ incidence**	**1% ↑ incidence**	**ARCOS***
2001	5,666	5,666	5,666	5,666
2004	6,187	6,003	6,374	6,154
2006	6,494	6,176	6,825	6,439
2011	7,259	6,565	8,018	7,172
2016	8,329	7,163	9,670	8,252
2021	9,455	7,734	11,537	9,407
2026	10,959	8,524	14,054	10,895
2031	12,481	9,232	16,822	12,463
2036	14,044	9,879	19,894	13,956
2041	15,290	10,229	22,765	15,021
2046	16,208	10,311	25,362	15,714
2051	16,807	10,168	27,641	16,338

* annual change in age and sex incidence rates found across the three ARCOS studies



S1 = Stable incidence, S3a = 1% annual decline in incidence, S3b = 1% annual increase in incidence, S3c = annual decline in incidence by age and sex, from the three ARCOS studies

Figure 8.2 Projections of first-ever stroke cases (adjusted for age and sex) in New Zealand, up to 2051.

A number of studies have recently shown stable trends in the incidence rate of stroke over time.[239, 258, 268, 297, 298, 301, 315, 316, 328, 330] Therefore, Scenario 1 assumes stable incidence while adjusting for the changes in the age and sex projected population of New Zealand. Assuming no change in the incidence of stroke over time, the number of new stroke cases will increase by nearly 200% between 2001 and 2051, leading to an increase of 4% per annum. An optimistic decline of 1% in the annual incidence rate of stroke, as shown in the review of trends in stroke incidence in ideal studies (Chapter 3), was assumed in Scenario 3a. This led to an 80% increase in the number of new stroke cases from 5,666 in 2001 to 10,168 in 2051, an annual increase of 2%. However, assuming a more pessimistic change in the incidence of stroke of a 1% increase per annum (Scenario 3b), as shown in a number of European stroke incidence studies,[318, 319] will produce a dramatic 8% increase in the number of new stroke cases of per annum. The annual change in the age and sex specific incidence rates found across the three ARCOS studies were applied to the projected population in Scenario 3c, as trends in incidence were shown to vary by age and sex, with larger declines in males and also for ages 75 to 84 years. This produced projections similar to those where stable incidence was assumed, where positive declines in some demographics groups were outweighed by stable trends in others. However, if an optimistic decline in the incidence of stroke of 2% per annum, as recently found in Oxford,[38] was assumed, the future number of new stroke cases would remain relatively stable over time (data not shown here).

In Chapter 6 it was shown that there were ethnic disparities in stroke incidence, as well as in trends over time. Therefore, a sensitivity analysis was conducted to control for the effects of ethnicity. The age, sex and ethnic specific incidence rates from the ARCOS 2002-2003 study were applied to the age, sex and ethnic specific population projections from 2001 to 2021.[402] Similar increases in the number of new stroke cases were found using Scenarios 1, 3a and 3b. However, when the past age, sex, and ethnic specific trends in stroke incidence were applied to the projections, there was a dramatic increase in the number of new stroke cases. This was mainly due to the increasing rates in Māori and Pacific populations, particularly in females

and small numbers in the population denominators, by age, sex and ethnic group, leading to over inflated projections.

Figure 8.3 presents ethnic specific projections of the number of new stroke cases, assuming the overall annual percentage change in incidence for each ethnic group and adjusting for age changes in the population. The will be a 2% increase in the annual number of first-ever New Zealand European stroke cases, from 4519 in 2001 to 6672 in 2021. There will be a 9% annual increase in the number of Māori and Asian & Other ethnic groups (Māori: 467 in 2001 to 1319 in 2021; Asian & Other: 209 in 2001 to 592 in 2021). The largest increase in the number of new stroke cases will occur in the Pacific ethnic group, with an increase of 16% per annum, from 232 in 2001 to 972 in 2021. This is mainly due to ageing at a greater rate in the minority ethnic groups compared to New Zealand Europeans and increases in immigration in the Pacific and Asian populations.

