IMPROVING CARE AND OUTCOMES AFTER STROKE: A FOCUS ON HOSPITALS AND COMMUNITY-BASED INTERVENTIONS

A thesis submitted for the degree of Doctor of Philosophy

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Bachelor of Science (Hons)

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In loving memory of

my granduncle, Professor S. Shan Ratnam

and

Aunty Nirmaladevi

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Summary

Stroke is a leading cause of mortality and chronic disability around the world, including in Australia. Many survivors of stroke have long-term physical, sensory, cognitive and psychological consequences that impact their quality of life, and have an increased risk of subsequent vascular events. This causes a huge burden on survivors, families and health care systems.

Provision of evidence-based care according to the clinical guidelines increases the likelihood of survival and aids better recovery. However, there is evidence that adherence to recommended clinical care varies between hospitals managing patients with stroke and in the community. Opportunities exists to develop effective interventions that target improvements in clinical practice to facilitate best practice care at the acute level (i.e. when in hospital) and over the long-term (i.e. when in the community).

In Chapters 1 and 2, I provide the rationale, objective, aims and the necessary background to stroke. In Chapter 3, I highlight the importance of collecting incidence, mortality, and case-fatality rates to assess the burden of stroke, and how it varies across the globe. Where data lacks, quality clinical registries may be in place in some countries to obtain epidemiological data. These registries can also play a vital role in improving the quality of care provided in hospitals. In Chapter 4 and 5, I highlight how registry data and behaviour change strategies may be used to improve care for stroke in acute hospitals. I then focus on the strategies to reduce the burden of anxiety or depression following stroke. In Chapters 6 and 7, I describe the processes involved and the benefits of using comprehensive linked data to understand factors that may be associated with post-stroke anxiety or depression. The factors most strongly

associated with post-stroke anxiety or depression were a prior diagnosis of anxiety or depression, dementia, being at home with support, and low socioeconomic advantage compared to high. The assessment of the convergent validity, sensitivity and specificity of the anxiety or depression domain of the EQ-5D-3L survey as a suitable screening tool for anxiety or depression in survivors of stroke is presented in Chapter 8. The EQ-5D-3L anxiety or depression domain had a strong correlation and excellent AU-ROC with either subscales of the Hospital Anxiety and Depression Scale. The sensitivity and specificity of the EQ-5D-3L anxiety or depression domain for anxiety were 89% and 71%, respectively. Whereas, the sensitivity and specificity of the EQ-5D-3L anxiety or depression domain for depression were 85% and 79%, respectively.

Finally, as presented in Chapters 9 and 10, mindfulness-based interventions (MBIs) appear beneficial in moderating some of the highly prevalent risk factors for stroke, such as hypertension, diabetes and cholesterol, and maybe an adjunct therapy to current rehabilitation strategies. There is a need to further unpack these beneficial changes on the pathophysiological pathways leading to therapeutic changes to some of these highly modifiable risk factors for stroke. In Chapter 11 a formative evaluation of the processes involved in developing a yoga-based MBI designed for survivors of stroke living in the community was described. The chapter is also used to highlight how ‘co-design’ is an important aspect of intervention development, where consumers contributed to the four stages of development that led to the final design of the program, which is now ready for testing in a clinical trial. The results of this thesis are an important step towards understanding the burden of stroke, and the potential strategies to improve stroke care and outcomes across the patient care continuum, with a primary focus on anxiety or depression.

General declaration

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 a total of 5 publications; 3 original papers published in peer reviewed journals, 1 article under editorial review. This thesis also includes one published article as a narrative with my contribution at 45% [Chapter 3]).

Signature: 

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Date: 30/11/2018

Thesis including published works declaration

Monash University

Declaration for thesis based, or partially based, on conjointly published or unpublished work.

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 a total of 5 publications; 3 original papers published in peer reviewed journals, 1 article under editorial review. This thesis also includes one published article as a narrative with my contribution at 45% [Chapter 3]).

The core theme of the thesis is ***Improving care and outcomes after stroke: A focus on hospitals and community-based interventions.*** The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the ***Translational Public Health and Evaluation Division, Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University***, under the supervision of ***Professor Dominique Cadilhac, Dr Nadine Andrew, Dr Rene Stolwyk*** and ***Professor Amanda Thrift.***

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research. The details of the contribution for publications where my contribution is >50% is provided in the table below.

Chapters 5, 7, 9 and 10, 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***
5	Understanding the role of external facilitation in hospitals to drive quality improvement: a case study from stroke	Submitted	70%. Data collection and management, statistical analysis, interpretation, and writing of first draft	1. **Nadine E Andrew,** Input into manuscript 6% 2. **Rohan Grimley,** Input into manuscript 3% 3. **Enna Salama,** Input into manuscript 2% 4. **Brenda Grabsch,** Input into manuscript 2% 5. **Kelvin Hill,** Contributed to study design and input into manuscript 2% 6. **Greg Cadigan,** Input into manuscript 2% 7. **Tara Purvis,** Input into manuscript 1% 8. **Libby Dunsta**n, Input into manuscript 1% 9. **Sandy Middleton**, Input into manuscript 1% 10. **Dominique A Cadilhac**, Contributed to study design and input into manuscript 10%	No No No No No No No No No No
7	Factors influencing self-reported anxiety or depression following stroke or TIA using linked registry and hospital data	Published	80%. Concept, data management, analysis, interpretation and writing of first draft.	1. **Nadine E Andrew,** Statistical support, input into manuscript 8% 2. **Monique F Kilkenny**, Input into manuscript 1% 3. **Rene Stolwyk,** Input into manuscript 1%	No No No

				4. **Amanda G Thrift**, Input into manuscript 1% 5. **Rohan Grimley**, Input into manuscript 1% 6. **Trisha Johnston**, Input into manuscript 1% 7. **Vijaya Sundararaja**n, Input into manuscript 1% 8. **Natasha Lannin**, Input into manuscript 1% 9. **Dominique A Cadilhac**, Contributed to study design and input into manuscript 5%	No No No No No No
9	Understanding the potential for yoga and tai chi interventions to moderate risk factors of stroke – a scoping review	Published	80%. Concept, literature search, data management, analysis, interpretation and writing of first draft.	1. **Maarten A Immink**, Input into manuscript 5% 2. **Philip Stevens**, Input into manuscript 3% 3. **Susan Hillier**, Input into manuscript 1% 4. **Amanda G Thrift**, Input into manuscript 1% 5. **Amy Brodtmann**, Input into manuscript 1% 6. **Leeanne Carey**, Input into manuscript 1% 7. **Monique F Kilkenny**, Input into manuscript 1% 8. **Dominique A Cadilhac**, Input into manuscript 7%	No No No No No No No No

10	Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis	Published	75%. Concept, literature search, data management, analysis, interpretation and writing of first draft.	1. **Nadine E Andrew**, Statistical support, input into manuscript 10% 2. **Maarten A Immink**, Input into manuscript 2% 3. **Susan Hillier**, Input into manuscript 1% 4. **Philip Stevens**, Input into manuscript 2% 5. **Rene Stolwyk**, Input into manuscript 1% 6. **Monique F Kilkenny**, Input into manuscript 1% 7. **Dominique A Cadilhac**, Input into manuscript 8%	No No No No No No No

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

Student signature: [redacted] **Date:** 30/11/2018

The undersigned 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 signature [redacted] **Date:** 30/11/2018

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Publications included in thesis

1. **Thayabaranathan T**, Andrew NE, Grimley R, Salama E, Grabsch B, Hill K, Cadigan G, Purvis T, Dunstan L, Middleton S and Cadilhac DA. Understanding the role of external facilitation in hospitals to drive quality improvement: a case study from stroke (Under review at Implementation Science 2018).

2. **Thayabaranathan T**, Immink MA, Stevens P, Hillier S, Thrift AG, Brodtmann A, Carey L, Kilkenny MF, Cadilhac DA. Understanding the potential for yoga and tai chi interventions to moderate risk factors of stroke – a scoping review. Future Neurology, 2018; 13(4)239-252.

3. **Thayabaranathan T**, Andrew NE, Kilkenny MF, Stolwyk R, Thrift AG, Grimley R, Johnston T, Sundararajan V, Lannin NA, Cadilhac DA on behalf of the Stroke123 investigators and AuSCR consortium. Factors influencing self-reported anxiety or depression following stroke or TIA using linked registry and hospital data. Quality of Life Research. 2018; August 4. doi.org/10.1007/s1113 6-018-1960-y.

4. **Thayabaranathan T**, Andrew NA, Immink MA, Hillier S, Stevens P, Stolwyk R, Kilkenny MF, Cadilhac DA. Determining the potential benefits of yoga in chronic stroke care: A systematic review and meta-analysis. Topics in Stroke Rehabilitation, 2017; 24(4):279-287 doi: 10.1080/10749357.2016.1277481.

5. Thrift AG, **Thayabaranathan T**, Howard G, Howard VJ, Rothwell PM, Feigin VL, Norrving B, Donnan GA, Cadilhac DA. Global Stroke Statistics. International Journal of Stroke, 2017;12(1):13–32, doi: 10.1177/1747493016676285.

Published abstracts

1. **Thayabaranathan T**, Immink MA, Stevens P, Hillier S, Thrift AG, Brodtmann A, Carey L, Kilkenny MF, Cadilhac D. Movement-based mindfulness interventions and potential pathophysiological pathways for moderating stroke risk – a scoping review. International Journal of Stroke, 2018; Vol.13(1S):p31.

2. **Thayabaranathan T**, Andrew N, Kilkenny M, Stolwyk R, Thrift A, Grimley R, Johnston T, Sundararajan V, Lannin N, Cadilhac D. Is self-reported anxiety or depression between 90–180 days post-stroke associated with patient factors or quality of acute care received? International Journal of Stroke, 2017; Vol. 12(3S):p23.

3. **Thayabaranathan T**, Andrew N, Immink MA, Hillier S, Stevens P, Stolwyk R, Kilkenny M, Cadilhac D. Benefits of mindfulness-based interventions for stroke care: A systematic review. International Journal of Stroke, 2015; 10 (S3):38.

4. **Thayabaranathan T**, Andrew N, Branagan H, Salama E, Grabsch B, Hill K, Cadigan G, Grimley R, Middleton S, Cadilhac D. Understanding the benefits of external support for quality improvement activities in public hospitals for acute stroke: A sub study of Stroke123. International Journal of Stroke, 2015; 10 (S3):10-11.

Other publications

1. Thrift AG, Howard G, Cadilhac DA Howard VJ, Rothwell PM, **Thayabaranathan T**, Feigin VL, Norrving B, Donnan GA. Global stroke statistics: An update of mortality data from countries using a broad code of "cerebrovascular diseases". International Journal of Stroke, 2017;12(8):796–801.

2. Luker JA, Bernhardt J, Graham ID, Middleton S, Lynch EA, **Thayabaranathan T**, Craig L, Cadilhac DA. Interventions for the uptake of evidence-based recommendations in acute stroke settings. Cochrane Database of Systematic Reviews, 2017: Issue 1. Art. No.: CD012520. DOI: 10.1002/14651858.CD012520.

Conference presentations

1. **Thayabaranathan T**, Immink MA, Stevens P, Hillier S, Thrift AG, Brodtmann A, Carey L, Kilkenny MF, Cadilhac DA (2018). Movement-based mindfulness interventions and potential pathophysiological pathways for moderating stroke risk – a scoping review. Presented as a poster at Monash Research Week, 5-9 November.

2. **Thayabaranathan T,** Immink MA, Stevens P, Hillier S, Thrift AG, Brodtmann A, Carey L, Kilkenny MF, Cadilhac DA (2018). Movement-based mindfulness interventions and potential pathophysiological pathways for moderating stroke risk – a scoping review. STROKE 2018 annual scientific meeting in Sydney, 7-9 August **[finalist best abstract for e-poster session].**

3. **Thayabaranathan T**, Andrew N, Kilkenny MF, Stolwyk R, Thrift AG, Grimley R, Johnston T, Sundararajan V, Lannin N, Cadilhac DA (2017). Is self-reported anxiety or depression between 90-180 days post-stroke associated with patient factors or quality of acute care received? Presented as a poster at Monash Research Week, 10-17 November.

4. **Thayabaranathan T**, Andrew N, Kilkenny MF, Stolwyk R, Thrift AG, Grimley R, Johnston T, Sundararajan V, Lannin N, Cadilhac DA (2017). Is self-reported anxiety or depression between 90-180 days post-stroke associated with patient factors or quality of acute care received? STROKE 2017 annual scientific meeting in Queenstown, 23-25 August **[finalist for New Investigator Award].**

5. **Thayabaranathan T**, Andrew N, Branagan H, Salama E, Grabsch B, Hill K, Cadigan G, Grimley R, Middleton S, Cadilhac D (2016). Benefits of external support for quality improvement activities in stroke. Presented as a poster at Monash Research Week, 21-26 November

6. **Thayabaranathan T**, Andrew N, Branagan H, Salama E, Grabsch B, Hill K, Cadigan G, Grimley R, Middleton S, Cadilhac D (2015). Benefits of external support for quality improvement activities in stroke. Presented as a poster at 4th Annual NHMRC Symposium on Research Translation jointly with CIPHER in Sydney, 27-28 October.

7. **Thayabaranathan T**, Andrew N, Branagan H, Salama E, Grabsch B, Hill K, Cadigan G, Grimley R, Middleton S, Cadilhac D (2015). Understanding the benefits of external support for quality improvement activities in public hospitals for acute stroke – a sub study of Stroke123, STROKE 2015 annual scientific meeting in Melbourne, 2-4 September **[Bursary Award].**

8. **Thayabaranathan T**, Andrew N, Immink M, Hillier S, Stevens P, Stowyk R, Kilkenny M, Cadilhac D (2016). Benefits of mindfulness-based interventions for stroke care: A systematic review. Presented as a poster at Monash Research Week, 21-26 November.

9. **Thayabaranathan T**, Andrew N, Immink M, Hillier S, Stevens P, Stowyk R, Kilkenny M, Cadilhac D (2015). Benefits of mindfulness-based interventions for stroke care: A systematic review. Presented as an oral presentation at the STROKE 2015 annual scientific meeting in Melbourne, 4 September **[finalist for New Investigator Award].**

Invited presentations

1. Thayabaranathan T, Andrew N, Branagan H, Salama E, Grabsch B, Hill K, Cadigan G, Grimley R, Middleton S, Cadilhac D (2015). Understanding the benefits of external support for quality improvement activities in public hospitals for acute stroke – a sub study of Stroke123, Symposium on Stroke, 9th Health Services and Policy Research Conference, 7-9 December.

2. Quality of stroke care in acute hospitals and long-term impacts of stroke in survivors of stroke, School of Public Health and Preventive Medicine, November 2015.

3. Understanding the benefits of external support for quality improvement activities in public hospitals for acute stroke – a sub study of Stroke123, The Florey Institute of Neuroscience and Mental Health, August 2015.

Media

- Podcast complementing the Global Stroke Statistics paper (2016). https://www.podbean.com/media/share/pb-3tgdr-64fd44.

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Committees and other groups

- Stroke123 Queensland Quality Improvement & Evaluation sub-committee
- Stroke123 Data Linkage sub-committee
- Yoga Program Working Group and Advisory Group
- School of Clinical Sciences Student Symposium organising committee

List of Abbreviations

AF	Atrial fibrillation
AHA	American Heart Association
ASA	American Stroke Association
AUD	Australian dollar
AU-ROC	Area Under the curve of the Receiver Operating Characteristic
AuSCR	Australian Stroke Clinical Registry
BMI	Body mass index
CVD	Cardiovascular disease
DOI	Digital Object Identifier
HADS	Hospital Anxiety Depression Scale
HADS-A	Hospital Anxiety Depression Scale- Anxiety subscale
HADS-D	Hospital Anxiety Depression Scale- Depression subscale
HbA1c	Haemoglobin A1c
HDL	High density lipoprotein
hospital ID	Project specific hospital identification
ICD-10-AM	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification
ICH	Intracerebral haemorrhage

ICHOM	International Consortium for Health Outcomes Measurement
IF	Impact factor
IQR	Interquartile range
kg/m^2	Kilogram-meter squared
LACI	Lacunar cerebral infarct
LDL	Low density lipoprotein
MBI/s	Movement-based mindfulness intervention/s
mmHg	Millimetre of mercury
NHMRC	National Health and Medical Research Council
NPIS	National Performance Indicator Set
PACI	Partial anterior circulation infarcts
PARIHS	Promoting Action on Research Implementation in Health Services
PDSA	Plan, Do, Study, Act
PoC	Clinical processes of care
POCI	Posterior circulation infarct
Pt ID	Project specific patient identification
QHAPDC	Queensland Hospital Admitted Patient Data Collection
QI	Quality improvement
QLD	Queensland
RCT/s	Randomised Controlled Trial/s
SAH	Subarachnoid haemorrhage

SES	Socioeconomic status
STAI	State-Trait Anxiety Inventory
TACI	Total anterior circulation infarct
TIA	Transient Ischaemic attack
tPA	Tissue plasminogen activator
TX, USA	Texas, United States of America
UND	Undetermined
VAS	Visual Analogue Scale
WHO	World Health Organisation

Introduction and thesis objectives

Chapter 1: Introduction and thesis objectives

1.1 Introduction

Stroke is a leading cause of mortality and chronic disability around the world, including in Australia.[1] Approximately 50,000 Australians suffer a stroke each year, costing about AUD 2 billion per year.[2] Many survivors of stroke have long-term physical, sensory, cognitive and psychological consequences that impact their quality of life.[3] Survivors of stroke are also at an increased risk of subsequent vascular events, including recurrent stroke (~16% within 1 year, 32% within 5 years, and 43% within 10 years).[4] Moreover, the consequences of recurrent strokes are often more severe than initial strokes and are a major cause of further comorbidity and mortality.[5] These recurrent events impart additional burden on survivors, families and health care systems.[6]

Stroke is a condition that may be treated and prevented, with best practice recommendations detailed in national clinical guidelines.[7] Provision of evidence-based care according to the clinical guidelines increases the likelihood of survival and aids better recovery. However, there is evidence that adherence to recommended clinical care (e.g. access to stroke units) varies between hospitals managing patients with stroke[8] and in the community.[9] Such discrepancies are concerning given that variability in patient management has been shown to adversely affect health outcomes and lead to ineffective use of health care resources.[8, 10] With a rising number of people living with the impacts of stroke, ensuring evidence-based management of survivors throughout their stroke journey is essential, yet becoming increasingly challenging. Therefore,

opportunity exists to develop effective interventions that target improvements in clinical practice to facilitate best practice care at the acute level (i.e. when in hospital) and over the long-term (i.e. when in the community).

Quality improvement (QI) programs have been developed to reduce the variation in care provided at acute hospitals. More specifically, these QI programs monitor clinical hospital performance and evaluate their means to improve the quality of care provided. In Australia, QI programs for acute stroke care have been developed and tested in a number of hospitals with support from state governments. In these QI programs, an important strategy for improving the delivery of evidence-based care is to support clinician behaviour change. Facilitation has been identified as a key component of QI programs.[11] In order to successfully implement change, an external facilitator may be used to help clinicians, teams and organisations actualise an implementation plan and, thereby, change evidence-based practice through interactive problem solving and support.[12] However, the effectiveness of external facilitation, as part of complex multifaceted interventions aimed at improving acute stroke care, is uncertain.[13]

Once patients leave hospital they can experience a range of comorbid consequences associated with adapting to life after stroke.[3, 14] Approximately 20-40% of survivors of stroke are affected by mood disorders, such as anxiety or depression.[15] Management of anxiety or depression following stroke (i.e. prescription of anti-depressant medication, psychological assessments) is one of a number of evidence-to-practice gaps that has remained relatively unchanged over a number of years.[16] Anxiety or depression following stroke can occur as a primary consequence of the stroke or secondary to the impact of stroke on the survivor's life. Those with anxiety or depression after stroke are reported to have greater dependence in activities of daily living, institutionalisation and mortality, and poorer overall quality of life.[14] There is also evidence that survivors of stroke who do not receive evidence-based care experience worse physical and

psychological outcomes following stroke.[10] Findings from a recent audit indicated that only 17% of patients were assessed for anxiety or depression when in hospital. Among these patients, only 37% identified with mood impairment were assessed by a psychologist.[17] This highlights the need for strategies to reduce these evidence-to-practice gaps to improve patient outcomes. However, it is unclear whether the quality of acute stroke care received in hospital impacts the risk of developing anxiety or depression in survivors of stroke. There is also a lack of understanding on whether the type of stroke or any other premorbid conditions influence the development of anxiety or depression following stroke.

Given the complexities associated with stroke, patients returning to the community require ongoing support and care.[3, 8, 18-22] In particular, there is a definite need for better management and prevention options to reduce the risk of developing anxiety or depression and other chronic and long-term issues. Behavioural therapies using movement-based mindfulness interventions (MBIs), such as yoga, may be one way of addressing these problems.[23-27] However, differences in the types of MBIs used, and a lack of controlled studies, make it difficult to determine the efficacy of MBIs for survivors of stroke.[28] Therefore, further research is required to assess the suitability of MBIs, within the context of stroke, as a recovery option.

As highlighted, there are various opportunities to support patients who experience stroke to achieve better outcomes. Research is urgently needed to address variation in management of acute stroke care, and provide evidence for the use of community-based interventions to avoid complications, including anxiety or depression, following stroke.

1.2 Thesis objective and aims

This doctoral project has been undertaken to *outline the burden of stroke and then the potential strategies to improve stroke care and outcomes across the patient care continuum.* The thesis is broken into three parts, and includes aims that address the overall objective as seen below:

1.2.1 Specific aims

Part A: The global burden of stroke and strategies to reduce this burden

Thesis aim 1: To contribute to a greater understanding of stroke incidence, mortality, and case-fatality in different countries, and explore the limitations of current data.

Part B: Strategies to improve quality of care in hospitals

Thesis aim 2: To address evidence-to-practice gaps in the acute care setting using data from a national clinical registry for quality improvement within an Australian context.

Part C: Strategies to reduce the burden of anxiety or depression following stroke

Thesis aim 3: To investigate the association between the quality of acute stroke care, patient factors and clinical factors with self-reported anxiety or depression at 90-180 days following admission for stroke or TIA.

Thesis aim 4: To examine the convergent validity of the EQ-5D-3L anxiety or depression domain as a reliable screening tool for anxiety or depression in the early period following stroke.

Thesis aim 5: To systematically evaluate published evidence on the effectiveness of MBIs for moderating risk factors of stroke, and reducing the risk of poor patient outcomes or comorbidity, including anxiety or depression.

Thesis aim 6: To undertake a formative evaluation of the processes involved in developing a community-based yoga program.

1.3 Thesis outline and guide to chapters

This thesis is organised into four main parts. Part A (The global burden of stroke and strategies to reduce this burden) includes the thesis objectives and two literature review chapters. Chapter 1 includes the thesis introduction, objectives and specific aims. In Chapter 2, a summary of the pathophysiological definition, risk factors, chronic and long-term consequences of stroke are outlined. Chapter 3 includes a systematic review on the incidence, mortality, and case-fatality rates of stroke in different countries (aim 1).

Part B (Strategies to improve quality of care in hospitals) comprises two chapters and is focussed on strategies to improve care for stroke in acute hospitals. Chapter 4 provides an overview of current evidence-based practices for treatment of acute stroke and gaps in delivery of evidence-based care in Australian public hospitals. In this chapter I also describe the data collection systems used for monitoring acute stroke care specific to Queensland and the importance of using these data to reduce evidence-to-practice gaps through targeted quality improvement activities. In Chapter 5, I describe a strategy to address evidence-to-practice gaps in the acute care setting in Queensland using data from the Australian Stroke Clinical Registry (aim 2). This is presented as a manuscript (currently under review).

Part C (Strategies to reduce the burden of anxiety or depression following stroke) comprises six chapters. Chapter 6 includes a detailed description of the methods used in the study presented in Chapter 7. This includes the process of developing an analytic dataset, using the linked data obtained as part of a larger project, Stroke123. In Chapter 7, I used these comprehensive linked data to answer aim 3 of my research program. Chapter 8 contains methods and preliminary results of a project on the convergent validity, sensitivity and specificity of the anxiety or depression domain of the EQ-5D-3L survey as a suitable screening tool for anxiety or depression in survivors of stroke (aim 4). Chapters 9 and 10 are then

focussed on the evidence base for using MBIs to reduce the long-term consequences of stroke, from the preventive and disability perspective. Chapter 9 contains a published paper on the potential pathophysiological mechanisms of MBIs for moderating risk factors for stroke (scoping review), and Chapter 10 contains a published paper on the potential benefits of MBIs on outcomes of stroke (systematic review with meta-analyses). In Chapter 11, I describe the processes involved with developing a yoga program designed for survivors of stroke living in the community based on the principles of formative evaluation.

Part D is a single chapter providing an overview of the findings presented in the thesis, and the overall contribution of this body of research to the area of stroke. In this last chapter, I also discuss the future implications and recommendations.

PART A:

Introduction to stroke and

global burden

Chapter 2: Background to stroke

This chapter provides an overview of the pathophysiological definition of stroke, and risk factors for stroke. It also provides details of some of the chronic and long-term consequences of stroke.

2.1 Definition of stroke

The World Health Organization defines stroke as a 'rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin'.[29] Recently, the definition of stroke was revised by the American Heart Association/American Stroke Association (AHA/ASA).[30] The clinical diagnosis of stroke now includes a tissue based diagnosis of infarction to account for 'silent infarcts' based on pathology or radiological information, irrespective of duration of symptoms. Stroke is categorised into specific types: ischaemic stroke, haemorrhagic stroke (intracerebral haemorrhage (ICH) or subarachnoid haemorrhage (SAH)), transient ischaemic attack (TIA), and undetermined (UND). These stroke sub-types are further described below.

Nearly 80% of first-ever strokes are diagnosed as ***ischaemic strokes***. This type of stroke occurs when there is a vascular occlusion of cerebral arteries, resulting from either a thrombus or an emboli. A thrombus or blood clot forms in a blood vessel, thereby blocking blood flow to the subsequent part of the brain. Emboli also result in blockage and originate from a blood clot formed elsewhere in the body. Part of this clot breaks off and is then carried through the blood

stream to the brain, thereby causing partial or complete obstruction of blood flow to the brain. As a result, that territory of the brain is damaged. Ischaemic strokes can be classified as one of the following sub-types: posterior circulation infarcts (POCI), total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI) or lacunar cerebral infarct (LACI).[31]

Haemorrhagic strokes occur when an artery ruptures and bleeds into the surrounding brain tissue. The rupture is generally caused by an aneurysm (thinning of the artery wall which is then prone to rupture) or arteriovenous malformation (cluster of abnormal formed blood vessels). Haemorrhagic strokes can either be classified as an ICH or a SAH, based on the origin and site of bleeding. In an ICH the blood from the ruptured vessel diffuses into the surrounding tissue. Bleeding into the subarachnoid space surrounding the brain is known as a SAH. Approximately 15% of first-ever strokes are ICH. It is one of the most severe types of stroke, leading to high mortality within the first year of stroke. It also results in significant long-term disability, with approximately 2 fold that of an ischaemic stroke. The mortality rate of those with SAH ranges 27% to 50%.[32] In this thesis, patients who have suffered a SAH have been excluded for analyses. This is because this type of haemorrhagic stroke is rare and managed very differently to other types of stroke (i.e. surgical intervention).

A ***TIA***, commonly known as a 'mini-stroke', has previously been classified as a temporary episode of brain clot lasting less than 24 hours. TIAs are generally classified separately to stroke although TIAs have similar pathological symptoms and mechanisms to an ischaemic stroke. In the mid-1960s, TIA was defined as episodes of temporary and focal dysfunction of vascular origin, which are variable in duration by lasting less than 24 hours, and with no permanent injury to the brain.[30] In 2013, a new definition was proposed by the AHA/ASA where a clinical diagnosis of a TIA allows for a tissue-based diagnosis from imaging techniques. TIA is now commonly defined as 'a transient episode of neurological dysfunction,

caused bifocal brain, spinal cord, or retinal ischaemia without acute infarction'.[30] After an initial TIA event, the risk of subsequent stroke is between 2% and 17% within the first 90 days.[5]

2.2 Consequences of stroke

Stroke is not only a leading cause of mortality, but is also a long-term chronic condition with multiple consequences for survivors, their families, health systems and society. The consequences of stroke are diverse and largely depends upon which part of the brain is affected. Survivors may experience physical disability, cognitive impairment, fatigue and psychological problems such as anxiety and depression.[8, 21, 33-35] In a recent Australian national survey commissioned by the Stroke Foundation, survivors reported having on-going problems that were inadequately addressed by the Australian health care system. They particularly reported issues with psychological function such as cognition, memory, mood and fatigue two years after stroke.[3]

2.3 Stroke reoccurrence

Patients surviving an initial stroke are known to be at significantly greater risk of further strokes.[36, 37] There is considerable variation in the estimation of risk of stroke reoccurrence in both the immediate phase (<6 months) and in the long-term (≥6 months) after first stroke. The cumulative risk of stroke reoccurrence within 1 year is reported to be approximately 16%, and between 19% to 32% at 5 years.[4, 36-38] The consequences of recurrent strokes are often more severe than initial stroke and contribute further to greater comorbidities and mortality.[6] With a rising number of people living with the consequences of stroke, it is essential that all survivors of stroke have their risks of stroke managed to avoid recurrent events.

2.4 Reducing the burden of stroke

There are three main ways that provide opportunities to intervene to reduce the burden of stroke. These are: (1) primary prevention (i.e. prevention a first-ever event), (2) acute stroke care (i.e. care provided in hospital), and (3a) ongoing secondary prevention, and (3b) long-term recovery; Figure 1.1).

1. Primary prevention is focussed on reducing the incidence of first-ever stroke. It involves identifying modifiable risk factors in those at risk of but without a prior history of stroke, and then controlling their risk factors using lifestyle changes or prescribing medications. For example, screening of the general public at pharmacies or clinics to identify those with high blood pressure.[39]

2. Acute stroke care includes the use of evidence-based strategies to diagnose and treat patients with stroke in the early stages of symptom onset and within the first week.[40] Care is provided in hospital and includes treatments to reduce the extent of brain damage, promotion of recovery through rehabilitation (i.e. sub-acute/in-hospital rehabilitation) and avoidance of complications.[7]

3. (a) Ongoing secondary prevention and (b) long-term recovery is initiated after a first stroke event, to prevent the likelihood of further stroke events, and aid long-term recovery. This stage of care includes patient rehabilitation at outpatient clinics, as well as lifestyle changes (e.g smoking cessation) and medication to control modifiable risk factors such as high blood pressure, cholesterol, or glycaemic control in diabetes. Blood-thinning medication is also recommended for those with ischaemic events, while anticoagulants are recommended for patients with atrial fibrillation. In addition to secondary prevention strategies, community-based interventions (e.g. group exercise programs)[41, 42] can assist with long-term recovery

following stroke and hence reduce the societal burden (i.e. costs of healthcare utilisation and worker productivity in the general society) of this condition.[43]

More detail on risk factors for stroke is provided in the next section.

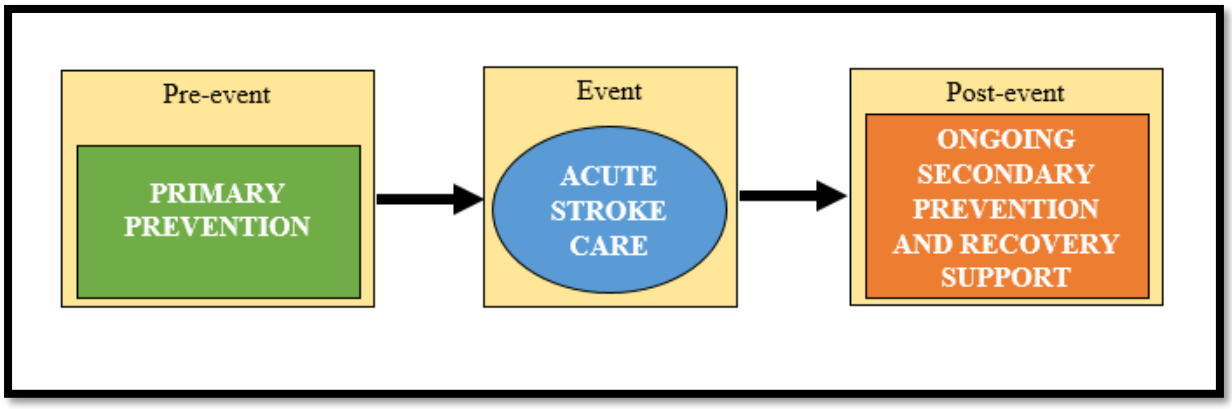

Figure 1.1. *Schema of the stroke care continuum*

2.5 Risk factors for stroke

2.5.1 General overview

The term 'risk factor' is one of the most central terms in epidemiological research, and it is defined as any patient characteristic, attribute or exposure that is independently associated with an increased risk of developing disease or injury.[44] Several risk factors for stroke have been identified and can be classified as modifiable or non-modifiable. The most recent comprehensive evaluation of the major risk factors for stroke were reported in the INTERSTROKE study, which was a large, multinational, case-control study with approximately 27,000 participants from 32 countries located in Africa, America, Asia, Australia, Europe and the Middle East.[45] In this study, approximately 92% of the risk for stroke

was attributed to ten modifiable risk factors. These included physiological factors such as hypertension (high blood pressure), diabetes mellitus (high blood glucose), dyslipidaemia (high blood cholesterol), atrial fibrillation and lifestyle factors such as smoking, unhealthy diet, inadequate physical activity, alcohol intake, as well as psychological issues such as stress and depression. Air pollution was also identified as an important contributor to the risk of stroke, particularly in low and middle income countries.[46]

There are also risk factors for stroke that cannot be modified. These include family history, ethnicity, gender and age.[47] Risk factors can be reduced or moderated to lower the risk of developing a first-ever stroke or recurrent stroke. Ideally, modifiable risk factors should be identified early, and managed with effective treatments as recommended in clinical practice guidelines.[7] Those individuals at high risk, as attributed by their risk factor profiles, should be provided with appropriate prevention and treatment strategies at the three levels of the continuum of care (Figure 1.1). In the section below, I will focus on the pathophysiology and burden of the major modifiable risk factors for stroke.

Most of the risk of stroke and attributed burden are associated with potentially modifiable factors. Individuals with multiple risk factors are at much greater risk of suffering from a recurrent stroke or cardiovascular event than those with a single risk factor.[47, 48] Careful management of these factors is crucial for primary and secondary prevention of stroke.

2.5.2 Modifiable risk factors for stroke

2.5.2.1 Medical factors

Hypertension

High blood pressure (i.e. hypertension) is diagnosed when systolic blood pressure is ≥ 140 mmHg and or diastolic blood pressure is ≥ 90 mmHg ideally obtained at an average of three

measurements per visit.[49] High blood pressure is the single most common risk factor for stroke, occurring in more than 60% of first-ever stroke events.[50] In Australia, nearly 80% of patients with stroke have high blood pressure. Generally, the risk of suffering a stroke is nearly three to four times greater in people with hypertension than among those without hypertension.[45, 51] High blood pressure causes stroke via many complex physiological pathways such as malfunctioned arterial baroreceptors, oxidative stress and inflammation.[52]

Diabetes

Diabetes, or high blood sugar, is a metabolic disease diagnosed when there is excess glucose in the blood (hyperglycaemia). It is usually diagnosed by measuring the levels of glycosylated haemoglobin (HbA1c) levels in the blood serum or fasting blood plasma glucose.[53]

Diabetes is an independent risk factor for stroke and is considered to be an underlying source of a global epidemic of stroke in the 21st century.[54] Approximately 1.7 million Australians are diagnosed with diabetes. More than 100,000 Australians have been diagnosed with diabetes in the past year, costing $14.6 billion to the health care system.[55] Those with diabetes are twice as likely to suffer an ischaemic stroke and 1.6 times likely to suffer from a brain haemorrhage, compared to those without diabetes.[56] More importantly, in survivors of stroke, the presence of high blood glucose increases the risk of recurrent stroke and increases the likelihood or severity or developing other comorbidities and greater mortality.[57]

There are several possible mechanisms wherein diabetes may lead to stroke. High blood glucose is caused by dysfunction of the pancreas resulting in inadequate secretion of insulin into the blood (Type 1), or progressive resistance of cells to insulin (Type 2). This leads to vascular endothelial dysfunction, increased arterial stiffness, systemic inflammation and thickening of the capillary basal membrane, which ultimately promote atherosclerosis or fatty deposits in the blood vessels.[58, 59]

Dyslipidaemia

Individuals with dyslipidaemia or high blood cholesterol have elevated levels of lipids in the blood stream, and these levels contribute to the development of atherosclerosis.[60] Elevated levels of total cholesterol, low-density lipoprotein (LDL), and triglycerides are proven risk factors for cardiovascular diseases, but the temporal association in stroke is varying.[61] The exact mechanism for the association between elevated blood lipids and stroke also remains unclear. Evidence is particularly inconsistent for both the type of lipid and type of stroke. The associations also depend on the specific lipid component considered, with stronger evidence for total cholesterol and LDL. There is evidence that the association between higher total cholesterol levels and increased risk of an ischaemic stroke.[62] In addition, in most observational studies an association between lower total cholesterol and LDL levels and increased risk of haemorrhagic stroke was found.[62, 63] Furthermore, a greater level of high-density lipoprotein (HDL) in the blood has been associated with a 40% reduction in the risk of an ischaemic stroke, but the association between and HDL and ICH remains uncertain.[62]

The exact pathophysiological mechanisms of the effect of lipids on the risk of stroke remains unclear. It is proposed that high levels of cholesterol in the blood can lead to deposits of cholesterol in the arteries and cause a plaque build-up (atherosclerosis) resulting in compromised or a blockage to normal blood flow to the brain and cause a stroke.[62]

Atrial fibrillation

Atrial fibrillation (AF) is a form of cardiac arrhythmia, and a major risk factor for stroke. Those with AF have abnormal heart rhythm which may be paroxysmal (i.e. occasional occurrence and then stops) or persistent, and is the cause of 20% of all cases of stroke.[64] AF is associated with a two- to five-fold greater risk of stroke particularly in the older population.[64] There is

evidence that patients with stroke and AF are often older, have more comorbidities, and experience worse outcomes following stroke than those without AF.[65]

Psychological conditions

Anxiety and depression are mood disorders that are the most common psychological conditions often associated with stroke.[15] The presence of anxiety or depression has been increasingly linked to the occurrence of first-ever and recurrent stroke.[45] Individuals with no prior history of stroke, but with anxiety, have a 14% increased risk of stroke.[66] Similarly those with depression have been reported to have a 40% increased risk of stroke.[67]

Anxiety or depression are often experienced by survivors of stroke, affecting 1 in 3 patients.[3, 8, 34] It is estimated that 31% will develop depression within 5 years following stroke and this increases the risk of recurrent events by 49% when compared to patients without depression.[68] Survivors of stroke may suffer from anxiety or depression as a result of the culmination of other risk factors such as excess smoking and alcohol consumption or purely due to the physical impairments, or, difficulties with speech or cognition as a result of stroke.[66, 67]

2.5.2.2 Lifestyle factors

Smoking and alcohol consumption

There is strong evidence for an association between smoking and the risk of stroke. Individuals who are current smokers have a two- to four-fold greater risk of suffering from stroke than never smokers or past smokers.[45, 69] Furthermore, smoking causes a greater risk for ischaemic stroke than ICH. In survivors of stroke, cigarette smoking is associated with further consequences such as 30% greater risk of mortality or recurrent stroke, when compared to non-smokers. The risk of stroke is greater in women who smoke when compared to men who smoke.[70] The pathophysiological mechanism for the association between smoking and

increased risk of stroke is thought to be aided by oxidative stress, inflammation and atherosclerosis.[71]

Excess alcohol consumption (> 14 standard alcoholic drinks per week)[45] is yet another major risk factor for stroke. The risk of stroke may also be dependent on the amount of alcohol consumed.[72] In a recent systematic review, where the authors assessed the effect of alcohol consumption on the risk of stroke, the risk of stroke increased by more than two folds in those individuals who consumed excessive alcohol compared to those who consumed no alcohol.[45] Vascular dysfunction, and increased irregular heartbeats and blood pressure are consequences of excessive alcohol consumption.

Unhealthy diet

A poor diet, insufficient in consumption of vegetables and fruits, increases the risk of stroke, and risk factors such as hypertension, hyperlipidaemia, diabetes and obesity which further increases the risk of stroke. Increased consumption of fatty and oily foods also results in an increase in lipids and associated risk of stroke.[73] In a recent meta-analysis, consuming 200 grams of fruits and vegetables daily reduced the risk of an ischaemic stroke by 32% and 11%, respectively. The pathophysiological mechanisms behind the association of adequate diet and risk of stroke is the benefits derived from the minerals, vitamins and nutrients that enrich the cells in the body to produce healthy energy. Optimal nutrition, vitamins, and antioxidants reduces the risk of vascular dysfunction and prevents hypertension.[74]

Physical inactivity

A lack of exercise is an independent risk factor for stroke.[45] There is growing evidence that regular exercise is associated with a reduced risk of stroke, and less severe strokes.[75] Regular exercise can also moderate the risk of stroke by altering other risk factors for stroke such as

hypertension and diabetes, thereby further reducing the overall 'absolute' risk of stroke.[45] In healthy individuals the intensity of exercises may vary from being moderate intensity (e.g. walking) to high intensity (e.g. running, swimming). However, not all survivors of stroke are able to take part in strenuous exercise activities. [41, 76]

Being overweight

There is strong evidence that obesity is independently associated with the risk of stroke.[77-79] The most recent data were obtained from a prospective cohort study, in which 13,700 individuals from the community were followed-up for 23 years.[80] In this study, individuals who were obese (body mass index (BMI) >30 kg/m^2) had a 30-80% greater risk of experiencing a stroke, and those who were overweight (BMI 25-29.9 kg/m^2) had a 20% greater risk of stroke when compared to healthy individuals with normal weight (BMI 18.5-24.9 kg/m^2).[80]

Increased fatty acids, or lipids, produce several inflammatory markers that contribute to vascular dysfunction and insulin resistance.[58, 59] Increased lipids causes an accumulation of excessive lipids in the blood vessels which result in blockages, disruption to blood flow and accelerates atherosclerosis.[62]

2.6 Summary

Stroke is a leading cause of death and disability, both globally and in Australia, resulting in a huge burden to patients, their families, society and the health care system. Most of the risk for stroke and attributed burden are associated with potentially modifiable risk factors. Evidence-based management of these risk factors is essential for the prevention of stroke. More research is needed to better understand the role of anxiety and depression and how best to avoid developing these comorbidities after stroke.

Chapter 3: Global Stroke Statistics

3.1 Overview

In Chapter 2, I provided a summary of the pathophysiological definitions and the consequences of stroke. I also highlighted some of the known evidence-based risk factors for stroke and the risk of stroke reoccurrence.

In this chapter these concepts are explored in greater detail through an in-depth assessment of the global effect of stroke. The effect of stroke can be described by incidence (number of new cases with a new diagnosis of stroke during a period of time), mortality (number of cases within a population who died from stroke) or case-fatality (number of cases of stroke who died within a set period of time), as well as disability.[1] With the growing global burden of stroke, there is a continued need to understand the characteristics of the disease and its effect on individuals and health systems in various countries.

In summary, the aims of the following paper were to (i) update our repository of the most recent country-specific data on stroke;[81] (ii) determine where data on incidence, mortality and case-fatality are missing; and (iii) determine countries where data on incidence, mortality and case-fatality from stroke are out-of-date. A further exploratory aim was to identify whether nationally-representative clinical registry data were being routinely obtained in countries where an incidence study was not undertaken or had outdated stroke data. This helped to describe whether registries were being used as a potential substitute for these data. This paper addresses the first aim of this thesis. My contribution is at 45%, and the nature of my contribution was

coordinating the author meetings, literature search, data management, analysis, interpretation, and writing parts of the manuscript.

This paper was published in the International Journal of Stroke (2017; Vol 12: 13-32).

3.2 Published paper

Global stroke statistics

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Global stroke statistics

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Abstract

Background: Up to date data on incidence, mortality, and case-fatality for stroke are important for setting the agenda for prevention and healthcare.

Aims and/or hypothesis: We aim to update the most current incidence and mortality data on stroke available by country, and to expand the scope to case-fatality and explore how registry data might be complementary.

Methods: Data were compiled using two approaches: (1) an updated literature review building from our previous review and (2) direct acquisition and analysis of stroke events in the World Health Organization (WHO) mortality database for each country providing these data. To assess new and/or updated data on incidence, we searched multiple databases to identify new original papers and review articles that met ideal criteria for stroke incidence studies and were published between 15 May 2013 and 31 May 2016. For data on case-fatality, we searched between 1980 and 31 May 2016. We further screened reference lists and citation history of papers to identify other studies not obtained from these sources. Mortality codes for ICD-8, ICD-9, and ICD-10 were extracted. Using population denominators provided for each country, we calculated both the crude mortality from stroke and mortality adjusted to the WHO world population. We used only the most recent year reported to the WHO for which both population and mortality data were available.

Results: Fifty-one countries had data on stroke incidence, some with data over many time periods, and some with data in more than one region. Since our last review, there were new incidence studies from 12 countries, with four meeting pre-determined quality criteria. In these four studies, the incidence of stroke, adjusted to the WHO World standard population, ranged from 76 per 100,000 population per year in Australia (2009–10) up to 119 per 100,000 population per year in New Zealand (2011–12), with the latter being in those aged at least 15 years. Only in Martinique (2011–12) was the incidence of stroke greater in women than men. In countries either lacking or with old data on stroke incidence, eight had national clinical registries of hospital based data. Of the 128 countries reporting mortality data to the WHO, crude mortality was greatest in Kazhakstan (in 2003), Bulgaria, and Greece. Crude mortality and crude incidence of stroke were both positively correlated with the proportion of the population aged $\geq$ 65 years, but not with time. Data on case-fatality were available in 42 studies in 22 countries, with large variations between regions.

Conclusions: In this updated review, we describe the current data on stroke incidence, case-fatality and mortality in different countries, and highlight the growing trend for national clinical registries to provide estimates in lieu of community-based incidence studies.

Keywords

Incidence, mortality, case-fatality, global, worldwide, stroke, burden, epidemiology

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Introduction

With the growing world-wide burden of stroke, there is a continued need to understand the characteristics of the disease and its impact in various countries. As found with our first report on global stroke statistics published in the International Journal of Stroke (IJS) in 2014 having a common repository of the latest published information on major determinants of the burden of stroke worldwide that was focused on stroke incidence and mortality is important.[1] We provide this update with additional information and consider this work as complementary to the information provided by the World Stroke Organization (WSO) and Global Burden of Disease (GBD) program.[2,3] As a flagship publication, we seek to regularly present comparative data for stroke in a readily accessible way, both in tabular and graphic form, using the latest available data at the time of publication which can be extracted from public records. We believe that such a compilation of data is a useful resource for all health care and related professions. This second report is part of an on-going series to update information on stroke mortality and incidence; and provides new information on case-fatality and the issues of potentially outdated data for some countries.

Aims

Our aims are to: (i) update our repository of the most recent country-specific data on stroke; (ii) determine where data on incidence, mortality and case-fatality are missing; and (iii) determine countries where data on incidence, mortality and case-fatality from stroke are out of date. A further exploratory aim was to identify whether nationally-representative clinical registry data were being routinely obtained in countries that

Figure 1. Screening and selection of articles with data on incidence or case-fatality.

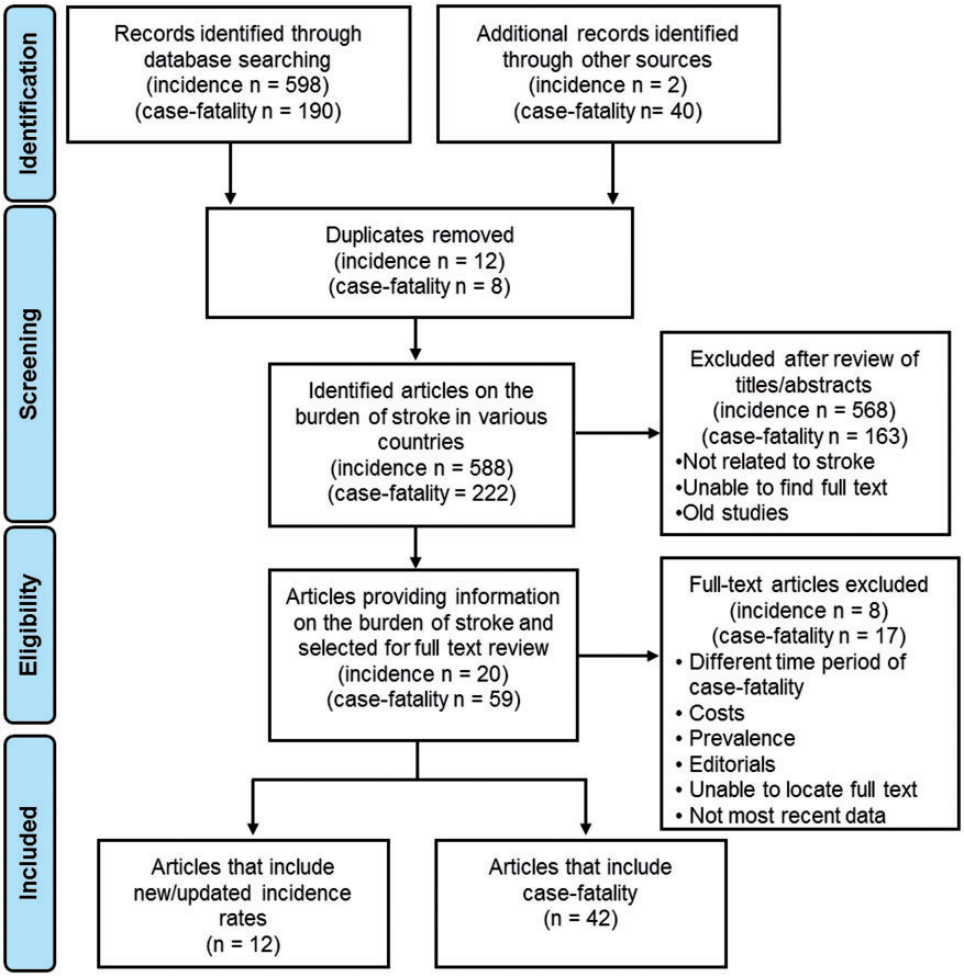


Figure 2. World map showing availability of studies with overall incidence. Old studies (in blue) indicate those that were included in the previous review, while new studies (in brown) indicate those published since that review.[1] The map is based on crude and/or adjusted incidence of stroke irrespective of age restriction, or adjustment method. The countries highlighted are therefore different to those in Figure 6.

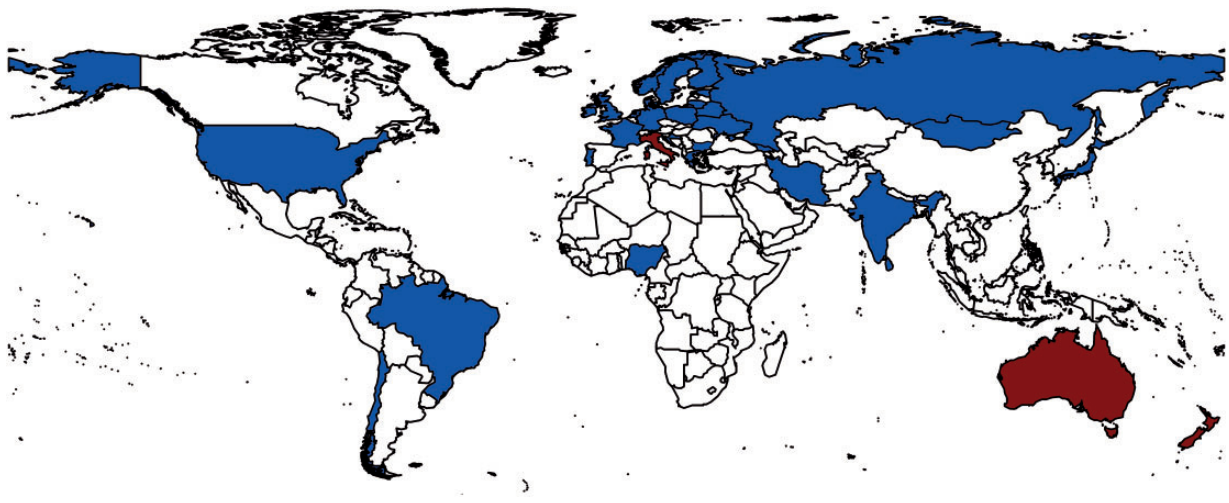
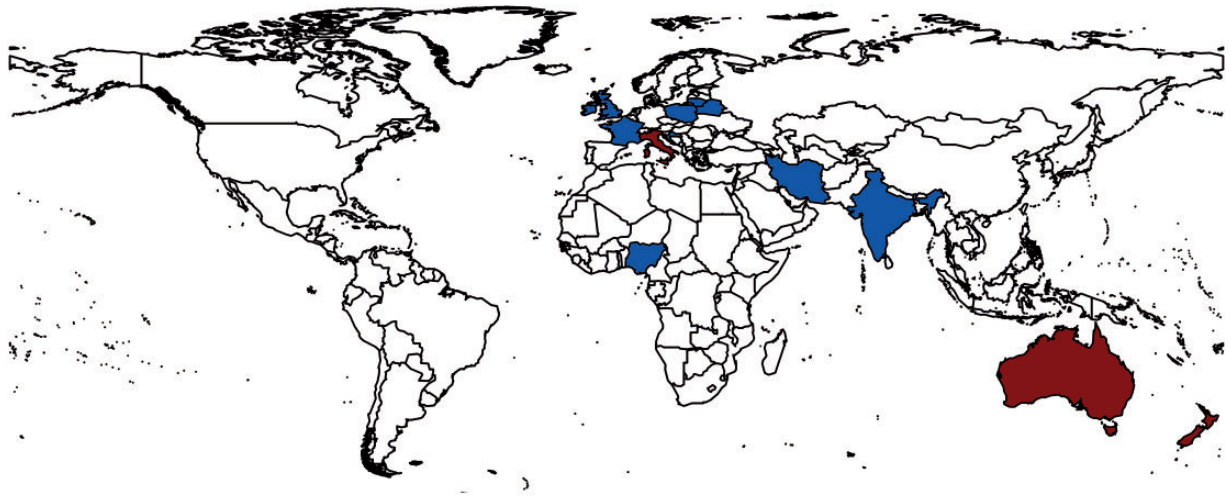


Figure 3. World map showing availability of studies with sex-specific incidence. The map is based on crude and/or adjusted incidence of stroke irrespective of age restriction, or adjustment method, hence it is different to Figure 6. Old studies are indicated in blue and new ones in brown.

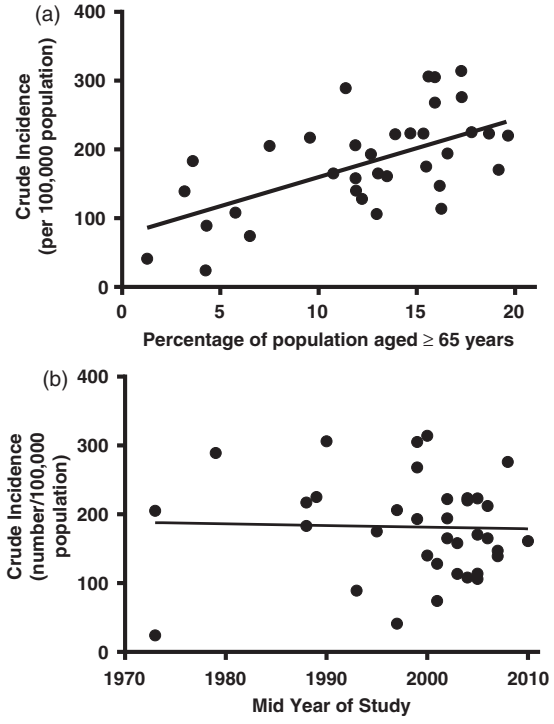


had not undertaken an incidence study or had outdated stroke data to describe whether these were being used as a potential substitute for these data.

Methods

We sought to present incidence, mortality and case-fatality data for 205 countries (source: www.infoplease.com/countries.html) out of which 194 are recognized by WHO (source: www.who.int/countries/en/), 192 countries are members of the United Nations (source: www.un.org/en/members/), and 182 countries are recognized by the World Bank (source: www.worldbank.org/en/country). Incidence data were compiled by conducting an updated literature review with a major focus on original papers, using only population-based incidence studies. Additionally, case-fatality data from population-based studies were also compiled. Relevant data were also drawn from published systematic reviews on these topics. We also acquired mortality

Figure 4. Crude incidence from stroke according to (a) the proportion of the population aged ≥ 65 years ($Y = 8.442*X + 75.32$, $p < 0.001$) and (b) the mid-year that the study was conducted ($Y = -0.2400*X + 661.4$, $p = 0.86$). These are for all countries that have reported crude incidence, and for which population estimates were reported to the WHO.[12,14,18–29]



data from the World Health Organization (WHO) mortality database, using the most current available estimates of stroke mortality and the corresponding population denominator.

Literature search and data extraction for incidence and case-fatality

We searched multiple databases (Medline, Scopus, Pubmed, Google Scholar, WHO library, and WHO regional databases) to identify relevant original papers and review articles published from 15 May 2013 to 31 May 2016 for data on stroke incidence around the globe. Similarly, an extensive search was conducted from 1980 and until 31 May 2016 for data on case-fatality of stroke.

The search strategy developed was adapted from our previously published review article.[1] Our pre-defined inclusion criteria comprised population-based studies that met, or potentially met, the ideal criteria (Supplementary Online Table 1), and a comprehensive determination of the overall incidence of stroke or on incidence among men and women separately. Ideal criteria included reports of first-ever in a lifetime stroke only to ensure that no figures were inflated by the inclusion of recurrent events. We also accessed papers where the incidence of any stroke type was reported, just in case the article contained overall incidence rates relevant to our aims. Data on types of stroke are not reported here. In addition, the search for case-fatality information was undertaken using terms such as case-fatality, mortality, and survival. We included case-fatality only from those studies that conformed to the ideal criteria for stroke incidence studies to ensure comparability between studies. Furthermore, only studies with published data on 7-day, 28-day, or 30-day case-fatality following stroke are included in this review.

As previously, citations identified were first screened by title and abstract. After this first screening stage, the full text was read by a single reviewer (TT). We included only original papers and systematic reviews clearly meeting the inclusion criteria (as stated above).

To supplement the database searches, we screened the reference lists of these papers to identify any potentially missing original papers or systematic reviews. Data were only included from reference lists on the incidence or case-fatality of stroke, which adhered to the same criteria as those for the database searches.

