Establishing high quality, integrated data for chronic disease management plans and secondary prevention medications and their effectiveness for patients after stroke: a substudy of STANDFIRM

A thesis submitted for the degree of *Doctor of Philosophy*

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Summary

Cardiovascular diseases (CVDs) encompass a range of acute and chronic conditions, such as stroke, and were responsible for 17.8 million deaths globally in 2017.[1] Almost 70,000 Australians were hospitalised for stroke in 2020.[2] Furthermore, approximately 32% to 43% of survivors of stroke will have a recurrent stroke within 5 to 10 years.[3] The current population of 445,000 survivors of stroke is estimated to grow to 820,000 survivors by 2050, if no action is taken.[2] This represents a considerable burden on the Australian population, health system and economy.[2]

Stroke and other CVDs have been identified as one of the Australian National Health Priority Areas for more than 20 years.[4] Stroke is one of the costliest disease groups in Australia. Each year, it costs approximately $6.2 billion in direct financial costs, and $26.0 billion due to premature mortality and short- and long-term disability.[2] Despite evidence for the contribution of risk factors to the burden of stroke, almost one half of Australians do not understand that stroke can be prevented.[5] This gap in the knowledge of risk factors among Australians represents a missed opportunity to prevent stroke through management of these modifiable risk factors.

In Chapters 1 and 2, I present the rationale, themes, aims and relevant background regarding stroke. In Chapter 3, I provide an overview of the importance and overall use of Medicare-subsidised Chronic Disease Management (CDM) plans in both Australia and a randomised controlled trial of patients with stroke. In this trial, the intervention comprised an individualised CDM plan and in-home tailored education about stroke prevention. Patient outcomes that were investigated at 12 months after stroke included overall cardiovascular risk factor profile and knowledge of medications. Compared with usual care, the intervention demonstrated little to no effect on outcomes in the intention-to-treat analyses of these

published studies. It was suspected that this lack of treatment effect was due to changing practice over time, whereby there was an increased uptake of CDM for not only the intervention group, but also the usual care group. Using linked data from Medicare and other national and state database sources I was able to examine this possibility and found that, at 12 months after recruitment, 64% in the intervention group and 36% in the usual care group were provided a CDM plan. This then enabled me to compare outcomes in patients who were given CDM plans with those who were not.

In Chapter 4, I detail the utility, strengths and limitations of using linked administrative data within a topical review published in *Stroke*, while in Chapter 5, I outline the application processes and datasets involved in my analyses.

In Chapters 6 and 7, which include two manuscripts that were submitted to the *Medical Journal of Australia*, I investigate how increasing exposure to CDM plans may affect CVD-related readmissions and adherence to secondary prevention medications after stroke. I found that at three years after stroke, being on a CDM plan for a longer duration (quintiles) was associated with fewer CVD-related readmissions (incidence rate ratio 0.86, 95% Confidence Interval (CI) 0.75-0.98, p=0.023) and adherence to antihypertensive (Odds Ratio (OR) 1.18, 95% CI 1.00-1.40, p=0.029) and antithrombotic medications (OR 1.22, 95% CI 1.03-1.46, p=0.024), but not lipid-lowering medications. In Chapter 8, which includes my paper published in the *British Journal of Clinical Pharmacology*, I found that the assumption of one dose per day was acceptable for estimating dosage for most medications, but not for medications that had large variations in prescribed daily dose. For example, 11.4% of patients were dispensed beta blockers within one year after stroke at an estimated rate of 2 pills/day.

The results from this thesis provide evidence that CDM plans may serve as a mechanism through which patients with strokes may be: (1) better managed, (2) are encouraged to control their modifiable risk factors and (3) return to consult with their GP.

Declaration

This thesis is an original work of my research and contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Signature:

Print Name: David Ung

Date: 24/11/2020

Thesis Including Published Works Declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes 2 original papers published in peer-reviewed journals and 2 submitted papers. The core theme of this thesis is ***Establishing high quality, integrated data for chronic disease management plans and secondary prevention medications and their effectiveness for patients after stroke: a substudy of STANDFIRM***. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the ***Epidemiology and Prevention division, Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University*** under the supervision of ***Professor Amanda Thrift, Associate Professor Monique Kilkenny*** and ***Professor Velandai Srikanth***.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of Chapters 4, 6, 7 and 8, my contribution to the work involved the following:

Thesis Chapter	**Publication Title**	**Status** *(published, in press, accepted or returned for revision, submitted)*	**Nature and % of student contribution**	**Co-author name(s) Nature and % of Co-author's contribution**	**Co-author(s), Monash student Y/N***
4	Promising Use of Big Data to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Research	Published	68%. Concept, literature search, analysis, interpretation and writing of first draft	1. **Joosup Kim**, input into manuscript 4% 2. **Amanda G Thrift**, input into manuscript 3% 3. **Dominique A Cadilhac**, input into manuscript 3% 4. **Nadine E Andrew**, input into manuscript 3% 5. **Vijaya Sundararajan**, input into manuscript 3% 6. **Moira K Kapral**, input into manuscript 3% 7. **Mathew Reeves**, input into manuscript 3% 8. **Monique F Kilkenny**, contributed to concept and interpretation, input into manuscript 10%	1. No 2. No 3. No 4. No 5. No 6. No 7. No 8. No
6	Longer duration on a chronic disease management plan is associated with fewer cardiovascular disease-related readmissions within 3 years of stroke	Submitted	59%. Concept, data collection and management, statistical analysis, interpretation and writing of first draft	1. **Richard P Gerraty**, contributed to data collection, input into manuscript 8% 2. **Judith Frayne**, contributed to data collection, input into manuscript 8% 3. **Monique F Kilkenny**, input into manuscript 3% 4. **Muideen T Olaiya**, input into manuscript 3% 5. **Joosup Kim**, input into manuscript 2% 6. **Thanh Phan**, input	1. No 2. No 3. No 4. No 5. No 6. No

				into manuscript 1% 7. **Dominique A Cadilhac**, input into manuscript 1% 8. **Henry Ma**, input into manuscript 1% 9. **Helen M Dewey**, input into manuscript 1% 10. **Mark R Nelson**, input into manuscript 1% 11. **Velandai K Srikanth**, input into manuscript 1% 12. **Christopher F Bladin**, input into manuscript 1% 13. **Sharyn M Fitzgerald**, input into manuscript 1% 14. **Amanda G Thrift**, conceived the study, interpretation, input into manuscript 9%	7. No 8. No 9. No 10. No 11. No 12. No 13. No 14. No
7	Longer duration on a Chronic Disease Management plan is associated with long-term adherence to antihypertensive and antithrombotic medications following stroke	Submitted	73%. Concept, data collection and management, statistical analysis, interpretation and writing of first draft	1. **Monique F Kilkenny**, contributed to concept, input into manuscript 5% 2. **Muideen T Olaiya**, input into manuscript 3% 3. **Joosup Kim**, input into manuscript 2% 4. **Thanh Phan**, input into manuscript 1% 5. **Dominique A Cadilhac**, input into manuscript 1% 6. **Henry Ma**, input into manuscript 1% 7. **Helen M Dewey**, input into manuscript 1% 8. **Mark R Nelson**, input into manuscript 1% 9. **Velandai K Srikanth**, input into manuscript 1%	1. No 2. No 3. No 4. No 5. No 6. No 7. No 8. No 9. No

				10. **Richard P Gerraty**, input into manuscript 1% 11. **Christopher F Bladin**, input into manuscript 1% 12. **Sharyn M Fitzgerald**, input into manuscript 1% 13. **Amanda G Thrift**, contributed to interpretation, input into manuscript 8%	10. No 11. No 12. No 13. No
8	Assuming one dose per day yields a similar estimate of medication adherence in patients with stroke: an exploratory analysis using linked registry data	Published	60%. Concept, literature search, data management, statistical analysis, interpretation and writing of first draft	1. **Lachlan L Dalli**, contributed to literature search, statistical support, input into manuscript 20% 2. **Derek Lopez**, statistical support, input into manuscript 5% 3. **Frank M Sanfilippo**, input into manuscript 3% 4. **Joosup Kim**, input into manuscript 3% 5. **Nadine E Andrew**, input into manuscript 1% 6. **Amanda G Thrift**, input into manuscript 1% 7. **Dominique A Cadilhac**, input into manuscript 1% 8. **Craig S Anderson**, input into manuscript 1% 9. **Monique F Kilkenny**, contributed to concept, input into manuscript 5%	1. Yes 2. No 3. No 4. No 5. No 6. No 7. No 8. No 9. No

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Student name: David Ung

Student signature: Date: 24/11/2020

I hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor name: Amanda G Thrift

Main Supervisor signature: Date: 24/11/2020

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I am deeply indebted to my family for their unwavering support towards not only my PhD, but also my entire educational journey. Last but not least, I am profoundly grateful for my best friend Michael Lewis. You have taken care of my mind, enriched my life and strengthened my resolve to complete my PhD and strive to do better. Thank you from the bottom of my heart.

Publications Included in Thesis

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- **[Chapter 4:]** Ung D, Kim J, Thrift AG, Cadilhac DA, Andrew NE, Sundararajan V, Kapral MK, Reeves M, Kilkenny MF. Promising Use of Big Data to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Research. *Stroke*. 2019;50:1302-1309. Available from: https://doi.org/10.1111/bcp.14468.
- **[Chapter 8:]** Ung D, Dalli LL, Lopez D, Sanfilippo FM, Kim J, Andrew NE, Thrift AG, Cadilhac DA, Anderson CS, Kilkenny MF. Assuming one dose per day yields a similar estimate of medication adherence in patients with stroke: an exploratory analysis using linked registry data. *Br. J. Clin. Pharmacol*. 2020. Available from: https://doi.org/10.1111/bcp.14468.

Other Publications

- Olaiya MT, Cadilhac DA, Kim J, Ung D, Nelson MR, Srikanth VK, Bladin CF, Gerraty RP, Fitzgerald SM, Phan TG, Frayne J, Thrift AG. Nurse-Led Intervention to Improve Knowledge of Medications in Survivors of Stroke or Transient Ischemic Attack: A Cluster Randomized Controlled Trial. *Frontiers in Neurology*. 2016;7:205. Available from: https://doi.org/10.3389/fneur.2016.00205
- Olaiya MT, Cadilhac DA, Kim J, Ung D, Nelson MR, Srikanth VK, Bladin CF, Gerraty RP, Fitzgerald SM, Phan TG, Frayne J, Thrift AG. Effectiveness of an intervention to improve risk factor knowledge in patients with stroke: a randomized controlled trial. *Stroke*. 2017;48(4):1101-1103. Available from: https://doi.org/10.1161/STROKEAHA.116.016229.

Published Abstracts

ORCID: https://orcid.org/0000-0002-7931-6387

- Ung D, Gerraty RP, Frayne J, Olaiya MT, Kim J, Srikanth VK, Phan T, Cadilhac DA, Nelson MR, Bladin CF, Thrift AG. Abstract P147: Longer Duration on a Chronic Disease Management Plan is Associated with Fewer CVD-Related Readmissions by 3 Years Among Australian Survivors of Stroke. *Circulation*. 2019;139:AP147.

- Ung D, Gerraty RP, Frayne J, Olaiya MT, Kim J, Srikanth VK, Phan T, Cadilhac DA, Nelson MR, Bladin CF, Thrift AG. Abstract P375: Using a Recalibrated Cardiovascular Disease Risk Score is Not Adequate to Predict Risk of Recurrence Within 3 Years in Australian Survivors of Stroke. *Circulation*. 2019;139:AP375.

- Ung D, Gerraty RP, Frayne J, Olaiya MT, Kim J, Srikanth VK, Phan T, Cadilhac DA, Nelson MR, Bladin CF, Thrift AG. Abstract TP396: Accuracy of Administrative Hospital, Emergency Department and Death Records. *Stroke*. 2019;50:ATP396.

Conferences and Invited Presentations

1. **2020 International Population Data Linkage Network Conference** (Online)
    i. [Live Oral Presentation] Longer duration on a Chronic Disease Management plan is associated with long-term adherence to antihypertensive and antithrombotic medications following stroke
2. **2019 International Stroke Conference** (Honolulu, Hawaii)
    i. [Poster] Accuracy of Administrative Hospital, Emergency Department and Death Records
3. **2019 EPI | Lifestyle Scientific Sessions** (Houston, Texas)
    i. [Poster] Longer Duration on a Chronic Disease Management Plan is Associated with Fewer CVD-Related Readmissions by 3 Years Among Australian Survivors of Stroke
    ii. [Poster] Using a Recalibrated Cardiovascular Disease Risk Score is Not Adequate to Predict Risk of Recurrence Within 3 Years in Australian Survivors of Stroke
4. **2018 Stroke Conference (Stroke Foundation) – Bridging the continuum** (Sydney)
    i. [Oral Presentation] Effectiveness of recalibrating a cardiovascular disease risk score to predict risk of recurrence within Australian survivors for stroke
5. **2018 National Stroke Data and Quality Improvement Workshop** (Melbourne)
    i. [Oral Presentation] Using linked data (MBS/PBS/Hospital/NDI) in the STANDFIRM trial
6. **2017 Department of Medicine 3 Minute Thesis (3MT) round** (Melbourne)
    i. [Oral Presentation] The missing data link in stroke care

Media

- A news article was published in *NeuroNews* based on the publication presented in Chapter 4 and is available at https://neuronewsinternational.com/issue-34/ (pages 1-2).

Awards

- Australian Government Research Training Program Scholarship (2016-2019)
- People's Choice award at Department of Medicine's Three Minute Thesis competition (2017)

Committees and Other Groups

- Chair of Stroke and Ageing Research Group Scientific Meetings held monthly (2018)
- Member of the National Stroke Data Linkage Interest Group (quarterly meeting)

List of Abbreviations

1DD	One dose per day
ACEI	Angiotensin-converting enzyme inhibitors
AIHW	Australian Institute of Health and Welfare
ATC	Anatomical Therapeutic Chemical
BP	Blood pressure
CDM	Chronic Disease Management
CI	Confidence interval
CVD	Cardiovascular disease
CVDL	Centre for Victorian Data Linkage
DBP	Diastolic blood pressure
ED	Emergency department
GP	General practitioner
GPMP	General practitioner Management Plan
HDL-C	High-density lipoprotein cholesterol
ICD-10-AM	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification
IMP	Individualised management plan
IRR	Incidence rate ratio
LDL-C	Low-density lipoprotein cholesterol
MADIP	Multi-Agency Data Integration Project
MBS	Medicare Benefits Schedule
MELDA	Multi-source Enduring Linked Data Asset
NDI	National Death Index
NIHSI AA	National Integrated Health Services Information Analysis Asset
PBS	Pharmaceutical Benefits Scheme
PDC	Proportion of days covered
PDD	Prescribed daily dose
RPBS	Repatriation Pharmaceutical Benefits Scheme
SAP	Statistical analysis plan
SBP	Systolic blood pressure
STANDFIRM	Shared Team Approach between Nurses and Doctors For Improved Risk factor Management
SURE	Secure Unified Research Environment
TCA	Team Care Arrangement
TIA	Transient ischaemic attack
VAED	Victorian Admitted Episodes Dataset
VEMD	Victorian Emergency Minimum Dataset

Chapter 1: Thesis Introduction, Objectives and Outline of Chapters

1.1 Introduction

This thesis will address the topic of 'establishing high quality, integrated data for chronic disease management plans and secondary prevention medications and their effectiveness for patients after stroke'.

Most of the analyses presented throughout this thesis were derived from patient-level data that had been linked from various national- and state-based datasets. Figure 1.1 outlines the datasets that were used for each chapter of my thesis. These datasets and the processes involved with linking data are primarily described in Chapters 4 and 5.

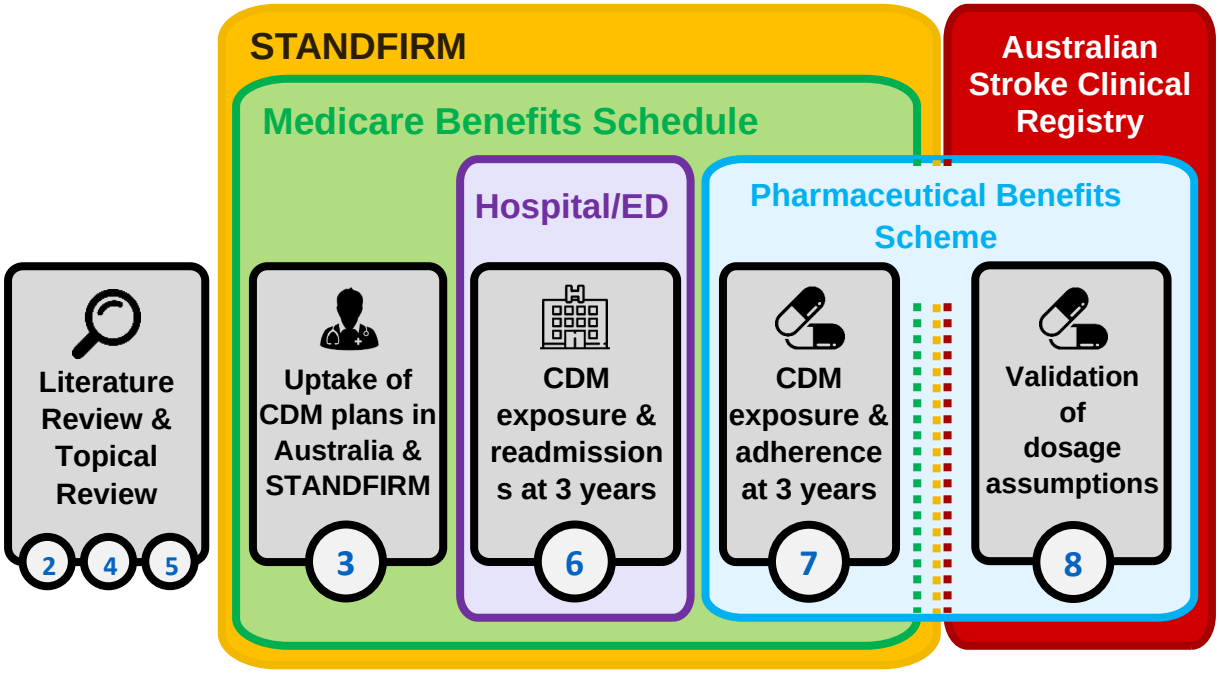


Figure 1.1. Overview of thesis topics (grey), associated chapters (circled) and the involved datasets within each.

Coloured areas that overlap denote which datasets were linked together.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; ED, emergency department; CDM, Chronic Disease Management.

1.2 Electronic Thesis Navigation

The electronic version of this thesis features hyperlinks and hexagonal icons. All icons and in-text mentions of parts, chapters, sections, tables and figures can be left-clicked to navigate to the corresponding location in this thesis (Figure 1.2). This also includes each figure and table listed within the List of Tables and List of Figures. Table and figure titles can also be left-clicked to return to the location of its first mention within the thesis. Some of the icons used throughout this thesis were made by *Freepik*, *Roundicons Freebies* and *Those Icons* from www.flaticon.com.

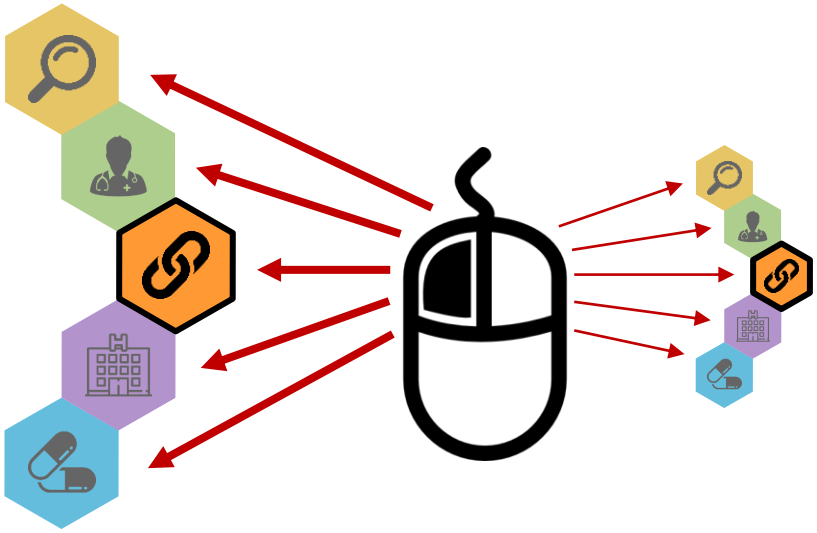


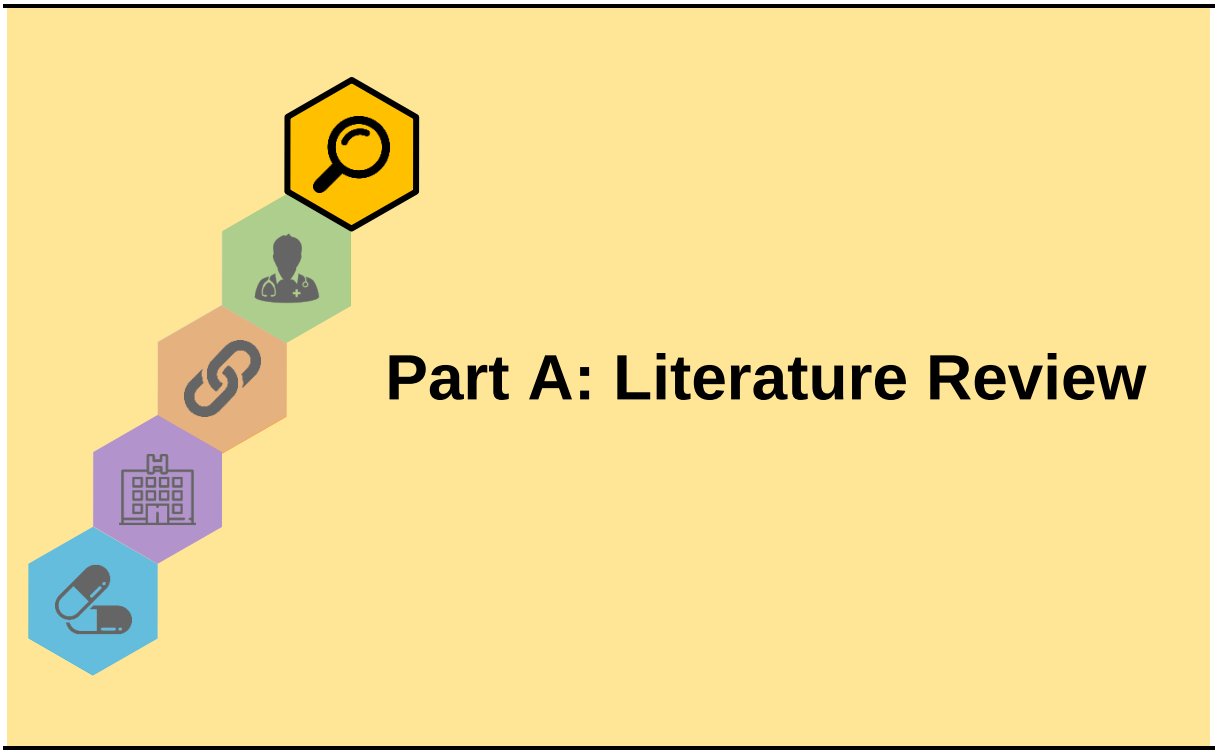
Figure 1.2. Left-clickable icons for electronic thesis navigation.
Hexagonal icons with a black border indicates the current Part (A-E) location in this thesis.

1.3 Thesis Objectives and Aims

The objective of this doctoral project was to examine how Chronic Disease Management (CDM) plans may improve outcomes after stroke by analysing linked data from clinical trial and administrative databases. The major themes and specific aims are provided below in Table 1.1. Chapters 4 and 8 have been published in peer-reviewed journals (*Stroke* and *British Journal of Clinical Pharmacology*), while the manuscripts in Chapters 6 and 7 have been submitted to the *Medical Journal of Australia*.

Table 1.1. Navigation icons and outline of thesis parts and specific aims of each chapter.

	Part:	**Part titles, chapters and specific aims of each chapter:**
	A	**Literature Review** **2)** To provide a summary of the current literature surrounding the epidemiology, impact, burden and modifiable risk factors of stroke.
	B	**Chronic Disease Management (CDM) Plans and the STANDFIRM trial** **3)** To determine the uptake of CDM plans in Australia and patients after stroke or transient ischaemic attack.
	C	**Understanding Data Linkage Within Australia: Strengths and Limitations to Investigate Outcomes After Stroke** **4)** To describe the utility, strengths, limitations and barriers of linking and using administrative data for stroke research. **5)** To describe the datasets, application process and barriers related to the data linkage used for this thesis project.
	D	**Effectiveness of CDM Plans Towards Rehospitalisations After Stroke** **6)** To determine whether being on a CDM plan for a longer duration is associated with a reduced recurrence rate of cardiovascular disease-related readmissions after stroke.
	E	**Effectiveness of CDM Plans Towards Medication Adherence After Stroke** **7)** To determine whether a longer duration on a CDM plan was associated with adherence to recommended secondary prevention medications after stroke. **8)** To compare three metrics for estimating duration covered by medications and assess whether this affects adherence to antihypertensive treatment among survivors of stroke in Australia.


Part A: Literature Review

Chapter 2: Epidemiology, Impact, Burden and Risk Factors of Stroke

2.1 Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, being responsible for 17.8 million deaths in 2017.[1] CVDs encompass a range of acute and chronic conditions, such as stroke, and carry a severe burden of morbidity and mortality in most countries.[1] The most recent definition for stroke, based on a consensus from the American Heart Association, incorporates a broad set of clinical and tissue criteria, whereby "*Central nervous system infarction is defined as brain, spinal cord, or retinal cell death attributable to ischemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury. Central nervous system infarction occurs over a clinical spectrum*".[6] The definition broadly includes ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage.

Almost 70,000 Australians were hospitalised for stroke in 2020 with 56% being male.[2] Furthermore, approximately 32% to 43% of survivors of stroke will have a recurrent stroke within 5 to 10 years and join a growing estimated population of 445,000 survivors of stroke, who may also be dependent on carers for activities of daily living.[2, 3] From a 2016 Swedish study of carers of patients 3 to 5 years after their stroke, 10% of patients were completely dependent on a caregiver and 33% were partially dependent.[7] Furthermore, it is estimated that by 2050, if no action is taken, the number of survivors of stroke could rise by more than 80% to almost 820,000 Australians.[2] This points towards a growing prevalence of the Australian population with stroke having at least some degree of cognitive impairment, handicap or disability.

Stroke and other CVDs have been identified as one of the Australian National Health Priority Areas for more than 20 years.[4] As a result of improvements in treatment and risk factors for stroke in Australia, the annual mortality rate has decreased from 71 per 100,000 people in 1988 to 26 per 100,000 people in 2018, representing an approximate 28% decrease with each decade.[8, 9] Despite this, incident and recurrent stroke remains a considerable burden on the population, health system and economy.[2]

2.2 Risk of Recurrence and Mortality After Stroke

Two serious consequences of stroke include an increased risk of recurrent stroke and mortality. Researchers in Australia found that the case-fatality at 30 days was 41% in those with a recurrent stroke, this being almost double that of the incident stroke (22%).[3] Furthermore, after 10 years of follow-up among those with an incident stroke, the risk of recurrent stroke was six times greater than the risk of the incident stroke in the general population.[3] In the global context, recurrence rates of stroke vary widely between regions. Overall, a worldwide meta-analysis of hospital- and community-based registries from 13 studies revealed that the pooled cumulative risk of a recurrent stroke, after an incident stroke, increased from 3% at 30 days to 39% at 10 years (Figure 2.1).[10]

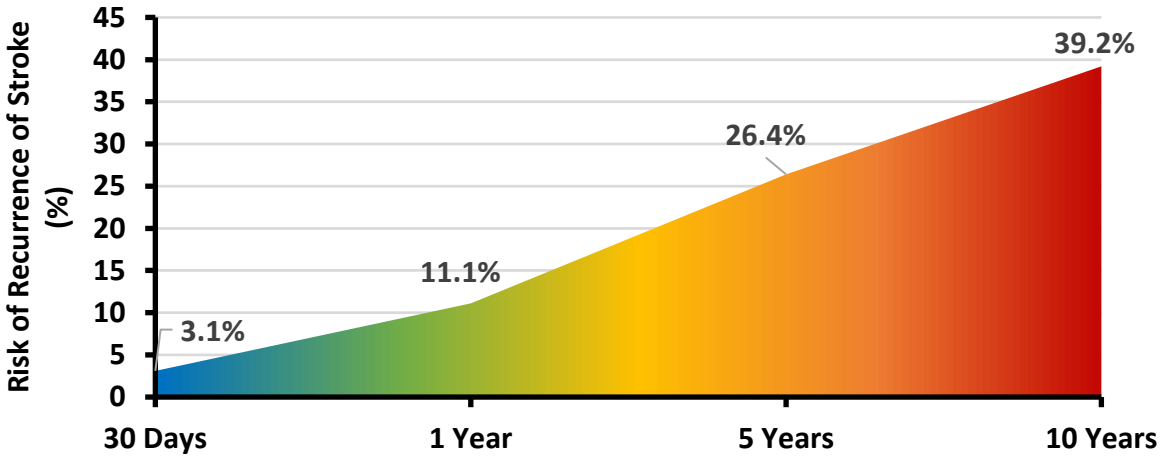


Figure 2.1. Risk of recurrent stroke over 10 years after the incident stroke.
Based on a meta-analysis of 9,115 survivors of stroke from 13 studies by Mohan et al.[10]

2.3 Costs

Stroke is one of the costliest disease groups in Australia. By 2020, stroke is expected to affect 820,000 Australians if nothing is done to reduce the number of incident strokes occurring.[2] The estimated average lifetime cost of having a stroke is approximately $103,566 AUD ($68,769 USD) per case of ischaemic stroke and $82,764 AUD ($54,956 USD) for intracerebral haemorrhage.[11] The overall economic impact of stroke in Australia has been estimated at $6.2 billion in direct financial costs each year, with an even greater cost of $26.0 billion attributable to premature mortality and short- and long-term disability.[2] Because stroke can be incredibly debilitating in terms of financial costs and disease burden, there is considerable incentive to preventing incident and recurrent strokes with better control and management of risk factors.

2.4 Risk Factors Associated With Stroke

Many risk factors for stroke are modifiable, in that they can be changed through 'modifications' to either behaviours, exposures or treatment. Modifiable risk factors that are associated with increasing the likelihood of stroke include hypertension (high blood pressure), dyslipidaemia (high blood cholesterol) and many others (Table 2.1).[12-17] Factors that cannot be changed are referred to as non-modifiable risk factors, such as sex (e.g. young men are at greater risk than young women), age, family history and race (e.g. risk of stroke is greater in black Americans than white Americans).[13]

Table 2.1. Major modifiable and non-modifiable risk factors for stroke.[12-14, 16, 17]

Modifiable	Non-modifiable
• Hypertension (high blood pressure)	• Age
• Dyslipidaemia (or high cholesterol)	• Sex
• Overweight/Obesity	• Genetics / Family History
• Diet	• Socio-economic environment
• Physical inactivity	
• Smoking	
• Alcohol consumption	
• Atrial fibrillation	
• Diabetes mellitus	
• Left ventricular hypertrophy	

Based on the INTERSTROKE case-control study of around 27,700 participants with stroke in 32 countries across the globe, the authors reported that more than 80% of strokes are potentially preventable with better management and control of ten common modifiable risk factors.[16] The ten risk factors that they examined were hypertension, smoking, waist-to-hip ratio, diabetes, physical activity, diet, alcohol intake, psychosocial factors, apolipoproteins and cardiac causes. Many of these risk factors are responsible for a significant proportion of the total disease burden in Australia (Figure 2.2).[15] In Australia, 96% of people who have suffered a stroke have two or more risk factors.[18] This is important as the risk of stroke is cumulative, with those having multiple risk factors being at greatest risk of incident or recurrent stroke.[19]

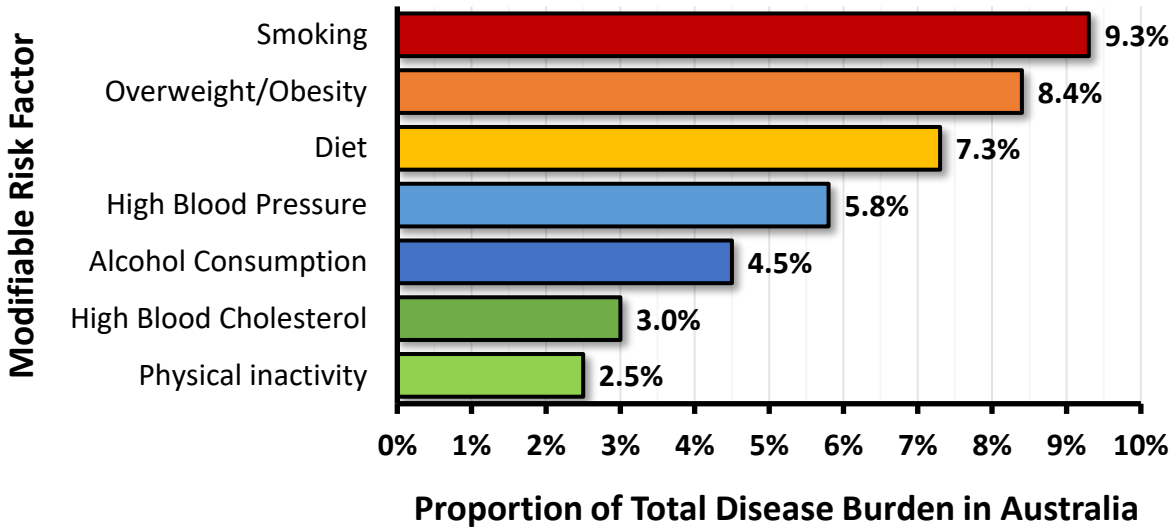


Figure 2.2. Proportion of total disease burden in Australians attributable to certain modifiable risk factors.[15]

Figure reproduced from estimates by the Australian Institute of Health and Welfare (2019), who estimated that 37.5% of the total disease burden in Australians was due to these modifiable risk factors.[15] Each risk factor was analysed independently and so these percentages cannot be combined to estimate the joint effect.

Despite evidence for the contribution of risk factors to the burden of stroke, knowledge about risk factors is poor in Australia, even in those who have suffered a stroke. In those recruited to a clinical trial of management following stroke, almost one third of two-year survivors were unable to name any risk factor, 40% could name at least one risk factor, while another third could name at least two risk factors.[20] This poor knowledge is also reinforced by findings from the Stroke Foundation, whereby awareness of risk factors was low in the community and almost one half of the Australians sampled did do not understand that stroke could be prevented.[5] This gap in knowledge of risk factors among Australians represents a missed opportunity to prevent stroke through management of these modifiable risk factors. In the following sections, I will limit my discussion of risk factors to those that are modifiable and can be treated with secondary prevention medications to improve management and reduce CVD events, this being the focus of my thesis.

2.4.1 Hypertension (High Blood Pressure)

For adults in Australia, hypertension is arbitrarily defined as use of antihypertensive medications or as having a blood pressure (BP) of at least 140 mmHg systolic and/or 90 mmHg diastolic. Those with a BP ranging from 120-139 mmHg systolic BP (SBP) and 80-89 mmHg diastolic BP (DBP) are classified as having prehypertension.[21] Furthermore, those with a SBP of 160 mmHg or greater, or a DBP of 100 mmHg or greater, are classified as having stage 2 hypertension.

Almost a fifth (22.8% or 4.3 million) of Australians had hypertension in 2017-18.[22] It accounted for 19% or 10.8 million of all deaths around the world in 2019 and remains the most important risk factor for mortality.[23] Those with hypertension have a three-fold increase in the risk of stroke than those with a normal BP.[16] In addition, despite BP being lower than in a hypertensive state, prehypertension still presents a greater risk of CVD than a normal BP of 120/80 mmHg or below.[21] Patients at stage 2 are recommended more intensive medical and lifestyle interventions, due to the high risk of mortality, stroke severity and risk of other CVD events.[24]

In a meta-analysis of 61 prospective observational studies, the relative risk of vascular complications in adults aged 50-89 years remained similar in those having a SBP up to 115 mmHg.[25] However, once SBP surpassed 115 mmHg, for ages 50-69 years, the relative risk of death, from stroke and other vascular events, approximately doubled for each consecutive rise of 20 mmHg.[25] Ultimately, a SBP of 180 mmHg at age 50-59 years, conferred a 16-fold risk of death compared to that at 115 mmHg. This demonstrates that SBP, above 115 mmHg, is a strong risk factor associated with stroke in older adults. Therefore, efforts to reduce BP, such as the use of antihypertensive medications, are likely to have a significant impact towards preventing future strokes.

Antihypertensive medications are commonly used to lower BP in those with hypertension with the aim of reducing BP to less than 140/90 mmHg, or among those with diabetes mellitus to less than 130/80 mmHg.[26] The American Heart Association recommends managing patients to these targets as being important to reduce stroke recurrences, improve survival, and improve health outcomes following stroke.[27] These medications commonly include angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor antagonists, calcium channel blockers and beta blockers, which exert their BP-lowering effects through different physiological mechanisms.[27]

Katsanos et al. recently undertook a meta-regression analysis to investigate the role of antihypertensive treatments on health outcomes following stroke.[28] Their analysis included 14 randomised controlled trials of varying drug classes of antihypertensive medications utilised for the secondary prevention of stroke and transient ischaemic attack (TIA).[28] The meta-regression analysis provided evidence that antihypertensive treatment, compared with placebo, lowered the risk of recurrent stroke by 27%, disabling or fatal stroke by 29% and cardiovascular-related death by 15%.[28] In a similar meta-regression analysis using a random effects model, Rashid et al. found that polytherapy with the combination of a diuretic with an ACEI was more effective at reducing the risk of stroke (risk ratio, 0.55; 95% confidence interval [CI], 0.44–0.68) than monotherapy with a diuretic (0.68; 0.50–0.92), beta blocker (0.93; 0.72–1.20) or ACEI (0.93; 0.75–1.14).[29] Based on evidence such as this, the Australian Stroke Foundation's *Clinical Guidelines for Stroke Management 2017* now includes a weak recommendation for dual therapy of an ACEI with a diuretic for those with stroke and a SBP of 120-140 mmHg, a recommendation that was not previously included in their 2010 guidelines.[30]

Promoting adherence to secondary prevention medications is one of the major recommendations for long-term care outlined in the Australian Stroke Foundation's clinical guidelines.[30] This is important as it has been estimated that up to 9% of all cardiovascular events can be directly attributed to poor adherence to medications.[31] However, the current proportion of patients with stroke being discharged from hospital with antihypertensive medications is approximately 77% in 2020, with a target benchmark of 91% to improve stroke care.[2] Another target benchmark is achieving an overall prevalence of 17% for uncontrolled hypertension in the Australian population (down from the current prevalence of 23%). Sub-optimal adherence to medications (non-adherence prevalence ≈ 26%) and prescription data in Australia indicate that there are many opportunities to reduce further strokes and other vascular events in the community.[31, 32]

2.4.2 Hypercholesterolaemia (High Blood Cholesterol) or Dyslipidaemia

There is some conflicting evidence across the literature regarding how high blood cholesterol (hypercholesterolaemia), which refers to a state of abnormal or elevated serum cholesterol, acts as a risk factor for stroke. The variations can be complex and appear to differ according to the type of stroke and to the type of cholesterol, i.e. high-density lipoprotein cholesterol (HDL-C) or low-density lipoprotein cholesterol (LDL-C). In Australia, high blood cholesterol is recognised as a risk factor for CVD and affects 8% of Australians.[33] This is particularly prevalent at older ages, whereby the proportion of Australians with high blood cholesterol increases by 7%, starting from age 45-54 years (7%), with each increase in age group by a decade (14% of those aged 55-64 years and 21% of 65 years or older).[33]

Cholesterol is primarily transported by serum LDL-C. Higher concentrations of LDL-C in the blood can lead to atherosclerosis: a process by which increased deposition of fatty material on the inner walls of blood vessels causes the formation of atherosclerotic plaques.[34, 35]

Consequently, thrombosis or clot formation may occur due to the narrowing or rupturing of these affected vessels.[35] Researchers from a prospective multicentre hospital-based study in 2001 found that dyslipidaemia was prevalent in patients who suffered an atherothrombotic stroke.[36] In a meta-analysis of data from 170,000 participants in 26 randomised controlled trials with statin therapy versus control, Baigent et al. calculated that per 1.0 mmol/L (≈38.6 mg/dL) reduction in LDL-C, the risk of one-year all-cause mortality was reduced by 10% and risk of major vascular events was reduced by 22%.[37]

In contrast to the mechanism of LDL-C, HDL-C can function to remove excess cholesterol from peripheral tissues and protect against atherosclerosis.[35] This protective relationship has been demonstrated in a pooled cohort of four large population studies without baseline atherosclerotic CVD and a median HDL-C of 1.24 mmol/L (48 mg/dL).[38] Singh et al. found patients with a HDL-C of 1.48 mmol/L or greater (highest quartile) had a 24% reduced relative risk of myocardial infarction and stroke compared with patients with a HDL-C of 1.04 mmol/L or lower (lowest quartile).[39]

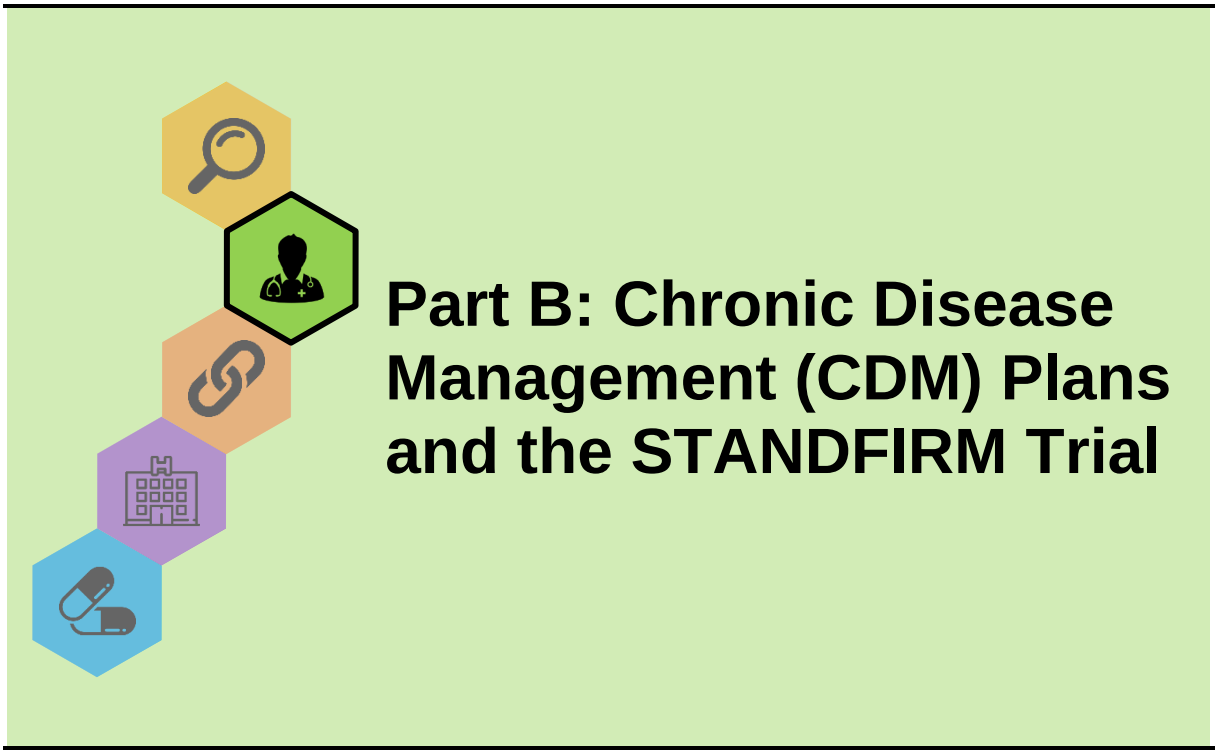
There also appears to be a dose-response relationship between total cholesterol and mortality, as shown in a 2007 meta-analysis of 61 prospective observational studies conducted mostly in North America and Western Europe.[40] In this meta-analysis. the authors reported that a decrease of 1.0 mmol/L in total cholesterol was significantly associated with a reduction in mortality, due to ischaemic heart disease, by 33% in those aged 40-49 years, and by 56% in those aged 50-69 years.[40] Total cholesterol has also been demonstrated to be inversely associated with haemorrhagic stroke, whereby the risk of haemorrhagic stroke increased as total cholesterol decreased.[41, 42] However, there is conflicting evidence regarding this inverse relationship from studies involving statin therapy. While some observational studies failed to detect an increased risk of intracerebral haemorrhage with statin therapy,[43, 44] other studies,

such as the SPARCL trial, have demonstrated an increased risk.[45] However, the possible slight increased risk of haemorrhagic stroke due to statins is outweighed by its beneficial effects for reducing the risk of ischemic stroke and mortality. Compared with placebo in a clinical trial of 4,731 patients with stroke or TIA, Amarenco et al. reported that treatment with 80 mg of atorvastatin per day reduced the five-year absolute risk of major cardiovascular events by 3.5%.[45] The use of atorvastatin was also associated with a 16% relative reduction in the risk of stroke. In a meta-analysis of 22 trials, which each had at least 1,000 participants and a treatment duration of at least two years, statin therapy provided per 1.0 mmol/L reduction, a proportional reduction in the rate ratio of vascular mortality by 12% and a reduction of major vascular events by 21%.[39]

The Stroke Foundation recommend that, regardless of baseline lipid levels, a statin should be prescribed to patients with ischaemic stroke or TIA with "*possible atherosclerotic contribution and reasonable life expectancy*".[30] This recommendation was provided following strong evidence from a meta-analysis by Tramacere et al., in which they found statin use was associated with a reduction in the absolute risk of ischaemic strokes and cardiovascular events.[46]

Summary of Part A

Stroke is a leading cause of death and disability in Australia and globally. The number of Australian survivors of stroke is growing alongside other countries with an ageing population. These patients with stroke represent a growing burden on the Australian population, health system and economy. However, there are opportunities in Australia to reduce this burden in primary care with systematic and better approaches towards the management of risk factors and secondary prevention for survivors of stroke.


Part B: Chronic Disease Management (CDM) Plans and the STANDFIRM Trial

Chapter 3: Uptake of CDM Plans in Australia and the STANDFIRM Trial

3.1 The STANDFIRM Trial

A detailed protocol and statistical analysis plan (SAP) for the Shared Team Approach between Nurses and Doctors For Improved Risk factor Management (STANDFIRM) trial have been published and are provided in Appendices A and B.[18, 47] As these methods have been described previously and are provided in the appendices, I will only provide an overview of the methods from the trial that are relevant to the analyses for this thesis.

3.1.1 Study Design and Population

The STANDFIRM trial for patients with stroke was a multicentre, cluster randomised controlled trial with blinded assessment of outcomes and intention-to-treat analyses.[18] The trial was undertaken between January 2010 to December 2015, and was led by researchers from the Stroke and Ageing Research group at Monash Health, School of Clinical Sciences, Monash University. Participants for this trial were recruited from four main hospitals across Victoria, Australia (Figure 3.1). To participate in the trial, patients needed to meet the following five inclusion criteria:

1. Hospitalised for stroke or TIA,
2. Aged ≥ 18 years,
3. Living within 50km of the closest participating recruitment centre,
4. Not admitted from or discharged to a nursing home, and
5. Not diagnosed with a concurrent rapidly deteriorating disease (e.g. terminal cancer) and were thus expected to survive for more than 12 months.

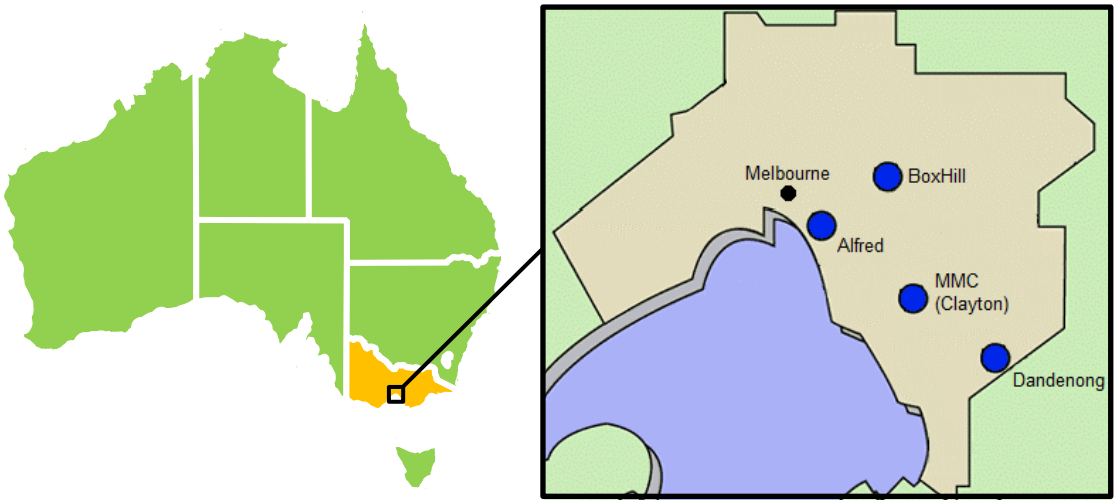


Figure 3.1. Location of the Australian state of Victoria and the four hospitals (Alfred Hospital, Monash Medical Centre, Box Hill Hospital and Dandenong Hospital) from which patients were recruited for the trial.

3.1.2 The Intervention

Recruited participants were then randomised to receive either an individualised management plan (IMP; intervention) or usual care (control) based on a block randomisation procedure. The IMP comprised two tailored components: a CDM plan and in-home tailored education about stroke prevention. An example form for the nurse-led education visit is provided in Appendix C. The CDM plan was constructed by an unblinded nurse with guidance from a stroke specialist (neurologist or geriatrician) and comprised recommendations for well-defined health targets and adherence to therapies for secondary prevention using guidelines for stroke care (Figure 3.2). An example form that was offered to general practitioners (GPs) is provided in Appendix D. The specific recommendations outlined in the CDM plan were based on the patients' health information obtained at baseline from an interview conducted by a blinded assessor.

MULTIDISCIPLINARY PATIENT NEEDS AND PLANNED ACTIONS		
Current Health Needs/Problems (Specialist/Nurse to complete)	**Goal**	**GP to Complete to Reflect Agreed Actions (tick those applicable)**
Blood Pressure management Measured blood pressure (at home): 148/59 mmHg 25/10/2012 BP of concern ☒ Yes ☐ No ☐ Please Review	**GOAL** Maintain blood pressure as close as possible to 120/80 if it is higher.	**Review:** ☐ Regularly monitor BP ☐ Add/titrate BP lowering medications ☐ Cease/reduce prohypertensive medications or other remedies ☐ Exercise ☐ Diet (reduce weight, salt, and alcohol where appropriate) ☐ After review, no action

Figure 3.2. Example of individual-tailored goal setting in the STANDFIRM trial intervention, provided with the Chronic Disease Management (CDM) plans.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management.

3.1.3 Assessments

The STANDFIRM trial adopted a three-layered approach, akin to surveillance studies, that utilised biochemical measurements, physical measurements and questionnaires to assess and monitor risk factors of recurrent CVD at baseline and at 3, 12 and 24 months (Figure 3.3). Table 3.1 provides a summary of the assessments that were used during the study and the data that were collected. Questionnaires that were used to record these assessment data are provided in Appendix E.

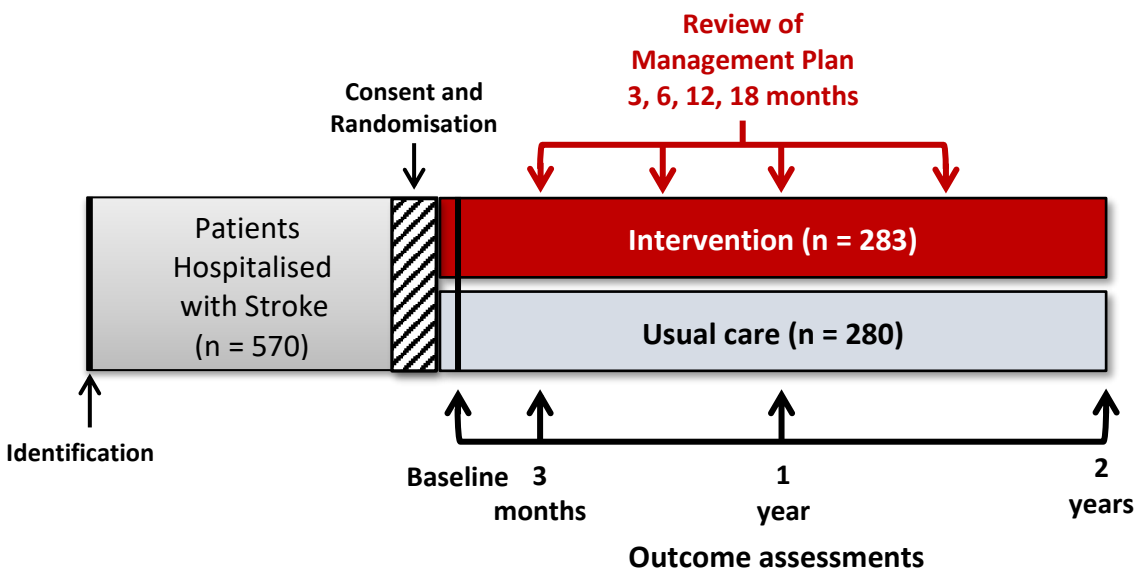


Figure 3.3. Study design and timing of outcome assessments in the trial (intention-to-treat).

Table 3.1 Summary of assessments used to evaluate biochemical, habitual and physical attributes of trial participants at baseline, 12 and 24 months after stroke.

Procedure	Data Collected
Physical Examination	Anthropometry: height, weight and skinfolds.
Sphygmomanometer	Systolic and diastolic blood pressure.
Questionnaires/Self-Report	Medical history, alcohol use, therapeutic drug use, physical activity and smoking status.
Blood Test	Serum glycosylated haemoglobin, fasting glucose, triglyceride, total-cholesterol, low-density lipoprotein and high-density lipoprotein cholesterol.
Urine Test	Cotinine (measure of smoke exposure) and 24-hour sodium excretion.

3.1.4 Suspected Increased Treatment Uptake by Usual Care Group

Assessment of the effect of the intervention, using an intention-to-treat approach, demonstrated little to no effect on outcomes such as risk factors (change in modified Framingham Risk Score at 12 months after stroke, adjusted Odds Ratio [OR] 0.9; 95% CI 0.6, 1.5) or knowledge about medications after stroke (good knowledge [composite knowledge score ≥5] at 12 months after stroke in medication users, adjusted OR 1.10;

95% CI 0.42, 2.92).[48, 49] A possible explanation of this inability to detect an effect of this intervention was due to a suspected increased uptake of CDM plans (treatment) by those in the usual care group. This would have reduced the potential for observing a difference between the usual care and intervention groups. However, prior to the initiation of the study, CDM plans were not often used by GPs in the usual care of their patients. This concern of increased treatment uptake by those in the usual care group could not be examined until years after the trial ended, at which time data from Medicare, regarding claims history for use of a CDM plan, were received and linked to each STANDFIRM trial participant. In the next sections, the impact of chronic diseases in Australia will be explored and CDM plans and their usage will be described in both Australia and the STANDFIRM trial.

3.2 Chronic Disease Management (CDM) Plans

3.2.1 Impact of Chronic Conditions in the Community

According to the Australian Institute of Health and Welfare (AIHW), 39% of hospitalisations in 2013-14, associated with chronic diseases such as CVD, were potentially preventable.[50] In terms of hospitalisations alone, CVD represents an annual expenditure of approximately $5 billion with preventable hospitalisations costing at least $1.3 billion.[50, 51]

In 2017-2018, almost one half (47.3%) of Australian adults reported having at least one chronic condition, an increase of more than 10% in prevalence since the prior decade (42.2% in 2007-08).[52] Heart disease, vascular disease and stroke represent 4.8% of the total number of chronic conditions affecting Australians. These individuals are more likely to be frequently interacting with primary healthcare providers, such as GPs, than the general population. In fact, of all encounters with GPs, 58% are by patients aged 45 years and over and 40% are for the management of a chronic condition.[53]

Using data from a continuous, national cross-sectional study of general practice activity in Australia, Harrison et al. developed a parsimonious model to predict patient use of general practice services in Australia.[54] They found that patients with chronic conditions visited a GP 1.06 times more than those without a chronic condition. Data from the Australian National Health Survey are consistent with this finding, with survivors of stroke visiting a GP 1.62 times more than the general population in the financial year of 2017-18.[52] These statistics indicate not only a growing need for GP capacity to support the Australian community, but also for this management to be cost-effective and beneficial towards chronic diseases such as stroke. One such approach to efficient management is the provision of CDM plans by GPs.

3.2.2 Overview of CDM Plans

Although there are many proven therapies for preventing stroke recurrence (e.g. BP-lowering and lifestyle modifications), uptake of treatments is poor.[55, 56] CDM plans, which include increased Medicare funded rebates for clinicians, aim to encourage GPs to provide better management of risk factors in those with chronic medical conditions. These conditions include cancer, diabetes, CVD and stroke, as well as conditions that have been, or are likely to be, present for at least six months.[57] CDM plans provide a coordinated approach to care, and may provide a means to improve patient: (1) knowledge about risk factors, (2) knowledge about appropriate use of medications, and (3) understanding about the changes to behaviours that can improve control of risk factors. Such knowledge may empower patients with stroke to adopt lifestyle changes and thereby prevent further CVD events.

3.2.3 The CDM Medicare Items

CDM plans are covered in the Medicare Benefits Schedule (MBS) by CDM items 721 (GP Management Plan; GPMP), 723 (Team Care Arrangements [TCAs] for those who required

multidisciplinary care) and 732 (Review of a GPMP or Coordination of a Review of TCAs).[58] These three items cost the Australian population more than $750 million each year.[59-62]

The preparation of a written CDM plan (Figure 3.4) involves the:

1. Careful assessment of the patient's health status and needs,
2. Discussion with the patient about action(s) to be taken,
3. Preparation of agreed upon management goals,
4. Identification and arrangement of ongoing treatments and services that are likely to be needed,
5. Arrangement to review the GPMP or TCA by a specific date.

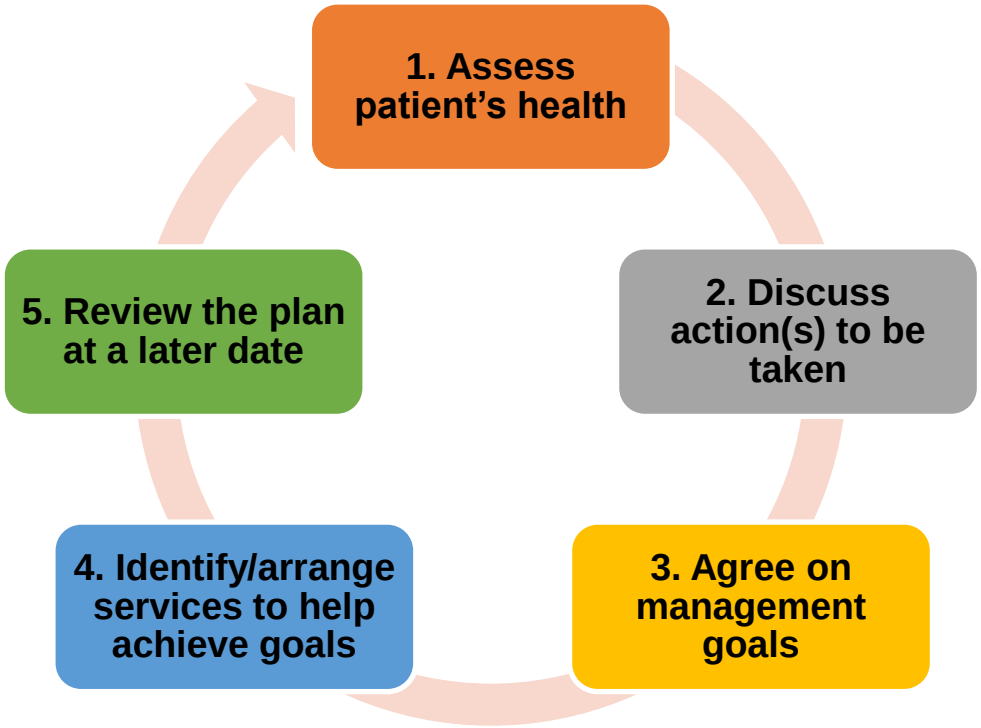


Figure 3.4. Overall steps involved in the preparation of a Chronic Disease Management plan.

3.2.4 Use of CDM Plans in Australia

In Australia, there has been increased adoption of CDM plans in clinical practice by GPs in the care of their patients (Figure 3.5). In fact, the use of CDM plans in Australia has increased

by 284% in the past 10 years (2008-2018) and 79% in the past 5 years (2013-2018; Table 3.2).[63] However, despite the extensive monitoring of disease burden in Australia, there is a clear lack of data and literature regarding the effectiveness of current strategies that target chronic diseases, such as the CDM plan.