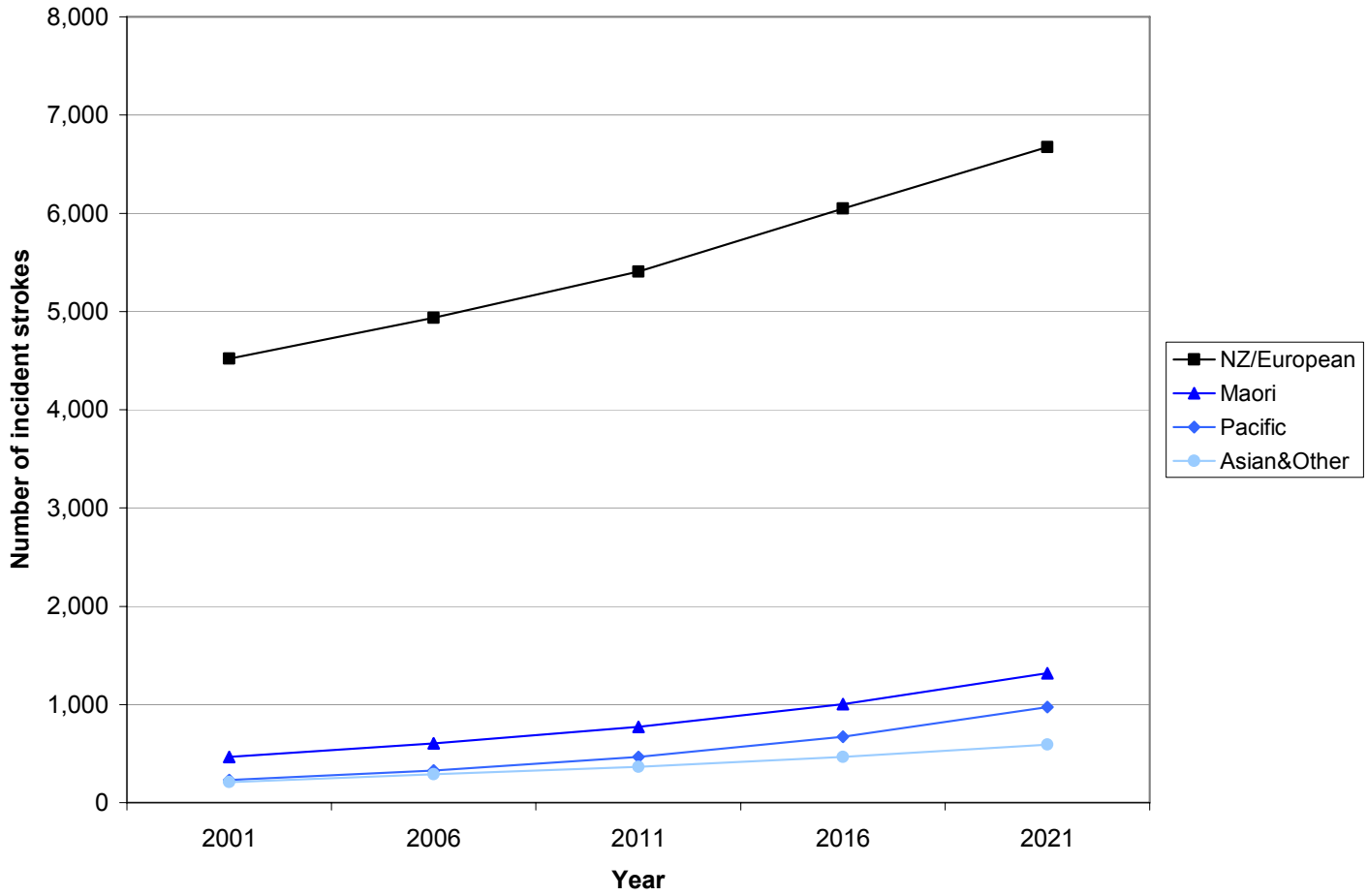


Figure 8.3 Ethnic specific projections of incident stroke cases (adjusted for age) in New Zealand, up to 2021.

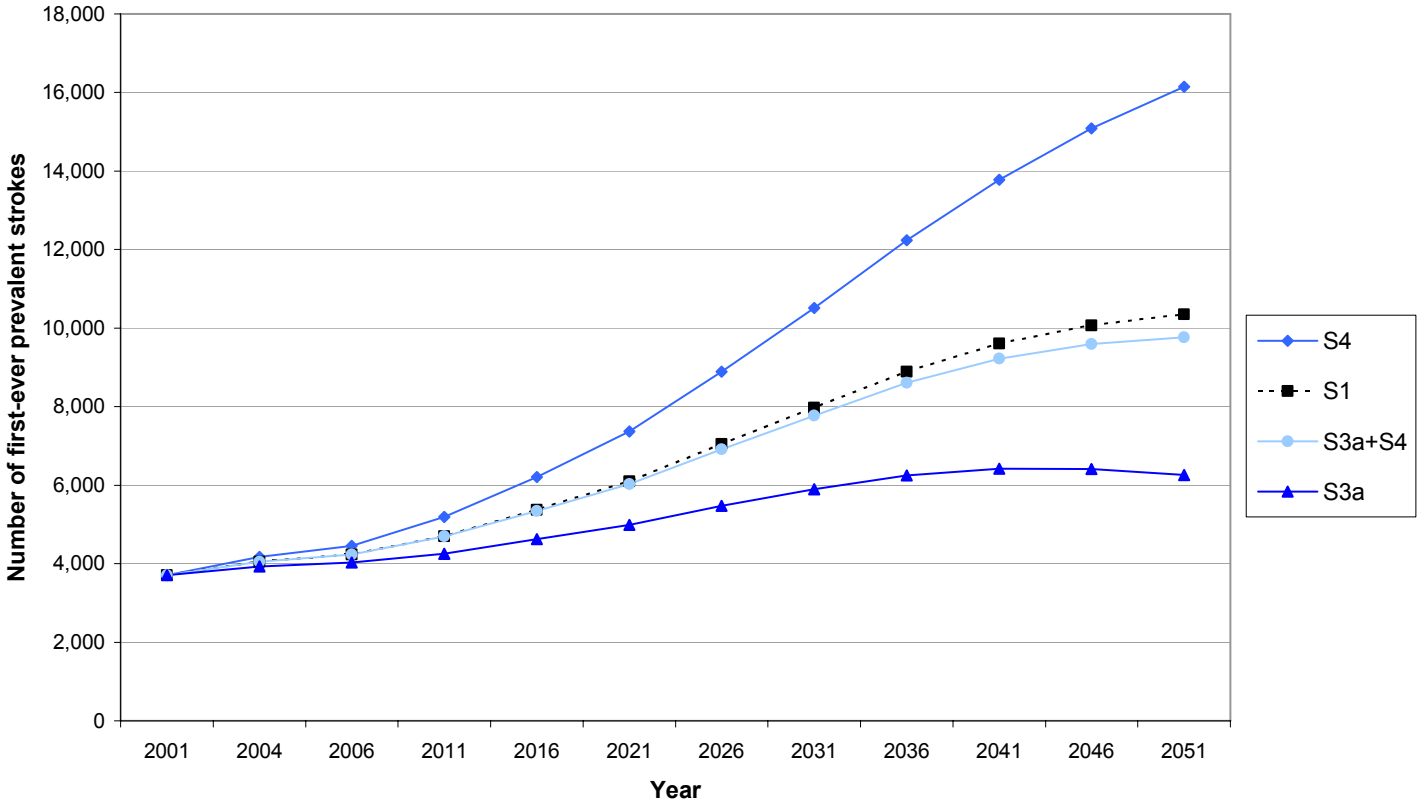
8.5. Projections of First-Ever Prevalent Cases

It is important to estimate the number of first-ever prevalent cases, and people living with lasting effects from stroke, to assess the burden on families, the community and health care providers. Prevalence is influenced by the incidence and the duration of the disease, survival. The future numbers of first-ever prevalent stroke patients were calculated by multiplying the projected population data by the age and sex prevalence rates from the most recent ARCOS study, 2002-2003 (Section 8.1). A combination of scenarios were used, assuming changes in incidence and survival, to provide an estimated range of projected prevalence over time and are presented in Table 8.8 and Figure 8.4.