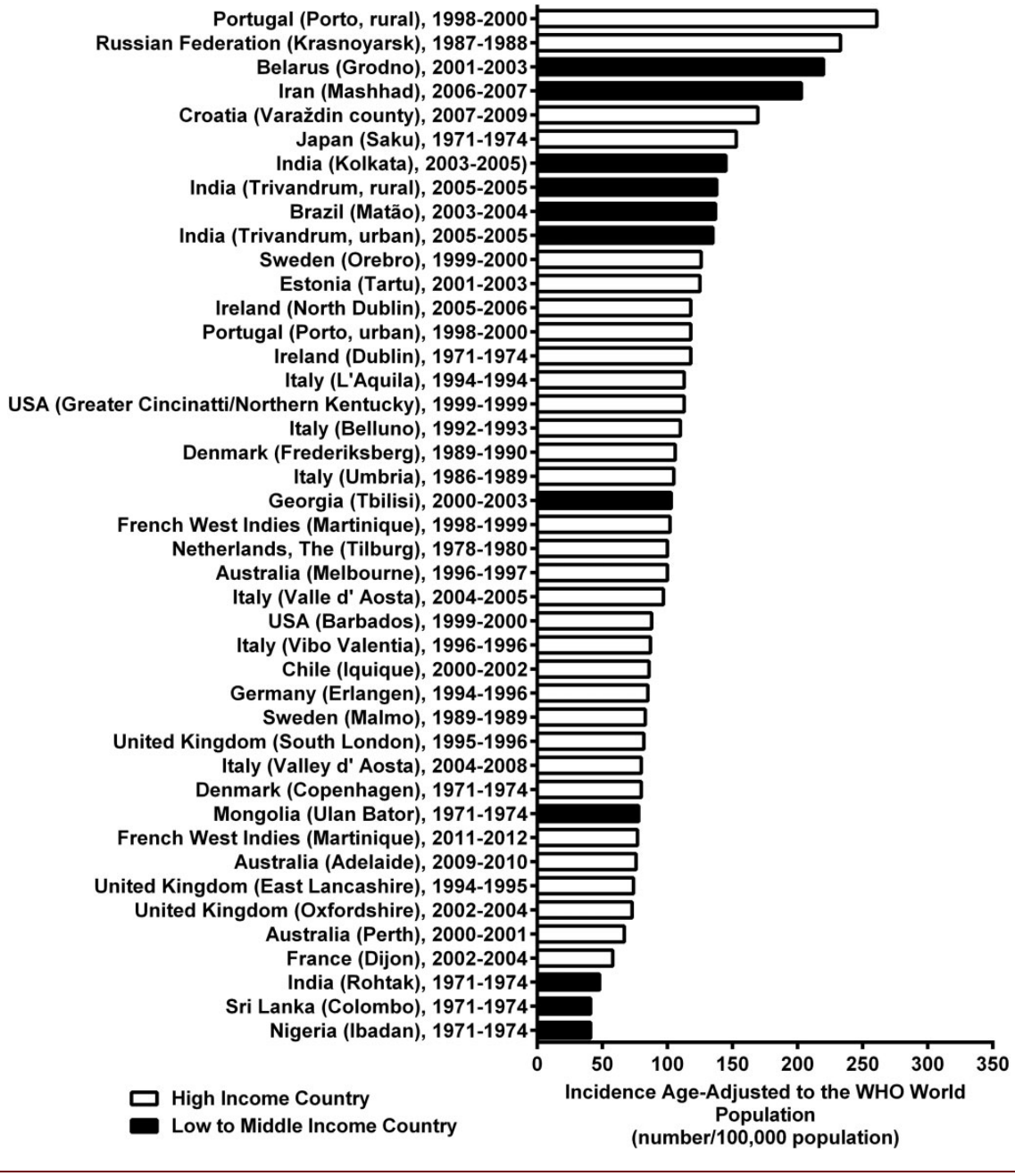
When new incidence or case-fatality data from one country were reported in more than one publication or online source, we linked the sources to prevent double-counting. For the heat maps on incidence, when there were data from the same country from both rural and urban regions, these countries were displayed as the mean value of these observations. Information from each paper was extracted by one reviewer (TT) and discussed among three reviewers (TT, AGT, DAC). All authors scrutinized the list of identified papers to assess whether any known papers were missing.

Data on the location of stroke clinical registries that are considered in their country to represent a national standardized dataset for acute stroke care and outcomes were obtained from a recently published systematic review.[4]

Incidence and mortality by age category

We have previously provided details of the assessment of incidence and mortality versus age category.[1] Briefly, for each country we undertook a regression analysis of crude incidence and/or mortality versus the proportion of the population aged ≥65 years. When possible, we used population data from the same year that incidence (and mortality) was assessed. When incidence was assessed over more than one year, the population data used was the mid-year of data collection. When the

Figure 5. Incidence of stroke, adjusted to World Health Organization World population.[7,10,12,14,16,18–20,22–26,30,31,34–39] High income countries are shown in the white bars, and low and middle income countries are shown in the black bars.



incidence studies spanned an even number of years, then the more recent of the two mid years was used. When there were no population data for the year in which the incidence study was conducted, we used the closest available year. For mortality, both population and mortality data were derived from the same year.

Because all of the new studies had data adjusted to the WHO World standard population, we only report data using this standard.

Collation and analysis of mortality data ability

Data for mortality and population denominators were obtained from the WHO website at www.who.int/healthinfo/statistics/mortality_rawdata/en/. These data comprise deaths registered in country civil registration systems, with deaths coded by the national authority within each country. Population data are also provided by many of these countries. The latest data files from

Figure 6. Heat map showing incidence of stroke adjusted to the WHO world population by quartiles.[5]

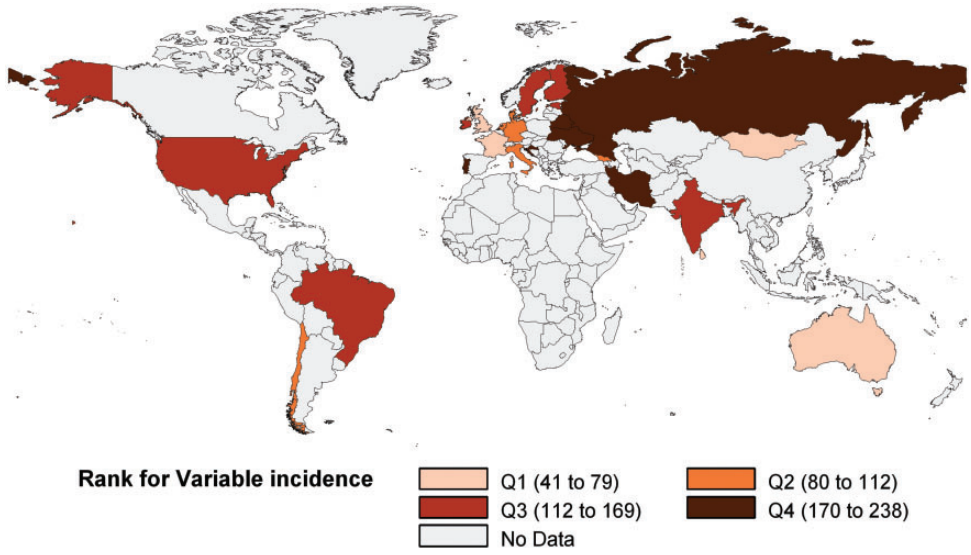


Table 1. Adjusted incidence of stroke in men and women. New studies are indicated by *.

Country, study period	Incidence rate per 100,000 population (95% confidence interval)		Standard criteria met[a]
	Men	Women	
Age adjusted to the European standard population			
Belarus (Grodno), 2001–2003[24]	356 (334–377)	236 (222–250)	Yes
Croatia (Varaždin county), 2007–2009[25]	282 (256–309.9)	181.1 (165.6–197.6)	No
France (Dijon), 2000–2006[34]	107.5 (98.3–116.8)	68.9 (62.7–75)	Yes
Italy (Sesto Fiorentino), 2004–2006[73,74]	101.2 (82.5–123)	63 (48.5–80.7)	Yes
Italy (Valle d' Aosta), 2004–2005[20]	159 (127–190)	100 (75–125)	Yes
Kuwait, 1989, 1992, 1993[75]	35.48 (35.39–35.56)	16.66 (16.59–16.73)	No
Lithuania (Kaunas), 2004[76]	239.3 (209.9–271.6)	158.7 (135–185.4)	Yes
Poland (Warsaw), 2005[26]	140 (132–147)	120 (114–127)	Yes
Spain (Castilla y León, Extremadura, and Comunitat Valenciana regions), 2005[35]	99 (81–117)	66 (53–80)	No
Spain (Menorca), 2004–2006[73,74]	116.3 (96.1–139.5)	65.8 (50.9–83.8)	No
*Spain (La Rioja), 2009[16]	206 (187.7–224.4)	139.3 (127.0–151.5)	No
United Kingdom (South London), 2004–2006[28]	121.1 (100.5–144.7)	78.1 (61.8–97.5)	Yes

(continued)

Table 1. Continued

Country, study period	Incidence rate per 100,000 population (95% confidence interval)		Standard criteria met[a]
	Men	Women	
Age adjusted to Segi's World population			
China (Beijing), 2000[36]	147.6 (134.6–162.6)	124 (113–137.4)	No
China (Changsha), 2000[36]	190 (175.2–207.3)	119.1 (108.5–132.3)	No
China (Shanghai), 2000[36]	87.3 (78.5–98.2)	68.1 (61–77.3)	No
France (Dijon), 2000–2006[34]	72.5 (65.9–79.1)	47.3 (45.5–52)	Yes
Iran (Mashhad), 2006–2007[18]	208 (180–236)	198 (170–226)	Yes
Age adjusted to WHO World standard population			
*Australia (Adelaide), 2009–2010[12]	91 (73–112)	61 (47–78)	Yes
Belarus (Grodno), 2001–2003[24]	266 (250–282)	180 (169–191)	Yes
Bulgaria (Rural), 2002[77]	909 (729.67–1132.41)	667 (529.24–840.61)	No
Bulgaria (Urban), 2002[77]	597 (491.2–725.59)	322 (255.14–406.637)	No
Croatia (Varaždin county), 2007–2009[25]	213.1 (194–233.3)	137.6 (126.3–150.9)	No
India (Trivandrum, rural), 2005[31]	163.4 (122.4–204.4)	115.3 (83–147.6)	Yes
India (Trivandrum, urban), 2005[31]	141.7 (122.1–161.3)	130.1 (113.3–146.9)	Yes
India (Kolkata), 2003–2005[78]	117.1 (87.8–152.6)	178.0 (102.4–223.2)	Yes
Italy (Valle d' Aosta), 2004–2005[20]	122 (94–150)	77 (55–99)	Yes
*Italy (Valle d' Aosta), 2004–2008[7]	100 (89–112)	62 (53–71)	Yes
*Japan (Iwate State)[15]	190 (172–209)	104 (91–118)	No
*Martinique (Caribbean)[14]	90 (79–101)	69 (60–78)	Yes
*New Zealand (Auckland)[10]	129 (120–138)	110 (103–119)	Yes
*Spain (La Rioja)[16]	131.0 (119.3–142.6)	86.2 (78.6–93.8)	No

[a]Standard criteria = multiple overlapping sources, World Health Organization definition of stroke, incidence cases, no upper age limit, and prospective design.

WHO were updated on 25 November 2015. Not all countries are listed in the mortality files provided by WHO. This is because (1) WHO does not receive mortality data from all countries; (2) some countries may provide data using non-standard codes; and (3) deaths may not be certified by a medical practitioner.

The files from WHO that we used include population denominators, country codes, and mortality data. The mortality codes used include those from ICD8, ICD9, and ICD 10 (Supplementary Online Table 2).

Data on deaths from cerebrovascular disease were merged with the population denominators for the same year as that in which mortality was coded. Crude mortality of stroke was obtained by dividing the overall deaths from cerebrovascular diseases for each country by the total population. These were then multiplied by 100,000 to obtain crude mortality per 100,000 population. The same calculations were conducted for men and women separately. We then calculated age-adjusted death rates standardized to the WHO world population using the direct method.[5]

Figure 7. Crude mortality from stroke in the most recent year reported to the World Health Organization, ordered according to the average mortality for men and women. Note that mortality data for China are for selected regions only and represent < 10% of all deaths in the country.

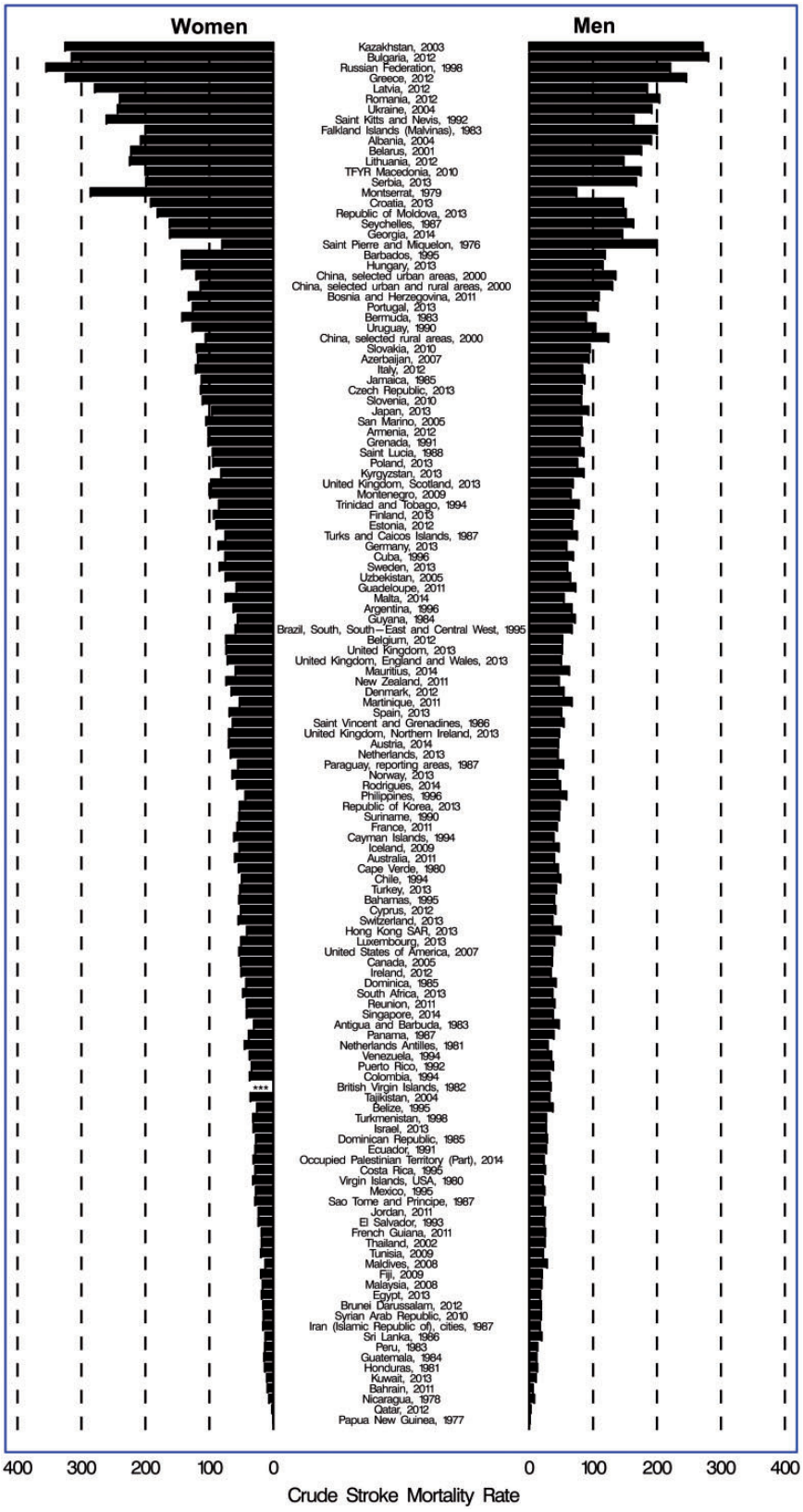
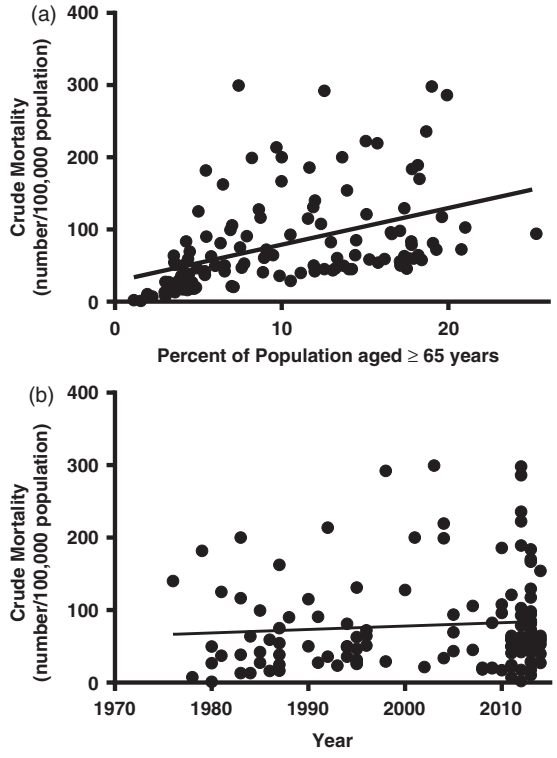


Figure 8. Crude mortality from stroke according to (a) the proportion of the population aged at least 65 years ($Y = 5.091*X + 28.08$, $p < 0.0001$) and (b) the year ($Y = 0.4675*X - 856.90$, $p = 0.35$). These are for all countries that have reported mortality to the World Health Organization, and are for the most recent year reported for each individual country.



Where possible, adjustments were made using 5-year age bands. In some instances, data on mortality were only provided in 10-year age bands, and so 10-year age bands are used for these countries. Some countries also had different upper age bands for mortality, ranging between ≥65 years and ≥95 years. We used the best available data for each country and adjusted for age using the maximum number of categories. We then removed all but the latest year data for each country.

Comparison of crude incidence and crude mortality

We assessed the relationship between the crude incidence and mortality for each country, using the same year for incidence and mortality, where possible. When the study was conducted over more than one year, we used population data from the middle year of the study, and when there was an even number of years the latter of the two mid years was used. When countries had not reported population data to WHO, even when mortality data were present, these countries were excluded. For countries that had no population data for the year in which the incidence study was conducted, but had population data for other years, the closest available year was used.

Results

Overall there were 12 countries in which new incidence data were reported. Of the 128 countries in which mortality data had been reported to the WHO, in 57 (44.5%) the figures were new or updated since our last review. In addition, data on case-fatality were reported for 22 countries.

Incidence

The literature search yielded 600 publications (see Figure 1 for selection process). In the first stage of screening, we retrieved 20 potential new articles on stroke incidence. In 12 of these articles, total crude stroke incidence was reported[6–17] with four conforming to our search criteria. In nine articles, separate rates were reported for men and women,[7–10,12–16] with four conforming to our strict criteria. Of those conforming to our strict methodological standards all were age-adjusted to the WHO population for both overall stroke incidence and sex-specific incidence rates.[7,10,12,14] In Figure 2, the location of these new published studies are highlighted in brown for overall stroke incidence, while Figure 3 shows all countries that provided sex-specific incidence rates. The updated data on crude incidence of stroke, including both old and new studies, varies greatly among countries (Figure 4, Supplementary Online Table 3).[12,14,18–29] Of the studies identified since our last review[1] that met our criteria, the largest crude stroke incidence rate was observed in Italy 2004–8) at 212/100,000 population per year,[7] with this population having a large proportion of people aged ≥65 years (19%; Figure 4(a)).[15] In contrast, Saku (Japan) had a relatively high crude incidence of stroke (205 per 100,000 per year) in the presence of a small population at risk (7.5% aged ≥65 years; Figure 4(a)).[22] Similar data are available for men and women in some regions (Supplementary Online Table 4).[7–10,12–16,18,19,23–27,29–33] There was no difference in incidence according to the year that the study was conducted (Figure 4(b)).

Using the WHO World standard population, the age adjusted incidence rates of the studies identified since our last review, and meeting our strict criteria, range

Figure 9. Age-adjusted mortality from stroke in the most recent year reported to the World Health Organization, ordered according to the average mortality for men and women. Note that mortality data for China are for selected regions only and represent < 10% of all deaths in the country.

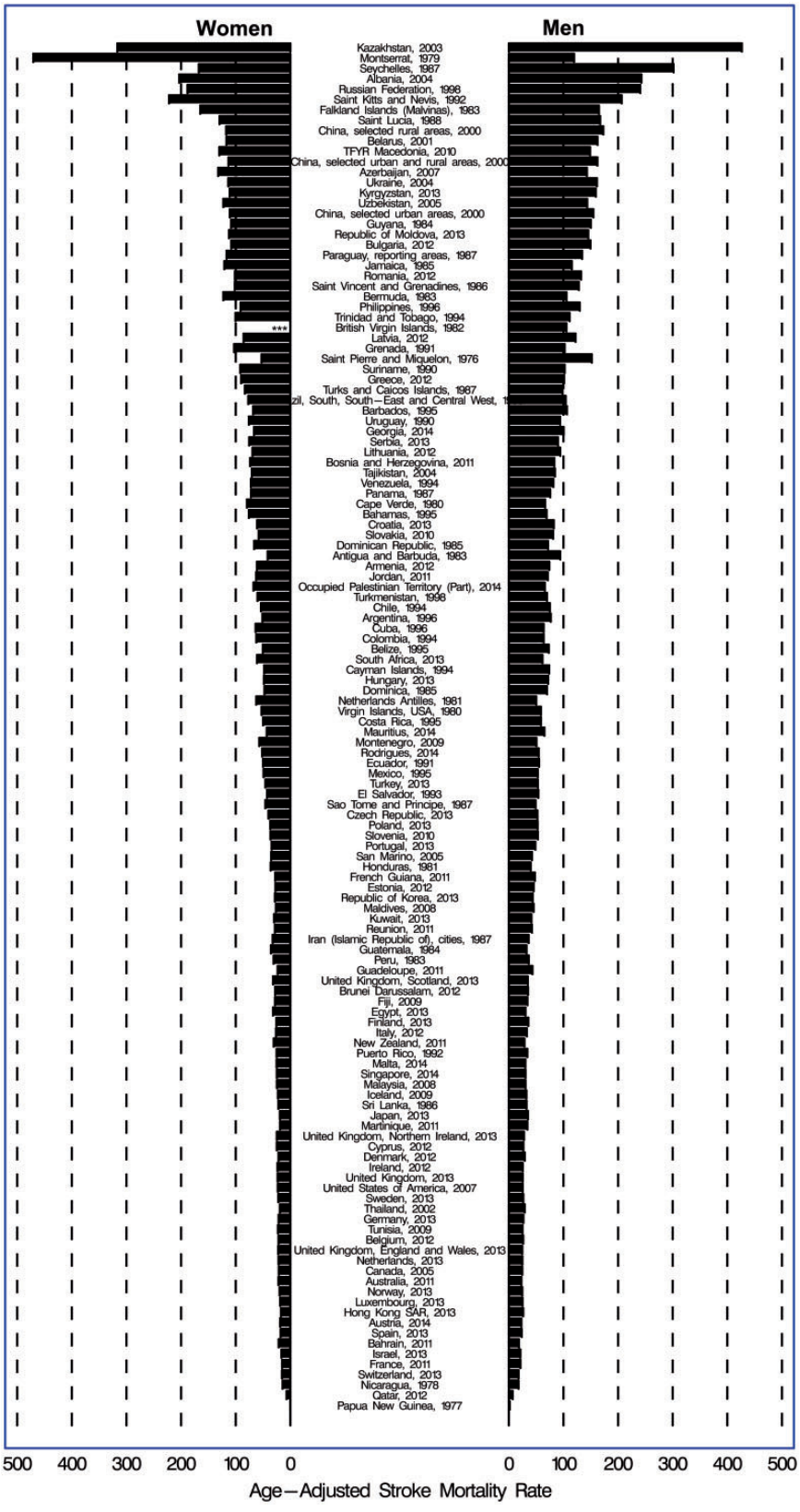


Figure 10. Heat map showing mortality from stroke adjusted to the WHO world population, by quintiles.[5]

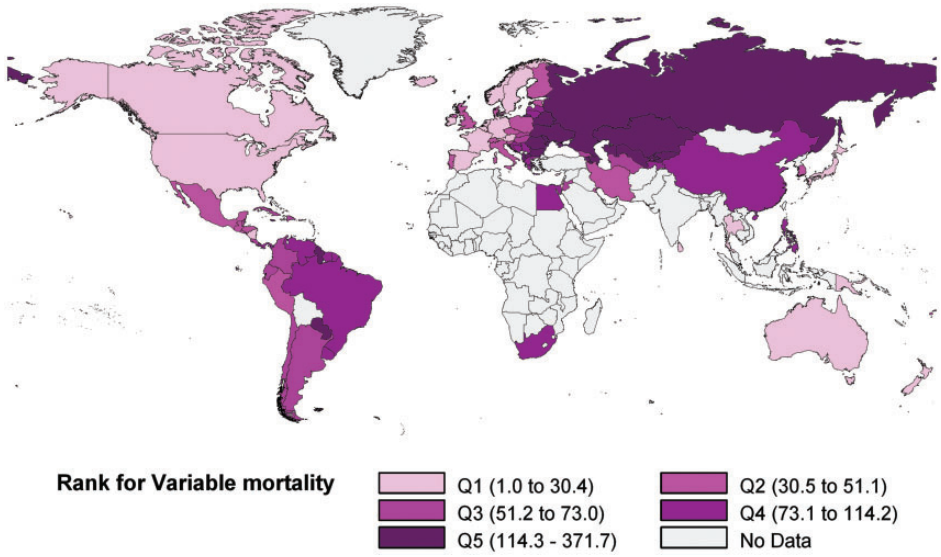
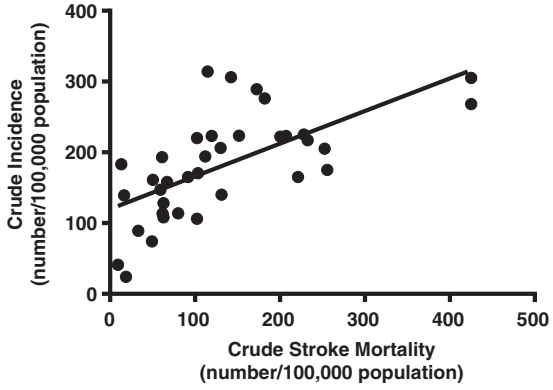


Figure 11. Regression of crude mortality from stroke versus incidence. These are for all countries that have reported mortality to the World Health Organization, and also have assessed the incidence of stroke for a similar year ($Y = 0.4616*X + 119.9$, $p < 0.0001$).



from 76 per 100,000 population per year in Adelaide, Australia (2009–10) to 119/100,000/year in Auckland, New Zealand (see Figures 5 and 6, and Supplementary Online Table 5).[7,10,12,14,16,18–20,22–26,30,31,34–39] This latter study was age-adjusted to the population aged ≥15 years and so incidence rates are greater than would occur if all age groups were included. New age-adjusted stroke incidence rates are greater in men than in women in all countries (Table 1).[14]

Mortality

Since our last review, where the most recent data available were for 2011, there are now new data for 2012 (14 countries), 2013 (28 countries), and 2014 (67 countries; see Supplementary Online Table 6).

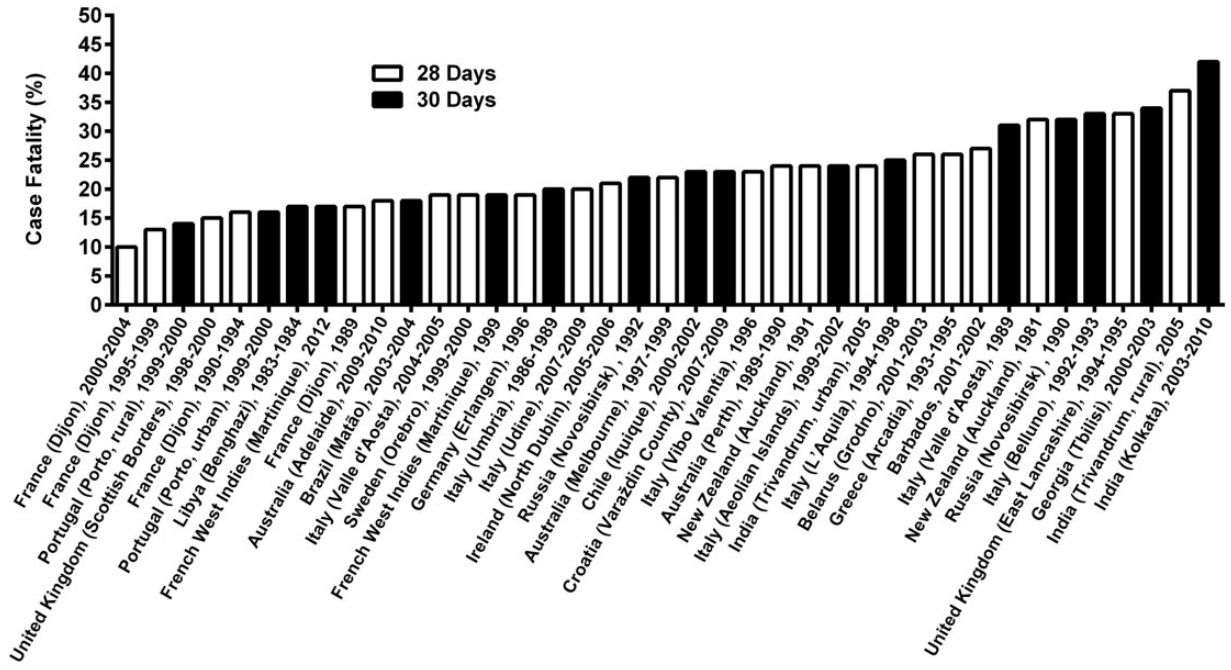
Kazhakstan remained the country with the greatest crude stroke mortality (number of deaths per 100,000 population per year) but there were no new data for this country since 2003. New data from Bulgaria and Greece (both 2012) were also similarly high (298/100,000 population per year for Bulgaria and 285/100,000 per year for Greece; Figure 7 and Supplementary Online Table 7). Countries with new mortality at the lower end of the spectrum included Qatar (2.2/100,000/year in 2012), Bahrain (7.5/100,000/year; 2011), and Kuwait (10.4/100,000/year; 2013).

Countries such as Austria and Switzerland have very low stroke mortality rates despite a large proportion of the population who are aged ≥ 65 years (Figure 8(a)). The largest mortality rates in countries with a relatively small proportion of the population aged ≥ 65 years include Montserrat (1979), the Seychelles (1987), and the British Virgin Islands (1982), but these data are relatively old, and the latter is based on a very small population.

The positive association between the year that the mortality data were collected and their crude mortality rates that we reported in our last review is no longer evident (Figure 8(b)), suggesting that crude mortality is not increasing.

When assessing mortality rates for stroke adjusted to the new world population, the countries with the

Figure 12. Overall 28-day and 30-day case-fatality of stroke that are reported in countries.[7,12,14,19,23–25,31,37,38,40–60]



10 largest rates remain the same as in our past review. None of these countries have provided updated data to WHO, and so these data are relatively old (Figures 9 and 10; Supplementary online Table 7).

There were 29 countries that had both crude incidence of stroke reported (all ages included) as well as mortality data provided to the WHO. There were an extra seven observations, as some countries had more than one incidence study in more than one region. There is a strong positive association between incidence and mortality from stroke (Figure 11). Even when removing the two regions of Portugal with the greatest incidence of stroke, the regression shows a strong association and a steep slope ($Y = 0.5652*X + 109.8$, $p = 0.0002$).

Case-fatality

The literature search yielded 222 publications (see Figure 1 for selection process). In the first stage of screening, we retrieved 59 potential articles and 42 provided usable data. In two of these, overall 7-day case-fatality were reported, being 13.1% in Barbados (2000) and 33% in Kolkata (2003–2010).[19,40] In 20 studies, overall case-fatality was reported at 28 days,[7,12,19,23,24,31,37,40–51] and 16 provided 30-day case-fatality.[14,25,38,45,52–60] Separate figures for men and women were reported for 17 studies.[14,24,25,44,50,51,55,57,58,61–63] Among these articles, 10 had 28-day sex-specific case-fatality,[24,44,50,51,61–63] and the remainder had 30-day sex-specific case-fatality.[14,25,55,57,58]

The data on case-fatality of stroke provide evidence for considerable variation among countries despite the strict criteria for inclusion (Figures 12 and 13). The greatest overall 28-day case fatalities were observed in India at approximately 37–42% at 28 days.[31,40] The least case-fatality was observed in Dijon (2000–2004) at 10% (28 days; Table 2).[43]

Discussion

In this updated review of global stroke statistics, we include evidence from new studies of stroke incidence ($n = 12$) and important updates of mortality data from 57 countries available from WHO. We also report case-fatality data as a new focus of attention. Important ongoing disparities in stroke incidence, mortality, and case-fatality were evident and provide an impetus for more effective prevention and improved clinical management of stroke.

Incidence rates presented in our review differ somewhat to those presented in the GBD Study (Figure 14), even though both were adjusted to the WHO World population.[64] These differences highlight the different aims of these studies. The GBD was undertaken to provide estimates of stroke in all regions using a systematic approach, and has the added advantage of enabling

Figure 13. Comparison of gender-specific 28-day and 30-day case-fatality of stroke that are reported in countries. ((a) men, (b) women)[14,24,25,44,50,51,55,57,58,61–63]

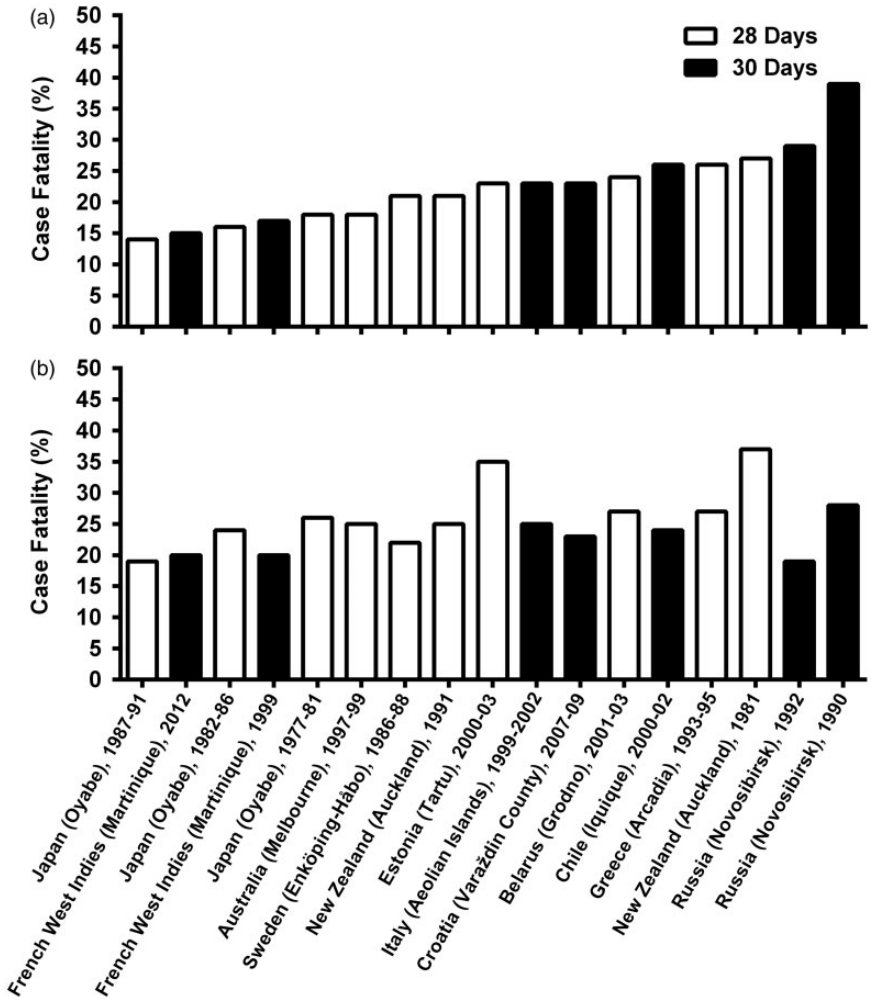


Table 2. Crude case-fatality (%) of stroke in countries: reported at 28–30[a] days.

Country	Overall % (CI)	Men % (CI)	Women % (CI)
Australia (Adelaide), 2009–10[12]	18 (14–24)		
Australia (Melbourne), 1997–99[50]	22.5 (20.0–25.1)	18.3 (14.7–21.8)	25.8 (22.3–29.4)
Australia (Perth), 1989–90[41]	24 (20–28)		
Belarus (Grodno), 2001–2003[24]	26.1	24.4	27.8
Brazil (Matao), 2003–04[38a]	18.5 (10.7–28.7)		
Chile (Iquique), 2000–02[57a]	23.3 (18.1–29.5)	26.2 (18.9–35.3)	24.2 (16.4–34.4)
Croatia (Varaždin County), 2007–09[25a]	23.5	23.6	23.4
Estonia (Tartu), 2000–03[63]		23	35

(continued)

Table 2. Continued

Country	Overall % (CI)	Men % (CI)	Women % (CI)
France (Dijon), 1989[43]	17.8 (15.4–20.5)		
France (Dijon), 1990–94[43]	16.6 (14.4–19.1)		
France (Dijon), 1995–99[43]	13.9 (11.8–16.3)		
France (Dijon), 2000–04[43]	10 (8.3–12.1)		
French West Indies (Martinique), 1998–99[14a]	19.3 (15.5–24.1)	17.9 (12.9–24.8)	20.7 (15.3–28.0)
French West Indies (Martinique), 2011–12[14a]	17.6 (13.3–23.4)	15.1 (9.2–24.6)	20.6 (14.8–28.7)
Georgia (Tbilisi), 2000–03[60a]	34.8 (28.7–41.3)		
Germany (Erlangen), 1994–96[49]	19.4 (16.1–23.3)		
Greece (Arcadia), 1993–95[51]	26.6 (22.9–32.2)	26.3 (21.3–31.1)	27.1 (21.4–32.6)
India (Kolkata), 2003–10[40a]	42 (38.6–45.6)		
India (Trivandrum, rural), 2005[31]	37.1		
India (Trivandrum, urban), 2005[31]	24.5		
Ireland (North Dublin), 2005–06[23]	21 (17.6–24.9)		
Italy (Aeolian Islands), 1999–2002[58a]	24.2 (19.2–36.8)	23.1 (9.0–43.7)	25 (12.2–42.2)
Italy (Belluno), 1992–93[56a]	33		
Italy (L'Aquila), 1994–98[45a]	25.6 (22.8–28.7)		
Italy (Udine), 2007–09[48]	20.6 (17.8–23.8)		
Italy (Umbria), 1986–89[59a]	20.3 (16.2–24.3)		
Italy (Valle d'Aosta), 1989[54a]	31		
Italy (Valle d'Aosta), 2004–08[7]	19		
Italy (Vibo Valentia), 1996[46]	23.7 (19.0–28.3)		
Japan (Oyabe), 1977–81[62]		18 (19.2–21.8)	26.8 (22.1–31.5)
Japan (Oyabe), 1982–86[62]		16.3 (12.2–19.8)	24.5 (19.4–29.6)
Japan (Oyabe), 1987–91[62]		14.2 (10.4–17.4)	19.1 (14.9–23.3)
Libya (Benghazi), 1983–84[52a]	17.3		
New Zealand (Auckland), 1981[44]	32.2 (28.4–36.5)	27.1 (21.7–32.6)	37.6 (31.8–43.5)
New Zealand (Auckland), 1991[44]	24.1 (21.4–26.7)	21.9 (18.1–25.7)	25.8 (22.3–29.4)
Portugal (Porto, rural), 1999–2000[53a]	14.6 (10.2–19.3)		
Portugal (Porto, urban), 1999–2000[53a]	16.9 (13.7–20.6)		
Russia (Novosibirsk), 1990[55a]	32.3 (25.8–38.8)	39.4 (27.0–51.7)	28.4 (20.7–36.2
Russia (Novosibirsk), 1992[55a]	22.7 (17.7–27.7)	29.1 (19.2–39.0)	19.1 (13.3–24.9)

(continued)

Table 2. Continued

Country	Overall % (CI)	Men % (CI)	Women % (CI)
Sweden (Enköping-Håbo), 1986–88[61]		21	22
Sweden (Orebro), 1999–2000[42]	19		
United Kingdom (Scottish Borders), 1998–2000[37]	15.9		
United Kingdom (East Lancashire), 1994–95[47]	33.8		
USA (Barbados), 2001–02[19]	27.8 (24.9–34.8)		

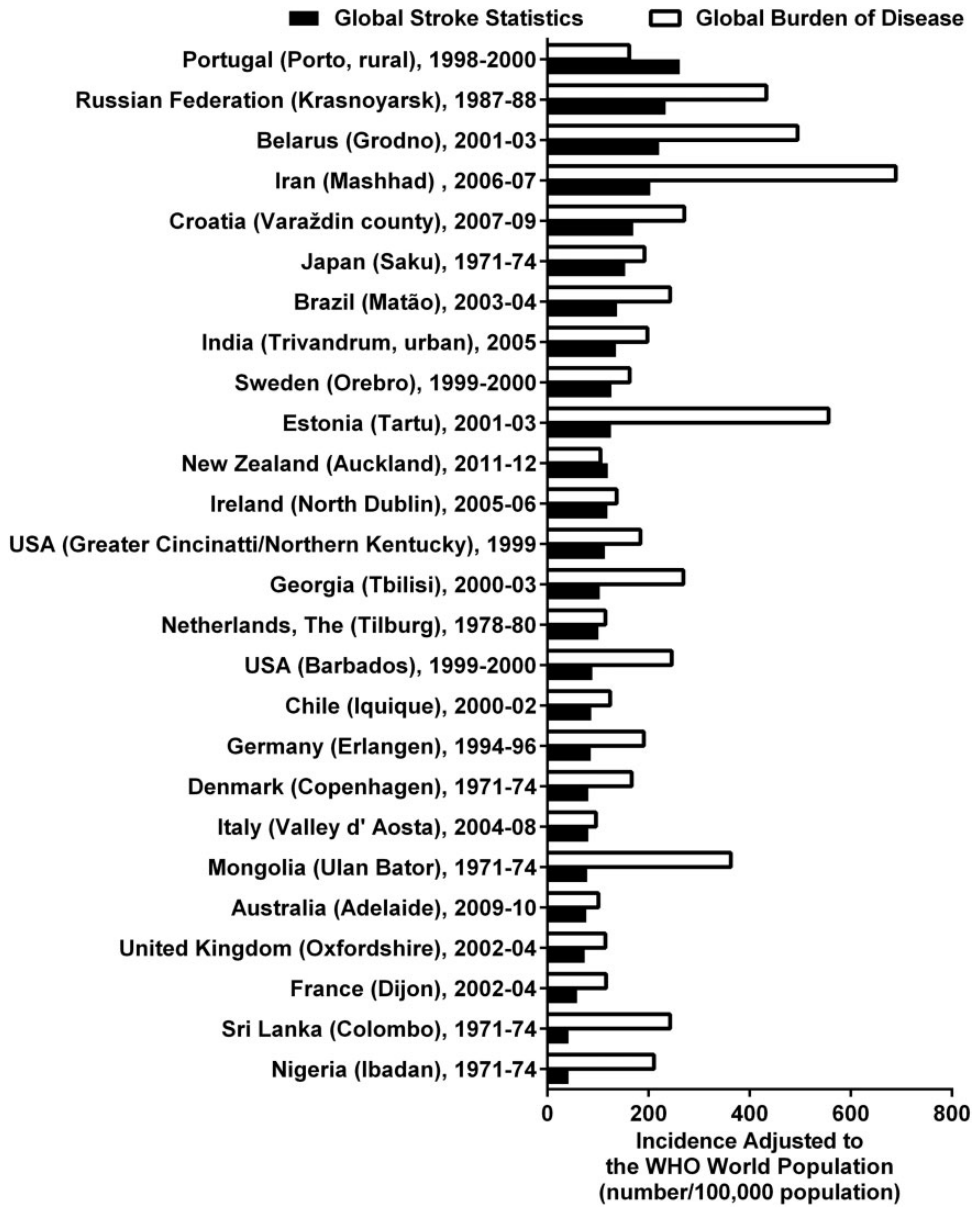
[a]30-Day case-fatality.

comparison across diseases. In contrast, our approach enabled us to identify countries with the most recent data on stroke incidence obtained using ideal methods,[65] and has the advantage of highlighting countries where data are lacking or out of date. Both approaches enable one to determine where there are hotspots in stroke occurrence. High quality data are needed to help plan and develop approaches to improve access to preventive strategies and stroke care. Knowing where important data are lacking, outdated or even where a country is ranked might help facilitate more research or greater policy attention in this field. This is important so that modifiable strategies that are within the control of health funders and providers of health care may be tackled using a data-driven approach. Recently, the WSO has provided guidelines and tools to support countries to review their health system and address improvements to the quality of care they provide for people who experience stroke.[66] In addition, there are more options now for primary prevention monitoring accessible to consumers which may help to encourage risk factor modification.[67] In particular, it is emphasized by WSO that although there are differences in resource availability among countries, it should always be feasible to increase stroke awareness, education, prevention, and treatment. By having standardized methods to compare and contrast countries over time it is possible to monitor progress. This includes the use of WSO Health System Indicators[66] recently showcased in the paper by Tse and colleagues whereby Australia, Singapore, and the USA[68] were compared on how well they align with the WSO Health System Indicators and the sources of routine data available to make such comparisons. Our report herein provides important information for two of the 10 WSO Health System Indicators: stroke incidence rates adjusted for age and sex in the population; and case fatality at 7 and 30 days.

Comparison of data for case-fatality provides two main challenges. First, case-fatality figures are presented in varying time periods; at 7 days, 28 days, and 30 days, making it difficult to compare outcomes across regions. Secondly, crude case-fatality figures do not take into account the fact that strokes occur at different ages across countries, and so greater case-fatality may actually reflect the age at which strokes are occurring and not differences in the management of stroke. Recommendations to provide data in standard time epochs, and providing case-fatality by 10-year age groups, would ensure better comparability among studies, including estimates of age-adjusted case-fatality figures.

Interestingly, we have noted that where incidence studies are not being undertaken or where incidence, case-fatality or mortality data are old, alternate methods of data collection are occurring in the form of clinical registries. In a recent systematic review, registries that were considered in their country to represent a national standardized dataset for acute stroke care and outcomes were summarized whereby 28 national stroke registries from 26 countries were identified.[4] When we overlaid the location of these registries to where the identified incidence studies had been undertaken we noted that in several countries this provided a reasonable explanation for why potentially more resource intensive community-based stroke incidence studies may not have been conducted or repeated (Figures 15 and 16). We accept that the majority of the included registries may not have full national coverage and in some countries there are large registries containing data on stroke that may include several stroke-mimicking conditions or be regionally based for example Catalonia.[4,69] However, these data provide an indication of changing methods of disease surveillance that may also be capturing aspects of the quality of care. In addition, hospitalization ratios differ

Figure 14. Comparison of incidence rates, age adjusted to the WHO world population, between this review and the Global Burden of Disease study.



between countries (e.g. ~90% in Sweden,[70] ~10% in Japan).[71] Therefore, registries may be a better proxy for important epidemiological measures in countries where the majority of incidence cases are treated in hospital.

The main strengths of this review include its comprehensiveness, lack of fixed time period restrictions, and the use of high quality studies that met strict criteria. The limitations include that we were only able to provide information using the available data reported for a country and the methods used in obtaining these data vary. This potentially makes any direct comparisons less reliable. Further, since the incidence and case fatality data are often obtained from one geographical region and may not be representative of other geographical regions within a country, this is a potential source of over- or underestimation of stroke incidence rates and case-fatality. Because mortality rates have been declining over time,[2,64] the rank position of a country may also be influenced by the currency of their data, differences in data collection policies for reporting deaths, and the potential misclassification of causes of death.[72]

Figure 15. World map showing availability of studies with overall incidence and national registries (pins). These include studies with either crude incidence and/or adjusted incidence figures irrespective of age restriction, or adjustment method.

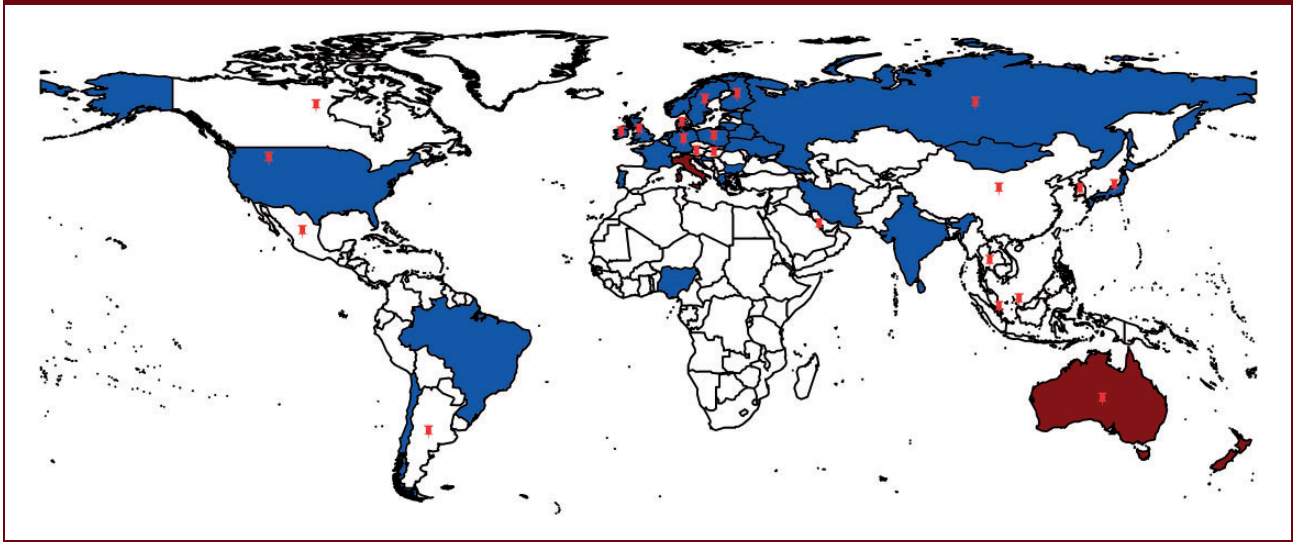
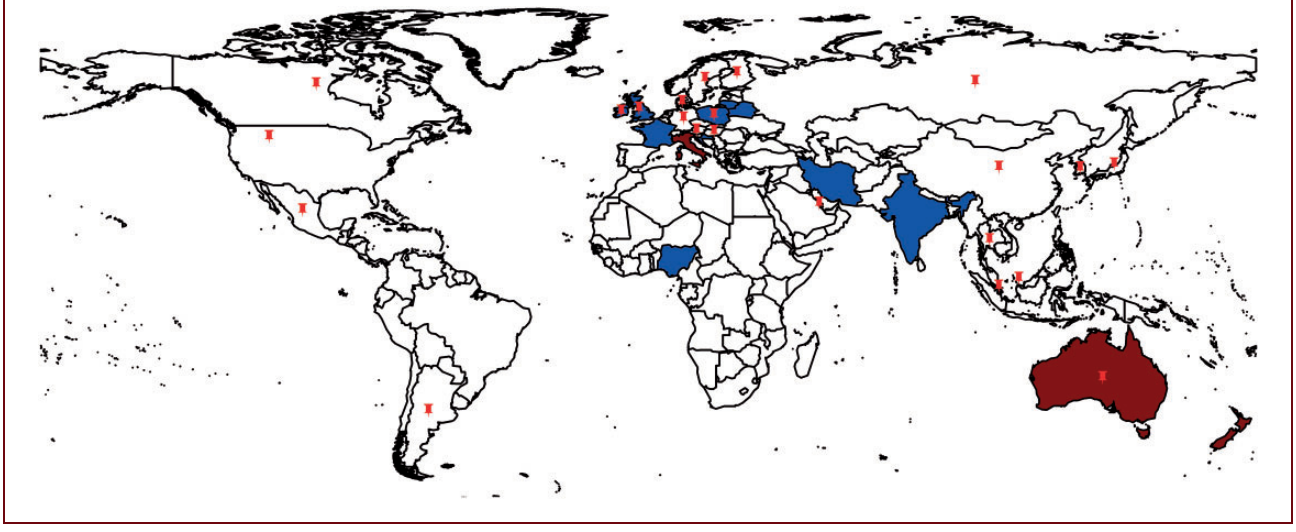


Figure 16. World map showing availability of studies with gender-specific incidence and national registries (pins). These include studies with either crude incidence and/or adjusted incidence figures irrespective of age restriction, or adjustment method.



Conclusion

In this updated data summary, we suggest that there is much that can be learned from countries that are managing to keep stroke incidence, case-fatality and mortality rates at low levels relative to other countries with similar demographic or socioeconomic circumstances. We further highlight the growing trend for national clinical registries to provide such estimates for stroke in lieu of community-based incidence studies.

Author contributions

AGT contributed to conception and design of the study, undertook the data analyses, wrote parts of the first draft of the manuscript and approved the final version.

TT undertook the literature search and data collection, wrote parts of the first draft of the manuscript and approved the final version.

GH contributed to the design of the study, undertook some of the analyses, interpreted the data, revised the manuscript, and approved the final version.

VJH contributed to the design of the study, interpreted the data, revised the manuscript, and approved the final version.

PMH contributed to the design of the study, interpreted the data, revised the manuscript, and approved the final version.

VLF interpreted the data, revised the manuscript, and approved the final version.

BN interpreted the data, revised the manuscript, and approved the final version.

GAD contributed to conception and design of the study, wrote parts of the first draft of the manuscript and approved the final version.