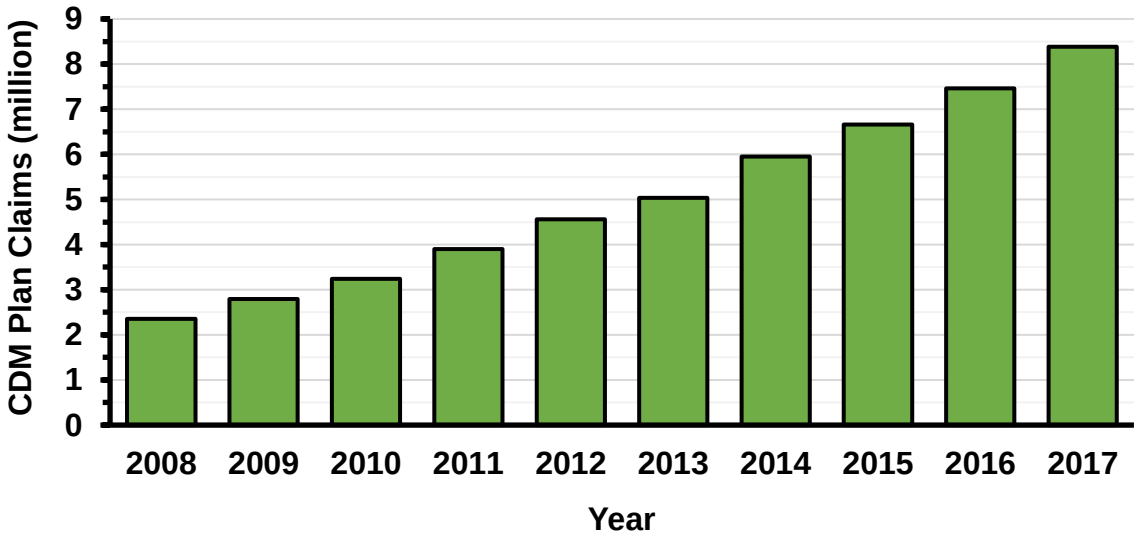


Figure 3.5. Annual uptake of Chronic Disease Management plans in Australia from 2008 to 2017.

Table 3.2. Number of Chronic Disease Management (CDM) Medicare items processed annually in Australia and Victoria and increase (%) in use in the past 10 years.

	Australia					Victoria				
	CDM Items Claimed (million)			Increase*		CDM Items Claimed (million)			Increase*	
Item	**2008**	**2013**	**2018**	**10-year**	**5-year**	**2008**	**2013**	**2018**	**10-year**	**5-year**
721	0.95	1.68	2.82	197%	68%	0.23	0.42	0.68	197%	64%
723	0.68	1.35	2.39	252%	78%	0.17	0.34	0.60	253%	75%
732	0.73	2.01	3.82	425%	90%	0.16	0.47	0.84	417%	79%
Total	2.35	5.03	9.03	284%	79%	0.56	1.23	2.12	278%	73%

* 10-year increase in the number of Medicare items processed annually was calculated from 2007 to 2016 and the 5-year was calculated for 2012 to 2016.

Statistics were derived from those reported on the Department of Health's online 'Medicare Item Reports' tool.[63]

3.3 Use of CDM plans in the STANDFIRM Trial

During the STANDFIRM trial, from 2010 to 2013, there was a 51.4% increase in the annual number of CDM plans claimed in Victoria. We found that there was no difference in the uptake of CDM plans provided for each participant in STANDFIRM prior to their stroke (Figure 3.6). Within a year, the proportion of participants with a CDM plan in the intervention group was more than double that of the usual care (control) group. However, reflecting the trend of increased uptake of CDM plans in Victoria from 2010 onwards, we can see that the usual care group becomes progressively contaminated over the three years since their stroke (Figure 3.6).

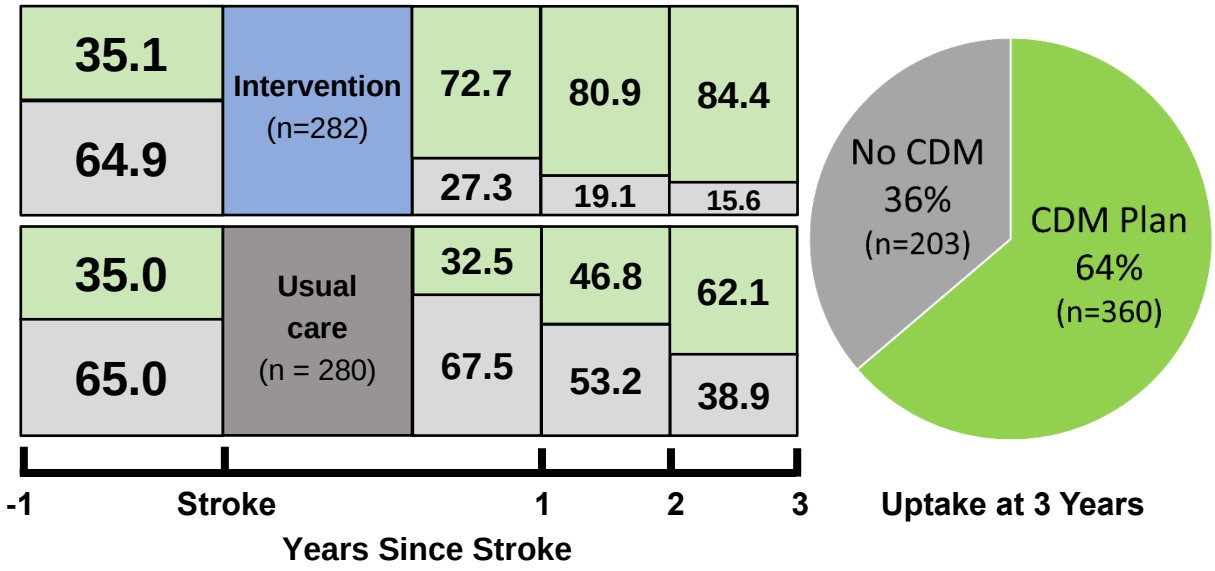


Figure 3.6. Percentage uptake before and after stroke, by treatment allocation and overall, of chronic disease management (CDM) plans (green) and no plan (grey).

The initial analysis of STANDFIRM was undertaken using an intention-to-treat approach, i.e. intervention vs usual care. However, the above data (Figure 3.6) shows that there was increased uptake of the treatment across both groups, although a larger proportion of the

intervention group received a CDM plan at each time point. This highlights the need to compare participants who were provided with a CDM plan from their GP after stroke against those were not, as presented in the following chapters. Intervention status was also included as a covariate in each of these analyses to adjust for any additional effect that the intervention may have had on the outcomes of readmissions (Chapter 6) and medication adherence (Chapter 7) after stroke. However, as previous publications have provided evidence for little to or no effect based on the intervention status on better control of risk factors, the perceived risk of this affecting the additional results remains low.

Summary of Part B

The linkage of data from participants in the STANDFIRM trial with data from the MBS has enabled us to (1) confirm that there was significant uptake of CDM plans (treatment) by the usual care and intervention groups, and (2) understand the changes during the past decade that occurred in the use of CDM plans in Australia and Victoria.

In Parts D and E we will explore the impact that CDM plans may have on readmissions following stroke (Chapter 6), and adherence to secondary prevention medications (Chapter 7). By doing so, we will generate evidence to fill the critical evidence gap in understanding what benefits CDM plans may have for patients after stroke.

Part C: Understanding Data Linkage Within Australia: Strengths and Limitations to Investigate Outcomes After Stroke

Chapter 4: Promising Use of Big Data to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Research

4.1 Overview

In Part A, I described the impacts of stroke, its modifiable risk factors and how secondary prevention for stroke is managed according to the Australian clinical guidelines. In Part B, I introduced the STANDFIRM trial, its intervention, CDM plans, and how these plans were used in both Australia and by the participants in this trial with stroke.

In this chapter, I will introduce the concept of 'data linkage', which is also known as data integration or record matching. Data linkage is a process by which information from different data collections can be brought together and linked for a particular purpose. I will also discuss the strengths and limitations of using secondary data, extracted from routinely collected administrative databases, for research into outcomes after stroke. The included topical review was published in the peer-review journal *Stroke* in 2019.

4.2 Published Paper

Promising Use of Big Data to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Research

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Topical Review

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Promising Use of Big Data to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Research

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The gold standard for outcome assessment in stroke is provided by longitudinal population-based incidence studies with full case-ascertainment and repeated outcome assessments over time.[1] This enables a comprehensive assessment of the burden of stroke that includes mortality, disability, adverse events, quality of life, and functional status and the effectiveness of the health system in relation to healthcare utilization. However, such purposeful collection of continuous data over a period of time for stroke surveillance is costly, and some patient-reported outcomes such as readmissions can be unreliable.[2] It is, therefore, unsurprising that the number of currently ongoing incidence studies is limited.[3] With the explosion of digital information, a broad range of health outcomes after stroke can be evaluated using new strategies for integrating administrative data with data from clinical studies or registries. In this article, we aim to describe approaches for the collection of outcomes data after stroke and their strengths and limitations. We further examine the utility of linking datasets to add value to stroke research, including ongoing stroke surveillance and outcomes reporting, and describe barriers to data linkage and to the use of administrative data in stroke research.

Methods of Collection of Health Outcomes After Stroke

The quality of outcomes data such as mortality, adverse events, and disability can vary by type and timing of the collected data, such as the in-hospital, short-term or long-term periods (Table 1).[4] There are 3 main approaches for collecting outcomes data after stroke (Figure):

1. **Clinical studies** comprise randomized controlled trials, population-based cohort or case-control studies. Assessments are typically undertaken in a systematic, organized manner, using specific clinical tools or scales. The measures may include a combination of diagnostic tests and assessments of biochemistry, anthropometry, costs, medication adherence, lifestyle behaviors, functional capacity, adverse events, and health-related quality of life. Minimizing the loss to follow-up of participants is challenging in clinical studies, as frequent follow-up contacts can be burdensome to patients.[5] Clinical studies usually have fewer total observations, on a selected sample of patients that typically require informed consent for participation, relative to the samples of patients in clinical registries and administrative databases. However, the information obtained at assessments in clinical studies can allow researchers to have a more nuanced and detailed understanding on the outcomes of patients with stroke.
2. **Clinical stroke registries** fill an important role in monitoring the delivery of healthcare and its quality (eg, acute therapies such as thrombolysis, admission to a stroke unit, and discharge medications). They can be important in tracking outcomes at a national, state, or health service level.[4] The expense and complexity of large scale patient follow-up means that for many patient registries, data regarding outcomes are limited to the in-hospital period (eg, in-hospital mortality, length of stay, and discharge destination).[4] The availability of validated quality of care indicators that are captured in registries help document real-world acute stroke practices that are not typically available in clinical studies and administrative databases. Information regarding stroke severity can also be captured and enables appropriate risk adjustment of outcomes, which is particularly important when comparing between countries.[6] Limitations of stroke registries include the potential for selection bias if case-ascertainment is poor and recording bias if there are variations in how data are collected between hospitals.[7]
3. **Administrative data** are routinely collected with the primary purpose of monitoring health service activity, provider billing, and overall health service operational costs. These databases are characterized by 4 Vs': large data volume (volume), heterogeneity and disparity (variety), rapid generation of data (velocity), and uncertainty regarding the reliability of the data (veracity).[8] Example databases include admissions to hospital, emergency department (ED) presentations, procedures, medical office visits, medical services provided such as rehabilitation, devices, equipment, pharmacy dispensing, and deaths (Table 1).[7] However it is important to understand the limitations of administrative databases, as these secondary data are not collected for research purposes.

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Table 1. Outcomes Data Typically Available by Type of Study Design

Type of Data Collection	Clinical Studies	Registries	Administrative Data
Examples	RCT, prospective cohort studies, or case-control studies	Hospital, regional, or national	Admissions, ED presentations, or pharmacy dispensing
Rationale	Comprehensive assessment of outcomes	Quality of stroke care and outcomes	Billing or claims data
Diagnostic accuracy	Clinical diagnosis	Clinical diagnosis	Diagnosis codes
Outcomes			
Adverse events			
In-hospital	A	A	A
Short-term	A/–	–	A
Long-term	A/–	–	A
Mortality			
In-hospital	A	A	A
Short-term	A/–	A/–	A
Long-term	A/–	–	A
Readmissions			
Short-term	A/–	A/–†	A
Long-term	A/–	–	A
Medications			
In-hospital	A	A	A/–
Short-term	A/–	A/–*	A
Long-term	A/–	–	A
Healthcare utilization			
In-hospital	A	A	A
Short-term	A/–	–	A
Long-term	–	–	A
PROMs			
In-hospital	A	A	–
Short-term	A/–	A/–†	–
Long-term	A/–	–	–

In-hospital defines outcomes collected during hospital stay; short-term, outcomes collected after discharge up to 90–180 days; and long-term, outcomes collected after 180 days and up to final follow-up. A indicates outcomes that are always collected; A/– , outcomes that are sometimes collected depending on the study or data source; and –, outcomes that are not collected; ED, emergency department; PROMs, patient-reported outcome measures; and RCT, randomized controlled trial.

*Recorded as being provided at discharge.

†In some clinical stroke registries,[4] PROMs (quality of life and disability) and readmissions are collected at 90- to 180-day follow-up.

Although not mutually exclusive, further details of the main strengths and limitations of these various methods of data collection are provided in the Supplemental materials (Table I in the online-only Data Supplement).

Strengths of Administrative Data in Health Services Research

Although administrative databases were not designed for research or clinical purposes, these databases (1) reflect real-world practice, (2) are large, (3) comprehensive, (4) population-based, (5) have potentially indefinite follow-up, and (6) are less expensive and resource intensive than clinical studies. The inclusion of data from a large number of individuals over many years enables detailed assessment of minority or rare disease groups.[7,9] For example, clinical studies rarely capture a representative sample of patients from specific ethnic backgrounds or socioeconomic positions, as it is uncommon for them to present within a given time period and location.[7] Rare risk factors and diseases associated with stroke can also be evaluated using databases that capture these well. Some successful examples include studies that have established an association between greater risk of stroke and the presence of Fabry disease,[10] congenital heart disease[11] or being Indigenous (only 3% of all Australians).[12] In Western Australia, longitudinal administrative hospital data have been used to compare stroke incidence between Indigenous and non-Indigenous populations.[12]

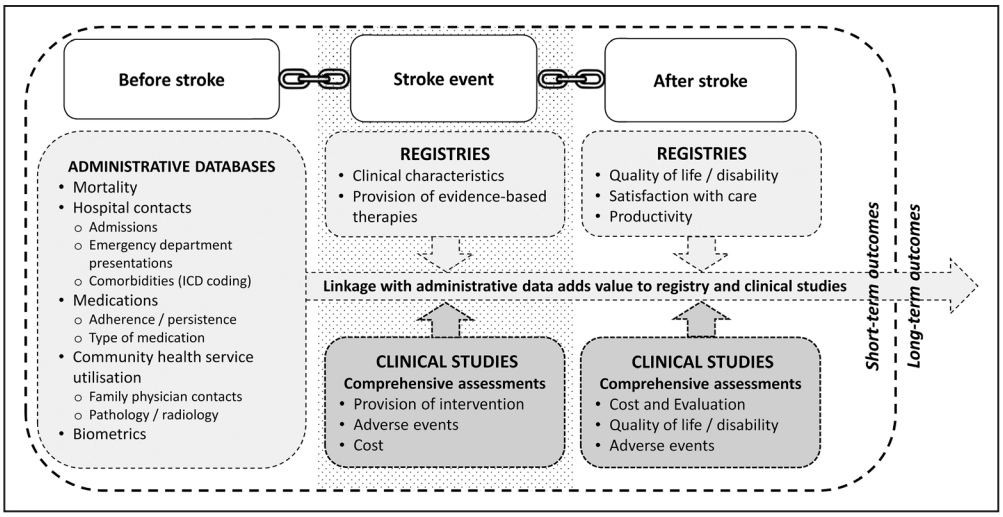

Figure. Stroke research using linked data. Administrative data adds value to registries and clinical studies. *ICD* indicates *International Classification of Diseases*.

For administrative hospital admissions databases, each admission is coded with details of principal and associated diagnoses and procedures.[7] Coding is undertaken using the International Statistical Classification of Diseases and Related Health Problems classification (*International Classification of Diseases*, *Ninth Revision [ICD-9]* or *International Classification of Diseases, Tenth Revision [ICD-10]*).[13] ICD codes can be reliably used to identify cases of stroke, provided that they have been validated within both the population of interest and administrative databases that capture these codes.[14] In Australia and Canada almost all patients with stroke are captured using ICD-10 diagnostic codes, which have been validated against physician diagnoses and demonstrate high sensitivity and positive predictive values.[2,15] However, other countries may have suboptimal accuracy of coding. There are variations between countries, coding systems and the criterion standard against which codes are compared that need to be taken into consideration.

Given the impracticalities of conducting regular gold standard population-based stroke incidence studies, using administrative admissions and ED data has the potential to be a cost-effective alternative for monitoring stroke incidence and burden.[16] By using look-back periods, first-ever strokes can be differentiated from recurrent strokes.[2] This process involves examining admission and ED data over a predefined period before a stroke event to confirm whether it is a first-ever or recurrent stroke. Longer look-back periods reduce the misclassification of recurrent strokes as first-ever strokes from more than 10%, using a 1-year look-back period, to 3.7% at 5 years and <1% at 10 years.[2,17] This process can also be used to discern first-ever administration of health plans, medications, and therapies. Adherence to secondary prevention medications is an important outcome to evaluate after stroke in clinical studies and registries given their effectiveness for preventing recurrent events.[18] Compared with self-report or clinical chart review, administrative medication databases can provide reliable data on medication dispensing with no additional burden of collecting the data directly from patients.[19,20] However, it is essential to understand the limitations of these dispensing databases, as information regarding whether the medications are actually being used or reasons for the prescription of these medications are not collected.[21]

Limitations of Administrative Data in Health Services Research

Because administrative data are not collected primarily for research purposes, there are caveats to their use in studying outcomes after stroke. First, selection biases can make it difficult to appropriately define the population. For example, patients with better access to healthcare (healthcare access bias) or who present with more severe and nonfatal symptoms (survival bias) may be more likely to be captured.[22] Additionally, participants who are misdiagnosed, inaccurately coded, or do not present to healthcare institutions may not be included. Second, the data in these databases may be inaccurate, incomplete, or do not encompass the entire population. In administrative databases on hospital admissions and ED presentations, coders are responsible for categorizing medical documentation into ICD-10 codes. Coders are often tertiary qualified health information managers or certified clinical coders and adhere to coding standards for classification to determine the primary and secondary diagnoses of a hospitalization.[7] Accuracy of diagnoses is further challenged when medical documentation is incomplete or illegible. Additionally, disease severity, race, ethnicity, and outcomes of interest, such as functional status and quality of life, may not be collected. As stroke severity is an important predictor of stroke outcomes, its absence in administrative data remains a serious limitation.[6] Third, another limitation arises when codes that lead to greater reimbursement of funds to hospitals are favored over the principal reason a patient is hospitalized. This phenomenon, termed code creep, has been estimated in an American study to increase payments for physician visits by 2.2% every year.[7,23] The combination of these factors not only impacts the ability to identify stroke cases, but also affects the ability to adjust outcomes by stroke severity and compare performance across health centers or hospitals. The reliability of administrative data to capture the outcomes of interest should be validated before its use in research, as has been done in stroke in Canada and Australia.[2,15]

What Is Data Linkage?

Record linkage was first proposed in 1946 by Dunn, where a book of life could be created for each individual based on a series of significant health and social events.[24] Technological advances in data storage, security, and analytics since then have enabled the scale of record linkage to expand to linking administrative databases to registries or clinical studies, a process commonly referred to as data linkage. Data linkage can be particularly valuable in stroke research as, in developed countries at least, most people attend healthcare–related services before, during, and after their stroke event (Figure). However, there are relatively few countries with frameworks and governing authorities to make this practical. Comprehensive data collected within clinical research or registries can be linked with administrative data or vice versa. As excessive resources are required to track outcomes after discharge, linkages with administrative data can provide an adjunct approach to cost-effectively and longitudinally capturing longer-term outcomes (eg, survival and readmissions) in both clinical studies and registries (Table 1).

Strengths and Opportunities of Data Linkage

Perhaps one of the greatest benefits of data linkage is its cost-effectiveness and efficiency. Not only does it reduce the overall time and financial costs associated with collecting these data, but it also reduces responder burden. Due to the availability of a unique patient identifier, referred to as the National Health Identifier (NHI), access to linked administrative data in New Zealand, Canada, Sweden, Finland, and Denmark is more easily facilitated.[19,25–27] However, most countries including Australia, the United States, and many Asian countries do not have a uniform NHI, and so linking databases is much more challenging.[25] In countries where NHIs are available, data linkage can be performed relatively quickly and accurately through direct matching known as deterministic linkage. When NHIs are unavailable, probabilistic linkage can be used. In this type of linkage, identifiers such as name, sex, date of birth, date of service, and postcode/zip code can be used to match individuals between databases.[16] In these instances, standardizing and cleaning the data or using pseudo-unique identifiers collected in both databases can help minimize the proportion of unmatched individuals.[28] For instance, matching between the Australian Stroke Clinical Registry to hospital and ED databases was 99% when unique identification numbers, derived from Australia's healthcare system (Medicare), were provided in addition to standard identifiers.[29]

Data linkage between large administrative databases and smaller research studies can enable exploration of how patient-level variables may affect outcomes after stroke. To illustrate this, provincial-level administrative hospital admissions and ED data for more than 15 000 stroke patients were linked to 552 patients enrolled in 4 clinical trials in Canada to determine whether there was a correlation between home-time and the modified Rankin Scale.[30] Home-time was defined using the administrative hospital data as the number of days spent outside a health institution in the first 90 days after index hospitalization. After comparing the 90-day home-times against the prospectively collected 90-day modified Rankin Scale scores, a lower 90-day modified Rankin Scale score was associated with a longer home-time after stroke. These results suggested that home-time could be used to track patient outcomes and healthcare use after stroke, in areas such as health policy evaluation and pragmatic clinical trials. This study approach demonstrates the value of linking prospectively collected data (eg, modified Rankin Scale) to outcomes (eg, home-time) that can be derived using administrative data.

There are many other examples of successful linkage between prospective stroke research cohorts or registry data with administrative data, to determine longer-term outcomes such as mortality, readmissions, use of medications, and physician services.[4,19,31] For example, in the United States, clinical data have been linked to Medicare claims data to assess hospital variation in 90-day and 1-year home-time after stroke,[32] whereas in Canada, Scotland, and Australia, stroke registries have been linked to death registry, hospital admissions and ED databases.[4,19,29,33] These linkages have provided the opportunity to determine outcomes after patients are discharged from hospital, validate the diagnosis of the index stroke, and enable capture of comorbidities. The Ontario Stroke Registry and Scottish Stroke Care Audit have also been linked to medication dispensing databases to understand adherence to secondary prevention medications after stroke.[19,20]

An important benefit of using data linkage for prospective studies is that it can minimize the effect of patients lost to follow-up. Administrative data can provide outcome data even when participants drop-out or relocate during the study. In most stroke registries, patient data are only collected during the hospital stay, and the status of the patient after discharge is typically not known.[4] In other stroke registries such as the Riksstroke and the Australian Stroke Clinical Registry, short-term patient outcomes are collected, typically between 30 and 180 days after discharge.[4,31] However, obtaining these data on a complete and representative sample is challenging and resource intensive. Longer-term outcomes beyond 180 days, such as mortality, readmissions, and stroke recurrence are also important to capture, but cannot feasibly be collected in registries. Indeed, follow-up interviews are no longer conducted in the Ontario Stroke Registry and patient outcomes are now obtained using linkages with administrative databases.[19] In some countries, linkages with stroke registries have been successfully maintained on an ongoing basis, such that a national dataset is periodically generated to inform annual or biennial reports on stroke care and hospital performance as demonstrated in Australia and Sweden.[4,31]

Another area where data linkage may be helpful is in evaluating the translation of research knowledge, or an evidence-based treatment, into routine practice by allowing observation of trends in treatment over time. This was recently demonstrated in a retrospective observational study in Australia involving person-level linkages between pharmaceutical claims data and hospital claims data for veterans and their dependents.[34] The authors found that the proportion of patients with ischemic stroke or transient ischemic attack dispensed antihypertensive, antithrombotic, and lipid-lowering drugs as recommended, almost doubled over a 7-year period from 24% in 2003 to 43% in 2009.[34] These data provided evidence that the dissemination of Australia's first guidelines for

acute stroke management in 2003 translated successfully into an increased use of secondary prevention medications.

Limitations and Challenges of Linking Data

Similar to the limitations for administrative data, the availability and quality of databases for linkage are country-dependent and can be inconsistent. Bohensky et al[35] reported on a framework for evaluating the quality of data linkage studies and emphasized that certain information should be reported. This information included descriptions of the data sources and linkage methods, variables used for linkage, match rate between data sources and coding definitions. To illustrate the use of this framework, we applied it to 2 prior data linkage studies: one involving linkage with 4 clinical trials and the other a stroke registry (Table 2).[30,33,35] By identifying limitations or gaps in reported information, these evaluations can also help researchers to enhance the quality of their own data linkage studies.

Delays in obtaining access to administrative data can be time-consuming and span many months or years, particularly when seeking approvals from ethics committees and data custodians to access and link these data.[25] The more data sources sought for linkage will compound these delays. Obtaining approvals may be difficult for smaller studies, where there could be a risk of reidentifying patients based on the data collected. When designing a clinical study or registry, forethought to include a clause regarding future data linkage with other health data, in patient consent forms, is extremely important as part of the ethics approval for data linkage.

Gliklich et al[36] have provided a comprehensive guide regarding technical, legal, and analytic considerations to linking registry data with other data sources. The processes for obtaining access to administrative data and data linkage vary significantly based on the country, state, and type of data being accessed. This can also vary over time in response to changes in legislation, technology, and data custodianship. Bradley et al[37] and the Agency for Healthcare Research and Quality[38] have described the existing infrastructure for linkage within the United States as being fragmented, costly, and limited in its accessibility to researchers. Andrew et al[25] have identified other challenges that can arise when establishing cross-jurisdictional data linkages and how these were overcome. Issues specific to linkages with a clinical registry were as follows: (1) the need for separation of data custodians from research staff, (2) concerns about releasing personal identifiers to other data linkage units for cross-jurisdictional linkages, resulting in complex data flows, and (3) coordinating multiple linkage applications that can have different requirements for approval.[25] Specialized ethics departments, such as those associated with data linkage units can facilitate these processes and assist researchers to avoid delays, impediments, and address concerns from data custodians.[25]

Public approval and governance are also potential impediments to linking data in some countries such as Taiwan and Australia.[25] Taiwan has a NHI, but according to Hsiew et al[39], researchers are prevented from linking clinical registry databases with administrative databases due to the public's concern for privacy, protests from human rights organizations against the collection and use of health and welfare data, and the amount of red tape necessary to get permission to link data. There are similar challenges worldwide that, as patients have increasing rights to control their own digital fingerprint in an increasingly digitalized and globalized world, this will decrease the availability of complete data for research; particularly in light of the recent General Data Protection Regulation introduced for all individuals within the European Union and European Economic Area.[40] These regulations introduce clearer rules that favor individuals regarding the provision of consent and repurposing personal data for scientific research. Although the impact of the General Data Protection Regulation should be minimal for researchers, this may represent a concerning trend where increasing individual control regarding privacy and confidentiality may ultimately impede research.

By understanding the nature, historical context and limitations of individual administrative databases, researchers can unpack these large data and use these to enrich comprehensive assessments in clinical studies for outcomes of stroke. Depending on the type of administrative data used and the research question, validated methodologies and sensitivity analyses should be conducted to correctly interpret the results of the study.

Future Directions

Over the last 25 years, high quality, complete, and linkable health data have been just around the corner. Only a few countries, such as Sweden, Denmark, Finland, Scotland, New Zealand, Canada, and Australia can claim to be realizing this promise, albeit at different stages.[4,19,25–27,31,41] The use of data linkage to study stroke-related outcomes in many countries is still in its infancy, as many population-based studies only link with a national death registry to ascertain mortality.[4,29] Furthermore, positive contributions resulting from large data linkage-based studies have yet to be demonstrated, likely owing to the time lags inherent to the translation of evidence from health research into changes in both policies and practice.[42] Following successful examples of data linkage in the research of stroke, there is a renewed impetus to use this approach around the world.[4,19,27,31] Many countries that do not currently use linked data in stroke research already possess systems capable of collecting routine health information at local and national levels, especially with the increasing adoption of electronic medical records. Unlocking this wealth of data could help generate new hypotheses in stroke, minimize data waste, and justify future comprehensive research into important and untested outcomes.

It is clear that the optimistic aspiration of data linkage is shared by many countries. These countries are encumbered by systems that must be robust and meet both national confidentiality and security standards for the protection of individual privacy. A lack of infrastructure and bioinformatics surrounding the optimal utilization of administrative data in healthcare may also be a barrier to routine data linkage. Compared with data collection systems for administrative data, clinical studies and registries are costly, labor intensive but more thorough and less subject to human error. However obtaining, linking,

Table 2. Example Evaluations of the Quality of Data Linkage in Stroke Registry[33] and Clinical Trial-Based[30] Studies Using a Framework Developed by Bohensky et al[35]

Framework Criteria	Linkage With a National Stroke Registry —Kilkenny et al[33]	Linkage With 4 Clinical Trials —Yu et al[30]
Completeness of source databases: This may include under-ascertainment of cases or differences in reporting practices and inclusion criteria between the data sources to be linked.		
1. A description of the data sources to be used in the study should be included.	Satisfied—Four data sources described: the AuSCR, national death and state hospital admission and ED presentation databases.	Satisfied—Five data sources described: pooled data from 4 clinical trials, acute care hospitals, ED, rehabilitation facilities, supportive living, and long-term care facilities databases.
2. The number of eligible records obtained from each dataset and the reasons for differences, if any, should be reported.	Satisfied—AuSCR registrants (16 214) were available for matching with data for 243 892 admissions, 90 823 emergency presentations, and 4183 corresponding NDI records. Data on AuSCR patients who opted-out were excluded.	Partially satisfied—Most Alberta residents (>99%) can be linked deterministically using the unique personal health number. Although the number of eligible records from each dataset is not reported, it is assumed that almost 99% from each database would be eligible. Data on patients <20 y of age and those with record of leaving against medical advice or failing to return after an out-of-hospital pass were excluded.
Accuracy of data sources: Incomplete/inaccurate data, especially if there is variation between sites or groups of patients.		
1. Variables selected by researchers for linkage and analysis should be reported.	Satisfied—Personal identifiers were used for linkage included name, date of birth, sex, address, admission and discharge dates, and Medicare numbers. Registry data used in analyses included demographic, clinical, and 90–180 days after admission to hospital follow-up data.	Satisfied—Unique personal health numbers were used for linkage. Clinical trial data were pooled from 4 clinical trials that enrolled acute ischemic stroke patients within 12 h of stroke onset. Extracted data used for analyses included age, sex, baseline NIHSS, date of enrollment, and 90-day mRS score.
2. The completion rate and accuracy of variables to be linked should be presented.	Satisfied—In total, 15 582 AuSCR registrants (98%) were matched to a hospital admission or ED presentation (or both). Concordance of demographic variables in AuSCR and hospital admissions datasets was excellent for age and sex (κ=0.99).	Satisfied—Unique personal health numbers were reported to cover most (>99%) Alberta residents.
3. Coding practices and the use of standardized definitions should be stated, if used.	Satisfied—A data dictionary was developed. A subcommittee comprised experts in data linkage processes, clinicians, and researchers was formed. Coding was independent.	Satisfied—ICD-10-CA codes used to identify cases for ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and transient ischemic attack were reported. Only the most responsible diagnosis was used, which in Canada implies that stroke accounted for the highest resource use during the admission.
Linkage methodology and technology: Linkage algorithm (ie, deterministic or probabilistic), technology, and linkage analysts used may affect the overall linkage rate.		
1. A measure of the validity of the linked data sets (eg, false-positive and false-negative rates, if available) should be given.	Satisfied—Positive predictive value of AuSCR in-hospital death status was 96.1%, the negative predictive value 99.9%.	Not reported
2. An analysis of potential sources of bias among nonlinked cases should be reported.	Not reported	Not reported
3. The denominator used to derive linkage rates and justification for this should be reported.	Satisfied—AuSCR registrants were available for matching after removing data for patients with missing admission dates (919 admissions) or 102 participants who had opted out of the AuSCR.	Not reported
4. A description of the data linkage methods (ie, deterministic or probabilistic) with a justification for these.	Satisfied—As Australian residents (16 214) do not have unique personal identifiers, a combination of deterministic and probabilistic linkage methods was used to link patients from different state hospital and ED databases to AuSCR.	Satisfied—As unique personal health numbers were available, data were linked deterministically.
Ethical and data security considerations		
1. Opt-in inclusion involving one or more of the data sources should be presented, if it was required.	Not applicable—Participation in the AuSCR is based on an opt-out process.	Not applicable—Clinical trial data were pooled from 4 clinical trials that enrolled acute ischemic stroke patients within 12 h of stroke onset. Written informed consent was obtained for 3 trials and a waiver of consent for the remaining trial.
2. Linkage consent practices (if consent-based) should be described.	Not applicable	Not applicable

AuSCR indicates Australian Stroke Clinical Registry; ED, emergency department; ICD-10-CA, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canadian Modification; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

cleaning, validating, and analyzing secondary administrative data also requires time, training and infrastructure, and these costs can still be considerable. Researchers should consider using data linkage as adjuncts to address their outcomes when the databases of interest are of appropriate quality, scope, and coverage. This also minimizes data waste and reduces responder burden. Continued advancements in streamlining data linkage, without compromising privacy, will not only lead to an explosive growth in the use of data linkage for stroke outcomes research, but it will also fill research gaps towards understanding other patient groups. These real-world data offer a promising opportunity for evaluations to improve evidence-based practice and policy decision-making.

Disclosures

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KEY WORDS: big data ■ cohort studies ■ data collection ■ data linkage ■ mortality ■ registries ■ stroke

SUPPLEMENTAL MATERIAL

The Promising Use of 'Big Data' to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Data

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- **Supplementary Table I: Potential strengths and limitations of clinical studies, registries and utilization of data linkage using administrative data.**

Supplementary Table I. Potential strengths and limitations of clinical studies, registries and utilization of data linkage using administrative data.

Strengths	**Clinical studies**	**Registries**	**Administrative data**
Demographic data collected	S++	S+	S
Monitor QoC	S	S	
Clinician-driven diagnosis of stroke	S	S	
Long-term follow-up data collected e.g. QoL	S+	S	
Standardized definitions for variables ensures comparability over time and across geographical areas	S	S	S
Standardized and validated measurements used e.g. mRS	S	S	S / –
Diagnosis codes are recorded in ICD format allowing comparability with other international data sources		S	S
Sample size allow investigation of subgroups and ethnicities in multiethnic populations		S	S
Provide data regarding patient admissions, ED, comorbidities, rehabilitation, medication, healthcare utilization and geographic location			S
Limitations			
Retrospective data collection system	L / –		+
Time limited data collection	L	L / –	L / –
Provides snap-shot measurement of QoC and outcomes for a period of interest	L	L / –	L / –
Completeness of case ascertainment may limit generalizability	L	L	L
Only a small sample of patients with stroke selected per hospital for a period of interest	L		
Follow-up data collected, e.g. readmissions	L	L	L
Over or under-ascertainment of data due to administrative nature of data			L
Reliability and validity of coding data can vary in quality, accuracy and detail depending on whether diagnosis recorded was stroke or TIA		L	L
Can have high levels of missing information		L	L
Labor intensive and expensive data collection	L	L	
Complex data management and analysis methods required for large datasets			L
Only a few or no QoC indicators collected	L		L

QoC, Quality of Care; QoL, Quality of Life; mRS, modified Rankin Scale; ICD, International Classification of Disease; ED, emergency department; TIA, transient ischemic attack; 'S' denotes that this strength is present; '+' indicate more data is collected; 'S / –', strength can be present depending on the study or data source; 'L' limitation is present; 'L / –' limitation can be present depending on the study or data source; and empty cells indicate that this strength or limitation is not present.

Chapter 5: Data Linkage in the STANDFIRM Trial: Overview of Processes, Challenges and Solutions

In Chapter 4, I discussed the approaches for the collection of data regarding outcomes after stroke, their strengths and limitations and the utility that data linkage can provide to the collection of outcomes after stroke. Many of the challenges described in my topical review were obstacles that we faced during my time as the lead of our data linkage application between STANDFIRM and both the AIHW and the Centre for Victorian Data Linkage (CVDL; formerly VDL).

5.1 Overview

In this chapter, I will: (1) summarise stages of the data linkage application process, from the development of the data request to receiving the data, (2) provide detail of the datasets used throughout my studies, and (3) provide insights into the current efficiency of data linkage in Australia and how to plan accordingly to form realistic timelines.

5.2 Application Process

The data integrating authorities involved with this project, during the data linkage application process, included the Commonwealth AIHW and the State of Victoria CVDL. These authorities are required to comply with strict security regimes outlined in the Commonwealth Privacy Act 1988 and the Privacy and Data Protection Act 2014.[64] Contained within the Privacy Act are the 13 Australian Privacy Principles that regulate how specific agencies collect, hold, use and disclose personal information.[65] Ultimately, any data linkage work or research must be (1) in the public interest, (2) stored securely, (3) destroyed if no longer required and (4) must not be accessed by an unauthorised third party.

Summarised in Figure 5.1 were the main steps used throughout the data linkage process for both the AIHW and CVDL. Each research proposal should be well-designed with a policy question or aims that can be strictly fulfilled by the data requested. As of 2020, the first three stages depicted in Figure 5.1 have been consolidated into the development of a 'technical assessment' (AIHW) or 'technical feasibility assessment' (CVDL). This form is used by researchers to provide details regarding the investigators, project background, the research proposal and aims and perceived benefits to the community. The form also includes: (1) what data are required, (2) how the data will be used, (3) an analysis plan and (4) evidence that the project has local ethics approval and meets all ethical prerequisites.

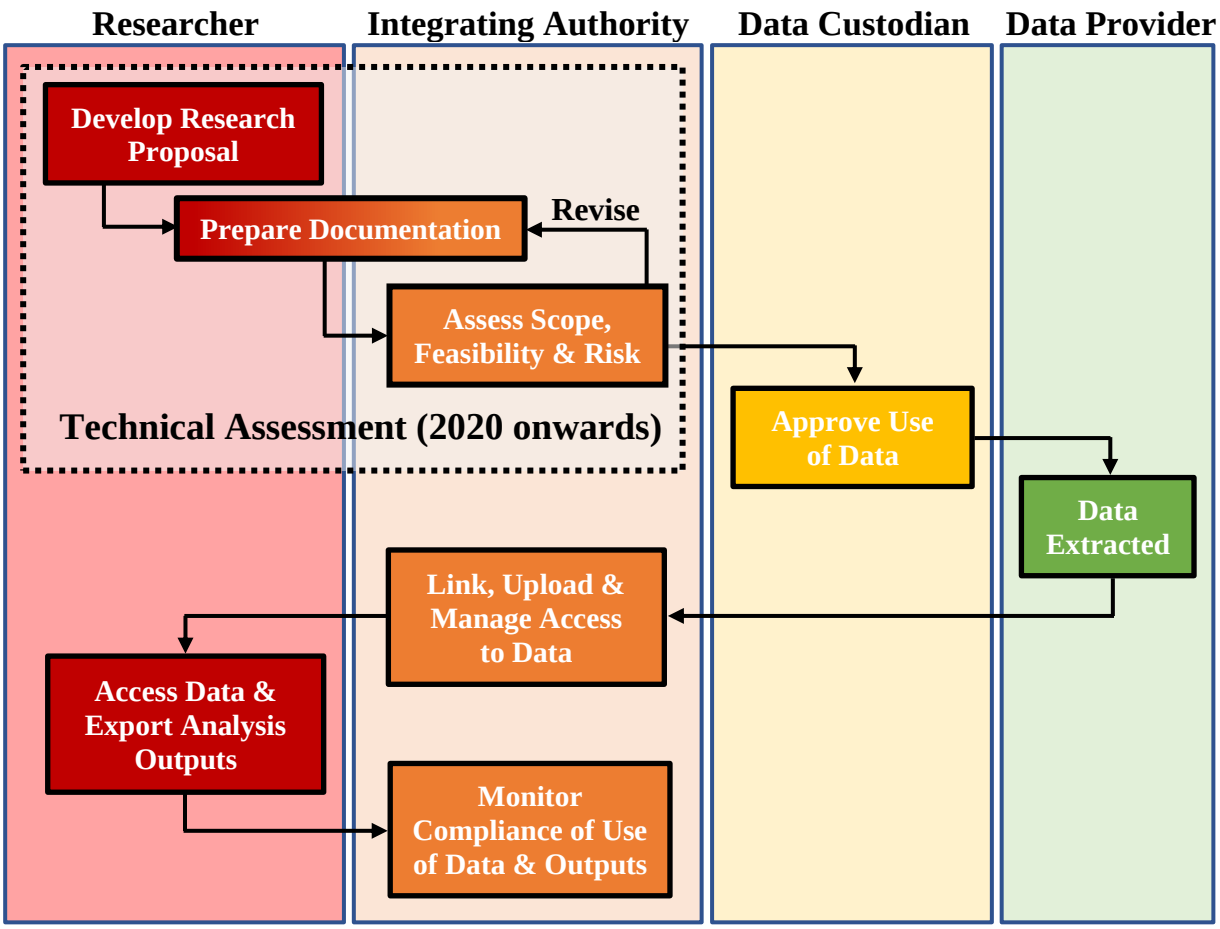


Figure 5.1. Stages and parties involved in the process of linking data to the Australian Institute of Health and Welfare (AIHW) and the Centre for Victorian Data Linkage (CVDL) as integrating authorities.

Stages encompassed in the dotted box have been consolidated, from 2020 onwards, into the preparation of a 'technical assessment' (AIHW) or 'technical feasibility assessment' (CVDL).

Data custodians will then be contacted to evaluate the feasibility of the data request, and if supported, the project will be considered at a subsequent ethics committee meeting for approval.[66] If approved by the data integrating authority, final approval will then be sought from the state or national Department of Health by the data integrating authority on behalf of the applicant.

5.2.1 AIHW's Involvement Within the Data Request Process

If access to Commonwealth or national datasets is required, a Public Interest Certificate must also be sought by the AIHW on behalf of the applicant. These national datasets include the: MBS, Pharmaceutical Benefits Scheme (PBS) and National Death Index (NDI). The Public Interest Certificate has to be signed by the Chief Data Steward or delegate of the Secretary of the relevant Commonwealth department.[66] On first contact with the AIHW, researchers are assigned a Project Manager who will provide guidance regarding the application process.[67] If required, they may also liaise with data custodians to address any concerns or queries regarding the feasibility of the proposed data request.

For all data linkage projects, data are provided de-identified when possible and for national data these must be accessed in an approved secure environment. An example of this is the Sax Institute's Secure Unified Research Environment (SURE).[68] The SURE is a remotely accessible computing environment in which data imports and exports are tightly controlled by a curated gateway. The AIHW are usually assigned as the curator that reviews and either rejects or approves for files to be uploaded to- or exported from the SURE. Figure 5.2 depicts the flow of identifiable and non-identifiable data between the requested datasets, until they are eventually linked and accessed by researchers in the SURE. Identifying information used for linking individuals to records included name, age, sex, postcode and address. These data were sent securely to the AIHW via the AIHW Secure Messaging system.

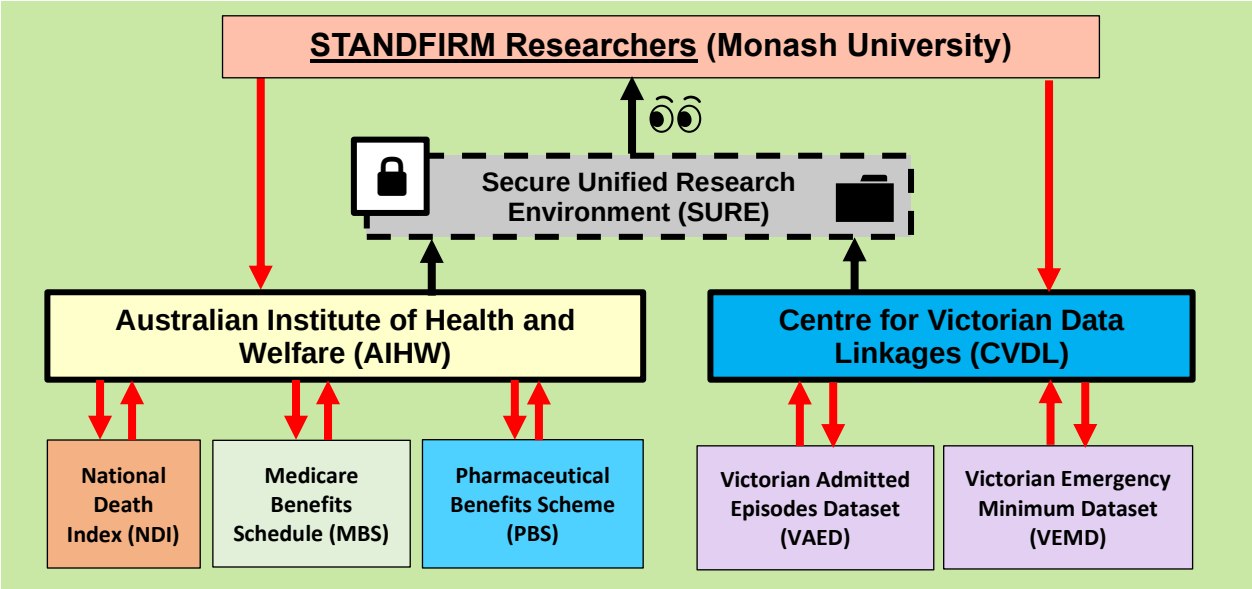


Figure 5.2. Data-linkage flowchart for participants with stroke from the STANDFIRM trial.

Red lines represent the flow of identifiable data (linkage variables such as name, age, sex, postcode, address), while black lines represent de-identified data.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management.

Approval from the AIHW for data extracts from the MBS, PBS and NDI Commonwealth datasets was granted in 2016 under the title "*Establishing high quality, integrated data for chronic disease management plans and secondary prevention medications and their effectiveness for patients after stroke: A substudy of STAND FIRM*" (Project ID: EO 2016/4/325; Figure 5.3).[69]

Establishing high quality, integrated data for chronic disease management plans and secondary prevention medications and their effectiveness for patients after stroke: A substudy of STAND FIRM (EO 2016/4/325)

Applicant: Monash University
Approval valid until: 31 December 2019

Approximately 50,000 Australians suffer a stroke each year. STAND FIRM, a research initiative, was designed to assist General Practitioners to manage stroke-related risk factors, and reduce stroke prevalence. STAND FIRM has recruited 570 stroke patients, randomly allocated to receive either an individualised management plan or standard care.

The STAND FIRM cohort will be linked with the National Death Index, Medicare Benefits Schedule and Pharmaceutical Benefits Schedule to meet the following objectives:

- Describe the uptake of chronic disease management plans within 12 and 24 months after a stroke
- Evaluate the effectiveness of chronic disease management plans, based on health outcomes (e.g., rates of hospitalisation, and mortality)
- Evaluate the effectiveness of secondary prevention medications

Findings will enable healthcare professionals to improve the management of stroke patients, and reduce the associated burden of disease.

Figure 5.3. Description of the data linkage project approved by the Australian Institute of Health and Welfare.

5.3 Datasets

Figure 5.4 depicts the information derived from each dataset and shows how linkage can provide a continuum of care over a typical patient's journey. Table 5.1 lists, for each dataset, the data custodian, the date ranges of the requested data and the number of records. Appendix F contains the full list of the data variables, from each dataset, that were uploaded to the SURE. Appendix G contains the data dictionary for variables that were uploaded to the SURE from the STANDFIRM trial database.

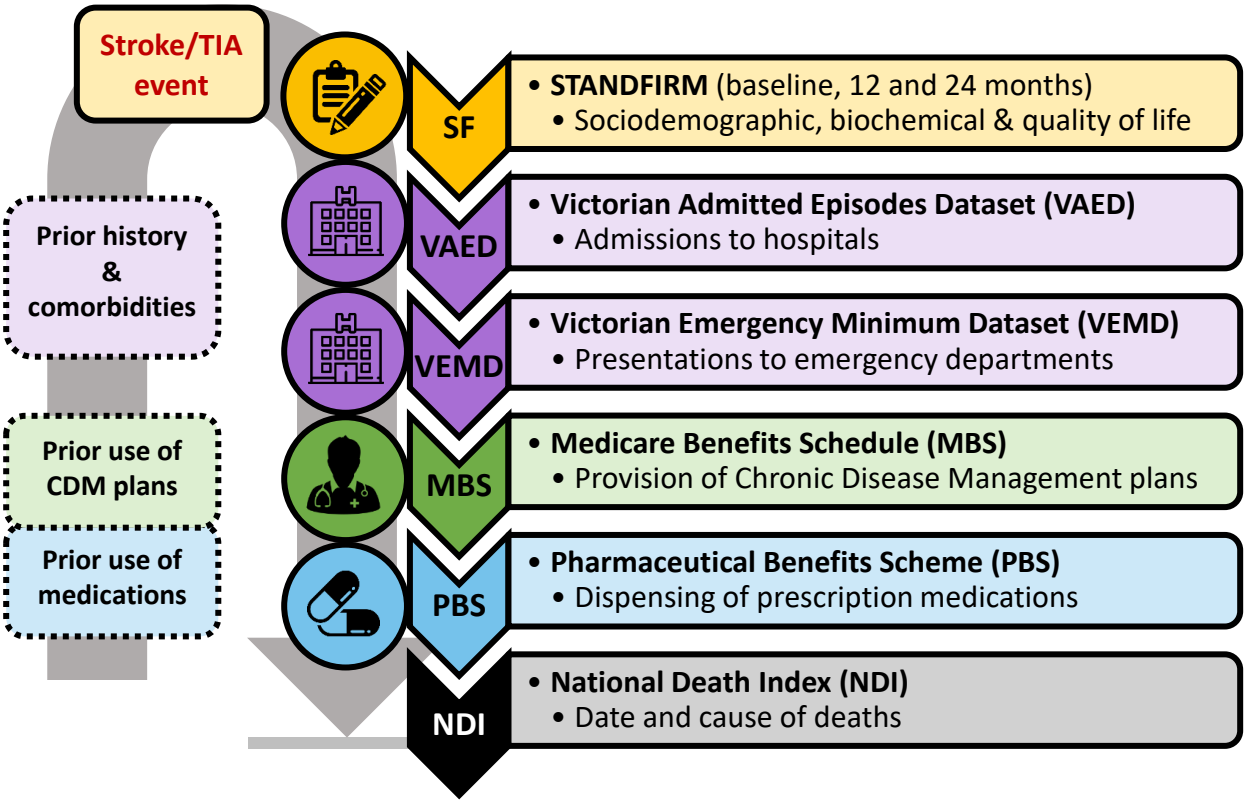


Figure 5.4. Depiction of key events, along the journey of a typical patient with stroke, that were derived from each dataset linked with the STANDFIRM trial.

The left-hand side of the arrow includes details obtained from before the hospitalisation, whereas the right hand side includes data obtained from after the event.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; TIA, Transient Ischaemic Attack.

Table 5.1. Summary of datasets utilised and linked for this project.

Data Custodian or Linkage Unit	Dataset	Earliest Date	Final Date	No. of Records*
STANDFIRM	**Assessments**	***Date of Stroke***	***24 Month Assessment***	566
		02 Jan 2010	13 Dec 2015	
AIHW (National Data)	**MBS**	***Date of Service***		3,970
		01 Aug 2005	28 Dec 2016	
	PBS	***Supply Date***		144,786
		01 Jan 2005	31 Dec 2016	
	NDI	**Death Date**		73
		31 Dec 2010	27 Dec 2016	
CVDL (State Data)	**VAED**	**Admission Date**	**Separation Date**	1,724
		16 Dec 2004	01 Jan 2017	
	VEMD	**Admission Date**		4,473
		01 Jan 2005	01 Jan 2017	

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; AIHW, Australian Institute of Health and Welfare; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme; NDI, National Death Index; CVDL, Centre for Victorian Data Linkage; VAED, Victorian Admitted Episodes Dataset; Victorian Emergency Minimum Dataset.

*Number of records prior to data cleaning stage.

5.3.1 STANDFIRM Dataset

The STANDFIRM study is described earlier in detail (Section 3.3) and the published protocol and SAP are included as Appendices A and B.[18, 47] Briefly, the STANDFIRM trial was a multicentre, cluster-randomised, controlled trial conducted in Melbourne, Australia. Participants with stroke were randomised to receive either an IMP (intervention) or usual care (control) and had follow-up assessments at 3 months, 12 months and 24 months. The trial was conducted from January 2010 to December 2015 and was led by researchers from the Stroke and Ageing Research group at Monash Health, School of Clinical Sciences, Monash University.

Randomisation of patients hospitalised for a stroke at four participating hospitals was based on a block procedure, so that each hospital had the same number of patients in each group. The IMP comprised two main components: a CDM plan and in-home tailored education about stroke prevention. The CDM plan was developed by a nurse with guidance from a stroke specialist (neurologist or geriatrician), and incorporated recommendations for well-defined health targets and adherence to therapies for secondary prevention using guidelines for stroke care.[18] The exact recommendations outlined in the CDM plan were based on the patients' health information acquired at baseline by a blinded assessor (Appendix D). The education component was conducted by nurses alongside the assessments at baseline, and 3 and 12 months (Appendix C). At these home visits, nurses provided individualised education about the secondary prevention of stroke. Further discussion took place about any needs and concerns that were raised by the participant. Specific education was also provided about the correct timing and dosage of medications, self-management skills and how to identify and address any potential side effects of medications.

The CDM plan provided to those in the intervention group of the STANDFIRM trial could be claimed by GPs through Medicare as it satisfied all of the aforementioned criteria (Section 3.2) for a GPMP (CDM item 721) or TCA (item 723). However, the actual uptake of CDM plans by participants in the intervention and usual care arm in STANDFIRM was unknown. Assessment of the use of these plans was required to assist in interpreting the findings from the STANDFIRM trial.

5.3.2 National Datasets

The AIHW has access to many national datasets that are owned and managed, as data custodians, by the Australian Government Department of Health. The AIHW hold extensive data on a wide range of health and welfare areas, including ageing, disability, disease, expenditure, hospitals,

injury, mental health, and the needs of Aboriginal and Torres Strait Islander people.[70] The datasets used in this study included the MBS, PBS and NDI. These datasets are described below:

Medicare Benefits Schedule (MBS)

The MBS contains historical and current records from January 2000 onwards of medical and hospital services that are subsidised by the Australian Government through the Medicare Program, including the CDM plan items. Please see Section 3.2 for more detail related to information collected in the MBS.

Medicare Enrolment File

The Medicare Enrolment File contains personal details (e.g. name, sex, date of birth and address) for all individuals registered with Medicare from November 1983 onwards. There are potentially multiple address records per person, due to changes in addresses over time. Therefore, the date that the Department of Human Services is notified of each change in address is also provided. It should be noted that only mailing addresses were provided to the AIHW and while mailing and residential addresses are the same for the vast majority of Australians, a proportion of these addresses are non-residential and include post office box addresses.

Pharmaceutical Benefits Scheme (PBS)

The PBS provides all permanent residents with access to subsidised prescription medicines and contains records of all prescriptions that were subsidised by the Australian Government. These include the PBS and Repatriation PBS (RPBS; since July 2002), as well as PBS/RPBS prescriptions priced below the patient co-payment that are not subsidised (since April 2012). The RPBS is a scheme administered by the Department of Veterans' Affairs under which the cost of prescription medications provided to veterans of Australia's defence force, their widows/widowers and dependants.

The PBS database includes details of all medications dispensed, including their type, strength and quantity, and although primarily collected for billing purposes, can facilitate pharmaco-epidemiological research.[71] An example dummy set of PBS data is provided in Table 5.2. All medications listed on the PBS schedule have an associated PBS "item code" that identifies the medications' form and strength, as well as a seven character Anatomical Therapeutic Chemical (ATC) code to identify medications, irrespective of strength.[72] For example, antihypertensive medications, most relevant to secondary stroke prevention include diuretics (ATC code C03), beta blockers (C07), calcium channel blockers (C08) and agents acting on the renin-angiotensin system (C09). A limitation of the PBS is that medications purchased over the counter or used during a hospital stay are not recorded. Furthermore, the PBS also lacks information on the actual daily dose prescribed by the GP to the patient. As most PBS quantities are intended for a 1-month supply, one potential solution used within some studies is to assume a prescribed daily dose (PDD) of one dose per day (1DD).[73, 74] Estimations or assumptions of daily dose and how these affect medication adherence estimates are evaluated in a large cohort of survivors of stroke in Chapter 8.

Table 5.2. Example of Pharmaceutical Benefits Scheme (PBS; blue) data linked with STANDFIRM trial data.

ID	Baseline date	Date of supply	Days since baseline	Drug	Quantity	Dosage*
1	17-Jan-12	07-Jan-12	-10	Atorvastatin	30	1
1	17-Jan-12	22-Jan-12	5	Atorvastatin	30	1
1	17-Jan-12	23-Feb-12	37	Atorvastatin	30	1
1	17-Jan-12	20-Mar-12	63	Simvastatin	30	1
1	17-Jan-12	17-Apr-12	91	Simvastatin	30	1
1	17-Jan-12	12-May-12	116	Simvastatin	90	1
1	17-Jan-12	07-Aug-12	203	Simvastatin	90	1

*Dosage (quantity/day) must be derived from another data source or estimated.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; TIA, Transient Ischaemic Attack.

National Death Index (NDI)

The NDI records all deaths in Australia since 1980 and is updated on a mid-monthly basis. Data in the NDI are obtained from the Registrars of Births, Deaths and Marriages in each State and Territory. As of 2017, the AIHW would usually require 18 months to access cause of death data of recent deaths. For example, for deaths registered in 2020, cause of death may only become available mid 2021 or later.

5.3.3 State Datasets

The CVDL was established in 2009 to develop the linkage capacity and infrastructure in Victoria and is the Victorian state node of the Population Health Research Network.[75, 76] Their services are provided free-of-charge to policymakers and researchers for approved projects. Similar to the AIHW, the CVDL can also serve as a trusted intermediary between researchers and data custodians to facilitate research, while maintaining the privacy of sensitive data. They are based in the Victorian Government Department of Health and Human Services, who serve as the data custodians of many health and non-health administrative collections. We sought linkage with two data collections through the CVDL: the Victorian Admitted Episodes Dataset (VAED) and Victorian Emergency Minimum Dataset (VEMD).

Victorian Admitted Episodes Dataset (VAED)

A minimum set of data is reported monthly by all Victorian public and private hospitals, for each admitted patient episode in the VAED since July 1993, and includes data from day procedure centres, extended care facilities and rehabilitation centres.[76] Comprehensive data are recorded in the VAED and include information related to demographics, date of arrival, use of hospital health services, diagnosis (coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification; ICD-10-AM), procedures, causes, effects, nature of illness and the immediate outcome following treatment.

Victorian Emergency Minimum Dataset (VEMD)

The VEMD details all presentations at Victorian public hospitals with designated emergency departments (ED) since July 2000. However, data from private hospitals are not captured. The VEMD includes fields relating to demographics, diagnosis, procedures, arrival and departure details.

5.4 Barriers and Limitations of Data Linkage

For data linkage projects, there are many barriers and limitations for undertaking this type of research. These are described in detail in my topical review (Chapter 4). Described here are some of the specific lessons learnt from pursuing a data linkage project in Victoria. For all projects, it is essential to plan out the analyses of a project prior to an application, such as creating an SAP or protocol, as any amendments will significantly delay receipt of the linked data. It would be realistic to expect that there may be delays in timelines, due to unforeseen circumstances and linkage complexities. An example of this was with the linkage we pursued with the CVDL. We found that our initial linkage rate for the STANDFIRM cohort was 97.0% (n=553/570). Based on advice from Kilkenny et al. of a similar study, we were able to improve this linkage rate to 99.5% (n=567/570) with the provision of uniquely identifying Medicare numbers.[77] This amendment added a few months to the linkage process. In some cases, it may take 1.5-3 years to receive all the requested data, so rather than specifying an end date for their data (e.g. 31 December 2017), applicants should request in their application that the latest available data are provided. This is because by the time the data are received, compared with the current date, the data may be up to three years older than originally anticipated and could affect the impact and implications of the study's findings.

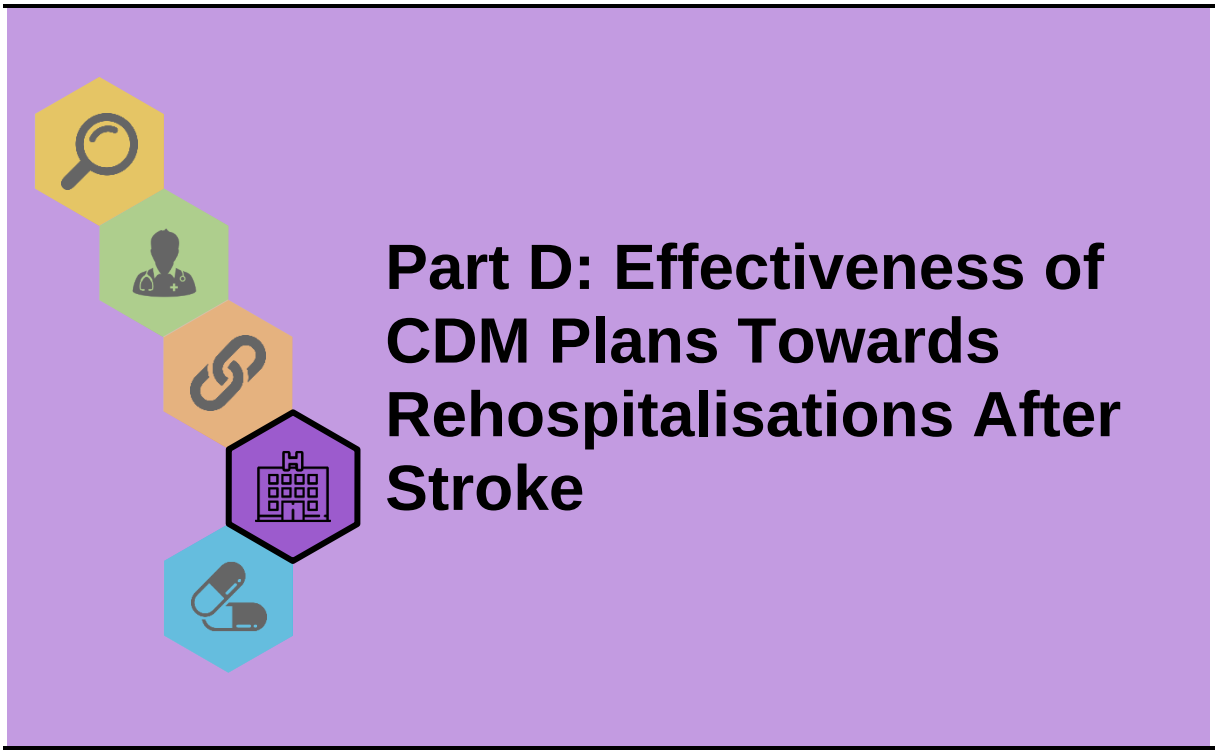
5.5 Summary

Pursuing a data linkage project in Australia can be time-consuming. However, there is a growing opportunity for data linkage to be used for research in Australia. Although, it is clear that there are still many obstacles to overcome to improve data linkage applications and build capacity to link routinely collected administrative data nationwide.