Scenario 1 presents the projected number of new stroke patients surviving one year after stroke, adjusting for the age and sex changes in the New Zealand population and assuming stable incidence and survival. This produced an increase in the number of prevalent stroke patients from 3,714 in 2001 to 10,347 in 2051, which is an absolute increase in the number of over 6,400 (178%), a 4% increase per annum. Whereas, assuming a 1% annual decline in the incidence of stroke and stable survival (Scenario 3a), the estimated number of prevalent cases is estimated to increase by 69% between 2001 and 2051, an increase of 1% per annum. Assuming an improvement in mean survival of 2.5 days per annum and stable incidence (Scenario 4), will increase the estimated number of prevalent cases by 335%, an increase of 7% per annum. However, combining the approximate trends found across the ARCOS studies (Scenario 3a + 4), by taking into account both a 1% annual decline in the incidence of stroke and a 2.5 day improvement in annual survival, the estimated number of prevalent cases will increase by 3% per annum. This is only slightly less than if no change in incidence or survival was assumed, so it appears that the improvement in the incidence and survival from stroke are additive and cancel each other out in the trends in prevalence.

Table 8.8 Projected number of first-ever prevalent stroke cases, using different scenarios of demographic and epidemiological change.

Year	S1 No change	S3a 1% ↓ incidence	S4 2.5 day ↑ survival	S3a + S4 1% ↓ incidence, 2.5 day ↑ survival
2001	3,714	3,714	3,714	3,714
2004	4,051	3,930	4,175	4,051
2006	4,238	4,030	4,455	4,237
2011	4,701	4,252	5,188	4,692
2016	5,374	4,622	6,212	5,343
2021	6,099	4,989	7,369	6,028
2026	7,040	5,476	8,885	6,911
2031	7,977	5,900	10,507	7,772
2036	8,889	6,253	12,232	8,605
2041	9,602	6,424	13,782	9,220
2046	10,072	6,408	15,085	9,597
2051	10,347	6,260	16,144	9,767



S1 = stable survival and incidence, S3a = 1% decline in incidence, stable survival, S4 = 2.5 day increase in mean survival, no change in incidence, S3a + S4 = 2.5 day increase in mean survival + a 1% decline in incidence

Figure 8.4 Projections of first-ever prevalent stroke cases (adjusting for age and sex), in New Zealand, up to 2051.

To estimate the projected population with lasting disability from stroke, the proportions (by age and sex) of those patients dependent or living in institutional care at the six month interview, were multiplied by the projected number of prevalent strokes. When the approximate trends in incidence and survival found across the ARCOS studies (Scenarios 3a + 4) were assumed, the number of patients dependent on others for activities of daily living will increase by 164%, from 681 in 2001 to 1801 in 2051, an increase of 3% per annum. Whereas, the number of patients living in institutional care six months after their stroke will increase by 271%, from 582 in 2001 to 2158 in 2051, a 5% increase per annum. This large increase is due to the large proportion of elderly patients living in institutional care. However, as shown in Table 8.3, there will not be a large change in the net proportion of people living in institutional care between before and after stroke.

8.6. Discussion

Extrapolation of historic trends into the future provides insight into the population groups most likely to suffer the highest burden of disease and creates a benchmark to guide future healthcare planning and prevention efforts. These results show dramatic increases in the future number of stroke deaths, new stroke cases and people living with the effects of stroke in New Zealand. A large part of this increase is an inevitable consequence of ageing of the New Zealand population, even in the light of decreasing trends in the rate of stroke. Increases in the number of people having a stroke will result in an increased burden on acute healthcare and improvements in survival will result in the increased burden on the long-term healthcare of survivors of stroke.

A dramatic increase in the number of stroke deaths occurring in New Zealand over the next 50 years was found. It was estimated, using the age and sex specific trends in stroke mortality found across the three ARCOS studies, that the number of stroke deaths would increase by 2% per annum. The New Zealand population is estimated to increase y 1% per annum over the same period. Therefore, only half of the increase in the stroke deaths could be attributed to increases in the age distribution of the New Zealand population.

Similar increases in the number of stroke deaths were found in a New Zealand Ministry of Health report that estimated a 3% increase per annum, assuming stable incidence and case fatality.[474] These results from New Zealand are comparable with 30 year projections of death from ischaemic stroke in the US, where it was found that the future number of stroke deaths would outpace the overall growth of the population.[22] This study assumed small declining trends in stroke mortality, adjusting for age, sex and ethnicity, and found an increase of 3% per annum, with the greatest projected increases occurring in ethnic minority groups.[22] An early study from Japan also found increases in the number of stroke deaths despite declining trends in stroke mortality.[475] If a 2% decline in the rate of mortality across all age and sex groups, was assumed in the current analyses, then the number of stroke deaths would still increase but to a lesser extent, which was mainly due to the increase in the older population of New Zealand.

As discussed previously in Chapter 3, trends in mortality are determined by trends in incidence and survival from stroke. The large increases in the number of stroke deaths are related, in part, to the large estimated increases in the number of new stroke cases occurring. Assuming the age and sex trends in incidence found across the three ARCOS studies, the numbers of new stroke cases were estimated to increase by 4% per year. These increasing future trends in the number of stroke cases were similar to those where stable trends in incidence overall were assumed. Therefore, it seems that the significant declines in incidence seen in males and among patients aged 65 to 74 years (shown in Chapter 5) were cancelled out by stable or non-significant declines in other demographic groups. If a 2% annual decline in the incidence of stroke, similar to that shown in Oxford[38] was assumed, then the number of new strokes cases would remain relatively stable over time. However, it seems that unless drastic action is taken to prevent new strokes, in the current climate, these large declines in incidence appear unattainable in New Zealand.

The large increase in the number of new stroke cases was greater than those found in other studies conducted around the world, an 0.8% annual increase

in the Netherlands,[21] 0.7% in the UK[380] and 2.6% in the US.[382] However these studies did not adjust for historical trends in incidence, assuming stable rates over time. A study from the Netherlands, assumed a declining trend in incidence, based on past trend data from Rochester, a decrease in the future number of stroke cases was found.[258] However, this study was based on trend data from before the 1980s and didn't take into account the stabilising trends during the 1980s and 1990s. The New Zealand population appears to be ageing at a faster rate than other populations around the world, with larger increases in the proportion of people aged over 65 years, which may explain the larger projected increases in the number of stroke cases estimated in New Zealand. There is also large ethnic variation within New Zealand and the projected increases in the number of strokes were larger in ethnic minority groups. These ethnic minority groups are expected to grow in future years due to increases in immigration and ageing at a faster rate than New Zealand Europeans.