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References

1. Thrift AG, Cadilhac DA, Thayabaranathan T, et al. Global stroke statistics. *Int J Stroke* 2014; 9(1): 6–18.
2. Feigin VL, Norrving B, George MG, Foltz JL, Roth GA and Mensah GA. Prevention of stroke: A strategic global imperative. *Nat Rev Neurol* 2016; 12(9): 501–512.
3. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016; 15(9): 913–924.
4. Cadilhac DA, Kim J, Lannin NA, et al. National stroke registries for monitoring and improving the quality of hospital care: A systematic review. *Int J Stroke* 2016; 11(1): 28–40.
5. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R and Inoue M. *Age standardization of rates: A new WHO world standard*. Geneva: World Health Organization, 2001 (GPE discussion paper series: No. 31; downloadable from www.who.int/whosis/indicators/compendium/2008/1mst/en/, accessed 6 January 2010.
6. Cantu-Brito C, Majersik JJ, Sánchez BN, et al. Door-to-door capture of incident and prevalent stroke cases in Durango, Mexico: The Brain Attack Surveillance in Durango Study. *Stroke* 2011; 42(3): 601–606.
7. Corso G, Bottacchi E, Giardini G, et al. Epidemiology of stroke in Northern Italy: The Cerebrovascular Aosta Registry, 2004–2008. *Neurol Sci* 2012; 34(7): 1071–1081.
8. Danesi MA, Okubadejo NU, Ojini FI and Ojo OO. Incidence and 30-day case fatality rate of first-ever stroke in urban Nigeria: The prospective community based Epidemiology of Stroke in Lagos (EPISIL) phase II results. *J Neurol Sci* 2013; 331(1): 43–47.
9. El-Tallawy HN, Farghaly WMA, Shehata GA, et al. Epidemiology of non-fatal cerebrovascular stroke and transient ischemic attacks in Al Quseir, Egypt. *Clin Interventions Aging* 2013; 8: 1547–1551.
10. Feigin VL, Krishnamurthi RV, Barker-Collo S, et al. 30-year trends in stroke rates and outcome in Auckland, New Zealand (1981–2012): A multi-ethnic population-based series of studies. *PLoS ONE* 2015; 10(8): e0134609.
11. Khealani BO, Hameed B and Mapari UU. Stroke in Pakistan. *J Pakistan Med Assoc* 2008; 58(7): 400–403.
12. Leyden JM, Kleinig TJ, Newbury J, et al. Adelaide stroke incidence study: Declining stroke rates but many preventable cardioembolic strokes. *Stroke* 2013; 44(5): 1226–1231.
13. Maredza M, Bertram MY and Tollman SM. Disease burden of stroke in rural South Africa: An estimate of incidence, mortality and disability adjusted life years. *BMC Neurol* 2015; 15(1): 1–12.
14. Olindo S, Chausson N, Mejdoubi M, et al. Trends in incidence and early outcomes in a black Afro-Caribbean population from 1999 to 2012: Etude Réalisée en Martinique et Centrée sur l'Incidence des Accidents Vasculaires Cérébraux II Study. *Stroke* 2014; 45(11): 3367–3373.
15. Omama S, Yoshida Y, Ogasawara K, et al. Incidence rate of cerebrovascular diseases in Northern Japan determined from the Iwate Stroke Registry with an inventory survey system. *J Stroke Cerebrovasc Dis* 2013; 22(8): e317–e322.
16. Ramalle-Gomara E, Ruiz E, Serrano M, Bártulos M, González M-Á and Matute B. Hospital discharges and mortality registries: 2. Complementary databases for the epidemiological surveillance of stroke. *J Stroke Cerebrovasc Dis* 2013; 22(8): e441–e445.
17. Demant MN, Andersson C, Ahlehoff O, et al. Temporal trends in stroke admissions in Denmark 1997–2009. *BMC Neurol* 2013; 13(1): 1–8.
18. Azarpazhooh MR, Etemadi MM, Donnan GA, et al. Excessive incidence of stroke in Iran: Evidence from the Mashhad Stroke Incidence Study (MSIS),

a population-based study of stroke in the Middle East. *Stroke* 2010; 41: e3–e10.
19. Corbin DOC, Poddar V, Hennis A, et al. Incidence and case fatality rates of first-ever stroke in a black Caribbean population: The Barbados Register of Strokes. *Stroke* 2004; 35(6): 1254–1258.
20. Corso G, Bottacchi E, Giardini G, et al. Community-based study of stroke incidence in the Valley of Aosta, Italy. CARe – cerebrovascular Aosta Registry: Years 2004–2005. *Neuroepidemiology* 2009; 32(3): 186–195.
21. Feigin VL, Lawes CM, Bennett DA and Anderson CS. Stroke epidemiology: A review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol* 2003; 2(1): 43–53.
22. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL and Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: A systematic review. *Lancet Neurol* 2009; 8(4): 355–369.
23. Kelly PJ, Crispino G, Sheehan O, et al. Incidence, event rates, and early outcome of stroke in Dublin, Ireland: The North Dublin Population Stroke Study. *Stroke* 2012; 43(8): 2042–2047.
24. Kulesh SD, Filina NA, Frantava NM, et al. Incidence and case-fatality of stroke on the east border of the European Union. *Stroke* 2010; 41: 2726–2730.
25. Pikija S, Cvetko D, Malojčić B, et al. A population-based prospective 24-month study of stroke: Incidence and 30-day case-fatality rates of first-ever strokes in Croatia. *Neuroepidemiology* 2012; 38(3): 164–171.
26. Sienkiewicz-Jarosz H, Gluszkiewicz M, Pniewski J, et al. Incidence and case fatality rates of first-ever stroke – Comparison of data from two prospective population-based studies conducted in Warsaw. *Neurologia I Neurochirurgia Polska* 2011; 45(3): 207–212.
27. Sugama C, Isa K, Okumura K, Iseki K, Kinjo K and Ohya Y. Trends in the incidence of stroke and cardiovascular risk factors on the isolated island of Okinawa: The Miyakojima Study. *J Stroke Cerebrovasc Dis* 2013; 22(7): e118–e123.
28. The European Registers of Stroke Investigators. Incidence of stroke in Europe at the beginning of the 21st century. *Stroke* 2009; 40(5): 1557–1563.
29. Zhang Y, Chapman AM, Plested M, Jackson D and Purroy F. The incidence, prevalence, and mortality of stroke in France, Germany, Italy, Spain, the UK, and the US: A literature review. *Stroke Res Treatment* 2012; 2012: 436125.
30. Benamer HT and Grosset D. Stroke in Arab countries: A systematic literature review. *J Neurol Sci* 2009; 284(1–2): 18–23.
31. Sridharan SE, Unnikrishnan JP, Sukumaran S, et al. Incidence, types, risk factors, and outcome of stroke in a developing country: The Trivandrum Stroke Registry. *Stroke* 2009; 40(4): 1212–1218.
32. Owolabi M. Taming the burgeoning stroke epidemic in Africa: Stroke quadrangle to the rescue. *West Indian Med J* 2011; 60: 412–421.
33. Connor MD, Walker R, Modi G and Warlow CP. Burden of stroke in black populations in sub-Saharan Africa. *Lancet Neurol* 2007; 6(3): 269–278.
34. Bejot Y, Osseby GV, Aboa-Eboule C, et al. Dijon's vanishing lead with regard to low incidence of stroke. *Eur J Neurol* 2009; 16(3): 324–329.
35. Vega T, Zurriaga O, Ramos JM, et al. Stroke in Spain: Epidemiologic incidence and patterns: A health sentinel network study. *J Stroke Cerebrovasc Dis* 2009; 18(1): 11–16.
36. Jiang B, Wang WZ, Chen H, et al. Incidence and trends of stroke and its subtypes in China: Results from three large cities. *Stroke* 2006; 37(1): 63–68.
37. Syme PD, Byrne AW, Chen R, Devenny R and Forbes JF. Community-based stroke incidence in a Scottish population: The Scottish Borders Stroke Study. *Stroke* 2005; 36(9): 1837–1843.
38. Minelli C, Fen LF and Minelli DP. Stroke incidence, prognosis, 30-day, and 1-year case fatality rates in Matao, Brazil: A population-based prospective study. *Stroke* 2007; 38(11): 2906–2911.
39. Sajjad A, Chowdhury R, Felix JF, et al. A systematic evaluation of stroke surveillance studies in low- and middle-income countries. *Neurology* 2013; 80(7): 677–684.
40. Ray BK, Hazra A, Ghosal M, et al. Early and delayed fatality of stroke in Kolkata, India: Results from a 7-year longitudinal population-based study. *J Stroke Cerebrovasc Dis* 2013; 22(4): 281–289.
41. Anderson CS, Jamrozik KD, Burvill PW, Chakera TM, Johnson GA and Stewart-Wynne EG. Ascertaining the true incidence of stroke: Experience from the Perth Community Stroke Study, 1989–1990. *Med J Aust* 1993; 158(2): 80–84.
42. Appelros P, Nydevik I, Seiger A and Terent A. High incidence rates of stroke in Orebro, Sweden: Further support for regional incidence differences within Scandinavia. *Cerebrovasc Dis* 2002; 14: 161–168.
43. Benatru I, Rouaud O, Durier J, et al. Stable stroke incidence rates but improved case-fatality in Dijon, France, from 1985 to 2004. *Stroke* 2006; 37(7): 1674–1679.
44. Bonita R, Broad JB and Beaglehole R. Changes in stroke incidence and case-fatality in Auckland, New Zealand, 1981–91. *Lancet* 1993; 342(8885): 1470–1473.
45. Carolei A, Marini C, Di Napoli M, et al. High stroke incidence in the prospective community-based L'Aquila registry (1994–1998). First year's results. *Stroke* 1997; 28: 2500–2506.
46. Di Carlo A, Inzitari D, Galati F, et al. A prospective community-based study of stroke in southern Italy: The Vibo Valentia incidence of stroke study (VISS). Methodology, incidence and case fatality at 28 days, 3 and 12 months. *Cerebrovasc Dis* 2003; 16: 410–417.
47. Du X, Sourbutts J, Cruickshank K, et al. A community based stroke register in a high risk area for stroke in north west England. *J Epidemiol Community Health* 1997; 51: 472–478.
48. Janes F, Gigli GL, D'Anna L, et al. Stroke incidence and 30-day and six-month case fatality rates in Udine, Italy: A population-based prospective study. *Int J Stroke* 2013; 8(Suppl A100): 100–105.
49. Kolominsky-Rabas PL, Sarti C and Heuschmann PU. A prospective community-based study of stroke in

Germany. The Erlangen stroke project (ESPro): Incidence and case fatality at 1, 3, and 12 months. *Stroke* 1998; 29: 2501–2506.
50. Thrift AG, Dewey HM, Sturm JW, et al. Incidence of stroke subtypes in the North East Melbourne Stroke Incidence Study (NEMESIS): Differences between men and women. *Neuroepidemiology* 2009; 32(1): 11–18.
51. Vemmos KN, Bots ML, Tsibouris PK, et al. Stroke incidence and case fatality in southern Greece: The Arcadia stroke registry. *Stroke* 1999; 30(2): 363–370.
52. Ashok PP, Radhakrishnan K, Sridharan R and el-Mangoush MA. Incidence and pattern of cerebrovascular diseases in Benghazi, Libya. *J Neurol Neurosurg Psychiatry* 1986; 49(5): 519–523.
53. Correia M, Silva MR, Matos I, et al. Prospective-community based study of stroke in Northern Portugal: Incidence and case fatality in rural and urban populations. *Stroke* 2004; 35(9): 2048–2053.
54. D'Alessandro G, Di Giovanni M, Roveyaz L, et al. Incidence and prognosis of stroke in the Valle d'Aosta Italy. *Stroke* 1992; 23: 1712–1715.
55. Feigin VL, Wiebers DO, Whisnant JP and O'Fallon WM. Stroke incidence and 30-day case-fatality rates in Novosibirsk, Russia, 1982 through 1992. *Stroke* 1995; 26(6): 924–929.
56. Lauria G, Gentile M, Fassetta G, et al. Incidence and prognosis of stroke in the Belluno Province, Italy: First-year results of a community-based study. *Stroke* 1995; 26: 1787–1793.
57. Lavados PM, Sacks C, Prina L, et al. Incidence, 30-day case-fatality rate, and prognosis of stroke in Iquique, Chile: A 2-year community-based prospective study (PISCIS project). *Lancet* 2005; 365(9478): 2206–2215.
58. Musolino R, La Spina P, Serra S, et al. First-ever stroke incidence and 30-day case fatality in the Sicilian Aeolian Archipelago, Italy. *Stroke* 2005; 36(12): 2738–2741.
59. Ricci S, Celani MG, La Rosa F, et al. SEPIVAC: A community-based study of stroke incidence in Umbria, Italy. *J Neurol Neurosurg Psychiatry* 1991; 54: 695–698.
60. Tsiskaridze A, Djibuti M, van MG, et al. Stroke incidence and 30-day case-fatality in a suburb of Tbilisi: Results of the first prospective population-based study in Georgia. *Stroke* 2004; 35(11): 2523–2528.
61. Åsberg KH and Parrow A. Event, incidence, and fatality rates of cerebrovascular diseases in Enköping-Håbo, Sweden, 1986–1988. *Scand J Pub Health* 1991; 19(2): 134–139.
62. Morikawa Y, Nakagawa H, Naruse Y, et al. Trends in stroke incidence and acute case fatality in a Japanese rural area: The Oyabe study. *Stroke* 2000; 31(7): 1583–1587.
63. Vibo R, Korv J and Roose M. The third stroke registry in Tartu, Estonia: Decline of stroke incidence and 28-day case-fatality rate since 1991. *Stroke* 2005; 36: 2544–2548.
64. Feigin VL, Forouzanfar MH, Krishnamurthi R, et al. Global and regional burden of stroke during 1990–2010: Findings from the Global Burden of Disease Study 2010. *Lancet* 2014; 383(9913): 245–254.
65. Sudlow CL and Warlow CP. Comparing stroke incidence worldwide: What makes studies comparable? *Stroke* 1996; 27(3): 550–558.
66. Lindsay P, Furie KL, Davis SM, Donnan GA and Norrving B. World Stroke Organization global stroke services guidelines and action plan. *Int J Stroke* 2014; 9(Suppl A100): 4–13.
67. Feigin VL, Krishnamurthi R, Bhattacharjee R, et al. New strategy to reduce the global burden of stroke. *Stroke* 2015; 46(9): 1740–1747.
68. Tse T, Carey L, Cadilhac D, Koh GC-H and Baum C. Application of the World Stroke Organization health system indicators and performance in Australia, Singapore, and the USA. *Int J Stroke* 2016; 11(10): 852–859.
69. Marti-Vilalta JL and Arboix A. The Barcelona Stroke Registry. *Eur Neurol* 1999; 41(3): 135–142.
70. Asplund K, Hulter Asberg K, Appelros P, et al. The Riks-Stroke story: Building a sustainable national register for quality assessment of stroke care. *Int J Stroke* 2011; 6(2): 99–108.
71. Kobayashi S. International experience in stroke registry: Japanese Stroke Databank. *Am J Prev Med* 2006; 31(6, Supplement 2): S240–S242.
72. Truelsen T, Krarup LH, Iversen HK, et al. Causes of death data in the Global Burden of Disease: Estimates for ischemic and hemorrhagic stroke. *Neuroepidemiology* 2015; 45(3): 152–160.
73. Heidrich J, Heuschmann PU, Kolominsky-Rabas P, Rudd AG and Wolfe CDA. Variations in the use of diagnostic procedures after acute stroke in Europe: Results from the BIOMED II study of stroke care. *Eur J Neurol* 2007; 14(3): 255–261.
74. Wolfe CD, Tilling K, Beech R and Rudd AG. Variations in case fatality and dependency from stroke in western and central Europe. The European BIOMED Study of Stroke Care Group. *Stroke* 1999; 30: 350–356.
75. Abdul-Ghaffar NU, El-Sonbaty MR, el-Din Abdul-Baky MS, Marafie AA and al-Said MM. Stroke in Kuwait: A three-year prospective study. *Neuroepidemiology* 1997; 16: 40–47.
76. Rastenyte D, Sopagiene D, Virviciute D and Juriene K. Diverging trends in the incidence and mortality of stroke register in Kaunas, Lithuania. *Scand J Pub Health* 2006; 34: 488–495.
77. Powles J, Kirov P, Feschieva N, Stanoev M and Atanasova V. Stroke in urban and rural populations in north-east Bulgaria: Incidence and case-fatality findings from a 'hot pursuit' study. *BMC Public Health* 2002; 2: 24.
78. Das SK, Banerjee TK, Biswas A, et al. A prospective community-based study of stroke in Kolkata, India. *Stroke* 2007; 38(3): 906–910.

Online Supplement

GLOBAL STROKE STATISTICS

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Supplementary Online Table 1. Ideal' Criteria for Stroke Incidence Studies (1-4)

Standard Definitions

- Stroke: World Health Organization definition (2)
- 1st ever in a life-time stroke

Methods

- Complete community-based ascertainment (hospital and non-hospital sources)
- Multiple overlapping sources
- Supplementary methods of case ascertainment, including referrals for imaging and follow-up of patients referred with transient ischaemic attack
- Prospective design using hot pursuit
- Population base should be large and stable
- Pathological subtyping by imaging in at least 90% of cases
- Time period should include whole years (because of the seasonality of stroke)

Data Presentation

- Standardisation of rates to standard populations
- Age bands should comprise mid-decade age bands
- Confidence intervals (95%) should be provided
- Male and female data should be presented separately

Supplementary Online Table 2. International disease classification codes used to estimate stroke mortality rates

International Disease Classification code	Codes used for mortality estimates by country	Comment
ICD8	The codes used for ICD8 are 431, 432, 433, 434, and for those countries using the condensed list of ICD codes the codes used were A085 and B030.	Codes for A085 and B030 correspond to ICD 8 codes 430-438.
ICD9	For ICD9, the codes used were B29, B290, B291, B292, B293, and B294, which are the codes obtained using the basic tabulation list. For China the code used was C051.	These codes equate to ICD9 codes 430-438.
ICD10	The codes used in the ICD10 database were: I60, I600, I601, I602, I603, I604, I605, I606, I607, I608, I609, I61, I610, I611, I612, I613, I614, I615, I616, I618, I619, I62, I620, I621, I629, I63, I630, I631, I632, I633, I634, I635, I636, I638, I639, I64, I67, I670, I671, I672, I673, I674, I675, I676, I677, I678, I679, I69, I690, I691, I692, I693, I694, I698.	These codes equate to ICD10 codes I60, I61, I62, I63, I64, I67, and I69.

Supplementary Online Table 3. Studies of stroke Incidence: crude incidence rates (men and women combined)

Country	Study Period	Incidence (95% CI)	Age range (years)	Standard criteria met*
Armenia (5)	2010	141.7 (-)	All ages	No
Australia (Adelaide) (6)	2009-2010	161 (141-183)	All ages	Yes
Australia (Melbourne) (7)	1996-1997	206 (182-231)	All ages	Yes
Australia (Perth) (8)	2000-2001	128 (109-146)	All ages	Yes
Bahrain (9)	1995	57 (-)	Ages 20+	Yes
Belarus (Grodno) (10)	2001-2003	222 (212-233)	Crude	Yes
Brazil (Matão) (8)	2003-2004	108 (84-131)	All ages	Yes
Bulgaria (11)	2002	622 (560-690)	Ages 45-84	No
Chile (Iquique) (8)	2000-2002	74 (65-82)	All ages	Yes
China (Beijing) (12)	2000	177.9 (-)	Crude	No
China (Changsha) (12)	2000	201.3 (-)	Crude	No
China (Shanghai) (12)	2000	159.8 (-)	Crude	No
Columbia (Sabaneta) (13)	1992-1993	89 (-)	Crude	No
Croatia (Varaždin county) (14)	2007-2009	276 (260-294)	All ages	Yes
Denmark (15)	2007-2009	322 (316-329)	All ages	No
Denmark (Frederiksberg) (8)	1989-1990	306 (269-344)	All ages	Yes
Egypt (Al Quseir City) (16)	2010-2011	181 (122-141)	Ages 20+	No
Estonia (Tartu) (8)	2001-2003	223 (202-244)	All ages	Yes
Finland (Espoo-Kauniainen), (8)	1989-1991	220 (203-238)	Ages 15+	Yes
Finland (Turku) (8)	1992	451 (412-490)	Ages 25+	Yes
France (Dijon) (17)	2000-2006	114 (107-120)	All ages	Yes
French West Indies (Martinique) (18)	2004-2008	147 (134-159)	All ages	Yes
French West Indies (Martinique) (8)	1998-1999	167 (154-181)	All ages	Yes
Georgia (Tbilisi) (8)	2000-2003	165 (144-186)	All ages	Yes
Germany (Erlangen) (8)	1994-1996	175 (156-193)	All ages	Yes
Greece (Arcadia) (8)	1993-1995	344 (315-372)	All ages	Yes
India (Mumbai) (8)	2005-2006	145 (132-159)	Ages 25+	Yes
India (Rohtak) (8)	1971-1974	27 (21-33)	All ages	Yes
Iran (Mashhad) (19)	2006-2007	139 (128-149)	All ages	Yes

Ireland (North Dublin), (20)	2005-2006	165 (150-179)	All ages	Yes
Italy (Belluno) (8)	1992-1993	224 (204-244)	All ages	Yes
Italy (L'Aquila) (8)	1994	275 (256-294)	All ages	Yes
Italy (Sesto Fiorentino) (21)	2004-2006	170.4 (-)	Crude	Yes
Italy (Umbria) (8)	1986-1989	254 (228-280)	All ages	Yes
Italy (Valle d' Aosta) (22)	2004-2008	212 (200-223)	All ages	Yes
Italy (Valle d' Aosta) (17)	2004-2005	223 (197-249)	All ages	Yes
Italy (Vibo Valentia) (8)	1996	179 (159-199)	All ages	Yes
Japan (Iwate State) (23)	2004-2008	290 (282-299)	All ages	No
Japan (Okinawa) (24)	2002-2005	220 (-)	Crude	No
Japan (Oyabe) (8)	1987-1991	411 (381-442)	Ages 25+	Yes
Japan (Saku) (8)	1971-1974	205 (190-220)	All ages	Yes
Japan (Shibata) (8)	1976-1978	261 (236-286)	Ages 20+	Yes
Lithuania (Kaunas) (21)	2004	223.44 (-)	Crude	Yes
Mexico (25)	2011	232 (-)	Ages 25+	No
Mongolia (Ulan Bator) (8)	1971-1974	50 (46-54)	All ages	Yes
The Netherlands, (Tilburg) (8)	1978-1980	289 (262-316)	All ages	Yes
New Zealand (Auckland) (26)	2011-2012	147 (140-150)	Ages 15+	Yes
New Zealand (Auckland) (8)	2002-2003	158 (150-166)	Ages 15+	Yes
Nigeria (Lagos) (27)	2007-2008	252 (216-288)	All ages	No
Nigeria (Ibadan) (8)	1971-1974	15 (13-17)	All ages	Yes
Pakistan[#] (28)	Not Stated	250	All	No
Peru (Cuzco) (13)	1988	183 (-)	Crude	No
Poland (Warsaw) (29)	2005	106 (87-124)	Crude	Yes
Portugal (Porto, rural) (8)	1998-2000	305 (265-344)	All ages	Yes
Portugal (Porto, urban) (8)	1998-2000	268 (244-293)	All ages	Yes
Qatar (9)	1997	41 (30.2-52.4)	Crude	No
Russia (Krasnoyarsk) (8)	1987-1988	217 (197-237)	All ages	Yes
South Africa (Rural Agincourt subdistrict) (30)	2011	259 (-)	All ages	No
South Africa (31)	1984-1985	101 (-)	Ages 20+	No
Spain (Castilla y Leon, Extremadura, and Coumunitat Valenciana regions) (17)	2005	141 (125-158)	Ages 14+	No

Spain (La Rioja) (32)	2009	304 (286-324)	All ages	No
Spain (Menorca) (21)	2004-2006	113.8 (-)	Crude	No
Sri Lanka (Colombo) (8)	1971-1974	24 (20-27)	All ages	Yes
Sweden (Lund-Orup) (8)	2001-2002	194 (177-212)	All ages	Yes
Sweden (Malmö) (8)	1989	225 (206-244)	All ages	Yes
Sweden (Örebro) (8)	1999-2000	314 (279-349)	All ages	Yes
Sweden (Söderhamn), (8)	1983-1986	353 (317-390)	Ages 25+	Yes
Ukraine (Uzhhorod) (8)	1999-2000	281 (248-313)	All ages	Yes
United Kingdom (East Lancashire) (8)	1994-1995	158 (146-171)	All ages	Yes
United Kingdom (Oxfordshire) (8)	2002-2004	145 (127-162)	All ages	Yes
United Kingdom (Scottish Borders) (33)	1998-2000	280 (258-304)	All Ages	Yes
United Kingdom (South London) (8)	1995-1996	130 (120-144)	All ages	Yes
USA (Barbados) (34)	2001-2002	140 (125-155)	All ages	Yes
USA (Greater Cincinnati) (8)	1999	193 (186-201)	All ages	Yes

*Standard criteria = multiple overlapping sources, World Health Organisation definition of stroke, incidence cases, no upper age limit, and prospective design; Grey shade = Incidence reported in new studies (May 2013 – March 2016); # estimated value

Supplementary Online Table 4. Studies of stroke Incidence: crude incidence rates in men and women

	Incidence (95% Confidence Interval)			
Country, Study Period	Men	Women	Age range (years)	Standard criteria met*
Australia (Adelaide), 2009-10 (6)	176 (147-201)	146 (120-176)	All	Yes
Bahrain, 1995 (9)	59 (-)	55	Ages 20+	No
Barbados, 1999-2000 (34)	115 (95-135)	163 (141-187)	All ages	Yes
Belarus (Grodno), 2001-3 (10)	234 (220-248)	211 (198-224)	All ages	Yes
Croatia (Varaždin county), 2007-9 (14)	265 (241-290)	287 (264-312)	All ages	Yes
Egypt (Al Quseir City), 2010-11 (16)	212 (121-302)	150 (75-227)	Ages 20+	No
France (Dijon), 2000-6 (17)	116 (106-126)	112 (103-121)	All ages	Yes
French West Indies (Martinique), 2011-12 (18)	171 (152-190)	126 (110-141)	All ages	Yes
India (Trivandrum, rural), 2005 (35)	131.6	105.2	All ages	Yes
India (Trivandrum, urban), 2005 (35)	110.5	121.6	All ages	Yes
Iran (Mashhad), 2006-7 (19)	144 (128-159)	133 (118-148)	All ages	Yes
Ireland (North Dublin), 2005-6 (20)	166 (145-187)	163 (142-185)	All ages	Yes
Italy (Valley d' Aosta), 2004-8 (22)	211 (195-228)	213 (197-229)	All ages	Yes
Italy (Valley d' Aosta), 2004-5 (17)	224 (186-261)	223 (186-260)	All ages	Yes
Japan (Iwate State), 2004-8 (23)	307 (295-320)	275 (264-286)	All ages	No
Japan (Okinawa), 2002-5 (24)	238	206	Age 30+	No
Libya, 1991-3 (9)	52	42	All ages	No
New Zealand (Auckland), 2011-12 (26)	148 (137-158)	146 (136-156)	Ages 15+	Yes
Nigeria (Ibadan), 1973-5 (36)	25	13	All ages	Yes
Nigeria (Lagos), 2007-8 (27)	28	21	All ages	No
Poland (Warsaw), 2005 (29)	109 (82-136)	103 (78-127)	All ages	Yes
Qatar, 1997 (9)	46	33 (23-49)	All ages	No
Saudi Arabia, 1989-1993 (9)	8.84	13.24	All ages	No
South Africa (Rural Agincourt	213 (198-243)	298 (296-372)	All ages	No

subdistrict), 2011 (30)				
South Africa, 1984-5 (31)	84	90	Ages 20+	No
Spain (Castilla y Leon, Extremadura, and Coumunitat Valenciana regions), 2005 (17)	148 (124-172)	134 (112-157)	Ages 14+	No
Spain (La Rioja), 2009 (32)	300 (273-326)	310 (282-337)	All ages	No
Zimbabwe, 1991 (31)	20	32	Ages 20 +	No

*Standard criteria = multiple overlapping sources, World Health Organisation definition of stroke, incidence cases, no upper age limit, and prospective design; Grey shade = Incidence reported in new studies (May 2013 – March 2016)

Supplementary Online Table 5. Adjusted incidence of stroke in men and women combined.

Country, Study Period	Incidence Rate per 100,000 population (95% Confidence Interval)	Standard criteria met*
Adjusted to European standard population		
Belarus (Grodno), 2001-2003 (10)	287 (274-301)	Yes
Croatia (Varaždin county), 2007-2009 (14)	223.6 (209.7-238.1)	Yes
France (Dijon), 2000-2006 (37)	85 (79.8-90.3)	Yes
Italy (Valley d' Aosta), 2004-2005 (38)	126 (106-146)	Yes
Kuwait, 1989, 1992, 1993 (9)	27.59 (-)	No
Poland (Warsaw), 2005 (29)	129 (122-136)	Yes
Spain (Castilla y Leon, Extremadura, and Coumunitat Valenciana regions), 2005 (39)	83 (72-94)	No
Spain (La Rioja), 2009 (32)	171.1 (160.4-181.8)	No
USA (Barbados), 1999-2000 (34)	135 (112-158)	Yes
Adjusted to Segi World population		
China (Beijing), 2000 (12)	135 (126.5-144.6)	No
China (Changsha), 2000 (12)	150 (141.3-160)	No
China (Shanghai), 2000 (12)	76.1 (70.6-82.6)	No
France (Dijon), 2000-2006 (37)	57.9 (54-61.8)	Yes
Iran , 2006-2007 (19)	203 (175-231)	Yes
United Kingdom (Scottish Borders), 1998-2000 (33)	110 (90-133)	Yes
USA (Barbados), 1999-2000 (34)	88 (70-106)	Yes
Adjusted to WHO World standard population		
Australia (Adelaide), 2009-2010 (6)	76 (59-94)	Yes
Australia (Melbourne), 1996-1997 (8)	100 (95-105)	Yes
Australia (Perth), 2000-2001 (8)	67 (56-79)	Yes
Belarus (Grodno), 2001-2003 (10)	220 (210-231)	Yes
Brazil (Matão), 2003-2004 (40)	137 (112-166)	Yes
Chile (Iquique), 2000-2002 (8)	86 (76-95)	Yes
China, 1980-2013 (41)	120 (26.17, 215)	No
Croatia (Varaždin county), 2007-2009 (14)	169.6 (159.8-181.4)	Yes
Denmark (Copenhagen), 1971-1974 (8)	80 (74-85)	Yes

Denmark (Frederiksberg), 1989-1990 (8)	106 (89-123)	Yes
Estonia (Tartu), 2001-2003 (8)	125 (113-138)	Yes
Finland (North Karelia), 1971-1974 (8)	141 (132-150)	No
France (Dijon), 2002-2004 (8)	58 (53-63)	Yes
French West Indies (Martinique), 1998-1999 (8)	102 (99-105)	Yes
French West Indies (Martinique), 2011-2012 (18)	77 (70-84)	Yes
Georgia (Tbilisi), 2000-2003 (8)	103 (72-133)	Yes
Germany (Erlangen), 1994-1996 (8)	85 (76-95)	Yes
India (Kolkata), 2003-2005 (42)	145 (120-175)	Yes
India (Rohtak), 1971-1974 (8)	48 (38-59)	Yes
India (Trivandrum, rural), 2005 (35)	138 (112-164)	Yes
India (Trivandrum, urban), 2005 (35)	135 (122-148)	Yes
Ireland (Dublin), 1971-1974 (8)	118 (108-128)	Yes
Ireland (North Dublin), 2005-2006 (20)	118 (107-129)	Yes
Italy (Belluno), 1992-1993 (8)	110 (100-121)	Yes
Italy (L'Aquila), 1994 (8)	113 (105-122)	Yes
Italy (Umbria), 1986-1989 (8)	105 (92-118)	Yes
Italy (Valley d' Aosta), 2004-2008 (22)	80 (73-87)	Yes
Italy (Valley d' Aosta), 2004-2005 (8)	82 (61-98)	Yes
Italy (Valley d' Aosta), 2004-2005 (38)	97 (80-114)	Yes
Italy (Vibo Valentia), 1996 (8)	87 (78-97)	Yes
Japan (Iwate State), 2004-2008 (23)	146 (130-163)	No
Japan (Saku), 1971-1974 (8)	153 (142-165)	Yes
Mongolia (Ulan Bator), 1971-1974 (8)	78 (71-84)	Yes
Netherlands, The (Tilburg), 1978-80 (8)	100 (81-119)	Yes
Nigeria (Ibadan), 1971-1974 (8)	41 (36-45)	Yes
Nigeria (Lagos), 2007-2008 (27)	54 (-)	No
Portugal (Porto, rural), 1998-2000 (8)	261 (249-273)	Yes
Portugal (Porto, urban), 1998-2000 (8)	118 (112-124)	Yes
Russia (Krasnoyarsk), 1987-1988 (8)	233 (212-256)	Yes
Spain (La Rioja), 2009 (32)	108 (101-115)	No
Sri Lanka (Colombo), 1971-1974 (8)	41 (35-47)	Yes
Sweden (Malmo), 1989 (8)	83 (74-91)	Yes
Sweden (Orebro), 1999-2000 (8)	126 (111-140)	Yes

Tanzania (Dar-es-Salaam, urban), 2003-2006 (11)	315.9 (282.43-353.34)	No
Tanzania (Hai, rural), 2003-2006 (11)	108.6 (89.55-131.71)	No
United Kingdom (East Lancashire), 1994-1995 (8)	74 (67-80)	Yes
United Kingdom (Oxfordshire), 2002-2004 (8)	73 (64-83)	Yes
United Kingdom (South London), 1995-1996 (8)	82 (80-84)	Yes
USA (Barbados), 2001 (8)	88 (79-98)	Yes
USA (Greater Cincinatti/Northern Kentucky), 1999 (8)	113 (102-126)	Yes
USA (Rochester), 1985-1989 (8)	102 (92-112)	No
West Ukraine (Uzhhorod), 1999-2000 (8)	238 (213-263)	No
Adjusted to WHO World standard population, 15+ years		
Finland (Espoo-Kauniainen), 1989-1991 (8)	100 (91-110)	Yes
New Zealand (Auckland), 2011-2012 (26)	119 (114-125)	Yes
New Zealand (Auckland), 2002-2003 (8)	126 (119-133)	Yes
Norway (Innherrred), 1994-1996 (8)	154 (138-171)	Yes
Adjusted to WHO World standard population, 18+ years		
Greece (Arcadia), 1993-1995 (8)	133 (120-146)	Yes
Adjusted to WHO World standard population, 20+ years		
Japan (Shibata), 1976-1978 (8)	223 (194-252)	Yes
Adjusted to WHO World standard population, 25+ years		
Finland (Turku), 1992 (8)	314 (283-344)	Yes
India (Mumbai), 2005-2006 (8)	151 (137-165)	Yes
Japan (Oyabe), 1987-1991 (8)	260 (254-265)	Yes
Mozambique (Maputo) hospitalised cases, 2005-2006 (43)	260.1 (-)	No
Sweden (Söderham), 1983-1986 (8)	312 (278-347)	Yes
Sweden (Lund-Orup), 2001-2002 (8)	133 (119-146)	Yes

*Standard criteria = multiple overlapping sources, World Health Organisation definition of stroke, incidence cases, no upper age limit, and prospective design. Grey shade = Incidence reported in new studies (May 2013 – March 2016)

Supplementary Online Table 6. Latest year available for mortality and population data:

	Countries	
Year	n	(%)
1976	1	(0.76)
1978	1	(0.76)
1979	1	(0.76)
1980	3	(2.29)
1981	1	(0.76)
1982	2	(1.53)
1983	4	(3.05)
1984	2	(1.53)
1985	3	(2.29)
1986	2	(1.53)
1987	6	(4.58)
1988	1	(0.76)
1990	2	(1.53)
1991	2	(1.53)
1992	2	(1.53)
1993	1	(0.76)
1994	5	(3.82)
1995	6	(4.58)
1996	3	(2.29)
1998	2	(1.53)
2000	1	(0.76)
2001	1	(0.76)
2002	1	(0.76)
2003	1	(0.76)
2004	3	(2.29)
2005	3	(2.29)
2007	2	(1.53)
2008	2	(1.53)
2009	4	(3.05)
2010	4	(3.05)
2011	10	(7.63)
2012	14	(10.7)
2013	28	(21.4)
2014	7	(5.34)
Total	131	(100.0)

Supplementary Online Table 7. Mortality of stroke in countries that have reported both mortality and population data to the World Health Organisation since 1976: data are reported as crude rates, and rates age-adjusted to the New World population.

	Crude Mortality per 100,000 population		Mortality age adjusted to the WHO World Population per 100,000 population	
Country_year	Male	Female	Male	Female
Albania, 2004	190.9	207.3	242.8	203.4
Antigua and Barbuda, 1983	46.5	30.5	94.0	41.6
Argentina, 1996	66.7	62.4	76.8	51.1
Armenia, 2012	83.0	101.6	74.1	61.2
Australia, 2011	39.3	60.1	22.8	21.5
Austria, 2014	45.6	69.6	22.9	18.9
Azerbaijan, 2007	93.6	117.9	142.9	132.1
Bahamas, 1995	39.4	53.6	69.1	76.0
Bahrain, 2011	5.9	9.0	18.4	21.2
Barbados, 1995	118.6	143.1	106.2	68.1
Belarus, 2001	175.5	222.3	162.4	117.1
Belgium, 2012	51.9	74.0	26.3	21.6
Belize, 1995	37.1	25.6	73.1	50.4
Bermuda, 1983	89.2	142.3	105.7	122.7
Bosnia and Herzegovina, 2011	109.3	132.4	83.1	73.6
Brazil (South, South-East and Central West), 1995	66.7	59.3	104.1	77.0
British Virgin Islands, 1982	33.9	0.0	105.4	0.0
Brunei Darussalam, 2012	18.9	16.1	35.2	27.8
Bulgaria, 2012	280.2	315.2	149.5	108.2
Canada, 2005	36.1	50.8	24.6	21.1
Cape Verde, 1980	45.2	54.1	66.5	79.1
Cayman Islands, 1994	38.5	61.3	73.9	48.0
Chile, 1994	49.1	49.3	75.1	53.8
China, selected urban and rural areas, 2000*	130.2	114.0	162.0	113.3
China, selected rural areas, 2000*	124.0	105.9	172.8	117.5

China (selected urban areas), 2000*	135.1	120.5	154.7	110.8
Colombia, 1994	32.1	37.1	63.7	62.3
Costa Rica, 1995	25.3	28.2	58.8	49.9
Croatia, 2013	147.3	191.5	82.3	60.9
Cuba, 1996	69.0	75.4	63.7	63.6
Cyprus, 2012	41.4	50.9	26.6	24.8
Czech Republic, 2013	82.3	113.4	52.3	40.0
Denmark, 2012	54.1	65.6	29.2	21.6
Dominica, 1985	41.8	42.4	69.8	47.4
Dominican Republic, 1985	28.1	27.2	71.7	66.3
Ecuador, 1991	26.8	28.0	55.5	50.0
Egypt, 2013	17.5	18.2	30.4	31.7
El Salvador, 1993	23.9	23.2	54.0	42.6
Estonia, 2012	67.0	89.3	45.4	27.3
Falkland Islands (Malvinas), 1983	200.0	200.0	165.0	165.0
Fiji, 2009	20.2	19.3	34.1	28.2
Finland, 2013	68.9	93.1	35.7	25.6
France, 2011	43.7	56.4	21.3	15.2
French Guiana, 2011	25.3	18.3	47.7	27.8
Georgia, 2014	145.9	161.7	100.3	66.5
Germany, 2013	58.7	85.9	26.6	21.5
Greece, 2012	245.7	324.8	101.1	90.0
Grenada, 1991	79.4	101.7	102.3	102.9
Guadeloupe, 2011	72.6	57.7	43.2	23.4
Guatemala, 1984	11.6	14.5	32.5	35.5
Guyana, 1984	71.8	55.8	150.0	108.4
Honduras, 1982	13.5	12.9		
Hong Kong SAR, 2013	49.7	41.4	26.3	17.1
Hungary, 2013	115.2	142.8	72.1	48.4
Iceland, 2009	46.4	53.3	32.1	22.9
Iran (Islamic Republic of), Cities, 1987	17.1	16.1	35.7	32.1
Ireland, 2012	34.1	50.2	25.5	23.6
Israel, 2013	26.7	31.1	21.0	16.4
Italy, 2012	83.1	121.4	33.1	26.4

Jamaica, 1985	86.8	112.1	115.2	120.9
Japan, 2013	92.7	95.5	35.0	19.1
Jordan, 2011	25.0	23.1	71.3	62.6
Kazakhstan, 2003	271.8	325.5	426.6	316.7
Kuwait, 2013	10.7	10.1	41.3	29.8
Kyrgyzstan, 2013	85.5	81.6	159.4	111.1
Latvia, 2012	184.6	278.9	122.1	85.7
Lithuania, 2012	147.9	224.5	94.1	69.4
Luxembourg, 2013	39.7	50.4	25.1	18.9
Malaysia, 2008	19.4	16.7	30.6	24.7
Maldives, 2008	28.1	12.4	45.3	26.5
Malta, 2014	54.3	74.8	30.3	25.1
Martinique, 2011	66.8	52.7	34.0	19.1
Mauritius, 2014	62.6	59.1	65.1	43.3
Mexico, 1995	24.1	27.3	53.0	49.1
Montenegro, 2009	65.2	99.0	50.6	56.9
Montserrat, 1979	74.1	285.7	119.4	470.6
Netherlands Antilles, 1981	29.2	44.9	50.2	62.4
Netherlands, 2013	45.0	66.6	24.8	21.7
New Zealand, 2011	46.7	73.8	28.6	30.5
Nicaragua, 1978	8.0	6.8	17.7	14.3
Norway, 2013	44.4	64.1	24.5	19.7
Occupied Palestinian Territory (Part), 2014	23.1	31.2	65.9	67.5
Panama, 1987	38.5	38.4	75.9	72.0
Papua New Guinea, 1977	1.2	0.3	1.7	0.4
Paraguay (Reporting Areas), 1987	53.6	55.3	134.1	116.8
Peru, 1983	13.1	13.2	36.4	30.7
Philippines, 1996	58.4	43.8	129.9	91.1
Poland, 2013	75.5	94.1	52.7	36.8
Portugal, 2013	107.7	126.1	48.5	34.4
Puerto Rico, 1992	37.7	33.9	33.8	25.1
Qatar, 2012	2.4	1.9	7.1	6.9
Republic of Korea, 2013	47.8	52.8	43.7	28.3
Republic of Moldova, 2013	151.2	181.0	145.4	112.4

Reunion, 2011	40.0	41.7	42.4	28.4
Rodrigues, 2014	48.7	56.7	54.6	51.7
Romania, 2012	203.7	240.1	132.1	101.6
Russian Federation, 1998	220.8	355.1	240.6	188.2
Saint Kitts and Nevis, 1992	163.6	260.9	206.5	222.1
Saint Lucia, 1988	85.4	94.8	167.1	129.6
Saint Pierre and Miquelon, 1976	200.0	80.0	152.0	52.7
Saint Vincent and Grenadines, 1986	54.3	63.7	128.2	101.8
San Marino, 2005	82.0	105.2	42.5	35.2
Sao Tome and Principe, 1987	21.5	28.4	48.9	45.7
Serbia, 2013	167.6	199.1	89.9	75.3
Seychelles, 1987	163.1	162.2	301.5	167.6
Singapore, 2014	37.5	41.8	30.5	24.8
Slovakia, 2010	95.2	119.7	81.0	57.9
Slovenia, 2010	81.7	110.6	53.1	36.3
South Africa, 2013	36.7	47.4	61.6	61.1
Spain, 2013	50.5	68.7	23.5	17.8
Sri Lanka, 1986	19.6	12.4	32.4	21.9
Suriname, 1990	47.0	53.5	102.2	91.8
Sweden, 2013	60.0	84.1	26.4	22.0
Switzerland, 2013	36.7	54.7	17.9	15.3
Syrian Arab Republic, 2010	18.8	15.3		
TFYR Macedonia, 2010	174.9	196.8	148.7	130.1
Tajikistan, 2004	31.9	35.7	84.4	70.5
Thailand, 2002	24.7	18.2	29.1	19.1
Trinidad and Tobago, 1994	77.8	85.0	111.2	100.5
Tunisia, 2009	21.9	19.4	25.1	22.9
Turkey, 2013	42.4	52.0	53.2	45.7
Turkmenistan, 1998	26.8	31.6	69.9	60.2
Turks and Caicos Islands, 1987	75.0	75.0	98.4	83.3
Ukraine, 2004	191.6	243.3	161.3	113.7
United Kingdom, England and Wales, 2013	50.1	71.7	24.6	22.4
United Kingdom, Northern Ireland, 2013	47.3	69.5	27.8	24.9

United Kingdom, Scotland, 2013	68.6	97.5	34.7	31.8
United Kingdom, 2013	51.6	73.8	25.5	23.3
United States of America, 2007	36.4	53.5	25.4	23.0
Uruguay, 1990	103.8	126.3	93.8	75.9
Uzbekistan, 2005	64.3	74.8	143.3	122.7
Venezuela, 1994	34.9	37.1	81.5	72.2
Virgin Islands (USA), 1980	21.6	31.7	58.8	52.8

*Data for China are only for selected urban and rural areas and represent less than 10% of all deaths occurring in the country, Grey shade = new mortality data

References:

1. Coull AJ, Silver LE, Bull LM, Giles MF, Rothwell PM. Direct assessment of completeness of ascertainment in a stroke incidence study. Stroke 2004;35(9):2041-5.
2. Hatano S. Experience from a multicentre stroke register: a preliminary report. Bull WHO 1976;54:541-53.
3. Malmgren R, Warlow C, Bamford J, Sandercock P. Geographical and secular trends in stroke incidence. Lancet 1987;2(8569):1196-200.
4. Sudlow CL, Warlow CP. Comparing stroke incidence worldwide: what makes studies comparable? Stroke 1996;27(3):550-8.
5. Danielyan KE, Oganesyn HM, Nahapetyan KM, et al. Stroke burden in adults in Armenia. Int J Stroke 2012;7(3):248-9.
6. Leyden JM, Kleinig TJ, Newbury J, et al. Adelaide Stroke Incidence Study: Declining Stroke Rates but Many Preventable Cardioembolic Strokes. Stroke 2013;44(5):1226-31.
7. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol 2003;2(1):43-53.
8. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 2009;8(4):355-69.
9. Benamer HT, Grosset D. Stroke in Arab countries: a systematic literature review. J Neurol Sci 2009;284(1-2):18-23.
10. Kulesh SD, Filina NA, Frantava NM, et al. Incidence and case-fatality of stroke on the east border of the European Union. Stroke 2010;41:2726-30.
11. Sajjad A, Chowdhury R, Felix JF, et al. A systematic evaluation of stroke surveillance studies in low- and middle-income countries. Neurology 2013;80(7):677-84.
12. Jiang B, Wang WZ, Chen H, et al. Incidence and trends of stroke and its subtypes in China: results from three large cities. Stroke 2006;37(1):63-8.
13. Saposnik G, Del Brutto OH, Iberoamerican Society of Cerebrovascular D. Stroke in South America: a systematic review of incidence, prevalence, and stroke subtypes. Stroke 2003;34(9):2103-7.
14. Pikija S, Cvetko D, Malojčić B, et al. A population-based prospective 24-month study of stroke: Incidence and 30-day case-fatality rates of first-ever strokes in Croatia. Neuroepidemiology 2012;38(3):164-71.
15. Demant MN, Andersson C, Ahlehoff O, et al. Temporal trends in stroke admissions in Denmark 1997–2009. BMC Neurology 2013;13(1):1-8.
16. El-Tallawy HN, Farghaly WMA, Shehata GA, et al. Epidemiology of non-fatal cerebrovascular stroke and transient ischemic attacks in Al Quseir, Egypt. Clin Interventions Aging 2013;8:1547-51.
17. Zhang Y, Chapman AM, Plested M, Jackson D, Purroy F. The incidence, prevalence, and mortality of stroke in France, Germany, Italy, Spain, the UK, and the US: A literature review. Stroke Research and Treatment 2012:Article ID 436125.
18. Olindo S, Chausson N, Mejdoubi M, et al. Trends in incidence and early outcomes in a black Afro-Caribbean population from 1999 to 2012: Etude Réalisée en Martinique et Centrée sur l'Incidence des Accidents Vasculaires Cérébraux II Study. Stroke 2014;45(11):3367-73.

19. Azarpazhooh MR, Etemadi MM, Donnan GA, et al. Excessive incidence of stroke in Iran: Evidence from the Mashhad Stroke Incidence Study (MSIS), a population-based study of stroke in the Middle East. Stroke 2010;41:e3-e10.
20. Kelly PJ, Crispino G, Sheehan O, et al. Incidence, event rates, and early outcome of stroke in Dublin, Ireland: The North Dublin Population Stroke Study. Stroke 2012;43(8):2042-7.
21. The European Registers of Stroke Investigators. Incidence of stroke in Europe at the beginning of the 21st century. Stroke 2009;40(5):1557-63.
22. Corso G, Bottacchi E, Giardini G, et al. Epidemiology of stroke in Northern Italy: the Cerebrovascular Aosta Registry, 2004–2008. Neurological Sciences 2012;34(7):1071-81.
23. Omama S, Yoshida Y, Ogasawara K, et al. Incidence rate of cerebrovascular diseases in Northern Japan determined from the Iwate Stroke Registry with an inventory survey system. J Stroke Cerebrovasc Dis;22(8):e317-e22.
24. Sugama C, Isa K, Okumura K, Iseki K, Kinjo K, Ohya Y. Trends in the incidence of stroke and cardiovascular risk factors on the isolated island of Okinawa: The Miyakojima Study. J Stroke Cerebrovasc Dis 2012.
25. Cantu-Brito C, Majersik JJ, Sánchez BN, et al. Door-to-door capture of incident and prevalent stroke cases in Durango, Mexico: The Brain Attack Surveillance in Durango Study. Stroke 2011;42(3):601-6.
26. Feigin VL, Krishnamurthi RV, Barker-Collo S, et al. 30-year trends in stroke rates and outcome in Auckland, New Zealand (1981-2012): A multi-ethnic population-based series of studies. PLoS ONE 2015;10(8):e0134609.
27. Danesi MA, Okubadejo NU, Ojini FI, Ojo OO. Incidence and 30-day case fatality rate of first-ever stroke in urban Nigeria: The prospective community based Epidemiology of Stroke in Lagos (EPISIL) phase II results. J Neurol Sci;331(1):43-7.
28. Khealani BA, Wasay M. The Burden of Stroke in Pakistan. Int J Stroke 2008;3(4):293-6.
29. Sienkiewicz-Jarosz H, Gluszkiewicz M, Pniewski J, et al. Incidence and case fatality rates of first-ever stroke - comparison of data from two prospective population-based studies conducted in Warsaw. Neurologia I Neurochirurgia Polska 2011;45(3):207-12.
30. Maredza M, Bertram MY, Tollman SM. Disease burden of stroke in rural South Africa: an estimate of incidence, mortality and disability adjusted life years. BMC Neurology 2015;15(1):1-12.
31. Connor MD, Walker R, Modi G, Warlow CP. Burden of stroke in black populations in sub-Saharan Africa. Lancet Neurol 2007;6(3):269-78.
32. Ramalle-Gomara E, Ruiz E, Serrano M, Bártulos M, González M-Á, Matute B. Hospital discharges and mortality registries: 2 Complementary databases for the epidemiological surveillance of stroke. J Stroke Cerebrovasc Dis;22(8):e441-e5.
33. Syme PD, Byrne AW, Chen R, Devenny R, Forbes JF. Community-based stroke incidence in a Scottish population: the Scottish Borders Stroke Study. Stroke 2005;36(9):1837-43.
34. Corbin DOC, Poddar V, Hennis A, et al. Incidence and case fatality rates of first-ever stroke in a black Caribbean population: The Barbados Register of Strokes. Stroke 2004;35(6):1254-8.
35. Sridharan SE, Unnikrishnan JP, Sukumaran S, et al. Incidence, types, risk factors, and outcome of stroke in a developing country: The Trivandrum Stroke Registry. Stroke 2009;40(4):1212-8.
36. Owolabi M. Taming the burgeoning stroke epidemic in Africa: stroke quadrangle to the rescue. West Indian Med J 2011;60:412-21.

37. Bejot Y, Osseby GV, Aboa-Eboule C, et al. Dijon's vanishing lead with regard to low incidence of stroke. Eur J Neurol 2009;16(3):324-9.

38. Corso G, Bottacchi E, Giardini G, et al. Community-based study of stroke incidence in the Valley of Aosta, Italy. CARe-cerebrovascular Aosta Registry: years 2004-2005. Neuroepidemiology 2009;32(3):186-95.

39. Vega T, Zurriaga O, Ramos JM, et al. Stroke in Spain: epidemiologic incidence and patterns; a health sentinel network study. J Stroke Cerebrovasc Dis 2009;18(1):11-6.

40. Minelli C, Fen LF, Minelli DP. Stroke incidence, prognosis, 30-day, and 1-year case fatality rates in Matao, Brazil: a population-based prospective study. Stroke 2007;38(11):2906-11.

41. Wu X, Zhu B, Fu L, et al. Prevalence, incidence, and mortality of stroke in the Chinese island populations: A systematic review. PLoS ONE 2013;8(11):e78629.

42. Das SK, Banerjee TK, Biswas A, et al. A prospective community-based study of stroke in Kolkata, India. Stroke 2007;38(3):906-10.

43. Damasceno A, Gomes J, Azevedo A, et al. An epidemiological study of stroke hospitalizations in Maputo, Mozambique: a high burden of disease in a resource-poor country. Stroke 2010;41(11):2463-9.

3.3 Summary

Gathering the data on incidence, mortality, and case-fatality for stroke are important for understanding the effect of stroke worldwide. It also enabled us to identify where health care intervention could be improved for primary or secondary prevention of stroke. In this paper, new data on incidence were extracted from new studies in four countries. Incidence rates presented in our review differ somewhat to those presented in the Global Burden of Disease Study (GBD), even though both were adjusted to the WHO World population.[82] The GBD had a different aim and was undertaken to provide estimates of stroke in all regions using a systematic approach, and has the added advantage of enabling comparison across other neurological diseases. In contrast, the approach taken in the paper presented in Chapter 3 helps us to identify countries and regions with the most recent data on stroke incidence obtained using ideal methods, and has the advantage of highlighting countries where data are lacking or out of date. Both approaches enable one to determine where there are 'hotspots' in stroke occurrence. These data are needed to help plan and develop approaches to improve access to preventive strategies and stroke care. In many countries, there were no new data on the incidence of stroke. However, national clinical registries may be used to provide such estimates for stroke in lieu of community-based incidence studies if they have adequate coverage of the population. The additional benefits of these registries is that they enable assessment of the quality of care provided in acute hospitals and subsequent patient outcomes.[83] The next section (Part B) of my thesis will describe a potential strategy to identity and address gaps in quality of care provided in hospitals with the use of data from clinical registry.

Summary of Part A

Stroke is the second leading cause of mortality, and the leading cause of disability globally. There are three essential facets that provide us with opportunities to intervene to reduce the burden of stroke. These are: (1) primary prevention (i.e. prevention of a first-ever event), (2) acute stroke care (i.e. care provided in hospital), and (3) secondary prevention (i.e.) prevention of a recurrent event and ongoing recovery support, Figure 1.1). Prevention opportunities exist because many risk factors for stroke are modifiable. Hypertension, diabetes, high cholesterol, physical inactivity, and inappropriate diet account for more than 80% of the risk of stroke.[84]

Region-specific or national clinical registries provide opportunities to estimate stroke incidence, mortality and case-fatality for stroke in lieu of community-based incidence studies. Additionally, clinical registries can also be used to assess the quality of stroke care provided at acute hospitals and subsequent patient outcomes.

In the next part of this thesis (Part B: Chapters 4 and 5), I will address the strategies, including data from clinical registries, that can be used to assess and improve the quality of care provided in acute hospitals for stroke care in Australia.

PART B:

Improving quality of evidence-based care in hospitals

Chapter 4: Strategies to use registry data to effectively change clinician behaviour for improving acute stroke care in Australia

Since the paper presented in Chapter 5 has its own methods section, in this chapter I will not reiterate methods that are subsequently outlined. This chapter includes a description of the evidence-based care for stroke in Australia, the various data collection systems and how they are used for QI at hospitals. Information on the various strategies that are known to effectively change clinician behaviour as part of QI programs, and the areas where data are lacking are also highlighted. Following this, a brief description of the QI component of the Stroke123 study is provided.

4.1 Evidence-based care for stroke in Australia

Receipt of evidence-based care for patients with acute stroke has been shown to be effective in reducing mortality and disability.[14, 85, 86] Countries around the world have developed clinical guidelines to provide recommendations for how care should be provided based on the best available evidence.[7, 87, 88]

4.1.1 The Australian Clinical Guidelines for Acute Stroke Management

In Australia, the Stroke Foundation have developed clinical guidelines for management with relevant experts that covers the whole stroke care continuum (treatment, rehabilitation and long-term care including secondary prevention).[7] The recommendations included in the

guidelines have been given an overall grade using criteria required by the National Health and Medical Research (NHMRC; Table 4.1). These guidelines set the standards of care expected for management of patients with stroke in Australia. A framework to guide the establishment of appropriate stroke services to support delivery of best practice care as outlined in clinical guidelines was first developed by the Stroke Foundation (with support from the Australian Government Department of Health and Ageing) in 2002. The most important guidelines were selected and formed part of the National Performance Indicator Set (NPIS) in 2011 as part of the Stroke Foundation Acute Stroke Services Framework 2011.[89] The NPIS was developed to guide and support the delivery of best practice stroke care in hospitals across Australia. The NPIS contains eight essential processes of care for acute stroke management. These include: (1) use of intravenous thrombolysis (tPA) for ischaemic strokes, (2) access to a stroke unit, (3) prescribed antihypertensive agents at discharge, (4) care plan developed with the patient and their family/carer at discharge, (5) mobilisation < 2 days of admission, (6) screen or swallow assessment < 24 hours of admission, (7) aspirin administration < 48 hours of admission if an ischaemic stroke, and (8) prescribed on antiplatelets or antithrombotics at discharge. Adherence to all eight clinical processes of care are recommended for collection by hospital staff for routinely monitoring their quality of care.[90]

Table 4.1. *Definition of NHMRC grades of recommendations*[91]

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

4.2 Acute data collection systems used for quality of care monitoring QI

Developing guidelines alone is not sufficient to improve care. It is also important to monitor the quality of care provided at hospitals by documenting adherence to guideline recommendations (i.e. via measures or indicators of the quality of care). Monitoring the quality of care is an important driver for change in practice. Information from the data collection systems that have been developed in Australia, based on the clinical guidelines, can be used to describe the quality of care and outcomes for patients with stroke at a national or state-level.

In Australia, the two common methods for standardised monitoring of the quality of care provided in hospitals are cross-sectional hospital audits of medical records or continuous collection of data through clinical registries. These data collection systems for Australia are briefly described in the following section.

4.2.1 The Australian Stroke Clinical Registry (AuSCR)

Clinical quality registries provide more reliable prospective measurement of the quality of care and patient outcomes, than cross-sectional audit data, because data are collected continuously on a large number of patients from multiple hospitals on an on-going basis. Stroke registries may often include long-term outcome information such as quality of life, or survival status.[83] These data are generally collected between 90 and 180 days.[92] However, the costs involved with running a registry are high because they can be labour intensive, especially if outcome data are collected directly from the patient. Consequently, the data collected in registries are often limited to a selected set of prioritised clinical process and outcome variables.[83]

The AuSCR was established in 2009 and is a collaborative national effort to monitor and improve the quality of acute stroke care (www.auscr.com.au). It was developed using the national operating principles and technical standards for quality registries.[93] Information on adherence to between 4 and 8 of the NPIS processes of care and patient outcomes is collected prospectively using an online web-tool for all eligible patients with a diagnosis of either stroke or TIA. Patients are also followed up between 90 and 180 days following their initial admission for stroke. The AuSCR was piloted in 2009 with six hospitals, as of August 2018 it was approved for use in 82 hospitals across Australia with 69 sites actively contributing data to the registry.[92]

4.2.2 The National Stroke Services Audit program

Clinical audits are conducted on a cross-sectional sample of patients using extraction of data from hospital medical records. They are often used to provide detailed clinical data on a large number of care processes and can be used to explain variations in patient outcomes at a particular hospital, indicating the quality of care provided to patients by clinicians, and highlighting gaps in a large number of areas relevant to different disciplines. The limitation of

audits is that they are often conducted cross-sectionally on only a relatively small number of patients. Further, long term outcomes are not captured and are generally limited to in-hospital mortality or morbidity. Moreover, the hospital medical record itself may vary in accuracy and completeness.

In Australia, audits have been undertaken at a national, state and local hospital level for monitoring of hospital performance in acute and rehabilitation settings. In this thesis, the Stroke Foundation acute audits are described as these were used to identify and report gaps in hospital management of acute stroke care and patient outcomes at a national level.

Since 2007, the Stroke Foundation has conducted the National Acute Stroke Services Audit program biennially to inform the gaps in stroke care.[94] These summary data are then fed back to the clinicians and hospital staff from hospitals that volunteered to participate. The audit program includes a clinical audit and an organisational survey. The clinical audit involves retrospectively auditing up to 40 medical records with a discharge International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) code for stroke within the last six month period from the audit date.[95] Patient information such as demographics, medical history, risk factors, stroke classification and severity, type of care received and discharge details are collected using a web tool known as the Australian Stroke Data Tool (https://tool.ausdat.org.au/auth/login). The organisational survey is a self-reported survey completed by one or more clinicians at each participating hospital.[96] The survey includes questions on the number of beds in each hospital, if the hospital has a dedicated stroke unit, and the number of strokes treated per year. A limitation of these audits is that performance feedback is only available every two years. However, these data have been used to demonstrate notable improvements in the quality of

stroke care over time.[97, 98] The biennial audit reports have also been used to provide information on the varying adherence to clinical indicators.[94-96, 99]

4.2.3 Hospital administrative datasets

Hospital administrative datasets provide information relating to emergency presentations and hospital admissions within defined geographical regions. There is a national minimum dataset that hospitals in all states in Australia are required to collect and submit to state and commonwealth governments for funding and policy purposes.[100] Clinical data are coded using the ICD-10-AM codes by trained coders. These data are used by government to monitor burden of disease. However, the reliability and validity of coded data may vary in quality, accuracy and detail depending on whether the diagnosis recorded was stroke or TIA.[101] Administrative datasets do not specifically include information on all quality of care indicators. However, a small number of indicators can be extracted, with variation between states. For example, some states have introduced an access to stroke unit variable. The use of tPA can be extracted through procedure codes. Moreover, hospital datasets do not provide post discharge information on patient outcomes, such as quality of life or survival.