Summary of Part C

In Part C, I introduced the concepts of data linkage, big data and the datasets used for this doctoral thesis. In Chapter 4, I discussed the strengths and limitations of using secondary data, based on routinely collected administrative databases, for research into outcomes after stroke. In Chapter 5, I described and outlined the processes and datasets used for undertaking a data linkage project within the context of the STANDFIRM trial. I also highlighted any lessons learnt and how data linkage should be approached in Australia and internationally.

In Parts D and E of my thesis, I will provide two examples of how data can be linked and analysed to evaluate readmissions and medication adherence after stroke.


Part D: Effectiveness of CDM Plans Towards Rehospitalisations After Stroke

Chapter 6: Longer Duration on a Chronic Disease Management Plan Is Associated With Fewer Cardiovascular Disease-Related Readmissions Within 3 Years of Stroke

6.1 Overview

In Part B, I outlined the increased uptake of CDM plans that had occurred for the usual care group in the STANDFIRM trial and that subsequent analyses of the use of CDM plans were to be undertaken using a per-protocol approach. In this chapter, we aimed to investigate the effectiveness of increasing exposure to a CDM plan on reducing CVD-related readmissions after stroke (primary outcome). The manuscript for this work was submitted to the *Medical Journal of Australia* and is presented in Section 6.3.

6.2 Summary of Primary Outcome Measure

Additional information is provided in the manuscript regarding how the primary outcome for this study was derived. Briefly, CVD-related readmissions to hospital/ED were captured during the two-year follow-up period via self-report and were adjudicated by two stroke specialists. A completed example of this form is provided in Appendix H. An additional one year of data (total of three years) were obtained via our linkage of the STANDFIRM trial participants with hospital admission (VAED) and ED presentation (VEMD) databases (Figure 6.1). Using the linked hospital/ED data, additional CVD-related readmissions within three years of stroke were determined based on ICD-10-AM diagnoses codes. Comorbidities, from up to five years prior to stroke, were also determined based on ICD-10-AM diagnoses codes derived from hospital and ED databases. The complete range of ICD-10-AM codes used to capture these CVD-related readmissions and comorbidities are provided in

Appendices I and J. Exposure to CDM plans within three years was calculated based on the cumulative amount of time each participant was on a plan. This is explained further in the included manuscript below.

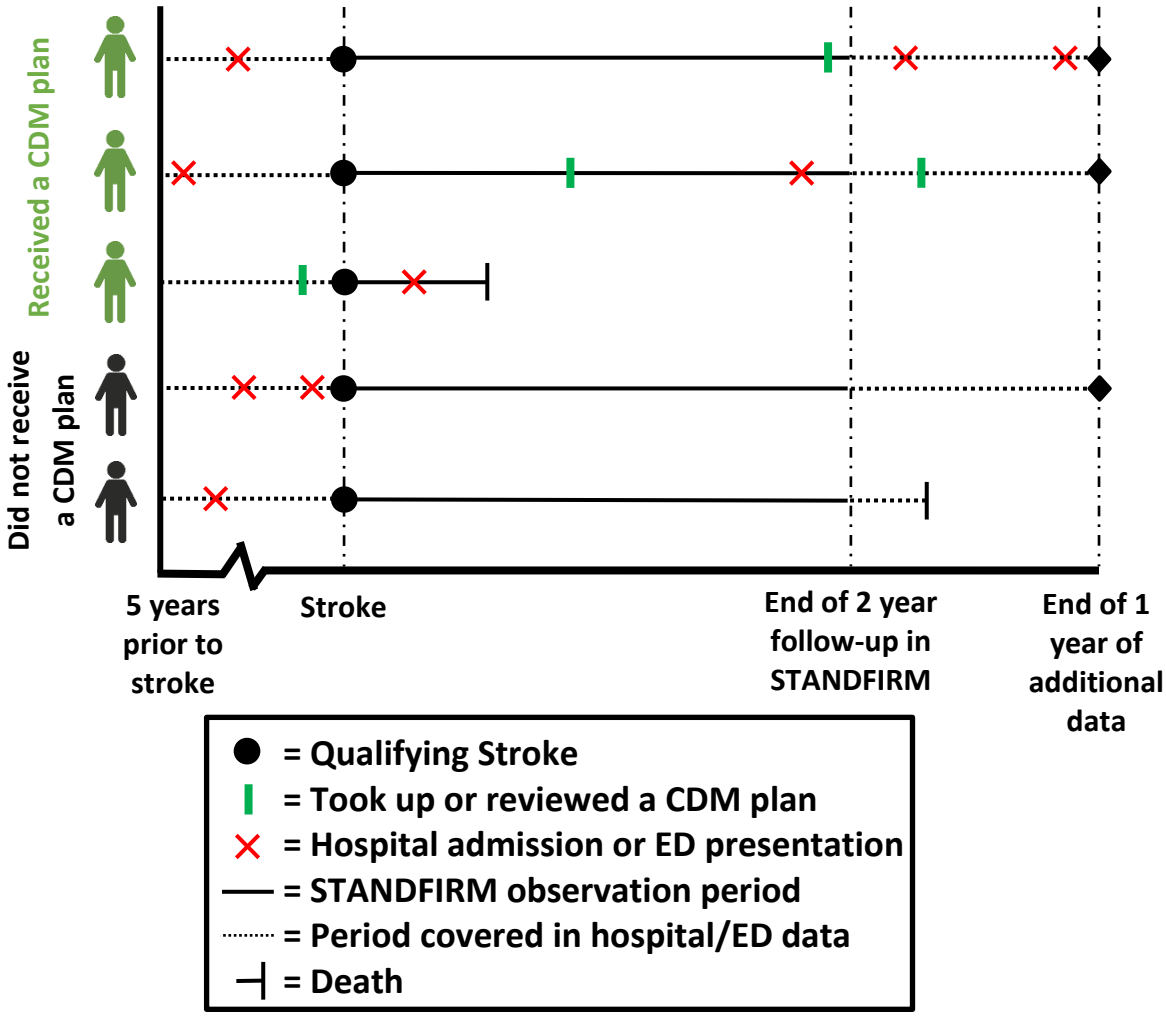


Figure 6.1. Occurrence of CVD-related readmissions, deaths and uptake of CDM plans for STANDFIRM trial participants with stroke.

CDM, Chronic Disease Management; ED, emergency department; STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management.

6.3 Submitted Paper

Longer duration on a chronic disease management plan is associated with fewer cardiovascular disease-related readmissions within 3 years of stroke

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Longer duration on a chronic disease management plan is associated with fewer cardiovascular disease-related readmissions within 3 years of stroke

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Abstract

Background and Purpose: Chronic Disease Management (CDM) plans are designed to better manage risk factors in those with chronic medical conditions, but there is limited evidence of their effectiveness in survivors of stroke. We aimed to determine whether being on CDM plans for longer was associated with a reduced rate of cardiovascular disease-related (CVD) readmissions.

Methods: Survivors of stroke or transient ischaemic attack, recruited for a clinical trial (2010-2013; registration ACTRN12608000166370), had comprehensive baseline data on risk factors. Patients were individually linked to death, hospital, healthcare claims and pharmacy dispensing databases. Negative binomial regression was conducted to determine the incidence rate ratio (IRRs) of CVD-related readmissions according to duration on a CDM plan, adjusting for confounding factors.

Results: In total, 562 participants were included (median age 70 years; 36% female). Within three years of stroke, 73% had a CDM plan with a median exposure of 1.75 years (Q_1: 1.00, Q_3: 2.43). In multivariable analysis, factors most strongly associated with fewer CVD-related readmissions were: longer duration on a CDM plan (IRR 0.86, 95% confidence interval [95% CI] 0.75-0.98; p=0.023), fewer comorbidities (IRR 1.24, 95% CI 1.06-1.45; p=0.008), more physically active occupation (IRR 0.63, 95% CI 0.43-0.92; p=0.018) and better baseline quality-of-life (IRR 0.25, 95% CI 0.10-0.58; p=0.001).

Conclusion: Being on a CDM plan for longer appeared to reduce the rate of CVD-related readmissions within three years of stroke. Patients should be encouraged to return for regular reviews of their CDM plans to enhance secondary prevention strategies and avoid CVD-related readmissions.

Introduction

Chronic conditions, such as stroke, cancer and diabetes, are responsible for 85% of the total burden of disease in Australia and contribute to 87% of deaths.[1] Stroke alone represents a significant burden affecting more than 50,000 Australians each year,[2] significant lifetime costs,[3] and more than $30 billion in due to loss of healthy life years and total burden of disease.[4] The Australian Government, through its universal health care system, Medicare, has made a commitment to reduce the growing demand on acute care services and avoidable hospital admissions in those with chronic diseases such as stroke.[1, 5] Specific Medicare-funded items, termed Chronic Disease Management (CDM), implemented at a primary care level are targeted at managing chronic diseases via self-management of risk factors and care coordination.[6]

The aim of these CDM plans is to provide a flexible, person-centred model of care to help manage risk factors and complex comorbidities in those with a chronic disease,[7] such as stroke. These Medicare-funded items require significant effort from GPs to tailor these plans to individuals.

Due to the comprehensive nature of these individualised CDM plans, GPs are recompensed for their time with extra government rebates. Despite use of CDM plans increasing markedly in recent years (see Supplementary Figure I in the online-only Data Supplement),[8-12] their effectiveness in stroke remains to be established. We aimed to determine the frequency and duration of use of CDM plans within three years of stroke, and to determine whether being on a CDM plan for a longer duration is associated with a reduced recurrence rate of cardiovascular disease-related (CVD) readmissions.

Methods

The patient cohort was derived from the Shared Team Approach between Nurses and Doctors For Improved Risk Factor Management (STANDFIRM) trial, conducted in Melbourne, Australia. STANDFIRM was a prospective clinical trial of patients with first-ever stroke or transient ischaemic attack (TIA) recruited between 2010 and 2013 and followed up for two years (see the online-only Data Supplement). Patients in the intervention arm of the trial were provided with in-home tailored education and had a CDM plan prepared for them. This prepared CDM plan was then sent to GPs for each patient in the intervention arm. However, the decision for whether the CDM plan was provided or not remained with each patient's GP. The study protocol and statistical analysis plan have been previously published.[13, 14]

For this study, data on STANDFIRM participants were linked to routinely collected administrative health and person-level data from four databases. This also extended the collection of outcomes and exposure to up to three years after stroke. The STANDFIRM trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12608000166370). Due to the sensitive nature of the data obtained for this study and ethical requirements for its use, we cannot provide these data upon request.

Data Sources and Linkage

The data used for this study comprised person-level data from the STANDFIRM study linked to three administrative databases (Figure 1):

1. The STANDFIRM trial, which included sociodemographic details, self-reported and measured risk factors at baseline and self-reported CVD-related readmissions over a two-year period following stroke (2010–2013; see online-only Data Supplement);

2. The Medicare Benefits Schedule contained healthcare claims for CDM plans (items 721, 723, 729, 731 and 732) obtained from the Australian government (2009–2016);

3. The Victorian Admitted Episodes Dataset and Victorian Emergency Minimum Dataset encompassed all public hospital admissions and emergency department (ED) presentations in Victoria (2010–2016);

4. The National Death Index is a registry of all deaths and their primary causes in Australia (2010–2016).

Ethics approval for this study was obtained from various sources (see online-only Data Supplement).

Sociodemographic information from STANDFIRM, such as age, sex and educational attainment were ascertained from self-report. We used the 10-year Framingham Risk Score as an overall estimate of each patient's baseline level of risk factors.[15] Other covariates included socio-economic position, disability, health status, anxiety and depression, risk factor profile and health-related quality of life (see online-only Data Supplement for how these measures were derived).

Primary Outcome

The primary outcome was the number of CVD-related readmissions within three years following stroke. Readmissions were primarily ascertained through self-report at 3, 12 and 24 months in-person interviews and were adjudicated by two stroke specialists (JF and RG) using supporting medical documentation. We supplemented this approach by identifying CVD-related readmissions from hospital admissions and ED presentation databases using primary and secondary International Classification of Diseases, 10th Revision, Australian Modification diagnoses codes for CVD. In this study, CVDs included stroke, myocardial

infarction, congestive heart failure and atrial fibrillation. Duplicate records from the administrative data, based on similar or overlapping dates of admission or discharge, were excluded to avoid double counting.

Measuring Exposure to a CDM Plan

The exposure variable of interest was the duration that patients were on a CDM plan within three years of stroke. Each patient's 'exposure' to a CDM plan was derived from Medicare's CDM items (see Supplementary Table I). The minimum claiming period for each CDM plan was used to calculate the overall exposure to a CDM plan within three years from baseline. Exposure periods were appropriately truncated at three years for CDM plans that continued beyond three years. The dichotomous variable for prior exposure to a CDM plan was determined based on whether a CDM item was claimed within the 12 months prior to the baseline date of assessment.

Statistical Analyses

We compared the number of CVD-related readmissions between those who were and were not provided a CDM plan within three years of stroke, using the Mann-Whitney U test with 1,000 bootstrap samples. The number of CVD-related readmissions was also compared between those with lesser and greater handicap, stratified using the median London Handicap Scale.

Due to the minimum claiming periods of 3 and 12 months for each CDM item, the cumulative exposure to a CDM plan was not normally distributed. Therefore, exposure to a CDM plan was stratified into quintiles. Using a stepwise negative binomial regression modelling approach, we evaluated whether increasing quintile of exposure to a CDM plan was associated with the incidence of CVD-related readmissions within three years after stroke. Variables with the largest p-value were sequentially removed from the model until

only those with a p-value ≤0.1 remained. All analyses were reported as incidence rate ratios (IRRs) and were adjusted for age, sex, stroke severity and intervention status at baseline, with these variables retained in the model even when their p-value >0.1. The negative binomial regression model was also censored for deaths, to account for reduced exposure time and so a reduced opportunity for receiving a CDM plan. Violin plots were also generated to break down the distribution of time until the first CVD-related readmission, based on provision of a CDM plan (see Supplementary Figure II). As a sensitivity analysis, we also investigated the possible confounding effect of medication use on the possible association of CDM plan exposure and CVD-related readmissions at three years after stroke (see Supplementary Table III). All analyses were performed using Stata version 13 or above.

Results

Among 570 participants, we achieved a 99.6% match between participant records from STANDFIRM with hospital, ED and death databases. Seven participants were excluded from all analyses because they were not randomised and one participant was excluded as an outlier because of a large number of (>35) hospitalisations over the three-year study period, primarily for atrial fibrillation.

Among the 562 participants included, the median age was 70 years, 36% were women, 78% were independent (mRS score of 0-1) and collection of baseline data occurred at a median 78 days following a participants' stroke. In total, there were 305 CVD-related readmissions within three years after stroke. One third (n=104) of the included CVD-related readmissions were self-reported, linked with hospital records and adjudicated. The remaining two-thirds (n=201) were derived from hospital and ED records. Most of the self-reported readmissions were for a CVD-related intervention (31.6%), ischaemic stroke (22.1%) and atrial fibrillation (11.6%). The median time until the first recurrent CVD-related readmission or death was 272

days and this was similar between those who did and did not have a CDM plan within three years of stroke (see Supplementary Figure II). Furthermore, we were unable to detect a difference in the number of CVD-related readmissions between those who were and were not provided a CDM plan for the total cohort (z-score=0.43; 95% confidence interval [CI] -1.54-2.41; p=0.661) or within subgroups of those who were least (z-score=-0.20; 95% CI -2.12-1.72; p=0.841) and most handicapped (z-score=1.17; 95% CI -0.81-3.15; p=0.248).

Uptake of Chronic Disease Management plans (Medicare data)

Within one year of stroke, uptake of CDM plans in the intervention group (72.7%) was more than double that in the usual care group (32.5%; see Supplementary Table II). Overall, 73.3% of participants in our cohort had a CDM plan within three years (Table 1) and had a median exposure of 1.75 years (Q_1: 1.00, Q_3: 2.43). The median time to receive or review a CDM plan after the index stroke was 0.54 years (Q_1: 0.27, Q_3: 1.17).

Participants who had a CDM plan within three years following stroke had a greater level of socio-economic disadvantage, greater handicap, a poorer quality of life and were more likely to be on antihypertensive or lipid-modifying medications at baseline than those who did not have a CDM plan (Table 1). They were also more likely to have a CDM plan if they were randomised to the intervention group. In multivariable analyses, fewer CVD-related readmissions occurred for those with a longer duration on a CDM plan (quintiles; IRR 0.86; 95% CI 0.75-0.98, P=0.023), greater level of education, more physically active occupation, a greater quality of life, a healthier risk factor profile and greater socio-economic advantage (Table 2; see Supplementary Figure III). In our sensitivity analysis, the IRR estimates for the association of CDM plan exposure with CVD-related readmissions did not differ (<10%

difference) from those when the model was also adjusted for medication use in the year prior to stroke (see Supplementary Table III).

Discussion

In this study we present important evidence of primary care management policy whereby being on a CDM plan for a longer duration was associated with a reduced incidence of CVD-related readmissions at three years after stroke. This association was independent of other factors, such as greater educational attainment and better quality of life, each of which were positively associated with a reduced incidence of CVD-related readmissions. Greater socio-economic advantage and a poorer risk factor profile were associated with an increased IRR.

We found that increasing duration on a CDM plan, and not historical use of a CDM plan, was associated with a reduced recurrence rate of CVD-related readmissions after stroke. This evidence suggests that there may be a dose-response to the effectiveness of this program after stroke and that the policy is effective for this patient group. Being on a CDM plan that is consistently reviewed by a GP every six months to a year may facilitate improvements in risk factor-related health behaviours and adherence to secondary prevention medications. Therefore, regular reviews of CDM plans, and opportunities this provides for education and reinforcement, may cement the longer-standing lifestyle changes required to reduce the likelihood of CVD-related readmissions.

This study has some limitations. Our approach likely captured most readmissions to public hospitals, some admissions to private hospitals may have been missed. In addition, we were unable to determine whether adhering to a CDM plan is sustainable beyond three years as we only had at least three years of data available for all patients in our study. As this is a non-randomised analysis, detection bias could result from patients who were on a CDM plan being more likely to willingly present to the hospital. Confounding by indication is another

potential limitation, whereby trial participants with hypertension may be more likely to be given a CDM plan than those without hypertension, and also more likely to be readmitted to hospital. However, our association estimates for CDM plan exposure, depicted in Supplementary Table III, did not differ by >10% when adjusted for prior use of each class of medication. In each of these models, CDM plan exposure remained inversely associated with CVD-related readmissions. Another limitation is that trial participants may be generally more motivated to optimise their health by remaining on CDM plans for longer and so these findings may not be reflective of the whole Australian population. Alternatively, GPs may be more likely to recommend CDM plans to those with a more favourable prognosis and are likely to adhere to these plans. To minimise these potential sources of bias, we have used a combination of both prospectively and retrospectively collected data to ascertain readmissions and adjusted our regression models for age, sex, stroke severity and group allocation. Finally, our finding that a more physically active occupation appeared to be associated with a reduced IRR in our final multivariable model, may be a result of residual confounding, where those with a non-sedentary occupation tended to remain on a CDM plan for longer than those in more sedentary occupations.

A major strength of this study is that one third of the readmissions were adjudicated by two stroke specialists and our risk factor assessments were systematically collected using strict methods. Another strength for our models is that we were able to adjust for pill burden in our multivariable model. Pill burden was associated with CVD-related readmissions after stroke and is likely to be attributable to the overall comorbidity load of each patient.

Further research is required to investigate whether: (1) the reduced incidence of readmissions, with longer duration of exposure to a CDM plan, can be sustained beyond three years; (2) those on a CDM plan tend to utilise healthcare or rehabilitation services differently than those

not on a plan; (3) adherence to CDM plans is associated with better control of risk factor-related health behaviour; and (4) these plans are cost-effective.

This study supports the current policy of subsidising GPs for developing CDM plans for those with stroke and potentially other chronic diseases.[16] To our knowledge, this is the first study undertaken to examine the temporal and dose-response association between the duration of being on a CDM plan and the recurrence of CVD-related readmissions in those following stroke. Although there has been an increase in use of CDM plans by GPs in the past decade (by 356% from 2008 to 2017), there is still room for improvement. Indeed, in our STANDFIRM study, within just the first year following a stroke more than twice as many people in the intervention group were provided with a CDM plan than those in the usual care group. The fact that this uptake was maintained for at least three years, despite the intervention concluding at two years, demonstrates some sustainability to our approach. Patients should be encouraged to adhere to regular reviews of their CDM plans with their GP to enhance secondary prevention strategies and avoid CVD-related readmissions.

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Disclosures

AGT reports being a Board Member of the Stroke Foundation (Australia). DAC reports grants from National Health and Medical Research Council, Stroke Foundation and the Heart Foundation. All other authors report no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Table 1. Baseline characteristics and cardiovascular disease-related (CVD) readmissions of the STANDFIRM cohort according to use of a Chronic Disease Management (CDM) plan within three years after stroke.

Factors	**Total* (N=562)**	**Did not take up a CDM plan* (N=150)**	**Had a CDM plan* (N=412)**	
	n (%)	**n (%)**	**n (%)**	**P-value**
Outcome variables				
CVD-related readmissions, median (Q_1, Q_3)	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.664
0 CVD-related readmission	399 (71.0)	104 (69.3)	295 (71.6)	0.600
1 CVD-related readmission	104 (18.5)	30 (20.0)	74 (18.0)	0.582
≥ 2 CVD-related readmissions	59 (10.5)	16 (10.7)	43 (10.4)	0.937
Exposure to a CDM plan				
Years on CDM plan:				
0	150 (26.7)	150 (100)	–	–
>0 – 1.0	60 (10.7)	–	60 (14.6)	–
>1.0 – 1.5	127 (22.6)	–	127 (30.8)	–
>1.5 – 2.3	112 (19.9)	–	112 (27.2)	–
>2.3 – 3.0	113 (20.1)	–	113 (27.4)	–
Used a CDM plan in prior year	197 (35.1)	Censored	Censored	<0.001
Baseline characteristics				
STANDFIRM intervention group	283 (50.4)	44 (29.3)	238 (57.8)	<0.001
Used in prior year:				
Antihypertensive drug(s)	329 (58.5)	73 (48.7)	256 (62.1)	0.004
Lipid modifying drug(s)	170 (30.3)	49 (32.7)	121 (29.4)	0.452
Antithrombotic drug(s)	265 (47.2)	60 (40.0)	205 (49.8)	0.040
Age, median (Q_1, Q_3)	70.2 (60.9, 78.7)	68.3 (57.8, 78.5)	71.0 (61.6, 78.8)	0.255
Men	362 (64.4)	105 (70.0)	257 (62.4)	0.095
Independent†	437 (77.8)	122 (81.3)	315 (76.5)	0.219
Married/living with a partner	369 (65.7)	90 (60.0)	279 (67.7)	0.088
Education level > high school	287 (51.1)	84 (56.0)	203 (49.3)	0.158
Non-sedentary occupation	334 (59.3)	87 (58.0)	246 (59.7)	0.715
IRSAD Percentile, median (Q_1, Q_3)	64.0	67.5	62.5	0.016

	(40.0, 80.0)	(45.0, 84.0)	(39.0, 78.0)	
London Handicap Scale score, median (Q_1, Q_3)	0.86 (0.73, 0.93)	0.89 (0.79, 0.97)	0.85 (0.71, 0.93)	<0.001
Diabetes	56 (10.0)	11 (7.3)	45 (10.9)	0.212
10-year Framingham Risk Score, median (Q_1, Q_3)	19.8 (10.9, 33.1)	18.4 (10.5, 29.3)	20.5 (11.1, 34.3)	0.227
Body Mass Index, median (Q_1, Q_3)	27.9 (24.6, 31.1)	27.1 (25.1, 30.4)	28.1 (24.3, 31.6)	0.147
Assessment of Quality of Life score, median (Q_1, Q_3)	0.70 (0.48, 0.85)	0.76 (0.59, 0.91)	0.66 (0.43, 0.84)	<0.001
Depression‡	77 (13.5)	17 (11.3)	59 (14.3)	0.329
Anxiety‡	102 (18.2)	23 (15.3)	79 (19.2)	0.296

* n (%) unless otherwise indicated.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; CVD, cardiovascular disease; CDM, Chronic Disease Management; mRS, modified Rankin Scale; IRSAD, Index of Relative Socio-economic Advantage and Disadvantage; Q_1, lower quartile; Q_3, upper quartile. Mann-Whitney U test was used to for continuous variables and Pearson's chi-squared test for categorical variables. To comply with ethical restrictions, cells were 'censored' in instances where a cell count could be calculated for cells that contained <5 individuals.

† Being independent was defined as having a modified Rankin Scale score of 0-1 and not independent if >1.

‡ Depression and anxiety were defined as having a HADS score >7.

Table 2. Negative binomial regression of factors associated with the number of cardiovascular disease-related readmissions within three years of stroke.

	Univariable		Multivariable*	
Factors	**IRR**	**P-value**	**IRR**	**P-value**
Adjustment variables				
Age, per year	1.03 (1.02, 1.05)	**<0.001**	1.02 (1.00, 1.04)	**0.012**
Male	0.92 (0.61, 1.38)	0.683	0.96 (0.65, 1.44)	0.855
modified Rankin Scale score	1.11 (0.88, 1.40)	0.374	0.84 (0.66, 1.08)	0.170
STANDFIRM Intervention group	1.17 (0.79, 1.72)	0.432	1.01 (0.70, 1.47)	0.955
Exposure to a CDM plan				
Duration on CDM plan (quintiles)†	0.89 (0.78, 1.01)	0.080	0.86 (0.75, 0.98)	**0.023**
Used a CDM plan in prior year	1.01 (0.68, 1.50)	0.961	–	–
Baseline characteristics‡				
Pill burden in prior year (quintiles)	1.42 (1.25, 1.62)	**<0.001**	1.41 (1.24, 1.61)	**<0.001**
Used in prior year:				
Antihypertensive drug(s)	1.87 (1.25, 2.81)	**0.002**	–	–
Lipid modifying drug(s)	2.02 (1.38, 2.94)	**<0.001**	–	–
Antithrombotic drug(s)	2.26 (1.52, 3.37)	**<0.001**	–	–
Education level > high school	0.89 (0.55, 1.43)	0.630	–	–
London Handicap Scale score	0.25 (0.06, 1.05)	0.059	–	–
10-year Framingham Risk Score	1.02 (1.00, 1.04)	**0.028**	–	–
BMI category§	1.36 (1.06, 1.74)	**0.017**	–	–
CCI category (comorbidity burden) ¶	1.35 (1.15, 1.59)	**<0.001**	1.24 (1.06, 1.45)	**0.008**
Diabetes	1.69 (0.92, 3.11)	0.089	–	–
Smoker	1.63 (0.95, 2.79)	0.074	1.80 (1.05, 3.08)	**0.033**
Depression#	1.16 (0.64, 2.11)	0.621	–	–
Anxiety#	1.37 (0.81, 2.33)	0.237	–	–
Assessment of Quality of Life score	0.25 (0.10, 0.60)	**0.002**	0.25 (0.10, 0.58)	**0.001**
Non-sedentary Occupation	0.82 (0.56, 1.20)	0.301	0.63 (0.43, 0.92)	**0.018**
Married or living with partner	1.01 (0.67, 1.51)	0.978	1.45 (0.96, 2.21)	0.080
IRSAD (quartile)	1.10 (0.91, 1.33)	0.308	–	–

IRR, incidence rate ratio; STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; CDM, Chronic Disease Management; BMI, Body Mass Index; CCI, Charlson Comorbidity Index; IRSAD, Index of Relative Socio-economic Advantage and Disadvantage. Data are expressed as IRRs.

* Baseline characteristics were sequentially removed until only those with a p-value ≤0.1 were retained in the model.

† Comparison group comprises patients not on a CDM plan at any time following stroke (i.e. 0 years; first quintile).

‡ Baseline characteristics in the univariable analyses were adjusted for age, sex, stroke severity (mRS) and intervention status.

§ BMI categories were underweight and normal (<25kg/m^2), overweight (25 - <30kg/m^2) and obese (>30 kg/m^2).

¶ CCI categories were none (0 comorbidities), moderate (1 comorbidity), severe (2 comorbidities) and very severe (≥3 comorbidities).

Depression and anxiety were defined as having a HADS score >7.

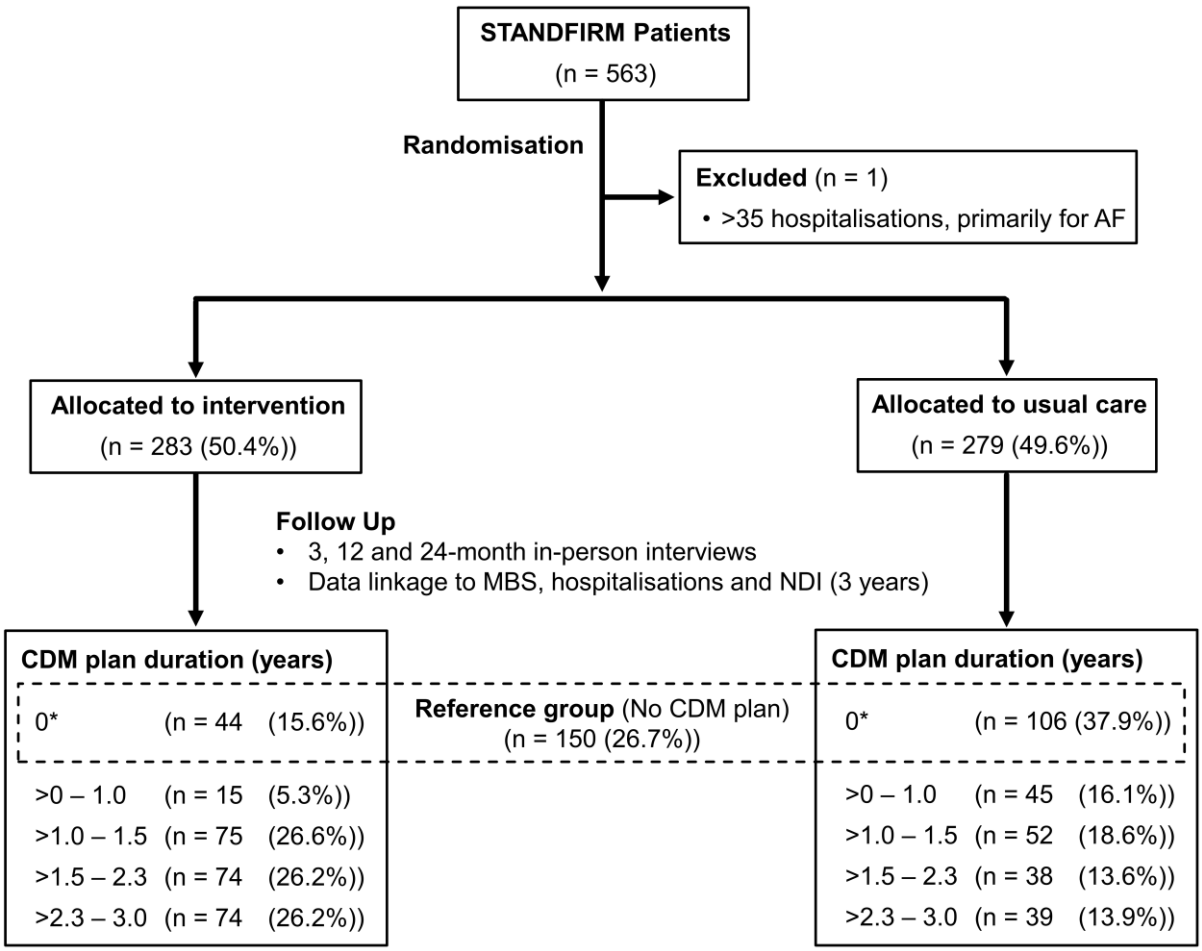

Figure 1. Flow diagram of participants included in analysis and cumulative exposure to Chronic Disease Management (CDM) plans.

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme; NDI, National Death Index; VAED, Victorian Admitted Episodes Dataset; VEMD, Victorian Emergency Minimum Dataset.

* A CDM plan was prepared for each participant in the intervention arm, and this was then sent to the participant's GP. As the GP could then decide whether or not to provide this plan to their patient, some participants in the intervention group were not provided a CDM plan.

SUPPLEMENTAL MATERIAL

Longer duration on a chronic disease management plan is associated with fewer cardiovascular disease-related readmissions within 3 years of stroke

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Supplemental Tables:

- **Supplementary Table I.** Description and minimum claiming period for Chronic Disease Management (CDM) items in the Australian health care system.
- **Supplementary Table II.** Uptake of Chronic Disease Management (CDM) plans before and within three years after stroke among patients in the STANDFIRM trial.
- **Supplementary Table III.** Multivariable incidence rate ratios (IRRs) of exposure to Chronic Disease Management (CDM) plans (quintiles) with number of cardiovascular disease-related readmissions within three years after stroke, determined within users and non-users of each medication class in year to stroke.

Supplemental Figures:

- **Supplementary Figure I.** Frequency of use of Chronic Disease Management (CDM) plans in Australia from 2008 to 2017. Frequency of CDM plan use was derived from claims that were processed for Medicare items 721, 723 and 732 within each year over this period.
- **Supplementary Figure II.** Horizontal violin plots of the distribution of time until first cardiovascular disease-related serious adverse event or death between those who took up (Yes) or did not take up (No) a Chronic Disease Management (CDM) plan within three years after stroke.
- **Supplementary Figure III.** Multivariable negative binomial regression of factors associated with recurrence of cardiovascular disease-related serious adverse events within three years of stroke.

Supplemental Methods

The STANDFIRM trial

Design

The Shared Team Approach between Nurses and Doctors For Improved Risk Factor Management (STANDFIRM) trial was a multicentre, cluster-randomized, controlled trial conducted to assess the effectiveness of an individualized management program (IMP) for managing risk factors following stroke, with blinded assessment of outcomes and intention-to-treat analyses. The trial was conducted in Melbourne, Australia between January 2010 and December 2015, and its study design and methods have been previously published.[1] Briefly, patients were recruited from four participating hospitals and were eligible if they were hospitalised for a stroke or transient ischaemic attack (TIA), aged at least 18 years and lived within 50 km of the closest recruitment hospital. Potential participants were excluded if they were admitted from or discharged to a nursing home, or were diagnosed with a rapidly deteriorating health condition. Participants were randomised to receive either an IMP (intervention) or usual care (control) based on a block randomisation procedure to obtain a similar distribution of study groups within each recruitment hospital. Written informed consent was obtained prior to any interview being conducted.

Intervention and usual care

The intervention in STANDFIRM comprised an IMP with two components: a Chronic Disease Management (CDM) plan, able to be subsidised by Medicare, and in-home tailored education about stroke prevention. The control arm was a group of survivors of stroke/TIA who were not provided an IMP by the study group and received ‘usual care’. The CDM plan was prepared by a nurse, who was aware of the group allocation of the patient, with guidance from a stroke specialist (neurologist or geriatrician). The plan comprised recommendations for well-defined

health targets and adherence to therapies for secondary prevention using guidelines for stroke care.[1] The exact recommendations outlined in the CDM plan were based on the patients' health information acquired at baseline by a blinded assessor and this management plan was sent to each patients' GP for use at future visits. The education component of the IMP comprised visits by a nurse to patients at approximately 2 weeks following each of the blinded assessments. During these visits individualised education was provided about self-management and the secondary prevention of stroke. Further discussion took place about any needs and concerns that were raised by the participant. Correct timing, dosages and how to identify and address any potential side effects of medications were also discussed.

Baseline covariates

Sociodemographic information, such as age, sex, educational attainment, marital status and residential address were ascertained via interview. Patients' residential addresses were used to identify their corresponding geographical area known as Statistical Areas Level 1 (SA1). These SA1s were then used to estimate their socio-economic position using the census-derived 2011 Socio Economic Indexes For Areas Index of Relative Socio-economic Advantage and Disadvantage (IRSAD) provided by the Australian Bureau of Statistics.[2] The IRSAD percentiles rank individuals from 1, for Australians living in the most socio-economically disadvantaged areas in Australia, to 100 for the most advantaged areas. The IRSAD were then stratified into quartiles from greatest disadvantage to greatest advantage for subsequent analyses. Nurses also conducted standardised assessments at baseline of disability (modified Rankin Scale), health status, anxiety and depression using validated questionnaires.

The Assessment of Quality of Life (AQoL) instrument is a multi-attribute utility scale that is used to measure health-related quality of life. This 15 item scale has been validated in an Australian population with stroke,[3] and a greater AQoL score indicates a greater quality of life. The London Handicap Scale (LHS) was used to measure health status over 6 domains: mobility,

physical independence, occupation, social integration, orientation and economic self-sufficiency.[4] A greater LHS score indicates less handicap. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression via two subscales, each containing 7 items;[5] a score greater than 7 in the relevant subscale was used to categorise participants as having depression or anxiety.

Data Linkage

De-identified person-level data from the STANDFIRM was linked with the Medicare Benefits Schedule and National Death Index databases by the Australian Institute of Health and Welfare. The Victorian Admitted Episodes Dataset (hospital admissions) and Victorian Emergency Minimum Dataset were provided by the Centre for Victorian Data Linkage.

Ethics

The STANDFIRM trial and this data linkage sub-study were approved by each participating hospital and Monash University (HREC number 2011000331). Ethics approval for data linkage was also obtained from the Australian Institute of Health and Welfare (project reference number EO 2016/4/325), which is an accredited integrating authority for data linkage.

Supplementary Table I. Description and minimum claiming period for Chronic Disease Management (CDM) items in the Australian healthcare system.[6]

Item Number	Description	Minimum Claiming Period*
721	Preparation of a GP Management Plan (GPMP)	12 months
723	Coordination of Team Care Arrangements (TCAs)	12 months
729	Contribution to a Multidisciplinary Care Plan, or to a Review of a Multidisciplinary Care Plan, for a patient who is not a care recipient in a residential aged care facility	3 months
731	Contribution to a Multidisciplinary Care Plan, or to a review of a multidisciplinary care plan, for a resident in an aged care facility	3 months
732	Review of a GPMP or Coordination of a Review of TCA	3 months

GP, General Practitioner.

*CDM plans may be provided more frequently in exceptional circumstances, such as if there is a significant change in a patient's clinical condition or care requirements. A TCA is designed for patients with chronic conditions who require multidisciplinary care from at least three different care providers, one of who is a medical practitioner.

Supplementary Table II. Uptake of Chronic Disease Management (CDM) plans before and within three years after stroke among patients in the STANDFIRM trial.

	STANDFIRM Cohort				
	Total* n (%) (n=562)	**Usual Care* n (%) (n=280)**	**Intervention* n (%) (n=282)**	**P-value**	**% uptake of CDM plans in intervention group versus usual care**
Use of a CDM plan in the year prior to stroke	197 (35.1)	98 (35.0)	99 (35.1)	0.979	-
Median (Q_1, Q_3) years on CDM plan†	1.09 (0, 2.18)	0.86 (0, 1.72)	1.69 (1.00, 2.42)	**<0.001**	50.8
Took up a CDM plan after stroke within:					
1 Year	296 (52.7)	91 (32.5)	205 (72.7)	**<0.001**	123.7
2 Years	359 (63.9)	131 (46.8)	228 (80.9)	**<0.001**	72.9
3 Years	412 (73.3)	174 (62.1)	238 (84.4)	**<0.001**	35.9

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management. Data are expressed as total count (proportion).

* n (%) unless otherwise indicated

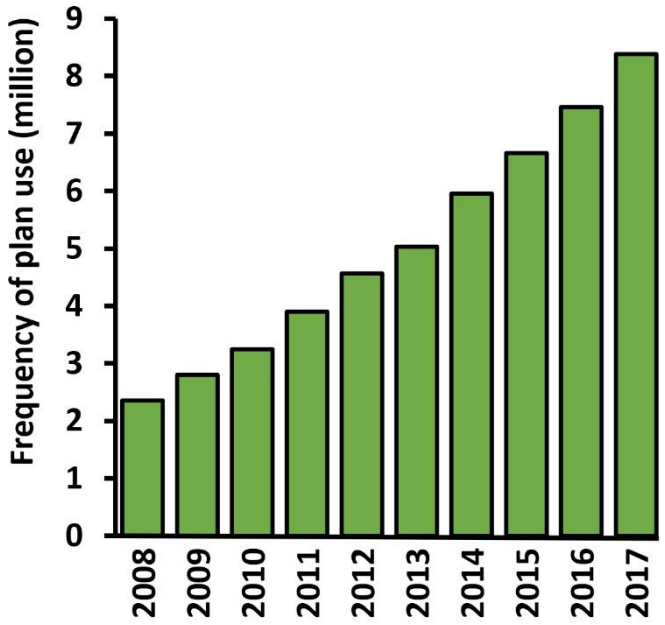
† Mann-Whitney U test was used for continuous variables.

Supplementary Table III. Multivariable incidence rate ratios (IRRs) of exposure to Chronic Disease Management (CDM) plans (quintiles) with number of cardiovascular disease-related readmissions, within three years after stroke (model 1) and with adjustment for users and non-users of each medication class (models 2-4).

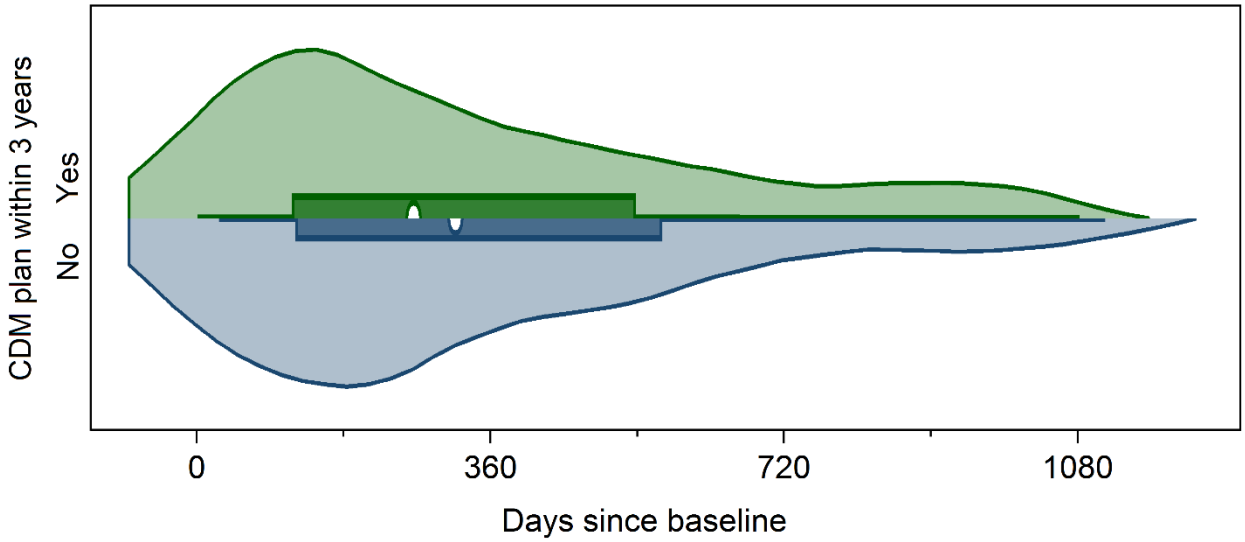
Model and Cohort	IRR of CDM exposure (95% CI)	SE	p-value	>10% difference in effect estimate?*
1. Full cohort (final model)	0.86 (0.75, 0.98)	0.06	0.023	Ref
2. AH user in prior year	0.87 (0.77, 1.00)	0.06	0.044	No
3. AT user in prior year	0.87 (0.76, 0.99)	0.06	0.035	No
4. LM user in prior year	0.86 (0.75, 0.98)	0.06	0.022	No

95% CI, 95% confidence interval; SE, standard error; AH, antihypertensive; AT, antithrombotic; LM, lipid modifying.

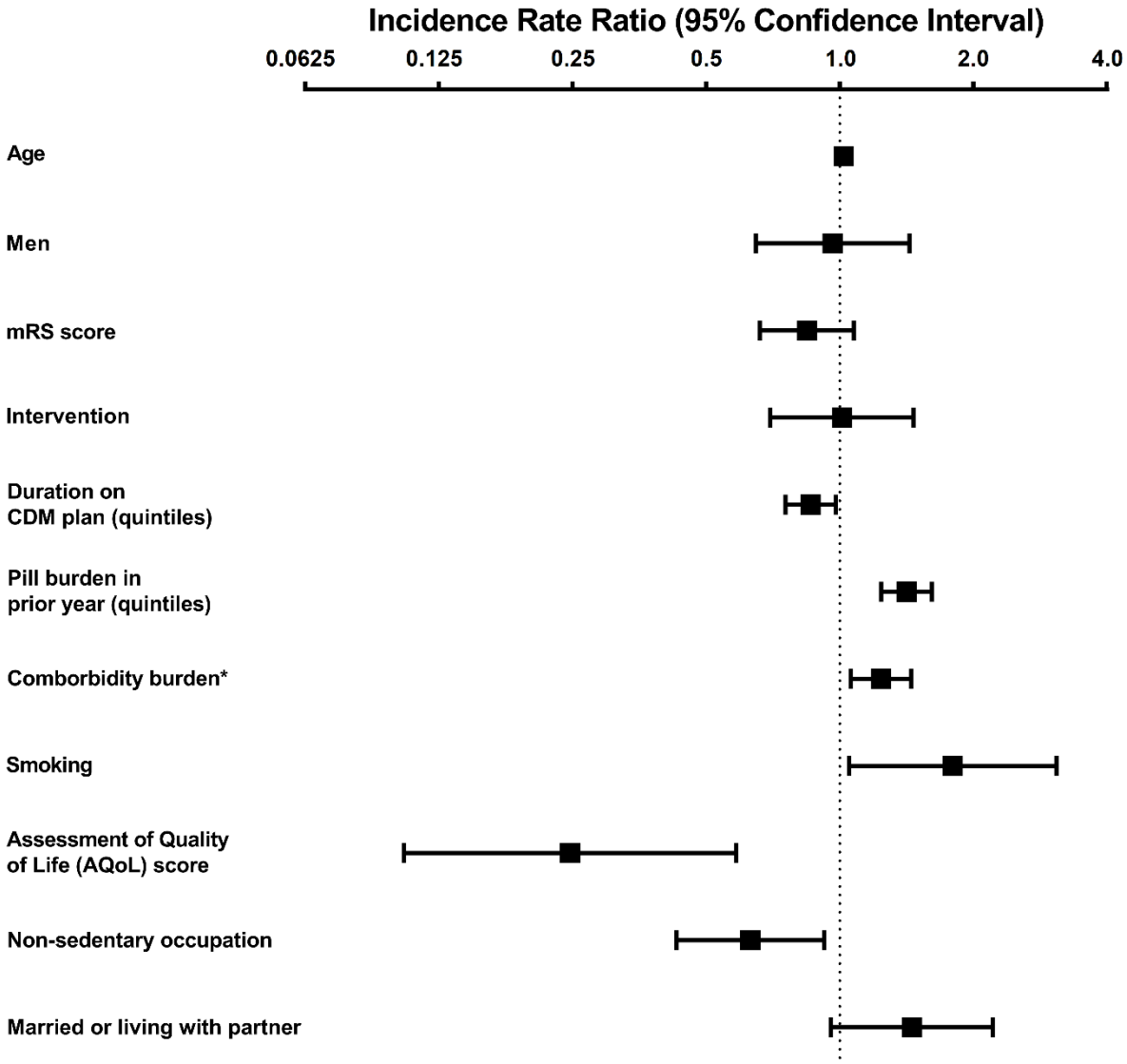
* Difference >10% when comparing IRR of current model with Model 1 for the full cohort.



Supplementary Figure I. Frequency of use of Chronic Disease Management (CDM) plans in Australia from 2008 to 2017. Frequency of CDM plan use was derived from claims that were processed for Medicare items 721, 723 and 732 within each year over this period.[7]



Supplementary Figure II. Horizontal violin plots of the distribution of time until first cardiovascular disease-related serious adverse event or death between those provided (Yes) or not provided (No) a Chronic Disease Management (CDM) plan within three years after stroke.



Supplementary Figure III. Multivariable negative binomial regression of factors associated with recurrence of cardiovascular disease-related serious adverse events within three years of stroke.

*Comorbidity burden was categorised into four groups: none (0 comorbidities), moderate (1 comorbidities), severe (2 comorbidities) and very severe (≥3 comorbidities).

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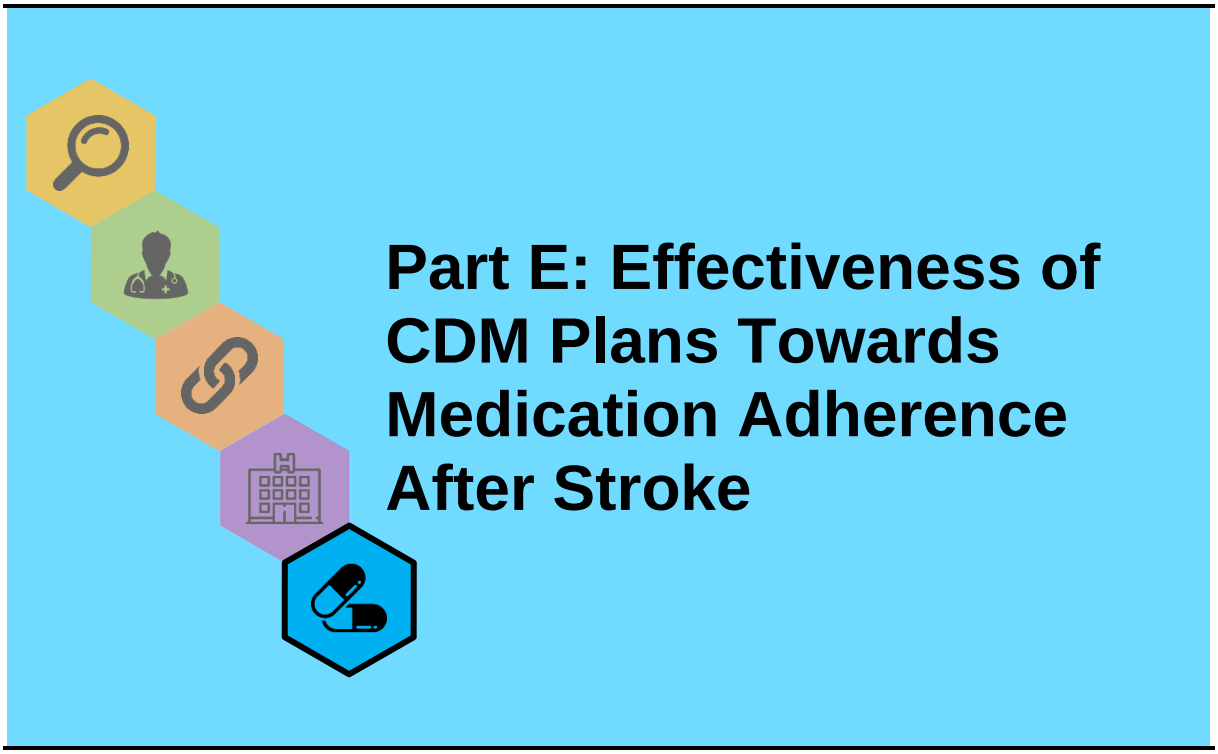
Part E: Effectiveness of CDM Plans Towards Medication Adherence After Stroke

Chapter 7: Longer Duration on a Chronic Disease Management Plan Is Associated With Long-Term Adherence to Antihypertensive and Antithrombotic Medications Following Stroke

7.1 Overview

The PBS allows for prescription drugs to be dispensed to Australian residents at Government-subsidised costs.[78] One of the underlying principles for providing this scheme is that the included medications cost-effectively preserve the health of all Australians. To gain the benefits of secondary prevention therapies, medications must be prescribed to patients and the specified dosage regimen adhered to. However, there is evidence that patients do not continue to take their medications, with only 86.6% continuing to take secondary prevention medications at 12 months after stroke.[79] Although factors such as timing of prescription (e.g. at hospital discharge) have been associated with adherence, the most important reasons for discontinuing medications remain unclear.[80-82]

Eight of the ten most subsidised drugs in Australia are associated with the primary and secondary prevention of stroke and other CVDs (i.e. cholesterol- and BP-lowering medications).[83] However, despite progress in Australia in reducing smoking rates and stroke mortality, there are no data regarding the effectiveness of CDM plans in improving adherence to secondary prevention medications.[4] In this chapter we will determine, via a per-protocol analysis, whether a longer duration on a CDM plan was associated with being adherent to secondary prevention medications after stroke. The included manuscript was submitted to the *Medical Journal of Australia*.

7.2 Submitted Paper

Longer duration on a Chronic Disease Management plan is associated with long-term adherence to antihypertensive and antithrombotic medications following stroke

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[MANUSCRIPT SUBMITTED TO MEDICAL JOURNAL OF AUSTRALIA]

Longer duration on a Chronic Disease Management plan is associated with long-term adherence to antihypertensive and antithrombotic medications following stroke

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Abstract

Background and Purpose: Chronic Disease Management (CDM) plans are used by general practitioners to manage chronic diseases such as stroke, but it is unclear whether these plans improve adherence to prevention medications. We aimed to assess whether a longer duration on a CDM plan was associated with better adherence to secondary prevention medications following stroke.

Methods: Patients with stroke or transient ischaemic attack participating in the STANDFIRM trial were individually linked to Medicare claims for CDM plans and dispensings of secondary prevention medications from the Pharmaceutical Benefits Scheme. We estimated (1) duration on a CDM plan based on the timing and frequency of these claims and (2) adherence using the proportion of days that patients would have been covered by these medications (PDC), while accounting for deaths and instances of over-supply. Logistic regression was used to evaluate factors associated with ≥80% adherence, up to three years after stroke, for each of antihypertensive, antithrombotic and lipid-modifying drugs.

Results: The median PDC for 563 patients (median age 70 years; 36% female) ranged from 92% to 95% among the three classes of medications. Approximately 27% did not take up a CDM plan, 33% were on plans for <1.5 years and 40% for 1.5-3 years. Duration on a CDM plan (quintiles) was associated with adherence to antihypertensive (odds ratio [OR] 1.18, 95% confidence interval [95% CI] 1.00-1.40, p=0.029) and antithrombotic (OR 1.22, 95% CI 1.03-1.46, p=0.024) medications, but not for lipid-lowering medications.

Conclusion: People on a CDM plan for longer had better adherence to antihypertensive and antithrombotic medications in the long-term after stroke. Use and ongoing reviews of CDM plans should be encouraged to improve adherence to secondary prevention medications following stroke.

Introduction

Survivors of stroke or transient ischaemic attack (TIA) are at greater risk of death and recurrent stroke.[1, 2] Within five years of stroke, approximately 10% to 26% of patients have a recurrent event.[2-4] Promoting adherence to secondary prevention medications is one of the major recommendations for long-term care outlined in the Stroke Foundation (Australia) clinical guidelines.[5] This is important as it has been estimated that up to 9% of all cardiovascular events can be directly attributed to poor adherence to medications,[6] so there are opportunities to reduce these further vascular events.

General practitioners (GPs) are integral to providing assessments for chronic diseases, including stroke and other conditions expected to persist for at least six months, advice regarding secondary prevention and arranging for visits to other specialists.[7] Included in this service are Medicare-funded GP Chronic Disease Management (CDM) plans. As regular reviews with a GP may enhance adherence to secondary prevention medications, we aimed to determine whether a longer duration on a CDM plan was associated with adherence to recommended secondary prevention medications after stroke.

Methods

Patients with first-ever stroke or TIA were recruited, between 2010 and 2013, as part of the Shared Team Approach between Nurses and Doctors For Improved Risk Factor Management (STANDFIRM) trial conducted in Melbourne, Australia. The study protocol and statistical analysis plan have been previously published and the STANDFIRM trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12608000166370).[8, 9] Briefly, sociodemographic information, such as age, sex, educational attainment, marital status and residential address were ascertained from hospital records and self-report at baseline. Physical assessments and questionnaires were used to obtain details of risk factors, disability,

anxiety, depression, and health-related quality of life within two years of follow-up after each qualifying stroke. We used the 10-year Framingham Risk Score (FRS), which is derived from modifiable and non-modifiable risk factors for CVD, as an overall estimate of each patient's baseline level of risk.[10]

Linkage and Administrative Datasets

We linked each patient's data from the STANDFIRM trial to routinely collected data from healthcare claims, medication claims and death databases. Healthcare claims for medical services subsidised by the Australian government, from January 2009 to December 2016, were obtained from the Medicare Benefits Schedule (MBS) claims database. Medication claims were obtained from Pharmaceutical Benefits Scheme (PBS) database, and these included details of medications that were dispensed to patients in Australia. From July 2012 onwards the PBS database recorded details for all medications dispensed, but prior to July 2012 only medications that attracted a subsidy were recorded. Medications dispensed in-hospital are not recorded in the PBS. Deaths from 2010 to 2016 were obtained from the National Death Index (NDI), this being a registry of all deaths that occurred in Australia.

Outcome Variable

The outcome was adherence to secondary prevention medications at three years after stroke. We included three recommended medication classes for the secondary prevention of stroke: (1) antihypertensive medications (AH; includes diuretics, beta-blocking agents, calcium channel blockers and agents acting on the renin-angiotensin system), (2) antithrombotic medications (AT; includes antiplatelet and anticoagulant medications) and (3) lipid-modifying (LM) medications.

We calculated adherence to each class of secondary prevention medication based on the proportion of days covered (PDC) method. This involves determining the overall proportion

of days in a patient's observation period that they have access to a supply of medication. The start and end dates for exposure to a class of secondary prevention medication was determined for each dispensing record. PDC calculations were also adjusted for deaths that occurred before three years. For example, a patient who died after two years would have a PDC of 100% if they were dispensed enough medications of that class to cover two years.

Using dosage assumptions from prior work,[12] we derived estimates of time until refill, for each medication strength and pack size, from a much larger cohort of patients with stroke from the Australian Stroke Clinical Registry. To allow for differences in prescribed dosages that may occur due to the initial stroke occurring more than a year ago, we calculated the 75th percentiles of days until next refill for each medication and strength. This number of days was used to calculate the daily dose (dosage) for each medication and strength by dividing the supply amount for each dispensing by this calculated number of days. The duration intervals for each dispensing was then determined by dividing the amount dispensed by these estimates of dosage derived from a population with stroke.

We adjusted the PDC for instances of 'stockpiling', a common phenomenon by which patients return to pharmacies to refill their prescriptions before their current supply was exhausted, but still finish their current supply before initiating the next. To achieve this, the subsequent supply date of refills were extended by the number of days of overlap between the prior supply's end date and subsequent supply's start date. Additionally, dispensing of secondary prevention medications within 40 days prior to each individuals' date of stroke were identified. This was used to account for instances where patients may have been told to exhaust their current supply before receiving a refill. The number of days of supply that would have continued past the date of stroke contributed to the total days covered by that

class of medication. A detailed explanation of this carry over method has been described by Arnet et al.[11]

Patients were considered 'adherent' if they had a PDC of 80% or greater, as this would indicate that these patients were dispensed enough medication to cover at least 80% of their observation period up to three years after stroke.

Measuring Exposure to a CDM Plan

Duration on a CDM plan was calculated as the cumulative exposure to CDM plans at three years after stroke. Each type of CDM plan was assigned a duration based on the minimum claiming period of each, which is the minimum amount of time before another claim for this item can be made. CDM items 721 and 723 had a minimum claiming period of 12 months, while 729, 731 and 732 were 3 months. Periods of exposure to a CDM plan were truncated if they continued beyond three years. Duplicate records, based on identical dates of service, were excluded to avoid double counting. The year prior to stroke was also monitored to determine prior exposure to a CDM plan.

Statistical Analyses

Three exposure contrasts were examined within our single cohort of patients with stroke. Our analyses included users and non-users of: (1) antihypertensive, (2) lipid-modifying and (3) antithrombotic medications. Patients were classified as a user of a medication if they were dispensed at least one medication for that class of medication during the observation period. Within each of these cohorts, factors associated with being adherent (PDC ≥80%) to that class of medication were examined using stepwise logistic regression models. Duration on a CDM plan was stratified into quintiles and examined as a potential covariate, among other risk and demographic factors. Variables with the largest p-value were sequentially removed from the model until only those with p-value ≤0.1 remained. We report both univariable odds

ratios (OR), multivariable ORs and 95% confidence intervals (95% CI) adjusted for age, sex, stroke severity and intervention status at baseline. All statistical analyses were performed using StataMP 15.0 (StataCorp, Texas).

Ethics approvals for the STANDFIRM trial were obtained at each participating hospital and Monash University (HREC number 2011000331). Ethics approvals were obtained for the subsequent data linkage in December 2016 from the Australian Institute of Health and Welfare (project reference number EO 2016/4/325).

Results

We were able to successfully match each of the 563 participants used within our analyses. Overall, the median age was 70 years, 35% were women, 78% were independent (mRS score of 0-1; Table 1). For those prescribed at least one class of secondary prevention medication within three years after stroke, the median PDC was 84.9% with approximately 54.9% of all participants being adherent (PDC ≥80%) to their medications. Adherence was greatest amongst users of antihypertensive medications (75.2% adherent; median PDC 94.8%), followed by users of lipid-modifying (65.7% adherent, median PDC 92.1%) and antithrombotic medications (63.3% adherent, median PDC 92.2%).