The estimates of prevalence presented in these analyses approximate the number of new stroke cases surviving one year after their stroke and provide insight into the burden on health care and services. These were crude estimates of prevalence, which do not take into account people already living with a history of stroke, so are likely to be underestimates of the total prevalence of stroke. Previous studies have estimated a stroke prevalence rate of up to 1000 per 100,000 in the community.[21, 169, 474, 476, 477] Assuming a 1% annual decline in the incidence of stroke and an improvement in survival of 2.5 days per annum, the overall trends found across the three ARCOS studies, the number of prevalent strokes were estimated to increase by 3% per annum. It seems that the trends in incidence and survival are additive, where the declining trends in incidence and the improvements in survival cancelled each other out in the projected number of prevalent stroke cases. Therefore, the results were similar to those where stable incidence and survival were assumed. Previous results from New Zealand projected the number of prevalent stroke cases from 1991 to 2001, assuming a 1% decline in incidence and a 1% decline in case fatality and found a 2% increase in stroke prevalence per annum.[474] When no change in incidence or case

fatality was assumed the annual increase in prevalence was approximately 3%. Therefore, although the estimates of prevalence presented in these analyses are crude, they present similar results of the increasing burden of stroke as shown in published data.

It is important to also approximate the number of new stroke patients that will live with lasting disability or dependency from their stroke, to estimate the burden on medium- to long-term healthcare. It was estimated that only 26% of the population alive at six months after their first-ever stroke, felt they had fully recovered. Approximately 20% were left with lasting disability and remained dependent on others for help with everyday activities of daily living and 15% were living in institutional care. However, it was shown in Section 8.1.1, that there will be only a small increase in the net proportion of patients dependent between pre- and post-stroke, with a decline in the net proportion living in institutional care. This is mainly due to the fact that older stroke patients, who were more likely to be dependent or living in institutional care before their stroke, were more likely to die as a result of their stroke. Similar results have been shown in a number of other studies conducted in the UK and Europe, where the number of newly dependent stroke cases, disabled as a result of their stroke, did not increase over time.[380, 381] Therefore, it appears that the increasing number of elderly stroke patients may result in a lessening in the burden on medium- to long-term healthcare of dependent stroke patients in the community. Hence, the increased in burden on healthcare is more likely to be as a result of increased use of acute care rather than from long-term disability. However, continued improvements in survival will result in a dramatic increase in the number of people living with the effects of stroke.

A number of different methods have been used to estimate future projections of stroke mortality, incidence and prevalence. Several investigators have used state-event transition models, integrating information about incidence and case fatality to model stroke event data and project rates into the future.[20, 21, 474] Such models have the potential to create more refined estimates of risk in the population but require multiple assumptions about incidence and mortality rates that can be difficult to estimate. Typically,

historical data from published studies have been used to determine trends in the risk of disease, not from their own population.[20, 21] Age-period-cohort modelling has also been used to model and forecast future stroke mortality in Sweden.[478] This type of model incorporates additional variables to account for factors present around the time of death (period effect) and factors present in early life (cohort effect) in their study population. Although such models are useful in identifying factors that account for changes in historical mortality data, their utility in making future projections is constrained by the multiple arbitrary assumptions that must be made to predict future cohort, age, and period effects.[479] Other studies have used simplistic modelling, simply multiplying current stroke rates by the projected population and not adjusting for historical trends in rates.[380, 381]

The current model used historical trends in the rate of stroke from the three ARCOS studies to project the most current event rates from the third ARCOS study (2002-2003), estimating the future number of strokes and stroke deaths occurring in New Zealand. The principal assumption of this model was that historical trends in stroke incidence and survival found in Auckland were applicable to the New Zealand population and will continue in the future. The various scenarios assumed that the trends were constant over time and provided optimistic and pessimistic limits within which the true projected number of strokes would fall. Assessing the likelihood that historical trends will continue over time, is complicated by the uncertainty about the causes of past changes in stroke rates. Dramatic improvements in primary and secondary prevention strategies will modify the projected increases in stroke incidence and mortality. Whereas, greater improvements in survival after stroke, will increase the number of people living with a history of stroke, but decrease stroke related mortality over time.

Future projections of stroke rates and numbers also depend on the reliability of the projected population. The Statistics New Zealand population projections rely on a number of assumptions about changes in fertility, mortality and net migration.[401] For the current analyses the mid-range projection (Series 5) was used to model future population changes. This

assumed that the total fertility rate would decrease to 1.85 births by 2016 and then remain constant, life expectancy at birth will increase to 83.5 years for males and 87.0 years for females, and from the year 2009 there will be a long-term annual net migration of 10,000 people.[401] Increases in the elderly population are estimated to be most marked in the ethnic minority populations in New Zealand.[19] These projections indicate that the doubling of the elderly population (≥65 years of age) over the next 50 years will be the predominant socio-demographic change affecting increases in the number of stroke cases and deaths. There is also greater uncertainty in the ethnic specific population projections, as there are small numbers in the age, sex, ethnic groups causing less precise estimates of fertility, migration and inter-ethnic mobility (changing ethnic identity over time).[402] Therefore, the ethnic specific population projections were only estimated for 20 years. The ethnic specific projections of the number of new stroke care are crude estimates, as rates from the Auckland population were applied to the New Zealand population. The ethnic projections were not based on prioritised ethnicity, as used in the ARCOS studies and rates, so people can belong to more than one ethnic group. This may have led to overestimation of the numbers of strokes within ethnic groups. A limitation in this analysis is that data on stroke rates based on the Auckland population were generalised to the NZ population. This may be problematic because of the ethnic structure of the Auckland population is different from the New Zealand population, with higher proportions of Pacific and Asian populations. However, the age and sex structures of the Auckland and New Zealand populations are quite similar.