4.3 Variability in acute stroke care

Substantial evidence exists to show that adherence to evidence-based clinical guidelines, such as admission to a stroke unit, can reduce in-hospital mortality and improve outcomes.[85] Despite this, evidence-based care for acute stroke management is not always provided. One of the issues is that the uptake of evidence-based care varies between hospitals and regions (e.g. discharge care planning).[86] Such discrepancies are concerning given that variability in patient management has been shown to adversely affect health outcomes and may lead to ineffective use of health care resources.[10]

Clinicians and hospital staff are important drivers of the care provided to patients with stroke. However, variability in care is often a result of (1) the use of different forms of evidence to inform their practice, (2) keeping up-to-date with the growth in evidence, (3) individual values and attitudes, and (4) time and resource constraints.[102]

4.4 Strategies to change clinician behaviour for quality improvement

There are various professional behaviour change strategies, defined by the Cochrane Effective Practice and Organisation of care group, that are considered effective and efficient for QI in clinical settings (Table 4.2).[103, 104] These behaviour change strategies are generic and can be used for QI programs by any health care organisation for any type of application, and not necessarily only in stroke. These strategies help clinicians to translate clinical evidence into practice. However, there is variation in the magnitude of the effectiveness of these strategies for changing clinician behaviour. An earlier study by Grimshaw and colleagues provided evidence that interventions involving educational outreach, a form of professional behaviour change strategy, resulted in a 7% median absolute improvement in care. However, there was a lot of heterogeneity between the developed interventions.[103] A more recent review by Squires and colleagues also offered no compelling evidence on what is an effective strategy to change clinician behaviour in clinical settings.[13]

In Australia, multifaceted state and national QI programs have been initiated to close the gap between evidence (what is recommended in clinical guidelines) and practice (what is shown to be happening in the health care system through data collection) (see section 4.5 below for an Australian example). In these QI programs, routine monitoring of performance is conducted and feedback provided to clinicians and hospital administrators. Ideally this should lead to an active process of strategy development to motivate clinicians and organisations to identify gaps in care and improve clinical outcomes by developing and implementing action plans. Audit

and feedback using both clinical audit and registry data, can provide hospitals and clinicians with regular feedback regarding adherence to stroke quality indicators and their performance in relation to other hospitals. Providing this type of feedback has been shown to be effective for improving adherence to stroke guideline recommendations.[105, 106]

Table 4.2. *Summary of literature on the effective strategies for achieving professional behaviour change (adapted: Grimshaw and colleagues).*[104, 107]

Intervention Review	Number of studies	Study population	Effect sizes (Median absolute improvement of care as %)
Printed educational materials	12 randomised trials 11 non-randomised	Healthcare professionals from all levels of care	4.3% (range -8.0% to +9.6%)
Educational meetings	81 randomised trials	Healthcare professionals from primary and secondary care (n=>11,000)	6.0% (IQR 1.8% to 15.3%)
Educational outreach	69 randomised trials	Healthcare professionals from primary and secondary care (n=>11,000)	5.6% (IQR 3.0% to 9.0%)
Local opinion leaders	18 randomised trials	>296 hospitals and 318 primary care physicians	12% (IQR 6.0% to 14.5%)
Audit and feedback	140 randomised trials	>5056 single healthcare professionals and clusters of healthcare professionals	Dichotomous outcomes: 4.3% (IQR 0.5% to Continuous outcomes: 1.3% (IQR 1.3% to
Reminders	35 randomised trials	Healthcare professionals from all levels of care	Cluster randomised controlled trials: 14.1% (range -1.0% to +34.0%) Patient randomised controlled trials: 5.4% (range -1.0% to 25.7%)
Computerized Reminders	28 randomised trials	Healthcare professionals from all levels of care	Median absolute improvement of care of 4.2% (interquartile range 0.8% to 18.8%).
Interprofessional collaboration	5 randomised trials	> 33 clusters of health professionals, 3090 patients	Can improve health care processes and outcomes, effect sizes not calculated due to small number of heterogeneous trials
Tailored interventions	26 randomised trials	Healthcare professionals mostly from primary care	Meta-regression using 12 randomised trials. Pooled odds ratio of 1.52 (95% CI, 1.27 to 1.82, p<.001)

4.5 The Stroke123 QI program

4.5.1 General overview

Stroke123 is a 4-year NHMRC funded controlled before-and-after study bthat commenced in 2012. The study and covered several main components pertaining to monitoring and improving hospital care and health outcomes associated with stroke. The QI component of Stroke123 was designed to assess the influence of hospital performance monitoring and implement a program of facilitated action planning for QI. Facilitated action planning was done primarily audit and feedback using data from the Stroke Foundation Audit data, and AuSCR for participating hospitals in Queensland (QLD), with the support of external facilitators. Steps taken by the facilitator included education, barrier assessment for modifiable and non-modifiable barriers and prioritising these. The evidence-based behaviour change strategies were then used to work out on an action plan template and consensus being achieved. The study protocol and statistical analysis plan for the main project were recently published.[108] The main results of this QI program have been analysed and are yet to be published.

4.5.2 The enhanced StrokeLink program for QI

StrokeLink was a QI program that commenced in 2008 by the Stroke Foundation in QLD. The program was a single workshop, conducted by external facilitators who used Stroke Foundation audit data to inform clinicians or hospital staff on the quality of care provided at their hospital. In Stroke123, the Strokelink program was enhanced by including data from the AuSCR as part of the audit and feedback process which included patient outcome data. The enhanced StrokeLink program was underpinned by the Promoting Action on Research Implementation in Health Systems (PARIHS) theoretical framework[109] (described below) and the plan-do-study-act (PDSA) model.[110] The PDSA model is the cycle of review action planning that is

used to test agreed improvement strategies. In StrokeLink, active review of hospital performance was done using data from the Stroke Foundation Audit and AuSCR during the Stroke123 intervention period.

The PARIHS framework can be used to guide the implementation of evidence into practice for changing clinician behaviour.[108] This framework is dependent on 1) the level and nature of the evidence; 2) the context or environment into which the evidence is to be provided; and 3) the method or way in which the process is facilitated.[111] The originators of the framework suggest that facilitators have a key role in helping individuals and teams understand what they need to change and how to change it to successfully implement evidence into practice. Project leads, educational outreach workers, opinion leaders, facilitators from external agencies are individuals that could be appointed as facilitators.[112] During the Stroke123, intervention facilitators who were external to the hospitals provided ongoing support to clinicians and hospital staff through face-to-face meetings, conference calls, and e-mail support. The ongoing support of trained external facilitators throughout the process of implementing change in hospitals is deemed beneficial[113] and so was also provided. The external facilitation components that were provided as part of Stroke123 were consistent with this theoretical framework.[109] However, how much facilitation (i.e. dosage of external support) that is required to reduce evidence-based practice gaps at a clinician level is not well understood.

The next chapter includes a submitted paper (*Implementation Science*, November 2018) describing the process of external facilitation for QI at the hospital-level for improving acute stroke care using data obtained in the enhanced StrokeLink program for the Stroke123 study.

4.6 Summary

In this chapter I briefly described the acute stroke data collection systems (audits, registry and hospital administrative data) used in Australia, and how these data can be used to monitor the quality of care provided at hospitals. I also highlighted the various strategies that are known to effectively change clinician behaviour as part of QI programs. However, it is not yet clear what the most effective behaviour change strategies are within the context of hospital care for stroke. I also provided an example of a QI program in Queensland, Australia. The next chapter (Chapter 5) comprises the submitted manuscript related to using data from clinical registry and audit in a QI program to help clinicians understand gaps in performance of stroke care as part of the Stroke123 project. In Chapters 6 and 7, I will demonstrate how linked AuSCR data and hospital administrative data, also obtained as part of a sub study of Stroke123 were used to investigate the potential areas of intervention to reduce practice gaps related to anxiety and depression in survivors of stroke.

Chapter 5: Case study of using registry and audit data to improve quality of care in acute hospitals

5.1 Overview

In Chapter 4, I outlined that audit data alone may be insufficient to provide information on the quality of care and subsequent patient outcomes. Continuous data from a clinical registry, such as the AuSCR, strengthens the data on hospital performance and can be used in QI program along with behaviour change strategies, to help clinicians close the gaps in stroke care. Data on their own would not change practice unless they are used to inform changes to clinical practice. In this chapter, I describe how data from the clinical registry and audit of participating hospitals in QLD, over a five year period, can be used to improve the quality of stroke care in hospitals by changing clinician behaviour.

Facilitators may have a role in helping clinicians identify, understand and address gaps in the delivery of care using implementation science theory and evidence.[12] However, little is known about the influence of external facilitation for improving practice within QI program.

As described in the previous chapter, Stroke123 was a partnership project that provided an opportunity to assess the influence of these data collection systems on improving adherence to evidence-based strategies for acute stroke care. The main results of this QI program have been

analysed and are yet to be published. The intervention results have been added as personal communication (Cadilhac et al. 2019). There was an 18% improvement in the net change in composite score (processes achieved vs processes eligible; 18% 95% CI: 12%, 24%) compared to no change in other non-participating Australian hospitals (95% CI:-3%, 3%). The largest improvement was observed following introduction of financial incentives (14%, 95% CI; 8%, 20%). The overall aim of the following paper was to evaluate the influence of the process of external facilitation for QI at the hospital-level for improving acute stroke care within an Australian context. This paper addresses aim two of this thesis: to address evidence-to-practice gaps in the acute care setting using data from a national clinical registry for quality improvement within an Australian context. My contribution is at 70%, and the nature of my contribution was data collection and management, statistical analysis, interpretation, and writing of first draft of the manuscript.

This manuscript has been submitted to 'Implementation Science' (IF 3.2) in November 2018.

5.2 Submitted paper

Understanding the role of external facilitation in hospitals to drive quality improvement: a case study from stroke

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Submitted to Implementation Science

Understanding the role of external facilitation in hospitals to drive quality improvement: a case study from stroke

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Abstract

Background: Quality improvement (QI) programs help support clinicians working in hospitals to reduce gaps in evidence and clinical practice. Facilitators may have a role in helping clinicians understand and address gaps in the delivery of care using implementation science theory and evidence. However, little is known about the influence of external facilitation in improving practice within the context of complex multifaceted QI programs. We aimed to evaluate the influence of external facilitation on the development and implementation of consensus-based action plans for improving acute stroke care. We also aimed to assess the influence of 'facilitator dose' with reference to the complexity of the actions plans, (i.e. number of actions to be addressed) on changes in adherence to eight clinical processes of care (PoC) measured before and after the intervention period.

Methods: An observational, process evaluation study was performed. Staff from participating Queensland hospitals were provided with support for action plan development and implementation by external facilitators from the StrokeLink program (Stroke Foundation). Additional, indirect support was provided by the Australian Stroke Clinical Registry staff (AuSCR) and the Queensland Statewide Stroke Clinical Network (government). We measured the number and mode of contacts; type of professional behaviour change support; and frequency of AuSCR site data reviews. Descriptive statistics were used to describe the association between dosage of external facilitation and simple versus comprehensive (addressed 4+ PoC) action plans. Data from the AuSCR (2010-2015) were used to assess the change in adherence to eight PoCs across the study period.

Results: 20/23 Queensland hospitals participated. There was no significant difference in support time from external facilitators to hospitals that developed a comprehensive action plan vs simple or no action plan: face-to-face (median [Q1,Q3]: 18 hours [11,24] vs 16 hours

[10,22] p=0.61); phone contact (6 hours [3,8] vs 3 hours [2,5], p=0.08). 8/12 hospitals selected all eight PoC for comprehensive action planning and there was an observed improvement in absolute change in only 4 PoCs. Most (95%) hospital staff reported accessing their AuSCR data for QI monitoring.

Conclusions: Faciliation for the development and implementation of a comprehensive action plan for QI may achieve greater outcomes in uptake of evidence-based practice. The dosage of external facilitation was similar and it is unclear whether hospitals with more comprehensive plans were more motivated to change practice. Further research is needed to understand the role of external facilitation as part of a multifaceted QI program that use audit and feedback strategies.

Key words: quality improvement, stroke, facilitation, behaviour change intervention, process evaluation

Background

Despite widely available evidence supporting clinical interventions that improve health outcomes for patients hospitalized for acute stroke, adherence to these recommended interventions is suboptimal [1, 2]. In Australia, there is evidence that adherence to recommended clinical processes of care vary between hospitals that treat patients with acute stroke [3]. Factors that may contribute to these variations include the ability to keep up to date with current evidence, 'clinicians' values and attitudes, unwillingness to change practice, and time constraints [4, 5]. Such discrepancies are concerning given that variability in acute patient care has been shown to adversely affect patient outcomes, and result in ineffective use of health care resources [6].

Grimshaw and colleagues provided an overview of the effectiveness of professional behaviour change strategies available to support quality improvement (QI) programs at a hospital level [7]. These strategies have been categorised by the Cochrane Effective Practice and Organisation of care group [8] and include techniques such as: *educational outreach visits* (face-to-face chat by a trained person to organisation staff on how to improve change and provide education materials); *audit and feedback* (using audit data to provide feedback on clinical performance over time); *interprofessional collaboration* (many health professionals from different fields work together with clinicians, patients, families, and caregivers to deliver the highest quality of care); *reminders* (to prompt clinicians to remember to perform critical tasks, such as monitoring of chronic conditions); and *tailored interventions* (to change professional practice following an investigation into the factors that explain current professional practice and any reasons for resisting new practice). However, the most effective implementation strategies are thought to be those that adopt a multifaceted approach [5, 9]. A more recent review offered no compelling evidence on what is an effective

strategy to change clinician behaviour in acute care settings [10]. Therefore, choosing QI interventions to change clinicians' behaviours to reflect best evidence is challenging.

A clear message from the implementation science literature is that information alone does not change behaviour and active facilitation in some form is required [4]. Successful implementation most likely when implementation processes are appropriately facilitated by either internal (i.e., inside the local site) and/or external (i.e., outside of the local site) facilitators [11]. Facilitators are individuals with the specific roles, skills and knowledge to help clinicians, teams and organizations deliver evidence-based care by changing their professional behaviour [12]. They have a key role in helping individuals and teams understand what they need to change and how they need to change practice. To Identify, engage, and connect stakeholders, facilitate collaboration, support communications and information sharing, changing evidence-based knowledge and evaluating practice change are some of the key attributes and skills of facilitators.[13] The aim of the primary study was to identify and address gaps in quality of care provided in acute hospitals. Facilitators may have a role in helping clinicians identify, understand and address gaps in the delivery of care using implementation science theory and evidence. However, very little is known about the type or dose of internal or external facilitation required to implement change.

In this study, the **primary aim** was to assess if mode and dosage of external facilitation influenced development of a comprehensive action plan as part of this multifaceted QI intervention.

The **secondary aim** was to assess the relationship between complexities of action plans and change in adherence to the eight clinical processes of care indicators for acute stroke post-intervention when compared to the pre-intervention period in the participating Queensland hospitals.

Methods

Study design: An observational, process evaluation study.

Population: Staff and clinicians from acute stroke hospitals

Queensland public hospitals participating in data collection using the Australian Stroke Clinical Registry (AuSCR) and who were part of the Queensland StrokeLink program [14] were eligible to participate in our quality improvement initiative known as 'Stroke123' (N=23). The interventions were delivered between May 2013 and August 2015.

Intervention detail

Stroke123 was a controlled before-and-after study designed to assess the influence of adding hospital level performance monitoring (i.e. assessing quality of stroke care using AuSCR data) to an existing QI program, StrokeLink [14, 15] In Stroke123, the enhanced StrokeLink QI intervention comprised of an externally facilitated program in which clinical performance and outcome data were presented to sites in a workshop format. These data were then to assist in identifying practice gaps. This data was used to target development of action plans and to monitor performance.

Our external facilitators were either StrokeLink staff, Queensland State-wide Stroke Clinical Network leads or AuSCR project coordinators. Facilitators all had health practitioner backgrounds, and a range of skills, based on their previous roles and experiences, including the capacity to provide focused attention for quality improvement. StrokeLink staff were the primary facilitators, with previous work experience, who conducted face-to-face meetings including barrier identification workshops, where they were able to develop clear and shared understanding of the local culture, values, beliefs, and attitudes of members of the hospitals. The StrokeLink staff had also been provided with standardised training, by a senior member

of the Stroke Foundation, in improvement science and theories of behaviour change including the application of the PDSA methods. The Strokelink staff were given a training manual and there was ongoing mentoring by a senior Stroke Foundation staff throughout the study period. They provided education on best practice care to the participating hospital staff as required, and used complementary performance data from the AuSCR to identify and describe local gaps in practice.[14] The external facilitator from the AuSCR supported local sites to access their own performance data via the AuSCR,, and understand practice gaps in evidence-based care. Qld State-wide Stroke Clinical Network leads provided education, and promoted linkage and shared learning with other stroke clinicians throughout the state, and encouraged use of data via health system reporting drivers. Change to stroke care was enacted through the development of an agreed action plan with hospital staff. An agreed action plan was consensus based and would only be counted if completed during the workshop. The external facilitators also provided ongoing peer support, via telephone, face-to-face or email, as required.

Data collection and analyses

A specifically designed data collection tool was developed to enter prospectively collect data from the external facilitators. Items recorded included the frequency, duration and mechanism of facilitation episodes (Table 1). The tool included pre-specified categories to ensure consistent data capture, and free text options for additional information as described below.

The primary outcome was the complexity of the action plan developed. Action plan was divided into: (i) a comprehensive action plan, defined as an action plan that aimed to address 4 or more clinical processes of care, and (ii) a simple plan, defined as an action plan that aimed to address 3 or fewer clinical processes. Dosage of external facilitation was determined

by frequency and duration professional behaviour change support provided to clinicians, mode of support delivery, and time spent delivering support. These parameters were used to understand the dose and types of external facilitation required to facilitate the development of different complexities of action plans.

Using the AuSCR data (from 2010 to 2015), a pre-post intervention design was used to compare change in adherence to the eight clinical processes of care indicators for acute stroke based on the complexity of action plans developed .See online-only data supplement for specific information on the AuSCR methodology.

Descriptive was analyses were undertaken. Normality tests were conducted to check the distribution of each continuous variable. The Wilcoxon Rank Sum Test was conducted to explore the association between dosage of external facilitation and the development of a simple or comprehensive action plan. Adherence to each of the 8 Queensland endorsed processes of care indicators were calculated as the proportion of patients with the documented measure divided by the number of patients eligible for the measure. Where applicable, eligibility criteria for an indicator is specified. For example, adherence to the use of aspirin within 48 hour is relevant only for patients presenting with ischemic stroke or transient ischemic attack. The percent adherence was calculated for each indicator overall for Queensland. Random-effect (multilevel) logistic regression, with level defined as patient and hospital, was used to compared adherence between pre- and post-intervention periods stratified by whether a complex or simple action plan was used. The dependent variable was the adherence to the indicator and the independent variable was the Stroke123 study period. Adjusted odds ratio and 95% confidence intervals were reported.

A p-value of < 0.05 was considered statistically significant. Data were analysed using Stata (Stata Statistical Software, Release 12.0; Stata Corporation, College Station, Texas, USA).

Results

Staff from 19 (out of 23 eligible) Queensland hospitals agreed to participate (urban hospitals: 55%; rural hospitals: 45%; 16% were teaching hospitals). During the course of the intervention (May 2013 to August 2015), nine external facilitators provided support to staff from the 19 hospitals. The most frequent activities provided by the facilitators were educational outreach (42%); followed by interprofessional collaboration (30%), review of audit data (11%) and reminders (6%) (Figure 1). Fourteen (74%) hospitals developed action plans. Five hospitals did not develop an action plan and reasons included: already developed QI plan, declined workshop and staff changes. Among the 14 hospitals that developed an action plan, 12 developed comprehensive action plans (i.e. plans involving four or more clinical processes of care). The number of times external facilitators provided professional behaviour change support and the mode of communication during the intervention period is shown in Table 2. The number of face-to-face contacts was greater in hospitals that developed a simple action plan. However, external facilitators provided more telephone and email contacts to sites that developed a comprehensive action plan compared toto those that developed a simple action plan (Table 2).Throughout the intervention 19 (95%) hospitals accessed their online AuSCR data for performance monitoring (overall number of times accessed AuSCR data: median [Q1,Q3]: 12 [7,18]. External facilitators had no more face-to-face contact time with staff from hospitals who developed a comprehensive action plan than those that developed a simple action plan (median: 18 hours vs 16 hours, p=0.61). Those who developed a comprehensive action plan had twice as much telephone contact time than those who developed a simple action plan (Figure 2; 6 hours vs 3 hours, p=0.08). However, this was not statistically significant.

The median total face-to-face and phone contact time was non-significantly lower (p=0.138) in those who reported significant improvement (22 hours: Q1:13, Q3:24) compared to those who reported modest improvement (27 hours: Q1:20, Q3:35). Overall the adherence improved more for the eight individual indicators in hospitals that developed a simple action action plan when compared to hospitals that developed a comprehensive action plan (Table 3 and 4). The individual processes of care indicators selected by hospitals as part of their action plan is shown in Figure 3. Most hospitals (8/12) selected all eight indicators for comprehensive action plan and observed an improvement in absolute change to four indicators. Those that developed a simple action plan (i.e. three indicators), observed greater improvement in absolute change to all three indicators when compared to hospitals with comprehensive action plan.

Discussion

This is one of the few studies in which the role of external facilitators has been assessed as part of a multicentre knowledge translation study. In this process evaluation study conducted alongside a controlled-before and after quality improvement project, we did not find a statistically significant association between either the mode, or dosage of external facilitation and complexity of action plans developed. However, a small but consistent trend across all forms of delivery of facilitation indicated that a larger dose of external facilitation was associated with more indicators being targeted in action plans. Sites with more directed action plans targeting fewer indicators, however, demonstrated greater improvement in indicators. Our study was underpowered to detect statistically significant differences, but this suggests that there may be a dose response, and that higher doses of facilitation may not be required or helpful. There is indication that the number and complexity of action plans is potentially a greater driver of improvement than the amount of facilitation.

To our knowledge, our study is the first to explore dosage of external facilitation in a complex multifaceted QI program in acute stroke care in Australia. It is important to evaluate the processes of a study so other researchers can reliably implement or build on the current intervention. According to the Template for Intervention Description and Replication (TIDieR) checklist, some of the key features of an evaluation study includes duration, dose or intensity, and mode of delivery of intervention, which can all influence efficacy and replicability of the program but are often poorly described [16]. In our study, external facilitators needed more contact time with staff from hospitals which chose a greater number of indicators. Several possible explanations for the correlations were observed: 1. Not targeting an achievable / manageable number of issues may have led to inefficient efforts with both extra time from facilitators and less improvement than sites that were targeted. 2. Sites with significant barriers to improvement, or less effective internal facilitation may have had greater need for external assistance but with lower ability to impact change. It is possible that higher doses of external facilitation are neither necessary, nor helpful for change, and that focussed efforts on a small number of issues is more efficient and effective.

In a recent study implementation of a care bundle comprising four indicators of acute care is associated with better patient outcomes (i.e mortality) [17]. In our study, greater absolute change was observed for a greater number of indicators in hospitals that developed a simple action plan when compared to hospitals that developed a comprehensive action plan (with 4 or more indicators). Staff at hospitals with simple plans only chose three indicators (i.e. swallow screen or assessment, prescribed antihypertensive agents at discharge, and discharged to the community with a care plan) for action planning. In addition, an improvement in absolute change for those three indicators were also observed in those hospitals with comprehensive action plans. Our results may indicate that simple action plans may be best. Focussing on more indicators as part of an action plan took more time and may

have resulted in poorer change. Therefore, focussing on targeting a few areas within a complex multifaceted intervention may be more efficient and effective.

The delivery of a complex multifaceted intervention to many sites required several different modes of contact. The presence of an external facilitator who provides support via face-to-face and telephone support, may ensure action plans are developed and implementation is followed through to support change in practice. Quality of care activities in the 'Get With The Guidelines Stroke' program evaluated the processes of workshops and impact of facilitation, which were shown to improve adherence to all primary performance measures, i.e. improve quality of care [18].

A lack of a definite dose-response is not evidence of an absence in effect of external facilitation, but may suggest that focus on the content of facilitation is more important than amount of time spent by facilitators. Limitation of total time will lead to more cost-effective and sustainable interventions. Anecdotal evidence from our facilitators suggests that future studies may also include a two-step process where the external facilitators first educate and identify the local barriers and enablers of the hospital, followed by a second meeting that is completely focussed on action planning.

The strengths of the study are the number and variety of hospitals that participated (e.g. teaching, urban and rural hospitals). Additionally, a standardised data collection tool was used to collect data from all external facilitators. The limitations of the study are that contact data were self-reported and only reflected the facilitators' perspectives, and not those from the hospital staff receiving the support. Also, no information on internal facilitation at a site level, if any, was available. Although most of the time the external facilitators provided data on a fortnightly basis, on some occasions there was a two month delay. Hence there may be a potential for recall bias. Nevertheless, the external facilitators kept personal diaries and email

records, and so had some objective data to ensure any recall bias was minimised. Also, the study was underpowered to find statistical difference. In-depth data on the content of the professional behaviour change support provided were not available. The number of staff and their relevant roles were also not provided by the external facilitators. In addition, future studies need to evaluate the effectiveness of external facilitation from those receiving support in-depth (i.e. clinicians and hospital staff), and directly assess the impact on adherence to care processes and patient outcomes.

Conclusion

To our knowledge, this is the first study to explore the process of external facilitation in a complex multifaceted QI program in acute stroke care. Action plans are important in complex multifaceted QI programs. It is also necessary to understand the optimal dosage of external facilitation required for successful development of action plans. The dosage of external facilitation was similar and it is unclear whether hospitals with more comprehensive plans were more motivated to change practice. Further research is needed to understand the dosage and benefits of external facilitation in developing the different types of action plans for multifaceted QI programs in acute stroke care.

List of abbreviations

Quality Improvement (QI)

Australian Stroke Clinical Registry (AuSCR)

Plan-Do-Study-Act (PDSA) model

Institute of Health care Improvement (IHI) score

Template for Intervention Description and Replication (TIDieR) checklist

Declarations

Ethics approval and consent to participate

Ethics approval was obtained from all participating hospitals, with the lead ethics committee in Queensland being the Metro South Human Research Ethics Committee (HREC/13/QPAH/31).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

DAC conceived the study design and developed the study protocol. TT collected data. TT and NA were involved with manuscript development and data analysis. All authors read and approved the final manuscript.

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References

1. Vestergaard AS, Ehlers LH: **A Health Economic Evaluation of Stroke Prevention in Atrial Fibrillation: Guideline Adherence Versus the Observed Treatment Strategy Prior to 2012 in Denmark.** *PharmacoEconomics* 2015, **33:**967-979.
2. Brien EC, Wu J, Zhao X, Schulte PJ, Fonarow GC, Hernandez AF, Schwamm LH, Peterson ED, Bhatt DL, Smith EE: **Healthcare Resource Availability, Quality of Care, and Acute Ischemic Stroke Outcomes.** *Journal of the American Heart Association* 2017, **6**.
3. Cadilhac DA, Lannin NA, Anderson CS, Kim J, Andrew N, Kilkenny M, Shehata S, Grabsch B, Levi C, Faux S, et al; The Australian Stroke Clinical Registry Annual Report 2015. The Florey Institute of Neuroscience and Mental Health; December 2016, Report No 7 , pages 42.

4. Grimshaw JM, Eccles MP, Walker AE, Thomas RE: **Changing physicians' behavior: What works and thoughts on getting more things to work.** *Journal of Continuing Education in the Health Professions* 2002, **22:**237-243.

5. Forsner T, Hansson J, Brommels M, Wistedt AÅ, Forsell Y: **Implementing clinical guidelines in psychiatry: a qualitative study of perceived facilitators and barriers.** *BMC Psychiatry* 2010, **10:**1-10.

6. Cadilhac DA, Carter RC, Thrift AG, Dewey HM: **Why invest in a national public health program for stroke?: An example using Australian data to estimate the potential benefits and cost implications.** *Health Policy* 2007, **83:**287-294.

7. Grimshaw JM, Eccles MP, Lavis JN, Hill SJ, Squires JE: **Knowledge translation of research findings.** *Implementation Science* 2012, **7:**1-17.

8. **Cochrane Effective Practice and Organisation of Care Group. Data collection checklist**

9. Grimshaw J, Eccles M, Tetroe J: **Implementing clinical guidelines: Current evidence and future implications.** *Journal of Continuing Education in the Health Professions* 2004, **24:**S31-S37.

10. Squires JE, Sullivan K, Eccles MP, Worswick J, Grimshaw JM: **Are multifaceted interventions more effective than single-component interventions in changing health-care professionals' behaviours? An overview of systematic reviews.** *Implementation Science : IS* 2014, **9:**152.

11. Gozdzik A: **Applying the PARiHS framework in a knowledge dissemination initiative.** *CANNT journal = Journal ACITN* 2013, **23:**48-50.

12. Stetler CB, Legro MW, Rycroft-Malone J, Bowman C, Curran G, Guihan M, Hagedorn H, Pineros S, Wallace CM: **Role of "external facilitation" in implementation of research findings: a qualitative evaluation of facilitation**

experiences in the Veterans Health Administration. *Implementation Science* 2006, **1:**23-23.

13. Bornbaum CC, Kornas K, Peirson L, Rosella LC: **Exploring the function and effectiveness of knowledge brokers as facilitators of knowledge translation in health-related settings: a systematic review and thematic analysis.** *Implement Sci* 2015, **10:**162.

14. Cadilhac DA, Andrew NE, Kilkenny MF, Hill K, Grabsch B, Lannin NA, Thrift AG, Anderson CS, Donnan GA, Middleton S, Grimley R: **Improving quality and outcomes of stroke care in hospitals: Protocol and statistical analysis plan for the Stroke123 implementation study.** *International Journal of Stroke* 2018, **13:**96-106.

15. Speroff T, O'Connor GT: **Study Designs for PDSA Quality Improvement Research.** *Quality Management in Healthcare* 2004, **13:**17-32.

16. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M, et al: **Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide.** *BMJ : British Medical Journal* 2014, **348**.

17. Turner M, Barber M, Dodds H, Murphy D, Dennis M, Langhorne P, Macleod M-J: **Implementing a Simple Care Bundle Is Associated With Improved Outcomes in a National Cohort of Patients With Ischemic Stroke.** *Stroke* 2015, **46:**1065-1070.

18. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, Ellrodt G, Cannon CP, Liang L, Peterson E, LaBresh KA: **Get With the Guidelines–Stroke Is Associated With Sustained Improvement in Care for Patients Hospitalized With Acute Stroke or Transient Ischemic Attack.** *Circulation* 2009, **119:**107-115.

Table 1. Information collected from external facilitators using the specifically designed data collection tool

Type of information
Number of contacts the external facilitators had with the relevant clinicians and hospital staff
Mode of contact (e.g. telephone, face-to-face, email)
Contact time in minutes for telephone and face-to-face contacts
Professional behaviour change support type provided (e.g. reminders, educational outreach)*
Action plan initiated by staff at participating hospitals (Yes/No)
Frequency of access by hospitals to their AuSCR data (by downloading online live reports)

* defined by the classifications by the Cochrane Effective Practice and Organisation of Care Group

Table 2. Frequency of contact for all modes of communication between external facilitators and hospital staff from participating hospitals

Mode of contact	Number of contacts Median (Q1, Q3)		
	All hospitals	**Hospitals that developed comprehensive action plan**	**Hospitals that developed simple action plan**
Face-to-face	5 (4.5, 11)	5 (3.5, 6)	8 (5, 11)
Telephone	8 (5, 12)	9 (6, 13.5)	6 (4.5, 10)
Email	22 (17, 36)	26 (17, 36)	20 (17, 36)

Table 3: Effect of intervention on adherence to individual indicators using the Australian Stroke Clinical Registry (AuSCR)

Intervention phase	***Pre-intervention (T1)***	***Stroke123 intervention (T2)***	***Post-intervention (T3)***	***Absolute change (%)***
Total Queensland (N=11,906)	***N=4,443***	***N=2,682***	***N=4,781***	
Hospitals that developed a comprehensive action plan (12 hospitals, N=8,525)	***N=3,265***	***N=1,850***	***N=3,410***	
Treated in a stroke unit (%)	2,394(73)	1,389 (75)	2,519 (74)	↑1
Swallow screen or assessment (%)	2,671 (82)	1,500 (81)	2,689 (79)	↓3
Prescribed antihypertensive agents at discharge (%)	1,965 (65)	1,224 (72)	2,224 (74)	↑9
Discharged to the community with a care plan (%)	682 (38)	448 (45)	1,060(57)	↑19
Mobilised during admission (%)	2,836 (87)	1,569 (85)	2,746 (81)	↓6
Ischaemic stroke only				
Received thrombolysis, if an ischemic stroke (%)	180 (10)	90 (8)	166 (9)	↓1
Aspirin within 48 hours (%)	2,142 (73)	1,225 (73)	2,226 (73)	-
Prescribed on antithrombotics at discharge (%)	2,266 (87)	1,369 (93)	2,409 (93)	↑6
Hospitals that developed a simple or no action plan (7 hospitals, N=3,381)	***N=1,178***	***N=832***	***N=1,371***	***Absolute change (%)***
Treated in a stroke unit (%)	852 (72)	625 (75)	1,179 (86)	↑14
Swallow screen or assessment (%)	931 (79)	693 (83)	1,236 (90)	↑11
Prescribed antihypertensive agents at discharge (%)	632 (59)	547 (73)	875 (69)	↑10
Discharged to the community with a care plan (%)	180 (28)	208 (49)	380 (51)	↑23
Mobilised during admission (%)	991 (84)	724 (87)	1,257 (92)	↑8
Ischaemic stroke only				
Received thrombolysis, if an ischemic stroke (%)	37 (5)	43 (9)	71 (8)	↑3
Aspirin within 48 hours (%)	719 (68)	530 (74)	916 (76)	↑8
Prescribed on antithrombotics at discharge (%)	697 (75)	595 (96)	1,006 (95)	↑20

T1 or Time period 1 is the pre-intervention/financial incentives period. Adherence to processes of care obtained from 2010-2013 AuSCR data.
T2 or Time period 2 is the enhanced StrokeLink period. Adherence to processes of care obtained from 2014 AuSCR data.
T3 or Time period 3 is the post-intervention period. Adherence to processes of care obtained from 2015 AuSCR data

Table 4: Effect of enhanced StrokeLink intervention on the change in adherence to indicators between post-intervention and baseline (multivariable analyses)*

Individual process indicators	*Odds ratio*	*95% CI*	*p-value*
Comprehensive action plan (12 hospitals, N=8,525)			
Treated in a stroke unit	0.86	0.76, 0.96	0.010
Swallow screen or assessment	0.70	0.62, 0.80	<0.001
Prescribed antihypertensive agents at discharge	1.40	1.25, 1.56	<0.001
Discharged to the community with a care plan	2.54	2.21, 2.93	<0.001
Mobilised during admission	0.56	0.49, 0.64	0.001
Ischaemic stroke only			
Received thrombolysis, if an ischemic stroke	1.04	0.83, 1.30	0.761
Aspirin within 48 hours	0.88	0.78, 0.99	0.028
Prescribed on antithrombotics at discharge	1.86	1.53, 2.28	<0.001
Simple or no action plan (7 hospitals, N=3,381)			
Treated in a stroke unit	2.32	1.89, 2.89	<0.001
Swallow screen or assessment	2.23	1.77, 2.81	<0.001
Prescribed antihypertensive agents at discharge	1.61	1.35, 1.93	<0.001
Discharged to the community with a care plan	2.78	2.20, 3.52	<0.001
Mobilised during admission	2.15	1.66, 2.77	<0.001
Ischaemic stroke only			
Received thrombolysis, if an ischemic stroke	1.12	0.73, 1.74	0.595
Aspirin within 48 hours	1.50	1.24, 1.82	<0.001
Prescribed on antithrombotics at discharge	7.59	5.42, 10.62	<0.001

*Dependent variable adherence to indicator, independent variable intervention phase, adjusted for clustering by hospital

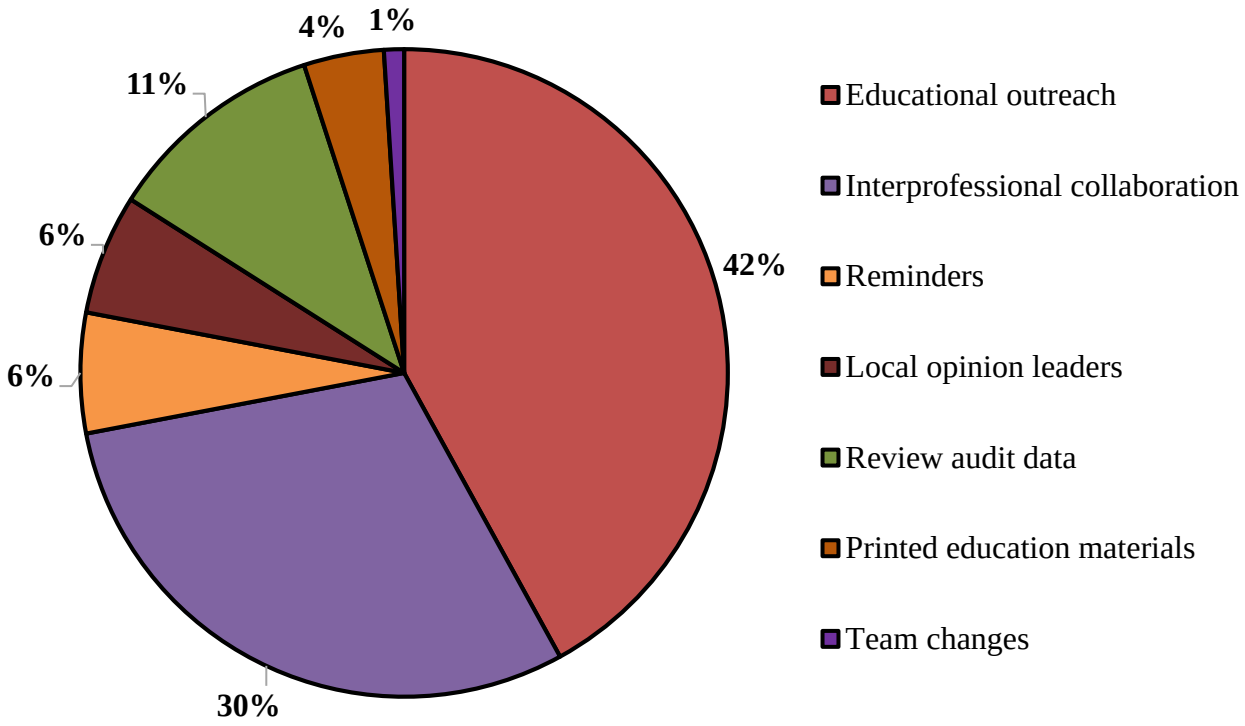

Figure 1. This pie chart shows the proportion of professional behaviour change interventions that were provided by the external facilitators for 20 hospitals in the study. These strategies have been categorised by the Cochrane Effective Practice and Organisation of care group [8].

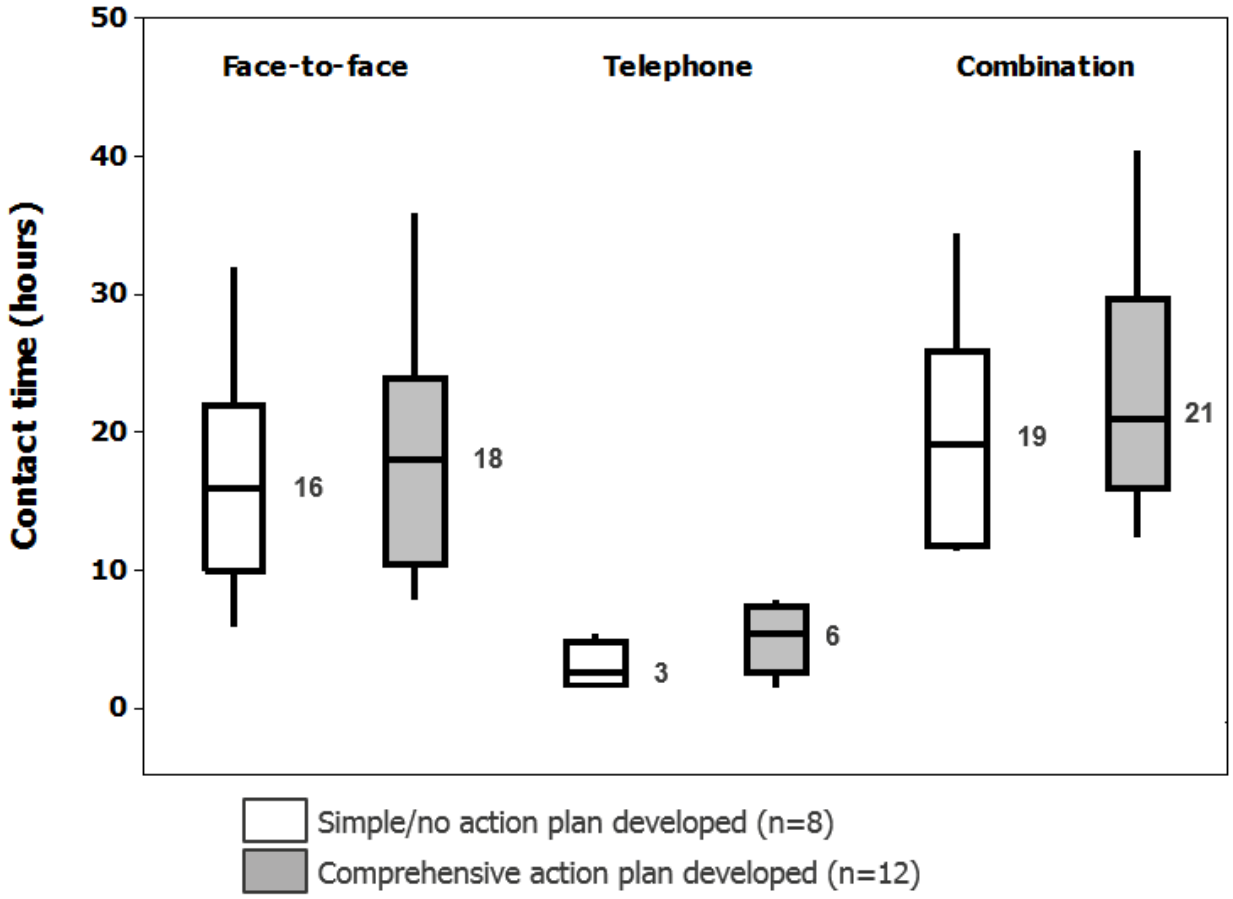

Figure 2. Association between median hours of external support and development of comprehensive action plan vs simple action plan

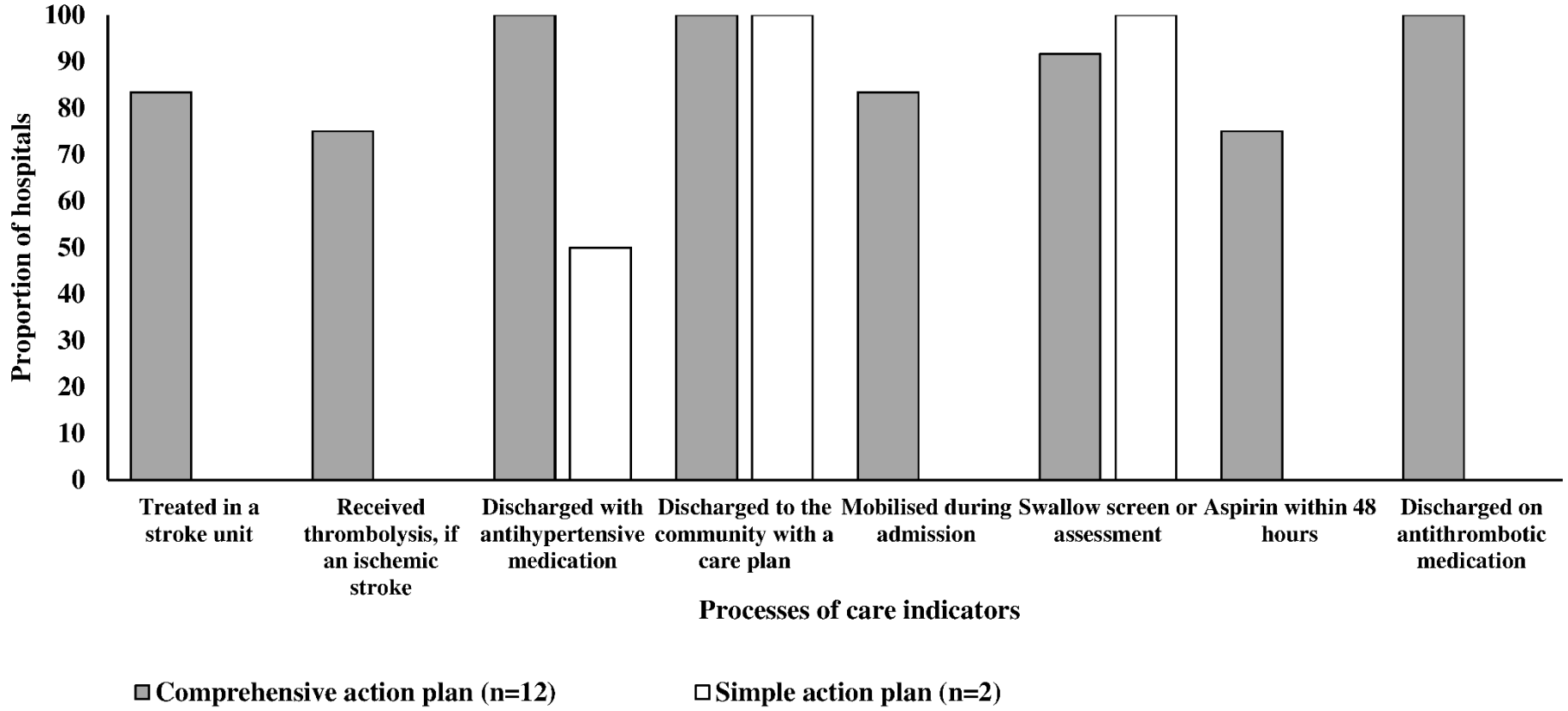

Figure 3. Proportion of hospitals that selected the individual indicators by complexity of action plan

5.3 Summary

Complex QI programs help support clinicians working in hospitals to reduce gaps in evidence and clinical practice. External facilitators may have a key role in helping clinicians understand and address gaps in the delivery of care. However, little is known about the dosage of external facilitation required for improving practice within the context of complex multifaceted QI programs. In the paper presented in Chapter 5, the influence of external facilitation on the development and implementation of consensus-based action plans for improving acute stroke care was evaluated. The influence of 'facilitator dose' with reference to the complexity of the actions plans, (i.e. number of actions to be addressed) on changes in adherence to eight clinical processes of care (PoC) measured before and after the intervention period was also evaluated.

This is one of the few studies in which the role of external facilitators has been assessed as part of a multicentre knowledge translation study. In this process evaluation study conducted alongside a controlled-before and after quality improvement project, we did not find a statistically significant association between either the mode, or dosage of external facilitation and the complexity of action plans developed. However, a small but consistent trend across all forms of delivery of facilitation indicated that a larger dose of external facilitation was associated with more indicators being targeted in action plans. Sites with more directed action plans targeting fewer indicators, however, demonstrated greater improvement in indicators. Our study was underpowered to detect statistically significant differences, but the work suggests that larger doses of facilitation may not be required or helpful. There is indication that the number and complexity of action plans is potentially a greater driver of improvement than the amount of facilitation.

Summary of Part B

In Part B, I described data sources available for monitoring the quality of acute stroke care (i.e. clinical registries and audit) and the objectives and methods for a QI program in which these data, along with behaviour change strategies, were used to improve adherence to evidence-based guideline. A way to reduce the burden of stroke is to ensure that when patients are in hospitals they receive the care they are eligible for as recommended in clinical guidelines. However, there is evidence that there is variability in the delivery of acute stroke care. I then further described external facilitation as a component of QI programs and how it may influence closing the evidence to practice gap, i.e. change clinician behaviour, between recommended care and current clinical practice.

In the next section (Part C), I focus on how data primarily from the clinical registry can be used to inform strategies to improve the development of hospital-based strategies in anxiety and depression, an area with a long-standing evidence to practice gap. I then also describe how a tailored MBI is beneficial in reducing the impact of anxiety or depression, and other comorbidities in survivors of stroke (Chapters 9, 10 and 11).

PART C:

Addressing the burden of anxiety or depression following stroke

Chapter 6: Detailed methods for the paper presented in chapter 7

6.1 Overview

In Chapters 4 and 5, I provided details of how audit, clinical registry, and hospital administrative data may be used to monitor the quality of stroke care provided in Australian hospitals and identify and help reduce disparities in stroke care, mortality and stroke reoccurrence in the community.

In this chapter and the next (Chapter 7), I will discuss how we can use clinical registry data linked with hospital administrative data to investigate potential areas for news interventions to reduce practice gaps related to anxiety and depression. By combining these routinely collected datasets it is possible to assess a wider range of factors specific to reducing the burden of anxiety or depression following stroke.

In this chapter I will provide extra detail on some of the complexities of using linked data. This will include a brief description of the data linkage component of the Stroke123 project and a detailed description of the processes involved to set up the final linked data set used for the analyses presented in Chapter 6.

6.2 Developing an analytic dataset using linked data

6.2.1 Data linkage conducted as part of the Stroke123 project

As described in Chapter 4, the AuSCR contains a minimum dataset of core demographic, clinical and quality indicator data items, but does not contain information on pre-existing comorbidities. In contrast, hospital administrative datasets do not contain clinical indicator or patient reported outcome data, but do contain coded information on primary and secondary (up to 40) diagnoses using ICD-10-AM codes. When appropriate 'look back' periods from hospital administrative datasets are included. These codes can be used to reliably identify common comorbidities to supplement the data in AuSCR. In this way we can obtain a more comprehensive dataset to enable us to answer questions about the quality of care received by patients in hospitals and outcomes, such as hospital readmissions and survival, following stroke (Figure 6.1). For this thesis I was able take advantage of this data linkage work to specifically answer questions relating to anxiety and depression.

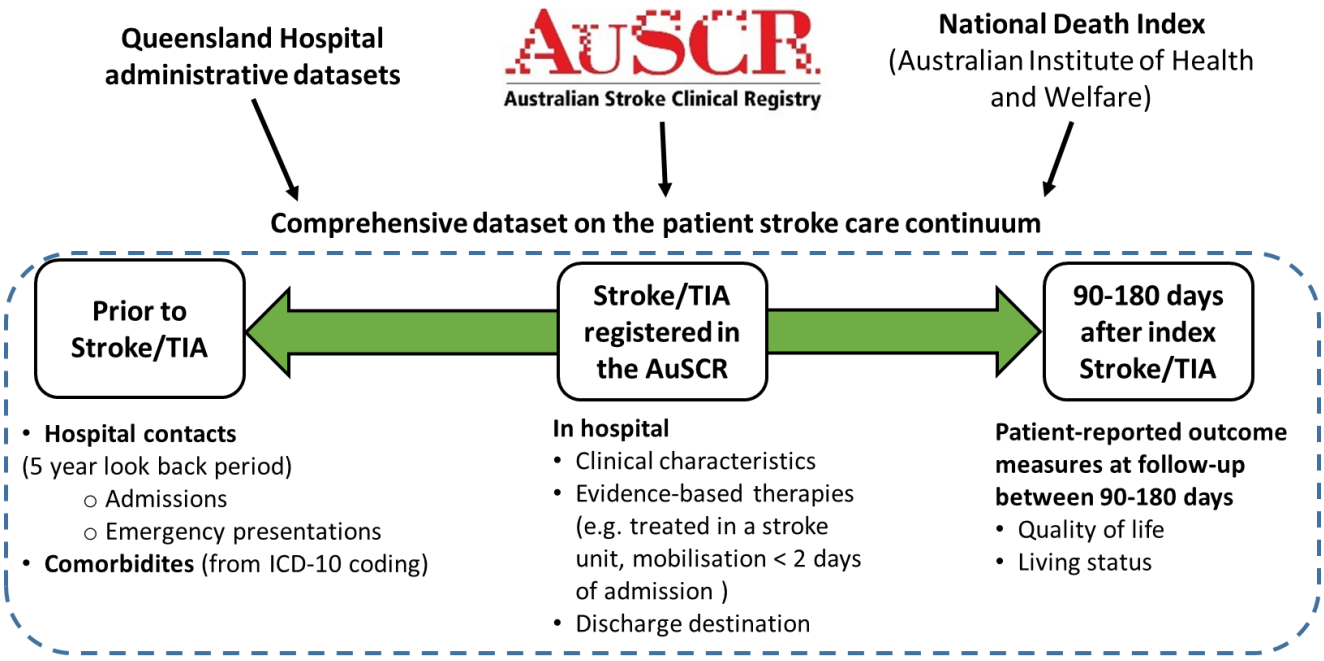

Figure 6.1. *Linking datasets for a complete patient stroke care journey: An overview*

One of the major components of the Stroke123 project (described in Chapters 3 and 4) was to establish high-quality, linked data for stroke using data from AuSCR, and routinely collected hospital and death data. The processes involved in the data linkage component of Stroke123 are further described in another paper involving supervisors Dr. Nadine Andrew, Prof. Amanda Thrift and Prof. Dominique Cadilhac.[114] The data used in this section of my thesis were obtained as part of Stroke123 and the datasets were merged and cleaned by Drs Nadine Andrew and Monique Kilkenny, prior to my use for the analysis.

A detailed description of the individual datasets are provided in the published manuscript (Chapter 7).

6.2.2 Selection of variables and merging process for my dataset

The primary purpose of using these combined datasets was to assess patient and hospital factors that may be associated with the development of anxiety or depression following stroke.

Approval to access the data for Queensland was obtained through the Queensland Public Health Act. Once this was completed, several steps were involved in obtaining the final dataset for the analyses of Aim 3 of this thesis. Following a review of all of the available data items in the merged datasets, I identified the required variables from each dataset (Figure 6.2) for my study. Pre-existing mental health problems were selected from the list of ICD-10-AM codes and verified with a Clinical Psychologist (i.e. my co-supervisor Dr. Rene Stolwyk). Mental health problems included dementia (F00, F01, F02, F03, F051), psychosis (F20, F22, F23, F24, F25, F28, F29, F302), bipolar disorder (F31), and anxiety and depression (F063, F064, F065, F066, F067, F068, F069, F051, F32, F33, F34, F38, F39, F41, F42, F43, F99). Other comorbidities had already been coded as part of the original Stroke123 data cleaning processes. The codes used for each illness are listed in the manuscript presented in the next chapter (online supplement, Table 1).

A list of the required variables were then provided to the data coordinators, Drs Nadine Andrew and Monique Kilkenny. These variables were identified from the appropriate dataset, selected from the secure file and merged into a final analytic dataset (Figure 6.2). The detailed statistical methods, results and discussion are presented as a published paper in the next chapter.

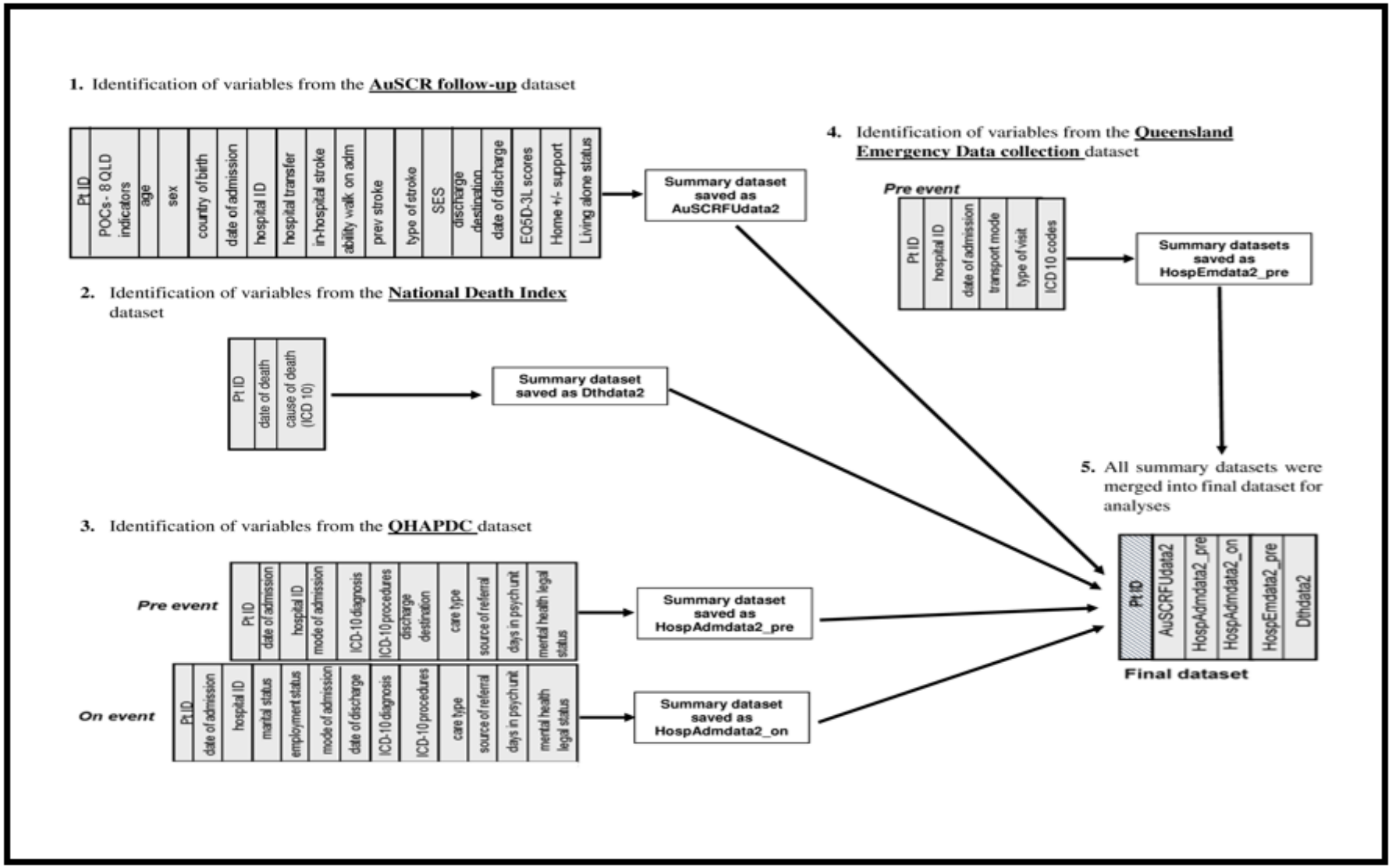

Figure 6.2. *Flow diagram showing the process used to merge datasets in the current study*

Pt ID: Project specific patient identification; PoC: Clinical processes of care; hospital ID: Project specific hospital identification; SES: Socioeconomic status; ICD-10: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (Australian Modification); QHAPDC: Queensland Hospital Admitted Patient Data Collection.

6.3 Summary

This chapter provided methodological details not contained in the main published paper with a focus on the data linkage aspects applied in order to derive the final dataset I used as part of this thesis. The complex processes involved to set up the final linked dataset used for the analyses presented in Chapter 6 were highlighted. In the next chapter (Chapter 7), I used these comprehensive linked data to answer aim 3 of my research program, i.e. to investigate the association between the quality of acute stroke care, patient factors and clinical factors with self-reported anxiety or depression at 90-180 days following admission for stroke or TIA.

Chapter 7: Anxiety and depression between 90 to 180 days following stroke: Demographic, clinical, and patient predictors using linked registry data

7.1 Overview

In Chapter 6, I provided a detailed description of the methods used to obtain the final dataset for a focussed analysis on mood outcomes after stroke. This research was undertaken using merged data from a range of sources that had been linked for the Stroke123 project (see section 5.2.1).

In this chapter the published paper that was the outcome of my research questions related to the third aim of this thesis is presented. The specific aims of the following paper were to use linked patient-level data to (i) identify patient and clinical factors associated with self-reported anxiety or depression at 90–180 days following stroke or TIA; (ii) explore the association between the quality of acute stroke care received in hospital and self-reported anxiety or depression at 90–180 days following a stroke or TIA admission; and (iii) assess whether there were any relationships between self-reported anxiety or depression, socioeconomic status and age.