Uptake of Chronic Disease Management plans (Medicare data)

Overall within three years of stroke, 73.4% of participants had either received a CDM plan or had a pre-existing plan reviewed (median duration 401 days; Table 1). There were no differences in uptake nor median duration of CDM plans within three years after stroke within each class of secondary prevention medication. Users of antihypertensive medications were 2.5-fold more likely to have been on a CDM plan within the year prior to their initial stroke than non-users.

Due to the minimum claiming periods of 3 and 12 months for each CDM item, exposure to a CDM plan was not normally distributed. We therefore stratified exposure to a CDM plan into approximate quintiles that each encompassed approximately 11% to 27% of the total cohort.

For patients who were dispensed medications in each class at baseline, we found that participants were more likely to be older, already using a medication from the same class, taking a greater number of medications and have poorer risk factor profile than those who were not dispensed (Table 1). Those attaining a university education appeared to be dispensed antihypertensive or lipid-modifying medication less often than those with a lesser education, while those with a greater body mass index appeared to more often use lipid-modifying or antithrombotic medication than those with a lesser body mass index. Those dispensed antihypertensive or antithrombotic medication more often had a greater number of comorbidities and reported a poorer quality of life than those who were not dispensed these agents. Smoking was also more common in those dispensed lipid-modifying medications. Interestingly those dispensed antithrombotic medications less often experienced a haemorrhagic stroke than those dispensed these agents.

In multivariable analyses, only greater age and pill burden in the year prior to stroke were associated with being adherent to the use of each class of secondary prevention medication. Increased exposure to a CDM plan was associated with being adherent in users of antihypertensive (OR 1.18, 95% CI 1.00-1.40, p=0.029) or antithrombotic medications (OR 1.22, 95% CI 1.03-1.46, p=0.024), but we were unable to detect an association between use of a CDM plan and lipid-modifying medications. The 10-year FRS was associated with being adherent in users of lipid-modifying (OR 0.98, 95% CI 0.96-0.99, p=0.005) and antithrombotic medications (OR 0.98, 95% CI 0.96-1.00, p=0.028), but not antihypertensive medications.

Discussion

In this Australian cohort of older adults with stroke, approximately a quarter were not provided a CDM plan and a third of users of each secondary prevention medication were not adherent to their medications. Non-adherence in our study ranged from 63% to 75%, which was similar to rates reported in a meta-analysis by McKenzie et al. for older Australians above 60 years of age.[13]

The relatively large proportion of people not adhering to their medications is particularly concerning when considering that the prescription rate of antihypertensive medications at hospital discharge for stroke is suboptimal (79%) according to a study involving 39 hospitals across Australia.[14] One of the benchmarks proposed by the Stroke Foundation in 2020 was achieving a antihypertensive prescription rate of 91% for patients discharged with stroke.[15] Our study provides evidence that this should be accompanied by approaches to improving adherence, such as CDM plans, for those prescribed.

An organised approach to care appears to serve to improve adherence to secondary prevention medications among survivors of stroke. This is supported by our finding that patients on a CDM plan for a longer duration were more likely adherent to using antihypertensive and antithrombotic medications than those not on an organised plan, a finding that was independent of age, sex, stroke severity, prior use of medications and pill burden. This finding is important as adherence to cardiac therapies has been estimated in Europe to be associated with a reduction in the risk of CVDs by 20% and all-cause mortality by 35%.[6]

Regimen complexity, knowledge of medications and concerns regarding side effects are some of the major barriers to achieving medication adherence and these may be addressed during the preparation of a CDM plan.[16] However adjunct strategies should be considered by

clinicians to address other commonly cited barriers, such as inability to self-care, burden of treatment and tendency for patients and carers to trivialise stroke.[16, 17]

There were some limitations in conducting this study. We had to make inferences about dose and duration of medications used, as we did not have details of the prescribing information from GPs or specialists. Additionally, even though we know that patients were dispensed these medications, we cannot infer that these medications were taken for the full supply period or even that their use was initiated. This may have had the effect of overestimating medication usage, but our finding that most patients were returning for repeats dispensings does not support this. Another limitation is the potential for protopathic bias, whereby patients who are returning more often for prescription refills may have more opportunities to receive or renew a CDM plan. This is important to consider and so we cannot infer that being on a CDM plan for longer results in greater adherence, rather that there is a strong association that warrants further study.

There were also some strengths to our study. This included our ability to adjust our analyses for age, sex, stroke severity and other potential confounding factors such as use of medications and pill burden in the year prior to stroke. Additionally, using this method of medications dispensed overcomes some of the inaccuracies that occur from self-report of medication use.[18]

In conclusion, patients provided CDM plans over a long period of time appeared to have better adherence to medications than those either not provided these plans, or those provided for a shorter duration. As better adherence reduces the risk of further vascular events, individualised management plans may be important for patients following their stroke.

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Table 1. Baseline characteristics and outcomes of the linked STANDFIRM cohort and between those who were and were not dispensed an antihypertensive, lipid-modifying or antithrombotic medication within three years after stroke.

		Antihypertensive medication*			**Lipid-modifying medication***			**Antithrombotic medication**		
Factors	**Total* (n=563)**	**Dispensed (n=509; 90.4%)**	**Not dispensed (n=54; 9.6%)**	**P-value**	**Dispensed (n=496; 88.1%)**	**Not dispensed (n=20; 3.6%)**	**P-value**	**Dispensed (n=455; 80.8%)**	**Not dispensed (n=108; 19.2%)**	**P-value**
Outcome										
PDC ≥ 80%	309 (54.9)	383 (75.2)	0 (0)	N/A	326 (65.7)	0 (0)	N/A	288 (63.3)	0 (0)	N/A
PDC (%), median (Q_1, Q_3)	84.9 (65.0, 95.3)	94.8 (80.7, 98.0)	0 (0, 0)	N/A	92.1 (63.1, 97.6)	0 (0, 0)	N/A	92.2 (55.3, 97.9)	0 (0, 0)	N/A
Exposure to CDM plan										
Used a CDM plan within 3 years	413 (73.4)	373 (73.3)	40 (74.1)	0.900	364 (73.4)	15 (75.0)	0.873	336 (73.9)	77 (71.3)	0.590
Days on CDM plan, median (Q_1, Q_3)	401 (0, 795.3)	408.5 (0, 820.8)	365.3 (0, 709.0)	0.200	403.8 (0, 791.9)	331.8 (43.1, 427.5)	0.069	406.6 (0, 787.1)	365.3 (0, 820.3)	0.999
Years on CDM plan										
0	150 (26.6)	136 (26.7)	14 (25.9)		132 (26.6)	5 (25.0)		119 (26.2)	31 (28.7)	
(>0 – 1.0)	60 (10.7)	54 (10.6)	6 (11.1)		51 (10.3)	5 (25.0)		50 (11.0)	10 (9.3)	
(1.0 – 1.5)	127 (22.6)	109 (21.4)	18 (33.3)		113 (22.8)	8 (40.0)		104 (22.9)	23 (21.3)	
(1.5 – 2.3)	113 (20.1)	Censored	Censored		102 (20.6)	Censored		93 (20.4)	20 (18.5)	
(2.3 – 3.0)	113 (20.1)	Censored	Censored	0.091	98 (19.8)	Censored	**0.029**	89 (19.6)	24 (22.2)	0.907
Used a CDM plan in year prior	196 (34.8)	188 (36.9)	8 (14.8)	**0.001**	177 (35.7)	5 (25.0)	0.327	167 (36.7)	29 (26.9)	0.053
Baseline characteristics										
Age (years), median (Q_1, Q_3)	70.2 (60.8, 78.7)	71.6 (62.0, 79.4)	60.5 (42.5, 67.0)	**<0.001**	70.2 (60.9, 78.7)	56.3 (33.0, 67.6)	**0.001**	71.9 (61.7, 79.6)	64.6 (55.4, 72.5)	**<0.001**
Men	363 (64.5)	328 (64.4)	35 (64.8)	0.956	319 (64.3)	10 (50.0)	0.192	294 (64.6)	69 (63.9)	0.887
mRS Score, median (Q_1, Q_3)	1 (0, 1)	1 (0, 1)	0 (0, 1)	**0.001**	1 (0, 1)	1 (0.5, 1.5)	0.646	1 (0, 1)	1 (0, 1)	0.531
Randomised to STANDFIRM intervention	283 (50.3)	252 (49.5)	31 (57.4)	0.270	247 (49.8)	8 (40.0)	0.390	220 (48.4)	63 (58.3)	0.062

Prior use of medications	385 (68.4)	328 (64.4)	Censored	**<0.001**	242 (48.8)	Censored	**0.003**	163 (35.8)	7 (6.5)	**<0.001**
Total pill burden (prior year), median (Q_1, Q_3)	390 (0, 1080)	480 (0, 1146)	0 (0, 0)	**<0.001**	390 (0, 1102)	0 (0, 355)	**0.002**	536 (30, 1244)	0 (0, 360)	**<0.001**
Haemorrhagic stroke	47 (8.3)	Censored	Censored	0.194	Excluded*	Excluded*	-	13 (2.9)	34 (31.5)	**<0.001**
Married or living with a partner	370 (65.7)	335 (65.8)	35 (64.8)	0.883	328 (66.1)	12 (60.0)	0.571	72 (66.7)	298 (65.5)	0.818
University educated	121 (21.5)	101 (19.8)	20 (37.0)	**0.003**	103 (20.8)	9 (45.0)	**0.010**	92 (20.2)	29 (26.9)	0.131
Non-sedentary occupation	334 (59.3)	309 (60.7)	25 (46.3)	**0.040**	296 (59.7)	8 (40.0)	0.079	274 (60.2)	60 (55.6)	0.375
IRSAD Percentile, median (Q_1, Q_3)	64 (40, 80)	63 (40, 79)	71 (41, 85)	0.424	64 (39, 80)	63.5 (47.0, 83.5)	0.703	63 (39, 79)	66 (44.5, 83.5)	0.373
LHS score, median (Q_1, Q_3)	0.86 (0.73, 0.93)	0.85 (0.73, 0.93)	0.90 (0.82, 0.97)	**0.013**	0.86 (0.74, 0.97)	0.86 (0.75, 0.92)	0.707	0.85 (0.73, 0.93)	0.86 (0.77, 0.97)	0.109
Diabetes	56 (10.0)	Censored	Censored	0.107	Censored	Censored	0.428	50 (11.0)	6 (5.6)	0.090
10-year FRS, median (Q_1, Q_3)	19.8 (10.9, 33.1)	20.6 (12.2, 33.7)	8.8 (2.8, 18.2)	**<0.001**	19.6 (10.9, 32.9)	10.2 (2.5, 24.7)	**0.017**	20.5 (11.4, 34.3)	16.7 (8.5, 27.8)	**0.009**
CCI score, median (Q_1, Q_3)	0 (0, 2)	0 (0, 2)	0 (0, 2)	**0.031**	0 (0, 2)	0 (0, 2)	0.355	0 (0, 2)	0 (0, 2)	**0.002**
BMI (kg/m^2), median (Q_1, Q_3)	27.9 (24.6, 31.1)	28.0 (24.7, 31.4)	27.0 (23.8, 29.3)	0.029	28.1 (25.1, 31.6)	24.8 (21.6, 27.7)	**0.001**	28.0 (24.7, 31.6)	27.0 (24.1, 30.3)	**0.044**
Smoker	89 (15.8)	80 (15.7)	9 (16.7)	0.856	76 (15.3)	7 (35.0)	**0.019**	68 (15.0)	21 (19.4)	0.249
AQoL score, median (Q_1, Q_3)	0.70 (0.48, 0.85)	0.67 (0.46, 0.84)	0.84 (0.67, 0.95)	**<0.001**	0.69 (0.47, 0.86)	0.76 (0.53, 0.91)	0.326	0.66 (0.44, 0.84)	0.79 (0.60, 0.89)	**<0.001**
Depression†	77 (13.7)	68 (13.4)	9 (16.7)	0.501	Censored	Censored	0.461	68 (15.0)	9 (8.3)	0.072
Anxiety†	103 (18.3)	93 (18.3)	10 (18.5)	0.964	90 (18.2)	7 (35.0)	0.059	79 (17.4)	24 (22.2)	0.240

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; CVD, cardiovascular disease; SAE, serious adverse event; CDM, chronic disease management; mRS, modified Rankin Scale; IRSAD, Index of Relative Socio-economic Advantage and Disadvantage; LHS, London Handicap Scale; FRS, Framingham Risk Score; CCI, Charlson Comorbidity Index; AQoL, Assessment of Quality of Life. Data are expressed as median (lower quartile (Q1), upper quartile (Q3)), and count (proportion), unless stated otherwise. Mann-Whitney U test was used for continuous variables and Pearson's chi-squared test for categorical variables. To comply with ethical restrictions, cells were 'censored' in instances where a cell count could be calculated for cells that contained <5 individuals.

* n (%) unless otherwise indicated

† People who experienced a haemorrhagic stroke were excluded from the cohort of users of lipid-modifying medications.

‡ Depression and anxiety were defined as having a corresponding Hospital Anxiety and Depression Scale score >7.

Table 2. Univariable and multivariable logistic regression of being adherent (proportion of days covered ≥80%) to each class of secondary prevention after stroke, baseline characteristics and adjusted for age, sex, stroke severity and the STANDFIRM intervention.

	Antihypertensive (AH) medication				**Lipid-modifying (LM) medication***				**Antithrombotic (AT) medication**			
	Univariable		**Multivariable†**		**Univariable**		**Multivariable†**		**Univariable**		**Multivariable†**	
Factors	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**
Adjustment variables												
Age	1.07 (1.05-1.09)	**<0.001**	1.04 (1.02-1.06)	**<0.001**	1.04 (1.02-1.05)	**<0.001**	1.04 (1.02-1.07)	**<0.001**	1.04 (1.02-1.05)	**<0.001**	1.03 (1.01-1.05)	**0.011**
Men	0.53 (0.34-0.84)	**0.006**	0.73 (0.43-1.22)	0.226	1.12 (0.77-1.62)	0.564	1.92 (1.19-3.12)	**0.008**	1.13 (0.76-1.68)	0.554	1.94 (1.14-3.28)	**0.014**
mRS score	0.99 (0.80-1.23)	0.948	1.04 (0.80-1.34)	0.788	1.22 (1.00-1.49)	0.054	1.30 (1.04-1.62)	**0.020**	1.06 (0.86-1.31)	0.578	1.07 (0.85-1.35)	0.544
Intervention	0.76 (0.50-1.13)	0.175	0.64 (0.39-1.05)	0.080	0.85 (0.59-1.22)	0.380	0.96 (0.65-1.41)	0.831	1.15 (0.79-1.69)	0.466	1.03 (0.65-1.61)	0.914
Exposure to CDM plan‡												
Duration on CDM plan since stroke (quintiles)	1.22 (1.04-1.43)	**0.014**	1.18 (1.00-1.40)	**0.029**	1.12 (0.98-1.29)	0.093	–	–	1.15 (0.99-1.32)	0.063	1.22 (1.03-1.46)	**0.024**
Took up CDM plan within 3 years	1.70 (1.03-2.79)	**0.037**	–	–	1.27 (0.82-1.96)	0.285	–	–	1.17 (0.74-1.86)	0.500	–	–
On CDM plan in prior year	1.07 (1.05-1.09)	**<0.001**	–	–	1.06 (0.72-1.57)	0.773	–	–	0.91 (0.60-1.38)	0.665	0.62 (0.37-1.02)	0.062
Baseline variables‡												
Haemorrhagic stroke	1.06 (0.49-2.31)	0.885	–	–	0.81 (0.38-1.72)	0.578	–	–	0.46 (0.15-1.45)	0.185	–	–
Prior user of this medication	4.86 (3.01-7.82)	**<0.001**	2.39 (1.15-4.95)	**0.019**	2.33 (1.57-3.46)	**<0.001**	1.20 (0.99-1.46)	0.062	2.12 (1.34-3.36)	**0.001**	–	–
Pill burden (prior year; quintiles)§	1.80 (1.48-2.18)	**<0.001**	1.38 (0.96-2.43)	**0.025**	1.39 (1.20-1.61)	**<0.001**	1.37 (1.17-1.59)	**<0.001**	1.65 (1.40-1.94)	**<0.001**	1.69 (1.43-1.99)	**<0.001**
University educated	0.77 (0.46-1.31)	0.338	–	–	0.73 (0.46-1.14)	0.160	–	–	0.89 (0.54-1.45)	0.639	–	–
LHS score	0.33 (0.05-1.97)	0.222	–	–	1.31 (0.30-5.69)	0.721	–	–	0.69 (0.15-3.10)	0.628	–	–
10-year FRS	1.00 (0.99-1.02)	0.644	–	–	0.98 (0.97-1.00)	**0.040**	0.98 (0.96-0.99)	**0.005**	0.98 (0.97-1.00)	0.063	0.98 (0.96-1.00)	**0.028**
BMI category¶	1.25 (0.94-1.66)	0.129	–	–	1.65 (1.29-2.12)	**<0.001**	1.57 (1.21-2.04)	**0.001**	1.27 (0.98-1.65)	0.069	–	–
Comorbidity burden#	1.05 (0.86-1.28)	0.665	–	–	1.03 (0.87-1.22)	0.719	–	–	1.08 (0.90-1.29)	0.398	–	–
Diabetes	1.54 (0.73-3.26)	0.260	–	–	1.26 (0.68-2.33)	0.466	–	–	1.49 (0.77-2.85)	0.234	–	–
Smoker	1.26 (0.71-2.25)	0.426	–	–	0.59 (0.35-0.97)	**0.038**	–	–	0.52 (0.30-0.89)	**0.018**	–	–

Depression**	1.03 (0.54-1.96)	0.930	–	–	0.84 (0.48-1.46)	0.534	–	–	0.91 (0.51-1.60)	0.737	–	–
Anxiety**	0.84 (0.49-1.45)	0.537	–	–	1.10 (0.67-1.81)	0.710	–	–	0.88 (0.52-1.49)	0.633	–	–
AQoL score	0.42 (0.14-1.22)	0.111	–	–	0.80 (0.34-1.89)	0.614	–	–	0.47 (0.19-1.17)	0.104	–	–
Non-sedentary occupation	1.66 (1.07-2.58)	**0.024**	1.52 (0.96-2.43)	0.076	1.38 (0.94-2.01)	0.099	–	–	1.22 (0.81-1.83)	0.337	–	–
Married or living with partner	0.72 (0.44-1.18)	0.191	–	–	0.79 (0.53-1.18)	0.253	–	–	0.96 (0.63-1.47)	0.862	–	–
IRSAD (quartile)	0.80 (0.64-1.00)	**0.047**	–	–	1.08 (0.90-1.30)	0.399	–	–	0.94 (0.77-1.15)	0.545	–	–
IRSD (quartile)	1.20 (0.97-1.48)	0.094	–	–	0.94 (0.79-1.12)	0.507	–	–	1.05 (0.88-1.27)	0.575	–	–

STANDFIRM, Shared Team Approach between Nurses and Doctors For Improved Risk factor Management; OR, odds ratio; mRS; modified Rankin Scale; LHS, London Handicap Scale; FRS, Framingham Risk Score; BMI, Body Mass Index; AQoL, Assessment of Quality of Life; IRSAD, Index of Relative Socio-economic Advantage and Disadvantage. Data are expressed as IRRs.

* People who experienced a haemorrhagic stroke were excluded from the cohort of users of lipid-modifying medications.

† Baseline characteristics were sequentially removed until only those with a p-value ≤0.1 were retained in the model.

‡ Exposure to CDM plan and baseline characteristics in the univariable analyses were adjusted for age, sex, stroke severity (mRS) and intervention status.

§ Quintiles of pill burden in the year prior to stroke were 0-56 (≈33% of total cohort), 58-386 (17%), 390-744 (17%), 750-1416 (17%) and 1420-4390 pills (17%).

¶ BMI categories were underweight and normal (<25kg/m^2), overweight (25 - <30kg/m^2) and obese (>30 kg/m^2).

Comorbidity burden categories, measured via the Charlson Comorbidity Index (CCI), were none (0 comorbidities), moderate (1 comorbidity), severe (2 comorbidities) and very severe (≥3 comorbidities).

** Depression and anxiety were defined as having a corresponding Hospital Anxiety and Depression Scale score >7

Chapter 8: Assuming One Dose per Day Yields a Similar Estimate of Medication Adherence in Patients With Stroke: An Exploratory Analysis Using Linked Registry Data

8.1 Overview

Outcomes such as persistence or adherence to medications can be efficiently determined using medication dispensing claims data, such as data from the PBS, without placing additional burden on patients to self-report or count their pills. However, assumptions regarding the PDD may affect the results of these types of analyses.

In this chapter, we will compare three approaches to estimating dosage in patients after stroke and, as a case study, whether this affects calculated 1-year adherence to antihypertensive medications. The included paper was published in the peer-reviewed *British Journal of Clinical Pharmacology* in 2020.

8.2 Published Paper

Assuming one dose per day yields a similar estimate of medication adherence in patients with stroke: an exploratory analysis using linked registry data

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ORIGINAL ARTICLE

Assuming one dose per day yields a similar estimate of medication adherence in patients with stroke: An exploratory analysis using linked registry data

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Purpose: Prescribed daily dose (PDD), the number of doses prescribed to be taken per day, is used to calculate medication adherence using pharmacy claims data. PDD can be substituted by (i) one dose per day (1DD), (ii) an estimate based on the 75th percentile of days taken by patients to refill a script (PDD_{75}) or (iii) the World Health Organization's defined daily dose (DDD). We aimed to compare these approaches for estimating the duration covered by medications and whether this affects calculated 1-year adherence to antihypertensive medications post-stroke.

Methods: We conducted a retrospective review of prospective cohort data from the ongoing Australian Stroke Clinical Registry linked with pharmacy claims data. Adherence was calculated as the proportion of days covered (PDC) for 1DD, PDD_{75} and DDD. Differences were assessed using Wilcoxon rank-sum tests.

Results: Among 12 628 eligible patients with stroke, 10 057 (80%) were prescribed antihypertensive medications in the year after hospital discharge (78.2% aged ≥65 years, 45.2% female). Overall, the 75th percentile of patient time until next medication refill was 39 days. The greatest variations in dose regimens, estimated using person- and dose-level refill times, were for beta blockers (11.4% taking two tablets/day). There were comparable levels of adherence between 1DD and the PDD_{75} (median PDC 91.0% *vs* 91.2%; $P = 0.70$), but adherence was slightly higher using DDD (92.3%; both $P < 0.001$). However, this would represent a clinically non-significant difference.

Conclusion: Adherence to antihypertensive medications shows similar estimates across standard measures of dosage in patients during the first year after an acute stroke.

KEYWORDS

antihypertensive agents, cohort studies, databases, drug prescriptions, drug utilisation, hypertension, pharmacoepidemiology, registries, secondary prevention, stroke

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1 | INTRODUCTION

Adherence to prevention medications following stroke is essential for reducing the risk of recurrent events,[1] but monitoring adherence to medications is not straightforward when using routinely collected administrative observational data where dosing information is not available.[2] The nonintrusive and population-wide coverage of pharmacy claims data makes it an increasingly popular method of objectively estimating adherence to medications compared with conventional self-reported measures. Other objective measures include counting pills and the use of electronic medication packaging devices, enabling one to monitor each time a pill is removed and assume it has been ingested.[2] In addition to providing comprehensive information on dispensing patterns over time, pharmacy claims data also reflect real-world practice at a whole population level, without responder burden and biases.[3] However, data elements and how these are collected can be inconsistent between countries and administrative Pharmaceutical Benefits Scheme (PBS) claims data in Australia lack actual prescribed daily dose (PDD) information. While there is no feasible gold standard for determining adherence to medications, one of the most widely used metrics is the proportion of days covered (PDC), ie, the percentage of days with access to medication in a defined period.[4–6]

In Australia, the PBS provides all permanent residents with access to subsidised prescription medicines. The PBS database includes details of all medications dispensed, including their type, strength and quantity, and although primarily collected for billing purposes, can facilitate pharmaco-epidemiological research.[7] However, the quantity of medication(s) taken per day or the PDD, are not recorded.[8] Without such information, it is not possible to determine the actual duration of exposure to each medication or assess whether therapeutic adherence is actually being achieved. As most PBS quantities are intended for 1-month supply, one potential solution used within some studies is to assume a PDD of one dose per day (1DD).[9,10] Another is to rely on a defined daily dose (DDD), as published by the World Health Organization (WHO).[11] Both of these approaches lack accuracy to account for potential differences in dosage due to the strength of products and do not account for differences in prescribing practices within and across regions, prescribing indication, severity of condition, or specific characteristics of the patient group.[12] Consequently, there can be imprecision in the estimates of medication adherence.[7]

A commonly used metric is to calculate the time taken for patients to refill scripts and estimate dosages by the application of the 75th percentile of refill times for each patient (PDD_{75}).[13–20] However, as shown in a recent study that included a measure of the PDD based on the 80th percentile of the time taken until the next refill of various antihypertensive classes in patients with heart failure,[21] there may be substantial differences between PDC and 1DD estimates.

Systematic evaluation of different dosage estimations for determining adherence to medications after stroke is lacking. We aimed to compare the 1DD, PDD and PDD_{75} metrics for estimating duration covered by medications and assess whether this affects 1-year adherence to antihypertensive treatment among survivors of stroke in Australia.

What is already known about this subject

- Pharmacy claims databases are frequently used to investigate medication use and adherence in many disease conditions.
- For databases without information on the prescribed daily dose, such as the Australian Pharmaceutical Benefits Scheme, it is unclear whether using the World Health Organization's defined daily dose (DDD) or assuming one dose per day (1DD) to estimate adherence produces similar results to dosages determined using pharmaco-epidemiological methods. One such metric is the prescribed daily dose (PDD_{75}), which is based on the 75th percentile of medication refill time for each patient.

What this study adds

- Antihypertensive medications were predominantly dispensed to patients with stroke at a rate which reflected 1DD.
- 1DD yielded similar medication adherence as PDD_{75} dosage estimates derived from the dispensing patterns of each patient.
- The DDD resulted in modest but significant differences in adherence compared to these methods.

2 | METHODS

2.1 | Study design

This was a retrospective review of prospective data from the ongoing Australian Stroke Clinical Registry (AuSCR) linked to PBS data. The AuSCR is a national clinical registry designed to routinely monitor the quality of care during acute hospital admission for patients with a clinical diagnosis of acute stroke or transient ischaemic attack (TIA) against their health outcomes at 90 to 180 days after hospital discharge.[22] To reduce sampling bias, an opt-out model of consent is used, with only 1–6% of registrants excluded from the AuSCR each year.[23] Annual linkages of the AuSCR registrants with the Australian National Death Index enable ascertainment of deaths beyond the 90–180-day follow-up period.

This study comprised adult patients who were registered in the AuSCR following an acute stroke or TIA, occurring between April 2010 and June 2014, and were linked to the PBS dataset.[7] All medications listed on the PBS schedule have an associated PBS "item code"

that identifies the medications' form and strength, as well as a seven-character Anatomical Therapeutic Chemical (ATC) classification code to identify medications irrespective of strength.[11] Antihypertensive medications most relevant to secondary stroke prevention include diuretics (ATC code C03), beta blockers (C07), calcium channel blockers (C08) and agents acting on the renin-angiotensin system (C09). Medications provided at discharge from hospital are recorded in the PBS, except for public hospitals in New South Wales and the Australian Capital Territory, where patients are typically discharged with a supply of medication for a maximum of 1 week.[24] Furthermore, medications purchased over the counter or during a hospital stay are not recorded in the PBS. Prior to July 2012, prescription medications costing less than the patient co-payment threshold were paid in full by the patient and were not recorded in the PBS as no government subsidy was received. From July 2012, it has been mandatory for all dispensed prescriptions medications to be recorded in the PBS. Although only medications that attracted a government subsidy were included in the PBS prior to July 2012, it is likely that many patients would have qualified for a healthcare (pension) concession card to receive subsidised medications as most patients with acute stroke are aged ≥65 years.[23]

We included patients who were dispensed at least one antihypertensive medication during the year following hospital discharge. Patients were excluded from analyses if they died during hospitalisation or were discharged before 1 April 2010 or after 30 June 2014, as linked PBS data were unavailable at these times. As part of a sensitivity analysis, we excluded patients who were discharged prior to July 2012 to investigate whether the co-payment threshold affected our findings.

2.2 | Variables

Data related to demographics, type of stroke, date of hospital discharge and discharge destination were obtained from the AuSCR dataset. Severity of stroke was determined according to an ability to walk on admission, a validated proxy measure.[25] Socioeconomic status was derived from the postcode of residence using the Index of Relative Socioeconomic Advantage and Disadvantage.[26] The date of hospital admission was substituted for those patients with missing date of hospital discharge (2%).

Patient-level data on adherence to antihypertensive medications in the year after hospital discharge were determined using the PDC method. This involved calculating the overall proportion of days in a patient observation period where there was access to a supply of medication, with various estimates for PDD (Figure 1). Patients were observed from their date of hospital discharge until the end of the observation period of 365 days or date of death, if earlier. The number of days covered is equal to the quantity of medication dispensed within the observation period divided by the estimate for PDD.[9] We also accounted for instances of pre-supply, stockpiling and early death (Supporting Information Figure S1). In Australia, patients can obtain refills of the same medications in advance of their current supply being exhausted or receive multiple repeat dispensings on a single occasion. These two approaches can lead to stockpiling, which can complicate estimates of medication adherence by introducing extended periods without a recorded refill.[7] To address this, we assumed that patients would exhaust their current supply before initiating the next supply of the same medication. Specifically, where multiple dispensing of the same drug overlapped for a patient, we extended the period of drug coverage such that each overlapping drug supply commenced the day after the previous drug supply had concluded. As suggested by Arnet et al,[8] carryover was granted for patients who switched between different strengths of the same medication class (eg, carvedilol 12.5 mg to 25 mg), but was not for therapeutic switches (eg, atenolol to carvedilol). As the PBS does not include any indication for the PDD, we used the following three approaches to calculating dose: (i) 1DD was applied to all secondary prevention medications (eg, a 30-tablet supply of 50 mg atenolol was assumed to result in 30 days covered in the observation period); (ii) the

$$\text{Days covered} = \sum_{t_1}^{t_n} \frac{\text{Quantity of medication}}{\text{Estimate of PDD}} = \sum_{t_1}^{t_{10}} \frac{30}{1} = 300$$

$$\text{PDC} = \frac{\text{Days covered}}{\text{Observation period}} \times 100\% = \frac{300 \text{ days}}{360 \text{ days}} \times 100\% = 83.3\%$$

FIGURE 1 Example calculation of medication adherence within 1 year, using the proportion of days covered (PDC) approach, for 10 dispensings of 30 tablets with an estimated prescribed daily dose of one dose per day (1DD). "Days covered" also accounted for overlapping periods (stockpiling) within a class of antihypertensive and death (Supporting Information Figure S1), which are not depicted here. t_1, first dispensing; t_n, last dispensing; DDD, defined daily dose; PDD_{75}, prescribed daily dose based on the 75th percentile of medication refill time for each patient; PDD, prescribed daily dose (estimate based on (i) 1DD, (ii) PDD_{75} or (iii) DDD)

WHO's DDD was applied to all medications of the same ATC code, irrespective of differences in strength (eg, 75 mg/day would apply to a 30-tablet supply of 50 mg atenolol over 20 days), combination therapies were assigned a fixed one DDD based on WHO guidelines for ATC classification and DDD assignment[11]; and (iii) the PDD_{75} was derived from the 75th percentile of the number of days between consecutive dispensing of specific PBS item codes, which uniquely identify specific medications, and their strength, pack size and form of delivery (Table 1). This 75th percentile represents the number of days in which individuals would return 75% of the time for a refill of the same item code. The PDD_{75} was calculated for each dispensing as being equal to the quantity dispensed divided by the population 75th percentile of time until refill for the corresponding item code. This would yield whole integers of dosage for capsules, but tablets could be dispensed at a half per day or greater. We used a PDC of ≥80% to define medication adherence in our cohort.[27]

2.3 | Statistical analysis

Descriptive statistics were used to describe the overall baseline characteristics of the cohort. Wilcoxon rank-sum tests were used to compare the median PDCs between each assumption of dosage. A two-sided $P < 0.05$ was considered statistically significant. All analyses were performed using StataMP 15.0 (StataCorp, Texas, USA).[27]

2.4 | Ethics and data availability

This study was approved by the ethics committees at Monash University (7864) and the Australian Institute of Health and Welfare (EO2017/1/346). Additional approvals for data linkage were obtained from the AuSCR Research Task Group and the Australian Department of Health. Medication and strength-level data relating to dosages are available in Supporting Information Table S1.

2.5 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in http://www.guidetopharmacology.org, the common portal for data from the IUPHAR/BPS Guide to PHARMACOLOGY.

3 | RESULTS

Of 17 980 AuSCR registrants discharged between 2010 and 2014, 95% were linked to PBS data. After excluding those ineligible (Figure 2), the final cohort comprised 12 628 patients (74.4% aged ≥65 years, 45.1% female, 49.6% unable to walk on admission; Table 2). There were 10 057 (80%) who were dispensed antihypertensive medication in the year after stroke (78.2% aged ≥65 years, 45.2% female, 48.8% unable to walk on admission). The most commonly prescribed classes of antihypertensive medications were angiotensin-converting enzyme inhibitors (50.0%), beta blockers (45.5%), calcium channel blockers (33.8%) and diuretics (29.0%). For the 152 982 antihypertensive medications dispensed, the 75th percentile of patients' time until next refill was 39 days (25th percentile, 25 days; median 30 days).

Most dispensed antihypertensive medications had a PDD_{75} of one dose per day (Table 3), and most were tablets (96.7%). Variations in the time until next refill were observed both within and between each class of antihypertensive medication (Supporting Information Table S1), being greatest for beta blockers (11.4% with two tablets/day) and diuretics (6.4% with 0.5 tablets/day). An example representation of the estimated PDD_{75} for beta blockers is provided in Supporting Information Figure S2.

Most (70.6%) patients were adherent (PDC ≥ 80%) to antihypertensive medications using the PDD_{75}, with the greatest adherence for medications acting on the renin-angiotensin system and worst for diuretics (Table 4). There were no significant differences in adherence

TABLE 1 Process for determining the population-level 75th percentile of time between consecutive refills for each PBS item code and PDD_{75}

Step	
1	Within a patient's 1-year dispensing history, determine the number of days between consecutive refills of the same PBS item code. All PBS item codes uniquely identify a specific combination of a medication, its form, strength and pack size.[a] For example, item code 01946 K identifies ramipril dispensed as a pack of 30 tablets with a strength of 5 mg.
2	For each item code, calculate the 75th percentile of the distribution of time until the next dispensing date for each person and the population.
3	For each person and item code, divide the quantity of medication by the 75th percentile of refill pattern to calculate dose per day. Assign an approximate individual PDD_{75}: • ≈ 0.5 if dose/day = 0.375–0.749 (for tablets) • ≈ 1 if dose/day = 0.375–1.499 (for capsules) • ≈ 1 if dose/day = 0.750–1.499 (tablets) • ≈ 2 if dose/day = 1.500–2.499 (tablets/capsules) • ≈ 3 if dose/day = 2.500–3.499 (tablets/capsules) • ≈ n if dose/day = (n-1).500 – n.499 (tablets/capsules) For each item code, individuals who had <5 dispensings for that item code are assigned the population's PDD_{75} instead.

[a]If an identifier similar to the PBS item code is not available, then consider using the seven-character Anatomical Therapeutic Chemical (ATC) code, which would identify the drug being dispensed. n represents any integer greater than 3.

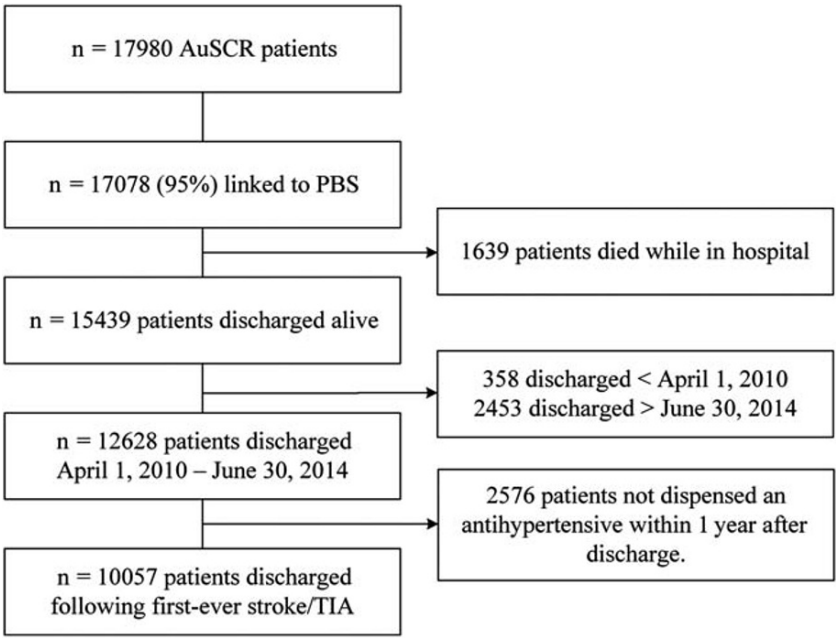

FIGURE 2 Flow diagram of cohort selection from the Australian Stroke Clinical Registry (AuSCR)

to any antihypertensive medication between the PDD_{75} and 1DD (median PDC 91.0% *vs* 91.2%; $P = 0.70$), but adherence was slightly higher using the DDD (92.3%; both $P < 0.001$). However, this represents a clinically nonsignificant difference. DDD-based PDC estimates tended to be inflated for each class of antihypertensive, except beta blockers and diuretics. These PDC estimates were significantly different from those calculated using either the PDD_{75} or 1DD.

After excluding patients, as part of a sensitivity analysis, who were either discharged before July 2012 (as PBS data is incomplete for medicines below the co-payment threshold) or not long-term concession card holders, 91.7% of the cohort remained (Supporting Information Table S2) and adherence remained similar overall and across each class of antihypertensive.

4 | DISCUSSION

In our evaluation of the different approaches to estimating medication adherence using Australian PBS data, we found that the simple 1DD approach was comparable to the more complex PDD_{75} in the first year in those who survived their hospitalisation for stroke, except for beta blockers. However, the WHO's DDD approach tended to overestimate the PDC.[28] There are strengths and weaknesses to each approach. For the PDD_{75} metric, the data-driven approach provides wide coverage, and efficient and flexible data on alternate dosage from the conventional 1DD (see Table 5 for more details).

Our finding of beta blockers being provided in many different doses was similar to the findings of a study of Alzheimer's disease, a population with similar characteristics to survivors of stroke in that they tend to be older adults with a high proportion of polypharmacy.[29] In the prior study, where **benzodiazepine temazepam** was commonly prescribed at either 0.5 or 1 tablet per day, the authors concluded that assumptions over a fixed dose (e.g. 1 tablet per day) required further validation. Our findings are also consistent with a South Australian study of users of antihypertensive therapy in 2007,[17] where the 75th percentile of time for most medications was 35 days. These findings support the current intended duration of 1-month supply prescriptions for chronic conditions in the PBS, as fixed-dose combination therapies are predominately provided in pack sizes of 28 or 30, or of 60 if medications are taken twice daily.[10,18]

The proportion of those adherent to each class of antihypertensive medication may have differed due to factors such as the side effects or differences in comorbidities, which lead to contraindications to the drug. The findings from the present study will form the basis of future research involving these data for estimation of medication adherence and investigations of the factors associated with greater adherence, such as age, type of stroke and socioeconomic status.

The strengths of our study include the ability to capture all medication dispensing for secondary prevention from a large registry and data on time of death reduced the overall observation time where this was the reason for drug cessation. There are, however, several limitations, such as the inferences that were made over the dose and duration of medication without supporting prescribing information from general practitioner or specialist records, or against pill counts. Additionally, being dispensed a medication does not imply that this medication was consumed by the patient.

In summary, our study has provided evidence that compared with the best assessment of exposure periods (PDD_{75}), the simpler approach of using 1DD to calculate the PDC provides similar results. Although the WHO's DDD produced significantly different PDCs for all antihypertensive agents used for patients with a recent stroke, 1DD is an equally valid metric for calculating the PDC in an Australian population. The application of 1DD for determining medication adherence using PBS dispensing data produced similar estimates for

TABLE 2 Characteristics of the final cohort of patients with stroke/TIA dispensed antihypertensive medications in the year following discharge

	All antihypertensive medication users
	n = 10 057
	n (%)
Female	4546 (45.2)
Age	
<65	2187 (21.8)
65–74	2497 (24.8)
75–84	3372 (33.5)
85+	1999 (19.9)
Type of stroke	
Intracerebral haemorrhage	1046 (10.4)
Ischaemic stroke	6917 (68.8)
Transient ischaemic attack	1778 (17.7)
Undetermined stroke	309 (3.1)
Severe stroke (unable to walk on admission)	4909 (48.8)
Previous history of stroke	2011 (21.2)
Socioeconomic position[a]	
Most disadvantaged	1053 (10.6)
Second most disadvantaged	1610 (16.3)
Third most disadvantaged	1989 (20.1)
Fourth most disadvantaged	2223 (22.4)
Least disadvantaged	3030 (30.6)
Year of admission	
2010	824 (8.2)
2011	1571 (15.6)
2012	2592 (25.8)
2013	3344 (33.3)
2014	1726 (17.2)
Discharge destination	
Home	5065 (50.3)
Rehabilitation	3143 (31.3)
Aged care	668 (6.6)
Other	1181 (11.7)
Class of antihypertensive medication dispensed[b]	
Any agent acting on RAS	8363 (83.2)
ACE inhibitor, plain	5027 (50.0)
ACE inhibitor, combination	803 (8.0)
ARB, plain	2803 (27.9)
ARB, combination	1391 (13.8)
Beta blocker	4574 (45.5)
Calcium channel blocker	3394 (33.8)
Diuretic	2913 (29.0)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; RAS, renin-angiotensin system.
[a]Determined using the Index of Relative Socioeconomic Advantage and Disadvantage.
[b]Due to coadministration of multiple antihypertensive medications, patients can be included in multiple medication groups.

TABLE 3 Estimated prescribed daily doses based on 75th percentile of the days until next dispensing (PDD_{75})

Class of antihypertensive	Total medication users	Total medications dispensed	Dose per day[a]		
			0.5 units	1 unit	2 units
	$n_{patients}$	$n_{scripts}$	%	%	%
Overall	10 057	152 982	0.7	96.9	2.4
Agents acting on RAS	8363	84 401	0.1	99.8	0.1
ACE inhibitor, plain	5027	43 291	<0.1	99.8	0.2
ACE inhibitor, combination	803	6142	<0.1	99.9	0.1
ARB, plain	2803	23 529	0.4	99.6	0.0
ARB, combination	1391	11 439	0.1	99.9	0.0
Beta blocker	4574	29 779	0.9	87.6	11.4
Calcium channel blocker	3394	27 771	<0.1	99.3	0.7
Diuretic	2913	11 031	6.4	93.6	0.0

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; RAS, renin–angiotensin system.
[a]Based on 75th percentile of individual patient's time until next dispensing.
[b]Due to coadministration of multiple antihypertensive medications, patients can be included in multiple medication groups.

TABLE 4 Adherence to antihypertensive medications within 1 year after stroke based on three different metrics of dosage, by overall and class use

Class of antihypertensive	Adherent[a]	PDC summary statistics (%)					
		Minimum	Q_1	Median	Q_3	Maximum	*P* value[b]
Any antihypertensive (n = 10 057)[c]							
1DD	70.8%	0.3	75.6	91.2	97.0	100	0.700
PDD_{75}	70.6%	0.3	75.3	91.0	97.0	100	<0.001
DDD	71.9%	0.3	75.6	92.3	98.1	100	<0.001
Agents acting on RAS (n = 8363)							
1DD	62.6%	0.3	64.9	87.1	95.1	100	0.998
PDD_{75}	62.6%	0.3	64.9	87.3	95.1	100	<0.001
DDD	65.9%	0.3	65.5	90.4	96.7	100	<0.001
Beta blocker (n = 4574)							
1DD	51.1%	0.3	52.6	80.8	93.2	100	0.061
PDD_{75}	49.7%	0.3	51.0	79.5	92.6	100	<0.001
DDD	42.3%	0.3	41.6	71.0	91.8	100	<0.001
Calcium channel blocker (n = 3394)							
1DD	46.5%	0.3	38.4	76.4	92.3	100	0.874
PDD_{75}	46.3%	0.3	38.4	76.4	92.3	100	<0.001
DDD	52.9%	0.3	43.8	82.7	94.7	100	<0.001
Diuretic (n = 2913)							
1DD	36.1%	0.3	34.0	67.1	85.8	100	0.322
PDD_{75}	37.0%	0.3	36.4	68.4	86.3	100	<0.001
DDD	32.8%	0.3	28.2	60.3	84.9	100	<0.001

Abbreviations: 1DD, one dose per day; DDD, defined daily dose based on work by the World Health Organization; PDC, proportion of days covered (measure of medication adherence); PDD_{75}, prescribed daily dose determined using the 75th percentile of the population's time until next dispensing for the same medication, strength and form; Q_1, 25th percentile; Q_3, 75th percentile; RAS, renin–angiotensin system.
[a]Being adherent was classified as having a PDC ≥ 80% within 1 year after stroke.
[b]*P* values were derived using Wilcoxon rank-sum tests and signify comparison between median PDC of the current and subsequent row, within each class of antihypertensive. The DDD of each class was compared with 1DD.
[c]Users of at least one of the following antihypertensive classes: agents acting on RAS, beta blocker, calcium channel blocker and diuretic.

TABLE 5 Strengths and weaknesses of different approaches for estimating duration on medications for the determination of medication adherence when prescribed daily dosage information is missing from a dataset[7,10,29]

Dosage estimation	Strengths	Weaknesses
All		• Do not differentiate between loading doses or maintenance doses
1DD	• Simple to implement • Found to be appropriate for most antihypertensive drug classes[a]	• May not provide a suitable estimate for beta blockers and other drugs with significant variation in prescribed daily dose • Does not consider disease severity or acute treatments, which may require higher or lower dosages
PDD_{75}	• Data-driven approach based on dispensing patterns for both individuals and the cohort • Discerns when medications appear to be predominately not taken at 1DD	• May slightly overestimate adherence • Estimates are specific to dispensing patterns and rules in the examined population, which could have limited generalisability to other countries
DDD	• Simple to implement	• Estimate is based on an average of international dosages in adults • May not be accurate due to the characteristics of those in the cohort being examined (eg, age and severity of disease) • May not reflect prescribed dose in Australia • Usually missing for combination medications • Inaccurate for variable-dose drugs

Abbreviations: 1DD, 1 dose per day; DDD, defined daily dose based on work by the World Health Organization; PDD_{75}, prescribed daily dose determined using the 75th percentile of the population's time until next dispensing for the same medication, strength and form.
[a]Antihypertensive classes were agents acting on the renin–angiotensin system, calcium channel blockers and diuretics.

antihypertensive medications, except for beta blockers. The PDD_{75} had the advantage of detecting variations in dosage for beta blockers and may be a more precise metric for this class of antihypertensive in the absence of data on actual PDD information (gold standard).

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COMPETING INTERESTS

D.A.C. is the current Data Custodian for the AuSCR. D.A.C., A.G.T., C.S.A. and M.F.K. are members of the AuSCR Steering or Management Committees. A.G.T. is a member of the Board of the Stroke Foundation. D.A.C. reported receiving restricted grants from Boehringer Ingelheim, Ipsen, Medtronic and Shire outside the submitted work.

CONTRIBUTORS

All authors contributed to the interpretation of the data and critical revisions of the manuscript for intellectual content. D.U. was also responsible for drafting the manuscript and alongside L.D. performed the statistical analysis and literature review. A.G.T and M.F.K were responsible for the initial conceptualisation and design of this study. N.E.A, D.A.C. and M.F.K acquired project funding to facilitate acquisition and linkage of data. All authors approved the manuscript for submission.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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SUPPLEMENTAL MATERIAL

Assuming one dose per day yields similar medication adherence in patients with stroke: an exploratory analysis using linked registry data

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Supplemental Results:

Supplemental Table I: Antihypertensive medications listed in the Australian Pharmaceutical Benefits Scheme and corresponding dosage information from the World Health Organisation's Defined Daily Dose and the 75th percentile of time taken by patients in cohort to return for a script refill.

Supplemental Table II: Sensitivity analysis for adherence to antihypertensive medications within 1 year after stroke, based on three different dosage assumptions, by overall and class. Cohort excluded those who were long-term non-concession card holders and discharged prior to 1st July 2012.

Supplemental Figure I: Calculation of medication adherence using the proportion of days covered (PDC) metric for 3 dispensings within the Pharmaceutical Benefits Scheme database. Example 1 depicts how the PDC would be calculated for an individual without accounting for stockpiling and death for a 1-year observation period. Example 2 contrasts the PDC that would result from accounting for stockpiling within a class of antihypertensive. Example 3 was used within the study and accounts for both stockpiling and deaths.

Supplemental Figure II: Proportion of patients with each estimated prescribed daily dose (PDD_{75}) of beta blockers dispensed in the year following discharge, by medication strength. This is based on each individuals' time until refill. For example, if for 75% of the time, they refilled a 30-tablet supply between 15 – 22 days, then we would estimate that they were taking this at a rate of 2 doses/day. See Table 1 for more details of how the PDD_{75} was determined.

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Supplemental Table I: Antihypertensive medications listed in the Australian Pharmaceutical Benefits Scheme and corresponding dosage information from the World Health Organisation's Defined Daily Dose and the 75th percentile of time taken by patients to return for a script refill.[1,2]

ATC code	PBS Item Code	PBS Drug Name	PBS Drug Form and Strength	Pack size	Q_3 of refill time (days)	PDD_{75}	DDD	DDD unit	PBS unit/day based on DDD
C03AA03	01484D	HYDROCHLOROTHIAZIDE	Tablet 25 mg	100	112	1	25	mg	1
C03BA04	01585K	CHLORTHALIDONE	Tablet 25 mg	50	86	0.5	25	mg	1
C03BA11	02436F	INDAPAMIDE	Tablet 2.5 mg	90	95	1	2.5	mg	1
C03BA11	08532C	INDAPAMIDE	Tablet 1.5 mg (sustained release)	90	98	1	2.5	mg	1.67
C03CA01	01810G	FRUSEMIDE	Tablet 20 mg	50	107	0.5	40	mg	2
C03CA01	02412Y	FRUSEMIDE	Tablet 40 mg	100	89	1	40	mg	1
C03CA01	02414C	FRUSEMIDE	Tablet 20 mg	100	99	1	40	mg	2
C03CA01	02415D	FRUSEMIDE	Tablet 500 mg	50	65	1	40	mg	0.08
C03CC01	08748K	ETHACRYNIC ACID	Tablet 25 mg	100	183	0.5	50	mg	2
C03DA01	02339D	SPIRONOLACTONE	Tablet 25 mg	100	98	1	75	mg	3
C03DA01	02340E	SPIRONOLACTONE	Tablet 100 mg	100	98	1	75	mg	0.75
C03DA04	08879H	EPLERENONE	Tablet 25 mg	30	34	1	50	mg	2
C03DB01	03109P	AMILORIDE HYDROCHLORIDE	Tablet 5 mg	50	44	1	10	mg	2
C03EA01	01280J	HYDROCHLOROTHIAZIDE with TRIAMTERENE	Tablet 25 mg-50 mg	100	169	0.5	1	TA	1
C03EA01	01486F	HYDROCHLOROTHIAZIDE with AMILORIDE HYDROCHLORIDE	Tablet 50 mg-5 mg	50	111	0.5	1	TA	1
C07AA02	02942W	OXPRENOLOL HYDROCHLORIDE	Tablet 20 mg	100	235	0.5	160	mg	8
C07AA02	02961W	OXPRENOLOL HYDROCHLORIDE	Tablet 40 mg	100	151	0.5	0.16	g	4
C07AA03	03062E	PINDOLOL	Tablet 5 mg	100	57	2	15	mg	3
C07AA03	03065H	PINDOLOL	Tablet 15 mg	50	35	1	15	mg	1
C07AA05	02565B	PROPRANOLOL	Tablet 10 mg	100	63	2	0.16	g	16

		HYDROCHLORIDE							
C07AA05	02566C	PROPRANOLOL HYDROCHLORIDE	Tablet 40 mg	100	62	2	0.16	g	4
C07AA05	02899N	PROPRANOLOL HYDROCHLORIDE	Tablet 160 mg	50	31	2	0.16	g	1
C07AA07	02043M	SOTALOL HYDROCHLORIDE	Tablet 160 mg	60	59	1	0.16	g	1
C07AA07	08398B	SOTALOL HYDROCHLORIDE	Tablet 80 mg	60	54	1	0.16	g	2
C07AB02	01324Q	METOPROLOL TARTRATE	METOPROLOL TARTRATE Tablet 50 mg	100	87	1	150	mg	3
C07AB02	01325R	METOPROLOL TARTRATE	METOPROLOL TARTRATE Tablet 100 mg	60	38	2	150	mg	1.5
C07AB02	08732N	METOPROLOL SUCCINATE	METOPROLOL SUCCINATE Tablet 23.75 mg (controlled release)	15	35	0.5	0.15	g	6.32
C07AB02	08733P	METOPROLOL SUCCINATE	METOPROLOL SUCCINATE Tablet 47.5 mg (controlled release)	30	35	1	0.15	g	3.16
C07AB02	08734Q	METOPROLOL SUCCINATE	METOPROLOL SUCCINATE Tablet 95 mg (controlled release)	30	36	1	0.15	g	1.58
C07AB02	08735R	METOPROLOL SUCCINATE	METOPROLOL SUCCINATE Tablet 190 mg (controlled release)	30	34	1	0.15	g	0.79
C07AB03	01081X	ATENOLOL	Tablet 50 mg	30	39	1	0.075	g	1.5
C07AB07	08604W	BISOPROLOL	Tablet 2.5 mg	28	34	1	10	mg	4
C07AB07	08605X	BISOPROLOL	Tablet 5 mg	28	33	1	10	mg	2
C07AB07	08606Y	BISOPROLOL	Tablet 10 mg	28	32	1	10	mg	1
C07AB12	09311C	NEBIVOLOL	Tablet 5 mg (as hydrochloride)	28	33	1	5	mg	1
C07AB12	09312D	NEBIVOLOL	Tablet 10 mg (as hydrochloride)	28	31	1	5	mg	0.5
C07AB12	09316H	NEBIVOLOL	Tablet 1.25 mg (as hydrochloride)	28	38	0.5	5	mg	4
C07AG01	01566K	LABETALOL HYDROCHLORIDE	Tablet 100 mg	100	57	2	0.6	g	6
C07AG01	01567L	LABETALOL HYDROCHLORIDE	Tablet 200 mg	100	52	2	0.6	g	3
C07AG02	08255L	CARVEDILOL	Tablet 3.125 mg	30	33	1	37.5	mg	12
C07AG02	08256M	CARVEDILOL	Tablet 6.25 mg	60	42	1	37.5	mg	6
C07AG02	08257N	CARVEDILOL	Tablet 12.5 mg	60	36	2	37.5	mg	3

C07AG02	08258P	CARVEDILOL	Tablet 25 mg	60	36	2	37.5	mg	1.5
C08CA01	01343Q	AMLODIPINE	Tablet 5 mg (as maleate)	30	38	1	5	mg	1
C08CA01	01345T	AMLODIPINE	Tablet 10 mg (as maleate)	30	36	1	5	mg	0.5
C08CA01	02751T	AMLODIPINE	Tablet 5 mg (as besylate)	30	36	1	5	mg	1
C08CA01	02752W	AMLODIPINE	Tablet 10 mg (as besylate)	30	35	1	5	mg	0.5
C08CA02	02361G	FELODIPINE	Tablet 2.5 mg (extended release)	30	34	1	5	mg	2
C08CA02	02366M	FELODIPINE	Tablet 5 mg (extended release)	30	33	1	5	mg	1
C08CA02	02367N	FELODIPINE	Tablet 10 mg (extended release)	30	34	1	5	mg	0.5
C08CA05	01694E	NIFEDIPINE	Tablet 10 mg	60	49	1	30	mg	3
C08CA05	01695F	NIFEDIPINE	Tablet 20 mg	60	47	1	30	mg	1.5
C08CA05	01906H	NIFEDIPINE	Tablet 30 mg (controlled release)	30	34	1	30	mg	1
C08CA05	01907J	NIFEDIPINE	Tablet 60 mg (controlled release)	30	35	1	30	mg	0.5
C08CA05	08610E	NIFEDIPINE	Tablet 20 mg (controlled release)	30	33	1	30	mg	1.5
C08CA13	08534E	LERCANIDIPINE	Tablet 10 mg	28	32	1	10	mg	1
C08CA13	08679T	LERCANIDIPINE	Tablet 20 mg	28	32	1	10	mg	0.5
C08CA13	08939L	LERCANIDIPINE HYDROCHLORIDE	Tablet 10 mg	30		1	10	mg	1
C08CA13	08940M	LERCANIDIPINE HYDROCHLORIDE	Tablet 20 mg	30	29	1	10	mg	0.5
C08DA00	01253Y	VERAPAMIL HYDROCHLORIDE	Tablet 160 mg	60	59	1	0.24	mg	1.5
C08DA01	01241H	VERAPAMIL HYDROCHLORIDE	Tablet 240 mg (sustained release)	30	35	1	0.24	mg	1
C08DA01	01248Q	VERAPAMIL HYDROCHLORIDE	Tablet 40 mg	100	56	2	0.24	mg	6
C08DA01	01250T	VERAPAMIL HYDROCHLORIDE	Tablet 80 mg	100	57	2	0.24	mg	3
C08DA01	01254B	VERAPAMIL HYDROCHLORIDE	Tablet 120 mg	100	88	1	0.24	mg	2
C08DA01	02206D	VERAPAMIL HYDROCHLORIDE	Capsule 160 mg (sustained release)	30	32	1	0.24	mg	1.5
C08DA01	02207E	VERAPAMIL	Capsule 240 mg (sustained release)	30	34	1	0.24	mg	1

		HYDROCHLORIDE							
C08DA01	02208F	VERAPAMIL HYDROCHLORIDE	Tablet 180 mg (sustained release)	30	34	1	0.24	mg	1.33
C08DB01	01312C	DILTIAZEM HYDROCHLORIDE	Capsule 180 mg (controlled delivery)	30	35	1	0.24	mg	1.33
C08DB01	01313D	DILTIAZEM HYDROCHLORIDE	Capsule 240 mg (controlled delivery)	30	35	1	0.24	mg	1
C08DB01	01335G	DILTIAZEM HYDROCHLORIDE	Tablet 60 mg	90	62	1	0.24	mg	4
C08DB01	08480H	DILTIAZEM HYDROCHLORIDE	Capsule 360 mg (controlled delivery)	30	35	1	0.24	mg	0.67
C09AA01	01147J	CAPTOPRIL	Tablet 12.5 mg	90	84	1	50	mg	4
C09AA01	01148K	CAPTOPRIL	Tablet 25 mg	90	64	1	50	mg	2
C09AA01	01149L	CAPTOPRIL	Tablet 50 mg	90	53	2	50	mg	1
C09AA02	01368B	ENALAPRIL MALEATE	Tablet 10 mg	30	34	1	10	mg	1
C09AA02	01369C	ENALAPRIL MALEATE	Tablet 20 mg	30	34	1	10	mg	0.5
C09AA02	01370D	ENALAPRIL MALEATE	Tablet 5 mg	30	39	1	10	mg	2
C09AA03	02456G	LISINOPRIL	Tablet 5 mg	30	36	1	10	mg	2
C09AA03	02457H	LISINOPRIL	Tablet 10 mg	30	34	1	10	mg	1
C09AA03	02458J	LISINOPRIL	Tablet 20 mg	30	34	1	10	mg	0.5
C09AA04	03050M	PERINDOPRIL	Tablet containing 2 mg perindopril erbumine	30	34	1	4	mg	2
C09AA04	03051N	PERINDOPRIL	Tablet containing 4 mg perindopril erbumine	30	34	1	4	mg	1
C09AA04	08704D	PERINDOPRIL	Tablet containing 8 mg perindopril erbumine	30	34	1	4	mg	0.5
C09AA04	09006B	PERINDOPRIL	Tablet containing 2.5 mg perindopril arginine	30	35	1	4	mg	1.6
C09AA04	09007C	PERINDOPRIL	Tablet containing 5 mg perindopril arginine	30	36	1	4	mg	0.8
C09AA04	09008D	PERINDOPRIL	Tablet containing 10 mg perindopril arginine	30	35	1	4	mg	0.4
C09AA05	01316G	RAMIPRIL	Tablet 10 mg	30	35	1	2.5	mg	0.25
C09AA05	01944H	RAMIPRIL	Tablet 1.25 mg	30	35	1	2.5	mg	2
C09AA05	01945J	RAMIPRIL	Tablet 2.5 mg	30	34	1	2.5	mg	1
C09AA05	01946K	RAMIPRIL	Tablet 5 mg	30	34	1	2.5	mg	0.5
C09AA05	08470T	RAMIPRIL	Capsule 10 mg	30	34	1	2.5	mg	0.25
C09AA05	09120B	RAMIPRIL	Capsule 1.25 mg	30	32	1	2.5	mg	2