There are a number of other limitations to the current analyses that need to be acknowledged. As mentioned previously, a crude measure of prevalence was used which does not take into account people already living in the population with a history of stroke before 2002, so the rates are underestimates of the total prevalence of stroke in Auckland. This measures the number of new stroke patients per year living with lasting effects from their stroke. Projections by stroke subtypes were not conducted because there were small numbers by age and sex, and past trends could not be estimated due to low rates of imaging in the earlier ARCOS studies. Changes in disability over time

could not be modelled because of slight variations in the study and questionnaire design between the three ARCOS studies. Therefore, changes in disability were inferred from the most recent ARCOS study. The projections did not take into account changes in co-morbid disease and changes in risk factors over time as it was not possible to obtain population data by the different risk factors. However, Struijs et al. found that adding changes in hypertension and smoking to the projection models modified the projected increase in the number of stroke cases by only a small amount.[21] The projections provided here are to act as a rough guideline for the probable future burden that will be placed on public healthcare over the next 50 years due to stroke or stroke related disability.

It is predicted that the increases in the ageing of the population in New Zealand is likely to place increased demand on health services, even in the light of declining trends in the rates of disease. Improved implementation of established prevention measures and the development of new therapies could result in lower than expected rates in stroke mortality or incidence. To reduce the number of strokes and stroke deaths occurring, more efforts need to be placed on primary and secondary prevention methods. Population-based approaches to reduce hypertension and smoking and improve population lifestyles through increased physical activity and better nutrition are effective primary prevention strategies. However, there is also a need to focus on high risk groups as disparities in the rates of stroke between population groups are growing over time.

9. CONCLUSIONS AND IMPLICATIONS

The main goal of this thesis was to investigate trends in stroke incidence and outcome in Auckland, New Zealand over the past two decades and explore disparities in these trends between ethnic groups. This was achieved by combining data from three large population-based ideal stroke incidence studies conducted in Auckland between 1981 and 2003. The historical trends in incidence and outcome were used to estimate the future burden of stroke in New Zealand to inform healthcare planners and policy makers of the impending burden.

9.1. Summary of Results

Trends in the incidence of stroke were found to be declining over time. However, these declines were not consistent across various demographic groups. Significant declines occurred in males, the "young-old" (aged 65 to 74 years) and among New Zealand Europeans. Increasing trends were found among Māori and Pacific ethnic groups, leading to growing ethnic disparities in the rate of stroke in New Zealand. This appears to be associated with the growing burden of major risk factors for stroke and the failure of primary and secondary prevention strategies in these groups.

Dramatic improvements in survival were found over the study period. Most of the improvement occurred during the acute period, within 28-days of the stroke, and between 1981 and 1991. These improvements in survival were consistent across most demographic groups. In survival modelling it was found that changes in patient and disease severity factors explained only part of the improvement in survival over time. However, when management factors such as changes in admission to hospital and the use of neuroimaging were adjusted for, most of the improvement in survival was explained.

Using these historical trends in stroke incidence and survival it was found that the future burden of stroke will increase by 3% per annum over the next 50 years. A third of this increase could be explained by the ageing of the New Zealand population over time. If the incidence of stroke could be reduced by

2% per annum, the number of new strokes occurring would remain relatively stable over time. The largest increase in the number of new strokes may be due to dramatic increases in the Pacific population in New Zealand, with increasing burden in Māori and Asian populations due to ageing at a faster rate than New Zealand Europeans. These results confirmed previous projections of the future burden of stroke in New Zealand and provide useful needs assessment for planning the funding and provisions of stroke services.[474]

9.2. Study Strengths and Limitations

The main strength of this study was that three large population-based stroke incidence studies were used to investigate trends in the rate of stroke over time. These three studies used similar case finding methods and definitions and have been shown to fulfil the stringent criteria for an ideal stroke incidence study, thereby enabling comparability of data over time. There are currently only a limited number of stroke incidence studies that have fulfilled the ideal criteria and investigated trends in the rate of stroke. This is the first to investigate ethnic disparities in these trends.

There are a number of possible limitations to these analyses that should be acknowledged. There were sampling methods used to ascertain cases of stroke in the first two studies. This, along with improvements in case ascertainment and neuroimaging over time, may have lead to the increased inclusion of milder cases of stroke in the third study. However, it was shown that all three studies fulfilled a number of international quality measures and the estimated number of patients missing, through capture recapture methods, was small in all three studies. Another limitation was that trends in rates across the major stroke subtypes could not be analysed due to the low levels of neuroimaging in the earlier studies. However, if a new study was to be conducted during the next decade more detailed trends by stroke subtype could be investigated. Finally, detailed analyses of changes in hospital management over time could not be since the 1981-1982 study only collected limited information on the hospital management of patients.

9.3. Implications for Future Research

There are only 12 ideal stroke incidence studies (including the current analysis) that have investigated trends in the incidence of stroke over time. Many of these studies were based on small populations with a limited number of strokes occurring per annum, leading to greater variation around the rates and trends over time. Therefore, there is a need for further population-based stroke incidence studies large enough to identify accurate trends in the rate of stroke within a population. Such studies need to focus on changes in management and prevention strategies to see how these effect trends in stroke incidence and outcome.

The STEPS-stroke program was developed by the WHO to encourage all countries worldwide to survey stroke using different levels of epidemiological data.[251] This will enable developing countries to add to the surveillance of stroke worldwide and how the burden is changing over time with respect to changing risk factors and treatment programs. It is recommended that countries progress through the stages of surveillance to eventually collect population-based information on stroke. This will provide comparable information on stroke worldwide and enable global investigations into trends and the future burden in the rate of stroke.

It was shown that ethnic disparities in the rate of stroke were growing over time. Therefore, population-based studies need to be conducted on ethnic disparate populations to identify ongoing disparities between groups and how these are changing over time. Future research will benefit from assessing ways to increase the uptake of interventions and lifestyle changes among different ethnic groups, thus aiding in reversing the disparities in stroke incidence. This data may be applicable to other ethnically disparate populations that haven't had the opportunity, or resources, to investigate population-wide trends in stroke.