To our knowledge, this is the first Australian study where data from a clinical registry, linked to hospital administrative datasets and the national death index, was used to conduct a comprehensive assessment of a broad range of factors that may be associated with the self-reported anxiety or depression in survivors between 90 to 180 days following their stroke. The study is presented as a paper that was published in Quality of Life Research (August 2018; doi: 10.1007/s11136-018-1960-y). This study addresses the third aim of my thesis: to investigate the association between the quality of acute stroke care, patient factors and clinical factors with self-reported anxiety or depression at 90-180 days following admission for stroke or TIA. My contribution is at 80%, and the nature of my contribution was concept, data management, analysis, interpretation and writing of first draft of the manuscript.

The following paper was published in Quality of Life Research (2018; Vol 27(12): 3145-3155).

7.2 Published paper

Factors influencing self-reported anxiety or depression following stroke or TIA using linked registry and hospital data

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Factors influencing self-reported anxiety or depression following stroke or TIA using linked registry and hospital data

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Abstract

Purpose Approximately 30–50% of survivors experience problems with anxiety or depression post-stroke. It is important to understand the factors associated with post-stroke anxiety or depression to identify effective interventions.

Methods Patient-level data from the Australian Stroke Clinical Registry (years 2009–2013), from participating hospitals in Queensland ($n=23$), were linked with Queensland Hospital Emergency and Admission datasets. Self-reported anxiety or depression was assessed using the EQ-5D-3L, obtained at 90–180 days post-stroke. Multivariable multilevel logistic regression, with manual stepwise elimination of variables, was used to investigate the association between self-reported anxiety or depression, patient factors and acute stroke processes of care. Comorbidities, including prior mental health problems (e.g. anxiety, depression and dementia) coded in previous hospital admissions or emergency presentations using ICD-10 diagnosis codes, were identified from 5 years prior to stroke event.

Results 2853 patients were included (median age 74; 45% female; 72% stroke; 24% transient ischaemic attack). Nearly half (47%) reported some level of anxiety or depression post-stroke. The factors most strongly associated with anxiety or depression were a prior diagnosis of anxiety or depression [Adjusted Odds Ratio (aOR) 2.37, 95% confidence interval (95% CI) 1.66–3.39; $p<0.001$], dementia (aOR 1.91, 95% CI 1.24–2.93; $p=0.003$), being at home with support (aOR 1.41, 95% CI 1.12–1.69; $p=<0.001$), and low socioeconomic advantage compared to high (aOR 1.59, 95% CI 1.21–2.10; $p=0.001$). Acute stroke processes of care were not independently associated with anxiety or depression.

Conclusions Identification of those with prior mental health problems for early intervention and support may help reduce the prevalence of post-stroke anxiety or depression.

Keywords Anxiety · Depression · Stroke · Registries · Data linkage · Quality of life · Comorbidity

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11136-018-1960-y) contains supplementary material, which is available to authorized users.

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Introduction

Many survivors of stroke have long-term psychological consequences that impact their quality of life [1, 2]. In 2012, the Stroke Foundation commissioned a national survey of the needs of survivors of stroke at least 12 months after their stroke [1]. Many participants reported ongoing unmet needs, 84% of which were associated with psychological issues. Among these, 73% of survivors had problems with emotions. Anxiety or depression after stroke have been associated with greater dependence in activities of daily living, institutionalisation and mortality, and poorer overall quality of life [3, 4].

There is a growing body of evidence about factors that may be associated with anxiety or depression in survivors of stroke. In a recent meta-analysis, history of mental illness was the highest ranking modifiable risk factor. Other risk factors that may impact on depression following stroke were sex, age (< 70 years), family history,and stroke severity [5]. There is a lack of understanding on whether the type of stroke or any other premorbid conditions may impact on anxiety or depression following stroke.

Furthermore, there is growing evidence that the quality of care received by patients in the hospital setting can directly influence long-term outcomes such as 90-day health status and survival [6]. In particular, acute care in a stroke unit, in which there is coordinated multidisciplinary care and better adherence to recommended clinical processes [7], has been shown to be associated with a reduction in death and disability, and improvement in quality of life [8]. However, it is unclear whether the quality of acute stroke care received in hospital may influence chronic self-perceived anxiety or depression in survivors of stroke.

Our aim was to use linked patient-level data to (i) identify patient and clinical factors associated with self-reported anxiety or depression at 90–180 days following stroke or TIA; (ii) explore the association between the quality of acute stroke care received in hospital and self-reported anxiety or depression at 90–180 days following a stroke or TIA admission; and (iii) assess whether there were any relationships between self-reported anxiety or depression, socioeconomic status and age.

Methods

Study design and datasets

This was a multicentre, prospective observational cohort study. Patient-level data from Queensland hospitals that had registered patients in the Australian Stroke Clinical Registry (AuSCR) between June 2009 and December 2013 were linked, using probabilistic methods, to the Queensland Emergency Data Collection and the Queensland Hospital Admitted Patient Data Collection (QHAPDC) from June 2004 to December 2015 as part of the Stroke123 project [9, 10].

The AuSCR includes information on all admitted patients with stroke or TIA at participating hospitals, based on a minimum dataset (demographic and clinical variables such as age, sex, stroke type, stroke severity, discharge destination) and acute stroke processes of care. The four acute stroke processes of care collected nationally are use of intravenous thrombolysis (tPA) for ischaemic strokes, access to a stroke unit, discharged on an antihypertensive agent and care plan provided at discharge. Four additional processes, recommended in the national clinical guidelines [7], were collected in Queensland: mobilisation < 2 days of admission, screen or swallow assessment < 24 h, aspirin administration < 48 h if an ischaemic stroke and discharged on antiplatelets or antithrombotics. These acute stroke processes of care are not routinely extractable in the administrative hospital datasets. This is because the Australian health system reimburses hospitals for all care elements bundled within a single payment for an episode of care using the Australian Refined Diagnosis Related Group. Collection of clinical indicator data is reliant on separate systems, such as the AuSCR. Patients were followed up by mail (or telephone if they did not respond) to determine their health outcomes (e.g. EQ-5D-3L, readmission status) between 90 and 180 days after the first stroke episode [11]. Follow-up was conducted centrally and independently of the participating hospitals.

In Australia, stroke care is provided mainly by public hospitals. In Queensland, there are 118 public acute health care facilities, many of which are very small and remote. The linked data include information on people who were treated at one of 58 reporting public hospitals with emergency departments in Queensland. Our patient cohort for this study, comes from the 23 hospitals (with stroke units). The ambulance service only directs patients with stroke to two private hospitals with emergency departments in Queensland. The Queensland Emergency dataset has a limited number of variables, and includes triage category, type and reason for emergency visit, discharge destination and primary diagnosis code [based on a subset of the International Classification of Diseases 10th Revision Australian Modification (ICD-10-AM) codes]. The QHAPDC contains details of demographic, administrative and clinical variables from all hospital inpatient separations from acute, public, private, repatriation and psychiatric hospitals in Queensland. The ICD-10-AM diagnosis codes (primary, secondary and other diagnoses) were used to identify comorbidities associated with hospital presentations within the 5 years prior to a stroke (see Table 1) [12]. Previous mental health problems

Table 1 Comparison of patient and clinical characteristics of AuSCR respondents between those who did and did not report anxiety or depression at 90–180 days after stroke

Anxiety/depression reported at 90–180 days following stroke/TIA	Yes ($n=1339$) n (%)	No ($n=1514$) n (%)	p value
Patient characteristics			
Age (years), median (Q1, Q3)	74 (62.6, 83.1)	74 (64.3, 81.7)	0.866
< 65	397 (29.7)	400 (26.6)	**0.001**
65–74	305 (22.9)	408 (27.2)	
75–84	371 (27.8)	463 (30.8)	
85+	262 (19.6)	232 (15.4)	
Female	630 (47.2)	639 (42.5)	**0.012**
Born in Australia	983 (73.4)	1,127 (74.4)	0.533
Interpreter required	20 (1.5)	13 (0.9)	0.113
Transferred from another hospital	227 (17.2)	259 (17.2)	0.979
In-hospital stroke	90 (6.8)	52 (3.8)	< **0.001**
Stroke type			
Ischaemic	829 (62.4)	877 (58.1)	< **0.001**
Haemorrhage	166 (12.4)	114 (7.6)	
TIA	285 (21.4)	463 (30.7)	
Unknown	54 (4.1)	56 (3.7)	
Stroke severity			
Unable to walk on admission	657 (54.5)	547 (41.0)	< **0.001**
Socioeconomic status			
Most advantaged	249 (18.6)	347 (22.9)	**0.001**
Second most advantaged	282 (21.1)	345 (22.8)	
Third most advantaged	248 (18.5)	241 (15.9)	
Fourth most advantaged	232 (17.3)	286 (18.9)	
Most disadvantaged	328 (24.5)	295 (19.5)	
History of comorbidities			
Cancer	111 (8.3)	131 (8.7)	0.729
Congestive Heart Failure	147 (11.0)	118 (7.8)	**0.003**
Diabetes with complications	126 (9.4)	130 (8.6)	0.442
Diabetes without complications	207 (15.5)	193 (12.8)	0.037
HIV	1 (0.1)	0 (0)	0.288
Liver disease	8 (0.6)	5 (0.3)	0.290
Myocardial infarction	157 (11.7)	170 (11.2)	0.678
Hemiplegia	750 (56.0)	640 (42.3)	< **0.001**
Ulcer	30 (2.2)	26 (1.7)	0.315
Peripheral vascular disease	67 (5.0)	51 (3.4)	0.029
Chronic renal disease	148 (11.1)	127 (8.4)	0.016
Dementia	91 (6.8)	49 (3.2)	< **0.001**
Angina	257 (19.2)	270 (17.8)	0.350
Hypertension	932 (69.6)	985 (65.1)	**0.010**
Smoking	309 (23.1)	274 (18.1)	**0.001**
Cholesterol	207 (15.5)	218 (14.4)	0.427
Obesity	85 (6.4)	58 (3.8)	**0.002**
Atrial fibrillation	392 (29.3)	397 (26.2)	0.069
Carotid stenosis	106 (7.9)	98 (6.5)	0.135
Psychoses/bipolar	11 (0.8)	17 (1.1)	0.415
Previous anxiety or depression	131 (9.8)	62 (4.1)	< **0.001**
CCI score, median (Q1, Q3)	3 (1, 3)	2 (1, 3)	< **0.001**
Number of comorbidities, median (Q1, Q3)	4 (3, 5)	3 (2, 5)	< **0.001**
Length of stay (days) if discharge, median (Q1, Q3)	6 (3, 12)	4 (2, 8)	< **0.001**

Table 1 (continued)

Anxiety/depression reported at 90–180 days following stroke/TIA	Yes ($n=1339$) n (%)	No ($n=1514$) n (%)	p value
Discharge destination			
Hospital	77 (5.9)	49 (3.3)	**< 0.001**
Rehabilitation (inpatient)	341 (26.1)	252 (16.9)	
Low-level residential care	17 (1.3)	12 (0.8)	
High-level residential care	67 (5.1)	24 (1.6)	
Home with supports	330 (25.3)	548 (36.8)	
Home without supports	286 (21.9)	440 (29.6)	
Transitional care service	10 (0.8)	11 (0.7)	
Other	10 (0.8)	11 (0.7)	

Bold: significant variables

Socioeconomic status is measured using the Index of Relative Socioeconomic Advantage/Disadvantage [28]

Low-level residential care includes residents of residential aged care services (i.e. nursing homes with low-level care, special accommodation and aged care hostels) who are able to function independently within a supportive environment with only occasional nursing care. High-level residential care includes residents of residential aged care services, who require frequent nursing care or a lot of assistance with activities of daily living

CCI Charlson Comorbidity Index [26, 27], *Q1* 1st quartile, *Q3* 3rd quartile, *HIV* human immunodeficiency virus

were identified using the ICD-10-AM codes 'F00'–'F99' [13].

Opt-out method of consent is used in the AuSCR. The processes involved in the AuSCR are described elsewhere [14]. Patient identifying information was used only for data linkage and was not accessed by the members of the research team who were conducting the analyses. Ethics approval for this project was obtained from the Monash University and Metro South Health (HREC/13/QPAH/31) Human Research Ethics Committees. Additional approvals were obtained from the AuSCR Research Task Group and the Queensland Department of Health.

Patient sample

The patient sample comprised AuSCR registrants who were aged at least 18 years, with a diagnosis of ischaemic stroke, intracerebral hemorrhage, TIA or stroke of unknown cause, who were followed up between 90 and 180 days following their stroke admission and provided responses to the EQ-5D-3L quality of life questionnaire. Approximately 71% of eligible AuSCR registrants provided outcome data. Patients with unknown or missing information were excluded (0.7%).

Outcomes

The EQ-5D-3L questionnaire is the health-related quality of life tool used within the AuSCR and was designed to measure overall quality of life and health status [15]. The quality of life component of the EQ-5D-3L has been shown to have good reliability and validity within the stroke population [16, 17]. The EQ-5D-3L is increasingly being used in large population-based studies [18, 19] and clinical registries [1, 20–22] to assess health-related quality of life as a measure of population health status to inform public health and health care policy. Using the EQ-5D-3L in the AuSCR also provides us with an opportunity for future comparisons with registries from other countries [21, 22]. Health status was measured over five domains: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Respondents self-rated their level of severity for each domain using a three-level scale: 1 = no problems, 2 = moderate problems, 3 = extreme or severe problems. They are also asked to rank their health status from 0 to 100 using the Visual Analogue Scale (VAS) where 100 is the best possible state and 0 the worst possible state [23]. Anxiety or depression was defined when patients reported yes to either being moderately anxious or depressed, or severely anxious or depressed on the anxiety/depression domain of the EQ-5D-3L questionnaire. Clinical relevance is based on an 8% or more difference on the EQ-utility score [24] which has been shown to correlate

well with a similar proportional difference on the EQ-VAS is ($r = 0.52$, $p < 0.001$) [25].

Variables

The EQ-5D-3L dimensions were dichotomised into "I am not anxious or depressed" (i.e. no; level 1) and "moderately or severely anxious or depressed" (i.e. yes; level 2 or 3). Comorbidities were classified according to the Charlson Comorbidity Index (CCI), a method of defining and weighting comorbidities, and has been widely utilised by health researchers to measure burden of disease and case mix [26, 27], and individually (see online supplement Table I). Socioeconomic status was measured using the Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) scores [28]. To address Aim 1, the first step of the model building process was to identify which model type (i.e. either individual comorbidities or CCI) was a better fit. Individual comorbidities were considered as covariates to adjust for modelling; however, when compared, the model with the CCI and previous anxiety or depression was a better fit.

Statistical analysis

Univariable analyses were performed using the Chi-squared test for categorical variables and the Wilcoxon Mann–Whitney rank-sum test for continuous variables. Levels were defined as patient and hospital to account for correlations among patients within individual hospitals. The patient's ability to walk on admission was used as a validated measure of stroke severity [29]. However, for patients that experience an in-hospital stroke, ability to walk is assessed within the first 24 h of onset of their stroke symptoms. Multivariable multilevel random effects logistic regression was to address Aim 1 and 2. Variables known to be associated with outcomes (evidence-based) such as stroke severity, stroke type and age were also included in the models.

To determine whether there was an association between self-reported anxiety or depression following stroke (dependent variable) and quality of acute stroke care received in hospital (Aim 1), eight separate multilevel, multivariable models were developed. The independent variables comprised each of the eight AuSCR acute stroke processes of care. All models were adjusted for patient characteristics (e.g. age, sex), clinical factors (e.g. transferred from another hospital), previous hospital admission for anxiety or depression and the CCI.

To identify patient (e.g. age, sex) and clinical factors (e.g. transferred from another hospital), associated with self-reported anxiety or depression at 90–180 days after a stroke (Aim 2), a parsimonious approach to model building was used. Independent variables, such as sex, country of birth, socio-economic status, comorbidities (see Table 1), previous anxiety or depression problems and CCI, were selected when p was < 0.2 in univariable analyses. Variables known to be associated with outcomes (evidence-based) such as stroke severity, stroke type and age were also included in the model independent of significance testing [30]. In situations where large numbers of variables met this criteria, manual backward stepwise regression was used to obtain the final model. The Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) were conducted to measure the goodness of fit for the logistic regression models developed, where smaller values of AIC and BIC indicate better model fit [31]. Likelihood ratio tests were also conducted as part of the model building process to check goodness of fit.

Standard techniques were implemented to check for collinearity. The area under the receiver operating characteristic curve (AUC-ROC) was also used as a measure of predictive accuracy of the logistic regression model. Multivariable results were reported as adjusted Odds Ratios (aORs) with 95% confidence intervals. Significance was set at $p < 0.05$.

Relationships between socioeconomic status, age and number of comorbidities variables were conducted. To illustrate these relationships, two-way contour plots were developed for age, total number of comorbidities, socioeconomic status (IRSAD score) and self-reported anxiety or depression. All analyses were performed using Stata (version 12.1, StataCorp, Texas).

Results

Out of those eligible for follow-up ($n = 4001$), 71% provided follow-up (outcome) data ($n = 2853$). There were 1148 non-respondents to the follow-up survey (29%). All those who provided outcome data at follow-up were included in the analyses. The median age was 74 years (Q1: 64; Q3: 84), 45% were female, 60% had suffered an ischaemic stroke, 13% suffered a hemorrhagic stroke and 24% had a TIA. The median follow-up time was 101 days (Q1: 96; Q3: 107). In total, 1339 (47%) reported moderately or severely anxious or depressed (Fig. 1). Those with anxiety or depression also reported having problems in the other domains of the EQ-5D-3L (pain and discomfort: 66%; usual activities: 63%; self-care: 72%; and mobility 36%). Moreover, those who reported having problems with anxiety or depression had a clinically relevant lower overall quality of life [median VAS score (Q1; Q3): 60 (45; 75)] compared to those who reported having no problems with anxiety or depression (median VAS score (Q1; Q3): 80 (70; 90), $p = < 0.001$) (Fig. 2). The non-respondents (28%) had similar characteristics to respondents, such as female, type of stroke, ability to walk on admission and stroke while in hospital (see Online Supplement Table II).

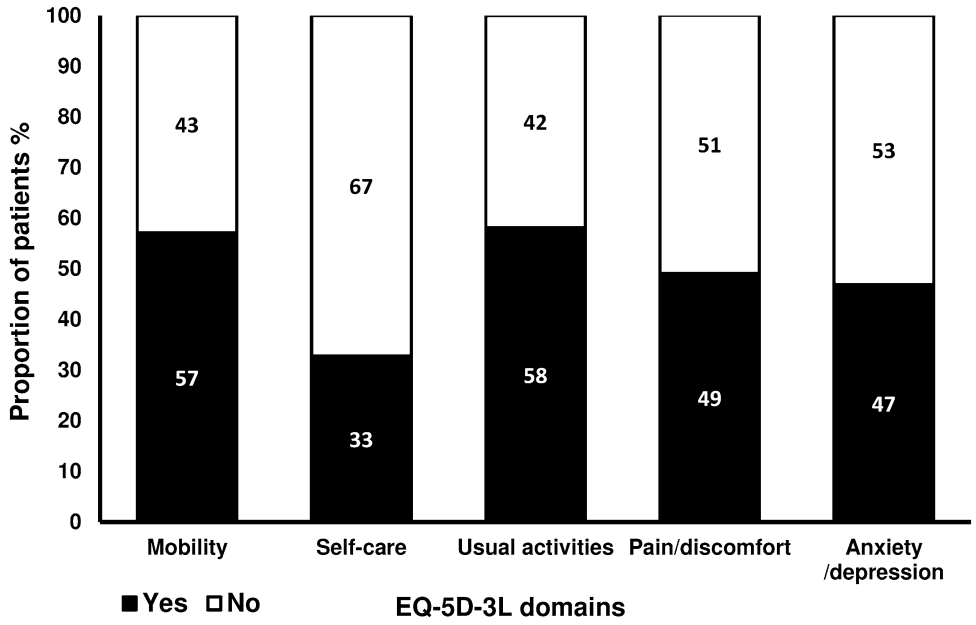

Fig. 1 The proportion of survivors of stroke in the Australian Stroke Clinical Registry in Queensland (years 2009–2013) who reported problems in each of the domains of EQ-5D-3L at 90–180 post-stroke

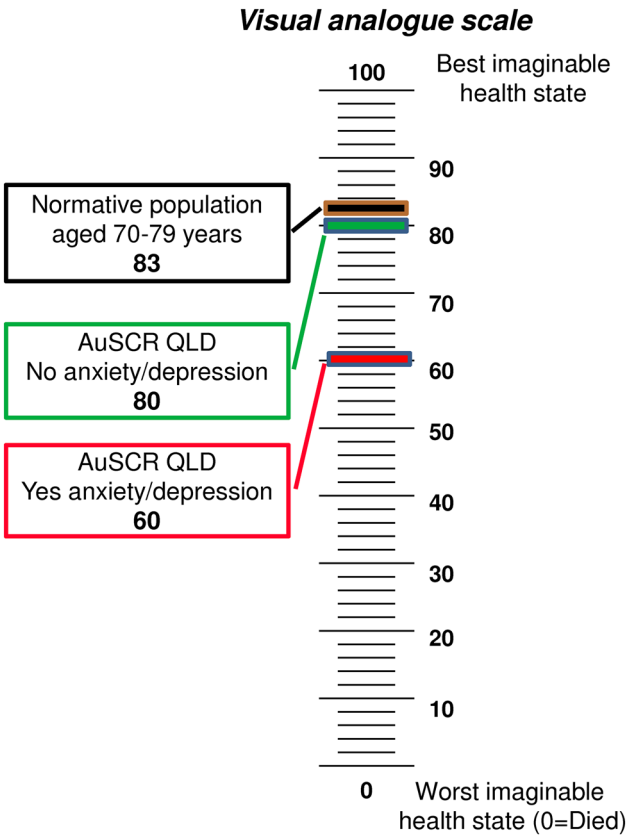

Fig. 2 Summary of visual analogue scale responses for 2009–2013 Australian stroke clinical registry registrants. Those who reported having issues with anxiety or depression have a lower overall quality of life than those who reported having no issues using the EQ-5D-3L

A significantly greater proportion of those who reported moderately or severely anxious or depressed were of working age (i.e. < 65 years), female, had stroke while in hospital, had an ischaemic stroke, were unable to walk on admission, were from a disadvantaged population and had a greater length of stay in hospital than those reported having no problems with anxiety or depression. In addition, those who reported being moderately or severely anxious or depressed were more likely to have a higher total number of comorbidities than those who did not (Table 1).

In multivariable analysis (AUC-ROC = 0.69; Table 2), the factors most strongly independently associated with anxiety or depression were diagnosis of either a mental health problem (aOR 2.37, 95% confidence interval (95% CI) 1.66–3.39; $p < 0.001$) or dementia during a prior hospital presentation (aOR 1.91, 95% CI 1.24–2.93; $p = 0.003$), being at home with support after stroke (aOR 1.41, 95% CI 1.12–1.69; $p = < 0.001$), and being from a socioeconomically disadvantaged compared to an advantaged population (aOR 1.59, 95% CI 1.21–2.10; $p = 0.001$). In the univariable analyses, the only two acute stroke processes of care that were significantly associated with post-stroke anxiety or depression responses were (i) aspirin administration less than 48 h in ischaemic stroke patients and (ii) mobilisation within 2 days of admission. However, after adjusting for covariates in the multivariable modelling, none of the eight processes of care were associated with self-reported anxiety or depression between 90 and 180 days following stroke (Table 3). A sub-group analysis was conducted in those without previous diagnosis of anxiety or depression. There was no association with acute stroke processes of care and self-reported anxiety or depression between 90 and 180 days

Table 2 Multivariable analysis: factors independently associated with self- reported anxiety or depression using the EQ-5D-3L at 90–180 days following stroke

Patients who completed the EQ-5D-3L anxiety or depression at 90–180 days following stroke ($n = 2404$)	Adjusted odds ratio (95% CI)	p value
Stroke type	0.85 (0.73–0.98)	0.024
Age		
< 65	Reference	
65–74	0.80 (0.63–1.01)	0.062
75–84	0.83 (0.66–1.05)	0.122
85+	1.16 (0.88–1.54)	0.300
Female	1.17 (0.98–1.39)	0.081
Home with supports	1.41 (1.12–1.69)	< 0.001
Length of stay (days) if discharged	1.01 (1.00–1.02)	0.010
Unable to walk on admission	1.21 (1.00–1.47)	0.040
Socioeconomic status		
Most advantaged	Reference	
Second most advantaged	1.19 (0.91–1.54)	0.203
Third most advantaged	1.48 (1.12–1.95)	0.006
Fourth most advantaged	1.13 (0.85–1.50)	0.398
Most disadvantaged	1.59 (1.21–2.10)	0.001
History of comorbidities		
Hemiplegia	1.46 (1.21–1.76)	< 0.001
Dementia	1.91 (1.24–2.93)	0.003
Smoking	1.31 (1.05–1.63)	0.018
Obesity	1.46 (0.98–2.18)	0.066
Carotid stenosis	1.38 (0.98–1.93)	0.061
Anxiety or depression	2.37 (1.66–3.39)	< 0.001

Socio-economic status is measured using the Index of Relative Socio-economic Advantage/Disadvantage [28]

Table 3 Adherence to processes of care according to self-reported anxiety or depression at 90–180 days follow-up following stroke: univariable and multivariable analysis

Patients who completed the EQ-5D-3L anxiety or depression at 90–180 days following stroke[b]	Model number	Total number of survivors	Univariable analysis			Multivariable analysis[a]	
			Yes ($n = 1339$) n (%)	No ($n = 1514$) n (%)	p-value	Adjusted odds ratio (95% CI)	p value
Treated in a stroke unit	1	2404	1027 (76.7)	1160 (76.6)	0.959	0.93 (0.73–1.18)	0.540
Screen or swallow assessment < 24 h	2	2853	590 (44)	705 (47)	0.180	0.94 (0.78–1.15)	0.111
Mobilisation < 2 days of admission	3	1960	746 (84)	969 (90)	**< 0.001**	0.92 (0.65–1.29)	0.615
Thrombolysis in ischaemic stroke	4	1451	76 (9.3)	71 (8.3)	0.463	0.98 (0.67–1.44)	0.900
Discharged on antihypertensive medication	5	2404	897 (68.7)	992 (66.7)	0.244	1.20 (0.96–1.41)	0.118
Discharge care plan provided	6	1486	273 (39.0)	360 (35.2)	0.104	1.20 (0.89–1.47)	0.302
Aspirin administration < 48 h in ischaemic stroke	7	2163	631 (54.0)	827 (59.2)	**0.008**	0.88 (0.71–1.09)	0.250
Discharged on antiplatelets or antithrombotics	8	2105	687 (62.5)	874 (65.3)	0.150	1.09 (0.85–1.40)	0.511

Bold: statistically significant ($p < 0.05$)

CI confidence interval

[a]Adjusted for stroke type, age, sex, interpreter needed, home with support, length of stay if discharged, unable to walk on admission, in-hospital stroke, discharge destination, Charlson Comorbidity Index [26, 27], socioeconomic status [28], previous anxiety or depression, level defined as hospital

[b]Recorded in the Australian Stroke Clinical Registry at 90–180 days following stroke

following stroke when analyses were restricted to this group. Some factors such as stroke severity, sex, previously admitted with diagnosis of dementia, and obesity were associated with self-reported anxiety or depression between 90 and 180 days following stroke in this sub-group (see Online Supplement Table III). A sub-group analysis was also conducted by excluding in-hospital stroke and transferred from another hospital (see Online Supplement Table IV).

In addition, the further display of relationships between continuous variables is shown in Fig. 3.

Discussion

Our study provides one of the largest assessments of factors associated with self-reported anxiety or depression following acute stroke or TIA. In our cohort, almost one in two respondents reported having anxiety or depression at follow-up. We were unable to detect an association between quality of care received in hospital and self-reported anxiety or depression following stroke. However, we did identify that patients with severe stroke, those from a disadvantaged population, and those with a history of anxiety, depression or dementia prior to admission were more likely to report being moderately or severely anxious or depressed between 90 and 180 days following stroke or TIA.

There was a lack of an independent association between the quality of acute stroke care received and anxiety or depression following stroke. So perhaps the quality and type of acute stroke care received does not independently impact on anxiety or depression following stroke in the same way as it appears to influence other types of post-stroke disabilities such as quality of life, stroke severity and survival [32, 33]. We were only able to assess eight acute stroke processes of care. However, these processes of care, although evidence-based and important for optimal management, do not specifically address anxiety or depression. It is also likely that the full impact of the stroke does not become apparent to the survivor until they are back home and they realise how much their life has changed following stroke [34]. It may be more important to target interventions during the early post-discharge period rather than the acute period. So perhaps more information is needed about the optimal timing of interventions for prevention and management of anxiety or depression, particularly during transition to home and integration back into the community.

Our results add to existing literature, which describe the complex interactions between poor physical well-being or disability and anxiety or depression experienced by survivors of stroke [5, 35]. Those with anxiety or depression also reported having problems with pain and discomfort, ability to perform usual activities, and mobility. In our study, we found that those who had more severe stroke (unable to walk on admission), and were more likely to require support at home between 90 and 180 days after their stroke, were more likely to report having anxiety or depression. We know that lack of physical activity and social interaction is a predictor of depression and anxiety in itself, which would also lead to a poor quality of life [36, 37]. It is important to have good quality of processes of care involved with patient transitions to home as it directly impacts on patient outcomes such as anxiety or depression. Perhaps transitions to home processes of care need to focus on psychological strategies that include education and skills training for patients, improving communication between families and caregivers and movement-based strategies to learn how to adapt and resume activities of daily living [38]. There is some emerging evidence that exercise-based interventions [39] or alternative therapies, such as mindfulness-based interventions, may be effective for ameliorating problems with depression and anxiety in survivors of stroke [40].

Personal history of anxiety or depression or dementia is regularly highlighted as one of the strongest predictors, and is likely to predispose people to subsequent development of these disorders following stroke [5, 41]. This was further confirmed in our study where those with previous hospital admissions with a diagnosis of anxiety or depression were twice as likely to report having problems with anxiety or depression at 90–180 days following stroke or TIA. Firstly, this could be due to the sudden change in life events and decline in health, both strong predictors of relapse [42]. Secondly, patient's coping and attribution styles that may have contributed to previous anxiety or depression episodes may still be in play in terms of how they process the sudden impact of stroke on their lives. Therefore, it is essential to gain a better understanding of why those with a history of anxiety, depression or dementia are more likely to experience problems with anxiety or depression following stroke and the types of supports and interventions that are required to mitigate this.

In a recent national stroke audit, almost 50% of patients were not provided with a mood assessment. In those who were assessed, two out of three patients who had been identified as having depression or anxiety were not provided with a further mood assessment or the necessary care [37]. Considering the high prevalence of anxiety or depression, blanket screening, and screening of those at high risk at different times during the transition period (e.g. while in hospital, early post-discharge and later post-discharge period) may be beneficial.

Our study also adds to the growing literature providing evidence that those with the most social advantage were less likely to experience anxiety or depression compared to the most disadvantaged socioeconomic group. This could be due to the lack of facilities and support available and poor accessibility to health services, lower levels of health literacy, and

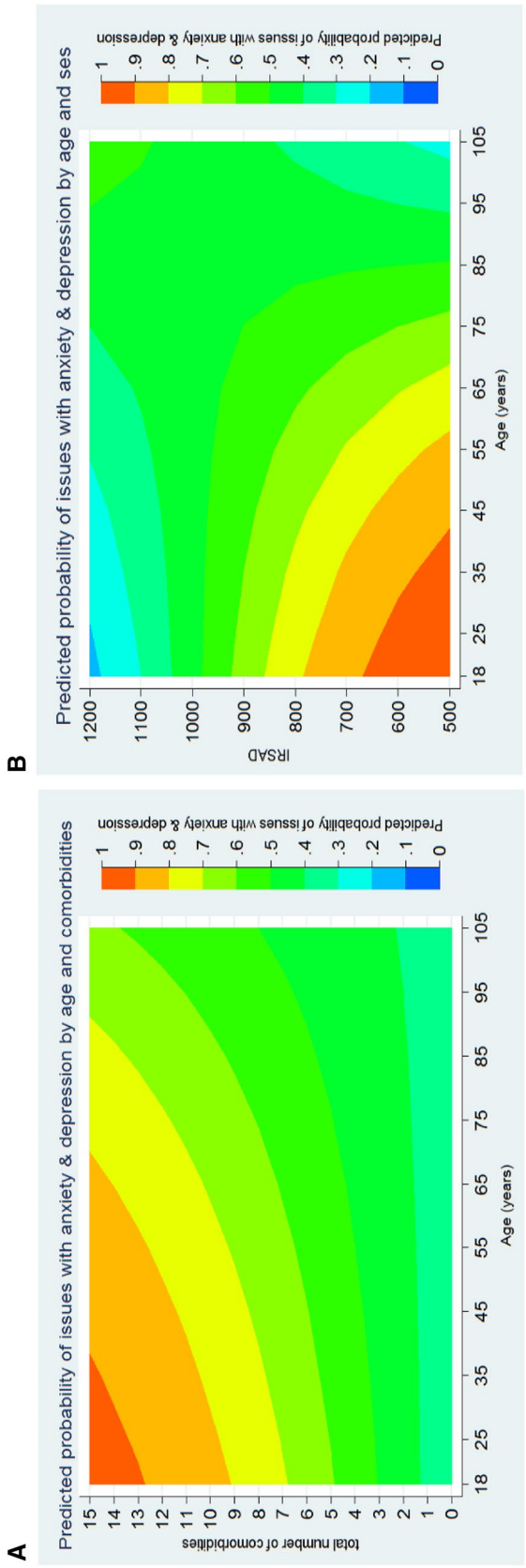

Fig. 3 Graphical representation of relationship between continuous variables and predicted probability of association with anxiety and depression. Age is on (*x* axis) and probability index (*z* axis). The y axis depicts total number of comorbidities (**a**) and socioeconomic status [The Index of Relative Socio-economic Advantage and Disadvantage (IRSAD)] summarises information about the economic and social conditions of people and households within an area, including both relative advantage (quantile 1) and disadvantage measures (quantile 5) [28] (**b**). The *z* axis effectively provides a 3-dimensional plot in which contours range from blue (lowest value of modelled probability) to red (highest value of modelled probability)

higher levels of financial stress in survivors living in the low socioeconomic areas [43, 44]. Therefore, designing and implementing psychosocial interventions for the promotion of mental health or providing social support in these communities of patients may be of benefit.

A major strength of this study is the use of a large linked dataset. Linking AuSCR data to hospital administrative datasets provided a much more comprehensive assessment of comorbidities and risk factors than would otherwise be available. Given the prevalence of anxiety and depression in our study cohort, having access to a comprehensive dataset enabled us to gain a more thorough understanding of factors that may impact on self-reported anxiety or depression in patients with stroke. This information may be useful for informing policy and practice improvements.

A limitation of this study is that the EQ-5D-3L mood domain does not differentiate between anxiety and depression. However, this scale provides a useful indicator of self-assessed problems with anxiety or depression. The EQ-5D-3L has not been validated as a measure of anxiety or depression. The authors are currently undertaking a study on the validity of the EQ-5D-3L as a measure of problems with mood. A further limitation is the lack of details on registrant's use of medications and other proven anxiety or depression treatments. This means that it is unclear whether those that had anxiety or depression, but were well managed, would have reported having anxiety or depression on the EQ-5D-3L. However, the higher rates of self-reported anxiety and depression among those with a previous diagnosis of anxiety or depression suggest that there are many patients where this is not the case.

In conclusion, identifying those with prior diagnosis of anxiety, depression or dementia for early intervention and support, especially when transitioning to home, may help reduce the prevalence of anxiety or depression following stroke. Future research specific to problems with mood, and patient outcomes throughout the patient's recovery journey would be of considerable importance in improving our understanding of anxiety or depression in survivors of stroke and to advance health care delivery in this area.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study as part of the registry.

References

1. Andrew, N. E., Kilkenny, M., Naylor, R., Purvis, T., Lalor, E., Moloczij, N., & Cadilhac, D. A. (2014). Understanding long-term unmet needs in Australian survivors of stroke. *International Journal of Stroke, 9*, 106–112.
2. Chrichton, S. L., Bray, B. D., McKevitt, C., Rudd, A. G., & Wolfe, C. D. A. (2016). Patient outcomes up to 15 years after stroke: Survival, disability, quality of life, cognition and mental health. *Journal of Neurology, Neurosurgery and Psychiatry, 87*, 1091–1098.
3. Broomfield, N. M., Quinn, T. J., Abdul-Rahim, A. H., Walters, M. R., & Evans, J. J. (2014). Depression and anxiety symptoms post-stroke/TIA: Prevalence and associations in cross-sectional data from a regional stroke registry. *BMC Neurology, 14*, 198.
4. Berg, A., Palomaki, H., Lehtihalmes, M., Lonnqvist, J., & Kaste, M. (2003). Poststroke depression: An 18-month follow-up. *Stroke, 34*, 138–143.
5. Shi, Y., Yang, D., Zeng, Y., & Wu, W. (2017) Risk factors for post-stroke depression: A meta-analysis. *Frontiers in Aging Neuroscience*. https://doi.org/10.3389/fnagi.2017.00218.
6. Cadilhac, D. A., Kilkenny, M. F., Longworth, M., Pollack, M. R. P., & Levi, C. R., on behalf of Greater Metropolitan Clinical T, Stroke Services New South Wales Coordinating C (2011). Metropolitan–rural divide for stroke outcomes: do stroke units make a difference? *Internal Medicine Journal, 41*, 321–326.
7. National Stroke Foundation.(2010). *Clinical guidelines for stroke management 2010*. Melbourne.
8. Stroke Unit Trialists C. (2007). Organised inpatient (stroke unit) care for stroke. *Cochrane Database of Systematic Reviews, 4*, 4.
9. Cadilhac, D. A., Andrew, N. E., Kilkenny, M. F., Hill, K., Grabsch, B., Lannin, N. A., Thrift, A. G., Anderson, C. S., Donnan, G. A., Middleton, S., & Grimley, R. (2017). Improving quality and outcomes of stroke care in hospitals: Protocol and statistical analysis plan for the Stroke123 implementation study. *International Journal of Stroke, 13*, 96–106.
10. Andrew, N. E., Sundararajan, V., Thrift, A. G., Kilkenny, M. F., Katzenellenbogen, J., Flack, F., Gattellari, M., Boyd, J. H., Anderson, P., Grabsch, B., et al. (2016). Addressing the challenges of cross-jurisdictional data linkage between a national clinical quality registry and government-held health data. *Australian and New Zealand Journal of Public Health, 40*, 436–442.

11. Lannin, N. A., Anderson, C., Lim, J., Paice, K., Price, C., Faux, S., Levi, C., Donnan, G., & Cadilhac, D. (2013). Telephone follow-up was more expensive but more efficient than postal in a national stroke registry. *Journal of Clinical Epidemiology, 66*, 896–902.
12. Preen, D. B., Holman, C. D. A. J., Spilsbury, K., Semmens, J. B., & Brameld, K. J. (2006). Length of comorbidity lookback period affected regression model performance of administrative health data. *Journal of Clinical Epidemiology, 59*, 940–946.
13. WHO (World Health Organization) (2007). *International statistical classification of diseases and related health problems*. Retrieved April 16, 2017. 10th Revision, Version for 2010.
14. Cadilhac, D. A., Lannin, N. A., Anderson, C. S., Levi, C. R., Faux, S., Price, C., Middleton, S., Lim, J., Thrift, A. G., & Donnan, G. A. (2010). Protocol and pilot data for establishing the Australian Stroke Clinical Registry. *International Journal of Stroke, 5*, 217–226.
15. Rabin, R., & de Charro, F. (2001). EQ-5D: A measure of health status from the EuroQol Group. *Annals of Medicine, 33*, 337–343.
16. Dorman, P. J., Waddell, F., Slattery, J., Dennis, M., & Sandercock, P. (1997). Is the EuroQol a valid measure of health-related quality of life after stroke? *Stroke, 28*, 1876–1882.
17. Hunger, M., Sabariego, C., Stollenwerk, B., Cieza, A., & Leidl, R. (2012). Validity, reliability and responsiveness of the EQ-5D in German stroke patients undergoing rehabilitation. *Quality of Life Research, 21*, 1205–1216.
18. Konig, H. H., Bernert, S., Angermeyer, M. C., Matschinger, H., Martinez, M., Vilagut, G., Haro, J. M., de Girolamo, G., de Graaf, R., Kovess, V., & Alonso, J. (2009). Comparison of population health status in six european countries: Results of a representative survey using the EQ-5D questionnaire. *Medical Care, 47*, 255–261.
19. McCaffrey, N., Kaambwa, B., Currow, D. C., & Ratcliffe, J. (2016). Health-related quality of life measured using the EQ-5D-5L: South Australian population norms. *Health and Quality of Life Outcomes, 14*, 133.
20. Jorgensen, T. S., Turesson, C., Kapetanovic, M., Englund, M., Turkiewicz, A., Christensen, R., Bliddal, H., Geborek, P., & Kristensen, L. E. (2017). EQ-5D utility, response and drug survival in rheumatoid arthritis patients on biologic monotherapy: A prospective observational study of patients registered in the south Swedish SSATG registry. *PLoS ONE, 12*, e0169946.
21. Christensen, M. C., Mayer, S., & Ferran, J. M. (2009). Quality of life after intracerebral hemorrhage: Results of the factor seven for acute hemorrhagic stroke (FAST) trial. *Stroke, 40*, 1677–1682.
22. Lindgren, P., Glader, E. L., & Jonsson, B. (2008). Utility loss and indirect costs after stroke in Sweden. *European Journal of Cardiovascular Prevention and Rehabilitation, 15*, 230–233.
23. Brooks, R. (1996). EuroQol: The current state of play. *Health Policy, 37*, 53–72.
24. Kim, S.-K., Kim, S.-H., Jo, M.-W., & Lee, S. (2015). Estimation of minimally important differences in the EQ-5D and SF-6D indices and their utility in stroke. *Health and Quality of Life Outcomes, 13*, 32.
25. Pickard, A. S., Neary, M. P., & Cella, D. (2007). Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health and Quality of Life Outcomes, 5*, 70.
26. Quan, H., Li, B., Couris, C. M., Fushimi, K., Graham, P., Hider, P., Januel, J.-M., & Sundararajan, V. (2011). Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *American Journal of Epidemiology, 173*, 676–682.
27. Charlson, M., Szatrowski, T. P., Peterson, J., & Gold, J. (1994). Validation of a combined comorbidity index. *Journal of Clinical Epidemiology, 47*, 1245–1251.
28. Australian Bureau of Stastistics. (2006). *Socio-economic indexes for areas (SEIFA)*. Canberra: Australian Bureau of Stastistics.
29. Counsell, C., Dennis, M., McDowall, M., & Warlow, C. (2002). Predicting outcome after acute and subacute stroke. *Stroke, 33*, 1041.
30. Royston, P., Moons, K. G. M., Altman, D. G., & Vergouwe, Y. (2009). Prognosis and prognostic research: Developing a prognostic model. *British Medical Journal, 338*, b604.
31. Spiegelhalter, D. J., Best, N. G., Carlin, B. P., & van der Linde, A. (2002). Bayesian measures of model complexity and fit. *Journal of the Royal Statistical Society Series B, 64*, 583–639.
32. Cadilhac, D. A., Pearce, D. C., Levi, C. R., & Donnan, G. A. (2008). Improvements in the quality of care and health outcomes with new stroke care units following implementation of a clinician-led, health system redesign programme in New South Wales, Australia. *Quality and Safety in Health Care, 17*, 329–333.
33. Cadilhac, D. A., Kim, J., Lannin, N. A., Levi, C. R., Dewey, H. M., Hill, K., Faux, S., Andrew, N. E., Kilkenny, M. F., Grimley, R., et al. (2016). Better outcomes for hospitalized patients with TIA when in stroke units: An observational study. *Neurology, 86*, 2042–2048.
34. Hackett, M. L., Yapa, C., Parag, V., & Anderson, C. S. (2005). Frequency of depression after stroke: A systematic review of observational studies. *Stroke, 36*, 1330–1340.
35. Kutlubaev, M. A., & Hackett, M. L. (2014). Part II: Predictors of depression after stroke and impact of depression on stroke outcome: An updated systematic review of observational studies. *International Journal of Stroke, 9*, 1026–1036.
36. Hackett, M. L., & Anderson, C. S. (2005). Predictors of depression after stroke. *Stroke, 36*, 2296.
37. Stroke Foundation. *National stroke audit—rehabilitation services report 2016*. Melbourne, Australia.
38. Cameron, J. I., O'Connell, C., Foley, N., Salter, K., Booth, R., Boyle, R., Cheung, D., Cooper, N., Corriveau, H., Dowlatshahi, D., et al. (2016). Canadian stroke best practice recommendations: Managing transitions of care following Stroke, Guidelines Update 2016. *International Journal of Stroke, 11*, 807–822.
39. Eng, J. J., & Reime, B. (2014). Exercise for depressive symptoms in stroke patients: A systematic review and meta-analysis. *Clinical Rehabilitation, 28*, 731–739.
40. Thayabaranathan, T., Andrew, N. E., Immink, M. A., Hillier, S., Stevens, P., Stolwyk, R., Kilkenny, M., & Cadilhac, D. A. (2017). Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis. *Topics in Stroke Rehabilitation, 24*, 279–287.
41. Ayerbe, L., Ayis, S., Rudd, A. G., Heuschmann, P. U., & Wolfe, C. D. (2011). Natural history, predictors, and associations of depression 5 years after stroke: The South London Stroke Register. *Stroke, 42*, 1907–1911.
42. Spuling, S. M., Wolff, J. K., & Wurm, S. (2017). Response shift in self-rated health after serious health events in old age. *Social Science and Medicine, 192*, 85–93.
43. Kapral, M. K., Wang, H., Mamdani, M., & Tu, J. V. (2002). Effect of socioeconomic status on treatment and mortality after stroke. *Stroke, 33*, 268.
44. Broomfield, N. M., Quinn, T. J., Abdul-Rahim, A. H., Walters, M. R., & Evans, J. J. (2014). Depression and anxiety symptoms post-stroke/TIA: Prevalence and associations in cross-sectional data from a regional stroke registry. *BioMed Central Neurology, 14*, 198.

Online Supplement

Full Title: Factors influencing self-reported anxiety or depression following stroke or TIA using linked registry and hospital data.

Journal name: Quality of Life Research

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Table I: Diagnostic categories and corresponding International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) codes

Condition	ICD-10 codes
Cancer	C0, C1, C2, C3, C40, C41, C43, C45, C46, C47, C48, C49, C5, C6, C70, C71, C72, C73, C74, C75, C76, C81, C82, C83, C84, C85, C883, C887, C889, C900, C901, C91, C92, C93, C940, C941, C942, C943, C9451, C947, C95, C96
Congestive heart failure	I50
Connective tissue disease	M050, M051, M052, M053, M058, M059, M060, M063, M069, M32, M332, M34, M353
Cerebrovascular accident	I60, I61, I62, I63, I64, I65, I652, I66, I670, I671, I672, I674, I675, I676, I677, I678, I681, I682, I688, I69, G450, G451, G452, G454, G458, G459, G46
Diabetes complicated	E102, E103, E104, E112, E113 E114, E132, E133, E134, E142, E143, E144
Diabetes uncomplicated	E101, E105, E109 , E111, E115, E119, E131, E135 E139, E141, E145, E149
HIV	B20, B21, B22, B23, B24
Mild liver disease	K702, K703, K717, K73, K740, K742, K743, K744 K745, K746
Metastatic cancer	C77, C78, C79, C80
Acute myocardial infarct	I21, I22, I252
Hemiplegia	G041, G81, G820, G821, G822
Peptic ulcer	K25, K26, K27, K28
Chronic pulmonary disease	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67
Peripheral vascular disease	I71, I739, I790, R02, Z958, Z959
Chronic renal disease	N01, N03, N18, N19, N25 N052, N053, N054, N055, N056, N072, N073, N074
Severe liver disease	K721, K729, K766, K767
Dementia	F00, F01, F02, F03, F051
Psychoses	F20, F22, F23, F24, F25, F28, F29, F302
Bipolar	F31
Anxiety or depression	F063, F064, F065, F066, F067, F068, F069, F051, F32, F33, F34, F38, F39, F41, F42, F43, F99
Angina	I20, I24, I250, I251
Hypertension	I10
Smoking	Z720, F172
Lipids	E78, E780, E781, E782, E783, E784, E785, E786, E788, E789
Obesity	E66, E660, E661, E662, E668, E669
Atrial fibrillation	I48
Carotid stenosis	I652, G451, S150
Atherosclerosis	I70

HIV: Human Immunodeficiency Virus

Table II: Demographic characteristics between AuSCR follow-up respondents and nonrespondents

	AuSCR follow-up respondents (n=2,853)	**AuSCR follow-up nonrespondents (n=1,148)**
Patient characteristics	**n (%)**	**n (%)**
Age (years), median (Q1,Q3)*	74 (64, 82)	72 (61, 83)
Female	1,285 (44.8)	526(44.3)
Born in Australia	2,135 (74.1)	825 (69.4)
In hospital stroke	145 (5.1)	65 (5.6)
Interpreter required*	34 (1)	25 (2)
Transferred from another hospital		
Stroke type		
Ischemic	1,701 (59.2)	680 (57.5)
Hemorrhage	283 (9.9)	107 (9.1)
TIA	738 (25.7)	301 (25.5)
Stroke severity		
Unable to walk on admission	1,346 (52.4)	492 (49.3)
*Socioeconomic status**		
Most advantaged	599 (21)	203 (17)
Second most advantaged	631 (22)	234 (20)
Third most advantaged	498 (17)	158 (13)
Fourth most advantaged	520 (18)	248 (21)
Most disadvantaged	633 (22)	345 (29)
Length of stay (days) if discharge, median (Q1,Q3)	5 (2,9)	5 (2,10)
*Discharge destination**		
Hospital	127 (5)	51 (5)
Rehabilitation (inpatient)	603 (21)	190 (17)
Low level Residential care	30 (1)	18 (2)
High level Residential care	95 (3)	67 (6)
Home with supports	885 (31)	341 (30)
Home without supports	727 (26)	252 (22)
Transitional care service	21 (1)	10 (1)
Other	22 (1)	24 (2)

*Statistically significant difference compared between AuSCR follow-up respondents and nonrespondents $p<0.05$)

Subgroup analyses

Table III: Multivariable analysis of factors independently associated with self- reported anxiety or depression using the EQ-5D-3L at 90-180 days following stroke in those without previous diagnosis of anxiety or depression

Patients who completed the EQ-5D-3L anxiety or depression at 90-180 following stroke (n=2404)	Adjusted Odds Ratio (95% CI)	p-value
Stroke type	0.86 (0.70 – 0.99)	0.040
Age		
<65	Reference	
65-74	0.79 (0.63 – 1.00)	0.053
75-84	0.85 (0.67 – 1.07)	0.157
85+	1.20 (0.89 – 1.55)	0.258
Female	1.20 (1.01 – 1.40)	0.036
Home with supports	1.41 (1.20 – 1.70)	<0.001
Length of stay (days) if discharged	1.01 (1.00 – 1.50)	0.008
Unable to walk on admission	1.23 (1.01 – 1.47)	0.042
Socioeconomic status		
Most advantaged	Reference	
Second most advantaged	0.60 (0.51 – 0.89)	0.010
Third most advantaged	1.52 (1.09 – 1.90)	0.005
Fourth most advantaged	1.13 (0.85 – 1.50)	0.398
Most disadvantaged	1.58 (1.20 – 2.10)	0.001
History of comorbidities		
Hemiplegia	1.44 (1.19 – 1.70)	<0.001
Dementia	2.16 (1.41– 3.30)	<0.001
Smoking	1.35 (1.09 – 1.69)	0.007
Obesity	1.54 (1.03 – 1.69)	0.035
Carotid stenosis	1.35 (0.97 – 2.29)	0.075

Socio-economic status is measured using the Index of Relative Socio-economic Advantage/Disadvantage [1].

Table IV: Multivariable analysis of factors independently associated with self- reported anxiety or depression using the EQ-5D-3L at 90-180 days following excluding 'in-hospital strokes and transferred from another hospital'

Patients who completed the EQ-5D-3L anxiety or depression at 90-180 following stroke (n=2404)	Adjusted Odds Ratio (95% CI)	p-value
Stroke type	0.84 (0.73 – 0.97)	0.020
Age		
<65	Reference	
65-74	0.79 (0.63 – 1.00)	0.056
75-84	0.83 (0.66 – 1.05)	0.114
85+	1.16 (0.87 – 1.54)	0.292
Female	1.17 (0.99 – 1.40)	0.071
Home with supports	1.42 (1.19 – 1.70)	<0.001
Length of stay (days) if discharged	1.01 (1.00 – 1.02)	0.003
Unable to walk on admission	1.19 (0.99 – 1.44)	0.066
Socioeconomic status		
Most advantaged	Reference	
Second most advantaged	1.18 (0.97 – 1.52)	0.199
Third most advantaged	1.48 (1.09 – 1.90)	0.005
Fourth most advantaged	1.09 (0.83 – 1.47)	0.332
Most disadvantaged	1.58 (1.20 – 2.10)	0.001
History of comorbidities		
Hemiplegia	1.44 (1.19 – 1.74)	<0.001
Dementia	1.95 (1.27– 2.99)	0.002
Smoking	1.30 (1.04 – 1.61)	0.021
Obesity	1.49 (1.00 – 2.22)	0.051
Carotid stenosis	1.39 (0.99 – 1.94)	0.056
Anxiety or depression	2.38 (1.66 –3.40)	<0.001
Acute stroke processes of care		
Treated in a stroke unit	0.92 (0.72 –1.16)	0.462
Screen or swallow assessment <24 hours	0.92 (0.77–1.12)	0.420
Mobilisation <2 days of admission	0.84 (0.56 –1.28)	0.433
Thrombolysis in ischemic stroke	0.97 (0.66 –1.43)	0.889
Discharged on antihypertensive medication	1.16 (0.96–1.40)	0.124
Discharge care plan provided	1.14 (0.89–1.47)	0.300
Aspirin administration <48 hours in ischemic stroke	0.88 (0.71–1.09)	0.240
Discharged on anti-platelets or antithrombotics	1.09 (0.85 –1.40)	0.498

Socio-economic status is measured using the Index of Relative Socio-economic Advantage/Disadvantage [1].

Co-investigators and other contributors to the Australian Stroke Clinical Registry
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References

1. Australian Bureau of Stastistics: Socio-economic indexes for areas (SEIFA). Canberra, Australia: Australian Bureau of Stastistics; Canberra. (2006).

7.3 Summary

In this paper I highlighted the importance of identifying those with prior diagnosis of anxiety, depression or dementia for early intervention and support when in hospital after stroke. This is especially important for those patients transitioning to home (i.e. into the community) straight from the hospital. Future research on how processes of care specific to psychological conditions provided in hospitals may influence the development of anxiety or depression in survivors of stroke is warranted. This would be of considerable importance for improving our understanding of anxiety or depression in survivors of stroke and to advance health care delivery in this area. However, an important limitation highlighted in this paper is the lack of validation of the EQ-5D-3L anxiety or depression domain. Therefore, in the next chapter I describe a study that I undertook to assess the convergent validity, sensitivity and specificity of the EQ-5D-3L anxiety or depression domain.

Chapter 8: Validating EQ-5D-3L to screen for anxiety or depression in stroke using AuSCR registrants

8.1 Overview

In this chapter, I describe a study that I undertook to assess the convergent validity, sensitivity and specificity of the EQ-5D-3L survey as a tool for screening anxiety or depression in people with stroke when used in population health research. As demonstrated in Chapters 4, 6 and 7, the EQ-5D-3L is increasingly being routinely collected in clinical quality registries, such as the AuSCR, to assess health-related quality of life. The EQ-5D-3L has good internal consistency when applied to a general population and has been validated as a health status measure in patients with stroke.[115, 116] However, to our knowledge there is no information on the validity of the EQ-5D-3L anxiety or depression domain as an indicator of these respective disorders in patients with stroke. Given the essential need for reliable indicators of anxiety and depression in survivors of stroke, I sought to examine whether the EQ-5D-3L could be used as a suitable screening tool, by assessing the convergent validity, sensitivity and specificity against the Hospital Anxiety and Depression Scale (HADS), for anxiety or depression in this patient population (aim 4 of my thesis).

8.2 Introduction

In Chapter 7, I highlighted mental health disorders, primarily anxiety and depression, which are the most common comorbidities reported by survivors of stroke. Anxiety or depression significantly alter outcomes following stroke, including the quality of the lives of patients with stroke, their families, social connectedness, and patient's ability to recover.[117] Despite these known impacts, evidence from the recent national audit results show little progress has been made in the provision of psychologist assessment, or follow-up of patients at risk of mental health disorders as a consequence of stroke.[17]

Understanding the breadth and scale of the problem of mental health disorders subsequent to stroke is paramount to improving clinical practice. The development and validation of self-reported data collection instruments to identify anxiety and depression at a population level has become an important area of outcomes research. However, to ensure reliability and validity, generic instruments require evaluation if they are to be used in a particular disease population. As described in Chapter 4, the AuSCR is a clinical quality disease registry that is used to prospectively collect important patient data, including type of stroke, quality of care received in acute hospital, and patient outcomes. Eligible registrants are followed-up between 90 to 180 days following stroke and data on survival, living situation, perceived general health, disability and quality of life, using the EQ-5D-3L instrument, are collected. The EQ-5D-3L is increasingly being used in large population-based studies[118-123] and clinical registries[124-126] to assess health-related quality of life as a measure of population health status to inform public health and health care policy. One of the domains that can be reported from the EQ-5D-3L is the presence or absence of anxiety or depression (see Chapter 7).

In the published paper presented in Chapter 7, the study sample (i.e. participants with anxiety or depression) was identified from those who did or did not report anxiety or depression on the

EQ-5D-3L anxiety or depression domain. One of the limitations of that study was that anxiety or depression status had not been measured using a disease-specific tool, such as the HADS. The EQ-5D-3L quality of life measure has been shown to have good internal consistency when applied, as a whole, to a general population and in groups of patients with chronic diseases, including stroke.[127] However, I was unable to find any publications with information on the validity of the EQ-5D-3L anxiety or depression domain as a suitable screening tool for anxiety or depression following stroke.

Factors such as fatigue, communication difficulties, and social isolation are often consequences of stroke reported by survivors, and may be associated with mental health disorders after stroke. Collecting new data on these variables as part of the AuSCR follow-up survey for this current study provided me with an opportunity to assess the temporal relationship between these factors and anxiety or depression.