C09AA05	09121C	RAMIPRIL	Capsule 2.5 mg	30	35	1	2.5	mg	1
C09AA05	09122D	RAMIPRIL	Capsule 5 mg	30	35	1	2.5	mg	0.5
C09AA06	01968N	QUINAPRIL	Tablet 5 mg (as hydrochloride)	30	34	1	15	mg	3
C09AA06	01969P	QUINAPRIL	Tablet 10 mg (as hydrochloride)	30	35	1	15	mg	1.5
C09AA06	01970Q	QUINAPRIL	Tablet 20 mg (as hydrochloride)	30	32	1	15	mg	0.75
C09AA09	01182F	FOSINOPRIL	Tablet 10 mg	30	36	1	15	mg	1.5
C09AA09	01183G	FOSINOPRIL	Tablet 20 mg	30	34	1	15	mg	0.75
C09AA10	02791X	TRANDOLAPRIL	Capsule 500 micrograms	28	35	1	2	mg	4
C09AA10	02792Y	TRANDOLAPRIL	Capsule 1 mg	28	31	1	2	mg	2
C09AA10	02793B	TRANDOLAPRIL	Capsule 2 mg	28	30	1	2	mg	1
C09AA10	08758Y	TRANDOLAPRIL	Capsule 4 mg	28	30	1	2	mg	0.5
C09BA02	08477E	ENALAPRIL with HYDROCHLOROTHIAZIDE	Tablet 20 mg-6 mg	30	32	1	1	TA	1
C09BA04	02190G	PERINDOPRIL with INDAPAMIDE	Tablet containing 2.5 mg perindopril arginine-0.625 mg indapamide hemihydrate	30	36	1	1	TA	1
C09BA04	02845R	PERINDOPRIL with INDAPAMIDE	Tablet containing 5 mg perindopril arginine-1.25 mg indapamide hemihydrate	30	35	1	1	TA	1
C09BA04	08449Q	PERINDOPRIL with INDAPAMIDE	Tablet containing 4 mg perindopril erbumine-1.25 mg indapamide hemihydrate	30	35	1	1	TA	1
C09BA06	08589C	QUINAPRIL with HYDROCHLOROTHIAZIDE	Tablet 10 mg (base)-12.5 mg	30	32	1	1	TA	1
C09BA06	08590D	QUINAPRIL with HYDROCHLOROTHIAZIDE	Tablet 20 mg (base)-12.5 mg	30	35	1	1	TA	1
C09BA09	08400D	FOSINOPRIL with HYDROCHLOROTHIAZIDE	Tablet 10 mg-12.5 mg	30	32	1	1	TA	1
C09BA09	08401E	FOSINOPRIL with HYDROCHLOROTHIAZIDE	Tablet 20 mg-12.5 mg	30	34	1	1	TA	1
C09BB02	09144G	ENALAPRIL and LERCANIDIPINE	Tablet 10 mg-10 mg	30	31	1	1	TA	1
C09BB02	09145H	ENALAPRIL and LERCANIDIPINE	Tablet 10 mg-20 mg	30	35	1	1	TA	1
C09BB04	09346X	PERINDOPRIL and AMLODIPINE	Tablet containing 5 mg perindopril arginine with 5 mg amlodipine (as besylate)	30	35	1	1	TA	1

C09BB04	09347Y	PERINDOPRIL and AMLODIPINE	Tablet containing 5 mg perindopril arginine with 10 mg amlodipine (as besylate)	30	33	1	1	TA	1
C09BB04	09348B	PERINDOPRIL and AMLODIPINE	Tablet containing 10 mg perindopril arginine with 5 mg amlodipine (as besylate)	30	34	1	1	TA	1
C09BB04	09349C	PERINDOPRIL and AMLODIPINE	Tablet containing 10 mg perindopril arginine with 10 mg amlodipine (as besylate)	30	34	1	1	TA	1
C09BB05	02626F	RAMIPRIL and FELODIPINE	Tablet 2.5 mg-2.5 mg (modified release)	30	22	1	1	TA	1
C09BB05	02629J	RAMIPRIL and FELODIPINE	Tablet 5 mg-5 mg (modified release)	30	34	1	1	TA	1
C09BB10	02857J	TRANDOLAPRIL and VERAPAMIL	Tablet 4 mg-240 mg (sustained release)	28	31	1	1	TA	1
C09BB10	09387C	TRANDOLAPRIL and VERAPAMIL	Tablet 2 mg-180 mg (sustained release)	28	95	1	1	TA	1
C09CA01	05452Y	LOSARTAN	Tablet containing losartan potassium 25 mg	30	33	1	50	mg	2
C09CA02	08397Y	EPROSARTAN	Tablet 400 mg (base)	28	52	0.5	0.6	g	1.5
C09CA02	08447N	EPROSARTAN	Tablet 600 mg (base)	28	30	1	0.6	g	1
C09CA03	09368C	VALSARTAN	Tablet 40 mg	28	37	1	80	mg	2
C09CA03	09369D	VALSARTAN	Tablet 80 mg	28	32	1	80	mg	1
C09CA03	09370E	VALSARTAN	Tablet 160 mg	28	31	1	80	mg	0.5
C09CA03	09371F	VALSARTAN	Tablet 320 mg	28	32	1	80	mg	0.25
C09CA04	08246B	IRBESARTAN	Tablet 75 mg	30	34	1	150	mg	2
C09CA04	08247C	IRBESARTAN	Tablet 150 mg	30	34	1	150	mg	1
C09CA04	08248D	IRBESARTAN	Tablet 300 mg	30	34	1	150	mg	0.5
C09CA06	08295N	CANDESARTAN	Tablet 4 mg	30	34	1	8	mg	2
C09CA06	08296P	CANDESARTAN	Tablet 8 mg	30	35	1	8	mg	1
C09CA06	08297Q	CANDESARTAN	Tablet 16 mg	30	35	1	8	mg	0.5
C09CA06	08889W	CANDESARTAN	Tablet 32 mg	30	35	1	8	mg	0.25
C09CA06	08997M	CANDESARTAN CILEXETIL	Tablet 8 mg	30	35	1	8	mg	1
C09CA06	08998N	CANDESARTAN CILEXETIL	Tablet 16 mg	30	118	0.5	8	mg	0.5
C09CA06	08999P	CANDESARTAN CILEXETIL	Tablet 32 mg	30	31	1	8	mg	0.25
C09CA07	05494E	TELMISARTAN	Tablet 40 mg	28	21	1	40	mg	1
C09CA07	05495F	TELMISARTAN	Tablet 80 mg	28	60	0.5	40	mg	0.5
C09CA07	08355R	TELMISARTAN	Tablet 40 mg	28	32	1	40	mg	1

C09CA07	08356T	TELMISARTAN	Tablet 80 mg	28	32	1	40	mg	0.5
C09CA08	02147B	OLMESARTAN MEDOXOMIL	Tablet 20 mg	30	33	1	20	mg	1
C09CA08	02148C	OLMESARTAN MEDOXOMIL	Tablet 40 mg	30	35	1	20	mg	0.5
C09CA08	05493D	OLMESARTAN MEDOXOMIL	Tablet 40 mg	30	49	0.5	20	mg	0.5
C09DA02	08624X	EPROSARTAN with HYDROCHLOROTHIAZIDE	Tablet 600 mg (base)-12.5 mg	28	31	1	1	TA	1
C09DA03	09372G	VALSARTAN with HYDROCHLOROTHIAZIDE	Tablet 80 mg-12.5 mg	28	25	1	1	TA	1
C09DA03	09373H	VALSARTAN with HYDROCHLOROTHIAZIDE	Tablet 160 mg-12.5 mg	28	31	1	1	TA	1
C09DA03	09374J	VALSARTAN with HYDROCHLOROTHIAZIDE	Tablet 160 mg-25 mg	28	55	0.5	1	TA	1
C09DA03	09481B	VALSARTAN with HYDROCHLOROTHIAZIDE	Tablet 320 mg-12.5 mg	28	33	1	1	TA	1
C09DA04	02136K	IRBESARTAN with HYDROCHLOROTHIAZIDE	Tablet 300 mg-25 mg	30	35	1	1	TA	1
C09DA04	08404H	IRBESARTAN with HYDROCHLOROTHIAZIDE	Tablet 150 mg-12.5 mg	30	35	1	1	TA	1
C09DA04	08405J	IRBESARTAN with HYDROCHLOROTHIAZIDE	Tablet 300 mg-12.5 mg	30	34	1	1	TA	1
C09DA06	08504N	CANDESARTAN with HYDROCHLOROTHIAZIDE	Tablet 16 mg-12.5 mg	30	35	1	1	TA	1
C09DA06	09314F	CANDESARTAN with HYDROCHLOROTHIAZIDE	Tablet 32 mg-12.5 mg	30	34	1	1	TA	1
C09DA06	09315G	CANDESARTAN with HYDROCHLOROTHIAZIDE	Tablet 32 mg-25 mg	30	35	1	1	TA	1
C09DA07	08622T	TELMISARTAN with HYDROCHLOROTHIAZIDE	Tablet 40 mg-12.5 mg	28	32	1	1	TA	1
C09DA07	08623W	TELMISARTAN with HYDROCHLOROTHIAZIDE	Tablet 80 mg-12.5 mg	28	31	1	1	TA	1
C09DA07	09381R	TELMISARTAN with	Tablet 80 mg-25 mg	28	32	1	1	TA	1

		HYDROCHLOROTHIAZIDE							
C09DA08	02161R	OLMESARTAN with HYDROCHLOROTHIAZIDE	Tablet 20 mg-12.5 mg	30	37	1	1	TA	1
C09DA08	02166B	OLMESARTAN with HYDROCHLOROTHIAZIDE	Tablet 40 mg-12.5 mg	30	35	1	1	TA	1
C09DA08	02170F	OLMESARTAN with HYDROCHLOROTHIAZIDE	Tablet 40 mg-25 mg	30	33	1	1	TA	1
C09DB01	05459H	AMLODIPINE and VALSARTAN	Tablet 5 mg (as besylate)-320 mg	28	32	1	1	TA	1
C09DB01	05460J	AMLODIPINE and VALSARTAN	Tablet 10 mg (as besylate)-320 mg	28	33	1	1	TA	1
C09DB01	09375K	AMLODIPINE and VALSARTAN	Tablet 5 mg (as besylate)-80 mg	28	30	1	1	TA	1
C09DB01	09376L	AMLODIPINE and VALSARTAN	Tablet 5 mg (as besylate)-160 mg	28	30	1	1	TA	1
C09DB01	09377M	AMLODIPINE and VALSARTAN	Tablet 10 mg (as besylate)-160 mg	28	32	1	1	TA	1
C09DB02	05292M	OLMESARTAN with AMLODIPINE	Tablet containing olmesartan medoxomil 20 mg with amlodipine 5 mg (as besylate)	30	36	1	1	TA	1
C09DB02	05293N	OLMESARTAN with AMLODIPINE	Tablet containing olmesartan medoxomil 40 mg with amlodipine 5 mg (as besylate)	30	34	1	1	TA	1
C09DB02	05294P	OLMESARTAN with AMLODIPINE	Tablet containing olmesartan medoxomil 40 mg with amlodipine 10 mg (as besylate)	30	34	1	1	TA	1
C09DB04	08978M	TELMISARTAN and AMLODIPINE	Tablet 40 mg-5 mg (as besylate)	28	31	1	1	TA	1
C09DB04	08979N	TELMISARTAN and AMLODIPINE	Tablet 40 mg-10 mg (as besylate)	28	33	1	1	TA	1
C09DB04	08980P	TELMISARTAN and AMLODIPINE	Tablet 80 mg-5 mg (as besylate)	28	31	1	1	TA	1
C09DB04	08981Q	TELMISARTAN and AMLODIPINE	Tablet 80 mg-10 mg (as besylate)	28	31	1	1	TA	1
C09DX01	05285E	AMLODIPINE with VALSARTAN and HYDROCHLOROTHIAZIDE	Tablet 5 mg (as besylate)-160 mg-12.5 mg	28	31	1	1	TA	1

C09DX01	05286F	AMLODIPINE with VALSARTAN and HYDROCHLOROTHIAZIDE	Tablet 5 mg (as besylate)-160 mg-25 mg	28	35	1	1	TA	1
C09DX01	05287G	AMLODIPINE with VALSARTAN and HYDROCHLOROTHIAZIDE	Tablet 10 mg (as besylate)-160 mg-12.5 mg	28	35	1	1	TA	1
C09DX01	05288H	AMLODIPINE with VALSARTAN and HYDROCHLOROTHIAZIDE	Tablet 10 mg (as besylate)-160 mg-25 mg	28	33	1	1	TA	1
C09DX01	05289J	AMLODIPINE with VALSARTAN and HYDROCHLOROTHIAZIDE	Tablet 10 mg (as besylate)-320 mg-25 mg	28	31	1	1	TA	1
C09DX03	02836G	OLMESARTAN with AMLODIPINE and HYDROCHLOROTHIAZIDE	olmesartan medoxomil 40 mg + amlodipine 10 mg + hydrochlorothiazide 12.5 mg tablet	30	31	1	1	TA	1
C09DX03	02864R	OLMESARTAN with AMLODIPINE and HYDROCHLOROTHIAZIDE	olmesartan medoxomil 40 mg + amlodipine 5 mg + hydrochlorothiazide 25 mg tablet	30	28	1	1	TA	1
C09DX03	02880N	OLMESARTAN with AMLODIPINE and HYDROCHLOROTHIAZIDE	olmesartan medoxomil 40 mg + amlodipine 5 mg + hydrochlorothiazide 12.5 mg tablet	30	31	1	1	TA	1
C09DX03	02953K	OLMESARTAN with AMLODIPINE and HYDROCHLOROTHIAZIDE	olmesartan medoxomil 40 mg + amlodipine 10 mg + hydrochlorothiazide 25 mg tablet	30	62	0.5	1	TA	1
C09DX03	10005N	OLMESARTAN with AMLODIPINE and HYDROCHLOROTHIAZIDE	olmesartan medoxomil 20 mg + amlodipine 5 mg + hydrochlorothiazide 12.5 mg tablet	30	29	1	1	TA	1

ATC denotes Anatomical Therapeutic Chemical; DDD, defined daily dose; PBS, Pharmaceutical Benefits Scheme; PDD, Prescribed Daily Dose; Q_3; 75th Percentile; and TA, Tablet

Pack size represents the quantity of tablets typically dispensed for each PBS item code.

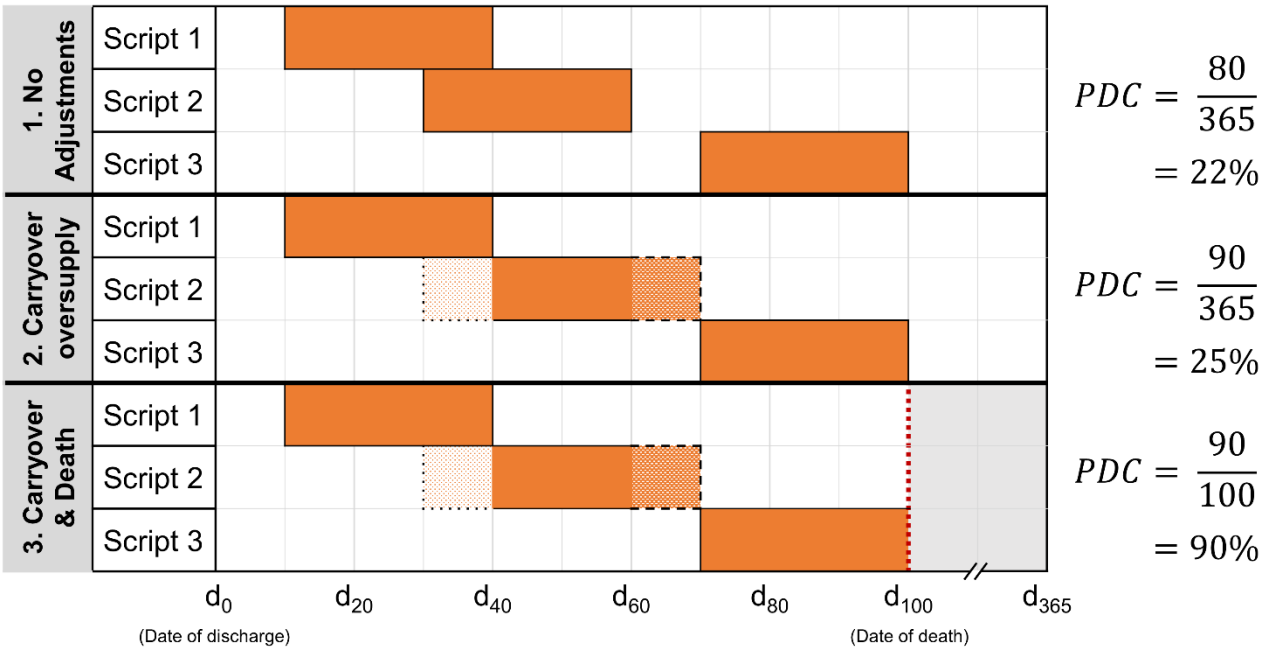
DDD unit column provides doses for the World Health Organisation's Defined Daily Dose (DDD) column.

Supplemental Table II. Sensitivity analysis for adherence to antihypertensive medications within 1 year after stroke, based on three different dosage assumptions, by overall and class. Cohort excluded those who were long-term non-concession card holders and discharged prior to 1st July 2012.

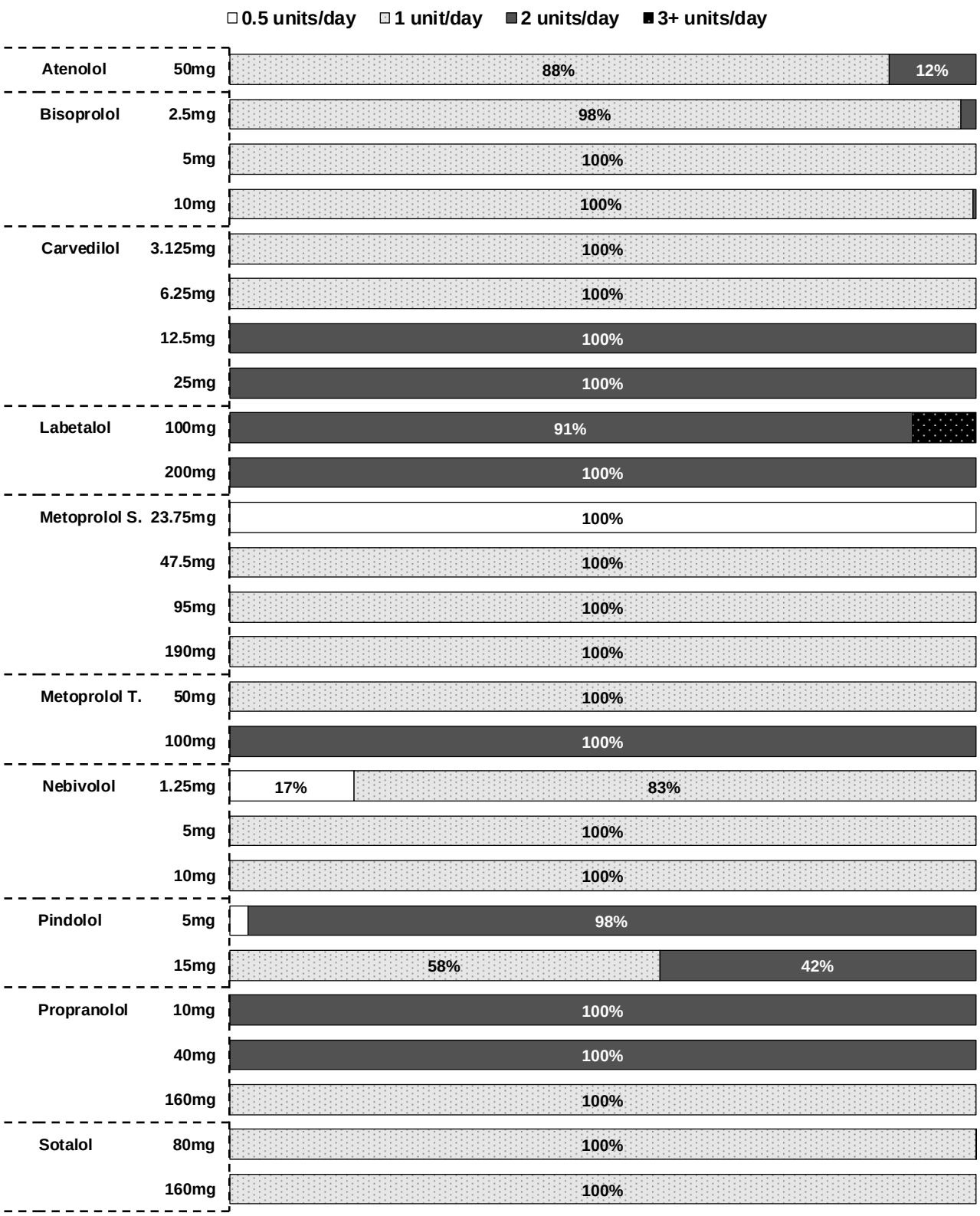
	Adherent[a]	**PDC summary statistics**				
	n (%)	min	Q_1	median	Q_3	max
Before exclusion						
Overall (N=10057)						
1 dose/day	70.8%	0.27	75.6	91.2	97.0	100
PDD_{75}	70.6%	0.27	75.3	91.0	97.0	100
DDD	71.9%	0.27	75.6	92.3	98.1	100
Agents acting on RAS (N=8363)						
1 dose/day	62.6%	0.27	64.9	87.1	95.1	100
PDD_{75}	62.6%	0.27	64.9	87.3	95.1	100
DDD	65.9%	0.27	65.5	90.4	96.7	100
Beta-blocker (N=4574)						
1 dose/day	51.1%	0.27	52.6	80.8	93.2	100
PDD_{75}	49.7%	0.27	51.0	79.5	92.6	100
DDD	42.3%	0.27	41.6	71.0	91.8	100
Calcium channel blocker (N=3394)						
1 dose/day	46.5%	0.27	38.4	76.4	92.3	100
PDD_{75}	46.3%	0.27	38.4	76.4	92.3	100
DDD	52.9%	0.27	43.8	82.7	94.7	100
Diuretic (N=2913)						
1 dose/day	36.1%	0.27	34.0	67.1	85.8	100
PDD_{75}	37.0%	0.27	36.4	68.4	86.3	100
DDD	32.8%	0.27	28.2	60.3	84.9	100
After exclusion						
Overall (N=9448)						
1 dose/day	73.0%	0.5	77.8	91.8	97.3	100
PDD_{75}	73.0%	0.5	77.8	91.5	97.3	100
DDD	74.2%	0.5	78.9	92.9	98.1	100
Agents acting on RAS (N=7847)						
1 dose/day	65.1%	0.27	67.9	88.5	95.3	100
PDD_{75}	65.1%	0.27	67.9	88.5	95.3	100
DDD	68.3%	0.27	69.3	91.2	97.0	100
Beta-blocker (N=4332)						
1 dose/day	52.1%	0.27	54.2	81.6	93.4	100
PDD_{75}	50.7%	0.27	51.9	80.5	92.7	100
DDD	43.4%	0.27	43.3	72.3	92.1	100
Calcium channel blocker (N=3220)						
1 dose/day	47.8%	0.27	41.4	77.8	92.6	100
PDD_{75}	47.6%	0.27	41.4	77.5	92.3	100
DDD	54.1%	0.27	46.1	83.6	94.8	100
Diuretic (N=2814)						
1 dose/day	36.8%	0.27	34.8	67.9	86.3	100
PDD_{75}	37.9%	0.27	37.3	69.0	86.6	100
DDD	33.7%	0.27	30.1	60.4	85.2	100

PDC, the proportion of days covered used as a measure of medication adherence; Q_1, 25th percentile; Q_3, 75th percentile; PDD_{75}, prescribed daily dose determined using the 75th percentile of the population's time until next dispensing for the same medication, strength and form; DDD, defined daily dose based on work by the World Health Organisation; RAS, renin–angiotensin system.

[a] Being adherent was classified as having a PDC ≥80% within 1 year after stroke.



Supplemental Figure I. Calculation of medication adherence using the proportion of days covered (PDC) metric for 3 dispensings within the Pharmaceutical Benefits Scheme database. Example 1 depicts how the PDC would be calculated for an individual without accounting for stockpiling and death for a 1-year observation period. Example 2 contrasts the PDC that would result from accounting for stockpiling within a class of antihypertensive. Example 3 was used within the study and accounts for both stockpiling and deaths.[3]



Supplemental Figure II. Proportion of patients with each estimated prescribed daily dose (PDD_{75}) of beta blockers dispensed in the year following discharge, by medication strength. This is based on each individuals' time until refill. For example, if for 75% of the time, they refilled a 30-tablet supply between 15 – 22 days, then we would estimate that they were taking this at a rate of 2 doses/day. See Table 1 for more details of how the PDD_{75} was determined.

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Chapter 9: Summary of Findings and Future Implications

As outlined in my literature review (Part A), there are many opportunities to improve the secondary prevention of stroke and its risk factors. CDM plans can assist by addressing the need for standardised, yet individualised management of patients with stroke. Education regarding medications, risk factors and how these should be managed are important for patients to understand for secondary prevention. It is particularly concerning that this knowledge can also still be poor in patients with a diagnosed chronic disease.

The four studies included in this thesis address the topic of '*establishing high quality, integrated data for chronic disease management plans and secondary prevention medications and their effectiveness for patients after stroke*'. To our knowledge at the time of initiation, this project was one of the few studies of stroke that incorporated the use of national and state data that were linked to a clinical trial. This trial also had comprehensive baseline phenotyping and long-term follow-up to two years. Prior to this study, many trial studies of stroke were, at most, linked with a single database, such as a death registry.[84, 85]

9.1 Promising Use of Big Data

Summary and Findings

As detailed in the paper presented in Chapter 4, there are various approaches for collecting outcomes after stroke. However, when data linkage is feasible, it has the added advantage of enabling a time- and cost-effective method to collect extra detail about the care received throughout the patient journey, and stroke-related outcomes. The aims of this topical review were to: (1) describe approaches for the collection of outcomes data after stroke and their strengths and limitations; (2) examine the utility of linking datasets to add value to stroke

research, such as ongoing stroke surveillance and reporting of outcomes; and (3) describe barriers to the use of linking these administrative data in stroke research. In this review, there were co-authors from the United States and Canada with expertise in using linked data. This facilitated to broaden the scope of this review to capture the current international landscape of using linked data for stroke-related outcomes.

The main findings of this topical review were that:

1. The ideal method needed to capture outcomes after stroke can be contingent on the type and timing of the data required to meet the aims of the study. These required specifications can include the need for the data to be derived from comprehensive assessments, have clinician-validated assessments/diagnoses, collected both during the in-hospital period or over the long-term.
2. Administrative databases can (a) reflect real-world practice, (b) be large, (c) comprehensive, (d) population-based, (e) have potentially indefinite follow-up, and (f) be less expensive and resource intensive than clinical studies and registries.
3. As administrative data are usually not primarily designed to be utilised for research or clinical purposes, it is important to understand the context surrounding how the data are collected and entered. These factors can affect the quality of the data and may present limitations in the interpretation of findings.

Future Implications

For the past 25 years, the promise of high quality, complete, and linkable health data to use in stroke research has been just around the corner. Our review of the literature reported that most of the research output relevant to stroke, albeit at differing stages, had taken place in only a few countries, such as Australia, Canada, Denmark, Finland, New Zealand, Scotland

and Sweden. This indicates that the use of data linkage to study stroke-related outcomes is still in its infancy in many countries.

Many countries already have technology capable of collecting routine health information at a national level. However, implementing and maintaining an infrastructure that could support data linkage for research can be a significant and costly barrier. In many cases, the findings from these data linkage studies have yet to influence policy and practice, likely due to the known time lag inherent to the translation of evidence from health research.[86]

As highlighted in Chapter 5, there are continual advancements and collaborations in Australia for streamlining the processes involved with linking state and national data. In fact, the development of Multi-source Enduring Linked Data Assets (MELDAs) are an example of this and in the future may be available for researchers in Australia.[87] The two foremost developments of MELDAs are the Multi-Agency Data Integration Project (MADIP) by the Australian Bureau of Statistics and the National Integrated Health Services Information Analysis Asset (NIHSI AA) by the AIHW. The NIHSI AA in particular has 27 analysis projects currently approved to use this data, which includes de-identified and linked healthcare data from MBS, PBS, hospital admissions, ED presentations, residential aged care and mortality databases.[87] However with this growth in the field of data linkage and stroke research, all data custodians and researchers must ensure that linked data is used responsibly as a part of well-designed studies, without compromising the privacy of individuals.[86]

9.2 Use of CDM Plans and Readmissions After Stroke

Summary and Findings

Despite a marked increase in the number of claims for CDM plan items and a commitment from the Australian Government to fund these plans via greater reimbursements for GPs within Medicare, there is limited evidence regarding their efficacy for people with stroke. As

part of Chapter 6, I aimed to determine whether being on CDM plans for a longer duration was associated with a reduced rate of CVD-related readmissions after stroke.

The main findings from this manuscript were that:

1. For 412 patients who were provided a CDM plan within three years after stroke (median exposure of 1.75 years; Q_1: 1.00, Q_3: 2.43), longer duration on a CDM plan was associated with fewer CVD-related readmissions within three years after stroke (quintiles, incidence rate ratio (IRR) 0.86, 95% CI 0.75-0.98, p=0.023).
2. Fewer comorbidities (IRR 1.24, 95% CI 1.06-1.45; p=0.008) and having a more physically active occupation (IRR 0.63, 95% CI 0.43-0.92; p=0.018) were also associated with fewer CVD-related readmissions within three years after stroke.

Future Implications

The findings within this manuscript contributes to filling the current gap in health service research regarding the efficacy of CDM plans for chronic conditions such as stroke. In this study we present important evidence that this policy initiative within primary care may improve outcomes. Our findings that being on a CDM plan for a longer duration was associated with a reduced incidence of CVD-related readmissions, at three years after stroke, provides important evidence that the Australian government should continue to fund these Medicare items. We also found that use of a CDM plan alone was not associated with a reduced rate of CVD-related readmissions after stroke. There is evidence that there may be a dose-response to the effectiveness of this program after stroke, and so it may be beneficial for patients to remain on a CDM plan that is consistently reviewed by a GP every six months to a year. Such continuation of use of CDM plans may facilitate improvements in risk factor-related health behaviours and thereby ultimately reduce the likelihood of CVD-related readmissions.

Future studies should be undertaken to investigate: (1) whether those on a CDM plan tend to utilise healthcare or rehabilitation services differently to those not on a plan, and (2) whether these plans are cost-effective.

9.3 Medication Adherence and the Use of CDM Plans After Stroke

Summary and Findings

One of the major recommendations for long-term post-stroke care from the Australian Stroke Foundation clinical guidelines is adherence to secondary prevention medications. During the provision of CDM plans, GPs could be a valuable resource to promote the importance of medication adherence to their patients with stroke or other chronic conditions. However, it is unclear as to how effective, if at all, CDM plans may be towards improving adherence to secondary prevention medications in patients with stroke.

The main findings from this manuscript were that:

1. The median PDC for 563 patients with stroke (median age 70 years; 36% female) ranged from 92% to 95% among the three classes of medications (Figure 9.1).
2. Approximately 27% did not take up a CDM plan, 33% were on plans for <1.5 years and 40% for 1.5-3 years.
3. Duration on a CDM plan (quintiles) was associated with adherence to antihypertensive (odds ratio 1.18, 95% CI 1.00-1.40, p=0.029) and antithrombotic (odds ratio 1.22, 95% CI 1.03-1.46, p=0.024) medications, but not for lipid-lowering medications.

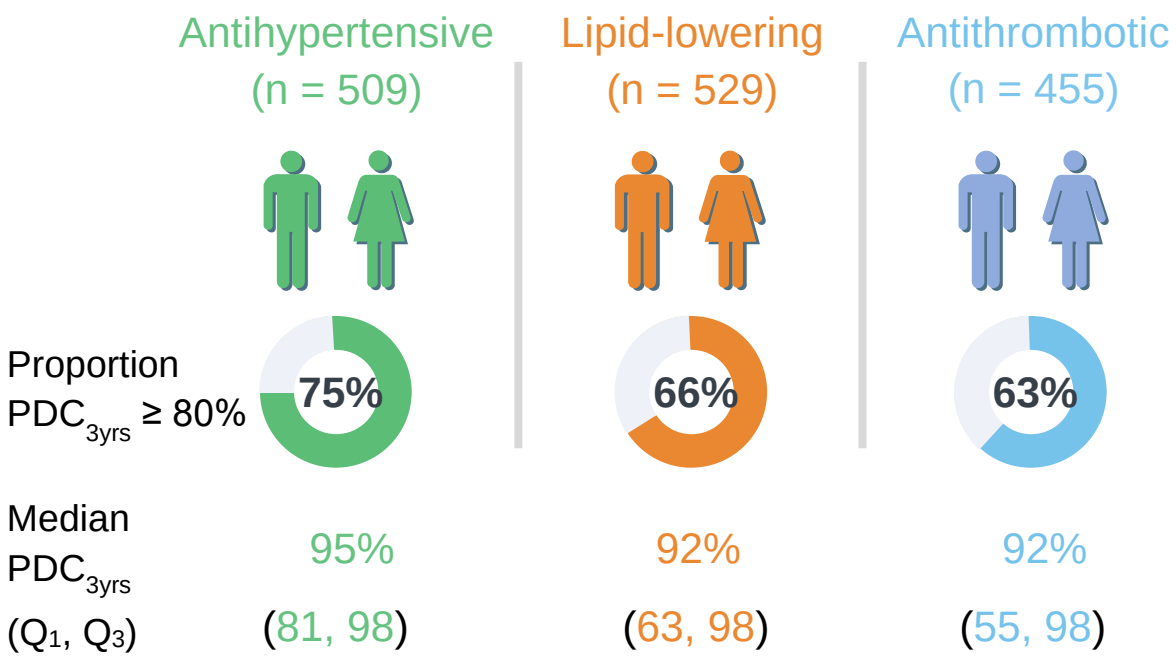

Figure 9.1. Summary statistics for the proportion of days covered (PDC) measure of medication adherence, in patients with stroke who were dispensed each class of secondary prevention medication.

Future Implications

There is evidence that an organised approach to care is associated with improving adherence to secondary prevention medications among survivors of stroke. This was supported by our finding that patients on a CDM plan for a longer were more likely to be adherent to their antihypertensive and antithrombotic medications, than those not on an organised plan. This finding was independent of age, sex, stroke severity, prior use of medications and pill burden.

Our findings provide evidence for the preparation of individualised management plans, as these may address patient-level barriers to achieving medication adherence, such as regimen complexity, knowledge of medications and concerns regarding side effects. However, as discussed in Chapters 2 and 7, adjunct strategies should be considered by clinicians to address other common barriers, such as inability to self-care, burden of treatment and tendency for patients and carers to trivialise stroke.

9.4 Assumptions of Dosage for Estimating Medication Adherence After Stroke

Summary and Findings

As highlighted in our paper for Chapter 8, there are different approaches to estimating the dosage, or pills per day, at which patients are prescribed or are taking their medications. Assuming patients are taking medications at a dosage of 1DD is a popular and simple assumption used in many early studies.[73, 74] The World Health Organization's DDD is another approach. However, it lacks accuracy to account for differences in strength of drugs and prescribing practices around the world. This information on dosage is then used to determine intervals in which a patient was likely to be exposed to a drug, based on the quantity they were dispensed. However, it is unclear the degree to which this reflects real-world practice and whether opting for a more population-specific estimation of dosage might affect the findings of study on medication adherence after stroke.

The main findings from this manuscript were:

1. Antihypertensive medications were predominantly dispensed to patients with stroke at a rate which reflected 1DD.
2. The 1DD estimates yielded similar medication adherence to those from the PDD_{75}, derived from the dispensing patterns of each patient.
3. Compared to the 1DD and PDD_{75} methods, the DDD overestimated adherence for the use of any antihypertensive medication, agents acting on RAS, and calcium channel blockers, while underestimating adherence for beta blockers and diuretics.

Future Implications

In our evaluation of the different approaches to estimating medication adherence using Australian PBS data, we found that the simple 1DD approach was comparable to the more

complex PDD_{75} for all the antihypertensive medications assessed, except from beta blockers. Our findings provide evidence for researchers to consider using the 1DD approach to estimate intervals of medication usage, when gold standard PDD information is lacking.

9.5 Concluding Remarks

This thesis has provided insight into the utility of data linkage and the potential benefits of being on CDM plans after stroke, towards reducing readmissions and improving adherence to secondary prevention medications. Building upon the evidence presented in this thesis, CDM plans may also serve as a mechanism to encourage patients to return and regularly consult with their GPs. This will increase the likelihood that they will be well managed and adherent with secondary prevention therapies and lifestyle modifications, for potentially improved risk factor control. Further analyses using the STANDFIRM trial data could be used to differentiate the effect of the in-home tailored education, independent of the provision of a CDM plan. This could potentially evaluate which of these two components may provide additional, or the most, benefit to outcomes after stroke. Future research using data linkage should identify patterns in the utilisation of health services for patients with stroke on a CDM plan. This could be essential for exploring what aspects of these plans are responsible for providing the most benefit to populations with chronic conditions. Ultimately, this could also positively contribute to policy and clinical practice to ensure all survivors of stroke adhere to secondary prevention clinical guidelines.

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Abbreviations:

STANDFIRM, Shared Team Approach between Nurses and Doctor For Improved Risk factor Management; GPMP, general practitioner management plan; GP, general practitioner; SAE, serious adverse events; ICD-10-AM, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification; CVD, cardiovascular disease.

[Appendix A] STANDFIRM Trial – Protocol

Protocols

Risk factor management in survivors of stroke: a double-blind, cluster-randomized, controlled trial

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Background **Comprehensive community care has the potential to improve risk factor management of patients with stroke or transient ischaemic attack.**
Aim **The primary aim is to determine the effectiveness of an individualized management program on risk factor management for patients discharged from hospital after stroke.**
Design **Multicentre, cluster-randomized, controlled trial, with clusters by general practice. Participants are randomized to receive intervention or control after a baseline assessment undertaken after discharge from hospital. The general practice they attend is marked as an intervention or control accordingly. All subsequent participants attending those practices are automatically assigned as intervention or control. Baseline and all outcome assessments, including an analysis of risk factors, are undertaken by assessors blinded to patient randomization.**
Intervention Details **Based on the results of blinded assessments, the individualized management program group will receive targeted advice on how to manage their risk factors using a standardized, evidence-based template to communicate 'ideal' management with their general practitioner. In addition, patients randomized to the individualized management program group will receive counselling and education about stroke risk factor management by an intervention study nurse. Individualized management programs will be reviewed at three-months, six-months, 12 months, and 18 months after stroke, at which times they will be modified if appropriate. Stroke risk management will be evaluated using changes in the Framingham cardiovascular risk score. Analysis will be on an intention-to-treat basis using analysis of covariance or generalized linear model to adjust for baseline risk score and other relevant confounding factors.**

Key words: multicenter cluster-randomized controlled trial, risk factor management, secondary prevention

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Introduction

Recurrent stroke and other vascular events are common after stroke (1–3) and transient ischaemic attack (TIA) (1,4). Of the estimated 50 000 annual stroke events in Australia, approximately 30% are recurrent (5). Generally, recurrent events are more severe (6). Therefore, patients who have suffered a stroke are more likely to gain benefit from evidence-based prevention interventions.

People who have suffered a stroke often exhibit risk factors, e.g. approximately 50% have high blood pressure (BP), 18% smoke daily, 77% undertake insufficient physical activity, and 31% have high blood cholesterol (7). Moreover, 96% have two or more stroke risk factors, many of these factors also being risk factors for other vascular events (7). Patients with multiple risk factors have the greatest risk of stroke, as risk is cumulative with the number of risk factors present (8).

Both pharmacological and nonpharmacological interventions have been shown to prevent recurrent stroke and other vascular events within this high-risk population. Effective pharmacological interventions include BP lowering after stroke or TIA (9), use of antiplatelet and cholesterol-lowering drugs after ischaemic stroke or TIA (10), and anticoagulant drugs in patients with a cardioembolic stroke due to atrial fibrillation (AF) (11,12). The evidence for the effectiveness of behavioural interventions mostly originates from primary prevention studies. These modifying behaviours include: dietary modifications to lower cholesterol levels (13); motivational interviewing to lower body weight, cholesterol, and BP (14); diabetes management via behavioural changes (15,16); simplified drug regimens, reminders, and motivational interviewing to promote medication compliance (17,18); smoking cessation (19,20); reducing dietary salt (21–23); increasing consumption of fruit and vegetables (24); increasing physical activity to reduce BP (25); and reducing alcohol consumption (26).

Similar to other countries, there is evidence that secondary prevention strategies may not always be adopted in eligible people with stroke in Australia (27). Although this may occur for valid clinical reasons or patient preferences, patients may not be prescribed medications according to evidence-based clinical guidelines and some continue behaviours that place them at greater risk. For example,: approximately 30% of stroke survivors have BP ≥140/90 mmHg at five-years post-stroke (28); 17% of patients with ischaemic stroke or TIA are not prescribed

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antiplatelet drugs (personal communication, Cadilhac – based on the Bettering the Evaluation and Care of Health study (29)); only 16% of hospitalized AF cases are prescribed warfarin on discharge (30); and most stroke survivors who smoke continue to do so (31). This suboptimal adoption of secondary prevention measures may leave many survivors of stroke susceptible to recurrent stroke and worse outcomes.

However, multidisciplinary interventions aimed at promoting comprehensive and coordinated care may improve secondary stroke prevention measures. Such interventions are effective for smoking cessation, BP control, and diabetes management (32–34). Similarly, an individualized management program (IMP), which includes a tailored management plan and regular review and input from a multidisciplinary team, may be effective for managing risk factors in patients with stroke or TIA.

Aim

The primary aim is to determine the effectiveness of an IMP for patients discharged from hospital after stroke or TIA. Secondary aims are to ascertain the effect of an IMP on risk factor management, the risk of subsequent adverse events (AE; e.g. recurrent strokes, myocardial infarctions), and the utilization of preventive therapies when compared to patients that receive usual care. Cost-effectiveness of the IMP will also be assessed.

Hypotheses

Primary hypothesis

Survivors of stroke given an IMP will show greater improvements in terms of overall stroke risk, defined as a 4–6% net change in absolute risk at 12 months (35), when compared to those who are provided usual care.

Secondary hypotheses

When compared with survivors of stroke undergoing usual care in the community, those given an IMP will:

1. Have significant improvements to risk profiles as measured by a change in modified absolute risk score at 12 months (as measured using the score sheet) (35);
2. Have fewer AEs and serious adverse events (SAEs) at 12 months;
3. Have greater reductions in systolic and diastolic BP;
4. More often be taking therapy according to evidence-based practice;
5. More often engage in low-risk behaviours (e.g. greater fruit and vegetable consumption, greater physical activity, cessation of smoking).

Also, we hypothesize that the intervention will be cost-effective defined as a cost per quality adjusted life-year (QALY) gained <$50 000.

Methods

Design

Shared Team Approach between Nurses and Doctors For Improved Risk factor Management (STAND FIRM) for patients with stroke is a multicentre, cluster-randomized, controlled trial with blinded assessment of outcomes and intention-to-treat analysis. Participants are randomized to receive an IMP or usual care after hospital discharge (Fig. 1). As the intervention is delivered by general practitioners (GPs), the general practice the participant attends is marked as an IMP or usual care cluster accordingly in order to minimize contamination. All subsequent participants attending those practices are automatically assigned as intervention or usual care. A computer-generated, blocked randomization procedure will ensure that each hospital has a balance of participants in each group as post-acute treatment may vary slightly at each patient recruitment site.

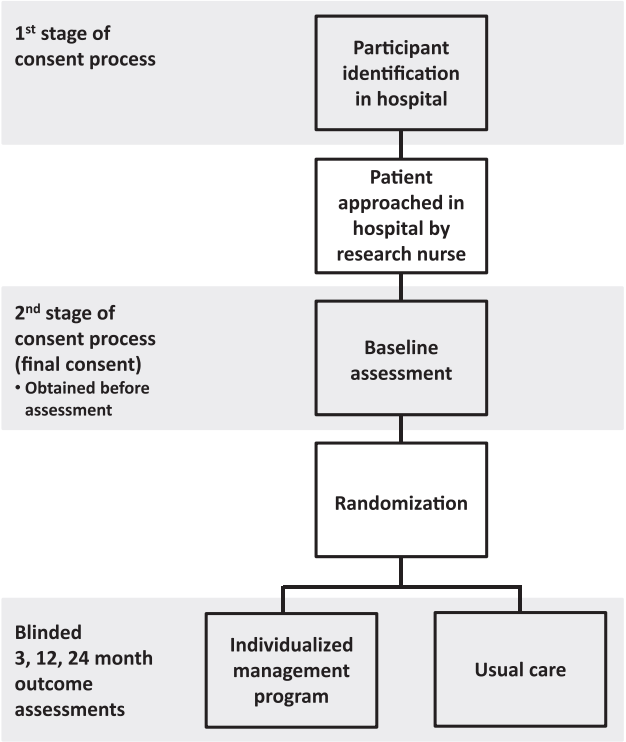

Fig. 1 Study design.

A pilot study was successfully conducted in 2008 (unpublished). Subsequently, a National Health and Medical Research Council project grant (ID: 586605) was obtained in 2009. Participant recruitment for the full study commenced in 2010. Ethics approval has been obtained at all participating hospitals (Alfred Hospital, Box Hill Hospital, Dandenong Hospital, and Monash Medical Centre).

Participant eligibility

Patients hospitalized for stroke or TIA, aged ≥18 years, and living within 50 km of the closest recruitment centre are eligible for recruitment. Individuals are excluded if they are participating in another clinical trial, are admitted from or discharged to a nursing home, or are not expected to survive the study follow-up as a result of concurrent diagnosis of a rapidly deteriorating disease. Potential participants identified by research nurses and a stroke physician are approached to request consent for participation. Final consent is obtained at an in-home patient visit. Following consent, a baseline assessment occurs and participants are then randomized to receive the intervention or usual care. The

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two-step process of obtaining consent was designed following our experience in the pilot study. This has helped to screen patients unlikely to follow study protocol and has therefore minimized dropouts after randomization.

Baseline and outcome assessments

During hospitalization, the following data are obtained: demographic information of participants, details of the stroke or TIA, the results of diagnostic tests performed, and a list of all discharge medications prescribed to the participant. The details of the stroke or TIA recorded include the history and onset of main symptoms, presence or absence of risk factors, and other relevant history and comorbidities, enabling an aetiological classification of stroke.

Baseline (2–8 weeks after discharge to home) and outcome assessments (three-months, one-year, and two-years after randomization) are undertaken by nurses blinded to treatment allocation (assessment nurses). The summary of assessments undertaken is shown in Table 1.

Assessment nurses administer a number of questionnaires at each time point to assess costs due to stroke, standard medical history, risk factor management (nutrition, physical activity, smoking, and alcohol intake), mental health, handicap (modified Rankin Scale (39) and London Handicap Scale (36)), and quality of life using the Assessment of Quality of Life (AQoL) instrument, a multi-attribute utility scale that has been validated in a stroke population (38). In addition, the following physical measurements occur: height measurement using a portable stadiometer, weight measurement using validated scales, waist and hip circumference measurement using measuring tape, and skinfold measurement using callipers. BP is measured using the OMRON Digital Automatic Blood Pressure Monitor (HEM 907) according to the European Society of Hypertension protocol (40).

Blood samples are collected from participants after an eight-hour fasting period and are used to assess cholesterol levels, triglycerides, glycosylated haemoglobin (HbA1c), creatinine, fasting glucose levels, and, in patients that are taking warfarin, international normalized ratio.

A 24-h urine sample is collected to assess salt excretion, cotinine (for smoking exposure), and creatinine (for kidney health).

Details of AEs that participants experience after discharge are also recorded. These include: the date of onset, description, severity, duration, and medical diagnosis if known. AEs comprise any untoward medical occurrence in any participant involved in the study and which does not necessarily have a causal relationship to the study intervention. This includes any worsening of a pre-existing event. SAEs are defined as any medical occurrence that is fatal, life-threatening, requires or prolongs hospitalization, results in significant permanent disability or is incapacitating, requires medical or surgical intervention to prevent permanent impairment or damage, and an accidental or intentional overdose.

Table 1 Summary of assessments undertaken by all participants

Assessment	Baseline	Three-months, one- and two-years
Patient history	✓	–
Patient history follow-up	–	✓
Lifescripts*	✓	✓
LHS/HADSI (36,37)	✓	✓
AQoL (38)	✓	✓
Management of risk factors	✓	✓
Modified Rankin scale† (39)	✓	✓
Service use	✓	✓
Carer quality of life	✓	✓
Healthcare needs, medications	✓	✓
Blood pressure, blood tests	✓	✓
Weight, waist, skin folds	✓	✓
24-h urine	✓	✓
Adverse events	–	✓
Serious adverse events	–	✓
Post-acute costs of stroke	–	✓

*Lifescripts is a national initiative, which provides tools for primary care clinicians to promote risk factor management in partnership with patients to promote self-efficacy. (http://www.health.gov.au/lifescripts). †Pre-stroke modified Rankin scale questionnaire is administered at baseline. LHS, London Handicap Scale; HADSI, Hospital Anxiety and Depression Scale and Irritability; AQoL, Assessment of Quality of Life.

Intervention details

Using results from the baseline assessment, a patient-specific management plan is prepared by a stroke clinician and an unblinded intervention nurse (Table 2). A standard management plan format is adapted to each intervention patient based on their risk factor profile. Clear health goals are itemized on the management plan for each risk factor present. The management plan is then provided to the patient's GP. The IMP meets the standard for Medicare item numbers in Australia, which means the participating GPs actions can be remunerated under the universal Medicare health insurance scheme. This provides an incentive for the GPs to participate in the trial (as the GPs will be paid for using the prepared documentation) and also is a pathway for implementation of the trial outcomes. The intervention nurse then makes an in-home visit to educate the patients about modifying their risk

Table 2 Summary of the intervention

Assessment	Baseline*	Three-months*	Six-months	12 months*	18 months
Management plan devised and sent to GP	✓	–	–	–	–
Management plan modified and sent to GP	–	✓	✓	✓	✓
Risk factor management education (in-home visit)	✓	✓	–	✓	–
GP visit organized	✓	✓	–	✓	–
Telephone interview	–	–	✓	–	✓

*Blinded outcome assessments occur at a separate visit prior to these intervention visits. GP, general practitioner.

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factors. Types of advice provided may include the benefits of healthy eating, healthy weight, physical activity, smoking cessation, alcohol moderation, adherence to medication, and other lifestyle changes. After the interview, the intervention nurse arranges an appointment for the patient to see their GP to further discuss their management plan.

Patient's healthcare needs and problems and potential goals are also assessed. If further services are required by a patient in the IMP group, another plan is devised that incorporates visits with other healthcare professionals. At each appointment, GPs may modify the proposed plan in consultation with the patients.

Following the three- and 12-month outcome assessments, the intervention nurse reviews the patient's management plan during in-home visits. At this visit, the intervention nurse discusses problems identified at earlier visits and barriers to achieving health goals. The nurse further supports lifestyle change by educating the patients about the benefits of risk factor management. Any problems identified at the intervention visit and the results of the outcome assessments are taken into consideration when changes to the management plan are made, with input from a stroke specialist. Another GP appointment is arranged.

At six and 18 months, patients are telephoned by an intervention nurse to discuss their management plan. Appropriate changes to the management plans are made at these dates as outlined earlier and are relayed to the patient's GP.

The interventions described earlier are only provided to patients in the intervention group and not to those in the control group. This ensures that the follow-up for controls is maintained as close to 'usual practice' as possible.

Primary outcome

The primary outcome measured is a mean change in absolute risk in the updated Framingham cardiovascular disease (CVD) risk score at 12 months (35). Factors included in the Framingham CVD risk score are age, gender, systolic BP, total cholesterol levels, high-density lipoprotein cholesterol levels, glycosylated haemoglobin levels, and smoking status (35).

The Framingham CVD risk score was initially designed to assess a patient's risk of vascular events in primary prevention settings, but is appropriate for use in STAND FIRM as most components of the Framingham CVD risk score are sensitive to change with better management of risk factors. Also, risk factors for incident stroke are similar to those for recurrent stroke. Achieving a lower Framingham CVD risk score (i.e. lower 10-year risk of CVD) is also likely to be associated with fewer subsequent vascular events. We acknowledge that the use of this Framingham CVD risk score may underestimate overall risk in participants (especially the very elderly), but this does not affect the magnitude of change and so any underestimate will be the same for both groups.

Secondary outcomes

Secondary outcomes measured will be:

- A change in modified absolute risk score at 12 months (as measured using the score sheet) (35). The score sheet method comprises 0, 1, 2, 3, etc scores for each item. In addition to the factors included earlier, this score incorporates the use of therapy (0 = treated, 1 = untreated) according to evidence-based practice (antihypertensive agents, antiplatelet drugs, anticoagulation therapy, and cholesterol-lowering drugs);
- Change in systolic BP and diastolic BP at one-year.
- AEs and SAEs.
- Use of at least one antihypertensive agent, defined as any antihypertensive agent prescribed to the patient.
- Use of antiplatelet therapy daily (in patients with ischaemic stroke or TIA), defined as any antiplatelet agent prescribed to the patient.
- Use of antithrombotic therapy in ischaemic stroke patients, defined as any antiplatelet agent prescribed to the patient or prescription of anticoagulants in patients with comorbid AF.
- Current smoking. A urinary cotinine test (a measure of smoking exposure) will provide validation for the self-report.
- Consumption of ≥5 servings of vegetables and ≥2 servings of fruit per day, determined by self-report.
- Salt excretion determined from a 24-h urine sample.
- Physical activity is assessed by self-report and pedometer counts (measured as mean steps/day).
- Risky drinking level (i.e. ≥4 standard drinks/day for men and ≥2 standard drinks/day for women). This is assessed by careful interview of the participant using pictures of standard drinks to help prompt patient recall.

Economic evaluation

Resource utilization is collected from a broad health sector perspective using a simplified version of questionnaires previously devised (41). Data collected include doctor appointments, medications, aids and equipment, rehabilitation, hospital re-admissions, community services, out-of-pocket costs to participants, as well as the costs of running the program. QALYs will be estimated from data obtained using the AQoL instrument (38). Cost-effectiveness of the intervention is defined as the net cost/QALY gained <$50 000. This is a commonly used threshold (42) and is consistent with the willingness-to-pay threshold reflected in previous policy decisions for healthcare programs in Australia (43).

Blinding

This study involves blinding of participants, assessment nurses, and clinicians. Participants, assessment nurses, and GPs are unaware of the nature of the intervention and are blinded to the treatment groups of participants. Stroke physicians review management plans for participants at other recruitment sites to ensure that they are blinded to the treatment status of the participants they treat. Intervention nurses coordinate the IMPs.

Safety monitoring

A data safety monitoring committee (DSMC) meets at least every six-months to adjudicate AEs and to discuss the study progression. The DSMC provides feedback to improve the study conduct.

Statistical analyses

Analysis will be performed based on intention to treat. Differences in baseline characteristics between groups will be analysed using chi-square tests, *t*-tests, or analysis of variance as appropriate.

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Framingham risk score changes from baseline to 12 months will be analysed using analysis of covariance or generalized linear models. These techniques allow adjustment for baseline risk score and other relevant confounding factors. Binary logistic regression analysis will be performed to compute odds ratios with 95% confidence intervals. The same techniques will be used to analyse mean BP reductions. Differences in the proportion of AEs and SAEs between groups will be compared using Poisson regression for count outcomes. Logistic regression will be used to assess differences between groups according to risk-reducing behaviours and evidence-based therapy.

Incremental cost-effectiveness ratios or the net difference in cost and outcomes will be calculated. Standard discounting will be applied to both costs and outcomes. Sensitivity and uncertainty analysis will be performed using @RISK software (Palisade Corporation, 2005). Probabilistic multivariable analysis will be used to account for variability in point estimates.

Sample size

Given the breadth of the IMP and intensity of monitoring, we estimate a minimal clinically significant change in absolute risk score between groups of 4–6%. Based on our pilot data, the mean 10-year risk of vascular events among stroke patients is estimated to be 23·60% with a standard deviation of 14·04%. This gives a requirement for 160 patients per group with a power of >80% to detect a 4·5% difference in 10-year Framingham CVD risk scores. Power calculations relied on assumptions derived from preliminary pilot data, as no other data exist for these estimates. We estimated that 5% of participants will drop in to the intervention (as their GP already utilizes the IMP) and 20% will drop out. This results in an adjusted sample size of 285 per group ($N^* = N/(1 - 0{\cdot}20 - 0{\cdot}05)^2 = 160/(0{\cdot}75)^2 = 285$), 570 patients in total. Study recruitment commenced on 16/02/2010 and 300 patients from four hospitals have been recruited as of 31/05/2012.

Conclusions

Comprehensive post-stroke care delivered through an IMP may be the solution to address the deficiencies that currently exist in the management of stroke survivors. IMPs will be tailored to the needs of the patients at three-months, six- months, 12 months, and 18 months after stroke to overcome the problems that stroke survivors may usually experience in adhering to post-stroke therapies. Thus, patients receiving an IMP are expected to have better control of risk factors and as a result have better Framingham CVD risk scores and fewer recurrent events when compared to patients given usual post-stroke care.

If the IMP is successful for stroke survivors, it can be readily implemented into Australian clinical practice without changes to policy as there are already Medicare-funded initiatives to support implementation.

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[Appendix B] STANDFIRM Trial – Statistical Analysis Plan

Protocol

Statistical analysis plan (SAP) for Shared Team Approach between Nurses and Doctors For Improved Risk Factor Management (STANDFIRM): a randomised controlled trial

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Key words: prevention, protocol, randomized controlled trial, risk factors, secondary prevention, statistics

With reducing case fatality following stroke (1), many more people in the community are living with stroke and are at risk of further vascular events. There are many proven treatments that prevent further vascular events in survivors of stroke. These include blood pressure (BP) lowering (2), antiplatelet therapy (3), anticoagulant therapy in people with nonrheumatic atrial fibrillation (4,5), and use of HMG CoA reductase inhibitors (6,7).

Behavioral changes are also effective for improving risk factor profiles, with most evidence coming from cohort studies of primary prevention. Effective strategies include dietary counselling and review by trained specialists to lower cholesterol levels (8,9); diabetes management using exercise regimes, and pharmacotherapy for BP, cholesterol, and glycemic control; simplified drug regimens and education to improve medication compliance (10–13); smoking cessation (14,15); reducing dietary salt (16–18); consuming a diet high in vegetables and fruit (19), particularly among those with dyslipidemia (20,21) and obesity (22); increasing physical activity (23); and reducing alcohol consumption (24). Behavior change has been more effective by tailoring lifestyle interventions to an individual (25), and providing educational and motivational counseling (8,9), e.g., 'Lifescripts' was a national initiative in Australia, which provided tools for general practitioners (GPs) to encourage risk factor management in partnership with patients to promote self-efficacy (26).

There is strong evidence that secondary prevention strategies for people with stroke are currently underutilized (27,28), e.g., about 30% of stroke survivors have BP levels ≥ 140/90 mmHg (29). In addition, only about 16% of patients hospitalized with atrial fibrillation and eligible for warfarin therapy were discharged on warfarin at the time the study commenced (30), although this has improved somewhat in recent years (31). Patients who do not receive these agents may be more susceptible to recurrent strokes and other poor outcomes.

The potential gains of secondary prevention are considerable. Using mathematical modeling, we assessed the cost per quality adjusted life year (QALY) gained of different BP lowering strategies to reduce the burden of stroke in Australia. We tested the impact of increasing the proportion of patients being treated for hypertension to 60% (from current estimates of 50%). Using a combined angiotensin converting enzyme inhibitor/diuretic therapy, we estimated that 2859 strokes would be prevented each year (32), with a minimal cost per QALY saved of $2120 (32). In other estimates, about 1700 recurrent strokes could be avoided in Australia each year (with a mean cost per case avoided) using any one of: voluntary smoking cessation (no cost), long-term aspirin use in those with ischemic stroke ($2000), or use of cholesterol-lowering drugs ($41 000) (33). Thus, considerable health gains could be made over and above that obtained with current practice at minimal extra cost. Moreover, a combined approach may achieve even better results.

In Australia, nurse-assisted interventions for coronary heart disease (and heart failure) have been proven effective in reducing rehospitalizations (34). Interventions include education of patients and caregivers on factors such as adherence to treatment, introduction of a simple exercise regimen, referral to other clinicians when required, and regular telephone follow-up. No such studies of stroke in Australia have been published. Only one long-term study has been completed in patients with stroke elsewhere (35). This Canadian study, focusing on quality of life, had a small sample size (96 patients/group). No hard end-points, such as recurrent events or management, were included. Fewer specialist visits occurred in the intervention group, this being the only difference observed. In another very short-term study (three-months), only 47 patients were recruited per group (36). Despite their positive outcome, it is important to assess whether management can be sustained in the longer term, particularly as management is often not finalized this early.

General practices are ideally placed to coordinate the long-term preventive care needs of people with stroke. In Australia, a

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'National Service Improvement Framework' for heart, stroke, and vascular disease has been developed recently to encourage optimal management of chronic disease (37). Processes include the Chronic Disease Management (CDM) plan Medicare item 721 (with remuneration of more than $140) which uses a structured approach to encourage optimal quality of care in patients with a chronic disease. Other practice incentive payments are available for recall registries and employing nurses. Despite the financial incentives, these items are used by GPs in only 1–3% of attendances (38). This is at least partly attributable to the complexity and administrative burden associated with these items. By overcoming these burdens, we aim to increase the uptake of these strategies.

Specific features of the CDM plan include:

1. counseling on lifestyle advice including nutrition, smoking cessation, and physical activity;
2. screening for depression;
3. collaborative care planning between patients, families, and healthcare teams;
4. written individualized management plans to promote shared involvement in management. A written plan is a major element in effective chronic illness care, as it involves the patient and promotes optimal, evidence-based care (39);
5. a patient education component; and
6. six monthly review of the management plan.

Despite the extensiveness of this CDM plan and the government commitment to fund it, there is no evidence of its effectiveness in stroke (40). There is also no coordinated approach in the plan to ensure efficient transition of treatment from inpatient hospital settings to the community. This uncertainty led us to conduct a randomized trial of chronic disease management in general practice. Our aim is to test whether the CDM plan can be used to reduce the 10-year CVD risk in stroke survivors.