The most recent ARCOS study (2002-2003) collected detailed data on stroke subtypes, management and outcome. Therefore, a similar study conducted during the next decade will provide more in depth detail as to the explanations

for the changing trends in incidence and outcome and delineate the trends in ethnic disparities. A detailed follow up of the 2002-2003 study cohort will enable comparisons of outcome data with previous follow ups of the 1981-1982 and 1991-1992 cohorts, leading to the investigation of trends in long-term survival, dependency and quality of life after stroke. It may also be possible to develop a prognostic model of short- to long-term outcome after stroke based on the 2002-2003 study, which could be validated on a future study conducted in Auckland. This will be useful for assessing the risk of death and disability in patients and guiding the treatment and secondary prevention of stroke and other co-morbid diseases.

9.4. Implications for Policy and Practice

The current results show small declines in the incidence of stroke with dramatic improvements in survival over time. It is also expected that the future number of stroke patients will increase even in the light of declining trends. It is important that stroke related health policies aim to reduce the number of strokes occurring through primary and secondary prevention methods, reduce the severity of strokes through the timely treatment and management of the disease and improve disability and outcome from stroke through the appropriate medium- to long-term care of the patient. Incidence reductions could be achieved through population-wide stroke prevention strategies, such as health education programs targeting smoking cessation, promoting increased physical activity and healthy eating, and reducing fat and salt content in manufactured foods. Better cardiovascular risk management in the primary health care setting will be important including established strategies complemented by new tools, such as electronic decision support and perhaps in the future by technologies such as the poly-pill.

These findings also emphasise the importance of additional community-based intervention and prevention programs targeting those at highest vascular risk, ethnic minority groups, older age groups and people with recent TIA. It was estimated that the future burden of stroke will be greater in ethnic minority groups. However, case fatality was similar between the ethnic groups in the 2002-2003 study. Therefore, the reduction of disparities due to stroke in New

Zealand will require particular efforts in primary prevention. These programs need to be tailored for specific ethnic groups and are culturally appropriate, so cultural community leaders and health-professionals need to be consulted in the development of any new programs, such as smoking interventions in Māori and nutrition education in Pacific populations. There are already a number of policies developed by the New Zealand Ministry of Health that aim to reduce disparities in health and major cardiovascular risk factors.[152, 443, 480, 481] Most of these policies involve population-wide initiatives, along with ethnic specific targets and education programs. However, the current study highlights stroke as a growing problem in New Zealand, with increasing disparities between ethnic groups which needs to be addressed in the revision of old and development of new health strategies.

The increasing number of new strokes occurring will place increased burden on an already stretched acute stroke care system. The New Zealand stroke guidelines recommend that every stroke patient should benefit from multidisciplinary care either in a stroke unit or similar.[206] However, there are only limited organised stroke care teams and units throughout New Zealand. It is important that organised stroke care is initiated in all hospitals around New Zealand, to ensure equal quality of care and essentially improving outcome after stroke. Therefore, more healthcare resources need to be invested into acute stroke services in New Zealand.

The positive improvements in survival shown in this study, will lead to an increasing number of people living with the effects of stroke, which in turn, will produce increasing numbers of patients, dependent or institutionalised. This along with declines in the length of stay in hospital will lead to increased use of post-acute care facilities and increased burden on families and informal care givers. Therefore, more medium- to long-term care facilities are needed in the future to accommodate this increased burden. However, it was shown that the increase in the net proportion of stroke patients dependent or institutionalised as a result of their stroke is likely to be small, as patients dependent or institutionalised pre- stroke are more likely to die as a result of their stroke. Given the estimates of ethnic specific projections, the nature of

long-term care will need to cater for a wide range of ethnicities and cultures. The development of Māori and Pacific Health models and strategies have identified the different philosophies towards health and home care within ethnic groups.[439, 482] The current analysis has identified stroke as a growing burden within these populations which needs to be addressed in future revisions of these strategies, highlighting stroke care and education in these groups.

It is important to educate stroke patients, and their families and carers about stroke and its related disabilities, how to care for stroke victims and the increased risk of secondary stroke and other diseases. This information needs to be cross cultural, as well as culturally specific as typical care varies between cultures. This is particularly important for Pacific ethnic groups, as it has been shown that recurrent stroke is increasing in these populations over time. There is also a need to educate the general public about the risks of stroke, as well as the typical signs and symptoms and the need to access emergency medicine as quickly as possible is needed to maximise treatment benefits in the acute phase of the disease. The initiation of stroke week in New Zealand is a good start but more frequent discussions on radio and television are needed to maintain current awareness of the disease.

10. REFERENCES

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11. APPENDICES

Appendix 1 List of ICD-9 and ICD-10 codes used to search the NZHIS database for strokes.

ICD-9 codes	
430	Subarachnoid Haemorrhage
431	Intracerebral Haemorrhage
432	Other and Unspecified Intracranial Haemorrhage
433	Occlusion and Stenosis of Precerebral Arteries
434	Occlusion of Cerebral Arteries
435	Transient Cerebral Ischaemia
436	Acute, but ill-defined cerebrovascular disease

ICD-10 codes	
G45.	Transient Cerebral Ischaemic Attacks
G46.	Vascular Syndromes
I60.	Subarachnoid Haemorrhage
I61.	Intracerebral Haemorrhage
I63.	Cerebral Infarction
I64.	Not Specified Stroke
I67.	Other Cerebrovascular Diseases
I68.	Cerebrovascular Disorders
I69.	Sequelae of Cerebrovascular Disease

Appendix 2 MEDLINE search strategy for trends in stroke.

1. exp Cerebrovascular Disorders/mo, ep, eh,et, hi [Mortality, Epidemiology, Ethnology, Etiology, History]
2. (stroke$ or poststroke$ or cva$).tw.
3. (cerebrovascular$ or cerebral vascular).tw.
4. (cerebral or cerebellar or brain$ or vertebrobasilar).tw.
5. (infarct$ or ischemi$ or ischaemic$ or thrombo$ or emboli$ or apoplexy).tw.
6. (cerebral or intracereberal or intracranial or brain$).tw.
7. (haemorrhage or hemorrhage or bleed$).tw.
8. 4 and 5
9. 6 and 7
10. 1 or 2 or 3 or 8 or 9
11. (ethn$ or incident$ or prevalen$ or case fatality or mortality or morbidity or epidemiol$).mp, hw.
12. 10 and 11
13. trend$.mp. or decline$.mp, hw. [mp=title, abstract, name of substance, mesh subject heading]
14. 12 and 13