Given the need for anxiety and depression screening in survivors of stroke, I sought to examine the whether the EQ-5D-3L, a routinely collected measure, could be a suitable screening tool for anxiety or depression in this patient population. The primary objective of this study was to assess the convergent validity (i.e. extent to which two measures capture a same or similar construct)[128], sensitivity and specificity of the EQ-5D-3L anxiety or depression domain as a measure of self-reported mood disturbance in patients with stroke. A secondary objective was to determine what factors may be associated with anxiety or depression post-stroke, including whether the presence of concurrent fatigue, communication difficulties or social isolation influence these outcomes.

8.3 Aims

8.3.1 Primary

(i) To assess the convergent validity, sensitivity and specificity of the EQ-5D-3L instrument as a screening tool for self-reported anxiety and depression following stroke.

8.3.2 Secondary

(ii) To determine factors that may be associated with anxiety or depression including presence of fatigue or problems with cognition, social participation or communication.

8.4 Methods

8.4.1 Participants

Registrants from the AuSCR admitted with stroke or TIA to 3 participating hospitals in Queensland, and aged over 18 years were eligible to participate.

8.4.2 Study design

To compare the convergent validity, sensitivity and specificity of the anxiety or depression domain of the EQ-5D-3L against the HADS, I undertook a cohort study whereby a sample of survivors of stroke registered in AuSCR were simultaneously requested to complete these two surveys as part of the standard AuSCR 90-180 days follow-up procedure.

8.4.3. Survey instruments

All data were collected according to the standard follow-up procedures for the AuSCR (see section 8.4.4.2) The EQ-5D-3L questionnaire is a tool designed to measure overall quality of life and health status from patients (or carers).[127] The health status is measured in terms of five domains; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The

mobility domain is an indication of the person's walking ability, while the self-care domain is about the ability to wash or dress by oneself, and the usual activities dimension measures performance in participant's ability to work, study, do housework, and attend family or leisure activities. The pain/discomfort domain, is an indication of how much pain or discomfort they have, and the anxiety/depression domain, is about how anxious or depressed they are at that point in time. The respondents self-rate their level of severity for each domain using a three-level scale; 1=no problems, 2=moderate problems, 3=extreme/severe problems. A summary index or utility score with a maximum score of 1 and minimum score of 0 can be derived from these 5 domains by conversion with a table of scores.[129] The maximum score of 1 indicates the best health state, and lower scores indicate increasingly worse health states. In addition, respondents are asked to rank their health status from 0-100 using a visual analogue scale (VAS) whereby 100 is the best possible state and 0 the worst possible state.[129] The instrument was designed to be generic enough to use in any patient populations, and is short so can be completed quickly.[130]

The disease-specific tool used as a reference in this study is the HADS. This was chosen over the other diseases-specific screening tools as it is short, and most importantly includes items to assess both disorders, anxiety and depression separately (Table 8.1). Good reliability, validity, and excellent screening properties have been reported for the use of the HADS in the general population, and for various clinical populations.[131] The HADS is a 14 item questionnaire sensitive for detecting anxiety and depression, and is commonly used and has been validated in acute stroke and other chronic illness populations.[131, 132] It was originally developed to indicate the possible presence of anxiety and depressive states in the setting of a medical out-patient clinic.[133] The HADS contains two scales: one for anxiety (HADS-A) and one for depression (HADS-D). Each scale contains seven domains, with each domain rated from 0 (best) to 3 (worst). The scale scores are calculated by summing the responses to the domains

up to a maximum score of 21 points (severe case) per scale. A subscale score higher than 7 indicates a possible anxiety disorder or a depression.[134] Scale scores of between 8 and 10 identify mild, 11–15 moderate, and 16 or above severe cases of anxiety or depression.[135] In the stroke population, the sensitivity of the HADS-A is 52%, and specificity is 90% for a score ≥8.[136] The sensitivity of the HADS-D ranges from 64%-73%, and specificity ranges from 82%-89% for a score ≥8.[132, 137]

Table 8.1. *Description of anxiety or depression specific screening tools validated in the stroke population*

Screening tools	Number of items	Time taken to complete (minutes)	What does the tool measure?
Hospital Anxiety Depression Scale	14	5	anxiety and depression
Irritability, Depression and Anxiety Scale	18	10-15	irritability, anxiety and depression
Hamilton Anxiety Rating Scale	14	10-15	anxiety
Beck Anxiety Inventory	21	5-10	anxiety
State-Trait Anxiety Inventory	40		anxiety
Patient Health Questionnaire-9	9	5	depression
Symptom Checklist-90	16 depression specific	15	depression
Hamilton Depression Rating Scale	17	20	depression
Zung Self-rating Depression Scale	20		depression
Stroke Aphasic Depression Questionnaire	21	4	depression
Beck Depression Inventory	21	5-10	depression
Geriatric Depression Scale	30	8-10	depression
General Health Questionnaire-28	28	5	psychological well-being

8.4.4 Data collection

Ethics approval for this project was obtained from the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC/18/QRBW/73). Site-specific applications were also obtained from the governance offices of the 3 hospitals from which their registry patients would be sent the survey.

8.4.4.1 New data collection through AuSCR

Study data were collected from May to October 2018, eligible AuSCR registrants were administered the brief additional survey questions, which included the HADS and the 6 additional questions based on the International Consortium for Health Outcomes Measurement (ICHOM) standard set, (Appendix A), in addition to the routine 90-180 days AuSCR follow-up survey (Appendix B). The choice of these additional variables was informed by the ICHOM survey for stroke that was developed after the AuSCR was established and has been recommended for use to permit comprehensive international comparisons of patient reported outcomes.[138] The ICHOM: Standard Set for Stroke was established by a group of experts to enable the assessment of health care value in stroke management by recommending patient-centred stroke outcome measures.[138] ICHOM has also established similar measurement sets for other types of chronic illnesses.[139] The AuSCR, however, only collects certain patient information aligned with the ICHOM standard set for stroke such as the modified Rankin Scale and the EQ-5D-3L (Figure 8.1). An additional question on taking medications for anxiety or depression was also included in the new survey. In order to understand the implications and value of adding additional variables, such as fatigue, communication difficulties and use of medications for anxiety or depression, to the follow-up survey of AuSCR there was an opportunity to add these variables and use them in the current study as part of completing the

secondary aim. The additional questions were approved by the ethics committee as being optional for survey respondents to complete.

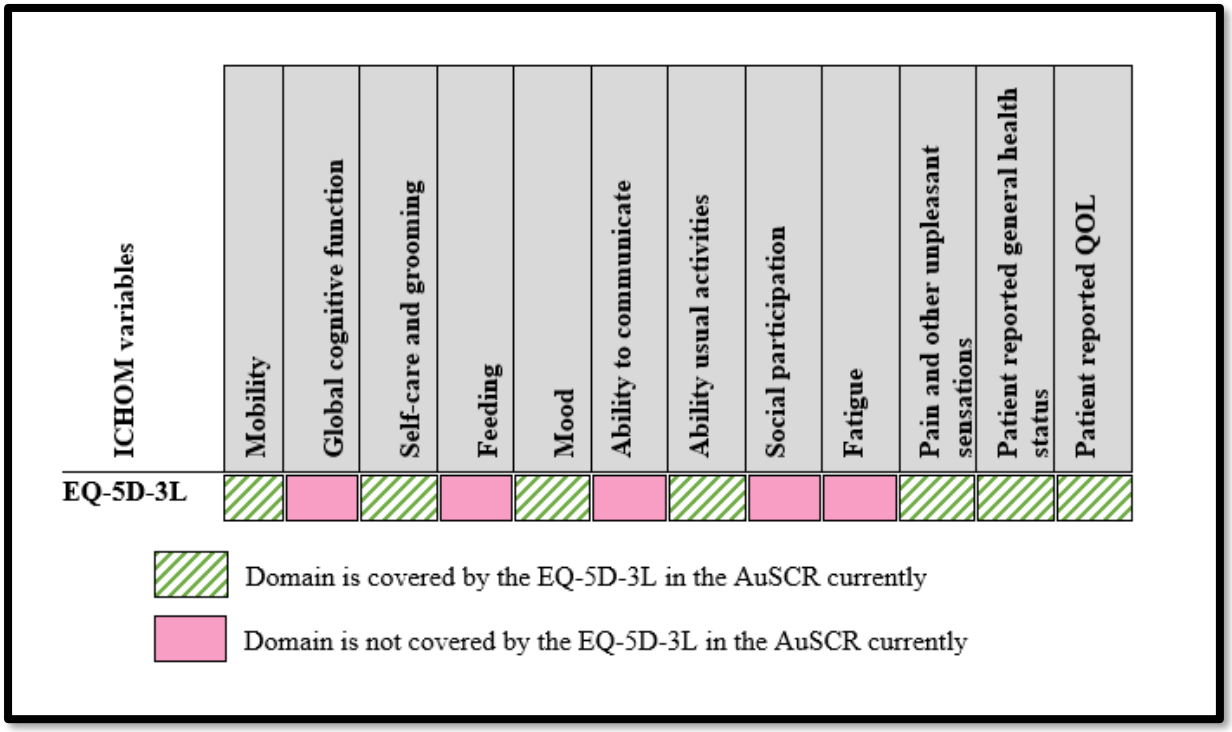

Figure 8.1. *Comparing the ICHOM variables against the EQ-5D-3L collected in AuSCR*

8.4.4.2 AuSCR follow-up procedure

As per the AuSCR follow-up procedures, a postal survey pack with cover letters (Appendix C and D), surveys and reply paid envelope was mailed to each registrant to collect the post-discharge information. If the surveys were not returned within four weeks, another set of surveys were posted to the registrant and/or next of kin. After another 4 week period, a comprehensive telephone attempt to the registrant (and/or next of kin) was conducted. If all forms of contact were unsuccessful, then the registrant was deemed lost to follow-up. As per

usual AuSCR procedures, the completed surveys were returned to the AuSCR office at the Florey Institute of Neuroscience and Mental Health (Heidelberg, Victoria, Australia).

8.4.4.3 Data entry and preparation of the dataset

The AuSCR staff transposed written responses into the online registry database. The AuSCR data manager then extracted the required study data into a password protected excel file. The version of the data provided to me was de-identified by the National Data Manager of AuSCR, whereby all personal identifiers were removed and a project ID was added for each registrant, and sent to me for analysis via a secure CloudStor data file transfer. The dataset contained the following information: project specific ID, age, gender, country of birth, preferred language, stroke type, stroke admission date, stroke severity, whether the registrant is Aboriginal and/or Torres Strait Islander, current living situation, living on own, recurrent stroke status, self-reported readmission status and date, responses to EQ-5D-3L domains, VAS scores, responses to the additional survey questions, based on the ICHOM survey, and survey completion date. For data verification purposes, a copy of the data is securely kept at the AuSCR office.

8.4.5 Sample size

The sample size was pragmatic for what could be achieved within the timeframe and budget of the study. Recruitment of consecutive eligible registrants with an assumed response rate of 40% was anticipated and I sought to obtain a minimum of 280 participant responses (from approximately 700 surveys distributed). A previously published validation study of the EQ-5D-3L and HADS in another patient population had approximately 151 participants.[140]

8.4.6 Statistical analysis

Descriptive statistics were computed for all variables in the overall sample to understand the characteristics and proportion of patients in each category of the HADS-A, HADS-D and EQ-

5D-3L domain. The response rates and missing data for all additional questions, as well as the standard AuSCR variables were assessed. The feasibility of EQ-5D-3L anxiety or depression domain and HADS was investigated by calculating the percentage of missing values. Any registrants with missing data were not included in the convergent validity analyses.

8.4.6.1 Convergent validity analyses

For descriptive analyses, the HADS-A and HADS-D scores were calculated and then categorised into 'no symptoms' (i.e. no; level 1), 'mild or moderate symptoms' (i.e. mild/moderate; level 2, and 3), and 'severe symptoms' (i.e. severe; level 4). A comorbid score was also calculated using the HADS-A and HADS-D sub-scales where 'no' in HADS-A or HADS-D, was considered 'no comorbid symptoms', 'mild/moderate' in HADS-A or HADS-D was considered 'mild/moderate comorbid symptoms', and 'severe' in HADS-A or HADS-D was considered 'severe comorbid symptoms'. The EQ-5D-3L anxiety or depression domain was dichotomised into 'I am not anxious or depressed' (i.e. no; level 1) and 'moderately or severely anxious or depressed' (i.e. yes; level 2 or 3).

However, the convergent validity of the EQ-5D-3L anxiety or depression domain was assessed by examining the correlation with HADS scores categorised into two levels 'no symptoms' (i.e. no; level 1), and 'mild or moderate or severe symptoms' (i.e. yes; level 2, 3 and 4).[141] A comorbid score was also calculated using the HADS-A and HADS-D sub-scales. Were 'no' in HADS-A and/or HADS-D, was considered 'no comorbid symptoms', and 'yes' in HADS-A and/or HADS-D was considered 'mild or moderate or severe comorbid symptoms'. Validity coefficients were computed as Spearman's rank correlation coefficients (r), with $r > 0.5$ considered as a strong correlation, 0.3 to 0.5 as a moderate correlation and 0.2 to 0.3 as a weak correlation.[142]

The sensitivity (the ratio between true positives and positives), the specificity (the ratio between true negatives and negatives), and the area under the receiver operator characteristics (AU-ROC) were also calculated.[143] An AU-ROC of 0.50 was considered no discrimination, 0.70 to 0.80 was considered acceptable, 0.80 to 0.90 was considered excellent, and more than 0.90 was considered outstanding.[144] Any participant who did not complete either of the HADS sub-scales were considered missing, and not included in the analyses.

8.4.6.2 The association of additional ICHOM variables with anxiety or depression

Feasibility, including response rates and missing data, of the 6 additional questions based on the ICHOM Standard Care Set for Stroke was assessed.

All analyses was conducted using Stata version 15 (StataCorp LP, College Station, TX, USA) and statistical significance was set at a p-value of 0.05.

8.5 Preliminary results

8.5.1 Summary of responses to the EQ-5D-3L and HADS

Until the 31 October 2018, surveys from 53 AuSCR registrants has been received. Overall 37 completed the EQ-5D-3L including the anxiety or depression domain (70% response rate). Forty-three participants completed the HADS survey (81% response rate). Characteristics of the included 37 participants are presented in Table 8.2. The median age of participants was 74 years (Q1, Q3: 64, 81); 42% were female, and a majority were born in Australia.

Table 8.2. *Demographic characteristics of studied population with stroke*

Variables	**Follow-up**
Sample size	37
Age (years)	
median (Q1, Q3)	74 (64, 81)
Female, n (%)	15 (42)
Born in Australia, n (%)	27 (73)
Interpreter required, n (%)	0 (0)
In hospital stroke, n (%)	2 (5)
Ischaemic, n (%)	28 (76)
Haemorrhage, n (%)	6 (16)
TIA, n (%)	2 (5)
Unknown, n (%)	1 (3)
Unable to walk on admission, n (%)*	22 (59)

Q1: Quartile 1, Q3: Quartile 3, TIA: Transient Ischaemic Attack, * missing data for 8 participants

Using the EQ-5D-3L anxiety or depression domain, 57% reported having no problems with anxiety or depression (level 1), 32% reported having moderate problems with anxiety or depression (level 2), and 11% reported having severe problems with anxiety or depression (level 3; Table 8.3).

The proportion of participants who reported having none, mild/moderate or severe problems (i.e. across 3 categories) with anxiety and depression using the HADS-A and HADS-D is also shown in Table 8.3. The median HADS-A score was 4 (Q1, Q3: 2, 8) with 24% screening positive for possible anxiety symptoms (levels 2-4). The median HADS-D score was 4 (Q1, Q3: 2, 7) with 35% screening positive for possible depressive symptoms (levels 2-4).

Table 8.3. *Distribution of EQ-5D-3L anxiety or depression domain and HADS responses at AuSCR follow-up between 90 to 180 days*

Categories*	Follow-up N =37*			
	EQ-5D-3L anxiety or depression domain	Hospital Anxiety and Depression Scale		
		HADS-A	HADS-D	HADS-A and/or HADS-D
All	n (%)	n (%)	n (%)	n (%)
No problems	21 (57)	28 (76)	24 (65)	33 (89)
Moderate problems	12 (32)	5 (13)	11 (30)	2 (5)
Severe problems	4 (11)	4 (11)	2 (5)	2 (5)
Males (n=21)				
No problems	12 (57)	16 (76)	13 (62)	19 (90)
Moderate problems	7 (33)	3 (14)	7 (33)	1 (5)
Severe problems	2 (10)	2 (9)	1 (5)	1 (5)
Females (n=15)				
No problems	9 (60)	11 (73)	10 (67)	13 (87)
Moderate problems	4 (27)	2 (13)	4 (27)	1 (7)
Severe problems	2 (13)	2 (13)	1 (7)	1 (7)

*data presented as N (%); Data for sex available for 36 participants (missing for n=1)

8.5.2 Convergent validity of EQ-5D-3L in screening for anxiety symptoms

A strong correlation was observed between the EQ-5D-3L anxiety or depression domain and HADS-A (rho = 0.65, p=<0.001). The EQ-5D-3L anxiety or depression domain against the HADS-A observed an excellent AU-ROC (0.80; 95% CI: 0.66, 0.94). Sensitivity and specificity were 89% and 71%, respectively (Figure 8.2).

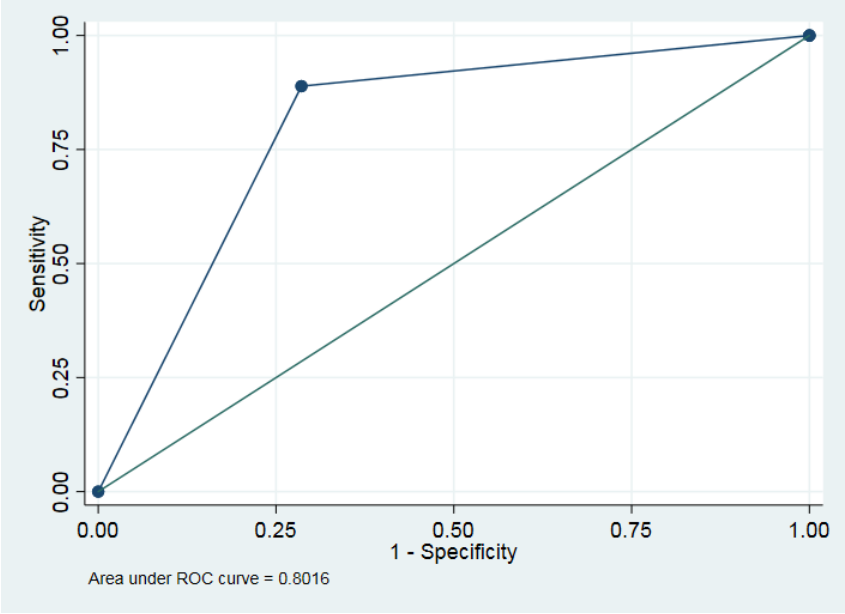

Figure 8.2. *Overall AU-ROC for the performance of EQ-5D-3L anxiety or depression domain and HADS-A in screening for anxiety symptoms (N=37).*

8.5.3 Convergent validity of EQ-5D-3L in screening for depression symptoms

A strong correlation was observed between the EQ-5D-3L anxiety or depression domain and HADS-D (rho = 0.68, p=<0.001). The EQ-5D-3L anxiety or depression domain against the HADS-D observed an excellent AU-ROC (0.82; 95% CI: 0.69, 0.95). Sensitivity and specificity were 85% and 79%, respectively (Figure 8.3).

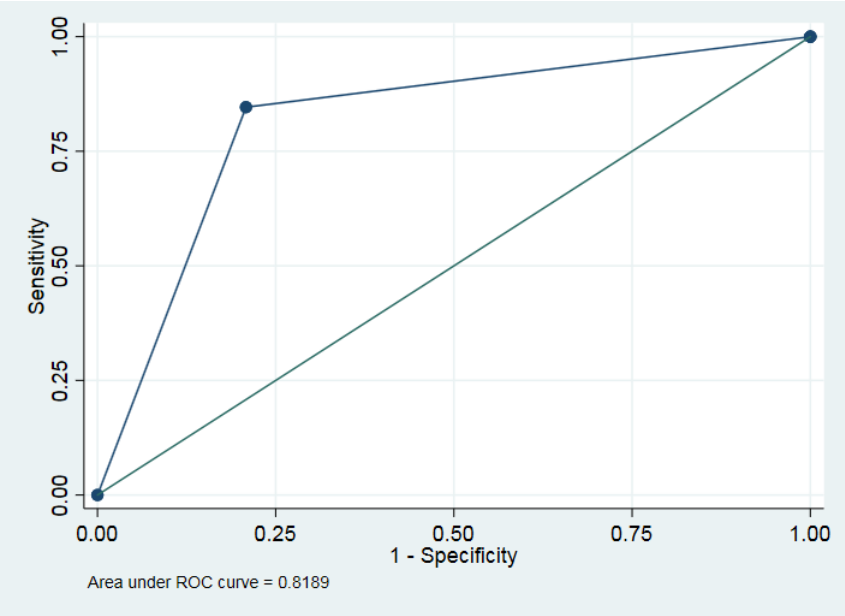

Figure 8.3. *Overall AU-ROC for the performance of EQ-5D-3L anxiety or depression domain and HADS-D in screening for anxiety and depressive symptoms (N=37).*

8.5.4 Convergent validity of EQ-5D-3L in screening for comorbid anxiety or depression

A moderate correlation was observed between the EQ-5D-3L anxiety or depression domain and comorbid anxiety or depression symptoms (rho = 0.47, p=0.002). The EQ-5D-3L anxiety or depression domain against the comorbid anxiety or depression symptoms observed an excellent AU-ROC (0.82; 95% CI: 0.62, 1.00). Sensitivity and specificity were 100% and 64%, respectively (Figure 8.4).

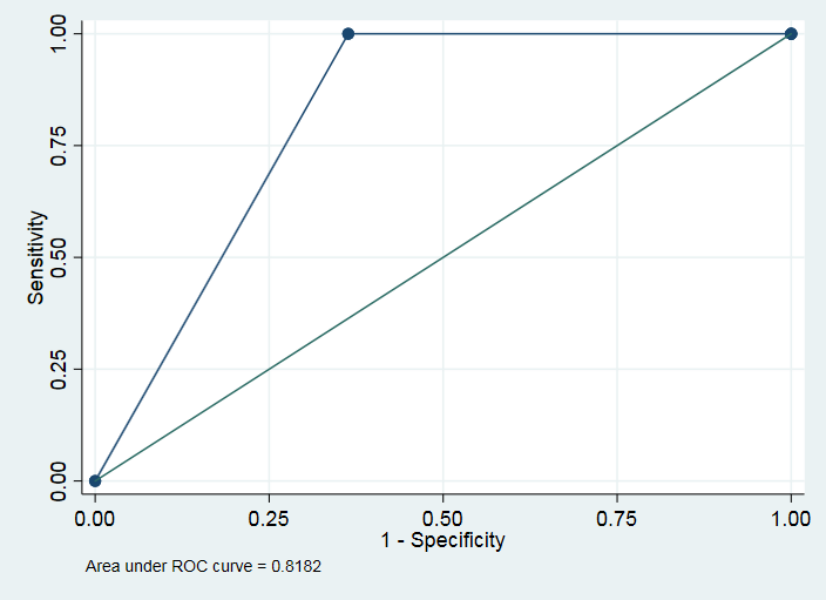

Figure 8.4. *Overall AU-ROC for the performance of EQ-5D-3L anxiety or depression domain and combined HADS-A and HADS-D in screening for anxiety and depressive symptoms.*

8.5.5 Feasibility of the explanatory factors that may be associated with anxiety or depression.

Forty-three participants completed the additional questions based on the ICHOM survey (81% response rate). Data were only comparable for 37 participants and will be the basis of a future publication. Table 8.4 provides a summary of the responses to these questions based on the presence of anxiety or depression as self-reported from the EQ-5D-3L domain responses.

Table 8.4. *Summary of responses to additional questions based on the ICHOM survey*

Anxiety/depression reported at 90–180 days following stroke/TIA using EQ-5D-3L	**Yes (n=16) N (%)**	**No (n=21) N (%)**	**p value**
ICHOM extra questions			
Ability to think			
Excellent	1 (6)	1 (5)	
Very good	3 (19)	5 (24)	
Good	4 (25)	2 (10)	
Fair	8 (50)	7 (33)	
Poor	0 (0)	6 (28)	0.154
Need tube for feeding			
No	16 (100)	21 (100)	
Yes	0 (0)	0 (0)	N/A
Problems with communications or understanding			
No	10 (63)	19 (90)	
Yes	6 (37)	2 (10)	0.041
Satisfaction with social activities and relationships			
Excellent	3 (19)	3 (19)	
Very good	3 (19)	3 (19)	
Good	5 (31)	5 (31)	
Fair	4 (25)	4 (25)	
Poor	1 (6)	1 (6)	0.569
Fatigue in the past 7 days			
None	2 (13)	0 (0)	
Mild	5 (31)	5 (26)	
Moderate	3 (19)	9 (47)	
Severe	4 (25)	3 (16)	
Very severe	2 (12)	2 (11)	0.295
Other			
On medications for anxiety or depression			
No	12 (80)	17 (81)	
Yes	3 (20)	4 (19)	0.943

8.6 Discussion

To our knowledge, this is the first study on the convergent validity, sensitivity and specificity of the EQ-5D-3L anxiety or depression domain in the stroke population. With a strong correlation to the reference measure (HADS), and acceptable sensitivity and specificity, the EQ-5D-3L anxiety or depression domain may be a suitable tool to screen for anxiety and depressive symptoms in survivors of stroke at 90-180 days following stroke. Preliminary data were presented because comparable data were only available for 37 participants at the time of initial analyses. Data collection is currently ongoing. Nonetheless, strong indications of the sensitivity and specificity of the EQ-5D-3L anxiety or depression domain against the HADS.

The convergent validity of the EQ-5D-3L anxiety or depression domain, with HADS as the reference measure, has only been studied in patients with anxiety and depression disorders, and acute lung injury before. [140, 145] In these studies, the correlation of the EQ-5D-3L anxiety or depression domain was strongest with HADS-A, and only moderate with HADS-D. However, in my study, the preliminary correlation was strongest with HADS-D (rho: 68) and then EQ-5D-3L anxiety or depression domain with HADS-A (rho: 65).

More importantly, for screening purposes, a high sensitivity is more important than a high specificity.[146] Having a high specificity may be important for a diagnostic tool, where those correctly identified without the disease, need not undergo invasive treatments. In the case of population screening for anxiety or depression, it is important to be able to identify those with a serious but treatable disorder. In my study, the sensitivity was greatest at 100%, with a high AU-ROC, in comorbid conditions, suggesting that the EQ-5D-3L may be very sensitive in identifying those at risk in either disorders, anxiety or depression. Moreover, when assessing the disorders separately, an optimal balance between sensitivity and specificity was achieved

when anxiety or depression was defined by a score of 8 or above on both HADS-A and HADS-D, respectively.

Several factors need to be considered to use the EQ-5D-3L survey for the purpose of screening for anxiety or depression symptoms. The study period for responding to this question based on the perception of the respondent 'today', and the domain refers to the severity of the problem, and not the frequency. Moreover it is not possible to separate out symptoms of anxiety from symptoms of depression. The main advantage of the EQ-5D-3L is that it is short and easy to complete in a number of settings and often routinely collected. Since the EQ-5D-3L is not disease-specific but a general health outcome survey, it can allow comparisons across a number of clinical populations. Moreover, the EQ-5D-3L offers the ability to screen for anxiety and depressive symptoms using only one question representing, 'anxiety or depression domain'. To use the HADS as a screening tool, one needs to answer all of the 14 items, and apply the scoring algorithm to obtain the respective anxiety and depression scores. Interestingly, in this study the response rate for the EQ-5D-3L anxiety or depression domain was lower than the HADS response rate (70% vs 81%). Nevertheless, given that the EQ-5D-3L is increasingly being used in large population-based studies[118, 123]and clinical registries such as the AuSCR[124] to assess health-related quality of life, I provide evidence that it can be reliably used for routine mood disorders screening in the stroke population.

Several limitations should be considered in the interpretation of the results of this study. First, anxiety and depressive symptoms assessment was based on self-report, so may be subjected to responder bias. Secondly, although the HADS is used as an established screening measure of anxiety and depression symptoms as a reference standard, it is not a 'gold standard'. Therefore, comparing the performance of the EQ-5D-3L to clinical assessments of these symptoms would provide a more robust conclusion about its suitability for this purpose. Nevertheless, in our

study of survivors of stroke, the EQ-5D-3L anxiety or depression domain did demonstrate good convergent validity with a widely used disease-specific measures of anxiety or depression. Thirdly, the EQ-5D-3L anxiety or depression domain cannot delineate between anxiety and depression. These disorders are often comorbid, but are separate disorders with different treatment strategies. An important limitation of dichotomising scores in HADS into "no" and "yes" is that information on the severities of the disorder is not accounted for in the group of "yes". However, categorisation allows the data to be comparable with the EQ-5D-3L, and is based on the manuals of both surveys.[129, 133]

This study provides information regarding the usefulness of the EQ-5D-3L for population health research of initial clinical screening purposes (i.e., to identify possible 'sub-clinical symptoms'). Despite ongoing concerns regarding the use of generic quality of life measures for clinical decision making, such as the EQ-5D-3L, in mental health,[147] our findings lend some support for the possible use of the EQ-5D-3L for population screening purposes to report the prevalence of conditions such as anxiety or depression, in the stroke population.

In addition, in the preliminary data obtained, the response rate to the additional questions based on the ICHOM survey was quite high. This suggests that these additional questions may be collected on an ongoing basis as part of AuSCR follow-up. However, the association of these additional variables with anxiety or depression could not be assessed with this dataset due to the small sample size.

8.7 Conclusion

This is the first study to assess the convergent validity, sensitivity and specificity of the EQ-5D-3L anxiety and depression domain as a measure of anxiety or depression in the stroke population. The EQ-5D-3L anxiety or depression domain was found to be a suitable tool for

screening of anxiety and depressive symptoms in survivors of stroke at 90-180 days following stroke. The tool presents a unique opportunity for a standardised approach for routine mental health screening as part of large clinical registries such as the AuSCR.

Chapter 9: The potential for movement-based mindfulness interventions on moderating risk factors for stroke

9.1 Overview

In Chapters 6 and 7, the strategies for early intervention (i.e. when in hospital or transitioning to home) that could help reduce the impact of anxiety or depression following stroke was highlighted. In Chapter 8, I undertook a validation study on the EQ-5D-3L anxiety or depression domain to assess if this survey could be used as a potential screening tool for patients with a high risk of developing these mood disorders. In this chapter and the next (Chapter 10), I provide the evidence base for a community-based intervention that could help reduce some of the long-term impacts of stroke, including problems with anxiety or depression. Behavioural therapies using MBIs, such as yoga, may be one way of addressing these problems.[23-27] However, differences in the types of MBIs used, and a lack of controlled studies, make it difficult to determine the efficacy of MBIs for survivors of stroke.[28] Therefore, further research is required to assess the suitability of MBIs, within the context of stroke, as a recovery option.

In this chapter, I explore how MBIs may have a role in moderating risk factors for stroke in order to prevent recurrent events. This chapter and the following chapter address the fifth aim of my thesis: to systematically evaluate published evidence on the effectiveness of MBIs for

moderating risk factors of stroke, and reducing the risk of poor patient outcomes or comorbidity, including anxiety or depression.

The aim of the following paper was to provide a scoping review of the existing evidence of how MBIs may influence some of the modifiable risk factors for stroke and CVD. This paper was the first review to comprehensively explore the potential effectiveness of yoga and tai chi, in moderating modifiable risk factors for stroke and CVD, thus expanding the scope of intervention types and focus. My contribution is at 80%, and the nature of my contribution was concept, literature search, data management, analysis, interpretation and writing of first draft of the manuscript.

The following paper was published in Future Neurology (2018; Vol 13(4): 239-252).

9.2 Published paper

Understanding the potential for yoga and tai chi interventions to moderate risk factors of stroke – a scoping review

Thayabaranathan T, Immink MA, Stevens P, Hillier S, Thrift AG, Brodtmann A, Carey L, Kilkenny MF, Cadilhac DA

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Review

Future NEUROLOGY

Understanding the potential for yoga and tai chi interventions to moderate risk factors for stroke – a scoping review

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Following an initial stroke, approximately two in five people will experience another stroke within 10 years. Recurrent strokes are often more severe and fatal. Mindfulness-based interventions (MBIs) that use movement to focus attention, such as yoga and tai chi, may offer a lifestyle strategy in addition to standard rehabilitation options, for moderating risk factors for stroke. We conducted a scoping review to explore the potential for yoga or tai chi to moderate modifiable risk factors for stroke. 26 papers between 1985 and 2017 were identified using online and gray literature databases. Overall, yoga or tai chi may reduce hypertension (up to 16/9 mmHg), and to a lesser extent some lipid and blood sugar levels. Study designs were heterogeneous. Further research on mediating pathways of MBIs, such as yoga or tai chi, on modifiable risk factors for stroke is warranted.

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Keywords: lifestyle • mindfulness • risk factors • review • stroke • tai chi • yoga

Stroke is a major neurological disease that accounts for nearly 5.7 million deaths and 16 million new stroke events globally in 2005. It is projected to cause 7.8 million deaths and 23 million new stroke events by 2030 [1]. Survivors of stroke are at an increased risk of recurrent stroke, being approximately 16% within 1 year, 32% within 5 years and 43% within 10 years [2]. Critically, the consequences of recurrent strokes are more severe than initial strokes and is a major cause of further comorbidities and mortality, thereby causing greater burden on survivors, families and healthcare systems [3].

Modifiable risk factors for stroke [4] include smoking, high blood pressure, high cholesterol levels, physical inactivity, overweight, diabetes, poor diet, mood and excessive intake of alcohol. On the other hand, risk factors such as family history, ethnicity and age cannot be changed [4]. There is also evidence that mental health comorbidities, such as stress, anxiety and depression, which are often experienced by patients following a stroke [5] can increase the risk of future stroke events [6], and mortality [7]. Individuals with multiple risk factors are at much greater risk of suffering from a recurrent stroke or cardiovascular events than those with a single risk factor [8–10]. Ideally, modifiable risk factors should be identified early, and managed with effective treatments as recommended in clinical practice guidelines. Some risk factors for stroke are the same as in cardiovascular diseases (CVD; e.g., high blood pressure, cholesterol and diabetes), and therefore the benefits of secondary prevention strategies may relate to both conditions [11].

Behavioral (lifestyle) strategies, such as increasing physical activity and improving diet, and pharmacological interventions have important roles in reducing the future risk of recurrent stroke [12]. Exercise has well-documented health benefits, but survivors of stroke often find it difficult to participate in exercise regimens particularly when

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they have significant residual physical impairments [13]. There are a range of mindfulness-based interventions (MBIs) and these include meditation, mindfulness-based stress reduction, yoga, tai chi, qigong or reiki. The major common component in MBIs is the aim of establishing states of mindfulness where purposeful attention is directed to the present moment enabling a full awareness of experiences in a nonjudgemental and accepting manner [16]. MBIs that include movement to focus attention may have a relevant role after stroke. Movement-based MBIs are thought to promote disposition for calm alertness, composure and acceptance of body through training with movement-based techniques that emphasise focusing attention on movement [17–19]. In people with stroke, the ability to concentrate can be affected. Therefore, movement-based MBIs, such as yoga and tai chi, may be helpful in developing concentration levels in people who have difficulties with concentration. Yoga and tai chi are emerging as promising adjunct therapies, in addition to standard recommended rehabilitation options, for reducing risk factor profiles or comorbidities in patients with stroke or CVD in western countries [5,14,15].

In this scoping review, we aimed to synthesize the existing evidence of how yoga and tai chi may influence some of the modifiable risk factors for stroke and CVD.

Methods

Identifying the research question

The research question, developed using the Population, Intervention, Comparison, Outcome (PICO) framework [20] was: 'What is the current state of knowledge on the potential of how yoga and tai chi may influence some of the modifiable risk factors for stroke and CVD?'

Ethics & dissemination

Formal ethics was not required as individual patient data were not collected. We conducted a scoping literature review. The scoping review was guided by Arksey and O'Malley's methodological framework [21] which includes: identifying the research question; searching for relevant studies; selecting studies; charting the data and collating, summarizing and reporting the results. The aim of a scoping review is to map existing literature in a given field when the topic is of a heterogeneous nature and has not been extensively reviewed [22]. While the scoping review has a number of similarities to a systematic review, it does not typically involve quality assessment of the included literature, and the findings are reported in a narrative format.

Identifying relevant studies

An electronic database search was conducted for original studies or review articles, using MEDLINE, CINAHL, Scopus, Google Scholar and The Cochrane Library, searching dates between 1 January 1985 and 31 December 2017 using the keywords: pathophysiology or pathways and stroke or cardiovascular diseases or brain and mindfulness or meditation or yoga or tai chi for each of the databases. The reference lists of included papers were also manually searched to identify any potentially relevant studies or reviews not found in the electronic search. Only full papers, in the English language, were considered.

Study selection

Each potentially eligible publication was independently assessed for inclusion and quality. One author (TT) performed the initial review of publications using the following inclusion criteria: studies with a focus on yoga- or tai chi-based MBIs and their impact on various modifiable stroke risk factors, no preselected criteria for assessment time periods, settings included primary care hospitals, mental health centers and community health, studies that were randomized controlled, controlled or descriptive and had retrospective or prospectively collected data, multi-case and single-case studies without original data and any systematic reviews that highlighted the impact of MBIs on any modifiable risk factor.

The following criteria were set for exclusion of studies: did not include yoga or tai chi as the MBI intervention, programs that were not related to chronic illnesses, studies where stroke risk factors were not investigated, and finally opinion pieces and conceptual studies. TT filtered abstracts or full articles using the eligibility criteria. Other authors provided input if uncertainty for inclusion was raised, or if they were aware of other relevant papers not identified.

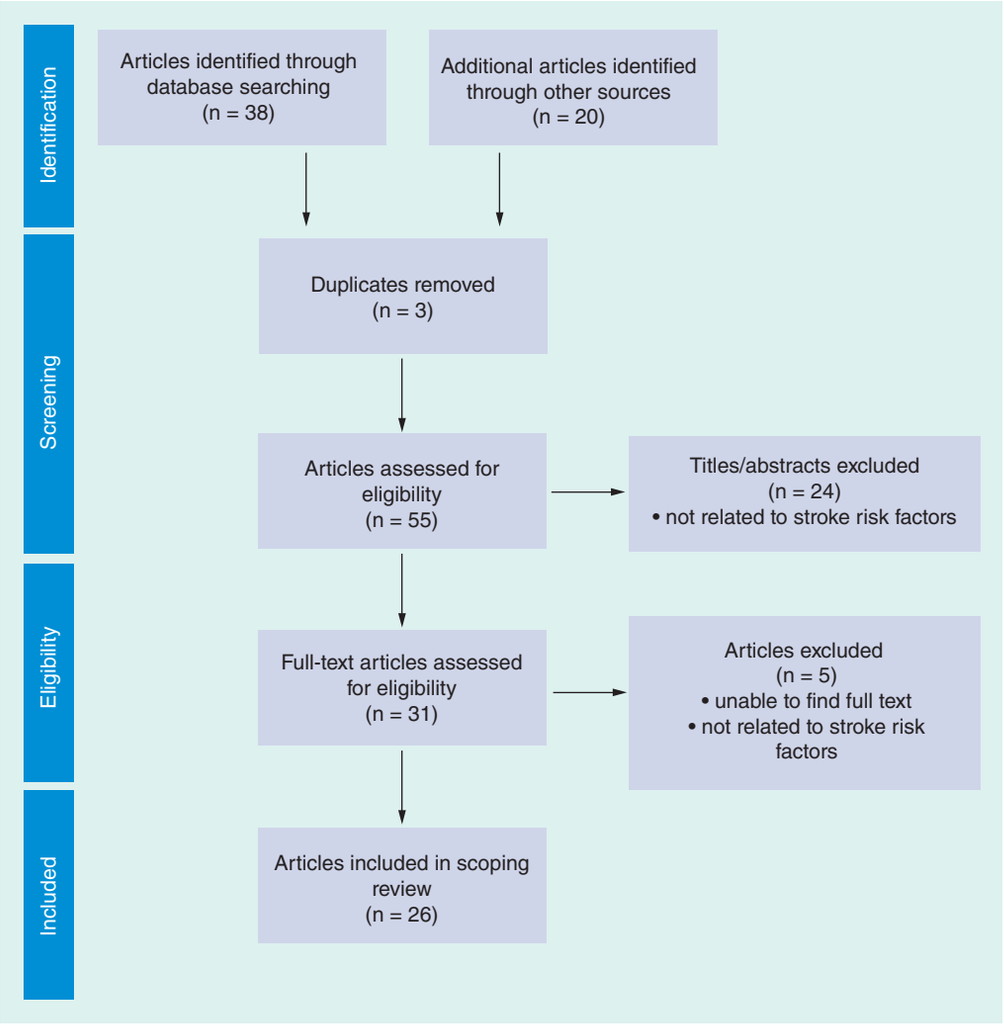

Figure 1. PRISMA flow diagram showing study selection.

Charting the available evidence

Articles that met the inclusion criteria were reviewed in detail. A Word-based (Microsoft Office version 15) extraction table was designed and used to summarize data using the following descriptors: study (year), article type, study design and targeted population, participant characteristics, sample size, MBI frequency and type, risk factors/pathways assessed, relevant results and limitations.

Results

In total, 55 articles were identified (Figure 1). Following eligibility assessments, 26 articles; 19 original and seven reviews (Table 1) were included in this review based on the selection criteria. Among the 19 original research studies, 15 studies were pilot randomized controlled trials [23–37] and four were before-after intervention designs [38–41]. Overall there were 15 articles on the effects of yoga on moderating risk factors for stroke and CVD [5,23–28,38–45] and 11 articles associated with tai chi [30–37,46–48]. In particular, authors of 21 articles described the impact of the MBI on the traditional stroke risk factors such as blood pressure, cholesterol and blood glucose levels [24–28,30–38,40,42–44,46–48].

Table 1. Summary of studies.

Study (year)	Article type	Study design	Study population	Participant characteristics	Sample size	MBI frequency and type	Risk factors assessed	Change observed	Important limitations
Hagins *et al.* (2013) [43]	Review	–	Patients with hypertension	–	–	No specific style of yoga	Blood pressure	SBP: -3.5 (-4.7 to-2.4) DBP: -2.5 (-2.6 to -1.5)	English articles only Included studies that reported complete blood pressure values
Okonta (2012) [44]	Review	–	Patients with hypertension	–	–	No specific style of yoga	Blood pressure Cholesterol Blood glucose weight	Significant reduction in BP, blood glucose, cholesterol and weight	English articles only
Anderson *et al.* (2008) [42]	Review	–				Meditation	Blood pressure	SBP: -4.7 (-7.4 to -1.9) DBP: -3.2 (-5.4 to -1.3)	None
Thayabaranathan *et al.* (2017) [5]	Review	–	Patients with stroke		118	Yoga	Anxiety Depression	Between group differences State anxiety symptoms: 6.05, 95% CI:-0.02–12.12; p = 0.05 Depression: 0.50, 95% CI:-0.01–1.02; p = 0.05	Mixed methodologies
Riley *et al.* (2015) [45]	Review	–	–	–	–	Yoga	Stress	Reduction in stress levels	Small sample sizes Lack of control groups nonrandomization
Lauche *et al.* (2017) [47]	Review	–	Patients with hypertension, high cholesterol, diabetes and obesity		1604	Tai Chi	Blood pressure blood glucose weight	SBP: -15.55 (-21.16 to -9.95) DBP: 10.66 (-14.90 to -6.43) FBG: -9.6 (-17.28 to -1.91) BMI: -1.65 (-3.11 to -0.20)	Language Heterogeneity Unclear risk of bias
Wang *et al.* (2013) [48]	Review	–	Patients with hypertension	Age: 35–75 years	1371	Tai Chi	Blood pressure	Systolic BP: -12.43 (-12.62, -12.24) < 0.00001 Diastolic BP: -6.03 (-6.16, -5.90)	Small sample size Poor methodological qualities of included trials
Wong *et al.* (2014) [28]	Original	RCT	Postmenopausal women with obesity	Age: 50–65 years	28	Yoga 50 min $\times$ 3 days per week for 8 weeks	Blood pressure	There were significant decreases in brachial SBP ($p < 0.05$), aortic SBP ($p < 0.01$), aortic DBP	None
Mourya *et al.* (2009) [27]	Original	RCT	Patients with hypertension	Age: 20–60 years	60	Yoga 30 min $\times$ 7 days per week for 12 weeks	Blood pressure	SBP: -4.6 (-7.4 to -1.9) DBP: -3.2 (-5.4 to -1.3)	Repeated measures of blood pressure Unable to tease out effect of antihypertensive drug on autonomic functions
Gordon *et al.* (2008) [24]	Original	RCT	Patients with Type 2 diabetes	Mean age: 64	77	Hatha yoga 60 min $\times$ for 24 weeks + home practice	Blood glucose Blood cholesterol	FBG intervention vs control decreased by 29.48% and 27.43% respectively ($p < 0.0001$) Significant reduction in serum total cholesterol in both groups ($p < 0.0001$)	None

BMI: Body mass index kg/m^2 (95% confidence interval); DBP: Diastolic blood pressure; FBG: Fasting blood glucose mg/dl (95% confidence interval); HDL: High-density lipoprotein; LDL: Low-density lipoprotein; MBI: Mindfulness-based intervention; RCT: Randomized controlled trial; SBP: Systolic blood pressure mmHg (95% confidence interval); TG: Triglyceride.

Table 1. Summary of studies (cont.).

Study (year)	Article type	Study design	Study population	Participant characteristics	Sample size	MBI frequency and type	Risk factors assessed	Change observed	Important limitations
Manchanda *et al.* (2003) [25]	Original	RCT	Patients with coronary artery disease	Mean age (±SD): 51.5 (9.5)	42	Yoga 4 days at yoga centre + fortnightly evaluation	Blood cholesterol Weight	Decrease in body weight. serum total cholesterol, LDL and TG levels	Small sample size Not blinded Self-reported yoga and diet compliance
Bernardi *et al.* (2000) [38]	Original	Before-after	Healthy males	Mean age: 29	12	Yoga controlled breathing 15 breaths/min for 3 min	Blood pressure	Decrease in blood pressure	None
Conrad *et al.* (2007) [39]	Original	Before-after	Patients with panic disorder	Mean age (±SD): 39.15 ± 15.58	13	Controlled breathing	Anxiety Depression	Decrease in anxiety and depression	Small sample size Not powered Patients were on medications
Lakkireddy *et al.* (2013) [41]	Original	Before-after	Symptomatic paroxysmal atrial fibrillation	Mean age (±SD): 60.6 ± 11.5	49	Yoga 60 min × 2 per week for 3 months	Atrial fibrillation Anxiety Depression	Symptomatic atrial fibrillation episodes (3.8 ± 3 v. 2.1 ± 2.6, $p < 0.001$), symptomatic non-AF episodes (2.9 ± 3.4 v. 1.4 ± 2.0; $p < 0.001$), asymptomatic AF episodes (0.1 ± 0.44 vs 0.04 ± 0.20; $p < 0.001$) Zung self-rated anxiety pre: 34.0 (31.5–37.0) post: 25.0 (23.0–30.0) Zung self-rated depression pre: 31.0 (27.0–37.0) post: 27.0 (22.0–31.0)	Lack of investigation on autonomic tone, systemic inflammatory markers, and endothelial function Small sample
Hunter *et al.* (2016) [40]	Original	Before-after	Patients with obesity	Mean age (±SD): 43 (12)	43	Bikram yoga 90 min × 3 per week for 8 weeks	Body composition Blood pressure	BMI Pre: 32.6 ± 4.3 Post: 32.2 ± 4.4 SBP Pre: 121 ± 18 Post: 118 ± 14 DBP Pre: 70 ± 11 Post: 68 ± 10	Lack of nonyoga time control group Small sample size Lack of measures providing physiological mechanisms
Mcdermott *et al.* (2014) [26]	Original	RCT	Healthy, risk of diabetes	Mean age (±SD): 47 (9.7) Males: 9	21	Yoga 75 min × 3–6 per week for 8 weeks	Blood pressure Weight Waist circumference Cholesterol Insulin resistance	Yoga vs control Weight: -0.8 ± 2.1 vs 1.4 ± 3.6, $p = 0.02$ Waist circumference -4.2 ± 4.8 vs 0.7 ± 4.2, $p < 0.01$ BMI -0.2 ± 0.8 vs 0.6 ± 1.6, $p = 0.05$). There were no between group differences in fasting blood glucose, postprandial blood glucose, insulin resistance	Cultural influence Small sample size

BMI: Body mass index kg/m^2 (95% confidence interval); DBP: Diastolic blood pressure; FBG: Fasting blood glucose mg/dl (95% confidence interval); HDL: High-density lipoprotein; LDL: Low-density lipoprotein; MBI: Mindfulness-based intervention; RCT: Randomized controlled trial; SBP: Systolic blood pressure mmHg (95% confidence interval); TG: Triglyceride.

Table 1. Summary of studies (cont.).

Study (year)	Article type	Study design	Study population	Participant characteristics	Sample size	MBI frequency and type	Risk factors assessed	Change observed	Important limitations
Brewer *et al.* (2011) [23]	Original	RCT	Treatment-seeking, nicotine-dependent adults	Mean age (±SD): 45.9 (10.2) Males: 54	88	Yoga 90 min × 2 per week for 4 weeks + home-based	Smoking	Reduction in cigarette use and maintained these gains during follow-up (F = 11.11, p = 0.001) Participants also exhaled reduced amount of carbon monoxide at the end of treatment vs control (36 vs 15%, p = 0.063), which was sustained significantly at the 17-week follow-up (31 vs 6%, p = 0.012)	Single site Moderate sample size Short intervention duration
Chen *et al.* (2010) [46]	Original	RCT	Patients with Type 2 diabetes and obesity	Mean age (±SD): 59. (6.2) Male: 25	56	Tai Chi 60 min × 3 per week for 12 weeks	Blood glucose BMI Cholesterol	Blood glucose did not decrease (8.9 vs 8.3, p = 0.064) BMI (33.5 vs 31.3, p = 0.038) triglyceride (21447 vs 171340.012, p = 0.012) HDL (3816 vs 4518; p = 0.023) tended to decrease from baseline (2.660.78 vs 2.310.55; p = 0.035)	Nonexercising control group Influence of change in diet
Dechamps *et.al.* (2009) [30]	Original	RCT	Women with obesity	Mean age (±SD): 44.4 (11.9)	21	Tai Chi 120 min × 1 per week for 10 weeks + diet program vs exercise + diet	Weight Body composition Heart rate Blood pressure Mood	Between group Weight: -1.8 (-8.5 to 4.9) BMI: -0.6 (-3.4 to 2.2) Heart rate: -12.5 (-28 to 3) SBP: -10.8 (-24.8 to 3.1) DBP: -2.3 (-14.5 to 9.8) Depression: -2.1 (-9.4 to 5.1)	Did not account for patient's expectations Small sample size
Lam *et al.* (2008) [31]	Original	RCT	Patients with Type 2 diabetes	Mean age (±SD): 63.2 (8.6)	53	Tai Chi 60 min × 2 per week for 12 weeks + 1 per week for further 12 weeks	Blood glucose Blood pressure Cholesterol	Between group measures not statistically significantly different	None
Liu *et al.* (2015) [32]	Original	RCT	Patients with abdominal obesity	Mean age (±SD): 52 (12) Males: 64	213	Tai Chi 90 mins × 3 per week for 12 weeks vs usual care	Mood Stress Blood glucose Blood pressure Cholesterol	Between group mean difference Depression: -5.6 units, $p < 0.001$), Anxiety (-2.3 units, $p < 0.01$), Stress (-3.6 units, $p < 0.001$) Glucose: 0.1 units, p = 0.43 SBP: 0.5 (p = 0.64) DBP: 0.9 (p = 0.15) TGL: 0.01 (p = 0.94)	Recruited patients with depression diagnosis – limits generalizability No active control group

BMI: Body mass index kg/m^2 (95% confidence interval); DBP: Diastolic blood pressure; FBG: Fasting blood glucose mg/dl (95% confidence interval); HDL: High-density lipoprotein; LDL: Low-density lipoprotein; MBI: Mindfulness-based intervention; RCT: Randomized controlled trial; SBP: Systolic blood pressure mmHg (95% confidence interval); TG: Triglyceride.

Table 1. Summary of studies (cont.).

Study (year)	Article type	Study design	Study population	Participant characteristics	Sample size	MBI frequency and type	Risk factors assessed	Change observed	Important limitations
Song *et al.* (2015) [33]	Original	RCT	Patients with obesity	Mean age (±SD): 59.6 (4.72)	15	Tai Chi 6 months	Cholesterol	Total cholesterol Pre: 6.92 ± 0.51 Post: 6.31 ± 0.44, $p < 0.05$ TG Pre: 2.37 ± 0.29 Post: 2.09 ± 0.25, $p < 0.05$ LDL Pre: 3.57 ± 0.32 Post: 3.20 ± 0.30, $p < 0.05$ HDL Pre:1.03 ± 0.22 Post: 1.05 ± 0.18	-
Sun *et.al.* (2015) [34]	Original	RCT	Patients with hypertension	Age: 45–80 years	266	Tai Chi 180 min for 3 weeks + home practice for 12 months	Blood pressure Weight	SBP: -0.15 (-0.25 to -0.04) p = 0.005 DBP: 0.24 (0.06 to 0.42) p = 0.01 BMI: 0.40 (-0.81 to 0.01) p = 0.05	Recruited patients from two regions in China Older adults
Tsai *et al.* (2003) [35]	Original	RCT	Patients with hypertension	Mean age (±SD): 51.6 (16.3)	76	Tai Chi 40 min × for 3 per week for 12 weeks	Blood pressure Cholesterol Anxiety	SBP: decrease by 15.6 DBP by 8.8 mmHg. Total cholesterol by 15.2 HDL: increased by 4.7 mg/dl. Anxiety decreased	Lack of active control
Tsang *et al.* (2008) [36]	Original	RCT	Patients with Type 2 diabetes	Mean age (±SD): 65 (8)	38	Tai Chi Mins × 2 per week for 16 weeks vs sham	Insulin resistance Blood glucose	There were no effects of time or group assignment on insulin resistance or blood glucose (-0.07 ± 0.4% Tai Chi vs 0.12 ± 0.3% Sham; p = 0.13) at 16 weeks. Improvement in blood glucose was related to decreased body fat (r = 0.484, p = 0.004) and improvement in insulin resistance related to decreased body fat (r = 0.37, p = 0.03)	Nonblinded outcome assessments
Zhang *et al.* (2008) [37]	Original	RCT	Patients with diabetes	Mean age (±SD): 57.4 (6.2)	20	Tai Chi 60 min × 5 days per week for 14 weeks	Blood glucose Cholesterol Blood pressure Heart rate	Between group measures not statistically significantly different	None

BMI: Body mass index kg/m^2 (95% confidence interval); DBP: Diastolic blood pressure; FBG: Fasting blood glucose mg/dl (95% confidence interval); HDL: High-density lipoprotein; LDL: Low-density lipoprotein; MBI: Mindfulness-based intervention; RCT: Randomized controlled trial; SBP: Systolic blood pressure mmHg (95% confidence interval); TG: Triglyceride.

A summary of the main findings on the effect of MBIs, in other words yoga and tai chi, on potentially moderating stroke risk factors

Blood pressure

In 16 articles a description of the association between MBIs and blood pressure was provided [26–28,30–32,34,35,38,40,42–44,47,48]. A meta-analysis of nine randomized controlled trials of the effect of MBIs on blood pressure provided evidence for a reduction in systolic blood pressure (by 4.7 mmHg) and diastolic blood pressure (by 3.2 mmHg) was observed among those in the intervention group compared with the control group [42]. In another meta-analysis, Hagins *et al.*, reported a similar decrease in blood pressure (systolic blood pressure by 3.5 mmHg and diastolic blood pressure by 2.5 mmHg) [43]. Moreover, a greater reduction in systolic blood pressure (range: 12.4–15.6 mmHg) and diastolic blood pressure (6.03–10.7 mmHg) was observed in two other meta-analyses [47,48]. In a study by Tsai *et al.,* patients with hypertension were observed to have a significant reduction in systolic blood pressure (15.6 mmHg) and diastolic blood pressure (8.8 mmHg) after completing a 12 weeks MBI intervention [35]. In two other randomized controlled trials (n = 266), there was no significant between group differences in blood pressure [31,32].

Cholesterol

Ten articles included evaluation of the effectiveness of practicing MBIs on cholesterol levels, and the results appeared to vary [24–26,31,32,35–37,44,46]. Tsai *et al.* found that in among 76 participants' total cholesterol levels were significantly reduced by 15.2 mg/dl ($p < 0.05$) [35]. A decrease in total cholesterol was also observed in another study by Song *et al.* (n = 15) [33]. MBIs appeared to reduce the levels of low density lipoprotein (LDL) by 0.37 mmol/l in patients with obesity [33]. A decrease in LDL was also seen in patients with type 2 diabetes and coronary heart disease [24,25]. However, the effectiveness of MBIs on regulation of high density lipoproteins (HDL) and triglycerides is less consistent. In the study by Tsai *et al.* (n = 76), HDL levels increased by 4.7 mg/dl [35]. Levels of HDL also increased post-MBI intervention in two other studies [33,46]. In one study, the levels of triglycerides were lowered by 0.28 mmol/l [33]. While in other studies, MBIs did not appear to affect participants' HDL or TG levels [25,32,37].

Diabetes

In nine studies there was promising evidence reported that MBIs can reduce diabetic symptoms [24,26,31,32,36,37,44,46,47]. In the study by Gordon *et al.*, those with type 2 diabetes (n = 77) and completing 6 months of a MBI intervention, had a reduction fasting blood glucose levels by 29.48% versus the conventional exercise group (27.43%; $p < 0.0001$) [24]. Reductions in blood glucose levels were also observed in one original study and two reviews [31,44,47]. However, in some studies no significant change in blood glucose or insulin sensitivity was observed in those at high risk [26,36,46]. Interestingly, an association between blood glucose and body fat was reported in one study [36].

Atrial fibrillation

Only one before-after study was identified that provided evidence of the effect of an MBI intervention on the burden of atrial fibrillation (AF) in 49 patients. MBI significantly reduced symptomatic AF episodes by 1.7% ($p < 0.001$), symptomatic non-AF by 1.5% ($p < 0.001$), and asymptomatic AF episodes by 0.08% ($p < 0.001$) [41].

Smoking & alcohol consumption

Only one randomized-controlled trial was identified that assessed the impact of an MBI on smoking cessation in 88 nicotine-dependent adults [23]. Those who completed the 4-week MBI intervention showed a greater rate of reduction in cigarette use and maintained these gains during follow-up ($F = 11.11$; $p = 0.001$). Participants also exhaled a reduced amount of carbon monoxide at the end of treatment (36 vs 15% [usual care]; $p = 0.063$), which was sustained at the 17-week follow-up (31 vs 6% [usual care]; $p = 0.012$) [23]. No studies were identified that assessed the effectiveness of an MBI on alcohol consumption.