In this article, we describe our prespecified statistical analysis plan (SAP) for the main and secondary analyses of this cluster randomized controlled trial (see Supporting Information Appendix S1). This SAP adds further detail about the analysis that was not included in our original protocol (41), and was finalized before data collection was complete, and before any of the investigators or statisticians were unblinded to the dataset. Our SAP outlines how we will analyze and present the data, including the baseline characteristics and the outcomes. This SAP provides more comprehensive details of our planned analyses, and ensures transparency so that readers of the study results can judge their validity.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Statistical analysis plan.

STATISTICAL ANALYSIS PLAN

for

STAND FIRM: Shared Team Approach between Nurses and Doctors for Improved Risk Factor Management for stroke patients – A Randomised Controlled Trial

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1 Introduction

Survivors of stroke are at greater risk of subsequent vascular events,[1] and these events contribute significantly to morbidity and mortality.[2, 3] The costs of recurrent stroke are also large and are estimated to be USD 21,482 (AUD 32,354) per case in the year this occurs.[4]
The majority of survivors of stroke have at least two risk factors for stroke.[5] Many of these risk factors also contribute to the risk of other vascular events.[5] Systematic reviews of randomised controlled trials provide evidence that treatment of many of these risk factors reduces the risk of recurrent stroke, other vascular events, and death.[6-11] Behavioural changes are also effective for improving a person's risk factor profile, with most evidence coming from cohort studies of primary prevention. These include interventions targeting medication compliance;[12-15] smoking cessation;[16, 17] diet; [18-23] physical activity;[24] and alcohol consumption.[25] In addition, tailoring lifestyle interventions to an individual has been shown to improve behaviour change.[26]

Uptake of secondary prevention strategies for people with stroke is poor;[27, 28] many patients are not discharged on appropriate preventive agents such as blood pressure lowering medications, [29] antiplatelet agents, [29] statins, [29] and most patients eligible for warfarin therapy are not discharged on this agent.[30, 31] Clearly opportunities exist to improve uptake of these secondary prevention agents.

Nurse-led supported or structured approaches have been shown to be effective in smoking cessation, control of blood pressure and care of diabetes.[32] However, there has been little evidence for effectiveness of these approaches to improve use of secondary prevention therapies in stroke,[33, 34] and none in longer term use of these therapies.

In Australia a 'National Service Improvement Framework' for heart, stroke and vascular disease has been implemented to encourage optimal management of chronic disease.[35] This includes use of Chronic Disease Management plans that incorporate a structured approach to encourage optimal quality of care in patients with a chronic disease. Enhanced primary care item numbers exist that can be used to financially support implementation of the study in general practice through the Health Insurance Commission.

2 Study Aim and Hypotheses

In this pragmatic ***cluster randomised controlled trial (cRCT)*** we aim to determine whether a structured approach to management can improve control of risk factors in people who have suffered a stroke.

2.1 Primary Hypothesis

Our primary hypothesis is that patients with stroke undertaking a comprehensive Chronic Disease Management plan will have better management of risk factors, as measured by a change in the updated Framingham Cardiovascular Disease (CVD) Risk Score at 12 months,[36] than those undergoing usual care.

2.2 Secondary Hypotheses

When compared to patients with stroke undergoing usual care in the community, patients with stroke undertaking a comprehensive chronic disease management will:

1. Have improved changes to risk profiles as measured by a change in absolute CVD risk score;
2. Have greater reductions in blood pressure (BP) than those undergoing usual care;
3. Have fewer adverse events at 1 year;
4. More often be taking therapy according to evidence-based practice;
5. More often have behaviours that help manage risk factors:
   a) Less often smoke; and less often drink ≥4 (males) or ≥2 (females) standard drinks daily;
   b) More often eat ≥5 serves of vegetables and ≥2 serves of fruit daily and have salt intake <5g;
   c) Will have greater physical activity;
6. The intervention will be cost-effective defined as a cost per Quality Adjusted Life Year (QALY) gained < $50,000.

3 Rationale for the Statistical Analysis Plan

The study protocol has been described in detail previously,[37] and is briefly outlined in Section 4 below. In addition, the study has been published on the Australian and New Zealand Clinical Trials Registry (number: ACTRN12608000166370), and details of the study design, and all changes, have been itemised on this site. This statistical analysis plan has been produced to specify, in detail, the main analyses to be reported in the initial report of the study findings. The general analytic approaches to be undertaken in subsequent reports are also provided, where known. The economic analyses will be described separately.

4 Trial Design and Intervention Plan

4.1 Trial Design

This is a cluster randomised controlled trial with blinded assessment of outcomes and intention-to-treat analysis. Up to 570 patients with stroke were to be recruited from four main centres; Alfred Hospital, Monash Medical Centre, Box Hill Hospital, and Dandenong Hospital. All of these centres are located in suburbs of Melbourne, Australia. The patients and outcome assessors were blind to treatment allocation. It was not possible to blind the nurses who provided the intervention to treatment allocation. The development and evaluation of the study intervention were in accordance with the Medical Research Council framework on complex interventions.[38] The primary outcome assessment at 12 months occurred in the patients' homes, and this was undertaken by an outcome assessor who was unaware of the treatment allocation. The study was funded by the National Health and Medical Research Council (586605).

4.2 Eligibility

All patients aged ≥ 18 years and hospitalised with ischaemic or haemorrhagic stroke or TIA were eligible for inclusion. The following patients were excluded:

(1) Patients living >50 km from the closest centre;

(2) Patients recruited to another clinical trial;

(3) Patients admitted from or discharged to a nursing home; and

(4) Patients not expected to survive post-stroke more than 12 months as a result of concurrent diagnosis of rapidly deteriorating disease (e.g. terminal cancer).

4.3 Randomisation

Potentially eligible patients entered a run-in period until they reached home. The purpose of this phase was to minimise dropouts before randomisation. This is because, in our pilot work, we found that some patients refused blood tests and/or refused to collect 24 hour urine samples once they were home (these tests provide critical data for our primary and secondary outcomes). Research nurses assessed the participant's competence to give consent using an Abbreviated Mental Test Score (AMTS) tool prior to randomisation.[39] When patients had an AMTS score less than 7, the spouse or any other caregiver who has authority to act on behalf of the patient was approached for potential consent. Patients were randomised immediately after the baseline visit. This enabled us to ensure that all the details required for randomisation, including details of the patients' General Practitioner (GP), were known.

A computer-generated, blocked randomisation procedure[40] was used to ensure that each hospital had a balance of patients in each group as post-acute treatment may vary slightly at each hospital. This process was adopted to ensure equal representation across groups within centres; removing the chance of treatment bias between centres. The treatment order was randomly permuted within each block, and they were exactly balanced at the end of each block. No further stratification occurred. Randomisation was clustered by GP practice to minimise contamination. This meant that, when a new patient was recruited, their nominated GP was checked against a list of all GPs already with a patient in the study. If the patient's GP, or the practice to which the GP belonged, did not already have a patient in the study, then the GP was randomly allocated according to the next random allocation within the block. However, if the GP already had a patient in the study, then the patient was allocated to the same treatment group as the GP's previous patient. This method

was adopted to minimise contamination between intervention and usual care groups.

4.4 Intervention

Participants were randomised to receive either usual care alone, or usual care in addition to the experimental intervention, chronic disease management. Usual care patients were given usual care as per the standard arrangements of the hospital secondary prevention clinic and usual GP practice. Chronic disease management participants received usual long term GP care, and were provided an additional chronic disease management plan and stroke-specific education. Apart from receiving the individualised management plan for their patients in the study, no further training was provided to GPs. Participants and outcome assessors were blinded to intervention group.

The schedule for trial assessments is summarised below (Table A).

Table A. Assessment Schedule for both intervention and usual care groups

Assessment	Baseline* Day 0	Follow up† 3, 12, and 24 Months
Medical History	✓	✓
Blood Pressure,‡ Blood Tests	✓	✓
Weight, waist, skin fold	✓	✓
24 hour Urine collection	✓	✓
Physical Assessments	✓	✓
Modified Rankin Scale§	✓	✓
Quality of Life[41]	✓	✓
Assessment of risk factors[42] and their management	✓	✓
Handicap, Anxiety, Irritability and Depression [43-45]	✓	✓
Healthcare needs	✓	✓
Adverse Events and Serious Adverse Events	–	✓
Utilisation of Services	✓	✓

* Research Nurse conducted all of the assessments at the participants' homes.
† Blinded Outcome assessor undertook all measurements at the participants' homes.
‡ Blood Pressure (BP) was measured using the OMRON Digital Automatic Blood Pressure Monitor (HEM 907) according to the European Society of Hypertension protocol.[46] At least 3 measurements were taken, until the last two measurements differed by less than 10/6 mmHg (up to 5 measurements were taken). The mean of the last two measurements was used.
§Pre-stroke Modified Rankin Scale was administered at baseline.

4.4.1 Intervention immediately following baseline assessment

Using the details obtained at the baseline assessment a patient-specific management plan was prepared by a stroke clinician and an unblinded intervention nurse. Clear goals were outlined according to the risk factor profile of the patient. This management plan was sent to the patients GP. In addition, the unblinded intervention nurse visited the patient at home to provide individualised education about their risk factors, and recommended behavioural changes to reduce their likelihood of having a further stroke. At this time, the nurse also made an appointment for the patient to visit their GP for further discussion of their management plan.

4.4.2 Intervention at 3 months after baseline

After the blinded outcome assessor had visited the patient at 3 months, the intervention nurse made an appointment to visit all intervention patients. The following occurred at this time:

a. Each of the problems identified at the initial visit were reviewed;
b. All identified barriers to achieving targets were discussed and itemised, as well as potential ways to overcome these barriers;
c. When required, further education was provided about the benefits of managing risk factors;
d. An appointment was made for the patient to visit their GP, and a copy of a review of the

management plan was sent to the GP.

4.4.3 Intervention at 6 months

Based on the results of the 6-month outcome telephone interview, the intervention nurse prepared a review of the management plan and provided it to the patient's GP.

4.4.4 Intervention at 12 months

Based on the results of the 12-month outcome interview, the intervention nurse prepared a new management plan and provided it to the patient's GP. The nurse also provided further education to the patient about their risk factors.

4.4.5 18 months

Based on the results of the 18-month outcome telephone interview, the intervention nurse prepared a review of the management plan and provided it to the patient's GP.

4.5 Blinding

There were numerous processes in place to ensure blinding of patients, nurses and treating doctors:

4.5.1 Blinding of Patients

1. Ethics committees approved blinding of participants. Information sheets did not outline the details of management approaches, but simply described them as "A" and "B".

2. Each participant was visited by a nurse on at least three occasions over a 1-year period. Participants in the control group were unaware that the intervention group had up to six visits over the first 12 months, while those in the intervention group were unaware that control participants received fewer visits.

3. The blinded outcome assessor was unaware of treatment allocation for each participant, and so was unable to inform them about their allocation group.

4.5.2 Blinding of Nurses

Intervention nurses could not be blinded to the intervention. However, the outcome assessors were unaware of the study aims and the intervention protocol. Outcome assessments were removed in time from the intervention.

The intervention was carried out by a nurse whose sole responsibility was to conduct the intervention. This nurse usually visited the patient about 1-2 weeks after the blinded nurse outcome assessor had conducted the outcome assessment.

4.5.3 Blinding of Clinicians

1. Patients in ***both*** intervention and control arms were visited by study staff at each follow-up period. Thus, if patients informed their clinician that they were visited by a nurse in their home, the specialist would remain unaware about the allocation group.

2. None of the hospital clinicians were informed about the status of each study participant and so management within the secondary prevention clinic is unlikely to be altered. The stroke specialists approving the management plans were not the patients' usual clinicians and had no contact with the patients themselves. For example, specialists at Monash Medical Centre assessed the management plans of patients recruited at the Alfred Hospital. Therefore when patients returned to their own specialist for routine follow-up, the specialist remained unaware of the patient group allocation.

4.6 Sample Size Considerations

The study was designed to detect a 4.5% clinically significant difference in 10-year Framingham CVD risk scores between the groups, with >80% power. This was based on a 23.6% mean 10-year

risk of vascular events among patients with stroke, with a standard deviation of 14.04%. These estimates give a requirement of 160 patients per group. A sample size of 570 (285 per group) was estimated with adjustments for 5% dropping in to the intervention (envisaging that some GPs in the control arm already utilise the management plan) and 20% dropping out. A detailed calculation of the sample size has already been reported.[47]

5 Outcome Assessments

Standard outcome assessments were conducted at 3 months, 1 and 2 years. To enable a comparison between the intervention and control groups we used valid and reliable outcome measures in common usage that had previously been used in stroke clinical trials. All outcomes were assessed by a person who remained blind to group allocation (see above). All outcomes will be interpreted with caution, keeping in mind the inclusion criteria and the run-in phase.

6 Definitions of Outcomes

6.1 Primary Outcomes

The primary outcome for this study will be a change in risk score between baseline and 12 months (assessed by comparing 12-month risk and adjusting for baseline risk). For the purpose of this study, the Framingham Risk Score (FRS) will be used. The original FRS is a validated risk prediction model, using the Cox model algorithm.[48] The algorithm was initially developed for predicting 10 years risk of coronary heart disease but later modified for the prediction of all cardiovascular diseases.[36] The baseline and one-year risk score will be estimated for individual participants using this later modified risk score. The following factors are required for the estimation of the risk score: gender, age, total cholesterol (TC), HDL cholesterol (HDL), systolic BP (SBP), use of antihypertensive medications, smoking status (smoking) as measured by urinary cotinine level (detected), and uncontrolled diabetes as measured by glycosylated haemoglobin levels (HbA1c ≥7.0%). Most of these items included in the latest Framingham CVD Risk score are factors that are sensitive to change with better management of risk factors (e.g. smoking). Therefore, improvements in management of risk factors, our primary aim, will result in lower Framingham CVD Risk scores.

Table B: Framingham Risk Score regression coefficients, 10-year baseline survival rates, population mean risk factor score and calibration factor for stroke

	Men	Women
Correlation factors		
Age (β_{Age})	3.06117	2.32888
Total cholesterol (β_{TC})	1.12370	1.20904
HDL cholesterol (β_{HDL})	- 0.93263	- 0.70833
SBP if treated with medications (β_{SBP})	1.99881	2.82263
SBP if not treated with medications (β_{SBP})	1.93303	2.76157
Smoking if yes ($\beta_{Smoking}$)	0.65451	0.52873
Smoking if no ($\beta_{Smoking}$)	0	0
Diabetes if present ($\beta_{Diabetes}$)	0.57367	0.69154
Diabetes if not present ($\beta_{Diabetes}$)	0	0
Baseline 10-year survival ($S_0(10)$)	0.88936	0.95012
Framingham population mean risk factor score (RFF)	23.98020	26.19310

The formula for the estimation of CVD risk score based on Cox model of proportional hazards is as follows and incorporates the coefficients in Table B, with differing coefficients for men and women:[36]

$$P_{CVD} = 1 - S_{0(10)}^{\exp(RFI - RFF)}$$

$$RFI = (\ln(Age) x \beta_{Age}) + (\ln(TC) x \beta_{TC}) + (\ln(HDL) x \beta_{HDL}) + (\ln(SBP) x \beta_{SBP}) + \beta_{Smoking} + \beta_{Diabetes}$$

Where:
P_{CVD} is the 10-year absolute risk of developing CVD;
ln is the natural logarithm;
$S_{0(10)}$ is the baseline 10-year survival from CVD;
RFI is individual's score for risk factor(s);
RFF is Framingham population mean risk factor score; and
β is Framingham Risk Score regression coefficients

6.2 Secondary Outcomes

1. A change in modified risk score at 12 months (as measured using the score sheet).[36] The score sheet method comprises 0, 1, 2, 3, etc scores for each item (see Tables C1 and C2 below). In addition to the factors included above, it will include other factors currently incorporated in secondary prevention guidelines (0 = treated, 1 = untreated). These include:
   (a) Antihypertensive therapy (already included in assessment of BP and so no new variable);
   (b) Daily antiplatelet therapy (in patients with ischaemic stroke/TIA not prescribed anticoagulants);
   (c) Anticoagulation therapy in patients with ischaemic stroke/TIA with one of atrial fibrillation, cardioembolic stroke from valvular heart disease, or recent myocardial infarction, unless a contraindication exists (e.g. poor compliance, major bleeding risk);
   (d) Use of lipid lowering medications (in patients with ischaemic stroke/TIA).
2. Change in SBP and DBP at 1 year. BP will be measured according to the criteria proposed by the European Society of Hypertension and assessed as a continuous outcome.[49] Protocol for BP measurement is provided in the legend of Table A.
3. Adverse events (AEs) and serious adverse events (SAEs). SAEs are defined as any event that is fatal; life-threatening; requires or prolongs hospitalisation; results in significant permanent disability or is incapacitating; requires medical or surgical intervention to prevent permanent impairment or damage; and an accidental or intentional overdose. AEs are defined as any adverse event that occurs that are not an SAE. Patients will be asked about any re-hospitalisations they have had, what this was for, and where they attended.
4. Use of at least one antihypertensive agent. This is defined as any antihypertensive agent prescribed to the patient. Patients will be asked to show the packets of medications prescribed, and they will be further asked about how often they take each medication.
5. Use of cholesterol lowering therapy daily (in patients with ischaemic stroke or TIA). This is defined as any lipid lowering agent prescribed to the patient. Patients will be asked to show the packets of medications prescribed, and they will be further asked about how often they take each medication.
6. Use of antiplatelet therapy daily (in ischaemic stroke or Transient Ischaemic Attack (TIA) patients). This is defined as any antiplatelet agent prescribed to the patient. Patients will be asked to show the packets of medications prescribed, and they will be further asked about how often they take each medication.
7. Use of antithrombotic therapy daily (in patients with ischaemic stroke or TIA). This includes the use of anticoagulants in patient with co-morbid atrial fibrillation, as well as the use of antiplatelet agents. This will be assessed by viewing patient medications and determining the presence or absence of atrial fibrillation. Patients will be asked to show the packets of medications prescribed, and they will be further asked about how often they take each medication.
8. Current smoking. This will be assessed by self-report questionnaire. A urinary cotinine test (a measure of smoking exposure) will provide validation for the self-report. When the questionnaire and urinary cotinine results do not agree, the latter will be used as the outcome measure.

Table C: Score sheet methods for determining risk score,[36] together with added columns for medication use:
C1. Calculation of points for men

Points	Age, years	HDL	Total Cholesterol	SBP Not Treated	SBP Treated	Currently smoking	Diabetic	Treated With		
								Antiplatelet Agents in Ischemic Stroke	Anticoagulant Agents in Atrial Fibrillation	Cholesterol-Lowering Agents in Ischaemic Stroke
-2		60+		<120						
-1		50-59								
0	30-34	45-49	<160	120-129	<120	No	No	Yes	Yes	Yes
1		35-44	160-199	130-139				No	No	No
2	35-39	<35	200-239	140-159	120-129					
3			240-279	160+	130-139		Yes			
4			280+		140-159	Yes				
5	40-44				160+					
6	45-49									
7										
8	50-54									
9										
10	55-59									
11	60-64									
12	65-69									
13										
14	70-74									
15	75+									

C2. Calculation of points for women

Points	Age, years	HDL	Total Cholesterol	SBP Not Treated	SBP Treated	Currently smoking	Diabetic	Treated With		
								Antiplatelet Agents in Ischemic Stroke	Anticoagulant Agents in Atrial Fibrillation	Cholesterol-Lowering Agents in Ischaemic Stroke
-3				<120						
-2		60+								
-1		50-59			<120					
0	30-34	45-49	<160	120-129		No	No	Yes	Yes	Yes
1		35-44	160-199	130-139				No	No	No
2	35-39	<35		140-149	120-129					
3			200-239		130-139	Yes				
4	40-44		240-279	150-159			Yes			
5	45-49		280+	160+	140-149					
6					150-159					
7	50-54				160+					
8	55-59									
9	60-64									
10	65-69									
11	70-74									
12	75+									

9. Consumption of at least 5 servings of vegetables and 2 servings of fruit per day will be determined by self-report using short-answer questions. Research nurses then calculate the number of servings based on subjects' descriptions of their daily intake. Although these short answer questions are not recommended for assessing precise intake of foods, they are considered adequate when gross estimates of fruit and vegetable intake are required.[50] The cut-off of 5 servings of vegetables and 2 servings of fruit is based on recommendations in the dietary guidelines for Australians.[51] Consumption of fruit and vegetables will each be converted into a dichotomous outcome for those who are meeting the daily requirements for vegetables (5 servings) and fruit (2 servings) and those not meeting these requirements (consuming less than these amounts).
10. Salt excretion will be measured using a 24 hour urine sample. This will converted to a dichotomous outcome with a cut-off of <5 grams of salt per day (versus ≥5 grams per day). Although the Dietary Guidelines for Australian Adults,[51] suggest that the recommended level of salt is <6 grams per day, the World Health Organization recommends <5 grams per day of salt (<2 grams per day of sodium) in adults.[52]
11. Physical activity will be assessed using a questionnaire. Physically active is defined when participants report undertaking 30 minutes or more of moderate-intensity activity or 20 minutes or more of vigorous-intensity physical activity at least 3 times a week. Moderate-intensity physical activity is that which increases the heart rate or causes breathing harder than normal. Vigorous-intensity physical activity is that which causes sweat, or puff and pant. As a validation we also have pedometer counts of steps per day (measured as mean steps per day) in some patients.
12. Risky drinking level (i.e. 4 or more standard drinks per day for men and 2 or more drinks per day for women). This will be assessed by careful interview of the participant using pictures of standard drinks to help prompt patient recall.

7 Data Analysis

Outcomes will be reported in clinical terms of absolute risk reduction, relative risk reduction, and numbers needed to treat. All analyses will be based on intention to treat. This means that patients will be analysed according to the group in which they were allocated, regardless of whether or not they received the intervention or deviated from the protocol.

The primary efficacy analysis will compare risk scores at 12 months, adjusted for baseline risk scores and other covariates. Secondary analyses include evaluations of proportion on treatment, mean blood pressure reduction at 12 months, smoking or drinking at risky levels, consuming appropriate amounts of fruit and vegetables or with a daily salt intake < 5g, physical activity levels, adverse events, and carer outcome. Statistically significant results will be identified using two-sided 5% significance levels. The estimates of this study will be reported with 95% confidence intervals.

7.1 Descriptive Characteristics

In order to assess balance between the intervention and control groups, a baseline comparison will be carried out. This will include a summary table (Table 1), reporting descriptive statistics and/or frequency, according to treatment arm. The data to be reported include the following: demographic and anthropometric characteristics; urine and serum biochemical variables; type of stroke; medical history; and drug use. Demographic variables include age and sex. Anthropometric measures of body mass index (BMI) will also be reported. Biochemical variables include measures of systolic BP, diastolic BP, total cholesterol, HDL- and LDL-cholesterols, fasting plasma glucose, glycated haemoglobin (HbA1c), triglycerides, urinary cotinine, urinary protein, and estimated glomerular filtration rate (eGFR). Type of stroke includes any of ischaemic stroke, intracerebral haemorrhage and transient ischaemic attack, based on the clinical diagnosis. Medical history includes smoking and drinking status at baseline, a history of prior stroke, and a history of selected relevant conditions such as diabetes, hypertension, high cholesterol, atrial fibrillation and other vascular conditions.

Continuous variables will be summarised as absolute means and standard deviations. Non-normally distributed data will be summarised as medians and interquartile ranges. Categorical variables will be summarised as frequency counts and percentages.

7.2 Missing baseline variable

If there are missing values for the baseline assessment, variables will be replaced with measurements obtained at the 3-month outcome assessment. This is particularly essential since any missing information on potential covariates will lead to the exclusion of the entire patient in the adjusted multivariable adjusted analysis. Moreover, since the statistical analysis of this study will be based on intention to treat, substituting missing data will ensure statistical efficiency and minimise bias.

7.3 Primary Outcome

The primary outcome for this study will compare risk scores at 12 months, adjusted for baseline risk scores and other covariates (see 7.3.3). The Framingham Risk Score (FRS) is a validated risk prediction model, using the Cox model algorithm.[36] The algorithm was initially developed for predicting 10 years risk of coronary heart disease but later modified for the prediction of all cardiovascular diseases. It was also developed for primary care, although others have used it in a clinical trial of secondary prevention.[53] The methods for the calculation of the risk score are described in Section 6.1. The following factors are required for the estimation of the risk score and are directly taken from the study participants during outcome assessments: systolic BP, total cholesterol, HDL cholesterol, diabetes as measured by glycosylated haemoglobin (HbA1c) levels, and smoking status as measured by urinary cotinine level. Other factors required include use of antihypertensive medications, age and gender.

7.3.1 Missing values for primary outcome assessment

If there are missing values in any of the variables to be used for the primary outcome assessment, we will undertake the following procedures. If the patients were alive at 12 months, and measurements are available after baseline, we will use the data recorded in the 3-month outcome assessment. The importance of replacing these variables has been stated earlier.

If blood pressure was measured fewer than three times or was not otherwise measured according to the protocol, the following procedures will be undertaken. If blood pressure was measured only three times and the last two measurements differed by 10/6 mmHg or more, the mean of the last two measurements will still be used as the BP level. If blood pressure was measured only twice, irrespective of whether or not the last two measurements differed by 10/6 mmHg or more, the mean of these two measurements will be used as the BP level. If blood pressure was measured only once, this measurement will be used as the BP level.

If measurements of urinary cotinine are not available for baseline and 3-month outcome assessments, current smoking will be determined using self-reported data obtained at baseline assessment. Decision will be made using the following procedure: a subject will be defined as a non-current smoker if he or she had never smoked nor had exposure to passive smoking at the time of assessment, or quit smoking at least 2 years before the date of assessment; a subject will be defined as a current smoker if he or she currently smokes and/or has exposure to passive smoking, or quit smoking within 2 years prior to the date of assessment.

If measurements of HbA1c are not available for baseline and 3-month outcome assessments, a decision on the baseline diabetes status will be made using the following procedure. If the measurements of fasting plasma glucose (FPG) are available at baseline and 3-month outcome assessments, the baseline diabetes status will be determined using either or both FPG measurements. If the FPG values are not available at both baseline and 3-month outcome assessments, the HbA1c measurements obtained during hospitalisation will be used. If there were no HbA1c measurements up to the time of 3-month outcome assessment, and no FPG measurements at baseline and 3-month outcome assessments, the FPG measurement obtained

during hospitalisation will be used.

7.3.2 Univariable analysis

The effect of the intervention will be estimated using analysis of covariance (ANCOVA). In this model, the intervention groups will be defined as the independent variable, the 12 months risk score as the dependent variable, while the baseline risk score will serve as the covariate. ANCOVA has been shown to improve statistical efficiency in the assessment of change from baseline.[54, 55] It is a preferred method over the simple analysis of change scores (SACS) as it provides unbiased estimates of treatment/intervention effects even if study groups show baseline imbalance.[56] This will produce the estimate of the change in FRS between baseline and 12 months. The proposed format for presenting the results is shown in Table 2. The magnitude of the change in the components of the risk score, and other selected prognostic variables, will also be reported.

7.3.3 Covariate adjusted analysis

The objective of this analysis is to support or provide additional context for the estimates of the univariable analysis. This will help test the robustness of the estimates of the intervention effect on the primary outcome. A multivariable analysis of covariance (MANCOVA) or generalised linear model (GLM) will be undertaken to adjust for relevant confounding factors. The predictive variables reported in Table 1 will be eligible for inclusion in the covariate adjusted analysis. The criteria for inclusion and exclusion of variables in the covariate adjusted model are as follow:

Exclusion criteria

- Variables that make up the risk score.
- Correlates of variables that make up the risk score (to avoid collinearity).

Inclusion criteria

- Variables that demonstrate a possible association with a change in risk score in the univariable model will be based on a Likelihood Ratio Test (LRT) p-value ≤0.15. These will be identified as potential confounding factors even if they show minimal imbalance between intervention groups.[57, 58]
- Baseline variables with possible heterogeneity between the intervention groups will be based on a LRT p-value ≤0.15. These will be identified as potential confounding factors even if they show a weaker association in the univariable model.[57, 58]

A two-sided p-value of ≤0.15 is well above the conventional 0.05, thus no statistical inference should be drawn from it. This p-value is set to assess the level of homogeneity between the intervention groups.[59]

All predictive variables that meet the inclusion criteria will be incorporated into a maximum covariate adjusted model. To obtain a final model, a stepwise elimination of variables will be performed, if the multivariable LRT p-value is >0.10. The adjusted estimate of change in risk score will be reported as the effect of intervention.

7.3.4 Subgroup analyses

Specific investigation of the effect of the intervention may be warranted in several subgroups in this study:

- Age and gender subgroups: there is evidence of age and gender differences in primary care visits and medication utilisation.[60]
- Risk factor subgroups: there is evidence that nurse-led community care is effective for the management of atrial fibrillation,[61] hypertension,[62] diabetes[63] and cholesterol levels.[64]
- Clinical subgroups: there is evidence that programs of organised care in the community are effective for the management of heart failure[65] and coronary heart disease.[66]

Test of differential effects of intervention on the primary outcome for each will be conducted using a test of interaction obtained from a logistic regression model. The adjusted odds ratio and p-value for interaction term will be reported.

7.3.5 Additional analyses: complex interrelationships

Linear structural equation model or path diagram model will be used to investigate the complex interrelationships among metabolic syndrome, stroke, and socio-economic factors.

7.3.6 Additional analyses: Drop outs and loss to follow-up

Although the calculated sample size for this study was increased (to 570) to account for a possible 20% dropout rate, it is still important to compare the baseline characteristics of dropouts or participants lost to follow-up with those that undertake the primary outcome assessment. This is important in order to minimise possible selection bias and to ensure internal validity of our study estimates. This analysis will be restricted to only the major vascular risk factors including, but not limited to, variables that make up the risk score.

7.4 Secondary Outcomes

7.4.1 Secondary Outcomes at 12 months

Table 3 shows the planned presentations of secondary outcomes occurring at 12 months. The secondary outcomes will be compared between treatment arms as outlined below:

- A change in the modified FRS between baseline and 12 months will be assessed using ANCOVA or GLM as described earlier.
- The effect of the intervention on systolic BP and diastolic BP will be estimated using ANCOVA and GLM.
- Differences in adverse events will be assessed using Student's t-test or Wilcoxon rank sum test, and Poisson regression for count outcomes.
- Differences in proportion of participants on antihypertensive medications**,** and those with ischaemic stroke or TIA on antiplatelet medications, will be estimated using Chi-square test and logistic regression.
- Differences in proportion of participants smoking, daily consuming desirable amounts of vegetables and fruits, and salt, performing sufficient exercise, and drinking at risky levels will be estimated using Chi-square test and logistic regression.
- These analyses will be adjusted in the same fashion as the primary outcome. Both adjusted and unadjusted analyses will be presented (Table 4).

7.4.2 Secondary Outcomes at 2 years

All primary and secondary outcome analyses conducted at 12 months will be repeated for the 2 year time point.

7.5 Compliance and data quality analyses

7.5.1 Protocol deviations in consent process

These will be tabulated and explained.

7.5.2 Protocol deviations in eligibility

These will be tabulated and explained. These participants will be included in the intention-to-treat analysis.

7.5.3 Sensitivity analyses

Sensitivity analyses will be conducted by determining the treatment effect on the primary outcome after adjustment for centre. This analysis will be performed using logistic regression. We will also undertake sensitivity analyses to explore the effects of missing data for the primary outcome. Similar analyses will be performed for the secondary outcome analyses.

8 Proposed data tables in the main publication

Table 1. Baseline Characteristics

	Intervention group N (%)	Usual Care group N (%)
Demographic measurements		
Age (years)		
Mean/Median (SD/IQR)		
≤60		
61-70		
71-80		
>80		
Female		
Body mass index (kg/m^2)		
Mean/Median (SD/IQR)		
<25.00		
25.00-29.99		
≥30.00		
Biochemical measurements*		
Systolic blood pressure (mmHg)		
Diastolic blood pressure (mmHg)		
Glucose (mmol/L)		
Triglyceride (mmol/L)		
Total cholesterol (mmol/L)		
LDL cholesterol (mmol/L)		
HDL cholesterol (mmol/L)		
Urinary protein (mg/day)		
eGFR (mL/min/1.73m^2)		
Type of stroke		
Ischaemic stroke		
Intracerebral haemorrhage		
Transient Ischaemic Attack		
Medical history		
Diabetes		
Hypertension		
Atrial fibrillation		
High cholesterol		
Proteinuria		
Stroke		
Other cardiovascular disease		
Behavioural factors		
Smoking†		
Never smoker		
Current smoker		
Ex-smoker		
Current risky drinking ‡		
Drug use		
Antihypertensive therapy		
Antiplatelet therapy		
Anticoagulant therapy		
Cholesterol lowering therapy		

* Data are expressed in mean (SD) or median (IQR). For any variables with more than 5% missing observations, the denominator will be reported in the footnote.
†Current smoker is defined as smoking at the time of assessment or quitting in the last two years. Ex-smoker is defined as quitting more than 2 years ago. ‡ Risky drinking is defined as 2 or more drinks per day for women and 4 or more drinks per day for men.

Table 2. Within- and between-group changes in primary outcomes for intervention and control groups

	Intervention			Control			
	Baseline	**Follow-up**	**Difference (95% CI)**	**Baseline**	**Follow-up**	**Difference (95% CI)**	**Difference* (95% CI) between group**
CVD Risk Score†							
Components							
Age (years)							
Male sex							
Systolic BP (mmHg)							
HbA1c (%)							
Total cholesterol (mmol/L)							
HDL cholesterol (mmol/L)							
Current smoking (%)							
Antihypertensive therapy (%)							
Potential covariates							
BMI (kg/m^2)							
Triglyceride (mmol/L)							
Urinary protein (mg/day)							
eGFR (mL/min/1.73m^2)							
Current risky drinking ‡ (%)							
Antiplatelet therapy (%)							
Antithrombotic therapy (%)							
Cholesterol lowering therapy (%)							
Multivariable adjusted CVD risk score §							

Data are expressed in mean (SD) or median (IQR) unless otherwise stated. For any variables with more than 5% missing observations, the denominator will be reported in the footnote.

CVD, cardiovascular disease; CI, confidence interval; BMI, body mass index; BP, blood pressure; HbA1c, glycosylated haemoglobin; LDL, low density lipoprotein; HDL, high density lipoprotein; eGFR, estimated glomerular filtration rate; SD, standard deviation; IQR, interquartile range

*Change at 12-month outcome assessment between groups adjusted for baseline measurements

† CVD Risk Score is an algorithm comprising age, sex, systolic blood pressure, serum total and HDL cholesterol, diabetes defined as HbA1c ≥7.0%, current smoking status defined by the urinary cotinine level, and use of antihypertensive medication

‡ Risky drinking is defined as 2 or more drinks per day for women and 4 or more drinks per day for men.

§ Adjusted for potential confounding factors in generalised linear model

Table 3. Within- and between-group changes in secondary outcomes for intervention and control groups

	Intervention			Control			
	Baseline	**Follow-up**	**Difference (95% CI)**	**Baseline**	**Follow-up**	**Difference (95% CI)**	**Difference* (95% CI) between group**
Modified CVD Risk Score†							
Systolic BP (mmHg)							
Diastolic BP (mmHg)							
Adverse events (AEs)							
All AEs							
Serious AEs							
Deaths							
Antihypertensive therapy (%)							
Cholesterol lowering therapy (%)							
Antiplatelet therapy (%)							
Antithrombotic therapy (%)							
Current smoking ‡ (%)							
Current risky drinking § (%)							
Healthy eating							
≥5 servings of vegetables daily (%)							
≥2 servings of fruit daily (%)							
<5g salt daily (%)							
Physically active ǁ (%)							

Data are expressed in mean (SD) or median (IQR) unless otherwise stated. For any variables with more than 5% missing observations, the denominator will be reported in the footnote.
CVD, cardiovascular disease; CI, confidence interval; BP, blood pressure; SD, standard deviation; IQR, interquartile range
*Change at 12-month outcome assessment between groups adjusted for baseline measurements
† Modified CVD Risk Score is an algorithm comprising age, sex, systolic blood pressure, serum total and HDL cholesterol, diabetes defined as HbA1c ≥7.0%, current smoking status defined by the urinary cotinine level, use of antihypertensive therapy, use of antiplatelet therapy, use of anticoagulation therapy and use of lipid lowering medications.
‡ Current smoker is defined as smoking at the time of assessment or quitting in the last two years. Ex-smoker is defined as quitting more than 2 years ago.
§ Risky drinking is defined as 2 or more drinks per day for women and 4 or more drinks per day for men.
ǁ Physically active is defined when participants report undertaking 30 minutes or more of moderate-intensity activity or 20 minutes or more of vigorous-intensity physical activity at least 3 times a week. Moderate-intensity physical activity is that which increases the heart rate or causes breathing harder than normal. Vigorous-intensity physical activity is that which causes sweat, or puff and pant.

Table 4. Unadjusted and adjusted analyses of the effect of intervention on the secondary outcomes

	Unadjusted		Adjusted	
	Effect estimate* (95% CI)	P-value	Effect estimate† (95% CI)	P-value
Modified CVD Risk Score‡				
Systolic BP (per mmHg)				
Diastolic BP (per mmHg)				
Adverse events (AEs)				
All AEs				
Serious AEs				
Deaths				
Antihypertensive therapy				
Cholesterol lowering therapy (%)				
Antiplatelet therapy				
Antithrombotic therapy (%)				
Current smoking §				
Current risky drinking ‖				
Healthy eating				
≥5 servings of vegetables daily				
≥2 servings of fruit daily				
<5g salt daily				
Physically active ¶				

CVD, Cardiovascular; CI, confidence interval; BP, blood pressure; SD, standard deviation; IQR, interquartile range. For any variables with more than 5% missing observations, the denominator will be reported in the footnote.

* Estimates of the univariable unadjusted analyses undertaken

† Estimates of the multivariable analyses adjusting for potential confounding factors

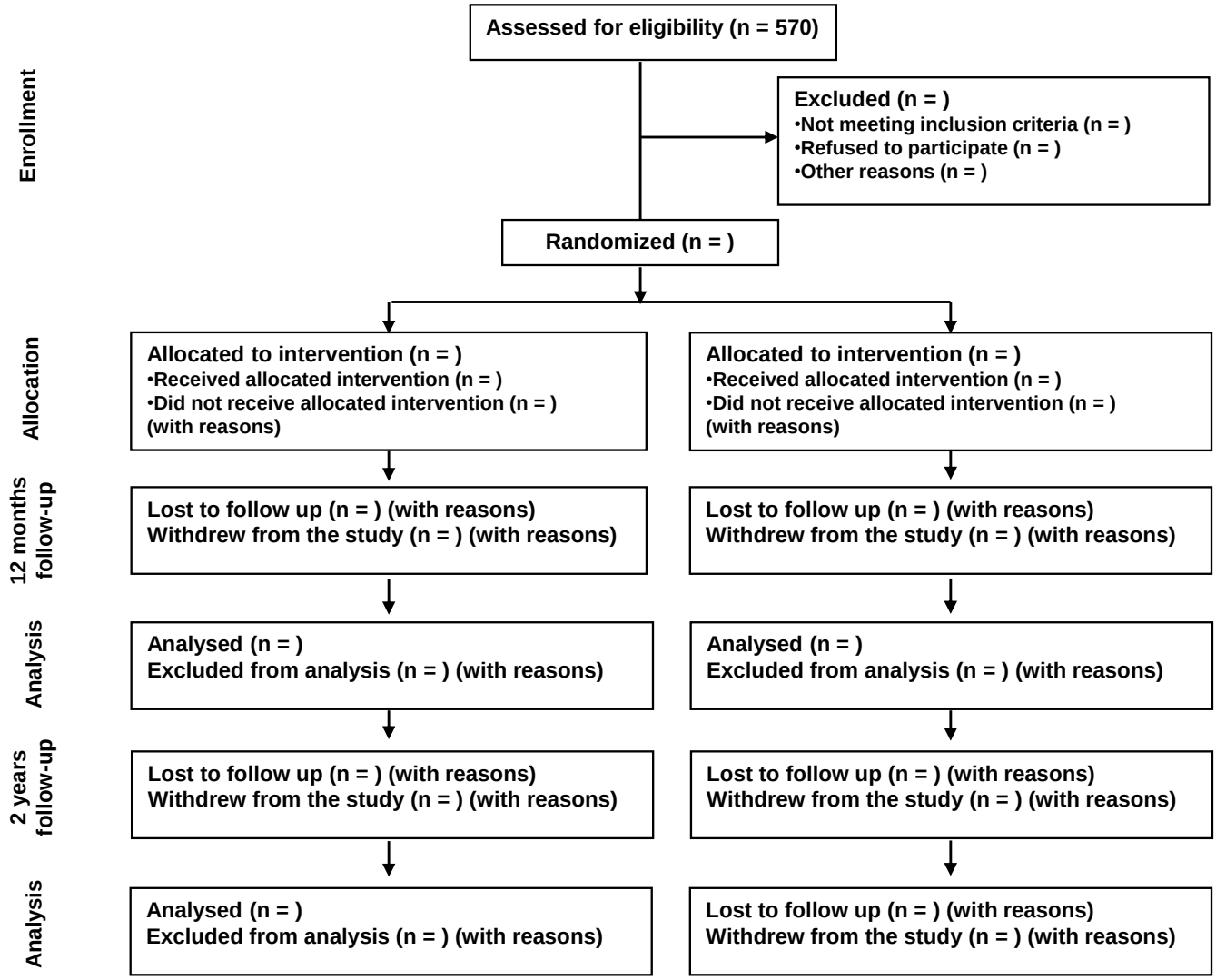
‡ Modified CVD Risk Score is an algorithm comprising age, sex, systolic blood pressure, serum total and HDL cholesterol, diabetes defined as HbA1c ≥7.0%, current smoking status defined by the urinary cotinine level, use of antihypertensive therapy, use of antiplatelet therapy, use of anticoagulation therapy and use of lipid lowering medications.

§ Current smoker is defined as smoking at the time of assessment or quitting in the last two years. Ex-smoker is defined as quitting more than 2 years ago.

‖ Risky drinking is defined as 2 or more drinks per day for women and 4 or more drinks per day for men.

¶ Physically active is defined when participants report undertaking 30 minutes or more of moderate-intensity activity or 20 minutes or more of vigorous-intensity physical activity at least 3 times a week.

Figure 1. CONSORT Flow Diagram



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[Appendix C] STANDFIRM Trial – Example Syllabus for Nurse Education Visit

Template of STAND FIRM syllabus for nurse education visit
Summary for Patient Education Visit **ID No:**

PATIENT DETAILS	**GP DETAILS**
Date of Birth: **Gender:** **Language Spoken:** **Interpreter may be required:**	
Details of stroke	
Date of stroke:	Type of stroke: Ischaemic Stroke
Hospital Name:	Baseline Visit:

MEDICAL HISTORY

Diabetes
Hypertension
High cholesterol
Ischemic heart disease
Heart failure
Atrial fibrillation

Other notes or comments relevant to the patient's management plan:

Heart Attack, Stent Inserted
Cataracts Both Eyes
Enlarged prostrate

FAMILY HISTORY (Reported by patient)

Family history of heart disease
Family history of diabetes

MEDICATIONS

Atorvastatin 40mg Daily
Karvezide 300/12.5mg Daily
Physiotens 0.2mg Twice Daily
Trajenta 5mg Daily
Norvasc 10mg Daily
Amaryl 4mg Daily
Diabex 1000mg Twice Daily
Betaloc 50mg Twice Daily
Jezil 600mg Twice Daily
Apidra 20 Units Daily

ALLERGIES

Nil Known

I. What are your main concerns about having a stroke?

If they are worried about having another stroke, discuss available options for support (use help after stroke card):

- National Stroke Foundation Helpline
- Encourage to discuss with GP
- If you experience symptoms dial 000 (and offer emergency card)

Please document main issues for the participant and advice offered

Participant has heard of National Stroke Foundation from hospital. Discussed and showed participant the NSF fact sheets.
Participant has been with GP for a long time. Participant states GP is easy to discuss problems with. GP refers participant to specialists: endocrinologist, dermatologist, urologist, ophthalmologist, and neurologist.
Participant would call 000 if needed.

If they are worried about living with the effects of stroke provide details about:

- Peer support (i.e. Stroke Association of Victoria, and Carers Australia)
- National Stroke Foundation Helpline
- Encourage to discuss with GP
- Beyond Blue Helpline
- Functional and impairment concerns (e.g. continence, speech, inability to walk, mood)

Please document main issues for the participant and advice offered

- Mobility
- Driving
- Speech/Communication
- Medication Use
- Support system at home
- Sexual Dysfunction

1. Participant had 95% recovery post-stroke.
2. Participant was unable to drive initially post-stroke, but no issues now.
3. No issues with communication.
4. Participant is compliant with medication use, generally no issues. Participant is more aware of Insulin.
5. Participant is independent.
6. Participant has no issues.

II. Stroke Prevention Education

SMOKING

Past smoker, ceased XX/XX/XX Cotinine: None detected

Education: The risk of heart disease halves within 12 months of quitting. The risk of stroke

becomes the same as that for a never smoker after 5 years. Lung function improves within 3 months. Passive smoking is associated with a high risk of stroke to a similar level as for people who smoke, and exposure must be avoided in the home and other social environments.

Goal: Cease smoking (or remain smoke-free) and to steer clear of exposure to smoking (including in the home). Ban or restrict smoking by others in the home.

Interest in quitting (score out of 7; 7 = very keen): out of 7. What would need to happen to make you more keen to quit - say to give a score of 6 or 7 out of 7 instead?

Confidence in quitting (score out of 7; 7 = very confident): out of 7. What would be the hardest thing about quitting? What made it difficult to quit the last time you tried? What would need to happen to increase your confidence to 6 or 7? Explore and tackle barriers (e.g. withdrawal, stress reduction, weight control). Identify support, e.g. partner, GP. Refer to Quitline.

Exposure to passive smoking. Determine whether passive smoking is an issue in the home, car and elsewhere. Discuss strategies to avoid exposure to environmental tobacco smoke (e.g. banning smoking inside the home or in cars).

Please document main issues for the participant and advice offered
Participant is not exposed to passive smoking.

BLOOD PRESSURE

Measured blood pressure at home on XX/XX/XX; BP = 158/69 mmHg

Weight Assessed at home on XX/XX/XX; BMI =35.1 kg/m^2 Waist (<80 F, < 94 M) = 126 cm Waist-Hip Ratio: 1.0

Participant has gained more than 10 kg since late teens or early twenties. Participant has tried to lose weight 1 time since late teens or early twenties.

Participant exercises vigorously (≥ 20 minutes) 0 times/wk. Walks 30 minutes or more 1 time/wk. Undertakes moderate-intensity activity that increases heart rate (≥30 minutes) 0 times/wk.

Participant adds salt to food at the table.
Salt excretion per day (Recommended range 40-220): 141 mmol/day

Education: It is recommended that all people who have had a stroke, regardless of blood pressure level, should receive blood pressure lowering therapy (unless you are prone to dizziness from very low blood pressure). Other ways to help reduce blood pressure include weight loss, increasing physical activity (to help with weight loss, improve cardiovascular fitness and mood, and reduce stress), reduce salt intake to less than 1 teaspoon per day, avoid processed food because these have high sources of salt and fat (particularly bread and ice cream), and increasing fruit and vegetable intake. GPs and pharmacists can provide support in these areas.

Goal: Lower blood pressure irrespective of baseline level. This minimizes damage to small blood vessels throughout the body.

Snoring and or sleep apnoea: Determine whether patient has ever been told that they have

sleep apnoea. Are they being treated for sleep apnoea? Presence of sleep apnoea may increase blood pressure and treatment has been shown to lower blood pressure (Continuous Positive Airway Pressure (CPAP)).

Please document main issues for the participant and advice offered
Participant sees GP once a month. GP takes BP measurement at each visit. Participant has been on BP medications for over 10 years. Participant is aware to also watch out for low BP.
Participant has gained weight since stroke, and knows connection of increasing weight with increasing BP, but has lacked incentive to reduce weight.
Participant is now looking at dietary changes and increasing exercise.
Participant does not think he has a snoring issue.

ATRIAL FIBRILLATION

Heart Rhythm: Regular

Education: Irregular heart beat is associated with a very high risk of stroke and stroke recurrence. Medication can reduce this risk. Smoking may exacerbate this condition. Atrial fibrillation can be difficult to control. It is important to have your response to medication regularly monitored. Regular contact with your general practitioner may be needed. Teach the participant how to take their pulse and check for AF.

Goal: If AF present or suspected, seek medical advice (GP).

Please document main issues for the participant and advice offered
Participant has had AF since 2000, sees cardiologist.
Participant does note when heart rate is irregular (occurs every 2-3 months), and gets concerned that it may lead to a heart attack.
Discussed associated risk factors, e.g. weight.

DIABETES

Date of Blood Tests: XX/XX/XX; Fasting HbA1c: 7.4% Glucose (Recommended < 7.0): 7.7 mmol/l
[A level of less than 7% is very good, a level between 7% & 8% is adequate, between 8% & 9% suggests the need for improvement, and over 9% is associated with poor control of blood sugar levels]

Diabetic status: Determine how long participant has been aware of diabetic status, and current management strategies.

Education: The risk of heart disease, stroke and recurrent stroke is much greater in people with diabetes. Control of your glucose levels significantly reduces these risks. Ways to improve your blood sugar levels are:

- A healthy eating plan (e.g. lower total fat intake and find substitutes for saturated fat, reduce sugar intake, and increase consumption of fruit and vegetables)
- Optimizing weight
- Regular physical activity to improve metabolic control
- Medication may be required, but does not substitute for healthy eating and activity
- Encourage participant to discuss diabetes management with GP
- Advise that there is a Diabetes Australia Helpline for further information and support (see contacts

card).
Goal: Achieve a stable blood glucose level that is below 7 mmol.

Potential referral: Determine interest in seeing a dietitian.

Please document main issues for the participant and advice offered
Participant has had diabetes for 30 years, under endocrinologist and with Baker IDI Institute for follow-ups. Participant does blood BSL QID.
Participant has good knowledge of medications.
Participant does not have diabetic educator, but sees dietician.
Participant reads symptoms and recognises if BSL < 4, does get symptomatic.
Participant's GP now monitors and tests urine monthly.
We discussed the use of Diabetes App to monitor BSL, foods, and calorie intake.

CHOLESTEROL
Total cholesterol level: 4.1 mmol/l LDL: 2.4 mmol/l HDL: 0.9 mmol/l
Triglycerides: 1.7 mmol/l

Education: High cholesterol levels are associated with a greater risk of heart disease and stroke recurrence. It is recommended that all people who have had an ischaemic stroke should receive cholesterol lowering therapy. Other ways to help reduce cholesterol levels include increase physical activity, avoid processed food because these have high sources of fat, and increased fruit and vegetable intake. GPs and pharmacists can provide support in these areas.

Goal: Maintain a normal cholesterol level, and have an annual cholesterol test.

Please document main issues for the participant and advice offered
Participant has had high cholesterol for over 10 years and has been on medication.
Participant has tried dietary changes, does not have fatty foods and uses low fat butter/margarine, occasionally takes cheese, fish and chips, and pizza.
Participant's cholesterol levels have come down since taking medications.
Participant also hopes to reduce weight and increase exercise. Participant said "it's a slow progress".

EXCESSIVE ALCOHOL INTAKE
The participant drinks once a month or less. On each occasion, the participant takes 1 to 2 drinks

Education: Heavy drinking can raise your blood pressure and increase your risk of stroke. It is a good idea to discuss your alcohol intake with your doctor as alcohol may interact with some of your medications or make it harder to control blood pressure.

Goal: Limit daily alcohol consumption to 2 standard drinks for men and 1 standard drink for women (show pictures). Everyone should have at least one or two alcohol free days every week.

If heavy drinker: Determine whether they may be dependent or not. If dependency is suspected, administer AUDIT questionnaire.

Interest in cutting down. Determine whether the patient is interested in cutting down.

Confidence about succeeding. Determine how confident the patient is in cutting down. Find out what would be required to increase their confidence in cutting down. Discuss barriers to reducing alcohol. Negotiate and set realistic goals.
Potential referral: Determine interest in seeing an alcohol dependency specialist.

Please document main issues for the participant and advice offered
Participant rarely takes alcohol. Participant is aware that heart rate goes up when he does.

OVERALL WELL-BEING (Physical Activity, Weight Loss, and Nutrition)

Exercise: the participant:

- Exercises vigorously 0 times/week;
- Walks 30 minutes or more 1 time/week;
- Undertakes moderate-intensity activity 0 times/week.

Weight assessed at home: XX/XX/XX; BMI = 35.1 kg/m^2; Waist circumference = 126 cm; Waist-Hip Ratio: 1.0

The participant:

- Has gained more than 10kg since his late teens and early twenties;
- Has tried to lose weight 1 time since his late teens and early twenties.

Nutrition:

- Does not choose low fat dairy products;
- Eats 3 serves of vegetables per day (Recommended = 5 serves/day);
- Eats 3 serves of fruit per day (Recommended = 2 serves/day);
- Does not eat pies, pastries, fried foods or takeaway meals more than once a week;
- Does not drink soft drinks, cordials, sport drinks or fruit juice on most days of the week;
- Sodium excretion (Recommended range 40-220): 141 mmol/day
- Adds salt to food at the table;
- Does not add more than 1 teasoon salt per day at the table.

Education: Physical activity, weight, and nutrition all impact on the occurrence of risk factor (e.g. high blood pressure, cholesterol). People who exercise regularly are about 30% less likely to have a stroke and 50% less likely to have cardiovascular disease. Regular exercise can reduce the risk of stroke by lowering blood pressure, assisting in weight loss and reducing cholesterol.

Losing weight improves blood pressure and blood glucose levels.

Diets rich in fruit and vegetables are associated with a lower risk of heart disease and stroke, and reduce the likelihood of developing type 2 diabetes and high blood pressure.

Activity Goal: Just 30 minutes per day of moderate-intensity physical activity (either continuous or in bouts of 10-minute intervals) provides health benefits.
Weight Goal: Reduce weight if BMI > 25kg/m^2
Nutrition Goals:

- Include 5 serves of vegetables in your diet every day
- Include 2 serves of fruit in your diet every day
- Avoid eating saturated fats in your diet (e.g. butter, cheese, hidden fats in cakes and pastries)

Potential referral: Determine interest in seeing a dietitian.

Please document main issues for the participant and advice offered
Participant has been increasing exercise regime slowly. Participant has treadmill, uses it for 5-10 minutes 4-5 times a week. Participant hopes to increase time on it slowly.
Participant has also reduced diet to 2 meals a day. Participant now drinks a lot of soup.
Participant has seen a dietician for advice.
We discussed the issue of weight gain, participant hopes to decrease weight.

MEDICATIONS AFTER STROKE

The patient is currently taking 10 medications.

Education: There are many different medications that your doctor may prescribe to reduce your risk of having another stroke or TIA.

Goal: If your doctor prescribes medication, it is important to continue taking it unless the doctor tells you to stop. If you have difficulty in remembering to take your medications then you can try:

- Taking your medication at the same time every day. It is important to get into a routine.
- Using a pill box or dispenser that notes day and times. You can organize this with your local pharmacist.
- Using a medication diary or daily chart to keep track of your medications.

Your doctor will help you to work out the right medication, dosage and timing for your lifestyle. Never stop taking your medication or change how much you take without talking to your doctor. In some cases, suddenly stopping your medication can be dangerous.

If you do not understand any of these things, please discuss with your doctor. Also remember to report any side-effects of your drugs to your doctor. Also remember to tell your doctor about any other medications that you may be taking that were not prescribed by the doctor.

Encourage patient to talk to their doctor about the medications they are taking.

Please document main issues for the participant and advice offered
Participant has reduced the amount of Insulin intake since stroke. And it is continually monitored and changed accordingly.
Other medications are well tolerated.
Participant has a good understanding of the medications being taken and why.

Please list other family members involved in discussion, and responsibility (e.g. spouse cooking or son smoking).
Interviewed alone. Independent.

Make appointment with GP for Management Plan in about 1 week (remember to tell receptionist that this will be for a long visit).

[Appendix D] STANDFIRM Trial – Example GPMP Provided to GPs

General Practitioner's Management Plan (Item 721)

For Patients with Multidisciplinary Care Needs

General Practice Management Plan or Team Care Arrangements each 2 years. Review after 6 months
New General Practice Management Plan or Team Care Arrangements after 12 months if clinical conditions change markedly.
Review General Practice Management Plan or Team Care Arrangements after 3 months if clinical conditions change markedly.
Copies to be given to the patient and other team members as appropriate.

All participants undertake to retain confidentiality

Date:

To claim the rebate for item 721 from Medicare, the following must be completed:

- Patient consent must be obtained
- Agreed actions in the right hand column must be completed where a risk factor is present.

PATIENT DETAILS	**File No:** **Medicare No:** **Date of Birth:** **Gender:** **Language Spoken:** **Interpreter may be required:**
Details of stroke Date of stroke: Hospital Name: XYZ Date of Admission: Date of Discharge: Discharged to: XYZ Home ☒ Rehabilitation ☐	**Type of event:** Ischaemic Stroke Other _____ **Mechanism of ischaemic stroke** Cardioembolic ☐ Non-cardioembolic ☒

GP DETAILS	
	Is patient eligible for Veteran Affairs? **Yes** ☐ **No** ☐ **Send a copy to DVA:** **Yes** ☐ **No** ☐ **GP Management Plan prepared by:** _____

Absolute Risk of Stroke in the next 10 years: 4.27%

Date of last Care Plan/GP Management Plan (if done):

RECOMMENDED PLAN FOR STROKE PREVENTION	
Summary of Management Plan for Patient/Carer	***GP to Consider based on information provided***
☒ BP lowering medications ☒ Lipid lowering therapy ☒ Antiplatelet therapy ☐ Anticoagulant therapy ☐ Measures to cease or avoid exposure to smoking ☒ Increase physical activity ☐ Reduce alcohol consumption ☒ Increase fruit and vegetable intake ☒ Reduce fat intake (meat and dairy) ☒ Reduce salt intake	☐ Referral to dietician (for cholesterol/diabetes/kidney) ☐ Referral to nephrologist (for kidney function) ☐ Information on medications, reminders, self-monitoring, reinforcement, counselling, family therapy ☐ Interventions for mood (e.g. counselling, psychotherapy etc.) ☐ Multi-compartment medication compliance device

MEDICAL HISTORY
Other notes or comments relevant to the patient's management plan: Appendectomy

Kidney Stenting -

FAMILY HISTORY (Reported by patient)
Family history of high cholesterol
Family history of heart disease
Family history of hypertension
Family history of diabetes

MEDICATIONS
ASPIRIN 100MG ONE TABLET DAILY

ALLERGIES
Penicillin

OTHER COMMENTS

NURSE SUMMARY OF HOME VISIT
Blood Pressure: **130/89 mmHg**

Overweight (BMI > 25kg/m^2): Yes ☐ No ☒
Weight Assessed:
BMI = 25.1 kg/m^2
Waist Circumference = 92 cm
Waist-Hip Ratio: 0.9

Smoker: Current ☐ Past ☐ Never ☒
Never smoker
Cotinine (a measure of recent smoking exposure): None detected

Alcohol:
How often drink? Never
No. occasions drinking ≥6 drinks: Never

Blood Tests
Cholesterol:

Total	[Recommended < 4.0]:	**5 mmol/L**
LDL	[Recommended <2.5]:	**2.9 mmol/L**
HDL	[Recommended >1.0]:	**1.2 mmol/L**
Triglycerides	[Ref Range <2.0]:	**1.9 mmol/L**

Diabetes: Yes ☐ No ☒

HbA1c	[Ref Range 0.0-6.0]:	**5.3%**
Glucose	[Ref Range 4.0-7.0]:	**3.9 mmol/L**

Physical Activity (as per Lifescripts)
No. times/week exercising vigorously (≥ 20 minutes): 0
No. times/week walking ≥30 minutes: 0
No. times/week undertaking other moderate-intensity physical activity that increases heart rate (≥30 minutes): 0
Interpretation of Physical Activity: Low physical activity.

Nutrition (as per Lifescripts)
Chooses low fat dairy products: Yes
No. serves vegetables/day: 3
No. serves fruit/day: 1
Eats pies, pastries, fried foods or take-away meals more than once a week: No
Drinks soft drinks, cordials, sports drinks or fruit juice on most days of the week: No
Salt added to food at the table: Yes
Adds >1 teaspoon salt to meals/day: No
Salt excretion per day (Recommended range 40-220): 173 mmol/day

Other Test Results

Creatinine	[Ref Range 45-80]:	**63 µmol/L**
24 hour urine:		
Sodium excretion	[Ref Range 40-220]:	**173 mmol/day**
Potassium excretion	[Ref Range 30-90]:	**60 mmol/day**
Creatinine excretion	[Ref Range 7.1-17.7]:	**13.9 mmol/day**
Protein excretion	[Ref Range 0.00-0.15]:	**0.06 g/day**

CONSENT TO PREPARE MANAGEMENT PLAN

My GP has explained the purpose of the Management Plan and I give / my carer gives permission to prepare a Management Plan.
Patient/Carer signature: ..... Date: .....