Appendix 3 Calculations for Percentage Change in the Literature Review of Trends in Ideal Stroke Incidence Studies

Overall percentage change (OC%) was calculated from data presented in each published 'ideal' stroke trends paper, using the published standardised data, from the rate of first time period (R_F) against the rate from the last time period (R_L)[312]

$$OC\% = \frac{R_L - R_F}{R_F}.$$

Confidence intervals were calculated by using Poisson Distribution where rate $(R) = \lambda$ and $var(\lambda) = \lambda$. In this analysis $\alpha = 0.05$ was used to calculate a 95% confidence interval.

$$OC\% \pm Z_{\alpha/2}\sqrt{\text{var}(\lambda_F) + \text{var}(\lambda_L)}$$

The percentage change (C%) between sequential study periods was calculated for each study. If there were only two study periods used this was the OC%. Annual percentage change (AC%) was calculated by taking the sum of these changes between study periods and dividing by the total number of years the study covered.

$$AC\% = \frac{\sum C\%_i}{\#\,years}.$$

To calculate the confidence interval the standard deviation for the OC% was divided by the number of years the study covered.

$$AC\% \pm Z_{\alpha/2}\sqrt{\frac{\text{var}(\lambda_F) + \text{var}(\lambda_L)}{\#\,years}}.$$

Appendix 4 Calculations for Pooled Estimates in the Literature Review of Trends in Ideal Stroke Incidence Studies

For each endpoint the inverse variance method was used to calculate a fixed effects estimate of the pooled effect size of the studies.[313] The individual study effect size is denoted by, θ_i. So the weighted average of the change in estimate for the individual studies is

$$\theta_{IV} = \frac{\sum w_i \theta_i}{\sum w_i}, \text{ where } w_i = \frac{1}{se(\theta_i)^2}.$$

The standard error of θ_{IV} is given by

$$se(\theta_{IV}) = \frac{1}{\sqrt{\sum w_i}}.$$

For each endpoint a test of heterogeneity was carried out. This tests for differences between the endpoints of the studies.

$$Q = \sum w_i (\theta_i - \theta_{IV})^2.$$

When the test for heterogeneity is significant the DerSimonian and Laird random effects model was used. This is given by

$$\tau^2 = \frac{Q - (k-1)}{\sum w_i - \left(\frac{\sum w_i^2}{\sum w_i} \right)},$$

where *k-1* is the degrees of freedom for the number of studies included in the meta-analysis. The effect size of each study is then weighted using this τ^2 formula by

$$w_i' = \frac{1}{se(\theta_i)^2 + \tau^2}$$

The overall pooled random effect is given by

$$\theta_{DL} = \frac{\sum w_i' \theta_i}{\sum w_i'}, \text{ with } se(\theta_{DL}) = \frac{1}{\sqrt{\sum w_i'}}.$$

Both the fixed and random effects are presented here to show the reader the difference between the fixed and random effects models. Sensitivity analyses were also conducted where studies with extreme results were removed to check the reliability of the pooled results.

Appendix 5 Crude event rates by age (10-year age bands) and sex

	1981				1991				2002			
	Person yrs	**n**	**Rate**	**95% CI**	**Person yrs**	**n**	**Rate**	**95% CI**	**Person yrs**	**n**	**Rate**	**95% CI**
Men												
15-24	73602	6	8	(-1,17)	79485	5	6	(1,12)	87552	4	5	(0,9)
25-34	60876	10	16	(2,31)	78396	11	14	(6,22)	87084	12	14	(6,22)
35-44	48531	32	66	(34,98)	67254	34	51	(28,73)	89706	28	31	(20,43)
45-54	38998	54	138	(86,191)	48546	51	105	(73,137)	70374	81	115	(90,140)
55-64	34493	102	296	(215,377)	35316	151	428	(336,519)	45423	148	326	(273,378)
65-74	22251	224	1007	(820,1193)	25452	290	1139	(947,1332)	28173	273	969	(854,1084)
75-84	8742	216	2471	(2005,2937)	11946	252	2109	(1768,2451)	15210	277	1821	(1607,2036)
85+	1509	46	3048	(1803,4294)	2421	41	1694	(1175,2212)	3633	95	2615	(2089,3141)
Total	289002	690	239	(214,264)	348816	835	239	(218,261)	427155	918	215	(201,229)
Women												
15-24	72966	2	3	(-3,8)	79002	4	5	(0,10)	89943	3	3	(0,7)
25-34	64743	2	3	(-3,9)	81912	9	11	(4,18)	98661	6	6	(1,11)
35-44	50037	16	32	(10,54)	70629	29	41	(26,56)	97668	20	20	(12,29)
45-54	37988	42	111	(63,158)	49152	48	98	(67,129)	74385	66	89	(67,110)
55-64	35878	84	234	(163,305)	35136	91	259	(190,328)	47310	116	245	(201,290)
65-74	27561	156	566	(440,692)	30936	222	718	(587,848)	31281	187	598	(512,683)
75-84	14223	282	1983	(1655,2310)	19755	359	1817	(1577,2058)	22605	390	1725	(1554,1897)
85+	4182	132	3156	(2395,3918)	6120	206	3366	(2799,3934)	8874	295	3324	(2945,3704)
Total	307578	716	233	(209,257)	372642	968	260	(239,281)	470727	1083	230	(216,244)
Overall												
15-24	146568	8	5	(0,11)	158487	9	6	(2,9)	177495	7	4	(1,7)
25-34	125619	12	10	(2,17)	160308	20	12	(7,18)	185745	18	10	(5,14)
35-44	98568	48	49	(29,68)	137883	63	46	(32,59)	187374	48	26	(18,33)
45-54	76986	96	125	(89,160)	97698	99	101	(79,124)	144759	147	102	(85,118)
55-64	70371	186	264	(211,318)	70452	242	343	(286,401)	92733	264	285	(250,319)
65-74	49812	380	763	(654,871)	56388	512	908	(795,1021)	59454	460	774	(703,844)
75-84	22965	498	2169	(1899,2438)	31701	611	1927	(1730,2125)	37815	667	1764	(1630,1898)
85+	5691	178	3128	(2478,3778)	8541	247	2892	(2460,3324)	12507	390	3118	(2809,3428)
Total	596580	1406	236	(218,253)	721458	1803	250	(235,265)	897882	2001	223	(213,233)