Overweight

Eight articles were identified that investigated the effect of an MBI intervention on moderating weight or body composition factors (e.g., BMI or waist circumference) [25,26,30,34,40,44,46,47]. BMI was reduced by 1.65 kg/m^2 in one meta-analysis [47], and significant weight reduction was also observed in the other review article [44]. In a

study by McDermott *et al.*, 41 healthy adults with a high risk of developing diabetes, were randomized to either complete an 8-week MBI intervention (n = 21) or an active control arm (n = 20) [26]. Between group weight differences were statistically significant in those that completed the MBI intervention (0.8 kg) compared with the control arm (gained 1.4 kg, p = 0.02). Similarly, BMI and waist circumference also decreased by 0.2 kg/m^2 and 4.2 cm, respectively, in the intervention participants, whereas BMI and waist circumference increased by 0.6 kg/m^2 (p = 0.05) and 0.7 cm (p < 0.01) in the participants who were in the control group.

Mental health comorbidity

A recent systematic review by our group compiled evidence on the effectiveness of yoga on moderating anxiety and depression in survivors following stroke [5]. The MBI was found to be beneficial in significantly reducing state anxiety symptoms and depression in the intervention group compared with the control group (mean differences for state anxiety 6.05, 95% CI: -0.02–12.12; p = 0.05 and standardized mean differences for depression: 0.50, 95% CI: -0.01–1.02; p = 0.05). In a before–after study by Lakkireddy *et al.* (n = 49), in those who completed the MBI intervention (n = 21), a reduction was observed in self-reported anxiety (9 points) and depression (4 points) [41]. In another study by Liu *et al.,* those who completed the 12-week intervention had a significantly greater reduction in anxiety (2.3 units) and depression (5.6 units) when compared with the control group (usual care) [32]. Anxiety and depression symptoms were also decreased in two other studies [35,39]

Discussion

This scoping review provides a summary of the current literature of the potential changes to stroke and CVD risk factors that are altered by MBIs, such as yoga and tai chi. Previous reviews had a different focus evaluating only some of the benefits of yoga for stroke rehabilitation [16,49]. A recent review explored the impacts of tai chi on moderating risk factors for stroke for primary prevention [47]. In this current review, the effectiveness of yoga and tai chi, and its potential to moderate all modifiable risk factors for stroke and CVD was comprehensively explored with an expanded scope of intervention types and focus. In addition, MBIs, such as yoga and tai chi, may offer a lifestyle strategy in addition to other standard medical treatments to moderate some of the risk factors for stroke. Understanding the potential risk reduction associated with MBIs is important for both researchers and practitioners to inform the choice of adjunct interventions and training programs implemented for those with high risk of recurrent stroke or CVD.

MBIs appear to moderate some of the major traditional risk factors for stroke. It is well known that high blood pressure is the single biggest modifiable risk factor for stroke [4]. There is increasing evidence that MBIs can be a very effective and noninvasive way of reducing hypertension in people with stroke [28,43,44]. Some evidence suggests that MBIs, through deep breathing, balance and stabilizing of the autonomic nervous system, resulting in the regulation of blood pressure [27,50]. However, extended deep breathing can lead to a sustained lower heart rate [27]. Also, practicing an MBI when experiencing stress is postulated to manage the 'fight or flight' response to negative stress, and thereby result in a lowered blood pressure [42]. Nearly a third of adults around the world suffer from high blood pressure, and it is forecasted to increase globally in the future [51]. Therefore, it is important to find interventions to help reduce blood pressure. In the PROGRESS trial, which had the aim of assessing prevention of strokes by lowering blood pressure in patients with cerebral ischemia using medications, blood pressure was reduced by 12/5 mmHg [52]. Although the measures are clinically meaningful, the magnitude of change was greater in a recent MBI-based trial (16/9 mmHg) [41]. Since blood pressure is hard to control, may be MBIs could be used in addition to other evidence-based medical treatments.

There is growing evidence that MBIs can reduce contributing factors of a diabetic profile in patients with high risk and symptoms. It is suggested that the practice of physical movements and deep breathing in MBIs assist in contracting and relaxing specific areas of the abdomen which stimulates the pancreas, thereby increasing blood and oxygen supply to the tissues and enhancing production of insulin [53]. As previously described, MBIs have been shown to reduce LDL cholesterol and triglyceride levels, both of which are often accompanying symptoms for diabetes [24]. Furthermore, MBIs may reduce diabetic profile by decreasing oxidative stress and improving antioxidant status [24]. People with diabetes are also more likely to have high blood pressure, which further increases the risk of a recurrent stroke [4]. This further highlights that stroke is a complex neurological illness and survivors with multiple risk factors have a much greater risk of a recurrent stroke event.

Moreover, high cholesterol levels are an important risk factor for stroke and CVD events. However, there is differing evidence of the impact of MBIs on blood cholesterol levels. The underlying pathophysiological mechanisms that result in moderating the cholesterol levels is not well understood.

Patients with AF generally experience more severe strokes [54]. MBIs appear to be beneficial in patients with AF; however, the precise underlying mechanisms remain unclear. Some authors suggest that MBIs may prevent the initiation of AF and perpetuation through its many effects such as increasing the activity of the parasympathetic nervous system; suppressing extreme fluctuations in the autonomic nervous system components via the hypothalamic–pituitary–adrenal axis; and decreasing the progression of the arrhythmias by preventing or minimizing change in atrial structure or function [41].

The risk of stroke in people who frequently smoke tobacco is two to fourfold greater when compared with lifelong non-smokers or individuals who have quit smoking more than 10 years prior [55]. In this review, we identified only one study that assessed the effectiveness of a MBI intervention on ceasing smoking. However, the plausible mechanisms were not provided [23]. There were no articles on the impact of MBIs on alcohol consumption. In the future, it may be important for researchers to further assess the effectiveness of MBIs in moderating smoking or alcohol consumption, and to also determine whether changes in the addiction process or other mechanisms mediate the effects of MBIs in smoking or alcohol cessation.

Out of the many consequences experienced by survivors of stroke, depression and anxiety are frequently reported. Approximately 30–50% of survivors of stroke suffer from anxiety and depression following stroke [56,57]. This could be attributed to factors such as the initial shock of a stroke incident, and feelings associated with loss of independence and physical function [58]. These symptoms are distressing for both the patients and their caregivers, and negatively influence the patient's quality of life [59]. Although there is growing literature of the effectiveness of MBIs on improving mental health [5,39,41], the underlying pathophysiological changes to the areas in the body that control emotional health is unclear. One way in which MBIs may impact on anxiety and depression is the modulation of GABA in the brain, which is vital for a well-functioning brain and CNS [60,61]. GABA helps to promote the feelings of calmness inside the body and a reduction in GABA levels is associated with depression and anxiety [62]. The other two proposed pathways that MBIs may reduce stress levels are via increased activation of the peripheral nervous system, and reducing the levels of cortisol via the hypothalamic–pituitary–adrenal axis [45,60]. Research evidence suggests that MBIs may increase default mode brain network connectivity within regions that are important for a wide range of high-level processes, such as attention, planning, reasoning and cognitive flexibility [63,64]. It is thought that this, in turn, improves emotion regulation, stress resilience and stress-related health outcomes. There is an urgent need for well-designed neuroimaging studies that particularly investigate the changes, due to MBIs, in brain structure and connectivity that control emotional and mental health in survivors of stroke.

There is a need to further unpack these beneficial changes to pathophysiological pathways leading to therapeutic changes to some of stroke's most harmful risk factors. We suggest that the investigated mechanisms of change of MBIs on some of the risk factors for stroke may overlap and may not be independent pathways. Future research must investigate the shared work between the various pathways.

A limitation of this scoping review is the inability to directly compare studies due to the varying study designs and the diversity of the disease populations studied. At this stage, it is not possible to report on any definite differential effect between yoga and tai chi. Based on the current findings of limited studies, heterogeneity among interventions and research designs including differing duration of the MBI intervention, and the paucity of data in the stroke population, it might not be feasible to conduct a systematic review and meta-analyses in the near future, until more research is conducted with better methodological consistency. Nevertheless, the current growing literature provides possible explanations for the pathophysiological pathways that may be influenced by MBIs in those with risk factors for stroke and CVD and provides an insight for future investigations. We also acknowledge that there may be the potential for publication bias. Yoga and tai chi are alternative interventions and relevant research may have been missed if not published in the common medical or sciences databases that we searched. We attempted to address publication bias by undertaking a manual search of complementary medicine journals to check for any research on MBIs in stroke populations and by electronic searches of the web via Google to identify relevant gray literature. Co-authors working in the field Maarten A Immink and Philip Stevens were also consulted, and we believe it is unlikely that we missed any article relevant to this review.

Conclusion

This was a large and comprehensive scoping review to inform the field on the current state of knowledge on the potential relationship between yoga or tai chi and stroke, and CVD risk factors. Despite extensive searches, we identified limited research on the effect of yoga or tai chi on risk factors for stroke and CVD. It appears that the pathways by which yoga or tai chi improves risk factor profiles are very complex. However, there are numerous methodological limitations that impact the generalizability of these promising study findings. Further research conducted to explore the potential causal effects of yoga or tai and other MBIs on different organ systems, and risk factors for stroke and CVD is warranted.

Future perspective

The authors of this scoping review highlight the lack of high-quality studies on MBIs to moderate risk factors and prevent recurrent stroke. There are no studies that are comparable because of the variation in intervention duration, study population, study design and outcome measures. Ideally, the first step is to conduct a high-quality randomized controlled trial in which the targeted movement-based mindfulness intervention is investigated. The trials should include appropriate power calculations to identify the required sample size to see a minimum meaningful effect. Given the economic burden in healthcare, these studies should include clinical effectiveness and cost effectiveness analyses.

Executive summary

Background

- The chance of recurrent stroke after an initial event is >40% within 10 years, and they are often more severe and fatal.
- Ideally, modifiable risk factors should be identified and managed with effective secondary prevention strategies according to the available evidence as recommended in clinical guidelines.
- Mindfulness-based interventions (MBIs) are emerging as promising adjunct lifestyle strategy for moderating risk factors for stroke.

Evidence

- There is growing evidence that movement-based MBIs, such as yoga and tai chi, may moderate some of the highly prevalent modifiable risk factors for recurrent stroke, such as high blood pressure, diabetes, cholesterol and mental health.
- The effectiveness of MBIs on reducing excessive smoking and alcohol intake, or decrease the burden of atrial fibrillation is not very well understood.

Discussion

- There is emerging interest in assessing the effectiveness of MBIs on chronic illnesses, but very little is known about the potential mechanism in preventing recurrent stroke.
- Developing an understanding of the various action mechanisms of MBIs is critically important to design and execute maximally informative clinical research.
- People with diabetes also more likely to have high blood pressure, and high cholesterol which further increases the risk of a recurrent stroke.
- The underlying pathophysiological mechanisms of MBIs on the changes to risk factors for stroke appears to overlap.
- Neuroimaging research on brain structure and neural connectivity, with MBIs as an intervention, is still in its infancy.
- Direct comparison between studies is problematic because of the varying study designs and the diversity of the disease population studied.

Recommendations

- Well-designed large randomized controlled trials are needed to further explore the potential causal effects of MBIs on the modifiable risk factors for stroke.

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References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

1 Kuklina EV, Tong X, George MG, Bansil P. Epidemiology and prevention of stroke: a worldwide perspective. *Expert Rev. Neurother.* 12(2), 199–208 (2012).

2 Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the perth community stroke study. *Stroke* 35, 731–735 (2004).

3 Feng W, Hendry RM, Adams RJ. Risk of recurrent stroke, myocardial infarction, or death in hospitalized stroke patients. *Neurology* 74(7), 588–593 (2010).

•• **A recent systematic review highlighting the important modifiable risk factors for stroke across regions of the world and different types of stroke.**

4 O'donnell MJ, Chin SL, Rangarajan S *et al.* Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case–control study. *Lancet* 388(10046), 761–775 (2016).

• **A recent systematic review and meta-analyses that investigated yoga for its potential benefit for recovery in survivors of stroke.**

5 Thayabaranathan T, Andrew NE, Immink MA *et al.* Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis. *Top Stroke Rehabil.*24 (4),279–287 (2017).

6 O'donnell MJ, Xavier D, Liu L *et al.* Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case–control study. *Lancet* 376(9735), 112–123 (2010).

7 Williams LS, Ghose SS, Swindle RW. Depression and other mental health diagnoses increase mortality risk after ischemic stroke. *Am. J. Psychiatry* 161(6), 1090–1095 (2004).

8 Immink MA, Hillier S, Petkov J. Randomised controlled trial of yoga for chronic poststroke hemiparesis: motor function, mental health, and quality of life outcomes. *Top Stroke Rehabil.* 21(3), 256–271 (2014).

9 Lai SM, Alter M, Friday G, Sobel E. A multifactorial analysis of risk factors for recurrence of ischemic stroke. *Stroke* 25(5), 958 (1994).

10 Sacco RL. Risk factors and outcomes for ischemic stroke. *Neurology* 45(2 Suppl. 1), S10–14 (1995).

11 D'agostino RB, Vasan RS, Pencina MJ *et al.* General cardiovascular risk profile for use in primary care. *Circulation* 117(6), 743–753 (2008).

12 Esenwa C, Gutierrez J. Secondary stroke prevention: challenges and solutions. *Vasc. Health Risk Manag.* 11, 437–450 (2015).

13 Yi TI, Han JS, Lee KE, Ha SA. Participation in leisure activity and exercise of chronic stroke survivors using community-based rehabilitation services in seongnam city. *Ann. Rehabil Med.* 39(2), 234–242 (2015).

14 Johansson B, Bjuhr H, Ronnback L. Mindfulness-based stress reduction (MBSR) improves long-term mental fatigue after stroke or traumatic brain injury. *Brain Inj.* 26, 1621–1628 (2012).

• **Provides a detailed definition of mindfulness meditation.**

15 Kabat-Zinn J. Mindfulness-based interventions in context: past, present, and future. *Clin. Psychol.* 10(2), 144–156 (2003).

16 Lawrence M, Booth J, Mercer S, Crawford E. A systematic review of the benefits of mindfulness-based interventions following transient ischemic attack and stroke. *Int. J. Stroke* 8, 465–474 (2013).

17 Bastille JV, Gill-Body KM. A yoga-based exercise program for people with chronic poststroke hemiparesis. *Phys. Ther.* 84(1), 33–48 (2004).

18 Evans E, Tsao JCI, Sternlieb B, Zeltzer LK. Using the biopsychosocial model to understand the health benefits of yoga. *J. Complement. Integr. Med.* 6(1), doi:10.2202/1553-3840.1183 (Epub ahead of print). (2009).

19 Garfinkel M, Schumacher Jr HR. YOGA. *Rheum. Dis. Clin. North Am.* 26(1), 125–132 (2000).

20 Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. *ACP J. Club* 123(3), A12–A13 (1995).

21 Arksey H, O'malley L. Scoping studies: toward a methodological framework. *Int. J. Soc. Res. Methodol.* 8(1), 19–32 (2005).

22 Pham MT, Rajic A, Greig JD, Sargeant JM, Papadopoulos A, Mcewen SA. A scoping review of scoping reviews: advancing the approach and enhancing the consistency. *Res. Synth. Methods* 5(4), 371–385 (2014).

•• **Benefits of mindfulness training on smoking cessation compared with standard care in smoking addicts.**

23 Brewer JA, Mallik S, Babuscio TA *et al.* Mindfulness training for smoking cessation: results from a randomized controlled trial. *Drug Alcohol Depend.* 119(1), 72–80 (2011).

24 Gordon LA, Morrison EY, Mcgrowder DA *et al.* Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with Type 2 diabetes. *BMC Complement. Altern. Med.* 8, 21 (2008).

25 Manchanda SC, Narang R, Reddy KS *et al.* Retardation of coronary atherosclerosis with yoga lifestyle intervention. In: *Frontiers in Cardiovascular Health.* Kluwer Academic Publishers Boston 535–547 (2003).

•• **Demonstrates the effectiveness of yoga for the reduction of blood glucose in people with Type 2 diabetes.**

26 Mcdermott KA, Rao MR, Nagarathna R *et al.* A yoga intervention for Type 2 diabetes risk reduction: a pilot randomized controlled trial. *BMC Complement. Alt. Med.* 14(212), (2014).

27 Mourya M, Mahajan AS, Singh NP, Jain AK. Effect of slow- and fast-breathing exercises on autonomic functions in patients with essential hypertension. *J. Altern. Complement. Med.* 15(7), 711–717 (2009).

28 Wong A, Figueroa A. Eight week of stretching training reduced aortic wave reflection magnitude and blood pressure in obese postmenopausal women. *J. Hum. Hypertens.* 28, 246–250 (2014).

29 Chen P, Lin K-C, Liing R-J, Wu C-Y, Chen C-L, Chang K-C. Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. *Qual. Life Res.* 25(6), 1585–1596 (2016).

30 Dechamps A, Gatta B, Bourdel-Marchasson I, Tabarin A, Roger P. Pilot study of a 10-week multidisciplinary tai chi intervention in sedentary obese women. *Clin. J. Sport Med.* 19(1), 49–53 (2009).

31 Lam P, Dennis SM, Diamond TH, Zwar N. Improving glycaemic and BP control in Type 2 diabetes. The effectiveness of tai chi. *Aust. Fam. Physician* 37(10), 884–887 (2008).

32 Liu X, Vitetta L, Kostner K *et al.* The effects of tai chi in centrally obese adults with depression symptoms. *Evid. Based Complement. Alternat. Med.* Article ID:879712 (2015). doi:10.1155/2015/879712.

• **Highlights the effectiveness of tai chi on reduction of body fat in patients with obesity.**

33 Song Q, Yuan Y, Jiao C, Zhu X. Curative effect of Tai Chi exercise in combination with auricular plaster therapy on improving obesity patient with secondary hyperlipidemia. *Int. J. Clin. Exp. Med.* 8(11), 21386–21392 (2015).

•• **Highlights the effect of tai chi in managing a number of risk factors associated with hypertension in older Chinese adults.**

34 Sun J, Buys N. Community-based mind-body meditative tai chi program and its effects on improvement of blood pressure, weight, renal function, serum lipoprotein, and quality of life in Chinese adults with hypertension. *Am. J. Cardiol.* 116(7), 1076–1081 (2015).

35 Tsai JC, Wang WH, Chan P *et al.* The beneficial effects of Tai Chi Chuan on blood pressure and lipid profile and anxiety status in a randomized controlled trial. *J. Altern. Complement. Med.* 9(5), 747–754 (2003).

36 Tsang T, Orr R, Lam P, Comino E, Singh MF. Effects of Tai Chi on glucose homeostasis and insulin sensitivity in older adults with Type 2 diabetes: a randomised double-blind sham-exercise-controlled trial. *Age Ageing* 37(1), 64–71 (2008).

37 Zhang Y, Fu FH. Effects of 14-week tai ji quan exercise on metabolic control in women with Type 2 diabetes. *Am. J. Chin. Med.* 36(4), 647–654 (2008).

38 Bernardi L, Wdowczyk-Szulc J, Valenti C *et al.* Effects of controlled breathing, mental activity and mental stress with or without verbalization on heart rate variability. *J. Am. Coll. Cardiol.* 35(6), 1462–1469 (2000).

39 Conrad A, Muller A, Doberenz S *et al.* Psychophysiological effects of breathing instructions for stress management. *Appl. Psychophysiol. Biofeedback* 32(2), 89–98 (2007).

40 Hunter SD, Dhindsa MS, Cunningham E *et al.* Impact of hot yoga on arterial stiffness and quality of life in normal and overweight/obese adults. *J. Phys. Act. Health* 13(12), 1360–1363 (2016).

41 Lakkireddy D, Atkins D, Pillarisetti J *et al.* Effect of yoga on arrhythmia burden, anxiety, depression, and quality of life in paroxysmal atrial fibrillation. *J. Am. Coll. Cardiol.* 61(11), 1177–1182 (2013).

42 Anderson JW, Liu C, Kryscio RJ. Blood pressure response to transcendental meditation: a meta-analysis. *Am. J. Hypertens.* 21(3), 310–316 (2008).

•• **A systematic review examining the effects of yoga on blood pressure among individuals with prehypertension or hypertension.**

43 Hagins M, States R, Selfe T, Innes K. Effectiveness of yoga for hypertension: systematic review and meta-analysis. *Evid. Based Complement. Alternat. Med.* Article ID: 649836 (2013). doi:10.1155/2013/649836.

44 Okonta NR. Does yoga therapy reduce blood pressure in patients with hypertension?: an integrative review. *Holist. Nurs. Pract.* 26(3), 137–141 (2012).

45 Riley KE, Park CL. How does yoga reduce stress? A systematic review of mechanisms of change and guide to future inquiry. *Health Psychol. Rev.* DOI: 10.1080/17437199.17432014.17981778 (Epub ahead of print) (2015).

46 Chen SC, Ueng KC, Lee SH, Sun KT, Lee MC. Effect of t'ai chi exercise on biochemical profiles and oxidative stress indicators in obese patients with Type 2 diabetes. *J. Altern. Complement. Med.* 16(11), 1153–1159 (2010).

47 Lauche R, Peng W, Ferguson C *et al.* Efficacy of Tai Chi and qigong for the prevention of stroke and stroke risk factors: a systematic review with meta-analysis. *Medicine* 96(45), e8517 (2017).

48 Wang J, Feng B, Yang X *et al.* Tai Chi for essential hypertension. *Evid. Based Complement. Alternat. Med.* Article ID: 215254 (2013). doi:10.1155/2013/215254

49 Lazaridou A, Philbrook P, Tzika AA. Yoga and mindfulness as therapeutic interventions for stroke rehabiliation: a systematic review. *Evid. Based Complement. Alternat. Med.* Article ID: 357108, (2013). doi:10.1155/2013/357108.

50 Tang YY, Ma Y, Fan Y *et al.* Central and autonomic nervous system interaction is altered by short-term meditation. *Proc. Natl Acad. Sci. USA* 106(22), 8865–8870 (2009).

51 Mills KT, Bundy JD, Kelly TN *et al.* Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. *Circulation* 134(6), 441 (2016).

52 Van Gijn J. The PROGRESS trial: preventing strokes by lowering blood pressure in patients with cerebral ischemia. *Stroke* 33(1), 319 (2002).

53 Bhagat U, Singh A. Effect of diabetes on daily life and role of yogic activities on diabetes. *Int. J. Yoga* 2(2), 338–340 (2017).

54 Jørgensen HS, Nakayama H, Reith J, Raaschou HO, Olsen TS. Acute stroke with atrial fibrillation. *Stroke* 27(10), 1765 (1996).

55 Shah RS, Cole JW. Smoking and stroke: the more you smoke the more you stroke. *Expert Rev. Cardiovasc. Ther.* 8(7), 917–932 (2010).

56 Cadilhac DA, Lannin NA, Anderson CS *et al.* The Australian stroke clinical registry annual report 2015. The Florey Institute of Neuroscience and Mental Health. Victoria, Australia (2016).

57 Hackett ML, Pickles K. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *Int. J. Stroke* 9(8), 1017–1025 (2014).

58 Cumming TB, Blomstrand C, Skoog I, Linden T. The high prevalence of anxiety disorders after stroke. *Am. J. Geriatr. Psychiatry* 24(2), 154–160

59 Cerniauskaite M, Quintas R, Koutsogeorgou E *et al.* Quality-of-life and disability in patients with stroke. *Am. J. Phys. Med. Rehabil.* 91(13), S39–S47 (2012).

60 Streeter CC, Gerbarg PL, Saper RB, Ciraulo DA, Brown RP. Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. *Med. Hypotheses* 78(5), 571–579 (2012).

61 Streeter CC, Jensen JE, Perlmutter RM *et al.* Yoga asana sessions increase brain GABA Levels: a pilot study. *J. Altern. Complement. Med.* 13(4), 419–426 (2007).

62 Brambilla P, Perez J, Barale F, Schettini G, Soares JC. GABAergic dysfunction in mood disorders. *Mol. psychiatry* 8(8), 721–737, 715 (2003).

63 Kilpatrick LA, Suyenobu BY, Smith SR *et al.* Impact of mindfulness-based stress reduction training on intrinsic brain connectivity. *NeuroImage* 56(1), 290–298 (2011).

64 Taren AA, Gianaros PJ, Greco CM *et al.* Mindfulness meditation training alters stress-related amygdala resting state functional connectivity: a randomized controlled trial. *Soc. Cogn. Affect. Neurosci.* 10(12), 1758–1768 (2015).

9.3 Summary

In this paper I summarised the current literature on the potential changes to risk factors for stroke and CVD that are altered by MBIs, such as yoga or tai chi. See Appendix E for example search strategy. Survivors of stroke often have multiple risk factors and, therefore, a greater absolute risk of experiencing another stroke or other CVD. MBIs appear beneficial in moderating some of the highly prevalent risk factors for stroke, such as hypertension, diabetes and cholesterol. However, there is a need to further unpack these beneficial changes to pathophysiological pathways leading to therapeutic changes to some of these risk factors. Understanding the potential risk reduction associated with MBIs is important for both researchers and practitioners to inform the choice of adjunct interventions and training programs implemented for those with high risk of recurrent stroke or other CVD.

Chapter 10: Yoga and its potential effect on improving anxiety, depression and quality of life following stroke

10.1 Overview

It is well understood that survivors of stroke have long-term physical and psychological consequences that influence their quality of life. Few interventions are available in the community to address these problems simultaneously, particularly problems with anxiety or depression. As highlighted in Chapter 9, there is potential for MBIs to moderate some of the long-term risk factors of stroke. In addition, in the recent times there appears to be more research conducted on yoga-based MBIs than other forms of MBIs. Yoga is also widely available in the general population and therefore more accessible to survivors than other forms of MBI. Yoga appear to be effective in improving anxiety, depression and quality of life in people with other chronic illnesses.[148-151] I wanted to further explore the potential for yoga to address psychological conditions reported by survivors of stroke. At the time this work was completed, only narrative reviews on this topic had been published.[152, 153]

The aims of the following paper were to conduct a systematic review of the existing evidence and perform meta-analyses of RCTs to provide a robust critical appraisal of the potential effectiveness of yoga for survivors of stroke. A comprehensive description of the feasibility of the yoga interventions was investigated, as well as the frequency and dosage of the intervention

used, and the outcomes that were measured, to provide guidance for the field. This paper contributes to addressing the fifth aim of my thesis: to systematically evaluate published evidence on the effectiveness of MBIs for moderating risk factors of stroke, and reducing the risk of poor patient outcomes or comorbidity, including anxiety or depression. My contribution is at 75%, and the nature of my contribution was concept, literature search, data management, analysis, interpretation and writing of first draft of the manuscript.

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10.2 Published paper

Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis

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Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis

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ABSTRACT

Background: Survivors of stroke have long-term physical and psychological consequences that impact their quality of life. Few interventions are available in the community to address these problems. Yoga, a type of mindfulness-based intervention, is shown to be effective in people with other chronic illnesses and may have the potential to address many of the problems reported by survivors of stroke.

Objectives: To date only narrative reviews have been published. We sought to perform, the first systematic review with meta-analyses of randomized controlled trials (RCTs) that investigated yoga for its potential benefit for chronic survivors of stroke.

Methods: Ovid Medline, CINHAL plus, AMED, PubMed, PsychINFO, PeDro, Cochrane database, Sport Discuss, and Google Scholar were searched for papers published between January 1950 and August 2016. Reference lists of included papers, review articles and OpenGrey for Grey literature were also searched. We used a modified Cochrane tool to evaluate risk of bias. The methodological quality of RCTs was assessed using the GRADE approach, results were collated, and random effects meta-analyses performed where appropriate.

Results: The search yielded five eligible papers from four RCTs with small sample sizes (n = 17–47). Quality of RCTs was rated as low to moderate. Yoga is beneficial in reducing state anxiety symptoms and depression in the intervention group compared to the control group (mean differences for state anxiety 6.05, 95% CI:–0.02 to 12.12; p = 0.05 and standardized mean differences for depression: 0.50, 95% CI:–0.01 to 1.02; p = 0.05). Consistent but nonsignificant improvements were demonstrated for balance, trait anxiety, and overall quality of life.

Conclusions: Yoga may be effective for ameliorating some of the long-term consequences of stroke. Large well-designed RCTs are needed to confirm these findings.

Abbreviations: AMED: Allied and Complementary Medicine Database; GRADE: Grading of Recommendations, Assessment, Development, Evaluation; MD: mean difference; SMD: standardized mean difference; RCT: randomized controlled trial; ITT: intention to treat

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Systematic review; meta-analysis; mindfulness; yoga; stroke

Introduction

Many survivors of stroke have long-term physical and psychological disabilities[1] that impact their quality of life. Difficulties experienced include physical function impairments, such as upper limb function, decreased gait speed, balance impairment, and fear of falling[2–7]that may lead to reduced willingness to participate in activities and sedentary lifestyle,[8] which further disrupt function and overall quality of life.[9] In addition, many survivors of stroke experience ongoing emotional health problems, including anxiety, fatigue, and depression.[1,10–12] It is estimated that 31% will develop depression within 5 years following stroke.[13] There are very few community-based therapy options available for long-term recovery and to reduce the incidence of further comorbidity.[14]

Yoga, as a program of health and well-being derived from Buddhist, Hindu, and other contemplative traditions,[2,15] might be a promising therapy to support the needs of survivors of stroke. The practices of yoga share characteristics with other practices derived from the Buddhist tradition such as those that cultivate mindfulness meditation including mindfulness-based stress reduction (MBSR).[16] Plausible mechanisms by which yoga has been proposed to provide benefits for the prevention and management of chronic conditions include exercise and promotion of mindfulness.[17–21] The exercise component of yoga involves movement and holding of postures (collectively known as asanas). The means of promoting mindfulness is when the low-impact exercise component of yoga is combined with focused attention to breathing (pranayama) and meditation (dharana).[22] Some of the benefits provided by yoga are common to other forms

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of physical activity and included building strength, as well as improving flexibility, balance and overall well-being in people with chronic illnesses.[23–26] Mindfulness is paying attention on purpose to the present moment with acceptance and nonjudgment.[16,27] This is quite similar to the principle of dharana in yoga, which is to sustain attention on the object of the yoga practice (e.g. holding posture or breathing). Yoga can improve mobility, mood, and quality of life in people who are older [6,28,29] who have chronic neurological conditions such as Parkinson,[30,31]or chronic conditions such as cancer[19] and coronary heart disease,[21] through a range of biopsychosocial benefits.[20] People with stroke also experience a complex range of problems like activity limitations, poor emotional well-being and lower quality of life in comparison with their age-matched peers.[8,32,33] Therefore, it is argued that yoga may improve well-being in chronic survivors of stroke by integrating the benefits of physical component and mindfulness into one process. Another advantage is that is applicable and accessible to people with different levels physical ability or health issues.[2,20,34,35]

Many survivors of stroke find it difficult to participate in regular physical activity and do not return to high-demand leisure activities that they were undertaking before their stroke. Many survivors prefer group-based training with an instructor.[36,37] Therefore, yoga may be a suitable physical activity for addressing a range of poststroke needs. However, to date, only narrative reviews on the benefits of yoga following stroke have been published.[35,38] Our *primary aim* was to conduct a systematic review of the existing evidence and perform meta-analyses of randomized controlled trial evidence to provide a robust critical appraisal of yoga and the potential effectiveness of yoga for survivors of stroke**.** Our *secondary aim* was to provide a comprehensive description of the feasibility of the yoga interventions investigated as well as the frequency and dosage, and outcomes that were measured to provide guidance for the field.

Methods

Search strategy, trial eligibility criteria, and data retrieval

We only included randomized controlled trials (RCTs) that had been conducted in adult populations (≥8 years of age); stroke diagnosis of any etiology or severity occurred at least within the 6 months prior to being recruited to the study, including transient ischemic attack, regardless of sex, ethnicity, language spoken, or number of events. We included trials with mixed populations, e.g., acquired brain injury, where stroke-only data could be extracted. Trial interventions could include either yoga postures (asanas); breathing (pranayama); or mindfulness meditation, or a combination of two or all three components of yoga. Trials were excluded if they included multimodal mindfulness interventions such as MBSR, mindfulness-based cognitive therapy, Tai Chi, or chanting where the effects of yoga could not be assessed separately. Comparators could include wait-list control, usual care, or an alternate "active therapy" to test against yoga as a stroke rehabilitation therapy irrespective of yoga style or dosage (frequency and intervention duration).

A systematic search strategy (online supplemental file) was formulated using subject headings and the combination of key terms (e.g. "yoga," "mindfulness," "stroke," "mood," and "quality of life") applied to each database. We searched using Ovid Medline, CINHAL plus, AMED, PubMed, PsychINFO, PeDro, Cochrane database, Sport Discuss, and Google Scholar for articles published between January 1950 and August 2016. We also searched the reference lists of included papers, review articles, and OpenGrey for Grey literature. Clinical trials platforms (e.g. the Australian and New Zealand Clinical Trial registry; ClinicalTrials.gov) were also searched for unpublished and ongoing trials. Key authors were contacted to establish whether any other important studies were missed or were being undertaken that warranted inclusion. Language filters were not applied.

The initial search and identification of trials were performed by the first author. Data extraction was conducted using an adapted Cochrane data extraction form.[39] For abstracts that appeared to meet the review criteria, full-text articles were retrieved and assessed. Final selection of eligible trials and uncertainty over eligibility was resolved by consensus with the second author, who also assessed the articles to ensure their conformity to the inclusion criteria.

Trials meeting the inclusion criteria were assessed for methodological quality and risk of bias using an appraisal framework adapted from the PeDro[40] and the Cochrane Risk of bias tool described in the Cochrane Handbook for Systematic Reviews of Interventions.[41] When the authors of the trials provided a satisfactory description for these quality assessment criteria, a positive value was assigned (+). If a criterion description was considered absent, unclear, or lacked the specified content, a negative value was assigned (−). To draw narrative conclusions across the included trials regarding the strength of evidence, the GRADE criterion was applied. Trials that scored 0–5 positive values were classified as low quality with a high risk of bias, 6–8 indicated a low to moderate quality with moderate risk of bias, 9–11 indicated a moderate quality with low to moderate risk of bias and 12 indicated high quality with a low risk of bias.[42]

TT independently extracted data from the included trials and entered into Review Managersoftware (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) that can used to combine data from multiple trials for quantitative analyses. Data entry was checked by second author and disagreements were discussed with a third review author. Extracted information, including information regarding patient demographics, study design features, methods of allocation, and blinding methods, was tabulated. In cases where data important to the review were unpublished, the corresponding authors were contacted and additional data obtained. Outcomes were assessed across three broad categories: physical function; mood; and quality of life. Adverse events, including falls or death, were also summarized.

Statistical analysis

Where we considered trials to be sufficiently similar, i.e. comparators and outcomes measured were the same, we conducted a meta-analysis by pooling the appropriate data using Review Manager (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) according to the PRISMA guidelines.[43] Means and standard deviation values were extracted for meta-analyses. Weighted effect sizes (standardized

mean difference and 95% CIs) were calculated for depression and quality of life where different outcome measures were used.

A random-effects model was used to pool the data. Statistical heterogeneity between trials was assessed using the Chi-square test.[44] We considered a p-value ≤0.10 as indicating significant heterogeneity. I^2 statistics were also reported by estimating the amount of variance in a pooled effect size accounted for by heterogeneity in the sample of trials.[45] An I^2 value of 0% indicated no observed heterogeneity, while values of 25%, 50%, and 75% indicated low, moderate, and high heterogeneity, respectively. If between-group effect sizes were not reported, where possible the postintervention between-group analysis was calculated using postintervention scores. Overall effect sizes were calculated from the mean difference, where a *p* value of <0.05 indicated statistical significance. For outcomes where it was impossible to pool quantitatively, we narratively summarized the results.

Results

The articles selection process is illustrated using a PRISMA flow diagram[46] (Figure 1). The electronic search and manual screening of references returned 557 potential articles to be assessed for inclusion in our review. After strict screening, 21 full-text articles were read, where five met the inclusion criteria and were selected for data extraction.[2,5,24,47,48] Results for one trial were reported in two articles,[5,24] therefore only four trials were available for analysis, and all were pilot studies.

Characteristics of included trials

The characteristics of each RCT are summarized in Table 1. Two trials were conducted in Australia, one in Sweden and the other in the United States of America. Three trials had a wait-list control design, while one had an active control group. The total number of participants was 118 (control and intervention), and sample sizes varied from 17 to 47. Hatha yoga was the most common type of yoga used for the intervention. The frequency and dosage of the yoga interventions varied across the trials from 6 weeks to 10 weeks (Table 1). Two trials had home practice components as part of the intervention for approximately 45 min for 6 days per week.[2,47] Dosage was not specified (i.e. frequency or duration of the intervention) for home practice in one trial.[5,24] Compliance (a measure of class attendance) was reported in three trials. For face-to-face group classes, compliance varied between

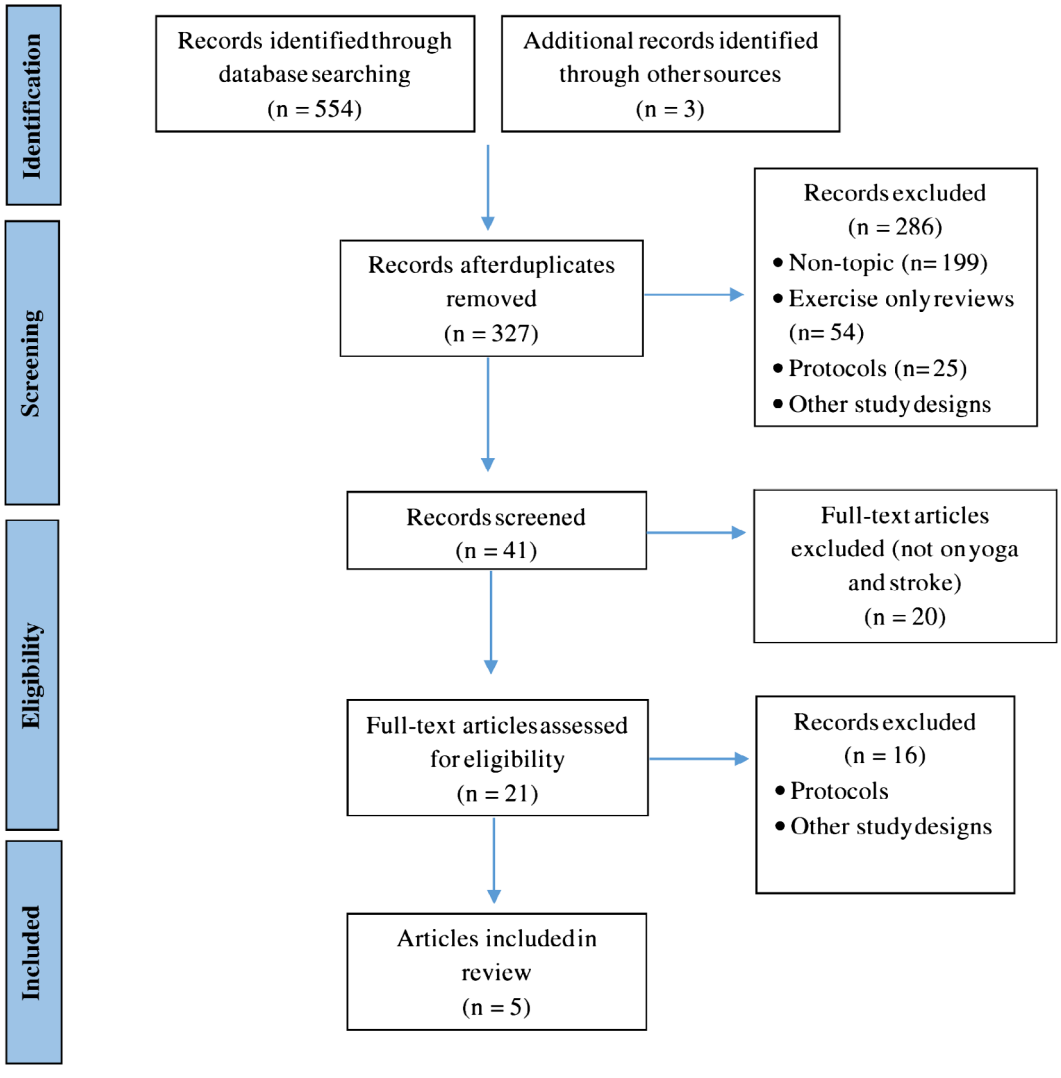

Figure 1. Flow diagram showing study selection for systematic review of trials on yoga and stroke care.

Table 1. Summary of characteristics of included randomized controlled trials.

Study/location	Design	Participants	Sample size	Yoga frequency and dosage	Type of yoga	Outcome measured and tools used for assessment	Adverse events	% drop-outs	Limitations
Immink, et al.[2] South Australia	Randomized controlled trial with wait-list control	Mean age: 60 chronic poststroke hemiparesis (>9 months)	25	90mins/week for 10 weeks + home practice	Hatha + meditation	Physical function • 9-Hole Peg test • Motor assessment scale • Berg Balance Scale • Comfortable gait Speed Mental health • Geriatric depression scale S25 • State-trait anxiety inventory Quality of life • Stroke impact scale	None	12	Use of motor imagery not monitored or recorded Study is underpowered – Small sample size Use of convenience sampling No intention-to-treat analysis No follow-ups Outcomes were only assessed at baseline and post-intervention (after 10 weeks) Did not include an active control group
Johansson, et al.[48] Sweden	Randomized controlled trial with wait-list control	Age:30–65 Stroke or traumatic brain injury (>12 months)	29	2.5 h/week for 8 weeks + home practice for 6x45 min /week for 8 weeks	Hatha	Mental health • Self-assessment scale for mental fatigue • Comprehensive psychopathological rating scale for depression & anxiety Cognitive • Process speed, attention & working memory using (Digital symbol-coding, verbal fluency test, Trail making test)	Not reported	10	No intention-to-treat analysis Study is underpowered – Small sample size
Schmid, et al.[5], Schmid, et al.[24] Indiana, USA	Randomized controlled trial with wait-list control	Mean age: 63 chronic stroke (>6 months)	47	2 × 60 min/week for 8 weeks + home practice	Not specified	Physical function • Range of motion • Upper extremity strength using arm curl test • Lower extremity strength using chair-to-stand test • Endurance using 6-min walk + 2-min step test • Berg Balance Scale Quality of life • Stroke-specific quality of life scale	Not reported	~16 ~16	Unblinded outcome assessment Relatively small sample size Low enrolment of women No intention-to-treat analysis
Chan, et al.[47] South Australia	Randomized controlled trial with active control	Mean age: 67 (intervention); 72 (control) Stroke type: chronic poststroke hemiparesis (>6 years)	17	Intervention: 90 min/week for 6 weeks + home practice + exercise weekly Active control: Exercise 50 min/week for 6 weeks	Hatha + meditation	Mental health • Geriatric depression scale • State trait anxiety inventory	None	18	Small sample size Unable to determine clinically relevant improvement was due to which treatment (yoga or exercise or combination of both) Length of interventions – 6 weeks is short Self-reporting of symptoms No intention-to-treat analysis

78% and 90%. However, home practice compliance was reported in one trial (82%).[2] Reasons for noncompliance included lack of transportation to attend group sessions, bad weather, illnesses not related to stroke, and work commitments.

Outcome measures used were inconsistent across the included RCTs (Table 1). Although most authors measured mood as an outcome, the assessment tools varied. Authors of three trials measured physical function outcomes.[2,5,24] Cognitive performance was assessed in one trial.[48] Longer-term postintervention follow-up to look for sustained effects were not reported by any of the authors.

Methodological quality of risk of bias

Table 2 shows the risk of bias assessment. In the two trials in which adverse events were recorded, no such events were reported.[2,47] In three trials, both between and within-group analyses were performed,[2,47,48] and none had an intention-to-treat (ITT) analysis. The lowest reported retention rate was 76%.[48] The risk of bias score varied between 5 and 8 (out of 12 points). Authors of two trials[2,47] described their method of randomization in detail and scored a maximum of 8 points therefore judged to have a moderate risk of bias. Authors of one trial-blinded participants to the nature of the intervention,[2] while the other blinded the outcome assessors.[47] Using the GRADE criteria, the overall quality of the trials was judged as low to moderate (Table 2).

Potential effects of yoga for stroke recovery

A summary of the main results from the included trials is presented in Table 3. Between group differences were not found for mobility and gait speed in one trial.[2] Pre–post improvements were significantly better in the intervention group than the control group for balance,[24] flexibility, strength and 6-min walking speed.[5]

In three trials mood outcomes were evaluated. A significant difference in postintervention mental fatigue scores was observed between the intervention and control group in one trial.[48] Between group differences were not found for depression,[2,48] overall anxiety[48] and state anxiety (participants perceived feeling of tension and anxiety at that moment of time)[2] – intervention. However, significant improvements postintervention was observed only in the intervention group for depression, anxiety, as well as cognitive scores.[48]

In one trial, with an active control group (general exercise), depression, state anxiety, and trait anxiety were not significantly different between intervention and at the 6-week follow-up assessment.[47]

Assessment for changes in quality of life was reported in two trials. Significant improvements were demonstrated between baseline and follow-up score in the intervention group only ($n = 37$) in one trial,[24] while significant improvements were only observed in the physical and memory domains of the stroke quality of life scale in the other trial.[2] No significant between group differences were observed between both groups at the end of the both trials.

Meta-analyses

No significant heterogeneity was detected in all meta-analyses. Only two trials were comparable for state and trait anxiety,[2,47]

Table 2. Results of the quality appraisal of the included yoga trials.

Citation	Eligibility criteria specified	Randomization procedure	Allocation concealed	Similarity of study groups	Blinding* of all subjects	Blinding of outcome assessors	Drop-outs	Compliance	Intention-to-treat analysis	Timing of outcome assessments	Between-group analysis used	Follow-up	Results
Randomized controlled trials													
Immink et al.[2]	+	+	–	+	+	–	+	+	–	+	+	–	8/12
Schmid et al.[5]	+	+	–	+	–	–	+	–	–	+	–	–	5/12
Johansson et al.[48]	+	+	–	+	–	–	+	–	–	+	+	–	6/12
Schmid et al.[24]	+	+	–	+	–	–	+	+	–	+	–	–	6/12
Chan et al.[47]	+	+	+	–	–	+	+	+	–	+	+	–	8/12

*For trials of interventions like yoga and mindfulness, it is not possible to blind those delivering interventions.

Table 3. Summary of study results from the included randomized controlled trials where common outcomes were reported.

First named author, year	Intervention group (postintervention period)			Control group (postintervention period)			Change or effect size (95% CI)
	Mean	*n*	SD	Mean	*n*	SD	
Mobility							
Immink[2]: Motor assessment scale	35.5	11	10.8	39.5	11	9.3	*4.00 (−4.42, 12.42)*
Immink[2]: 2-min walk distance (m)	90.2	11	51.9	104.0	11	49.1	*14.20 (−28.02, 56.42)*
Immink[2]: comfortable gait speed (m/s)	2.2	11	4.5	0.88	11	0.48	*−1.32 (−3.99, 1.35)*
Balance (Berg Balance Scale)							
Immink[2]	50.7	11	6.3	48.5	11	8	*2.20 (−3.82, 8.22)*
Schmid[24]	46.3	37	9.1	43.8	10	6.3	*2.50 (−2.38, 7.38)*
Depression (Geriatric Depression Scale and The Comprehensive Psychopathological Rating Scale)							
Immink[2]	2.7	11	2.9	4.8	11	3.3	*0.65 (−0.21, 1.51)*
Chan[47]	*3.56*	8	*4.12*	*3.17*	6	*1.9*	*−0.11 (−1.17, 0.95)*
Johansson[48]	*5.88*	12	*2.98*	*8.82*	14	*4.56*	*0.73 (−0.07, 1.53)*
State Anxiety (State Trait Anxiety Inventory)							
Immink[2]	33.4	11	7.1	41.8	11	12.2	*8.40 (0.06, 16.74)*
Chan[47]	*32.3*	8	*11.5*	*35.7*	*6*	*4.8*	*3.40 (−5.45, 12.25)*
Johansson[48]	NR	–	–	NR	–	–	
Trait Anxiety (State Trait Anxiety Inventory)							
Immink[2]	35.3	11	10.5	42	11	10.2	*6.70 (−1.95, 15.35)*
Chan[47]	*36.3*	8	*10.6*	*39.3*	*6*	*7*	*3.00 (−6.24, 12.24)*
Johansson[48]	NR	–	–	NR	–	–	
Quality of life (Stroke Impact Scale and Stroke Specific Quality of Life Scale)							
Immink[2]	*64.4*	11	*19.9*	*54.1*	11	*23.2*	*0.46 (−0.39, 1.31)*
Schmid[24]	*35.8*	37	*9.1*	*33*	10	*6.2*	*0.32 (−0.38, 1.02)*

Notes: Results presented in *italics* are author's own calculation or extrapolation from other data provided. SD: standard deviation, CI: confidence interval, NR: No comparable result.

three trials for depression,[2,47,48] and two trials for balance and overall quality of life scores.[2,24] Yoga appeared to be effective in reducing state anxiety symptoms, and depression in the intervention group compared to those in the control group, but this mean difference was borderline in being statistically different based on conventional criteria ($p = 0.05$; Figure 2(a) and Figure 3(a)). The mean difference in trait anxiety, balance and overall quality of life between intervention and control groups was not statistically significant (Figures 2(b), (c) and 3(b)).

Discussion

To our knowledge, this review is the first to include a meta-analytic approach following careful standardized quality assessment of the available RCTs to provide a summary of the current evidence on the benefits of practicing yoga for stroke recovery. Previous reviews were narrative appraisals that included a mix of observational and experimental study designs.[35,38] The majority of RCTs that met our inclusion criteria were small feasibility trials underpowered to detect differences in health outcomes. Our review, is consistent with the summation of others, that yoga is a feasible intervention and may promote well-being in survivors of stroke. Our meta-analyses provided the opportunity to have pooled the data from these small studies to assess for the likely impact on outcome in the areas of physical function, anxiety, depression, and overall quality of life.

Importantly, we found using meta-analytic techniques that yoga may ameliorate state anxiety symptoms, and depression in survivors of stroke. This finding is also supported by evidence from two observational before-after studies where the beneficial effect of yoga on state anxiety, and depression in survivors of stroke was reported.[49,50] These observational study designs make it difficult to determine whether the effects were specific to the yoga intervention or to other factors such as being part of a group with a shared experience.[51]

The physiological mechanisms of yoga on anxiety are not well understood. Practicing body postures and breathing, may act on the over active sympathetic nervous system and help reduce the objective indicators of anxiety (e.g. a racing heart, palpitations, increased blood pressure, signs of restlessness).[52] In addition, mindfulness helps raise awareness of body tension and may serve to increase self-confidence by promoting a personal sense of control and acceptance, thereby reducing perceived anxiety.[53,54]

Due to the limited number of trials on physical outcome, variations in outcome measures, measurement tools used and small sample sizes, there was insufficient evidence to draw firm conclusions on the evidence of yoga on physical effects poststroke. The lack of significant improvements on physical function may be related to the short intervention duration, with most trials lasting between 8 and 10 weeks. Buffart and colleagues suggested that 10 weeks may be too short to improve physical function and fitness and that longer intervention durations may be required in patients with chronic diseases.[19] Exercise training RCTs (non-yoga) aimed at improving fitness in people with chronic stroke included interventions lasting for a minimum of 12 weeks. These interventions provided significant improvements to physical function during this time period.[55,56] Therefore, a longer intervention duration may be required to achieve the full effectiveness potential of yoga as a therapy for chronic stroke recovery.

The potential benefits of yoga on stroke recovery beyond the benefits of general exercise interventions (strength training or aerobic exercise) is poorly researched. Chan's study[47] was the only study ($n = 17$) that used an active control (group exercise program). Lower effect sizes were shown in this trial, when compared to the results from the trials with different designs.[47] Although the American Heart Association recommends use of customized physical activity in survivors of stroke,[8] there is limited evidence regarding the effectiveness of exercise programs in stroke populations due to small sample sizes and methodological

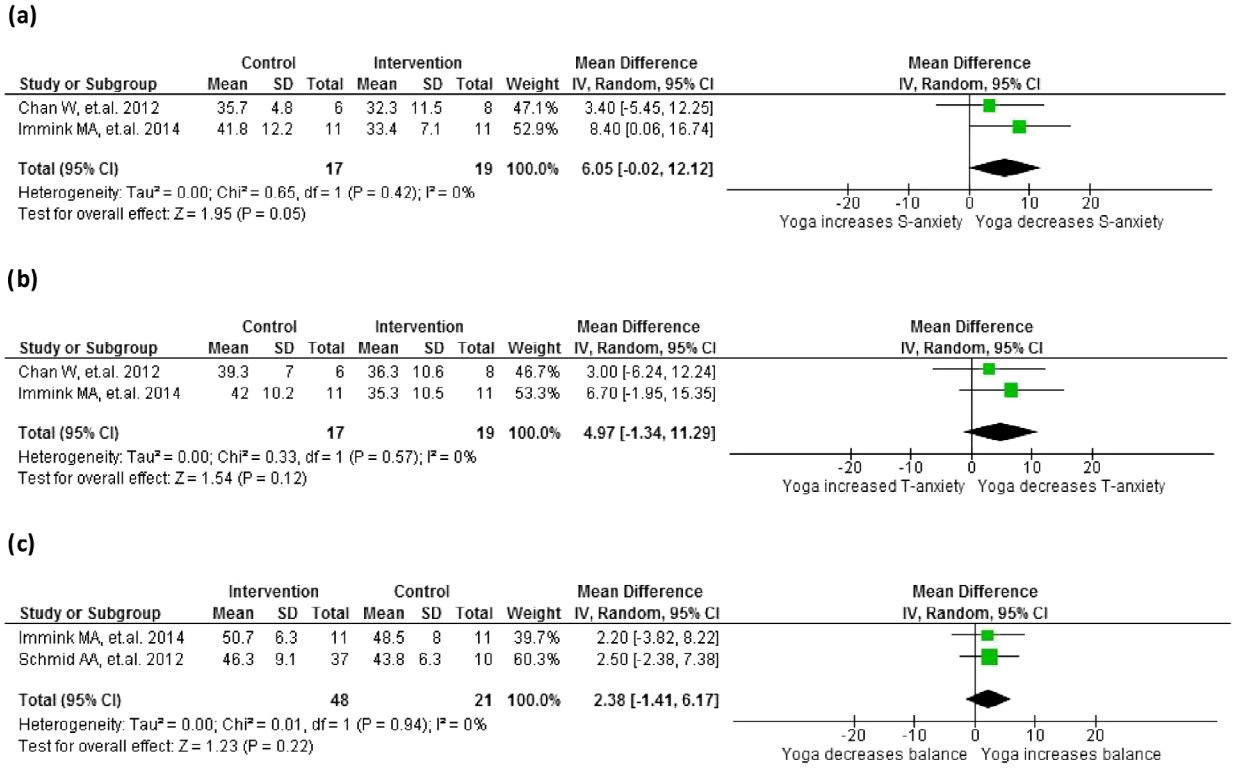

Figure 2. (a) Forest plot representing effect sizes of intervention and control groups in state anxiety (S-anxiety). (b) Forest plot representing effect sizes of intervention and control groups in trait anxiety (T-anxiety). (c) Forest plot representing effect sizes of intervention and control groups in balance outcome.

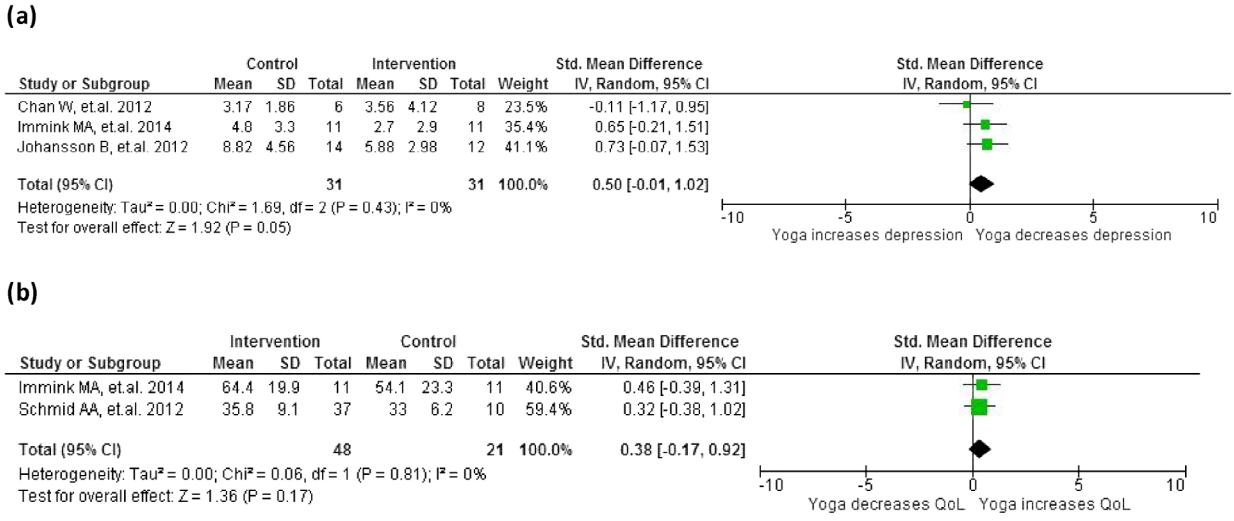

Figure 3. (a) Forest plot representing effect sizes of intervention and control groups in depression. (b) Forest plot representing effect sizes of intervention and control groups in quality of life (QoL) as an outcome.

variations. The evidence is also limited for strength training poststroke.[57] As reported by Erickson and colleagues, exercise training increases the size of the hippocampus and improves memory in older adults, reversing age-related loss in volume by 1–2 years.[58] Since stroke is often common in older adults this may offer some insights into potential mechanisms and may explain why an "active control" using an exercise intervention may equally reduce the observed effects of yoga. It is well understood that physical activity improves mood. In Chan's trial, participants observed smaller effects on mood. Whereas participants in wait-list control designed trials might be feeling good about being part of a group and engaging in social networking with other survivors, thereby providing a stronger signal for improving their mood.

For future trials in this area, the use of an active control is more appropriate for this type of multifaceted intervention over a wait-list control,[59] as it is difficult to differentiate the treatment effects specific to yoga. An active control with equivalent intervention duration and group session time is important to control for socialisation effects and the potential effects of general exercise.[59] Blinding the outcome assessors has not been rigorous in these trials and needs to be better considered in future trials. There is no definite answer to the ideal length or the "dosage" of a yoga intervention to bring about the best results but those who

participated were physically able to complete all planned yoga activities, and no injuries or adverse events were reported. This supports the notion that once enrolled in the intervention, the majority of the participants completed the intervention in most trials. Future studies on comparison of intervention duration and dose, as well as powered to detect differences in recovery outcomes are needed. A future RCT could also include funding for travel, and variety of class times, to improve participant compliance in group classes. Incorporating an ITT analysis would be important for larger RCTs to minimise retention bias, if they experience large number of drop-outs or missing data.