MULTIDISCIPLINARY PATIENT NEEDS AND PLANNED ACTIONS		
Current Health Needs/Problems (Specialist/Nurse to complete)	**Goal**	**GP to Complete to Reflect Agreed Actions (tick those applicable)**
Blood Pressure management Measured blood pressure (at home): 130/89 mmHg BP of concern ☐ Yes ☐ No ☒ Please Review	**GOAL** Maintain blood pressure as close as possible to 120/80 if it is higher.	**Review:** ☐ Regularly monitor BP ☐ Add/titrate BP lowering medications ☐ Cease/reduce prohypertensive medications or other remedies ☐ Exercise ☐ Diet (reduce weight, salt, and alcohol where appropriate) ☐ After review, no action
Antiplatelet Therapy **Type of event:** ☒ Ischaemic Stroke ☐ Intracerebral	**GOAL** For patients with ischaemic stroke or TIA: Daily antiplatelet therapy if not on anticoagulants for another	**Review:** Antiplatelet therapy: ☐ Low dose aspirin and modified release dipyridamole, ***or*** ☐ Aspirin alone, ***or***

Haemorrhage ☐ Transient Ischaemic Attack (TIA)	indication (unless otherwise contraindicated).	☐ Clopidogrel alone ☐ Not recommended (Specialist to tick if applicable) ☐ After review, no action
Anticoagulation Therapy Risk of cardioembolism: ☐ Yes ☐ No	**GOAL** For patients with ischaemic stroke or TIA: Daily anticoagulation therapy.	**Review:** ☐ After review, no action ☐ Oral anticoagulant therapy ☐ Not recommended ☐ Monitor INR
Lipid Lowering Therapy/Diet **Date of Blood Test:** **Cholesterol:** Total: 5 mmol/L LDL: 2.9 mmol/L HDL: 1.2 mmol/L	**GOAL** Total Cholesterol < 4.0 mmol/L LDL Cholesterol <2.5 mmol/L HDL Cholesterol >1.0 mmol/L Lipid-lowering therapy.	**Review:** ☐ After review, no action needed ☐ Annual lipid monitoring ☐ Lipid-lowering therapy ☐ Reduce fat intake (meat and dairy) ☐ Increase fruit and vegetable intake ☐ Referral to dietitian ☐ Statin not recommended
Alcohol Drinks alcohol Never Number of occasions drinking 6 or more drinks: Never	**GOAL** Limit daily alcohol consumption to 2 standard drinks for men and women.	**Review:** ☐ Reduce alcohol consumption ☐ After review, no action
Physical Activity Exercises vigorously 0 times/wk Walks 30 minutes or more 0 times/wk Moderate-intensity activity 0 times/wk	**GOAL** Undertake regular (daily) physical exercise. There is a link between low exercise and stroke risk.	**Review:** Current Physical Activity: Low physical activity. ☐ Provide written information ☐ Increase physical activity ☐ After review, no action
Smoking ☐ Current ☐ Past ☒ Never Never smoker Cotinine: None detected Check exposure to passive	**GOAL** Cease or avoid exposure to smoking. The risk of heart disease and stroke decreases after quitting.	**Review:** Consider ☐ Nicotine replacement therapy ☐ Bupropion or nortriptyline therapy ☐ Nicotine receptor partial agonist therapy ☐ Behavioural therapy

smoking.		☐ Recommend Quitline ☐ Avoid exposure to second hand smoking ☐ After review, no action
Self Management Skills **Medications** Patient is taking 1 medications. **Chronic disease self-management skills**	**GOAL** • Know and understand medications To learn about & increase chronic disease self management skills: • Healthy eating • Physical activity • Managing stress • Effective communication with health professionals • Setting personal health goals	Consider: ☐ Reminders, reinforcement, counselling, family therapy; ☐ Once daily and combination dosing ☐ Multi-compartment medication compliance device; ☐ Home medicines review ☐ After consideration, no action Consider: ☐ Patient education ☐ Counselling ☐ Referral to Allied Health Professional ☐ After consideration, no action
Overweight: (BMI > 25kg/m^2) ☐ Yes ☒ No Weight Assessed: BMI = 25.1 kg/m^2 Waist = 92 cm Waist-Hip Ratio: 0.9	**GOAL** Reduce weight if BMI > 25kg/m^2 or waist ≥ 80 cm (women) and ≥ 94 cm (men)	**Review:** ☐ Diet ☐ Exercise ☐ After review, no action
High Blood Sugar Levels **Diabetes:** ☐ Yes ☒ No **Date of Blood Tests:** HbA1c: 5.3% [Ref Range 0.0-6.0] Glucose: 3.9 mmol/L [Ref Range 4.0-7.0]	**GOAL in diabetes** Maintain glycosylated haemoglobin ≤ 7%. Glycosylated haemoglobin is a measure of how sugar is affecting the cells of the body. Levels of control are: • <7% (Very good) • 7-8% (Adequate) • 8-9% (Requires improvement) • >9% (Poor)	**Review:** ☐ 3-monthly blood test for HbA1c ☐ Diet ☐ Education ☐ Referral to dietitian ☐ Referral to diabetes educator ☐ After review, no action
Kidney Function	**GOAL**	**Review:**

Creatinine: 63 µmol/L [Ref Range 45-80] Protein: 0.06 g/day [Ref Range 0.00-0.15]	Monitor kidney function. This is achieved by assessing the amount of a protein in the urine, and by measuring the blood creatinine level.	☐ Annual urine test for urinary ACR ☐ Diet ☐ Education ☐ Referral to a nephrologist ☐ Referral to dietitian ☐ After review, no action
Mood Assessment HADS screening scores for: Depression* = 1 Anxiety† = 1 *For Scores ≥ 7 consider depression. † For scores ≥ 8 consider morbid anxiety.	**GOAL** Monitor for altered mood. Mood is frequently affected following stroke. The most common mood alteration is depression.	**Review:** ☐ Patient education ☐ Medication Consider: ☐ CBT ☐ Counselling ☐ Psychotherapy ☐ Relaxation training ☐ Referral to Allied Health Professional ☐ Referral to Psychiatrist ☐ After consideration, no action
Other, please state		

ISSUES ARISING FROM GP CONSULTATION
Other patient issues identified at home visit: ☐ Concern about ability to manage medications ☐ Safety concerns for falls ☐ Patient wanting to return to driving ☐ Loss of confidence in mobility ☐ Concerns about speech, communications and/or memory ☐ Sexual dysfunction ☐ Other _____ Summary of Management Plan for Patient/Carer:

Copy of Management Plan provided to patient: Yes ☐ No ☐

GP Management Plan Review Date:
(recommendations: 6 months after GP initiated Management Plan)

Will extra patient visits be required for risk factor management within this time period? Yes ☐ No ☐

Does patient need referral for Team Care Arrangement? Yes ☐ No ☐
(Consider referral in 4 weeks).

Please fax copy back to: Professor Amanda Thrift 990 24245
Please DO NOT SEND to Specialist

[Appendix E] STANDFIRM Trial – Questionnaires

11679

STAND FIRM for Stroke Patients
Assessment of Quality of Life (AQoL)

ID

INTERVIEWER INITIALS **DATE OF ASSESSMENT** / /

STATUS Patient ☐ Carer ☐

TIME Baseline ☐ 3 month ☐ 1 year ☐ 2 year ☐

PERSON RESPONDING

Index case ☐ Other relative ☐
Spouse/partner ☐ Friend/Associate/Neighbour ☐
Sibling ☐ Carer, e.g. nurse ☐
Son/Daughter ☐ Other, unspecified ☐
Parent ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household
Not living with index ☐ If living apart, note number of contacts per week
Prof carer in nursing home/hostel ☐

INSTRUCTIONS: Please tick the alternative that best describes you during the last week.

ILLNESS

1. Concerning my use of prescription medications:

I do not or rarely use any medicines at all ☐
I use one or two medicinal drugs regularly ☐
I need to use three or four medicinal drugs regularly ☐
I use five or more medicinal drugs regularly ☐

2. To what extent do I rely on medicines or a medical aid? (NOT glasses or a hearing aid). *E.g. walking frame, wheelchair, prosthesis etc*

I do not use any medicines and/or medical aids ☐
I occasionally use medicines and/or medical aids ☐
I regularly use medicines and/or medical aids ☐
I have to constantly take medicines or use a medical aid ☐

3. Do I need regular medical treatment from a doctor or other health professional?

I do not need regular medical treatment ☐
Although I have some regular medical treatment, I am not dependent on this ☐
I am dependent on regular medical treatment ☐
My life is dependent on regular medical treatment ☐

INDEPENDENT LIVING

4. Do I need help looking after myself?

I need no help at all ☐
Occasionally I need some help with personal care tasks ☐
I need help with the more difficult personal care tasks ☐
I need daily help with most or all personal care tasks ☐

5. When doing household tasks: *E.g. preparing food, gardening, using the video recorder, radio, telephone or washing the car*

I need no help at all ☐
Occasionally I need some help with household tasks ☐
I need help with the more difficult household tasks ☐
I need daily help with most or all household tasks ☐

6. Thinking about how easily I can get around my home and my community

I get around my home and community by myself without any difficulty ☐
I find it difficult to get around my home and community by myself with some difficulty ☐
I cannot get around the community by myself, but I can get around my home ☐
I cannot get around either the community or my home by myself ☐

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STAND FIRM for Stroke Patients
Assessment of Quality of Life (AQoL)

ID

SOCIAL RELATIONSHIPS

7. Because of my health, my relationships (e.g. - with my friends, partner or parents) are generally:

- Very close and warm ☐
- Sometimes close and warm ☐
- Seldom close and warm ☐
- I have no close and warm relationships ☐

8. Thinking about my relationships with other people:

- I have plenty of friends, and am never lonely ☐
- Although I have friends, I am occasionally lonely ☐
- I have some friends, but am often lonely for company ☐
- I am socially isolated and feel lonely ☐

9. Thinking about my health and my relationship with my family:

- My role in the family is unaffected by my health ☐
- There are some parts of my family role I cannot carry out ☐
- There are many parts of my family role that I cannot carry out ☐
- I cannot carry out any part of my family role ☐

PHYSICAL SENSES

10. Thinking about my vision, including when using my glasses or contact lenses if needed:

- I see normally ☐
- I have some difficulty focussing on things, or I do not see sharply. *E.g. small print, a newspaper, or seeing objects in the distance* ☐
- I have a lot of difficulty seeing things. My vision is blurred. *E.g. I can see just enough to get by with* ☐
- I only see general things, or am blind *E.g. I need a guide to get around* ☐

11. Thinking about my hearing, including when using my hearing aid if needed:

- I hear normally ☐
- I have some difficulty hearing, or I do not hear clearly ☐
- I have a lot of difficulty hearing things clearly ☐
- I hear very little indeed ☐

12. When I communicate with others:
E.g. by talking, listening, writing or signing

- I have no trouble speaking to them or understanding what they are saying ☐
- I have some difficulty being understood by people who do not know me. I have no trouble understanding what others are saying to me ☐
- I am only understood by people who know me well. I have great trouble understanding what others are saying to me ☐
- I cannot adequately communicate with others ☐

PSYCHOLOGICAL WELL-BEING

13. If I think about how I sleep:

- I am able to sleep without difficulty most of the time ☐
- My sleep is interrupted some of the time, but I am usually able to go back to sleep without difficulty ☐
- My sleep is interrupted most nights, but I am usually able to go back to sleep without difficulty ☐
- I sleep in short bursts only. I am awake most of the night ☐

14. Thinking about how I generally feel:

- I do not feel anxious, worried or depressed ☐
- I am slightly anxious, worried or depressed ☐
- I feel moderately anxious, worried or depressed ☐
- I am extremely anxious, worried or depressed ☐

15. How much pain or discomfort do I experience?

- None at all ☐
- I have moderate pain ☐
- I suffer from severe pain ☐
- I suffer unbearable pain ☐

STAND FIRM for Stroke Patients Lifescripts

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐ **DATE OF ASSESSMENT** ☐☐ / ☐☐ / ☐☐☐☐

TIME Baseline ☐ 3 month ☐ 1 year ☐ 2 year ☐

PERSON RESPONDING

Index case ☐
Spouse/partner ☐
Sibling ☐
Son/Daughter ☐
Parent ☐
Other relative ☐
Friend/Associate/Neighbour ☐
Carer, e.g. nurse ☐
Other, unspecified ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household ☐☐
Not living with index ☐
Prof. carer in nursing home/hostel ☐ If living apart, note number of contacts per week ☐☐

NUTRITION

Part 1

a) Are you pregnant or breast feeding? Yes ☐ No ☐ Not Applicable ☐

b) Have you lost weight recently without trying to? Yes ☐ No ☐

c) Do you have diabetes and use insulin or take oral medication for your diabetes? Yes ☐ No ☐

d) Do you have anaemia caused by iron deficiency? Yes ☐ No ☐

e) Do you have osteoporosis? Yes ☐ No ☐

f) Is it difficult for you to shop and cook for yourself? Yes ☐ No ☐

Part 2

a) Do you choose low-fat dairy products? Yes ☐ No ☐

b) Do you eat vegetables every day (fresh, frozen or canned)? Yes ☐ No ☐

c) Do you eat pies, pastries, fried foods or take-away meals more than once a week? Yes ☐ No ☐

d) Do you drink soft drinks, cordials, sports drinks or fruit juice on most days of the week? Yes ☐ No ☐

WEIGHT MANAGEMENT

3) Are you currently gaining weight without trying to? Yes ☐ No ☐

4) Have you gained more than 10kg weight since your late teens or early twenties? Yes ☐ No ☐

5) How many times have you tried to lose weight since you were in your late teens or early twenties? ☐☐

6) How interested are you in managing your weight in the long term? _____

7) **Do you have any other medical conditions, such as:**

a) High blood pressure Yes ☐ No ☐

b) High cholesterol Yes ☐ No ☐

c) Diabetes Yes ☐ No ☐

STAND FIRM for Stroke Patients
Lifescripts

ID ☐☐☐☐

PHYSICAL ACTIVITY

Please circle **one** option for each question.

8) How many times a week do you usually do 20 minutes or more of vigorous-intensity physical activity that makes you sweat or puff and pant? (e.g. heavy lifting, digging, jogging, aerobics or fast bicycling)

0 1 2 3 4 5 6 7+ Score ☐

9) How many times a week do you usually do 30 minutes or more of walking? (e.g. walking from place to place for exercise or recreation)

0 1 2 3 4 5 6 7+ Score ☐

10) How many times a week do you usually do 30 minutes or more of other moderate-intensity physical activity that increases your heart rate or makes you breathe harder than normal? (e.g. carrying light loads, bicycling at a regular pace or doubles tennis)

0 1 2 3 4 5 6 7+ Score ☐

TOTAL ☐☐

SMOKING

11) Do you smoke? Yes, current smoker ☐ No, past smoker ☐ No, never smoker ☐

12) If Yes, how many cigarettes do you smoke a day now? ☐☐

13) If previous smoker, when did you quit? ☐☐ / ☐☐ / ☐☐☐☐
Day Month Year

14) Have you been exposed to passive smoke in the past week? Yes ☐ No ☐

If CURRENT SMOKER, continue questions, if currently NON-SMOKER stop here.

15) How keen are you to stop smoking?
Circle the number that best matches your current attitude, from 0 (not at all keen) to 7 (very keen)

not at all keen to quit — very keen to quit

0 1 2 3 4 5 6 7 Score ☐

16) If you decided to stop smoking right now, how confident of success would you be?
Circle the number that best matches your current attitude, from 0 (not at all confident) to 7 (very confident)

not at all confident — very confident

0 1 2 3 4 5 6 7 Score ☐

17) When you wake up each day, how soon do you smoke your first cigarette? (tick **one** box)

more than 60 minutes ☐
31-60 minutes ☐
5-30 minutes ☐
less than 5 minutes ☐

18) How many cigarettes do you smoke on a typical day?

10 or less ☐
11-20 ☐
21-30 ☐
more than 30 ☐

TOTAL ☐☐

STAND FIRM for Stroke Patients Lifescripts

ID

ALCOHOL USE

Please tick **one** box for each question.

19) How often do you have drink containing alcohol ?

- Never ☐
- Monthly or less ☐
- 2 to 4 times a month ☐
- 2 to 3 times a week ☐
- 4 or more times a week ☐

20) How many standard drinks do you have on a typical day when you are drinking?

- 2 or less ☐
- >2 - 4 ☐
- >4 - 6 ☐
- >6 - 9 ☐
- 9 or more ☐

21) How often do you have 6 or more drinks on one occasion?

- Never ☐
- Less than monthly ☐
- Monthly ☐
- Weekly ☐
- Daily or almost daily ☐

STAND FIRM for Stroke Patients
Lifescripts

ID

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STAND FIRM for Stroke Patients
Management of Risk Factors

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐

DATE OF ASSESSMENT ☐☐ / ☐☐ / ☐☐☐☐

TIME Baseline ☐ 3 month ☐ 1 year ☐ 2 year ☐

PERSON RESPONDING

Index case ☐
Spouse/partner ☐
Sibling ☐
Son/Daughter ☐
Parent ☐
Other relative ☐
Friend/Associate/Neighbour ☐
Carer, e.g. nurse ☐
Other, unspecified ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐
Not living with index ☐
Prof carer in nursing home/hostel ☐

If living with index, note number of years living in the same household ☐☐

If living apart, note number of contacts per week ☐☐

This questionnaire is designed to include both closed and open-ended questions.
This is a semi-structured in-depth interview.

I would like to ask you some questions about your (his/her) smoking habits.

1. Have you (has he/she) ever smoked cigarettes, cigars, or a pipe at least once a day for 3 months or longer? Yes ☐ No ☐

If NO, Go To Q. 5. If YES, ask...

2. Were you (was he/she) smoking regularly at the time of your (his/her) stroke? Yes ☐ No ☐

3. Do you (does he/she) smoke now? Yes ☐ No ☐

If YES, Go To Q. 5. If NO, ask...

4. When did you (he/she) cease smoking?

a) Year Ceased Smoking ☐☐☐☐

b) Month Ceased Smoking

Jan ☐ May ☐ Sep ☐
Feb ☐ Jun ☐ Oct ☐
Mar ☐ Jul ☐ Nov ☐
Apr ☐ Aug ☐ Dec ☐

Now I would like to ask you some questions about any alcoholic beverages you (he/she) may have consumed.

5. Have you (has he/she) ever had periods when you (he/she) drank, on average, at least one glass of alcohol per month? Yes ☐ No ☐

IF NO, Go To Q. 8 (next page). If YES ask .....

6. Do you (does he/she) drink now? Yes ☐ No ☐

IF NO, Go To Q. 8. If YES ask .....

7. How many do you (does he/she) usually drink? (Record in grams alcohol).

Beer	☐☐☐.☐	per	day ☐ week ☐ month ☐
Red Wine	☐☐☐.☐	per	day ☐ week ☐ month ☐
White Wine	☐☐☐.☐	per	day ☐ week ☐ month ☐
Spirits	☐☐☐.☐	per	day ☐ week ☐ month ☐
Fortifieds	☐☐☐.☐	per	day ☐ week ☐ month ☐

STAND FIRM for Stroke Patients
Management of Risk Factors

ID ☐☐☐☐

Now I would like to ask you some questions about your (his/her) exercise habits during recreation, now and at other times in the past.

8. Since your (his/her) stroke have you (has he/she) ever engaged in any active exercise which caused you (him/her) to sweat and increase your (his/her) breathing rate (e.g. brisk walking, running, swimming, cycling, squash, vigorous team sports)?

Instruction: Exercising period must be for at least 20 minutes on each occasion. Breathless also includes people who are breathing more heavily than at rest.

Instruction: Do not count any daily activities which caused breathlessness (e.g. going to the bathroom), as exercise.

Yes ☐
No ☐

IF NO, Go To Q.11. If YES ask .....

9. Do you (does he/she) exercise regularly now? Yes ☐ No ☐

IF NO, Go To Q.11. If YES ask .....

10. How often do you (does he/she) engage in active exercise which causes you (him/her) to sweat and become breathless?

Number of times ☐☐ per day ☐ week ☐ month ☐

Now I would like to ask you about the way that you (he/she) manage(s) your (his/her) diet

11. Have you (has he/she) ever been advised to change your (his/her) diet? Yes ☐ No ☐

IF NO, Go To Q.16 (next page). If YES ask .....

12. What were you (was he/she) advised to do?

- Increase fibre ☐
- Increase fish intake ☐
- Increase fruit/vegetable intake ☐
- Reduce alcohol consumption ☐
- Reduce dairy intake ☐
- Reduce fat intake ☐
- Reduce meat intake ☐
- Reduce salt intake ☐
- Reduce sugar intake ☐
- Reduce overall intake ☐
- General advice (eat healthily) ☐
- Other (specify below) ☐

13. Why were you (was he/she) advised to change your (his/her) diet?

- Manage high blood pressure ☐
- Manage high cholesterol ☐
- Manage diabetes ☐
- Weight loss ☐
- Other (specify below) ☐

14. What difficulties did you (he/she) experience in carrying out this advice?

- Tried to change diet, but unsuccessful ☐
- Food is unappetising ☐
- I miss certain foods ☐
- I still eat cheese/salt and/or butter ☐
- I missed all the things I enjoyed ☐
- I don't enjoy eating as much ☐
- Unable to stick to diet for long ☐
- Unable to reduce size of meals ☐
- Sometimes I weaken ☐
- Unable to control diet in hostel/nursing home ☐
- Other (specify below) ☐

STAND FIRM for Stroke Patients
Management of Risk Factors

ID

15. What changes did you (he/she) find you (he/she) could act on and what did you (he/she) do?

- Cuts fat off meat/chicken ☐
- Increased fibre ☐
- Increased fish intake ☐
- Increased fruit/vegetable intake ☐
- No success ☐
- Reduced alcohol consumption ☐
- Reduce carb intake (e.g. pasta, bread, rice) ☐
- Reduced dairy intake ☐
- Reduced fat intake ☐
- Reduced red meat intake ☐
- Reduced salt intake ☐
- Reduced sugar intake ☐
- Reduced overall intake ☐
- General advice (eat healthily, and/or moderation) ☐
- Other (specify below) ☐

16. Have you (has he/she) ever been advised to change your (his/her) exercise habits?

Yes ☐
No ☐

IF NO, Go To Q.21 (next page). If YES ask .....

17. What were you (was he/she) advised to do?

- Advised to start exercising ☐
- Advised to exercise more regularly ☐
- Advised to increase intensity of activity ☐
- Other (specify below) ☐

18. Why were you (was he/she) advised to change your (his/her) exercise habits?

- Improve mobility (strength) ☐
- Increase fitness ☐
- Manage high blood pressure ☐
- Manage high cholesterol ☐
- Manage diabetes ☐
- Weight loss ☐
- Other (specify below) ☐

19. What difficulties did you (he/she) experience in carrying out this advice?

- Difficult to find the time ☐
- I became short of breath ☐
- I am afraid of falling ☐
- I am unable to exercise (poor balance/weakness) ☐
- Lack of motivation (incl. laziness) ☐
- No difficulties ☐
- Pain, limiting mobility (e.g. arthritis, pvd, swelling) ☐
- Other (specify below) ☐

20. What changes did you (he/she) find you (he/she) could act on and what did you (he/she) do?

- Started exercising ☐
- I exercise more often ☐
- I exercise more intensely ☐
- Changed type of exercise (e.g. lower to upper body) ☐
- Other (specify below) ☐

STAND FIRM for Stroke Patients
Management of Risk Factors

ID ☐☐☐☐

21. Have you (has he/she) ever been advised to take medications? Yes ☐ No ☐

IF NO, Go To Q.25. If YES ask .....

22. What were you (was he/she) taking medications for?
- Atrial fibrillation (irreg heart rhythm) ☐
- Diabetes ☐
- Heart failure ☐
- High blood pressure ☐
- High cholesterol ☐
- Prevention of another stroke ☐
- Don't know / unsure ☐
- Other (specify below) ☐

23. What difficulties did you (he/she) experience in following medication prescriptions?
- I don't want to take medications and so I don't ☐
- I sometimes forget to take my medications ☐
- No difficulties ☐
- Since changing medications (type/dose) I have no difficulties ☐
- They caused me to have unpleasant side effects ☐
- No longer take medications as no longer required ☐
- Other (specify below) ☐

24. What changes did you (he/she) find you (he/she) could act on and what did you (he/she) do?
- I have regular blood checks ☐
- I take my medications as prescribed ☐
- Health professional checks medication regularly ☐
- I use a dosette box to help me ☐
- My blood pressure is monitored regularly ☐
- Someone needs to remind me to take them ☐
- Other (specify below) ☐

25. Has your (his/her) blood pressure been checked in the past 12 months? Yes ☐ No ☐ Don't know ☐

26. Has your (his/her) cholesterol (blood fat) been checked in the past 12 months? Yes ☐ No ☐ Don't know ☐

27. Do you (does he/she) try to limit the amount of dairy products in your (his/her) diet? Yes ☐ No ☐ Don't know ☐

28. Do you (does he/she) try to limit the amount of sugar in your (his/her) diet? Yes ☐ No ☐ Don't know ☐

29. Do you (does he/she) try to limit the amount of salt in your (his/her) diet? Yes ☐ No ☐ Don't know ☐

30. Do you (does he/she) have a mechanical heart valve? Mechanical ☐ No ☐ Other heart valve ☐

31. How many servings of vegetables would you (he/she) eat per day? ☐☐☐.☐

32. How many servings of fresh fruit would you (he/she) eat per day? ☐☐☐.☐

33a. Do you (does he/she) add salt to your (his/her) food? Yes ☐ No ☐ Don't know ☐

33b. IF yes, In total would you (does he/she) have more than a teaspoon of salt added to your meals in one day? Yes ☐ No ☐ Don't know ☐

34. How many slices of bread would you (he/she) eat per day? ☐☐☐.☐

35. What is your height? Height in cm ☐☐☐.☐

36. What is your current weight? Weight in kg ☐☐☐.☐

STAND FIRM for Stroke Patients
Modified Rankin Scale

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐ **DATE OF ASSESSMENT** ☐☐ / ☐☐ / ☐☐☐☐

TIME Pre-stroke ☐ Baseline ☐ 3 month ☐ 1 year ☐ 2 year ☐

PERSON RESPONDING

Index case ☐ Other relative ☐
Spouse/partner ☐ Friend/Associate/Neighbour ☐
Sibling ☐ Carer, e.g. nurse ☐
Son/Daughter ☐ Other, unspecified ☐
Parent ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household ☐☐
Not living with index ☐
If living apart, note number of contacts per week ☐☐
Prof carer in nursing home/hostel ☐

General Instructions

Mark an x in the place corresponding to the patient's level of disability at the time of assessment.

No symptoms at all, no limitations and no symptoms ☐

No significant disability; symptoms present but not other limitations. ☐
Question: Does the person have difficulty reading or writing, difficulty speaking or finding the right word, problems with balance or co-ordination, visual problems, numbness (face, arms, legs, hands, feet), loss of movement (face, arms, legs, hands, feet), difficulty with swallowing, or other symptoms resulting from stroke?

Slight disability; limitations in participation in usual social roles, but independent for ADL. ☐
Questions: Has there been a change in the person's ability to work or look after others if these were roles before stroke? Has there been a change in the person's ability to participate in previous social and leisure activities? Has the person had problems with relationships or become isolated?

Moderate disability; need for assistance with some instrumental ADL, but not basic ADL. ☐
Question: Is assistance essential for preparing a simple meal, doing household chores, looking after money, shopping or traveling locally?

Moderately severe disability; need for assistance with some basic ADL, but not requiring constant care. ☐
Question: Is assistance required for eating, using the toilet, daily hygiene, or walking?

Severe disability; someone needs to be available at all times; care may be provided by either a trained or an untrained caregiver. ☐
Question: Does the person require constant care?

Dead ☐

STAND FIRM for Stroke Patients
Patient History

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐ **DATE OF ASSESSMENT** ☐☐ / ☐☐ / ☐☐☐☐

TIME Baseline ☐

PERSON RESPONDING

Index case ☐
Spouse/partner ☐
Sibling ☐
Son/Daughter ☐
Parent ☐
Other relative ☐
Friend/Associate/Neighbour ☐
Carer, e.g. nurse ☐
Other, unspecified ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household ☐☐
Not living with index ☐
Prof. carer in nursing home/hostel ☐
If living apart, note number of contacts per week ☐☐

DEMOGRAPHICS

1) Sex Male ☐ Female ☐

2) Marital Status
Never Married ☐
Now Married ☐
Separated but not divorced ☐
Divorced ☐
Widowed ☐
Living with partner ☐

3) Initials: First ☐☐ Surname ☐☐

4) Date of Birth ☐☐ / ☐☐ / ☐☐☐☐

5) Living Place Before Stroke OR Current Living Place at: 3mths, 1yr or 2yr
Own home or unit ☐
Home of Relative/Friend ☐
Special Accommodation ☐
Hostel ☐
Nursing Home ☐
Insufficient Data ☐

LANGUAGE

6) Country of Birth ☐☐☐

7) What is your (is his/her) preferred language? ☐☐

8) Are you (is he/she) fluent in English? Yes ☐ No ☐

9) What language do you (does he/she) mainly use at home? ☐☐

10) What language do you (does he/she) mainly use at work? ☐☐

11) What languages are you (is he/she) fluent in? ☐☐ ☐☐ ☐☐

12) What is your (is his/her) ethnic origin? ☐☐☐

STAND FIRM for Stroke Patients
Patient History

ID

SOCIAL HISTORY

13a) What is (was) your (his/her) occupation? (Specify)

13b) What are (were) the main tasks that you (he/she) usually performed in that occupation? (Specify)

13c) What is (was) the employers trading name?(Specify)

13d) What kind of industry, business or service was carried out by that employer? (Specify)

14a) What is (was) your (his/her) partner's occupation? (Specify)

14b) What are (were) the main tasks that they (he/she) usually performed in that occupation? (Specify)

14c) What is (was) the employers trading name?(Specify)

14d) What kind of industry, business or service was carried out by that employer? (Specify)

EDUCATION

15) Age Completed Education

16) Highest Level of Education Completed

- Never attended school ☐
- Primary School ☐
- Some High School ☐
- Completed High School ☐
- Completed a Trade ☐
- University ☐
- Other Vocational Training ☐

17) Social Class of Patient

- Professional, e.g. doctor, lawyer, accountant ☐
- Intermediate, e.g. manager, executive, teacher ☐
- Skilled non-manual, e.g. salesman, shopowner ☐
- Skilled manual, e.g. craftsman ☐
- Semi-skilled manual, e.g. driver ☐
- Unskilled manual, e.g. labourer ☐

STAND FIRM for Stroke Patients
Patient History

ID

MEDICAL HISTORY

18) While in hospital did you receive any stroke education about how to prevent stroke? Yes ☐ No ☐

Now I would like to ask you about any diseases or conditions which you (he/she) may have had.

If the subject answers YES to a query in column 1, ask the subsequent question in column 2, etc. If the subject answers NO, go to the next disease/condition.

19) Were you (he/she) ever told by a doctor that you (he/she) had....?

20) Was that condition treated with medication?

21) Were you (was he/she) ever admitted to hospital for the condition?

For each Box Option 1 = Yes 2 = No 9 = Unknown

	19)	20)	21)
High cholesterol/fat in blood	☐	☐	☐
Heart attack/coronary/M.I./angina/heart pain	☐	☐	☐
Atrial Fibrillation/Irregular pulse	☐	☐	☐
High blood pressure	☐	☐	☐
Stroke	☐	☐	☐
TIA/transient weakness/numbness	☐	☐	☐
Obstructive Sleep Apnoea/ Disrupted sleep (by snoring)	☐	☐	☐
Rheumatic Fever	☐	☐	☐
Diabetes	☐	☐	☐
Arthritis	☐	☐	☐
Migraines or other headaches	☐	☐	☐
Depression/Anxiety	☐	☐	☐

22) Do you drink any alcohol-containing beverages (e.g. wine, beer, spirits)?

Alcohol Use
- Never Drink Alcohol ☐
- Previously drunk alcohol ☐
- Currently drink alcohol ☐

23) Other relevant history/intercurrent illness: (Specify) _____

_____

24) Known Allergies: (Specify) _____

_____

Now I would like to ask you about any diseases or conditions which a <u>family member</u> may have had.

If the subject answers YES to a query in column 1, ask the subsequent question in column 2, etc. If the subject answers NO, go to the next disease/condition.

25) Was a family member (he/she) ever told by a doctor that he/she had....?

26) Was that condition treated with medication?

27) Was your family member ever admitted to hospital for the condition?

For each Box Option 1 = Yes 2 = No 9 = Unknown

	25)	26)	27)
High cholesterol/fat in blood	☐	☐	☐
Heart attack/coronary/M.I./angina/heart pain	☐	☐	☐
High blood pressure	☐	☐	☐
Diabetes	☐	☐	☐
TIA/transient weakness/numbness	☐	☐	☐
Stroke	☐	☐	☐

STAND FIRM for Stroke Patients
Patient History

ID ☐☐☐☐

BLOOD GLUCOSE, HAEMOGLOBIN AND LIPIDS

28) During the past 12 hours have you had anything to eat or drink other than water?
Yes ☐
Yes, but fasted overnight ☐
No ☐

29) Date and time of last meal and or drink, other than water (24 hour clock)
Date ☐☐ / ☐☐ / ☐☐☐☐
☐☐ **hrs** ☐☐ **mins**

30) Date and time of day of blood specimen taken (24 hour clock)
Date ☐☐ / ☐☐ / ☐☐☐☐ ☐☐ **hrs** ☐☐ **mins**

TEST			MEASUREMENT
31)	Cholesterol	Non-fasting ☐ Fasting ☐	☐☐☐.☐ **mmol/l**
32)	HDL Cholesterol	Non-fasting ☐ Fasting ☐	☐☐☐.☐ **mmol/l**
33)	LDL Cholesterol	Non-fasting ☐ Fasting ☐	☐☐☐.☐ **mmol/l**
34)	Creatinine		☐☐☐.☐ **umol/l**
35)	Triglyceride	Non-fasting ☐ Fasting ☐	☐☐☐.☐ **mmol/l**
36)	INR (for patients taking warfarin)		☐☐☐.☐ **ratio**
37)	HbA1c		☐☐☐.☐ **%**
38)	Glucose	Non-fasting ☐ Fasting ☐	☐☐☐.☐ **mmol/l**

URINE		MEASUREMENT
39)	Sodium Excretion	☐☐☐.☐ **mmol/day**
40)	Potassium Excretion	☐☐☐.☐ **mmol/day**
41)	Creatinine Excretion	☐☐☐.☐ **mmol/day**
42)	Protein Excretion	☐☐☐.☐☐ **g/day**
43)	Cotinine	None Detected ☐ Detected ☐

STAND FIRM for Stroke Patients
Patient History

ID ☐☐☐☐

HEIGHT AND WEIGHT

DATE HEIGHT AND WEIGHT ASSESSED ☐☐ / ☐☐ / ☐☐☐☐

44) Height — **In centimetres** ☐☐☐.☐

45) Weight *If too large for scale code 999.9* — **In kilograms** ☐☐☐.☐

WAIST AND HIP

46) *FOR WOMEN* Are you pregnant? — Yes ☐ No ☐ *If yes, skip waist*

47) Abdomen circumference — **In centimetres** ☐☐☐.☐

48) Hip circumference — **In centimetres** ☐☐☐.☐

49) Arm used — Left ☐ Right ☐

50) Arm circumference — **In centimetres** ☐☐☐.☐

51) Skin Fold

DATE SKINFOLDS ASSESSED ☐☐ / ☐☐ / ☐☐☐☐

Triceps ☐☐.☐ **mm**

Biceps ☐☐.☐ **mm**

Subscapular ☐☐.☐ **mm**

Supra-iliac ☐☐.☐ **mm**

BLOOD PRESSURE AND CARDIOVASCULAR SYSTEM

52) Cuff size used — Small ☐ Medium ☐ Large ☐

DATE BP ASSESSED ☐☐ / ☐☐ / ☐☐☐☐

53) Arm used — Left ☐ Right ☐

54) Position of Subject — Sitting ☐ Lying ☐

BP AND HEART RATE MEASUREMENTS

55)

		Systolic	Diastolic	Beats per minute
Reading 1		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 2		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 3		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 4	(Readings 4 and 5 are only required if the last two readings differ by >= 10/6 mmHg)	☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 5		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐

56) Heart Rhythm — Regular ☐ Irregular ☐

STAND FIRM for Stroke Patients
Patient History

ID

MEDICATIONS

57) What other medications have you been taking?

For each medication mentioned, ask: 53a) What were you taking _____ for?
53b) When did you start taking _____?
53c) When did you stop taking _____?
53d) Do you (Did he/she) always take your (his/her) medication as directed?

Name (units)	Medication Code	A.C*	Dose (per day)	Duration (Days)	C*	Meds seen/list provided
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐

*** A.C = Antihypertensive Class**

1 = diuretic
2 = ß-blocker
3 = Calcium blockers
4= ACE inhibitors
5 = vasodilators
6 = others

***Compliance (c)**

1= Yes
2 = No
3 = N/A
9 = Don't know

58) For any medications no longer being used, list and state reason:

Name (units)	Medication Code	Reason

STAND FIRM for Stroke Patients
Patient History - Follow Up

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐ **DATE OF ASSESSMENT** ☐☐ / ☐☐ / ☐☐☐☐

TIME 3 month ☐ 1 year ☐ 2 year ☐

PERSON RESPONDING

Index case ☐
Spouse/partner ☐
Sibling ☐
Son/Daughter ☐
Parent ☐
Other relative ☐
Friend/Associate/Neighbour ☐
Carer, e.g. nurse ☐
Other, unspecified ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household ☐☐

Not living with index ☐

Prof. carer in nursing home/hostel ☐ If living apart, note number of contacts per week ☐☐

DEMOGRAPHICS

1) Marital Status

Never Married ☐
Now Married ☐
Separated but not divorced ☐
Divorced ☐
Widowed ☐
Living with partner ☐

MEDICAL HISTORY

2) Other relevant history/intercurrent illness: (Specify) _____

_____

3) Known Allergies: (Specify) _____

_____

BLOOD GLUCOSE, HAEMOGLOBIN AND LIPIDS

4) During the past 12 hours have you had anything to eat or drink other than water?

Yes ☐
Yes, but fasted overnight ☐
No ☐

5) Date and time of last meal and or drink, other than water (24 hour clock)

Date ☐☐ / ☐☐ / ☐☐☐☐ ☐☐ **hrs** ☐☐ **mins**

6) Date and time of day of blood specimen taken (24 hour clock)

Date ☐☐ / ☐☐ / ☐☐☐☐ ☐☐ **hrs** ☐☐ **mins**

STAND FIRM for Stroke Patients
Patient History - Follow Up

ID ☐☐☐☐

TEST			MEASUREMENT
7)	Cholesterol	Non-fasting ☐ Fasting ☐	☐☐☐.☐ mmol/l
8)	HDL Cholesterol	Non-fasting ☐ Fasting ☐	☐☐☐.☐ mmol/l
9)	LDL Cholesterol	Non-fasting ☐ Fasting ☐	☐☐☐.☐ mmol/l
10)	Creatinine		☐☐☐.☐ umol/l
11)	Triglyceride	Non-fasting ☐ Fasting ☐	☐☐☐.☐ mmol/l
12)	INR (for patients taking warfarin)		☐☐☐.☐ ratio
13)	HbA1c		☐☐☐.☐ %
14)	Glucose	Non-fasting ☐ Fasting ☐	☐☐☐.☐ mmol/l

URINE		MEASUREMENT
15)	Sodium Excretion	☐☐☐.☐ mmol/day
16)	Potassium Excretion	☐☐☐.☐ mmol/day
17)	Creatinine Excretion	☐☐☐.☐ mmol/day
18)	Protein Excretion	☐☐☐.☐☐ g/day
19)	Cotinine	None Detected ☐ Detected ☐

HEIGHT AND WEIGHT

DATE HEIGHT AND WEIGHT ASSESSED ☐☐ / ☐☐ / ☐☐☐☐

20) Height **In centimetres** ☐☐☐.☐

21) Weight *If too large for scale code 999.9* **In kilograms** ☐☐☐.☐

STAND FIRM for Stroke Patients
Patient History - Follow Up

ID ☐☐☐☐

WAIST AND HIP

22) *FOR WOMEN*
Are you pregnant? Yes ☐ No ☐
If yes, skip waist

23) Abdomen circumference **In centimetres** ☐☐☐.☐

24) Hip circumference **In centimetres** ☐☐☐.☐

25) Arm used Left ☐ Right ☐

26) Arm circumference **In centimetres** ☐☐☐.☐

27) Skin Fold

DATE SKINFOLDS ASSESSED
☐☐ / ☐☐ / ☐☐☐☐

Triceps ☐☐.☐ **mm**
Biceps ☐☐.☐ **mm**
Subscapular ☐☐.☐ **mm**
Supra-iliac ☐☐.☐ **mm**

BLOOD PRESSURE AND CARDIOVASCULAR SYSTEM

28) Cuff size used Small ☐ Medium ☐ Large ☐

DATE BP ASSESSED ☐☐ / ☐☐ / ☐☐☐☐

29) Arm used Left ☐ Right ☐

30) Position of Subject Sitting ☐ Lying ☐

BP AND HEART RATE MEASUREMENTS		Systolic	Diastolic	Beats per minute
31) Reading 1		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 2		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 3		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 4	(Readings 4 and 5 are only required if the last two readings differ by >= 10/6 mmHg)	☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐
Reading 5		☐☐☐ **mmHg**	☐☐☐ **mmHg**	☐☐☐

32) Heart Rhythm Regular ☐ Irregular ☐

STAND FIRM for Stroke Patients
Patient History - Follow Up

ID

MEDICATIONS

33) What other medications have you been taking?

For each medication mentioned, ask: 33a) What were you taking _____ for?
33b) When did you start taking _____?
33c) When did you stop taking _____?
33d) Do you (Did he/she) always take your (his/her) medication as directed?

Name (units)	Medication Code	A.C*	Dose (per day)	Duration (Days)	C*	Meds seen/list provided
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐
			.			Yes ☐ No ☐

*** A.C = Antihypertensive Class**

1 = diuretic
2 = ß-blocker
3 = Calcium blockers
4= ACE inhibitors
5 = vasodilators
6 = others

***Compliance (c)**

1= Yes
2 = No
3 = N/A
9 = Don't know

34) For any medications no longer being used, list and state reason:

Name (units)	Medication Code	Reason

STAND FIRM for Stroke Patients
Post- Acute Costs of Stroke

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐

DATE OF ASSESSMENT ☐☐ / ☐☐ / ☐☐☐☐

PERSON RESPONDING

Index case ☐ Other relative ☐
Spouse/partner ☐ Friend/Associate/Neighbour ☐
Sibling ☐ Carer, e.g. nurse ☐
Son/Daughter ☐ Other, unspecified ☐
Parent ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES
AGE OF RESPONDENT ☐☐

TIME 3 month ☐ 1 year ☐ 2 year ☐

SEX OF RESPONDENT Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐
Not living with index ☐
Professional carer in nursing home or hostel ☐

If living with index, note number of years living in the same household ☐☐

If living apart, note number of contacts per week ☐☐

Instructions to the assessor: This cost questionnaire aims to obtain information about health care occurring subsequent to any acute admission to hospital after the initial stroke. Therefore subsequent admissions to rehabilitation or geriatric hospital or additional periods of hospitalisation for stroke related complications e.g. Aspiration pneumonia should be recorded in this questionnaire.

PLEASE ONLY ENTER WHOLE DOLLAR AMOUNTS WHERE COSTS ITEMISED.

Instructions to the person responding: These questions are about health care provided since returning home after your (his/her) stroke which occurred on

_____ or as a result of any further stroke.
Date of patients stroke

QUESTIONS ARE ABOUT HEALTH CARE SINCE MY LAST VISIT

I will be asking about health care such as visits to your local doctor, specialist doctor visits, medical tests, rehabilitation, therapy at home and equipment. To help us work out the cost of the stroke to the community and you (your husband, wife etc) I will be asking about how often services were provided, and also what it cost you (your husband, wife etc).

STAND FIRM for Stroke Patients
Post- Acute Costs of Stroke

ID ☐☐☐☐

1) DISCHARGE

Date of Discharge from Acute Care

☐☐ / ☐☐ / ☐☐☐☐

Acute Discharge Destination

- Home ☐
- Rehabilitation ward/hospital ☐
- Supported residential service (SRS) ☐
- Hostel ☐
- Nursing Home ☐
- Other ☐
- Unknown ☐

Date of Discharge from Inpatient Rehabilitation

☐☐ / ☐☐ / ☐☐☐☐

Leave dates BLANK if not applicable

Please note: inpatient rehabilitation is inclusive of geriatric evaluation and transitional care

Discharge Destination After Inpatient Rehab

- Home ☐
- Rehabilitation hospital ☐
- Supported residential service (SRS) ☐
- Hostel ☐
- Nursing Home ☐
- Other ☐
- Unknown ☐

Leave BLANK if not applicable

2) LIVING ARRANGEMENTS

Pre-stroke Residential Address

- Own house/flat - alone ☐
- Own house/flat - with family/relative/friend ☐
- Home of relative/friend ☐
- Supported residential service (SRS) ☐
- Hostel ☐
- Nursing Home ☐
- Other ☐
- Unknown ☐

Current Residential Address*

- Own house/flat - alone ☐
- Own house/flat - with family/relative/friend ☐
- Home of relative/friend ☐
- Supported residential service (SRS) ☐
- Hostel ☐
- Nursing Home ☐
- Other ☐
- Unknown ☐

**Please note if the subject is currently a hospital inpatient (acute or subacute), record their current residential address, NOT the hospital address*

STAND FIRM for Stroke Patients
Post- Acute Costs of Stroke

ID ☐☐☐☐

3) CHANGE IN LIVING ARRANGEMENTS

As a consequence of your stroke, have you needed to change your place of residence? Yes ☐ No ☐ Unknown ☐

*If NO, proceed to question 4. *Please note : if subject has been a hospital inpatient this is NOT a change of residence.*

	Date of Move	Location	Reason for Move
1)	☐☐ / ☐☐ / ☐☐☐☐	Own home or unit ☐ Home of relative ☐ SRS ☐ Hostel ☐ Nursing home ☐ Other ☐	
2)	☐☐ / ☐☐ / ☐☐☐☐	Own home or unit ☐ Home of relative ☐ SRS ☐ Hostel ☐ Nursing home ☐ Other ☐	
3)	☐☐ / ☐☐ / ☐☐☐☐	Own home or unit ☐ Home of relative ☐ SRS ☐ Hostel ☐ Nursing home ☐ Other ☐	
4)	☐☐ / ☐☐ / ☐☐☐☐	Own home or unit ☐ Home of relative ☐ SRS ☐ Hostel ☐ Nursing home ☐ Other ☐	

4) AMBULANCE TRANSFERS: EMERGENCY AND NON-EMERGENCY

As a consequence of your stroke, have you required ambulance transport after your acute admission to hospital?* Yes ☐ No ☐ Unknown ☐

If NO, proceed to question 5.

Count number of ambulance trips ☐☐

**Only Include transfers since Baseline visit*

STAND FIRM for Stroke Patients
Post- Acute Costs of Stroke

ID

5) HOSPITALISATION OR EMERGENCY DEPARTMENT ATTENDANCES

5a) Have you been readmitted to hospital or attended the emergency department as a consequence of another stroke or for any stroke related problems? Yes ☐

ONLY include information for admissions and attendances for stroke-related problems (see below for summary list of stroke-related problems for further **clarification)** No ☐

Unknown ☐

If NO, proceed to question 6.

5b) If YES, Start with the earliest admission or attendance. For each admission start by asking....

"WHAT WAS THE STROKE OR STROKE-RELATED PROBLEM/S THAT PRECIPITATED YOUR ADMISSION/S TO HOSPITAL?"

Admission		Hospital code	Date of Admission	Date of Discharge
1st	**Stroke or stroke-related problem code** (see below for list of problems)		/ /	/ /
2nd	**Stroke or stroke-related problem code**		/ /	/ /
3rd	**Stroke or stroke-related problem code**		/ /	/ /
4th	**Stroke or stroke-related problem code**		/ /	/ /
5th	**Stroke or stroke-related problem code**		/ /	/ /

Stroke-related problems include: 1. Recurrent stroke, 2. TIA or suspected TIA, 3. Seizure, 4. Pneumonia/chest infection, 5. UTI, 6. Urinary catheter-related problem, 7. Mood disorder, 8. Falls, 9. Fractures, 10. DVT, 11 Pulmonary Embolism, 12. Complications of stroke treatment or stroke prevention, 13. Haemorrhage, 14. Nutritional problem, 15. Gastroscopy/colonoscopy/barium enema or other procedure to investigate GI haemorrhage, 16. Cerebral angiography, 17. Carotid endarterectomy, 18. Carotid (or other cerebral vessel) angioplasty and/or stenting, 19. Surgery or procedural management of an atrial septal defect or patent foramen ovale, 20. Surgical or electrophysiological procedure to treat AF, 21 Inability to manage at home, 22. Increased confusion or cognitive impairment, 23. Constipation - investigation or treatment, 24. Urinary incontinence, 25. Post-stroke pain (incl. headache), 26 Pressure sores, 27 Complications of stroke event

STAND FIRM for Stroke Patients
Post- Acute Costs of Stroke

ID ☐☐☐☐

6) INPATIENT REHABILITATION HOSPITAL ADMISSION

After you first went home, were you then admitted to a Rehabilitation Hospital or other hospital where you received Rehabilitation treatment?
Please include admissions with the care type 'rehabilitation', 'geriatric evaluation' and 'transitional care'

Yes ☐
No ☐
Unknown ☐

If NO, proceed to question 7.
If YES, complete inpatient rehabilitation admission details, starting from your first inpatient rehabilitation admission.
If patient NOT discharged at 3 month assessment, leave discharge dates BLANK (complete dates at 12 month assessment)

Admission	Which hospital were you admitted to?	Rehab Hosp Code	What date were you admitted?	What date were you discharged?
1st	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
2nd	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
3rd	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐
4th	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐

7) OUTPATIENT REHABILITATION PROGRAM

Did you attend or are you attending an outpatient rehabilitation program as a consequence of stroke-related problems?
e.g. physiotherapy, occupational therapy, speech therapy, counselling, driving assessment

Yes ☐
No ☐
Unknown ☐

An outpatient rehabilitation program is any rehabilitation program where the patient attends a facility. The program can be located at a hospital or community facility.
If NO, proceed to question 8.
If YES, complete outpatient rehabilitation details, starting from your first outpatient rehabilitation visit.
If patient NOT discharged at 3 month assessment, leave discharge dates and number of days attended BLANK

Outpatient Rehabilitation Program	Which hospital did you attend?	Rehab Hosp Code	What date did you commence?	What date did you cease?	Total no. of days attended
1st	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐☐
2nd	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐☐
3rd	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐☐
4th	_____	☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐ / ☐☐ / ☐☐☐☐	☐☐☐

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8) REHABILITATION SERVICES PROVIDED AT HOME

Have you had a rehabilitation program provided to you at home as a consequence of your stroke?
e.g. with physiotherapy, occupational therapy, speech therapy

Yes ☐
No ☐
Unknown ☐

If NO, proceed to question 9.
If YES, complete rehabilitation details, starting from your first visit since your stroke..
If patient NOT discharged at 3 month assessment, leave discharge dates and number of days attended BLANK

Was this referred by your GP?

Yes ☐
No ☐

Admission	Which rehabilitation program did you attend?	Rehab Code	What date did you commence?	What date did you cease?	Total no. SESSIONS
1st	_____		/ /	/ /	
2nd	_____		/ /	/ /	
3rd	_____		/ /	/ /	
4th	_____		/ /	/ /	

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9) COMMUNITY SERVICES

9a) Did you receive any community services in the year PRIOR to your stroke? e.g. Royal District Nursing Service, Meals on Wheels, Home Help

Yes ☐
No ☐
Unknown ☐

If NO, proceed to question 9b.
If YES, which service/s did you receive in the year PRIOR to your stroke?

Community service codes
1 = Nursing Service
2 = Delivered Meals
3 = Housework Help
4 = Gardening/home maintenance
5 = Home respite
6 = Personal Carer
7 = Other Services, Specify

Which service did you receive? *One service code per line*							**How many times did you receive the service in the year PRIOR to your stroke?**
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐

If "other" (code 7), please specify
☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

9b) Have you received community services SINCE the stroke?
Community services are individual care services provided at home and do NOT include rehabilitation therapy.

Yes ☐
No ☐
Unknown ☐

If NO, proceed to question 10
If YES, which service/s did you receive AFTER your stroke?
For each service, complete a separate line.

Community service codes
1 = Nursing Service
2 = Delivered Meals
3 = Housework Help
4 = Gardening/home maintenance
5 = Home respite
6 = Personal Carer
7 =Other Services, specify

Which service did your receive AFTER your stroke?							**How many times did you receive the service?**	**How many minutes per service?**	**Was this referred by your GP?**	
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐	☐☐☐	Yes ☐	No ☐
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐	☐☐☐	Yes ☐	No ☐
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐	☐☐☐	Yes ☐	No ☐
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	☐☐☐	☐☐☐	Yes ☐	No ☐

If "other" (code 7), please specify
☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

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10) HOME MODIFICATIONS AND OTHER COSTS

Has your home been modified as a consequence of your stroke? Yes ☐ No ☐ Unknown ☐
e.g. installation of rails, bathroom modifications, installation of ramp(s), kitchen modifications, etc.

If NO, check whether there are other costs. If NO, proceed to question 11.
If YES, please indicate the type of modifications/costs, who supplied the modifications and estimate any personal cost to you

Suppliers 1 = Hospital/rehabilitation centre 2 = Patient/family 3 = Veteran's Affairs 4 = Local Council 5 = Housing Commission 6 = Charity 7 = Other, specify

Type of modification/Cost	Who supplied the modification or service?							If supplier is "other", please specify	
☐ Rail(s) for steps/stairs	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Ramp(s)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Platform step(s)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Shower, bath and toilet rail(s)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Shower(s) modifications	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Toilet modification(s)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Remove/modify door(s) from shower/toilet/bath	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Kitchen modifications	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
☐ Other cost (specify below)									
Other cost - 1	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**
Other cost - 2	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐		**Cost to you/family* - $**

If total costs includes any aids, describe in brief below:

***If an overall cost is provided, please indicate type of modifications above, and provide the total cost here, INCLUSIVE of any known itemised costs listed above:**

Overall Cost $

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11) SPECIAL EQUIPMENT AND AIDS

Have you been given, hired or purchased any special equipment, aids or special food as a consequence of your stroke? Yes ☐ No ☐ Unknown ☐

Prompt: These may have been provided by Occupational Therapist or Physiotherapist. What about a....?
If NO, proceed to question 12.

Walking Aids
- Single point stick ☐
- Three or four point stick ☐
- Walking frame - pick up ☐
- Walking frame - wheelie ☐
- Walking frame - gutter (forearm support) ☐
- Crutch(es) ☐

Mobility Aids
- Manual wheelchair ☐
- Electric wheelchair/scooter ☐
- Car steering wheel knob ☐

Eating Aids
- Built-up cutlery ☐
- Plate guard ☐
- Non-slip mat ☐
- Special food e.g. NG/PEG ☐
  If yes, number of days used: ☐☐☐

Kitchen Aids
- Tap handles ☐
- Chopping board ☐
- Modified knife ☐
- Vitamiser/blender ☐
- Non-slip mat ☐

Lounge and Bedroom Equipment
- Chair platform/blocks raise ☐
- Cushion to relieve pressure ☐
- Special chair (NOT wheelchair) ☐
- Table - bedside/wheelie ☐
- Bed platform - block raise ☐
- Bedstick ☐
- Hospital bed (e.g. height/tilt adjust) ☐
- Mobile hoist/lifter ☐

Bathroom Equipment
- Over-toilet seat ☐
- Toilet surround ☐
- Bathroom and grooming aids ☐
- Shower chair/stool ☐
- Over-bath seat ☐
- Hand held shower ☐
- Non-slip mat ☐

Continence Aids
- Urine bottle ☐
- Bedpan ☐
- Commode ☐
- Incontinence sheet (bed protector) ☐
- Incontinence sheet (kylie/bluey) ☐
  If yes, number of days used: ☐☐☐
- Incontinence pads ☐
  If yes, number of days used: ☐☐☐
- Catheter ☐
  If yes, number of days used: ☐☐☐

General Aids
- Long handled aid ☐
- Blood pressure machine ☐
- Treadmill ☐
- Stationary bike ☐
- Intercom (portable) ☐
- Modified tap handles ☐
  If yes, number supplied ☐☐
- Personal Alarm ☐
  If yes, number of days supplied: ☐☐☐

Any other aids/equipment, specify:

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐
☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Were any of these aids and/or equipment provided following contact with your GP and/or allied health care provider in the community? Yes ☐ No ☐

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12) PRIVATE THERAPY

Have you received private treatment (as listed below) related to your original stroke or for problems relating to a recurrent stroke? *(NOT while a hospital inpatient)* Yes ☐ No ☐

			If YES, how many times?	Was this referred by your GP?	
Private Physiotherapy	Yes ☐	No ☐	☐☐	Yes ☐	No ☐
Private Speech Therapy	Yes ☐	No ☐	☐☐	Yes ☐	No ☐
Private Dietetics	Yes ☐	No ☐	☐☐	Yes ☐	No ☐
Private Naturopathy	Yes ☐	No ☐	☐☐	Yes ☐	No ☐
Private Osteopathy	Yes ☐	No ☐	☐☐	Yes ☐	No ☐
Private Chiropractor	Yes ☐	No ☐	☐☐	Yes ☐	No ☐
If other: please specify _____			☐☐	Yes ☐	No ☐

13) RESPITE CARE

13a) As a consequence of your stroke, have you been admitted to a respite bed in a day centre, nursing home or hospital? Yes ☐ No ☐ Unknown ☐
If NO, proceed to question 14.

13b) If YES, how many days of respite have you received since your stroke? ☐☐☐

14) EMPLOYMENT STATUS/ PAID WORK

14a) Were you working up to the time of your stroke? Yes ☐ No ☐ Unknown ☐

If YES, what was the nature of this work? Full time ☐ Part time ☐

How many hours did you work each week? ☐☐

14b) Are you receiving a disability or aged care pension? Disability Pension ☐ Aged Pension ☐ Neither ☐ Unknown ☐

If YES, what is the source of the pension? Private Super ☐ Government ☐

14c) Since the stroke, did you return to work? Yes ☐ No ☐ Unknown ☐

Did you initially return to normal hours or decreased hours? Normal ☐ Decreased ☐

If NO, what year did you cease work? ☐☐☐☐

14d) If you did return to work (yes to 14c), are you still working? Yes ☐ No ☐ Unknown ☐

If YES, what was the nature of this work? Full time ☐ Part time ☐

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15) GENERAL PRACTITIONER CARE

15a) Since your stroke, have you been to your general practitioner? Yes ☐ No ☐
If NO, go to question 16

15b) If YES, do you have a regular appointment schedule with your GP? e.g. weekly, monthly etc Yes ☐ No ☐
If NO, go to question 15d

15c) If YES, how often do you see your GP?

- Weekly ☐
- Fortnightly ☐
- Monthly ☐
- Every 3 months ☐
- Other, specify below ☐

15d) Why do you see your GP?

Medication prescription	Yes ☐	No ☐
Blood pressure check	Yes ☐	No ☐
Blood tests	Yes ☐	No ☐
Other, specify below	Yes ☐	No ☐

15e) Are you bulk billed for consultations? ☐ Yes ☐ No

16) MEDICAL TESTS FOR STROKE

Have you had any medical tests or other tests as a result of your stroke, or a recurrent stroke? Yes ☐ No ☐
DO NOT include tests performed as a hospital inpatient

CT Brain scan	Yes ☐	No ☐	How many times did you have this test?
MRI Brain scan	Yes ☐	No ☐	How many times did you have this test?
Carotid duplex	Yes ☐	No ☐	How many times did you have this test?
Blood test	Yes ☐	No ☐	How many times did you have this test?
Angiogram	Yes ☐	No ☐	How many times did you have this test?
Echocardiogram	Yes ☐	No ☐	How many times did you have this test?
Transesophageal echocardiogram	Yes ☐	No ☐	How many times did you have this test?
Other	Yes ☐	No ☐	Specify

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17) PRESCRIPTION MEDICATIONS

Name of Medication	Medication Code	Compliant?	Medication seen?
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐
		Yes ☐ No ☐	Yes ☐ No ☐

Do you receive prescription medication at the reduced pensioner rate? Yes ☐ No ☐

For compliance ask "Do you use this medicine as directed by your doctor?" Yes ☐ No ☐

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18) INFORMAL CARE

Definition of Informal Carer: That person who is most closely involved in helping the person with stroke to live independently at home. Any assistance provided by an informal carer is **over and above the assistance provided by any formal support service**. A carer is usually a spouse or other member of the family but may be a friend or neighbour.

If the person with stroke needs help with any activities of daily living, the carer is the person who provides most of this help beyond that provided by any formal support services. Assistance that a carer could provide includes: help with community tasks (e.g. shopping, errands, appointments, transport); help with domestic tasks (e.g. house cleaning, garden maintenance, laundry, meal preparation, washing up); help with personal care tasks (e.g. bathing, toileting, transferring, walking indoors, feeding). Supervision of daily activities to ensure safety should also be included as care.

18a) Over the last week, have you received any assistance with your daily activities from a carer? Yes ☐ No ☐

This might include assistance with community tasks (such as help with your banking, paying your bills, shopping or transportation), assistance with domestic tasks (such as cooking and cleaning) or assistance with personal care tasks (such as bathing, toileting and feeding)

If the answer is NO, no further questions are required in this section

18b) If the answer is YES, OVER THE LAST WEEK did you receive any assistance with community tasks? Yes ☐ No ☐

Examples of assistance with community tasks include: banking and paying bills; errands such as posting letters or making appointments; transport to appointments or social occasions; shopping; your carer might also 'check up' on you by visiting or phoning.

If NO, go to question 18c)

If YES, can you estimate how much time your carer spent helping you with these tasks during the last week? ☐☐☐.☐ Hours

18c) OVER THE LAST WEEK did you receive any assistance with domestic tasks? Yes ☐ No ☐

Examples of assistance with domestic tasks include: gardening; handyman tasks; grounds and home maintenance; housework such as laundry, cleaning, washing up; supervision of medication; supervision or assistance to walk outside.

If NO, go to question 18d)

If YES, can you estimate how much time your carer spent helping you with these tasks during the last week? ☐☐☐.☐ Hours

18d) OVER THE LAST WEEK did you receive any assistance with personal care tasks? Yes ☐ No ☐

Examples of assistance with personal care tasks include: eating; grooming; bathing; dressing; toilet use; help with incontinence pads; moving from bed to chair or chair to chair; walking inside the house including stairs.