Appendix 6 Crude incidence rates by age (10-year age bands) and sex

	1981				1991				2002			
	Person yrs	**n**	**Rate**	**95% CI**	**Person yrs**	**n**	**Rate**	**95% CI**	**Person yrs**	**n**	**Rate**	**95% CI**
Men												
15-24	73602	6	8	(-1,17)	79485	4	5	(0,10)	87552	4	5	(0,9)
25-34	60876	10	16	(2,31)	78396	11	14	(6,22)	87084	11	13	(5,20)
35-44	48531	26	54	(24,83)	67254	30	45	(23,66)	89706	23	26	(15,36)
45-54	38998	48	123	(74,172)	48546	43	89	(59,119)	70374	68	97	(74,120)
55-64	34493	74	215	(145,284)	35316	109	309	(232,386)	45423	110	242	(197,287)
65-74	22251	158	710	(553,867)	25452	201	790	(628,951)	28173	198	703	(605,801)
75-84	8742	150	1716	(1328,2104)	11946	155	1298	(1038,1557)	15210	189	1243	(1065,1420)
85+	1509	38	2518	(1386,3651)	2421	34	1404	(932,1876)	3633	64	1762	(1330,2193)
Total	289002	510	176	(155,198)	348816	587	143	(125,161)	427155	667	156	(144,168)
Women												
15-24	72966	2	3	(-3,8)	79002	3	4	(0,8)	89943	3	3	(0,7)
25-34	64743	2	3	(-3,9)	81912	6	7	(1,13)	98661	5	5	(1,10)
35-44	50037	16	32	(10,54)	70629	28	40	(25,54)	97668	16	16	(8,24)
45-54	37988	32	84	(43,126)	49152	39	79	(51,108)	74385	57	77	(57,97)
55-64	35878	70	195	(130,260)	35136	74	211	(146,275)	47310	94	199	(159,239)
65-74	27561	102	370	(269,472)	30936	172	556	(437,675)	31281	138	441	(368,515)
75-84	14223	200	1406	(1131,1682)	19755	257	1301	(1096,1505)	22605	249	1102	(965,1238)
85+	4182	96	2296	(1646,2945)	6120	139	2271	(1833,2709)	8874	194	2186	(1879,2494)
Total	307578	520	169	(149,190)	372642	718	172	(154,190)	470727	756	161	(149,172)
Overall												
15-24	146568	8	5	(0,11)	158487	7	4	(1,8)	177495	7	4	(1,7)
25-34	125619	12	10	(2,17)	160308	17	11	(6,16)	185745	16	9	(4,13)
35-44	98568	42	43	(24,61)	137883	58	42	(29,55)	187374	39	21	(14,27)
45-54	76986	80	104	(72,136)	97698	82	84	(63,105)	144759	125	86	(71,101)
55-64	70371	144	205	(157,252)	70452	183	260	(209,310)	92733	204	220	(190,250)
65-74	49812	260	522	(432,612)	56388	373	661	(564,759)	59454	336	565	(505,626)
75-84	22965	350	1524	(1298,1750)	31701	412	1300	(1139,1460)	37815	438	1158	(1050,1267)
85+	5691	134	2355	(1791,2918)	8541	173	2026	(1684,2367)	12507	258	2063	(1811,2315)
Total	596580	1030	173	(158,188)	721458	1305	181	(168,194)	897882	1423	158	(150,167)

Appendix 7 Age-specific crude event rates by ethnicity per 100,000 in Auckland, New Zealand, 1981-2003.

	1981-1982				1991-1992				2002-2003			
Age group	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**
NZ/European												
15-64	422202	276	65	(55-76)	459267	293	64	(55-73)	501426	269	54	(47-60)
65-74	47481	354	746	(636-855)	52125	459	881	(764-997)	48633	303	623	(553-693)
75-84	22209	488	2197	(1922-2473)	30303	579	1911	(1709-2113)	34332	568	1654	(1518-1791)
85+	5577	174	3120	(2464-3776)	8253	241	2920	(2477-3364)	11790	345	2926	(2617-3235)
Total	497469	1292	260	(240-280)	549948	1572	286	(267-305)	596181	1485	249	(236-262)
Māori												
15-64	52179	46	88	(52-124)	63762	58	91	(63-119)	77742	60	77	(58-97)
65-74	1266	10	790	(98-1482)	1344	8	595	(183-1008)	2292	24	1047	(628-1466)
75-84	336	6	1786	(-235-3806)	429	14	3263	(1554-4973)	654	15	2294	(1133-3454)
85+	51	0	0	(0-0)	72	2	2778	(-1072-6628)	144	5	3472	(429-6516)
Total	53832	62	115	(75-156)	65607	82	125	(94-156)	80832	104	129	(104-153)

Appendix 7 Age-specific crude event rates by ethnicity per 100,000 in Auckland, New Zealand, 1981-2003.

	1981-1982				1991-1992				2002-2003			
Age group	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**	**N**	**n**	**Rate**	**(95% CI)**
Pacific												
15-64	33672	22	65	(27-104)	64506	65	101	(74-127)	89724	88	98	(78-119)
65-74	741	10	1350	(167-2532)	2025	33	1630	(899-2360)	3840	67	1745	(1327-2163)
75-84	213	0	0	(0-0)	597	13	2178	(536-3819)	1392	39	2802	(1922-3681)
85+	33	0	0	(0-0)	108	2	1852	(-715-4418)	246	8	3252	(999-5506)
Total	34659	32	92	(47-138)	67236	113	168	(131-205)	95202	202	212	(183-241)
Asian & Other												
15-64	10059	6	60	(-8-127)	37293	17	46	(17-74)	119214	64	54	(41-67)
65-74	324	6	1852	(-244-3947)	894	12	1342	(268-2416)	4689	55	1173	(863-1483)
75-84	207	4	1932	(-746-4611)	372	5	1344	(166-2522)	1437	34	2366	(1571-3161)
85+	30	4	13333	(-5146-31812)	108	2	1852	(-715-4418)	327	10	3058	(1163-4954)
Total	10620	20	188	(72-305)	38667	36	93	(54-132)	125667	163	130	(110-150)