If NO, you have finished the questions in this section

If YES, can you estimate how much time your carer spent helping you with these tasks during the last week? ☐☐☐.☐ Hours

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19) SPECIALIST CARE

Have you had a consultation with a medical specialist (as listed below) since your stroke/TIA? Yes ☐ No ☐

Please prompt the patient with the specialists listed on this page.

If NO, you have finished the questions.

			If YES, how many times since your stroke/TIA	Was this referred by your GP?
Neurologist	Yes ☐	No ☐		Yes ☐ No ☐
Cardiologist	Yes ☐	No ☐		Yes ☐ No ☐
Endocrinologist	Yes ☐	No ☐		Yes ☐ No ☐
Psychologist	Yes ☐	No ☐		Yes ☐ No ☐
Psychiatrist	Yes ☐	No ☐		Yes ☐ No ☐
Gastroenterologist	Yes ☐	No ☐		Yes ☐ No ☐
Rheumatologist	Yes ☐	No ☐		Yes ☐ No ☐
If other: please specify _____	Yes ☐	No ☐		Yes ☐ No ☐

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Run-In ID ☐☐☐☐

CONSENT OBTAINED Yes ☐ No ☐

INTERVIEWER INITIALS ☐☐

* COMPULSORY FIELDS (1, 3, 5, 6, 9, 10, 18 abcd, 42)

DEMOGRAPHICS

*** 1) Sex** Male ☐ Female ☐

2) Initials First ☐☐ Surname ☐☐

*** 3) Date of Birth** ☐☐ / ☐☐ / ☐☐☐☐

4) Medicare Number ☐☐☐☐☐☐☐☐☐☐

*** 5) Final Participant Status**
- First-ever in a life-time stroke ☐
- Recurrent Stroke ☐
- TIA ☐

*** 6) Final Diagnosis of Event**
- Ischaemic Stroke ☐
- Intracerebral Haemorrhage ☐
- TIA ☐

HOSPITAL/REHABILITATION

7) Hospital ☐☐☐☐☐☐☐☐☐☐

8) Hospital UR ☐☐☐☐☐☐☐

*** 9) Admission Date** ☐☐ / ☐☐ / ☐☐☐☐

*** 10) Discharge Date (if HITH, date sent home)** ☐☐ / ☐☐ / ☐☐☐☐

Date Hospital in the Home (HITH) completed ☐☐ / ☐☐ / ☐☐☐☐

11) Rehabilitation ☐☐☐☐☐☐☐☐☐☐

12) Rehabilitation UR ☐☐☐☐☐☐☐

13) Admission Date ☐☐ / ☐☐ / ☐☐☐☐

14) Discharge Date ☐☐ / ☐☐ / ☐☐☐☐

STROKE HISTORY

Date and time (24 hour clock) of: Time (24 hour clock)

15) Stroke Onset ☐☐ / ☐☐ / ☐☐☐☐ ☐☐☐☐

16) Maximal Deficit ☐☐ / ☐☐ / ☐☐☐☐ ☐☐☐☐

History of onset and main symptoms:

_____

_____

_____

_____

_____

_____

_____

_____

17) Summarise stroke symptoms:

a) _____

b) _____

c) _____

d) _____

e) _____

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18) Medical History of:

	Yes	No	Diagnosed during present visit	Unknown
* a) Diabetes	☐	☐	☐	☐
* b) Hypertension	☐	☐	☐	☐
* c) Atrial Fibrillation	☐	☐	☐	☐
* d) High Cholesterol	☐	☐	☐	☐
e) Stroke	☐	☐	☐	☐
f) Ischaemic Heart Disease	☐	☐	☐	☐
g) Heart Failure	☐	☐	☐	☐
h) Rheumatic fever	☐	☐	☐	☐
i) Pacemaker	☐	☐	☐	☐
j) Clinically Relevant Carotid Stenosis	☐	☐	☐	☐

19) Other relevant history/intercurrent illness: (Specify)

_____

_____

_____

_____

20) Alcohol Use

Never Drink Alcohol ☐
Previously drunk alcohol ☐
Currently drink alcohol ☐

CEREBRAL IMAGING

21a) Was a CT scan performed? Yes ☐ No ☐

21b) Date of initial CT scan ☐☐ / ☐☐ / ☐☐☐☐

21c) Date Image used ☐☐ / ☐☐ / ☐☐☐☐

21d) Number of days after stroke onset ☐☐

22a) Was an MRI scan performed? Yes ☐ No ☐

22b) Date of Initial M.R.I. ☐☐ / ☐☐ / ☐☐☐☐

22c) Date Image used ☐☐ / ☐☐ / ☐☐☐☐

22d) Number of days after stroke onset ☐☐

23) CT/MR FINDINGS:
(Visual or Report)

Cerebral Infarct ☐
Intracerebral Haemorrhage ☐
Subarachnoid Haemorrhage ☐
No Abnormalities detected ☐

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ELECTROCARDIOGRAPH

24) Was an ECG performed? Yes ☐ No ☐

25) Was the ECG abnormal? Yes ☐ No ☐

26) Is there ECG evidence of AF? Yes ☐ No ☐

Date Observed ☐☐ / ☐☐ / ☐☐☐☐

CAROTID DOPPLER

27) Was a carotid doppler test done? Yes ☐ No ☐

Date Observed ☐☐ / ☐☐ / ☐☐☐☐

	RIGHT % Stenosis	LEFT % Stenosis
a) Common carotid artery		
b) Internal carotid artery		
c) External carotid artery		
d) Vertebral artery		

BLOOD TEST (NOTE: all blood tests are taken from the last date of testing)

28)	Haemoglobin		Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**g/l**
29)	Glucose	Not tested ☐ Tested ☐	Non-fasting ☐ Fasting ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**mmol/l**
30)	Total Cholesterol	Not tested ☐ Tested ☐	Non-fasting ☐ Fasting ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**mmol/l**
31)	HDL Cholesterol	Not tested ☐ Tested ☐	Non-fasting ☐ Fasting ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**mmol/l**
32)	LDL Cholesterol	Not tested ☐ Tested ☐	Non-fasting ☐ Fasting ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**mmol/l**
33)	Triglyceride		Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**mmol/l**
34)	HbA1c		Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**%**
35)	Creatinine		Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**umol/l**
36)	Troponin (highest reading)		Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐.☐☐	**ug/l**
37)	Creatinine Kinase (highest reading)		Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐☐.☐	**u/l**
38)	**Warfarin Therapy** No ☐ Yes ☐	INR	Not tested ☐ Tested ☐	Date of test ☐☐ / ☐☐ / ☐☐☐☐	☐☐☐.☐	**ratio**

STAND FIRM for Stroke Patients
Run-In

ID ☐☐☐☐

HEIGHT AND WEIGHT

DATE HEIGHT AND WEIGHT ASSESSED ☐☐ / ☐☐ / ☐☐☐☐

39) Height stadiometer ☐ 2 x arm length ☐ *(Mid sternum to finger tip)* ☐☐☐.☐ **cm**

40) Weight *(If too large for scale code 999.9)* ☐☐☐.☐ **kg**

DISCHARGE MEDICATIONS

41) Medication Name	Medication Code	Medical Condition	Antihypertensive Class	Duration (Days)
a)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
b)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
c)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
d)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
e)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
f)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
g)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
h)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
i)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
j)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
k)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
l)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
m)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
n)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐
o)	☐☐☐☐☐	☐☐☐.☐	☐	☐☐☐☐☐

Antihypertensive Class
1 = Diuretics
2 = β- Blockers
3 = Calcium Channel Blockers
4 = ACE Inhibitors
5 = Vasodilators
6 = Others

REASON FOR NON-INCLUSION

*** 42)**

☐ Subject died
☐ Subject refused to follow study protocol
☐ Subject went to high level care

STAND FIRM for Stroke Patients
Serious Adverse Events

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐ **DATE OF ASSESSMENT** ☐☐ / ☐☐ / ☐☐☐☐

PERSON RESPONDING

Index case ☐ Other relative ☐
Spouse/partner ☐ Friend/Associate/Neighbour ☐
Sibling ☐ Carer, e.g. nurse ☐
Son/Daughter ☐ Other, unspecified ☐
Parent ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household ☐☐
Not living with index ☐
Prof carer in nursing home/hostel ☐ If living apart, note number of contacts per week ☐☐

To:	STAND FIRM Office	**Date:**	
Fax:	03 9902 4245	**From:**	
Address:	Epidemiology and Prevention Unit Stroke and Aging Research Centre (STARC) Department of Medicine, Monash Medical Centre Southern Clinical School, Monash Medical Centre Level 1/43-51 Kanooka Grove Clayton, Victoria, 3168	**Fax:** **Address:**	
Phone:	03 9594 7578	**Phone:**	

Please transcribe the AE number
(located in the far left column of the AE form)

AE Number ☐☐

SERIOUS ADVERSE EVENT DETAILS

Please attach the following documents (as appropriate - cross box if attached):

Adverse event page - One of these pages MUST be attached ☐
Demographics from Baseline ☐
Death report ☐
Death certificate ☐
Autopsy report (for death) ☐
Relevant laboratory reports (see requirements) ☐
Relevant diagnostic reports (see requirements) ☐
Discharge summary/referral letter (for hospitalisation) ☐
Other ☐

For a guide to relevant reports, please refer to completion instructions
Ensure that all attached information is identified by the site and patient number ONLY.

STAND FIRM for Stroke Patients
Serious Adverse Events

ID ☐☐☐☐

This Adverse Event is serious because it: (check one box only)

Resulted in death ☐

Is/was life threatening ☐

Requires/required inpatient hospitalisation** ☐

Resulted in persistent or significant disability/incapacity ☐

Admission Date ☐☐ / ☐☐ / ☐☐☐☐

Discharge Date ☐☐ / ☐☐ / ☐☐☐☐

**If hospitalised, complete admission and discharge dates

Time (24 hour clock)

When did the AE meet the criteria for serious? ☐☐ / ☐☐ / ☐☐☐☐ ☐☐☐☐

When did you become aware of the event? ☐☐ / ☐☐ / ☐☐☐☐ ☐☐☐☐

Was this serious adverse event unexpected? Yes ☐ No ☐

Date of patient's first stroke in STAND FIRM ☐☐ / ☐☐ / ☐☐☐☐

Description of Event:
(include onset, symptoms, course, diagnostic investigations, results, treatment of the event and any other relevant comments)

STAND FIRM for Stroke Patients
Serious Adverse Events

ID

Description of Event:
(include onset, symptoms, course, diagnostic investigations, results, treatment of the event and any other relevant comments)

Assessor's Initials

Assessor's Signature

Date / /

STAND FIRM for Stroke Patients
Serious Adverse Events

ID

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STAND FIRM for Stroke Patients
Your Health and Your Life & HAD

ID ☐☐☐☐

INTERVIEWER INITIALS ☐☐ **DATE OF ASSESSMENT** ☐☐ / ☐☐ / ☐☐☐☐

STATUS Patient ☐ Carer ☐

TIME Baseline ☐ 3 month ☐ 1 year ☐ 2 year ☐

PERSON RESPONDING

Index case ☐ Other relative ☐
Spouse/partner ☐ Friend/Associate/Neighbour ☐
Sibling ☐ Carer, e.g. nurse ☐
Son/Daughter ☐ Other, unspecified ☐
Parent ☐

Questionnaire completed with assistance e.g. read aloud to case Yes ☐ No ☐

FOR PROXIES **AGE OF RESPONDENT** ☐☐ **SEX OF RESPONDENT** Male ☐ Female ☐

LIVING ARRANGEMENT OF RESPONDENT

Living with index ☐ If living with index, note number of years living in the same household ☐☐
Not living with index ☐
If living apart, note number of contacts per week ☐☐
Prof carer in nursing home/hostel ☐

This questionnaire asks six questions about your *(his/her)* everyday life. Please answer each question. Read the instructions in each question and then answer by ticking the box next to the sentence which describes you *(him/her)* best. When answering the questions, it may help to think about the things you *(he/she)* have *(has)* done over the past week. Compare what you *(he/she)* can do with what someone like you *(him/her)* who is in good health can do.

GETTING AROUND

Think about how you *(he/she)* get*(s)* from one place to another, using any help, aids or means of transport that you *(he/she)* normally have *(has)* available.

1) DOES YOUR (HIS/HER) HEALTH STOP YOU (HIM/HER) FROM GETTING AROUND? *TICK ONE BOX ONLY*

NOT AT ALL: You go (He/she goes) everywhere you (he/she) want(s) to, no matter how far away. ☐

VERY SLIGHTLY: You go (He/she goes) most places you (he/she) want(s) to, but not all. ☐

QUITE A LOT: You (He/she) get(s) out of the house, but not far away from it. ☐

VERY MUCH: You don't (He/she doesn't) go outside, but you (he/she) can move around from room to room indoors. ☐

ALMOST COMPLETELY: You are (He/she is) confined to a single room, but can move around in it. ☐

COMPLETELY: You are (He/she is) confined to a bed or a chair. You (He/she) cannot move around at all. There is no one to move you (him/her). ☐

LOOKING AFTER YOURSELF (HIMSELF/HERSELF)

Think about things like housework, shopping, looking after money, cooking, laundry, getting dressed, washing, shaving and using the toilet.

2) DOES YOUR (HIS/HER) HEALTH STOP YOU (HIM/HER) LOOKING AFTER YOURSELF (HIMSELF/HERSELF)? *TICK ONE BOX ONLY*

NOT AT ALL: You (He/she) can do everything yourself (himself/herself). ☐

VERY SLIGHTLY: Now and then you (he/she) need(s) a little help. ☐

QUITE A LOT: You (He/she) need(s) help with some tasks (such as heavy housework or shopping), but not more than once a day. ☐

VERY MUCH: You (He/she) can do some things, but you (he/she) need(s) help more than once a day. You (He/she) can be left alone for a few hours. ☐

ALMOST COMPLETELY: You (He/she) need(s) help to be available all the time. You (he/she) cannot be left alone safely. ☐

COMPLETELY: You (He/she) need(s) help with everything. You (he/she) need(s) constant attention, day and night. ☐

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WORK AND LEISURE

Think about things like work (paid or not), housework, gardening, sports, hobbies, going out with friends, travelling, reading, looking after children, watching television and going on holidays.

3) DOES YOUR (HIS/HER) HEALTH LIMIT YOUR (HIS/HER) WORK OR LEISURE ACTIVITIES?

TICK ONE BOX ONLY

NOT AT ALL:	You (He/she) can do everything you (he/she) want(s) to.	☐
VERY SLIGHTLY:	You (He/she) can do almost all the things you (he/she) want(s) to do.	☐
QUITE A LOT:	You (He/she) find(s) something to do almost all the time, but cannot do some things for as long as you (he/she) would like.	☐
VERY MUCH:	You are (He/she is) unable to do a lot of things, but can find something to do most of the time.	☐
ALMOST COMPLETELY:	You are (He/she is) unable to do most things, but can find something to do some of the time.	☐
COMPLETELY:	You (He/she) sit(s) all day doing nothing. You (He/she) cannot keep yourself (himself/herself) busy or take part in any activities.	☐

GETTING ON WITH PEOPLE

Think about family, friends and people you (he/she) might meet during a normal day.

4) DOES YOUR (HIS/HER) HEALTH STOP YOU (HIM/HER) GETTING ON WITH PEOPLE? *TICK ONE BOX ONLY*

NOT AT ALL:	You (He/she) get(s) on well with people, see(s) everyone you (he/she) want(s) to see, and meet(s) new people.	☐
VERY SLIGHTLY:	You (He/she) get(s) on well with people, but your (his/her) social life is slightly limited.	☐
QUITE A LOT:	You are (He/she is) fine with people you (he/she) know(s) well, but you (he/she) feel(s) uncomfortable with strangers.	☐
VERY MUCH:	You are (He/she is) fine with people you (he/she) know(s) well, but you have (he/she has) few friends and little contact with neighbours. Dealing with strangers is very hard.	☐
ALMOST COMPLETELY:	Apart from the person who looks after you (him/her), you (he/she) see(s) no one. You have (He/she has) no friends and no visitors.	☐
COMPLETELY:	You don't (He/she doesn't) get on with anyone, not even people who look after you him/her).	☐

AWARENESS OF YOUR (HIS/HER) SURROUNDINGS

Think about taking in and understanding the world around you (him/her), and finding your (his/her) way around in it.

5) DOES YOUR (HIS/HER) HEALTH STOP YOU (HIM/HER) UNDERSTANDING THE WORLD AROUND YOU (HIM/HER)?

TICK ONE BOX ONLY

NOT AT ALL:	You (He/she) fully understand(s) the world around you (him/her). You (He/she) see(s), hear(s), speak(s), and think(s) clearly, and your (his/her) memory is good.	☐
VERY SLIGHTLY:	You have (He/she has) problems with hearing, speaking, seeing or your (his/her) memory, but these do not stop you (him/her) doing most things.	☐
QUITE A LOT:	You have (He/she has) problems with hearing, speaking, seeing or your (his/her) memory, which make(s) life difficult a lot of the time. But, you (he/she) understand(s) what is going on.	☐
VERY MUCH:	You have (He/she has) great difficulty understanding what is going on.	☐
ALMOST COMPLETELY:	You are (He/she is) unable to tell where you (he/she) are (is) or what day it is. You (He/she) cannot look after yourself (himself/herself) at all.	☐
COMPLETELY:	You are (He/she is) unconscious, completely unaware of anything going on around you (him/her).	☐

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AFFORDING THE THINGS YOU (HE/SHE) NEED(S)

Think about whether health problems have lead to any extra expenses, or have caused you (him/her) to earn less than you (he/she) would if you (he/she) were (was) healthy.

6) ARE YOU (IS HE/SHE) ABLE TO AFFORD THE THINGS YOU (HE/SHE) NEED(S)? *TICK ONE BOX ONLY*

YES, EASILY:	You (He/she) can afford everything you (he/she) need(s). You have (He/she has) easily enough money to buy modern labour-saving devices, and anything you (he/she) may need because of ill-health.	☐
FAIRLY EASILY:	You have (He/she has) just about enough money. It is fairly easy to cope with expenses caused by ill-health.	☐
JUST ABOUT:	You are (He/she is) less well-off than other people like you (him/her); however, with sacrifices you can get by without help.	☐
NOT REALLY:	You (He/she) only have (has) enough money to meet your (his/her) basic needs. You are (He/she is) dependent on government benefits for any extra expenses you (he/she) have (has) because of ill-health.	☐
NO:	You are (He/she is) dependent on government benefits, or money from other people or charities. You (He/she) cannot afford things you (he/she) need(s).	☐
ABSOLUTELY NOT:	You have (He/she) has no money at all and no government benefits. You are (He/she is) dependent on charity for your (his/her) most basic needs.	☐

HOSPITAL ANXIETY AND DEPRESSION (HAD) SCALE + IRRITABILITY

IMPORTANT NOTE FOR ASSESSOR: Do not complete this scale if the person is unable to communicate their answers. An interpreter may be used.

Has the HAD been completed? Yes ☐ No ☐ **Rating** Reliable ☐ Possible/Definitely Unreliable ☐ **Completed with assistance?** Yes ☐ No ☐

This Questionnaire is to help the doctors to know how you are feeling at present. Read each item and TICK the response that best shows how you are feeling now, or have been feeling in the last day or two.

1. I FEEL CHEERFUL *TICK ONE BOX ONLY*

- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

2. I CAN SIT AT EASE AND FEEL RELAXED *TICK ONE BOX ONLY*

- Definitely ☐
- Usually ☐
- Not often ☐
- Not at all ☐

3. I FEEL AS IF I AM SLOWED DOWN *TICK ONE BOX ONLY*

- Nearly all of the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

4. I LOSE MY TEMPER AND SHOUT OR SNAP AT OTHERS *TICK ONE BOX ONLY*

- Yes, definitely ☐
- Yes, sometimes ☐
- No, not much ☐
- No, not at all ☐

5. I FEEL TENSE OR 'WOUND UP' *TICK ONE BOX ONLY*

- Most of the time ☐
- A lot of the time ☐
- From time to time, occasionally ☐
- Not at all ☐

6. I FEEL LIKE HARMING MYSELF *TICK ONE BOX ONLY*

- Yes, definitely ☐
- Yes, sometimes ☐
- No, not much ☐
- No, not at all ☐

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7. I STILL ENJOY THE THINGS I USED TO ENJOY

TICK ONE BOX ONLY

- Definitely as much ☐
- Not quite so much ☐
- Only a little ☐
- Not at all ☐

8. I AM PATIENT WITH OTHER PEOPLE

TICK ONE BOX ONLY

- All of the time ☐
- Most of the time ☐
- Some of the time ☐
- Hardly ever ☐

9. I GET A SORT OF FRIGHTENED FEELING AS IF SOMETHING AWFUL IS ABOUT TO HAPPEN

TICK ONE BOX ONLY

- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

10. I GET ANGRY WITH MYSELF OR CALL MYSELF NAMES

TICK ONE BOX ONLY

- Yes, definitely ☐
- Sometimes ☐
- Not often ☐
- No, not at all ☐

11. I CAN LAUGH AND SEE THE FUNNY SIDE OF THINGS

TICK ONE BOX ONLY

- As much as I always could ☐
- Not quite so much now ☐
- Definitely not so much now ☐
- Not at all ☐

12. I FEEL I MIGHT LOSE CONTROL AND HIT OR HURT SOMEONE

TICK ONE BOX ONLY

- Sometimes ☐
- Occasionally ☐
- Rarely ☐
- Never ☐

13. I GET A SORT FRIGHTENETED FEELING LIKE BUTTERFLIES IN THE STOMACH

TICK ONE BOX ONLY

- Not at all ☐
- Occasionally ☐
- Quite often ☐
- Very often ☐

14. THE THOUGHT OF HURTING MYSELF OCCURS TO ME

TICK ONE BOX ONLY

- Sometimes ☐
- Not very often ☐
- Hardly ever ☐
- Not at all ☐

15. I CAN ENJOY A GOOD BOOK OR RADIO OR TV PROGRAMME

TICK ONE BOX ONLY

- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

16. PEOPLE UPSET ME SO THAT I FEEL LIKE SLAMMING DOORS OR BANGING ABOUT

TICK ONE BOX ONLY

- Yes, often ☐
- Yes, sometimes ☐
- Only occasionally ☐
- Not at all ☐

17. I GET SUDDEN FEELINGS OF PANIC

TICK ONE BOX ONLY

- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

18. LATELY I HAVE BEEN GETTING ANNOYED WITH MYSELF

TICK ONE BOX ONLY

- Very much so ☐
- Rather a lot ☐
- Not much ☐
- Not at all ☐

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19. WORRYING THOUGHTS GO THROUGH MY MIND

TICK ONE BOX ONLY

- A great deal of the time ☐
- A lot of the time ☐
- From time to time but not too often ☐
- Only occasionally ☐

20. I HAVE LOST INTEREST IN MY APPEARANCE

TICK ONE BOX ONLY

- Definitely ☐
- I don't take so much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

21. I FEEL RESTLESS AS IF I HAVE TO BE ON THE MOVE

TICK ONE BOX ONLY

- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

22. I LOOK FORWARD WITH ENJOYMENT TO THINGS

TICK ONE BOX ONLY

- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

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ID

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[Appendix F] STANDFIRM Trial – Example SAE Adjudication Form

STAND FIRM Outcome Adjudication
Serious Adverse Events

ADJUDICATOR INITIALS J S **SAE NO** 0 8 7 **PATIENT IDNO** 4 2 3 6

Provisional diagnosis (according to supporting documents)

Stroke/cerebrovascular accident followed by death

Opinion on provisional diagnosis: Agree ☐ Disagree ■ Unable to ascertain ☐

If you disagree with the provisional diagnosis, please provide below your opinion on cause of the event

Cerebral infarct

Please specify below the type of event based on the information provided in the supporting documents

Fatal events (deaths)

- Death due to stroke ■
- Death due to myocardial infarction ☐
- Sudden cardiac death ☐
- Death due to heart failure ☐
- Death due to other cardiovascular cause ☐
- Non-cardiovascular death ☐
- Undetermined cause of death ☐

Non-fatal events

- Acute myocardial infarction ☐
- Angina ☐
- Heart failure ☐
- Ischaemic stroke ☐
- Haemorrhagic stroke ☐
- Undetermined stroke ☐
- Transient Ischaemic Attack ☐
- Atrial fibrillation ☐
- Cardiovascular interventions ☐
- Non-cardiovascular events ☐
- Unable to be determined ☐

If you are unable to ascertain diagnosis, please specify below if further documentation may clarify this event

Signature: _____ **Date** 0 5 / 0 6 / 2 0 1 5

Additional comments:

[Appendix G] Variables Uploaded to the SURE From Each Dataset

Full list of variables from all datasets to be brought together (*AIHW Project EO2016/4/325*)

AIHW (Australian Institute of Health and Welfare)

Medicare Benefits Schedule (MBS)

- MBS item number
- MBS item description
- Date of service

National Death Index (NDI)

- Date of death
- State/territory the death was registered in
- Underlying cause of death code
- Codes for other causes of death

Pharmaceutical Benefits Scheme (PBS) and Repatriation PBS (RPBS)

- ATC code
- PBS item number
- Drug name
- Form and strength
- Form category/type
- Date of supply
- Date of prescribing
- Patient category
- Patient contribution
- Net benefit
- Number of dispensings/scripts
- Repeat prescription indicator
- Regulation 24 indicator
- Under co-payment indicator

VDL (Victorian Data Linkages)

As required by the data custodian, all dates within the VDL output to SURE will be encrypted as 'number of days from a set date' (unknown to researchers).

Victorian Admitted Episodes Dataset (VAED)

- Sex
- Date of admission (*encrypted*)
  - Month of admission (*not encrypted*)
  - Year of admission (*not encrypted*)
- Date of separation (*encrypted*)
  - Month of separation (*not encrypted*)
  - Year of separation (*not encrypted*)
- Length of stay
- Length of stay type
- Same day separation flag

Victorian Emergency Minimum Dataset (VEMD)

- Sex
- Date of arrival (*encrypted*)
  - Arrival month (*not encrypted*)
  - Arrival year (*not encrypted*)
- Date of departure (*encrypted*)
  - Departure month (*not encrypted*)
  - Departure year (*not encrypted*)
- Length of stay in ED

Victorian Admitted Episodes Dataset (VAED) – Restricted Data

- Age in years
- Separation mode
- ICD-10-AM Diagnosis (all codes)
- ICD-10-AM Procedure (all codes)

Victorian Emergency Minimum Dataset (VEMD) – Restricted Data

- Age in years
- Procedures (all codes)
- ICD-10-AM Diagnosis codes (all codes)

Variables from STAND FIRM (Shared Team Approach between Nurses and Doctors For Improved Risk factor Management) trial.
Please see accompanying "*[STAND FIRM] Variables to upload to SURE.docx*" document for full list containing descriptions, rationale, names and summary table with assessment time points for each variable.

Dates

(1) Date of stroke
(2) Date of dropout (if applicable)
(3) Date of baseline assessment
(4) Date of 3 month assessment
(5) Date of 12 month assessment
(6) Date of 24 month assessment

Demographics/Measurements

- **Demographics**
  - Age (at baseline/3/12/24 months)
  - Sex
  - Marital status
  - Highest completed level of education
  - Social class
  - Pre-stroke and current living arrangements
- **Anthropometrics**
  - Body mass index (BMI)
  - Waist-hip ratio (WHR)
- **Medication use**
  - Use of antihypertensive medication
  - Pensioner rate for medications or not
  - Medication tracking behaviour
- **Blood-related assessments**
  - Systolic blood pressure (SBP)
  - Diastolic blood pressure (DBP)
  - Total cholesterol
  - High-density lipoprotein (HDL) cholesterol

Serious Adverse Events (SAEs self-reported and adjudicated)

- Date of SAE admission
- Date of SAE discharge
- Reason adverse event is serious
- Hospitalisation type
- Death type

Patient History (self-report/health records)

- Comorbidities history
- Alcohol use history
- Smoking history

Health/management Assessments

- Assessment of Quality of Life (AQoL)
- London Handicap Scale (LHS)
- Hospital Anxiety and Depression Scale (HADS) and irritability
- Modified Rankin Scale (mRS)
- Exercises regularly or not
- Average vegetable and fruit consumption
- Adds salt to their food or not
- Working at time of stroke or not
- Worked after stroke or not
- Currently working or not

STAND FIRM trial variables

- **Run-In**
  - Qualifying stroke/TIA event type
  - Diagnosis type of qualifying stroke
- **Intervention or usual care group**
- Reason for dropout
- Total number of education contacts (at 24 months)
- Feedback on quality of after-stroke care received (at 24 months)
- Framingham Risk Score (FRS; health outcome)
  - Variables needed to calculate FRS: Age/SBP/total cholesterol/HDL cholesterol/smoking status/diabetes status.

Other variables

- Australian Statistical Geography Standard Remoteness Areas (ASGS-RA)
- Index of Relative Socio-economic Disadvantage (IRSD)
- Index of Relative Socio-economic Advantage and Disadvantage (IRSAD)

[Appendix H] STANDFIRM Trial – Data Dictionary

Data Dictionary for variables to be uploaded from **STAND FIRM** to **SURE**

- Data will be uploaded as two complete dataset in the form of STATA13 data (.dta) and/or Microsoft Excel 2013 (.xlsx) files, in the following format:

(Blue) Dataset 1 – STAND FIRM variables	(Green) Dataset 2 – STAND FIRM Serious Adverse Events (SAEs)

• Wide format.
• Each observation/row corresponds with an individual.
  ○ Uniquely identified by STAND FIRM ID numbers.
	• Long format.
	• May have duplicate STAND FIRM ID numbers.
	• Each observation/row corresponds with a single serious adverse event (SAE) that occurred within the 2-year follow-up period.
	  ○ Uniquely identified by admission/discharge dates with a STAND FIRM ID number.

- All STAND FIRM ID numbers will be replaced with randomly generated project specific IDs by the AIHW.
  - This mapping is unknown to researchers and will allow for linkage of this data to the datasets in the Secure Unified Research Environment (SURE) system.
- Variable names in the datasets to be uploaded to the SURE system may have the following prefixes based on which follow-up time point they were assessed at:
  - "**SF_**", time point not required; "**SFPS_**", pre-stroke; "**SFB_**", baseline; "**SF3_**", 3 months; "**SF6_**", 6 months; "**SF12_**", 12 months; "**SF24_**", 24 months.
- Missing data will be represented with "." in each STATA13 data field and/or blank in Microsoft Excel 2013 cells.

(B) (B/12/24) (24)	**----------STAND FIRM variables----------**	
Description and Rationale	**Possible Values**	**Variable Names in** ***STAND FIRM*** ¦ ***SURE***
Allocated to intervention or usual care group • To distinguish between those who were allocated to the intervention (GP management plan + regular nurse-led face-to-face and telephone education) and usual care groups.	0 = Usual Care group 1 = Intervention group	SF_Intervention
Australian Statistical Geography Standard Remoteness Areas (ASGS-RA) • STAND FIRM postcodes will be mapped against concordant ASGS-RA values from the Australian Bureau of Statistics (ABS) for measures of remoteness (accessibility to goods and services). • The ASGS-RA geographical classifications are essentially a measure of a location's level of access to goods and services. This remoteness measure is calculated using Accessibility/Remoteness Index of Australia (ARIA+) scores, where the lower the ARIA+ score for a location, the better its level of access to goods and services. • This could be an important proxy measure of access to health services to be accounted for in our health outcome analyses.	1 = Major cities of Australia 2 = Inner regional Australia 3 = Outer regional Australia 4 = Remote Australia 5 = Very remote Australia 6 = Migratory	SFB_ASGS_RA

(1) Index of Relative Socio-economic Disadvantage (IRSD) and **(2) Index of Relative Socio-economic Advantage and Disadvantage** (IRSAD) • STAND FIRM postcodes will be mapped against concordant IRSD/IRSAD scores from the Australian Bureau of Statistics (ABS) for measures of socioeconomic status (relative measures of advantage/disadvantage). • The IRSD/IRSAD scores are ordinal and are a weighted combination of Census variables for a particular Statistical Area Level 1 (SA1). These scores standardised to a distribution where the mean equals 1000 and the standard deviation is 100 for SA1s. For areas larger than SA1s (e.g. postcodes) the scores are a population weighted aggregation of constituent SA1 scores. • These scores are measures of socioeconomic position that will need to be accounted for in our health outcome analyses. • The percentiles and deciles will allow for us to create our own groups measured against Australia or Victoria, such as quartiles (which contains 25% of areas) or quintiles. ***Note:*** *All participant postcodes in STAND FIRM have an allocated Postal Area Code (POA).*	**(1) Index Score** • Ordinal • IRSD values = 506 – 1156 • IRSAD values = 588 – 1191	SFB_IRSDscore SFB_IRSADscore
	(2) Rank within Australia • Ordinal, percentiles • Percentiles: 1 – 100	SFB_IRSDpercentile SFB_IRSADpercentile
	(3) Rank within Victoria • Ordinal, deciles • Deciles: 1 – 10	SFB_IRSDdecile SFB_IRSADdecile
Total number of education contacts • These were received by those in the intervention group (Consisted of three contacts: two face-to-face visits and one telephone call) ○ **Number of face-to-face education visits** (occurred at 3, 12 and 24 months) ○ **Number of telephone calls** (occurred at 6 and 18 months) • Acts as a measure of the intensity/dosage of the education component of the STAND FIRM intervention.	**Total number of education contacts** • Count (out of 5)	SF24_totalcontacts
	Number of education visits • Count (out of 3)	SF24_educontacts
	Number of telephone calls • Count (out of 2)	SF24_telecontacts
(1) Date of stroke **(2) Date of dropout** **(3) Date of baseline assessment** **(4) Date of 3 month assessment** **(5) Date of 12 month assessment** **(6) Date of 24 month assessment** • These dates are required to ○ Determine the timing of outcomes of interest, such as: ▪ If participants were on a CDM plan prior to their stroke or took up a CDM plan after their stroke. ▪ How many cardiovascular-related hospitalisations/deaths occurred before each participants' 12 and 24 month assessments? ▪ The timing of participant drop-outs in the study (e.g. after 12 month assessment and before 18-month telephone education call). ○ Validate self-reported dates captured in STAND FIRM (i.e. >3 day disparity) ○ Correct possible administrative errors in VDL data received	**Derived from STAND FIRM variables:** (*Run-In*) AdmDateH8 (*Dropout*) DROPOUT_DAT (*Patient_History*) (*Time = 0*) DOASS (*PatientHistoryFU*) (*Time = 1 / 2 / 3*) DOASS	DD/MM/YYYY ***Note:*** *Follow-up interviews were based on baseline date of assessments and not date of stroke/admission* . ***Note:*** *3 month assessment dates should be validated against Costs and Medication Knowledge Forms' DOASS.*	SF_DOStroke SF_DODO SFB_DOASS SF3_DOASS SF12_DOASS SF24_DOASS

(B / 12m / 24m) (Time = 0 / 2 / 3)	----------Assessment of Quality of Life----------				
Description and Rationale	**Possible Values**	**Variable Names**			
		STAND FIRM *derived from:*	***SURE***		
			Baseline	***12 months***	***24 months***
Assessment of Quality of Life (**AQoL**) (consists of 5 dimensions) **total utility score** **(1)** Illness **(2)** Independent Living **(3)** Social Relationships **(4)** Physical Senses **(5)** Psychological Well-being • The AQoL utility scores are derived from dimensions 2 – 5 using formulae that account for the individual weighting of each item within each overall dimension. • The AQoL utility scores can be used to calculate quality-adjusted life years (QALYs) as a measure of disease burden for use in economic evaluation.	**Total AQoL utility score (dimensions 2-5)** • Out of 1 (up to 4 decimal places)	—	SFB_AQoL	SF12_AQoL	SF24_AQoL
	Utility score for each of the 5 dimensions • Out of 1 (up to 4 decimal places) ***Note:*** *Algorithm required to calculate the total and individual dimensions' weighted scores.*	ILLMEDS1 ILLAIDS2 ILLDOC3	SFB_AQoL1	SF12_AQoL1	SF24_AQoL1
		INDHLP4 INDTASKS5 INDHOM6	SFB_AQoL2	SF12_AQoL2	SF24_AQoL2
		SOCHLTH7 SOCFRDS8 SOCFAM9	SFB_AQoL3	SF12_AQoL3	SF24_AQoL3
		PHYSVIS10 PHYSHEAR11 PHYSCOMM12	SFB_AQoL4	SF12_AQoL4	SF24_AQoL4
		PSYCHSLP13 PSYCHFEEL14 PSYCHPAIN15	SFB_AQoL5	SF12_AQoL5	SF24_AQoL5

(3m / 12m / 24m) (Time = 1 / 2 / 3)	----------Post-Acute Costs of Stroke----------				
Description and Rationale	**Possible Values**	**Variable Names**			
		STAND FIRM	***SURE***		
			3 months	***12 months***	***24 months***
(1) Pre-stroke Living Arrangements **(2) Current Living Arrangements**	1 = Own house/flat – alone 2 = Own house/flat – family/relative/friend 3 = Home of relative/friend 4 = Supported residential service (SRS)	Prestroke_liv	SF3_Prestrokeliv	—	—

• Living arrangements at each time point could relate to overall disability and outcome.	5 = Hostel 6 = Nursing Home 7 = Other 8 = Unknown ***Note:*** *Follow-up (Prestroke_liv) answers will be used to verify baseline answers.*	PostStrkLiv	SF3_Currentstrokeliv	SF12_Currentstrokeliv	SF24_Currentstrokeliv
(1) Working at time of stroke **(2) Worked since stroke** **(3) Currently working** • Important measure of stroke recovery	1 = Yes 0 = No 9 = Unknown ***Note:*** *Follow-up (WORKPRIOR) answers will be used to verify baseline answers.*	WORKPRIOR	SF3_Workprior	—	—
		WORKPOST	SF3_Workpost	SF12_Workpost	SF24_Workpost
		WORKSTILL	SF3_Workstill	SF12_Workstill	SF24_Workstill
Were prescriptions received at the reduced pensioner rate? • To validate whether we receive data on those who were restricted (i.e. PBS medications obtained using a Department of Veteran's Affairs (DVA) card (gold, orange or white).	1 = Yes 0 = No	MEDPENS	SF3_Medspension	SF12_Medspension	SF24_Medspension

(B / 12m / 24m) **(Time = 0 / 2 / 3)**	**----------Your Health and Your Life & HAD----------**			
Description and Rationale	**Possible Values**	**Variable Names**		
		STAND FIRM *derived from:*	***SURE***	
			Baseline	***12 months***	***24 months***
London Handicap Scale (LHS) overall score (consists of 6 dimensions) **(1) Mobility** (getting around) **(2) Physical independence** (looking after self) **(3) Occupation** (work and leisure) **(4) Social integration** (getting on with people) **(5) Orientation** (awareness of his/her surroundings)	**Overall handicap severity score** (a) **Mobility** (b) **Physical independence** (c) **Occupation** (d) **Social integration** (e) **Orientation** (f) **Economic self-sufficiency**	—	SFB_LHSscore	SF12_LHSscore	SF24_LHSscore
		LHSMOB1	SFB_LHS1Mob	SF12_LHS1Mob	SF24_LHS1Mob
		LHSPI2	SFB_LHS2PI	SF12_LHS2PI	SF24_LHS2PI
		LHSOC3	SFB_LHS3Occ	SF12_LHS3Occ	SF24_LHS3Occ

(6) Economic self-sufficiency (affording the things he/she needs) • Used to measure health status and disadvantage in patients and evaluate the STAND FIRM intervention. • The scale generates a profile of handicaps on six different dimensions, where each dimension has six levels (6-point scale) that are arranged in order of increasing disadvantage.	• Each weighted score above is out of 1 (up to 4 decimal places) ***Note:*** *Algorithm required to calculate the total and individual dimensions' weighted scores*	LHSSI4		SFB_LHS4SI	SF12_LHS4SI	SF24_LHS4SI
		LHSOR5		SFB_LHS5Ori	SF12_LHS5Ori	SF24_LHS5Ori
		LHSESS6		SFB_LHS6ESS	SF12_LHS6ESS	SF24_LHS6ESS
Hospital Anxiety and Depression Scale (HADS) and Irritability **(1) Depression score** **(2) Anxiety Score** **(3) Outward Irritability Score** **(4) Inward Irritability Score** • Based on the validated and updated HADS and Irritability questions proposed by Snaith (1978). • Participants will be categorised as being depressed or having anxiety if their individual scores for each are > 7. Additionally, participants may be potentially categorised into quartiles for analyses.	**Depression score** • Integer (out of 21)	IDA1 IDA3 IDA7 IDA11	HADenjoy15 HADappear20 HADEnjoy22	SFB_HADSDep	SF12_HADSDep	SF24_HADSDep
	Anxiety score • Integer (out of 21)	IDA2 IDA5 IDA9 IDA13	HADPanic17 HADWorry19 HADrestless21	SFB_HADSAnx	SF12_HADSAnx	SF24_HADSAnx
	Outward irritability score • Integer (out of 12)	IDA4 IDA8	IDA12 IDA16	SFB_HADSOI	SF12_HADSOI	SF24_HADSOI
	Inward irritability score • Integer (out of 12)	IDA6 IDA10	IDA14 IDA18	SFB_HADSII	SF12_HADSII	SF24_HADSII

(Pre-stroke / B / 12m / 24m) **(Time = -1 / 0 / 2 / 3)**	**----------Modified Ranking Scale----------**					
Description and Rationale	**Possible Values**	**Variable Names**				
		STAND FIRM	***SURE***			
			Pre-stroke	***Baseline***	***12 months***	***24 months***
Modified Rankin Scale (mRS) • The mRS is a widely used clinical outcome measure in stroke clinical trials. It measures the degree of disability or dependence in the daily activities of people who have suffered a stroke.	**0** = No symptoms **1** = No significant disability **2** = Slight disability **3** = Moderate disability **4** = Moderately severe disability **5** = Severe disability **6** = Dead	RANKIN	SFPS_mRS	SFB_mRS	SF12_mRS	SF24_mRS

(B / 12m / 24m) (Time = 0 / 2 / 3)	----------Lifescripts----------		
Description and Rationale	**Possible Values**	**Variable Names**	
		STAND FIRM	**SURE**
(Q11) Do you smoke? ***Note:*** *Smoking status will be derived from Patient History's (& follow-up) cotinine detection and then verified against MoRF and lifescripts datasets.*	*1 = Yes, current smoker* *2 = No, past smoker* *3 = No, never smoker*	*Smoke*	*N/A (See Patient History below)*

(B / 12m / 24m) (Time = 0 / 2 / 3)	----------Management of Risk Factors----------				
Description and Rationale	**Possible Values**	**Variable Names**			
		STAND FIRM	**SURE**		
			Baseline	**12 months**	**24 months**
(1) Smoked regularly in the past (once a day for at least 3 months) **(2) Smoking regularly at time of stroke** Smoking is an important risk factor for stroke and other cardiovascular diseases.	1 = Yes 2 = No ***Note:*** *Follow-up answers will be used to verify baseline answers.*	(Q1) Ev_smoke1	SFB_Eversmoked	—	—
		(Q2) SmokStroke2	SFB_Smokestroke	—	—
Do you smoke now? ***Note:*** *use with MoRF (Q3) & lifescripts (Q11) datasets.*	*1 = Yes* *2 = No*	*(Q3) SmokNow3*	*N/A (See Patient History below)*		
(1) Exercises regularly **(2) Vegetable consumption (servings/day)** **(3) Fresh fruit consumption (servings/day)** **(4) Adds salt to their food** **(5) Adds more than one teaspoon of salt to food per day** These variables will show us if participants adopted the lifestyle changes recommended in the GP Management Plans (GPMP) and show any changes over time.	1 = Yes 2 = No	(Q9) Ex_Now9	SFB_Currentexer	SF12_Currentexer	SF24_Currentexer
	Servings to 1 decimal place e.g. 0.5 servings (per day) 3.0 servings (per day)	(Q31) Veg_serves31	SFB_Vegserves	SF12_Vegserves	SF24_Vegserves
		(Q32) Fruit_serves32	SFB_Fruitserves	SF12_Fruitserves	SF24_Fruitserves
	1 = Yes 2 = No 9 = Don't know	(Q33a) Add_salt_33a	SFB_Addsalt	SF12_Addsalt	SF24_Addsalt
		(Q33b) Amt_salt_33b	SFB_Add1teasalt	SF12_Add1teasalt	SF24_Add1teasalt

(Baseline only) (Time = 0)	----------Patient History----------		
Description and Rationale	**Possible Values**	**Variable Names**	
		STAND FIRM	***SURE***
(1) Highest completed level of education **(2) Social Class** These are broad measures of education and occupation that could reflect the socioeconomic status of participants in the analyses.	1 = Never attended school 2 = Primary School 3 = Some High School 4 = Completed High School 5 = Completed a Trade 6 = University 7 = Other Vocational Training	HighEd	SFB_Highestedu
	1 = Professional (e.g. doctor/lawyer) 2 = Intermediate (e.g. manager) 3 = Skilled non-manual (e.g. salesman/shopowner) 4 = Skilled manual (e.g. craftsman) 5 = Semi-skilled manual (e.g. driver) 6 = Unskilled manual (e.g. labourer)	SocClass	SFB_Socialclass
Was told by a doctor that they had: **(1) High cholesterol** **(2) Heart attack/coronary/ MI/angina/heart pain** **(3) Atrial fibrillation/ irregular pulse** **(4) High blood pressure** **(5) Stroke** **(6) TIA/transient weakness/numbness** **(7) Obstructive Sleep Apnoea/Disrupted sleep (by snoring)** **(8) Rheumatic Fever** **(9) Diabetes** **(10) Arthritis** **(11) Migraines or other headaches** **(12) Depression/Anxiety** These are important comorbidities to capture and validate within STAND FIRM. The presence of comorbidities will be used to adjust regression models in the statistical analyses.	1 = Yes 2 = No 9 = Unknown	HiChol	SFB_HxHC
		MI	SFB_HxMI
		AF	SFB_HxAF
		HiBP	SFB_HxHBP
		Str	SFB_HxStr
		TIA	SFB_HxTIA
		Snor	SFB_HxSleep
		RF	SFB_HxRF
		Diab	SFB_HxDiab
		Arth	SFB_HxArth
		Mig	SFB_HxMigr
		Anx	SFB_HxDepAnx
History of alcohol use ***Note:*** *Checked against Run-In response.*	1 = Never drink alcohol 2 = Previously drunk alcohol 3 = Currently drink alcohol	AlcUse *Alco39 (Ru-In)*	SFB_AlcUse

Education regarding excessive alcohol consumption being a risk factor for stroke was given as part of the intervention. Whether participants were alcohol consumers or not at baseline should be accounted for in the analyses.			

(B) & (12m / 24m) Time = (0) & (2 / 3)	----------Patient History AND Patient History Follow-up----------					
Description and Rationale	**Possible Values**		**Variable Names**			
			STAND FIRM	***SURE***		
				Baseline	***12 months***	***24 months***
Current marital status	1 = Never Married 2 = Now Married 3 = Separated but not divorced	4 = Divorced 5 = Widowed 6 = Living with partner	(Q2) & (Q1) Marital_Status	SFB_Marital	SF12_Marital	SF24_Marital
(1) Body Mass Index (BMI) **(2) Waist-hip ratio (WHR)** BMI and WHR are proxy measures of fat deposition or adiposity. ***Note:*** *W/H² & abdomen/hip circumference.*	**BMI** – Continuous, 4 decimal places – Range ≈ 17.00 – 63.49		Height Weight	SFB_BMI	SF12_BMI	SF24_BMI
	WHR – Continuous, 4 decimal places – Range ≈ 0.55 – 1.34		AbCircum Hip	SFB_WHR	SF12_WHR	SF24_WHR
Framingham Risk Score (FRS) • The FRS predicts the risk of developing a first-ever CVD event in people with no prior history of CVD. Calculation of the risk of individual CVDs (i.e. stroke, CHD and coronary heart failure). It is calculated using a statistical algorithm by D'Agostino *et al.* (2008). • The primary outcome of the STAND FIRM trial was the mean change in absolute risk in the updated Framingham cardiovascular disease (CVD) risk score (FRS) at 12 and 24 months. The factors included in the FRS are age, gender, systolic BP, total cholesterol levels, high-density lipoprotein cholesterol levels, glycosylated haemoglobin levels, and smoking status. • Although the FRS was initially designed to assess a patient's risk of vascular events in primary prevention settings, it is appropriate for use in STAND FIRM as most components of the FRS are sensitive to change with better management of risk factors. Also, risk factors for incident stroke are similar to those for recurrent stroke. Achieving a lower Framingham CVD risk score (i.e. lower 10-year risk of CVD) is also likely to be associated with fewer subsequent vascular events.	**FRS =** • 0 – 100 • 4 decimal places • Calculated using risk factor data below		—	SFB_FRS	SF12_FRS	SF24_FRS

Variables needed to calculate the FRS: **(1) Age (in years)** **(2) Mean SBP** **(3) Mean DBP** **(4) Antihypertensive medication use** **(5) Total cholesterol** **(6) HDL cholesterol** **(7) Smoking status** **(8) Diabetes status** • These are also needed to see where potential improvements occurred from baseline to 12 and 24 months in biochemical factors between those on a CDM plan and those who were not. ***Note:*** *Smoking status is derived from Patient History's (& follow-up) cotinine detection & then verified against MoRF (Q3) & lifescripts (Q11). DOB in Run-In checked against DOB in Pt_Hx (DOB4).*	**(1) Age** – Continuous, 4 decimal places	*DOB (Run-In)* DOASS	SFB_Age	SF12_Age	SF24_Age
	(2) SBP and **(3) DBP** – Continuous (mmHg), 4 decimal places	SBP(1-5)	SFB_SBP	SF12_SBP	SF24_SBP
		DBP(1-5)	SFB_DBP	SF12_DBP	SF24_DBP
	(4) Antihypertensive medication use 1 = Using medication(s) 0 = Not using medication(s)	MedCode (1-25)	SFB_AHmeds	SF12_AHmeds	SF24_AHmeds
	(5) Total cholesterol and **(6) HDL cholesterol** – Continuous, 1 decimal place – Range ≈ 21.11 – 95.34	Chol	SFB_Totalchol	SF12_Totalchol	SF24_Totalchol
		HDLChol	SFB_HDLchol	SF12_HDLchol	SF24_HDLchol
	(7) Smoking status 1 = Yes, current smoker 2 = No, past smoker 3 = No, never smoker	Cotin *Smoke* *SmokNow3*	SFB_Smoking	SF12_Smoking	SF24_Smoking
	(8) Diabetes status 1 = Diabetic (fasting plasma glucose ≥7.0mmol/L) 0 = Not diabetic	HbA1c	SFB_Diab	SF12_Diab	SF24_Diab

(3m / 12m / 24m) **(Time = 1 / 2 / 3)**	**----------Medication Knowledge and Adherence----------**				
Description and Rationale	**Possible Values**	**Variable Names**			
		STAND FIRM	***SURE***		
			3 months	***12 months***	***24 months***
(1) How does the pharmacist provide their medications? **(2) How do they keep track of taking their medications?** These reflect the medication tracking behaviour of participants and could be associated with their medication adherence over time (using PBS data).	1 = Pill bottle/package 2 = Webster packs 3 = Other	meds_package	SF3_Medspackage	SF12_Medspackage	SF24_Medspackage
	1 = Instructions on original pill container 2 = Medication diary 3 = Daily chart 4 = Dispenser 5 = Other 6 = Dosette box	meds_track	SF3_Medstrack	SF12_Medstrack	SF24_Medstrack

(Only at Baseline)	----------Run-In----------			
Description and Rationale	**Possible Values**		**Variable Names**	
			STAND FIRM	***SURE***
Sex	1 = Male	2 = Female	Male	SF_Male
Age (at each time point)	*See Patient History AND Patient History Followup above*			
STAND FIRM run-in participant status • Qualifying stroke/TIA event for study	1 = First-ever in a life-time stroke 2 = Recurrent Stroke	3 = TIA	FinStat3	SF_FinalStat
STAND FIRM run-in participant diagnosis • Type of stroke is important for stroke severity and contraindications.	1 = Ischaemic Stroke 2 = Intracerebral Haemorrhage 3 = TIA		FinalDx	SF_FinalDx
Date of stroke	*See STAND FIRM date variables at start of table*			

(0 – 24 months)	----------Serious Adverse Events (SAEs)----------		
Description and Rationale	**Possible Values**	**Variable Names**	
		STAND FIRM	***SURE***
Reason Adverse Event is Serious Will allow for validation of events and identify any hospitalisations not captured in STAND FIRM.	1 = Resulted in death 2 = Was life threatening 3 = Required inpatient hospitalisation 4 = Resulted in persistent or significant disability/incapacity	Serious	SF_ReasonSerious
(1) SAE Admission Date **(2) SAE Discharge Date** • These dates will allow for matching of serious adverse events (SAEs) in STAND FIRM that have been categorised as being cardiovascular-related or not. • Identify any hospitalisations not captured in STAND FIRM • Both dates are needed as one date may not match ***Note:*** *SAE dates are more accurate than AE dates.*	DD/MM/YYYY	AE_ADMIT_DAT	SF_AdmD
		AE_DISCH_DAT	SF_DischD

(0 – 24 months)	----------Serious Adverse Events Adjudication----------			
Description and Rationale	**Possible Values**		**Variable Names**	
			STAND FIRM	***SURE***
(1) Hospitalisation type **(2) Death type** • Hospitalisations and deaths were adjudicated as being cardiovascular related or not by two stroke specialists • Validate against hospital/death records • Will help categorise events alongside the algorithms previously proposed for grouping of ICD-10 codes. ***Note:*** *SAENOs will be matched using mapping file with SAEs using SAENO, IDNO and event date.*	1 = Acute myocardial infarction 2 = Angina 3 = Heart failure 4 = Ischaemic stroke 5 = Haemorrhagic stroke 6 = Undetermined stroke	7 = Transient Ischaemic Attack (TIA) 8 = Cardiovascular interventions 9 = Non-cardiovascular events 10 = Unable to be determined 11 = Atrial fibrillation	NON_FATAL	SF_NonFatal
	1 = Death due to stroke 2 = Death due to myocardial infarction 3 = Sudden cardiac death 4 = Death due to heart failure	5 = Death due to other cardiovascular cause 6 = Non-cardiovascular death 7 = Undetermined cause of death	DEATH_TYPE	SF_DeathType

(0 – 24 months)	----------Patient Dropout/Withdrawal----------		
Description and Rationale	**Possible Values**	**Variable Names**	
		STAND FIRM	***SURE***
Date of dropout	*See STAND FIRM date variables at start of table*		
Reason for dropout To assess patient retention in both the intervention and usual care groups.	1 = Unable to contact/find patient 2 = Patient no longer interested in participating 3 = Patient too sick to participate 4 = Other	Unable_contact Disinterested Too_sick	SF_DOreason

(only at 24 months)	----------Feedback Survey----------		
Description and Rationale	**Possible Values**	**Variable Names**	
		STAND FIRM	***SURE***
These questions were asked on a feedback survey form at the end of the study. The feedback responses will allow us to qualitatively assess how well the intervention was delivered compared with usual care and analyse for associations with 2-year health outcomes.			
Since stroke, most involved health care professional (HCP) ***Note:*** *5 binary variables were combined. In cases where >1 response was provided, these have been grouped.*	0 = No HCP specified 1 = General practitioner (GP) 2 = Nurse 3 = Personal care attendant (PCA) 4 = Medical specialist (e.g. neurologist, cardiologist, endocrinologist, psychologist, psychiatrist, rheumatologist) 5 = Allied health specialist (e.g. dietician, physiotherapist, occupational therapist, speech therapist, social worker) 7 = More than one HCP (combinations below)	(Q1) (String) impt_health_prof (0, 1) impt_gp (0, 1) impt_nurse (0, 1) impt_pca (0, 1) impt_med_spe (0, 1) impt_allied_hs	SF24_Important_HCP
	0 = N/A 1 = GP & Medical specialist		SF24_Important_GM
	0 = N/A 1 = GP & Medical specialist or PCA		SF24_Important_G_NP
	0 = N/A 1 = AHS & GP, Nurse, PCA and/or Medical specialist		SF24_Important_A_GNPM
Since stroke, participant was satisfied with how well organised their care was?	1 = Yes, definitely 2 = Yes, to some extent 3 = No, I am not satisfied	(Q2) care_satisfy	SF24_Satisfied
Since stroke, was there enough information given about their stroke (e.g. what is a stroke)?	1 = Yes, all the information I needed 2 = Yes, some information but not enough 3 = No	(Q3) stroke_info	SF24_Enoughinfo
Since stroke, has their GP helped in developing a stroke treatment or management plan that they could carry in their daily life?	1 = Yes 2 = No, but I would have liked it 3 = No, I did not want any treatment plan 4 = I am not sure	(Q5) use_imp	SF24_GPuseIMP
Since stroke, were they given enough information about their secondary prevention of stroke medications (e.g. benefits, side effects)?	1 = Yes, definitely 2 = Yes, to some extent 3 = No, but I would have liked to 4 = No, I did not need such information	(Q6) info_meds	SF24_Medsinfo

Since stroke, was there enough help with taking medications as prescribed?	1 = Yes, definitely 2 = Yes, to some extent 3 = No, I did not get enough help 4 = No, I did not want help 5 = I did not have difficulty in taking my medications	(Q7) help_take_meds	SF24_Medshelp
Since stroke, was there enough help in setting goals (e.g. wishes & expectations) towards preventing another stroke?	1 = Yes, definitely 2 = Yes, to some extent 3 = No, I did not get enough help 4 = I did not want help 5 = I did not set any goal towards improving my health	(Q11) info_health_goal	SF24_Goalshelp
Since stroke, were they involved as much as they wanted to be in decisions about their care/treatment?	1 = Yes, definitely 2 = Yes, to some extent 3 = No, but I would have liked to have been more involved 4 = No, but I did not mind 5 = Don't know/Can't say 6 = I have not had any care or treatment since my stroke	(Q12) decision_making	SF24_Decisions
Twelve months after their stroke, did their doctor discuss their risk of having another stroke with them?	1 = Yes 2 = No	(Q13) risk_comm	SF24_Riskdiscussed
Since stroke, was enough advice given to improve their diet (e.g. alcohol, sugar, fat, salt)?	1 = Yes, definitely 2 = Yes, to some extent 3 = No	(Q15) advice_diet	SF24_Dietadvice

Note: *There could be instances where data that's technically only needed at one time point (e.g. working at time of stroke only needed at 3 months), however due to missing data, the following assessment response would need to be used (Muideen has cleaned some of these, but need to be careful).*

----------Telephone Running Sheet----------	**----------Services----------**
----------Adverse Events----------	**----------Pedometers----------**
----------Patient Screening Log----------	**----------Protocol Violation----------**
----------Returned IMP----------	

[Appendix I] ICD-10-AM Codes Used to Identify Additional CVD-Related Readmissions

Diagnoses	ICD-10-AM extraction codes
Cardiovascular disease	I00 – I99
Coronary heart disease	I20 – I25
Acute myocardial infarction	I21
Angina	I20
Atrial fibrillation	I48
Cerebrovascular disease	I60 – I69
Stroke	I60 – I64
Transient ischaemic attack	G45
Heart failure and cardiomyopathy	I50, I25.5, I42.0, I42.5 – I42.9, I43
Heart failure	I50
Peripheral vascular disease	I70 – I74
Atherosclerosis of peripheral arteries	I70.2
Abdominal aortic aneurysm	I71.3 – I71.4
Acute rheumatic fever and chronic rheumatic heart disease	I00 – I09
Valvular heart disease	I05 – I08, I34 – I37, Q22 – Q23
Congenital heart disease	Q20 – Q28
Transposition of the great vessels	Q20.3
Tetralogy of Fallot	Q21.3
Hypoplastic left heart syndrome	Q23.4
Coarctation of the aorta	Q25.1
Diabetes	E10 – E11, E13 – E14, O24.0 – O24.4, O24.9
Chronic kidney disease	N00 – N09, N11 – N12, N14 – N16, N18 – N19, N25 – N28, N39.1 – N39.2, Q60 – Q63, T82.4, T86.1, Z49, Z94.0, Z99.2, E10.2, E11.2, E13.2, E14.2, I12 – I13, I14.0 – I15.1

ICD-10-AM, International Classification of Diseases, 10th Revision, Australian Modification; CVD, cardiovascular disease.

[Appendix J] ICD-10-AM Codes Used to Identify Comorbidities

Diagnoses	ICD-10-AM extraction codes
Any cancer tumour	C0 – C6, C40 – C41, C43, C45 – C47, C48 – C49, C70 – C76, C81 – C85, C91 – C93, C95 – C96, C883, C887, C889 – C901, C940 – C943, C947, C9451
Congestive heart failure	I50
Connective tissue disease	M32, M34, M050 – M053, M058 – M060, M063, M069, M332, M353
Cerebrovascular accident	G450 – G452, G454, G458 – G459, G46, I60 – I66, I681 – I682, I688, I69, I670 – I672, I674 – I679
Chronic pulmonary disease	J40 – J47, J60 – J67
Chronic renal disease	N01, N03, N052 – N056, N072, N073, N074, N18, N19, N25
Dementia	F00 – F03, F051
Diabetes (complicated)	E102- E104, E112 – E114, E132 – E134, E142 – E144
Diabetes (uncomplicated)	E101, E105, E109, E111, E115, E119, E131, E135, E139, E141, E145, E149
Hemiplegia	G041, G81, G820 – G822
HIV	B20 – B24
Metastatic cancer	C77 – C80
Mild liver disease	K702, K703, K717, K740, K742 – K746, K73
Moderate to severe liver disease	K721, K729, K766, K767
Myocardial infarction	I21, I22, I252
Peripheral vascular disease	I71, I739, I790, R02, Z958, Z959
Ulcer disease	K25 – K28

ICD-10-AM, International Classification of Diseases, 10th Revision, Australian Modification; HIV, human immunodeficiency virus.