Study limitations

Our review has some limitations. We acknowledge that there may be selection bias (because of the nominated inclusion criteria) and the potential for publication bias. Yoga has its roots in Hindu, Buddhist, Vedic and other contemplative traditions, and relevant research may have been missed if not published in the common medical or social sciences databases that we searched. We attempted to address publication bias through undertaking a manual search of complementary medicine journals to check for any research on yoga in stroke populations and by electronic searches of the web via Google to identify relevant grey literature. Coauthors working in the field MM and PS were also consulted, and we believe it is unlikely that we missed an RCT relevant to this review. We also acknowledge that one study did include patients with stroke or traumatic brain injury.

Conclusion

Despite the growing popularity of yoga in the general population and the potential benefits for survivors of chronic illnesses, there is limited evidence, in the form of large RCTs, on the effectiveness of yoga for long-term stroke recovery. However, evidence from these pilot trials assessed in this review highlights that yoga may be effective for improving some of the long-term consequences of stroke, particularly mood. It is strongly recommended that future research apply more stringent designs (e.g. randomization with active control and passive control groups as comparison, between-group analyses and ITT) to enable a robust evaluation of the effects of yoga among survivors of stroke.

Ethics approval and consent to participate

This systematic review of the literature did not involve human or animal research and did not require ethical approval. This systematic review was conducted as part of first author's PhD program.

Availability of data and materials

Data are presented in the main paper and additional supporting file.

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Disclosure statement

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References

1. Andrew NE, Kilkenny M, Naylor R, Purvis T, Lalor E, Moloczij N, et al. Understanding long-term unmet needs in Australian survivors of stroke. *Int J Stroke*. 2014;9:106–112.
2. Immink MA, Hillier S, Petkov J. Randomised controlled trial of yoga for chronic poststroke hemiparesis: motor function, mental health, and quality of life outcomes. *Top Stroke Rehabil*. 2014;21(3):256–271.
3. Kim CM, Eng JJ, MacIntyre DL, Dawson AS. Effects of isokinetic strength training on walking in persons with stroke: a double-blind controlled pilot study. *J Stroke Cerebrovasc Dis*. 2001;10(6):265–273.
4. Quaney BM, Boyd LA, McDowd JM, Zahner LH, He J, Mayo MS, et al. Aerobic exercise improves cognition and motor function Poststroke. *Neurorehabil Neural Repair*. 2009;23(9): 879–885.
5. Schmid AA, Miller KK, Puymbroeck MV, DeBaun-Sprague E. Yoga leads to multiple physical improvements after stroke, a pilot study. *Comple Ther Med*. 2014;22:994–1000.
6. Schmid AA, Puymbroeck MV, Koceja DM. Effect of a 12-week yoga intervention on fear of falling and balance in older adults: a pilot study. *Arch Phy Med Rehabil*. 2010;91:576–583.
7. Tyson SF, Hanley M, Chillala J, Selley A, Tallis RC. Balance disability after stroke. *Phy Ther*. 2006;86(1):30–38.
8. Billinger SA, Arena R, Bernhardt J, Eng JJ, Franklin BA, Johnson CM, et al. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45(8):2532–2553.
9. Schmid AA, Van Puymbroeck M, Altenburger PA, Dierks TA, Miller KK, Damush TM, et al. Balance and balance self-efficacy are associated with activity and participation after stroke: a cross-sectional study in people with chronic stroke. *Arch Phys Med Rehabil*. 2012;93(6):1101–1107.
10. Lerdal A, Gay CL. Fatigue in the acute phase after first stroke predicts poorer physical health 18 months later. *Neurology*. 2013;81(18):1581–1587.
11. Morrison V, Pollard B, Johnston M, MacWalter R. Anxiety and depression 3 years following stroke: demographic, clinical, and psychological predictors. *J Psychoso Res*. 2005;59(4):209–213.
12. Staub F, Carota A. Depression and fatigue after stroke. In: Barnes M, Dobkin B, Bogousslavsky J, ed. *Recovery after stroke*. Cambridge: Cambridge University Press; 2005:556–579.
13. Hackett ML, Pickles K. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *Int J Stroke*. 2014;9(8):1017–1025.
14. Hachinski V, Donnan GA, Gorelick PB, Hacke W, Cramer SC, Kaste M, et al. Stroke: working toward a prioritized world agenda. *Int J Stroke*. 2010;5(4):238–256.
15. Garfinkel M, Schumacher HR Jr. YOGA. *Rheum Dis Clin North Am*. 2000;26(1):125–132.

16. Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. *Gen Hosp Psychiatry*. 1982;4(1):33–47.
17. Niemiec R, Rashid T, Spinella M. Strong mindfulness: integrating mindfulness and character strengths. *J Mental Health Counsel*. 2012;34(3):240–253.
18. Evans E, Tsao JCI, Sternlieb B, Zeltzer LK. Using the biopsychosocial model to understand the health benefits of yoga. *J Comple Integr Med*. 2009;6(1):1–24.
19. Buffart LM, van Uffelen JGZ, Riphagen II, Brug J, van Mechelen W, Brown WJ, et al. Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. *BMC Cancer*. 2012;12. doi: http://dx.doi.org/10.1186/1471-2407-12-559.
20. Garrett R, Immink MA, Hillier S. Becoming connected: the lived experience of yoga participation after stroke. *Disabil Rehabil*. 2011;33(25–26):2404–2415.
21. Kwong JSW, Lau HLC, Yeung F, Chau PH, Woo J. Yoga for secondary prevention of coronary heart disease. *Coch Database Syst Rev*. 2015;(6). Art. No.: CD009506. doi: http://dx.doi.org/10.1002/14651858.CD009506.pub3.
22. Lin K-Y, Hu Y-T, Chang K-J, Lin H-F, Tsauo J-Y. Effects of yoga on psychological health, quality of life, and physical health of patients with cancer: a meta-analysis. *Evid Based Comple Alter Med*. 2011. doi: http://dx.doi.org/10.1155/2011/659876.
23. Galantino ML, Bzdewka TM, Eissler-Russo JL, Holbrook ML, Mogck EP, Geigle P, et al. The impact of modified hatha yoga on chronic low back pain: a pilot study. *Alter Ther Health Med*. 2004;10(2):56–59.
24. Schmid AA, Puymbroeck MV, Altenburger PA, Schalk NL, Diercks TA, Miller KK, et al. Poststroke balance improves with yoga: a pilot study. *Stroke*. 2012;43:2402–2407.
25. Tiedemann A, O'Rourke S, Sesto R, Sherrington C. A 12-week iyengar yoga program improved balance and mobility in older community-dwelling people: a pilot randomized controlled trial. *J Gerontol Series A Biol Sci Med Sci*. 2013;68(9):1068–1075.
26. Williams K, Steinberg L, Petronis J. Therapeutic application of iyengar yoga for healing chronic low back pain. *Int J Yoga Ther*. 2003;13(1):55–67.
27. Kabat-Zinn J. Mindfulness-based interventions in context: past, present, and future. *Clin Psychol Sci Pract*. 2003;10(2):144–156.
28. Roland KP, Jakobi JM, Jones GR. Does yoga engender fitness in older adults? A critical review. *J Ag Phy Act*. 2011;19:62–79.
29. Wang D. The use of yoga for physical and mental health among older adults: a review of the literature. *Int J Yoga Ther*. 2009;19(1):91–96.
30. Boulgarides LK, Barakatt E, Coleman-Salgado B. Measuring the effect of an eight-week adaptive yoga program on the physical and psychological status of individuals with Parkinson's disease. A pilot study. *Int J Yoga Ther*. 2014;24(1):31–41.
31. Sharma NK, Robbins K, Wagner K, Colgrove YM. A randomized controlled pilot study of the therapeutic effects of yoga in people with Parkinson's disease. *Int J Yoga*. 2015;8(1):74–79.
32. Andrew NE, Kilkenny M, Naylor R, Purvis T, Lalor E, Moloczij N, et al. Understanding long-term unmet needs in Australian survivors of stroke. *Int J Stroke*. 2014;9:106–112.
33. Cerniauskaite M, Quintas R, Koutsogeorgou E, Meucci P, Sattin D, Leonardi M, et al. Quality-of-life and disability in patients with stroke. *Am J Phy Med Rehabil*. 2012;91(13):S39–S47. doi:http://dx.doi.org/10.1097/PHM.0b013e31823d4df7.
34. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA*. 2007;298(14):1685–1687.
35. Lazaridou A, Philbrook P, Tzika AA. Yoga and mindfulness as therapeutic interventions for stroke rehabiliation: a systematic review. *Evid Based Comple Alter Med*. 2013;2013. doi: http://dx.doi.org/10.1155/2013/357108.
36. Banks G, Bernhardt J, Churilov L, Cumming TB. Exercise preferences are different after stroke. *Stroke Res Treat*. 2012;2012:890946.
37. Hildebrand M, Brewer M, Wolf T. The impact of mild stroke on participation in physical fitness activities. *Stroke Res Treat*. 2012;2012:548682.
38. Lynton H, Kligler B, Shiflett S. Yoga in stroke rehabiliation: a systematic review and results of a pilot study. *Top Stroke Rehabil*. 2007;14(4):1–8.
39. Higgins JPT, Deeks JJ, eds. Chapter 7: selecting studies and collecting data. In: Higgins JPT, Green S, eds. *Cochrane handbook for systematic reviews of interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from: www.cochrane-handbook.org
40. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. *Aust J Physiother*. 2009;55(2):129–133.
41. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
42. Huguet A, Hayden JA, Stinson J, McGrath PJ, Chambers CT, Tougas ME, et al. Judging the quality of evidence in reviews of prognostic factor research: adapting the GRADE framework. *Syst Rev*. 2013;2. doi:http://dx.doi.org/10.1186/2046-4053-2-71.
43. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.
44. Cochran WG. The combination of estimates from different experiments. *Biometrics*. 1954;10(1):101–129.
45. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–560.
46. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8(5):336–341.
47. Chan W, Immink MA, Hillier S. Yoga and exercise for symptoms of depression and anxiety in people with poststroke disability: a randomised, controlled pilot trial. *Alter Ther*. 2012;18(3):34–43.
48. Johansson B, Bjuhr H, Ronnback L. Mindfulness-based stress reduction (MBSR) improves long-term mental fatigue after stroke or traumatic brain injury. *Brain Inj*. 2012;26:1621–1628.
49. Joo HM, Lee SJ, Chung YG, Shin Y. Effects of mindfulness based stress reduction program on depression, anxiety and stress in patients with aneurysmal subarachnoid hemorrhage. *J Korean Neurosurg Soc*. 2010;47(5):345–351.
50. Marshall RS, Basilakos A, Williams T, Love-Myers K. Exploring the benefits of unilateral nostril breathing practice post-stroke: attention, language, spatial abilities, depression, and anxiety. *J Alter Comple Med*. 2014;20(3):185–194.
51. Kinser PA, Robins JL. Control group design: enhancing rigor in research of mind-body therapies for depression. *Evid Based Comple Alter Med*. 2013;2013:140467.
52. Vempati RP, Telles S. Yoga-based guided relaxation reduces sympathetic activity judged from baseline levels. *Psychol Rep*. 2002;90:487–494.
53. Hofmann SG, Sawyer AT, Witt AA, Oh D. The effect of mindfulness-based therapy on anxiety and depression: a meta-analytic review. *J Consult Clin Psychol*. 2010;78(2):169–183.
54. Speca M, Carlson LE, Goodey E, Angen M. A randomized, wait-list controlled clinical trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psycho Med*. 2000;62(5):613–622.
55. Globas C, Becker C, Cerny J, Lam JM, Lindemann U, Forrester LW, et al. Chronic stroke survivors benefit from high-intensity aerobic treadmill exercise: a randomized control trial. *Neurorehabil Neural Repair*. 2012;26(1):85–95.
56. Marsden DL, Dunn A, Callister R, Levi CR, Spratt NJ. Characteristics of exercise training interventions to improve cardiorespiratory fitness after stroke: a systematic review with meta-analysis. *Neurorehabil Neural Repair*. 2013;27(9):775–788.
57. Hill TR, Gjellesvik TI, Moen PMR, Tørhaug T, Fimland MS, Helgerud J, et al. Maximal strength training enhances strength and functional performance in chronic stroke survivors. *Am J Phy Med Rehabil*. 2012;91(5):393–400.
58. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci*. 2011;108(7):3017–3022.
59. Kinser PA, Robins JL. Control group design: enhancing rigor in research of mind-body therapies for depression. *Evid Based Comple Alter Med*. 2013. doi: http://dx.doi.org/10.1155/2013/140467.

Online Supplement

Title: Determining the potential benefits of yoga in chronic stroke care: A systematic review and meta-analysis

Supplemental methods: main database search strategy

The following search was constructed for Ovid Medline, and adapted for the other large databases:

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or vasospasm, intracranial/ or vertebral artery dissection/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
5. hemiplegia/ or exp paresis/ or exp Gait Disorders, Neurologic/
6. (hemipleg$ or hemipar$ or pareis or paretic).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. Yoga/ or mind-body therapies/ or exp breathing exercises/ or meditation/ or relaxation therapy/ or mindfulness/ or mindfulness therapy/ or mindfulness based interventions/ or attention
9. (yoga$ or yogic or relaxation or meditation or mind-body or (mind adj1 body) or postures).tw.
10. (breath$ adj3 (exercises or control$)).tw.
11. (hatha or ashtanga or bikram or iyengar or kripalu or kundalini or sivananda or vinyasa or raja or radja or bhakti or jnana or kriya or karma or yama or niyama or asana$ or pranayama or pratyahara or dharana or dhyana or samadhi or bandha or mudra).tw.
12. 8 or 9 or 10 or 11
13. 7 and 12
14. Randomized Controlled Trials as Topic/

15. RCT.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
16. random allocation/
17. Controlled Clinical Trials as Topic/
18. control groups/
19. clinical trials as topic/
20. double-blind method/
21. single-blind method/
22. Placebos/
23. placebo effect/
24. active control/
25. cross-over studies/
26. randomized controlled trial.pt.
27. controlled clinical trial.pt.
28. clinical trial.pt.
29. (random$ or RCT or RCTs).tw.
30. (controlled adj5 (trial$ or stud$)).tw.
31. (clinical$ adj5 trial$).tw.
32. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
33. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
34. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
35. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
36. (cross-over or cross over or crossover).tw.
37. (placebo$ or sham).tw.
38. trial.ti.
39. (assign$ or allocat$).tw.
40. controls.tw.
41. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39
42. exp animals/ not humans.sh.
43. 13 and 41

44. 43 not 42

45. 43 not 42

46. limit 44 to yr="2000 -Current"

Search limits: 1950-current, human studies, only RCTs
Medline: 262 hits

10.3 Summary

The findings of this paper provided important evidence that yoga is feasible and may provide both physical and psychological benefits for survivors of stroke. Yoga may ameliorate short-term anxiety symptoms (temporary perceived anxiety) and appears to have advantageous effects for depression, balance and quality of life. However, large well-designed randomised controlled trials (RCTs) are needed to confirm these findings. Since my publication, authors from another systematic review, published in 2018, also assessed the effects of yoga on the quality of life for survivors of stroke. However, only two studies were included in the meta-analysis. Similar to my review, the overall quality of the included studies in this review was assessed using the GRADE criteria, and considered very low with high risk of bias due to small number of trials. The authors also concluded that more good-quality research studies are needed to be certain that yoga has benefits for survivors of stroke.[154] Future research must particularly apply more stringent designs (e.g. randomization with active and passive control groups as comparison, and between group analyses) to enable a robust evaluation of the effects of yoga among survivors of stroke. Therefore, in the next chapter the process of developing a yoga-based mindfulness intervention designed for survivors of stroke living in the community is described based on principles of formative evaluation.

Chapter 11: The development of a new yoga-based mindfulness intervention for survivors of stroke: A formative evaluation

11.1 Overview

In this chapter the process of developing a yoga-based mindfulness intervention designed for survivors of stroke living in the community is described based on principles of formative evaluation. This chapter addresses the sixth aim of my thesis.

The intervention was developed as a yoga program presented in the format of a yoga teacher training manual. The manual was developed over two years (June 2016 to June 2018). The process consisted of interdisciplinary collaboration with the involvement of clinicians, researchers and three consumer representatives via three face-to-face meetings (2–3 hours each), six teleconferences (1 hour each), one focus group session (4-5 hours) and communication via email. Four practicing yoga teachers were selected, through purposeful sampling, for participation in the independent review stage. Pragmatic approach to formative evaluation of the manual was conducted throughout the design phase. Data collection and documentation included minutes of formal meetings, focus group discussions, researcher observations, and note taking. The data were iteratively synthesised by means of inductive thematic analysis. The 12-week program is now ready for testing with survivors of stroke.

11.2 Introduction

Stroke is a leading cause of death and disability in Australia. Survivors of stroke often experience problems with physical and psychological health following stroke. The impact of stroke in survivors has been described in detail in Chapters 1 and 2 of this thesis. The potential benefits of yoga to reduce the risk of comorbidities including recurrent events in survivors of stroke have been described in Chapters 8 and 9. This chapter includes the description of a formative evaluation of the process of developing a yoga-based mindfulness intervention designed as a program for survivors of stroke living in the community. The finalised intervention is to be tested for effectiveness in a future pilot trial and, subsequently, in a larger Phase III RCT.

A pilot study is an essential preliminary phase of a RCT for testing the effectiveness of a newly developed intervention.[155] However, if the new intervention to be tested is complex (i.e. has multiple components, or where there are several types of outcomes),[156] it must be designed carefully and systematically across different developmental stages. This is to ensure it will be standardised for application and be reproducible. Empirical data are needed to gain insight into the quality of the developed intervention, the design principles and what content needs to be revised for the next improved version.[157,158] For this reason, formative evaluation is an essential feature of the development and design phase of a new intervention or program. The focus of formative evaluation is to uncover the advantages and disadvantages of the intervention during its development process with the purpose of generating evidence to improving the intervention features so that it is implemented as intended, and will produce the hypothesised benefits for the patient group to which it will be applied.[158] Results of the formative evaluation give ground for improving the prototype of the intervention towards a high-quality and completed

intervention; and sharpening the underlying design principles towards a final set of design principles.[157]

The yoga program for survivors of stroke was designed in Australia by an interdisciplinary team that consisted of basic scientists, health services researchers, yoga experts, stroke rehabilitation experts (i.e. occupational therapists, physiotherapists) and consumers (i.e. survivors of stroke). The program is a MBI which targets attention control through the practice of yoga. Attention control has been suggested as having a significant impact on a survivor's outcomes by providing an opportunity to improve concentration and cognitive function.[159] Subsequently, this leads to improved self-awareness, acceptance and overall quality of life.[160] The yoga program for stroke was based on a 10-week intervention that was originally developed by collaborators from the University of South Australia.[161] The intervention was deemed feasible by the researchers based on successful implementation of the intervention and participant feedback and was detailed in their publication that I have cited. Significant improvements to self-acceptance and executive functioning in survivors of stroke were also found following a wait-list control trial among 21 participants with chronic stroke.[160, 161] However, only patients with chronic hemiparesis with minimum levels of physical ability (i.e. ability to walk for 10 metres or more with or without the use of an assistive walking device) were recruited to the study limiting the generalisability of the intervention.

The new intervention proposed in this chapter is a 12-week program and is described in the format of a yoga teacher training manual (see Appendix F for example of sections). No framework, intervention mapping or behaviour change wheel was used in this design and development phase of the trial. However, the newly developed intervention has not yet been formally evaluated for survivors of stroke.

In this chapter I describe the four phases of evaluation, based on principles of formative evaluation, that were undertaken to inform the final design of this new, contextually appropriate yoga-based mindfulness intervention for survivors of stroke. The chapter is also used to highlight how an interdisciplinary team with collaboration of consumers contributed to the formative process that led to the final design of the yoga program for stroke, in the form of a teacher training manual.

11.3 Methods

11.3.1 Study design

The formative evaluation was iteratively conducted during the two years in which the program was designed (June 2016 – June 2018). Multiple data sources were used in this mixed methods formative evaluation. My role was to support and coordinate the project governance committee (see below), advisory group, yoga teachers and consumers. My intellectual contribution to the project was to synthesise the existing evidence to support decision-making about the program design and undertake the formative evaluation work as outlines in this chapter, including contribution to the contents of the manual.

11.3.1.1 Project governance

The project lead investigators include Professor Dominique Cadilhac (my primary supervisor), Professor Susan Hillier (physiotherapist) and Dr Maarten Immink (exercise and movement physiologist, and yoga expert), who form the executive for the program development and intervention design. Professor Cadilhac leads the project and established the members of the advisory committee and yoga program working group.

11.3.1.2 Project phases

The development of the program in the format of a yoga teacher's training manual occurred over four main phases whereby the evaluation data were used to inform each subsequent phase. The four phases were:

Phase 1: Establishment of an advisory group to agree on the broad principles of the program and draft the template for the manual.

Phase 2: Development of the yoga teacher training manual to detail the program components and features in a standardised format by a working group.

Phases 3: Internal review of the draft manual between project investigators and experts.

Phases 4: External review of the training manual by independent yoga teachers, and finalisation of content.

11.3.2 Data collection and documentation

I collected and analysed the qualitative data based on an iterative and inductive approach and established the themes and subthemes through these data and my own experiential reflections since I was present at all review stages. These themes and subthemes were discussed with the lead PI including the summation for each and interpretation of the totality of the information gathered over two years. This provided the most pragmatic way to describe the iterative development process of the training manual that fostered co-production. Data sources included notes from advisory group team meetings, yoga program working group meetings, and focus groups with yoga teachers. Documentation analysis of: (1) email and phone correspondence between members of the yoga program working group and key members of the advisory group, (2) comments on hard copy drafts of the manual from consumers and yoga teachers, (3) minutes

of all advisory committee and lead investigators meetings and (4) my notes from researcher observation. Edits to the manual were tracked into a copy of the master document by all the different contributors. I managed the consolidation of the master document to ensure all relevant feedback was incorporated from each phase of the development process.

11.3.3 Data synthesis and interpretation

At every step I synthesised the feedback and, where relevant, used pragmatic inductive thematic analysis techniques. Identified themes were compared and collated. In this manner I worked with large amounts of detailed qualitative information in my attempt to identify core intervention and manual content features that were required to be modified. These changes were then discussed and amended, as required, with the three lead investigators of the project. Similarly, if there was mixed or conflicting advice, this was adjudicated on by the lead investigators.

11.4 Results

11.4.1 Phase 1: Advisory group established and program designed

For Phase 1, an advisory group was established that included experts from various fields including a clinical neuropsychologist, epidemiologist, statistician, occupational therapists, physiotherapists, exercise physiologist, yoga experts, basic scientists, and neuroscientist. As part of the design process it was acknowledged to involve survivors of stroke as consumer representation. Involving community members with whom the research will take place is essential to the success of a project.[162]

The agreed first aim of Phase 1 was to design a template of the yoga teacher training manual. During this first advisory group meeting, a literature review and a summary of the previous 10-

week intervention were presented (briefly described in section 11.2).[161] The advisory group then primarily discussed the study design, the length of the program, inclusion criteria, involvement of caregivers, possible outcome measures and strategies to maximise retention (e.g. accessibility to group classes). It was agreed at the first meeting that the program should be a 12-week intervention to allow sufficient time for progression and reinforcement of the main MBI techniques. The program was also to be based on a previously developed 10-week program designed by lead investigator Dr Immink.[161] The advisory group agreed to not duplicate efforts, but the new program will be an improved one based on the 10-week program, previously shown to be feasible in its application.

I coordinated the engagement with three consumers (two survivors of stroke and one carer) who practiced yoga, and invited them to provide their input to the design of the manual template. Phase I helped to maintain fruitful and open communication between the research team and consumers via regular emails and telephone calls. This phase also fostered a good working relationship between the consumers, researchers and clinicians. These consumer members of the advisory group had a key role in supporting other members of the advisory group to understand factors that needed consideration such as the structure of the intervention, accessibility and size of classes, influence of group participation, and involvement of caregivers in classes. The consumers provided information on the various benefits and difficulties of participating in standard (generic) yoga classes from their perspective, i.e. what has and has not helped with their participation, in generic yoga programs in the community, and recovery. This review process ensured the manual-based program would be practical, achievable, authentic and inclusive for participants.

Three major themes and four sub-themes were revealed that led to specific decisions being made in relation to the format of the yoga program. These are detailed below.

Length and content of program

At this stage it was decided that the intervention should be comprised of 12 different group classes progressing in intensity and duration for 12 weeks. It was also decided that the first class would be needed for participants to understand the objectives of the program and to familiarise themselves with the poses and transitions. It was also decided that the final weeks (weeks 11 and 12) would be used to reinforce the various aspects of the program, and provide tips to safely practice at home.

Assistant teachers

Based on the learnings of the previous 10-week program,[160, 161] the advisory groups agreed on having an assistant teacher present at every class. This was to ensure the yoga teacher could teach without interruption and the assistant could help correct the positions of participants or provide support in the transitions between poses to participant safety, as required.

Template design and sub-themes

- ***Background information on stroke for teachers***

A decision was made to include background information on stroke, including some of the major risk factors and consequences that may occur after stroke. This section would inform those yoga teachers and class assistants who may have limited understanding about stroke and its consequences. This section had not been part of the prior 10-week program, but was considered important if a larger number of yoga teachers were to be trained to deliver the program.

- ***Clear illustration of poses***

It was decided to invite survivors of stroke with different levels of impairment for a photo shoot to capture yoga poses that would be included in the manual (see pages 267-277, Appendix F)

and later could be used in the development of a the home-based practice guide for participants. The photos provide clear illustrations of how the poses should be done safely and, as relevant, with stable support materials (e.g. chair without wheels).

- ***Active therapy features***

Importantly, the yoga and allied health experts agreed that the manual must highlight the concept of 'mirroring' where participants with stroke, particularly those with physical disabilities, are encouraged to use their mind and picture themselves moving the non-functioning limb. This gives the patient the illusion of moving the non-functioning limb which is proposed to stimulate and reorganise function in damaged neural networks of the adult brain.[163]

- ***Mindfulness development***

There was consensus that the active ingredient of the yoga program for stroke as an intervention is the development and attainment of mindfulness, and the use of movement via the various poses and concentration on breathing was to focus the mind. Consistent with a standard yoga class structure (movement, focus on breathing throughout and meditation), the last part of each group class would have at least 10 minutes dedicated to mindfulness mediation. The focus was to ensure the purposeful allocation of attention so as to have full awareness of experiences in a non-judgemental and accepting manner.[28] It was decided that the duration of mindfulness meditation would be 10 minutes in the first few classes, with the duration to increase to 20 minutes by the end of 12 weeks. It was also highlighted that the poses and breathing would be guided with key points to re-emphasise to participants to focus their attention or be mindful as part of every process in the class.

11.4.2 Phase 2: Development of the training manual

The main aim of Phase 2 was to formulate the draft manual based on the information gathered in Phase 1 (see 11.4.1). Three major themes were identified in this phase.

Yoga program working group

The first step involved development of the terms of reference document highlighting the roles and responsibilities of the members of the yoga program working group. The working group consisted of the three project leads (see section 11.3.1.1) and me (i.e. project coordinator). The second step involved the development and execution of a collaborative agreement for the new yoga program for stroke between Monash University and the University of South Australia.

Program format and content

The program manual included developing a section on background information about stroke and its consequences, and the role of the teacher in ensuring program fidelity (see pages 264-265, Appendix F). The main headings were agreed upon by the yoga program working group and I wrote the initial draft for many of the subsections. Members of the advisory group with expertise in stroke contributed feedback for this section.

To ensure all yoga teachers would understand the underlying principles of the program, it was agreed to have a section outlining a set of 'golden rules' (i.e. guiding principles) of the main program features that must be adhered to throughout program. Group classes were designed to be delivered by an experienced yoga teacher in a series of discrete weekly one hour sessions over 12 weeks. It was thought having a shorter session (~10 minute) of *yoga nidra* or mindfulness meditation from week one to week five would make learning easier rather than a 20-minute session. A description of the various physical postures, possible variations to the

postures, and suggestions on appropriate use of language across the manual were included in the manual.

Photo shoot

The two survivors of stroke who were part of the advisory group, and another, were invited to take part as models in a photo shoot. Two females and one male survivor, with different levels of disabilities, attended the photo session. The photos captured in this session were used to illustrate some poses featured in the manual. At the beginning of the session, all three volunteers were provided with a session information sheet. They provided written consent, according to Monash University Privacy Policy, to participate in the photo shoot. The shoot was led by Dr. Maarten Immink (yoga expert and collaborator from the University of South Australia). I was the researcher who was observing the shoot. The shoot was held during one day over 6 hours. During the shoot I noted how the safe transition from one pose to another was important, especially for someone with severe physical disability who would require a strong and secure chair for support, or modified means of support in getting up and down from the ground (e.g. using the support of a wall or receiving help from an assistant). The models also mentioned that they had been practicing yoga and mindfulness meditation for a long time (>3 years) through generic programs in the community, and it definitely helped with their recovery process. All 3 models were very pleased to be a part of project, and were excited that a tailored intervention was being developed for use in survivors of stroke.

11.4.3. Phase 3: Internal review of the program by members of the advisory group and other consumers and allied health professionals

All members of the yoga program working group (described in 11.4.2) provided their expert opinion on the content and design of the developed manual. In addition, through purposeful sampling, allied health professionals (who were also stroke experts, n=3), and consumers (n=3)

were invited to collaborate and review the content and design of the drafted prototype manual (as described in Phase 2). Members of the advisory group (described in 11.4.1) were also asked to provide their view on the content, design, overall acceptability and feasibility of the content in the manual. This process lasted seven months (from January 2017 to August 2017). Four major themes were identified in this phase.

Refining manual format and content

Through written feedback, the allied health professionals and researchers commented on how particular activities could be better adapted to suit survivors of stroke, whilst maintaining the guiding principles of the program (see Figures 11.1 and 11.2 for examples). Changes in the class plans were made to (1) facilitate ease of implementation for teachers, (2) use materials that were available and acceptable for the cohort, and (3) promote implementation fidelity of the program. Key practice points were embedded under sections of each posture and class plans to reinforce key guiding principles of the program. It was also reinforced that an assistant teacher must be present within each class to optimise program delivery and patient safety.

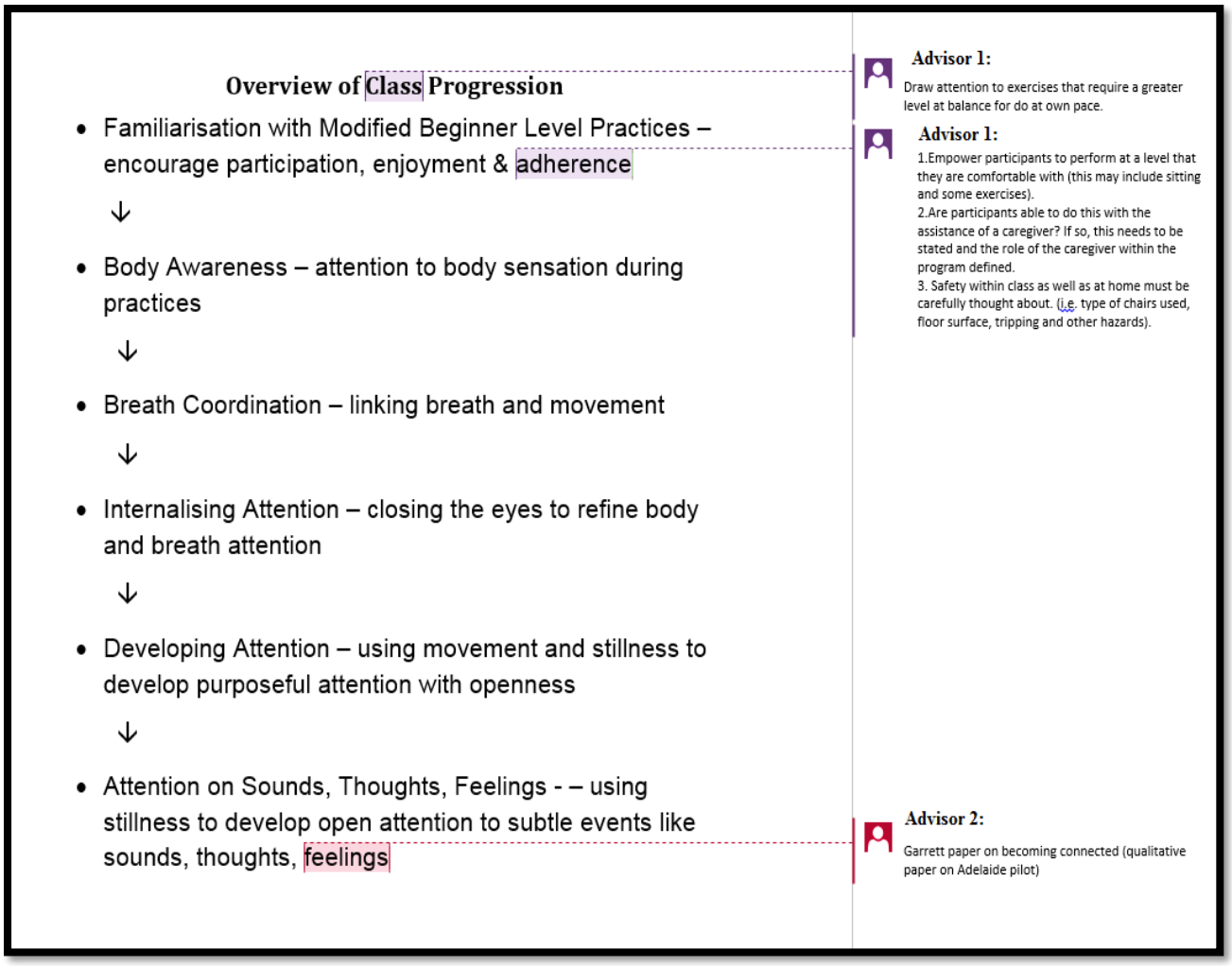


Figure 11.1. *Snapshot of comments provided as part of internal review of the manual by members of the advisory group*

Clear instructions on transitions

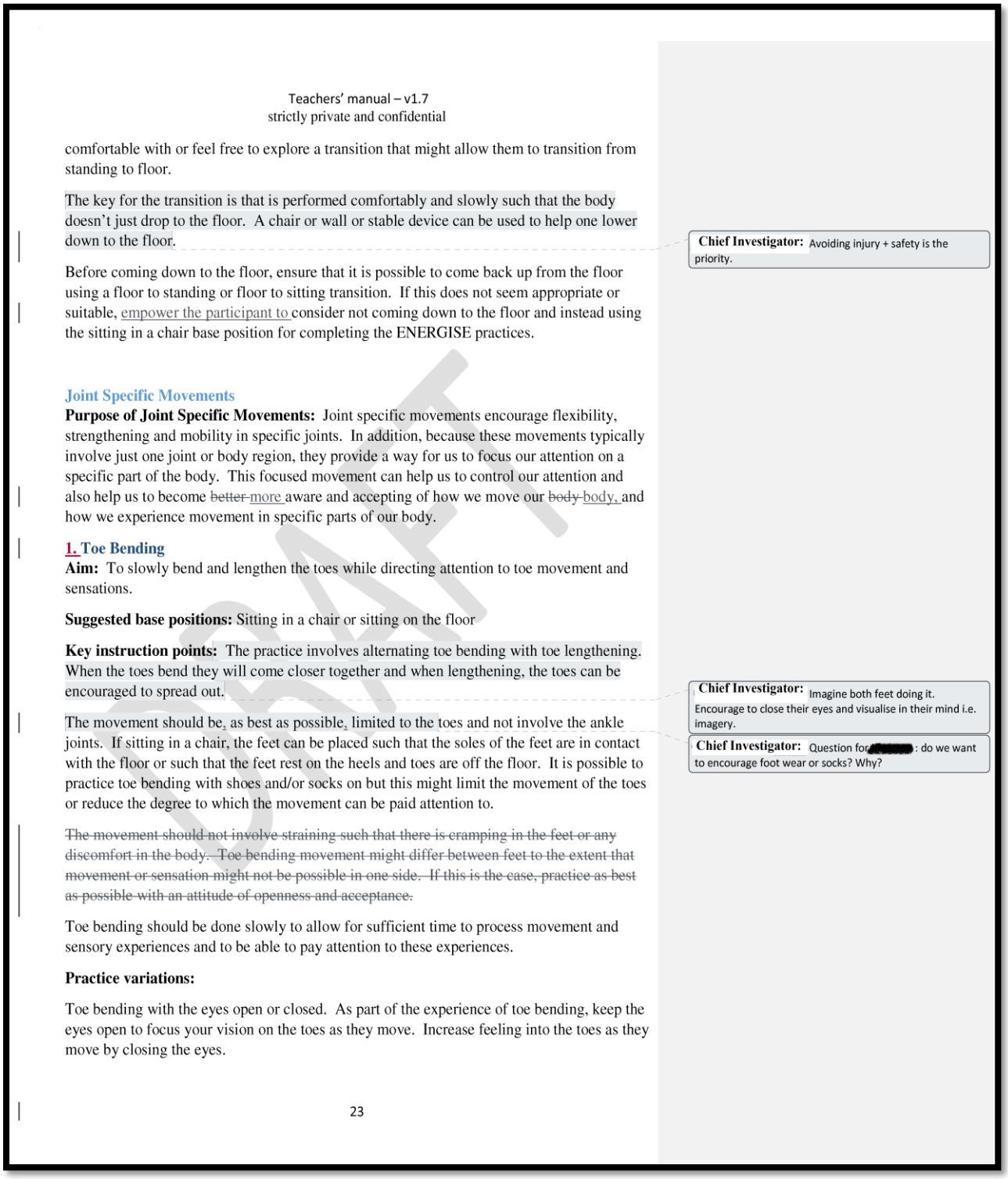
Importantly, greater detail on how to transition from one pose to another was added. Photos that provided an illustration of some of the poses were also updated to include more contextually appropriate photographs (e.g. avoid ones with roller chairs, encourage use of pillows for support).

Transitioning to home practice

It was also suggested that the content of week 11 and week 12 could largely focus on 'transition to home techniques' and included information on how to effectively continue practice at home, rather than traditional group class. Consumers also asked to include time at the end of every class to explore the manual and resources as a group to support implementation of practical lesson activities at home. The yoga teacher training manual will form the basis of a participant manual and an accompanying audio CD.

Story of the three models

The manual was personalised by adding the 'story' of the 3 models who had contributed to the photo shoot at the end of the manual (see pages 278-280, Appendix F). It was believed that, by including these stories, the yoga teachers undergoing training would gain some insights into what it is like to live with stroke and participate in yoga.



Teachers' manual – v1.7
strictly private and confidential

comfortable with or feel free to explore a transition that might allow them to transition from standing to floor.

The key for the transition is that is performed comfortably and slowly such that the body doesn't just drop to the floor. A chair or wall or stable device can be used to help one lower down to the floor.

Chief Investigator: Avoiding injury + safety is the priority.

Before coming down to the floor, ensure that it is possible to come back up from the floor using a floor to standing or floor to sitting transition. If this does not seem appropriate or suitable, empower the participant to consider not coming down to the floor and instead using the sitting in a chair base position for completing the ENERGISE practices.

Joint Specific Movements

Purpose of Joint Specific Movements: Joint specific movements encourage flexibility, strengthening and mobility in specific joints. In addition, because these movements typically involve just one joint or body region, they provide a way for us to focus our attention on a specific part of the body. This focused movement can help us to control our attention and also help us to become ~~better~~ more aware and accepting of how we move our ~~body~~ body, and how we experience movement in specific parts of our body.

1. Toe Bending

Aim: To slowly bend and lengthen the toes while directing attention to toe movement and sensations.

Suggested base positions: Sitting in a chair or sitting on the floor

Key instruction points: The practice involves alternating toe bending with toe lengthening. When the toes bend they will come closer together and when lengthening, the toes can be encouraged to spread out.

Chief Investigator: Imagine both feet doing it. Encourage to close their eyes and visualise in their mind i.e. imagery.

The movement should be, as best as possible, limited to the toes and not involve the ankle joints. If sitting in a chair, the feet can be placed such that the soles of the feet are in contact with the floor or such that the feet rest on the heels and toes are off the floor. It is possible to practice toe bending with shoes and/or socks on but this might limit the movement of the toes or reduce the degree to which the movement can be paid attention to.

Chief Investigator: Question for [redacted]: do we want to encourage foot wear or socks? Why?

~~The movement should not involve straining such that there is cramping in the feet or any discomfort in the body. Toe bending movement might differ between feet to the extent that movement or sensation might not be possible in one side. If this is the case, practice as best as possible with an attitude of openness and acceptance.~~

Toe bending should be done slowly to allow for sufficient time to process movement and sensory experiences and to be able to pay attention to these experiences.

Practice variations:

Toe bending with the eyes open or closed. As part of the experience of toe bending, keep the eyes open to focus your vision on the toes as they move. Increase feeling into the toes as they move by closing the eyes.

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DRAFT

Figure 11.2. *Snapshot of comments provided as part of internal review of the program manual by a Chief Investigator*

11.4.4 Phase 4: Independent review of the manual by yoga experts

Through the collaborative network of the chief investigator, and via email to the Yoga Australia Association, four yoga teachers (3 females, 1 male) not previously involved in the project were approached to provide independent review on the manual. These yoga teachers had different levels of experience and provided their expert opinion on the content, design and acceptability of the drafted manual over a four month period (August to December 2017). The yoga teachers also attended a focus group and quasi training workshop in December 2017 where they provided more feedback on the manual. Several modifications were identified that needed to be made to the manual to enhance its relevance and feasibility for use in program delivery (see Figure 11.3 and 11.4 for example comments). In this phase, three major themes were identified.

Use of consistent terminologies

The teachers indicated that it would beneficial to focus on key concepts of the program and the use of consistent language prior to delivering the first class. Clear terminologies (western or plain English) were suggested to be used instead of Sanskrit words, such as using ‘deep controlled breathing’ instead of ‘pranayama’ for better readability.

Alterative seating options

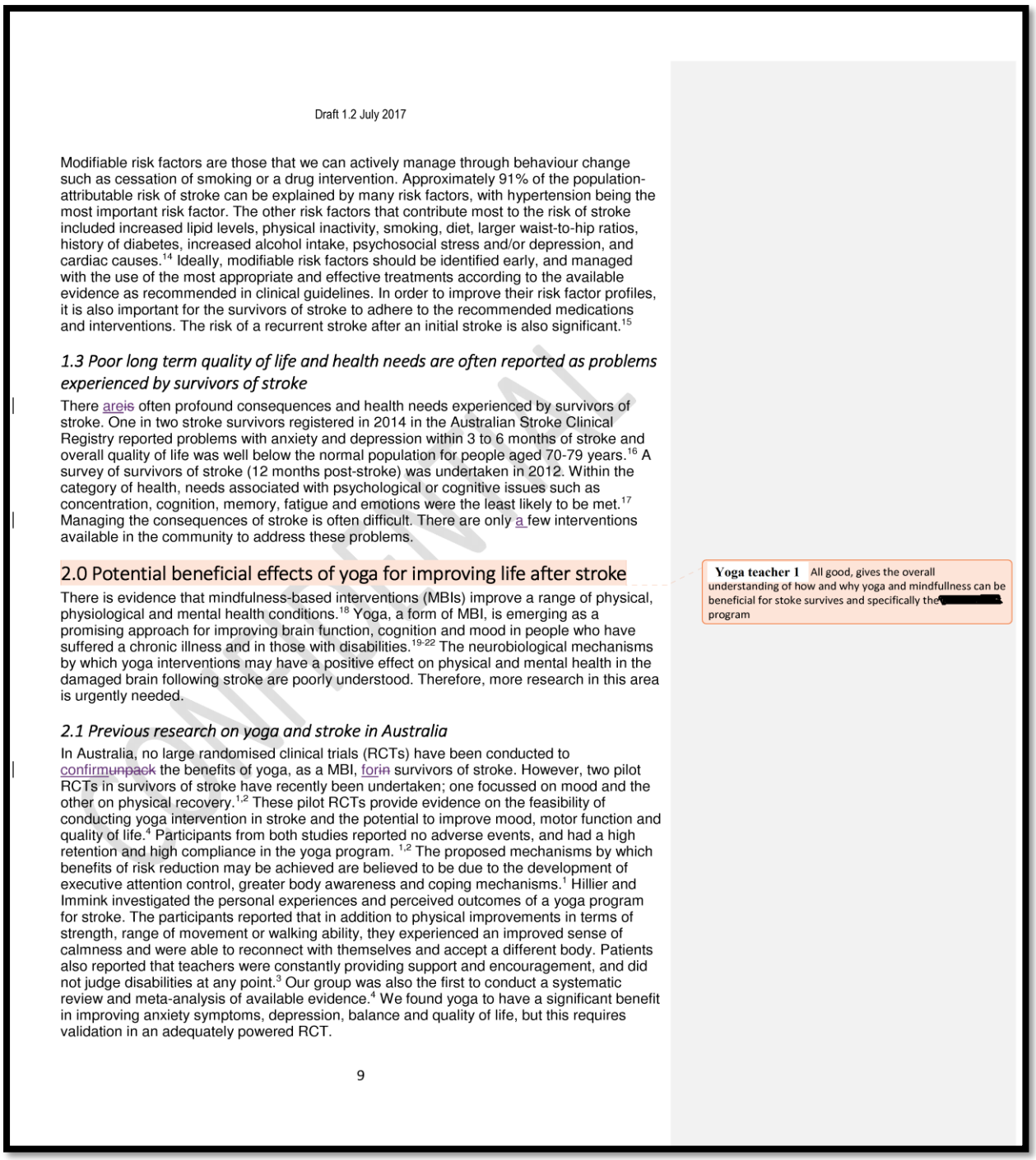
The teachers suggested including alternative seating options. For example, the use of chairs instead of standing for any ‘standing pose’ could easily be implemented in the group environment. So this type of practical information was included, where relevant.

Further refinement to other manual content

Teachers also provided information about the suitability of particular resources used in the classes, for example yoga bands for support of shoulder or arm poses. Advice on how to address

any concerns with safety and adverse events during class times were also advised to be included in the manual. Finally, the teachers suggested to add some information on the different types of stroke to the background on stroke section.

In response to the independent review, the yoga teacher training manual was modified. Table 11.1 shows the differences and similarities between the content of the original 10-week program[161] and the new 12-week program.



Draft 1.2 July 2017

Modifiable risk factors are those that we can actively manage through behaviour change such as cessation of smoking or a drug intervention. Approximately 91% of the population-attributable risk of stroke can be explained by many risk factors, with hypertension being the most important risk factor. The other risk factors that contribute most to the risk of stroke included increased lipid levels, physical inactivity, smoking, diet, larger waist-to-hip ratios, history of diabetes, increased alcohol intake, psychosocial stress and/or depression, and cardiac causes.[14] Ideally, modifiable risk factors should be identified early, and managed with the use of the most appropriate and effective treatments according to the available evidence as recommended in clinical guidelines. In order to improve their risk factor profiles, it is also important for the survivors of stroke to adhere to the recommended medications and interventions. The risk of a recurrent stroke after an initial stroke is also significant.[15]

1.3 Poor long term quality of life and health needs are often reported as problems experienced by survivors of stroke

There areis often profound consequences and health needs experienced by survivors of stroke. One in two stroke survivors registered in 2014 in the Australian Stroke Clinical Registry reported problems with anxiety and depression within 3 to 6 months of stroke and overall quality of life was well below the normal population for people aged 70-79 years.[16] A survey of survivors of stroke (12 months post-stroke) was undertaken in 2012. Within the category of health, needs associated with psychological or cognitive issues such as concentration, cognition, memory, fatigue and emotions were the least likely to be met.[17] Managing the consequences of stroke is often difficult. There are only a few interventions available in the community to address these problems.

2.0 Potential beneficial effects of yoga for improving life after stroke

There is evidence that mindfulness-based interventions (MBIs) improve a range of physical, physiological and mental health conditions.[18] Yoga, a form of MBI, is emerging as a promising approach for improving brain function, cognition and mood in people who have suffered a chronic illness and in those with disabilities.[19-22] The neurobiological mechanisms by which yoga interventions may have a positive effect on physical and mental health in the damaged brain following stroke are poorly understood. Therefore, more research in this area is urgently needed.

2.1 Previous research on yoga and stroke in Australia

In Australia, no large randomised clinical trials (RCTs) have been conducted to confirmunpack the benefits of yoga, as a MBI, forin survivors of stroke. However, two pilot RCTs in survivors of stroke have recently been undertaken; one focussed on mood and the other on physical recovery.[1,2] These pilot RCTs provide evidence on the feasibility of conducting yoga intervention in stroke and the potential to improve mood, motor function and quality of life.[4] Participants from both studies reported no adverse events, and had a high retention and high compliance in the yoga program. [1,2] The proposed mechanisms by which benefits of risk reduction may be achieved are believed to be due to the development of executive attention control, greater body awareness and coping mechanisms.[1] Hillier and Immink investigated the personal experiences and perceived outcomes of a yoga program for stroke. The participants reported that in addition to physical improvements in terms of strength, range of movement or walking ability, they experienced an improved sense of calmness and were able to reconnect with themselves and accept a different body. Patients also reported that teachers were constantly providing support and encouragement, and did not judge disabilities at any point.[3] Our group was also the first to conduct a systematic review and meta-analysis of available evidence.[4] We found yoga to have a significant benefit in improving anxiety symptoms, depression, balance and quality of life, but this requires validation in an adequately powered RCT.

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Yoga teacher 1 All good, gives the overall understanding of how and why yoga and mindfulness can be beneficial for stoke survives and specifically the [redacted] program

Figure 11.3. *Snapshot of comments provided as part of external review of the manual by a yoga teacher*

4.1.3 Sitting On The Floor

Aim: The sitting on the floor base position can provide a good level of stability for completing some of the ENERGISE practices but this base position has some requirements and might present challenges for some participants.

The sitting on the floor base position requires sufficient space to sit with the legs straight and also this base position requires a floor covering that provides some cushioning such as carpeting or a yoga mat. This position might also require some wall space to lean the body against to support the torso.

Challenges with the sitting on the floor base position include the mobility demands associated with getting down on to the floor and then getting up from the floor. Sitting on the floor also presents more challenge in keeping the body balanced and the torso in an upright position while seated and also while doing any of the movements or postures. Finally, it can be more challenging to keep a comfortable seated position while sitting on the floor.

Key instruction points: Suggestions for safety transitioning between base positions are provided in the following pages for coming down to the floor and then back up again. The guiding principles for deciding whether or not to use the sitting on the floor base position are 1) ensuring that emphasis is placed on being comfortable; and 2) working well within one's own limits or unique needs. Participants should be empowered to use devices to support their posture and comfort in this base position (e.g. blocks, blankets, bolsters, cushion). The teacher's aide should circulate around the room to ensure appropriate use of the support devices by correcting postures and provide comfort.

The torso should be balanced and upright, not slouching, while sitting on the floor and including when joint specific movements are completed in this base position. It is possible to have knees slightly bent for the sake of comfort. A folded blanket or thin cushion can be placed under the buttocks to support achieving an upright seated position. Whilst seating of completing joint specific movements involving the lower limbs, it is possible to place the hands on the floor beside or slightly behind the torso to support the torso.

Yoga teacher 2: This is a bad idea for people with disabilities. Even if no stroke, this is not appropriate. Back does not have support. Against a wall is better.

Advisor 6: For people who can get up and down it is actually really good. A lot of people with stroke miss out on getting down to the floor – this means they cant play with grandkids and they get frightened of the position. Please leave in for those who want to!!!!

Yoga teacher 3: -Key instructions; dot points
-Bend knees if can't maintain neutral spine
-Lean back against the wall, blanket under knees

Yoga teacher 1: Make use to have knees unlocked and bend them as much as required. Have fairly firm support to sit on or at the edge of

Advisor 6: This sentence doesn't make sense to me?

Figure 11.4. *Snapshot of comments provided as part of external review of the manual by yoga teachers*

Table 11.1. *Content of the 10-week yoga program as originally described and content of new program*

Contents	Yoga manual developed in Adelaide	New program manual
Information on stroke	No	Yes
Intervention period	10 weeks	12 weeks
Class duration	90 minutes	60 minutes
Class focus themes		
Weeks 1 & 2	Familiarise poses and encourage participation	Introduction to yoga
Weeks 3 & 4	Body awareness & breath coordination	Connecting with body sensations & breath
Weeks 5 & 6	Breath coordination	Breath and movement coordination
Weeks 7 & 8	Deep internalising & visualisations	Internalising & visualising the awareness
Weeks 9 & 10	Integrate body and breath awareness, internalisation & visualisation	Deepening body and breath awareness & stillness
Weeks 11 and 12	--	Transitioning to home
Class plans	Structured weekly class plans	Guided weekly class plans
Terminology	Sanskrit and English	English only
Images	Use of plastic chair, unstable ground, one volunteer used in the illustrations	Use of strong chair, flat ground, three volunteers used in the illustrations
Carer involvement	Discouraged	Encouraged
Individual pre-intervention meeting	No	Yes
Manual summary	No	Yes
Clear guiding principles	No	Yes
Clear practice variations	No	Yes
Key instruction points per pose	No	Yes
External interdisciplinary and consumer feedback	No	Yes
Total number of sections	4	8
Total number of pages	38	78

11.4 Discussion

Before a complex intervention, such as the yoga-based MBI as described in this chapter, is piloted in survivors of stroke, it is important that it is designed well to ensure relevance, and the ability to be standardised and replicated. Involvement in the project's formative stage by allied health professionals, clinical neuropsychologists, yoga experts and teachers, and consumers (carer and survivor) was essential to identifying features to include, barriers to program implementation and intervention delivery. Engagement of key research partners in the planning, adaptation and modification of the intervention was reliant on their early involvement in the project, and will facilitate a strong design for testing the program in future research. This process provides a model for other researchers and clinicians who aim to develop and implement complex interventions for survivors of stroke in the community. Illustrating how the yoga program for stroke was adapted and successfully integrated into a training manual for pilot testing provides insights into how this may be accomplished in similar contexts and other populations with chronic disabilities.

The development of the new yoga program for stroke involved 'co-design' whereby a team of allied health professionals, researchers, yoga experts and teachers, and consumers worked together.[164] The consumers provided mutually valuable contributions, via regular meetings, emails and focus group, and were regarded as equal and active agents and not merely passive subjects or recipients of services.[165] Moreover, the suggestions made by the consumers informed important practical modifications required to increase program adherence. This collaborative and phased approach was invaluable for identifying various aspects of the manual that needed to be modified to ensure relevance to the target population.

Overall, positive feedback was received from the allied health professionals, yoga teachers and consumers about the program and its potential utility. This manual has been designed to train

and then be used by yoga teachers to teach groups of survivors of stroke across a broad range of age groups and disabilities (see pages 262-280 for example sections, Appendix F). The program allows for progression of training intensity throughout the 12 weeks, giving an opportunity for survivors to gradually improve their mindfulness development and potentially enhance their physical and cognitive abilities, acceptance and awareness of themselves within the context of living with stroke. The program is suitable for people with all types of stroke impairments.

It is important to note some limitations of the present study. Firstly, the study involved only three survivors of stroke and one carer, and hence the findings may not be regarded as generalisable. However, the survivors of stroke have different abilities and have been practicing yoga for a long period of time. As a result their perspective on some of the information required for program implementation was deemed important. Secondly, there may be a possibility of responder bias since the survivors, teachers and researchers who provided independent review had great interest in yoga and may have been more committed to the project.

11.5 Conclusion

Multiple data sources were used in this mixed methods formative evaluation that was iteratively conducted during the two years in which the program was designed. The development of the program, in the form of a teacher training manual, involved the engagement of key stakeholders in the planning, adaptation and modification phases. By providing a program that is tailored to addressing the complexities that exist within survivors of stroke in the community, the conduct of a well-designed empirical study will be more feasible and acceptable for survivors of stroke. Ensuring that the program is clearly detailed will allow it to be replicated if found to be effective. Effective implementation and trialling of this program is key to delivering robust

evidence about the efficacy of a yoga-based MBI in survivors of stroke.[154, 166] This stroke specific yoga program will be subsequently evaluated in a future RCT, assessing the impact of the yoga-based mindfulness intervention on patient outcomes including quality of life and mental health disorders in survivors of stroke living in the community.

PART D:

Thesis summary and future implications

Chapter 12: Summary of findings and future implications

Stroke is a neurological disease that affects many people around the world.[1] There are various opportunities, across the stroke care continuum, to support patients who experience stroke to achieve better outcomes. There is a definite need to address the variation in management of stroke care within hospitals, and provide better management and prevention options to reduce the risk of developing anxiety or depression and other chronic and long-term issues in survivors of stroke.

The various studies presented in this thesis contribute to the overall theme 'Improving care and outcomes after stroke: A focus on hospital and community-based interventions' from different aspects of the patient care continuum. While there is emphasis on anxiety and depression, there is also a focus on global stroke burden and how gaps in acute hospital care are identified and addressed in relationship to long-term patient outcomes (Parts A and B). Part C then focusses on strategies to reduce the burden of anxiety or depression following stroke, a gap that has not been well addressed to date.

12.1 Summary of findings related to the Global Stroke Statistics paper (PART A)

As highlighted in the paper presented in Chapter 3, considering the worldwide impact of stroke, a compilation of epidemiological data on stroke, including incidence, mortality and case-fatality into one database, is a useful resource for all health care and related professions, and policy makers. The aims of this paper were to: (i) update a repository of the most recent country-specific data on stroke; (ii) determine where data on incidence, mortality and case-fatality were missing; and (iii) determine countries where data on incidence, mortality and case-fatality from stroke were out of date. Whether clinical registries were active in countries that had not undertaken an incidence study, or had outdated stroke data, to describe whether these were being used as a potential substitute for incidence was also explored.

The main findings of Chapter 3 were:

1. Incidence, adjusted to the WHO World standard population, ranged from 76 per 100,000 population per year in Australia (2009–10) up to 119 per 100,000 population per year in New Zealand (2011–12), with the latter being in those aged at least 15 years.
2. Data on case-fatality were available in 42 studies in 22 countries, with large variations between regions.
3. Some countries may be using clinical registries to provide such estimates for stroke in lieu of community-based incidence studies. These registries can also be used to assess the quality of care provided at acute hospitals and subsequent patient outcomes.

12.2 Future implications from the Global Stroke Statistics paper (PART A)

In many countries, stroke is a lower priority than other diseases despite its impact on public health. One issue is a lack of readily accessible comparative data to help make the case for the development of country-wide stroke strategies. To assist in this process, the Global Stroke Statistics publication provides an important common repository of the latest published information on the impact of stroke worldwide. We plan to update this repository annually and expand the scope to address other aspects of the burden of stroke.

Country-level data provide important information for citizens, clinicians, and policy makers to understand where an individual country sits within the global picture of stroke. These comparative data provides us with opportunities to explore what might be effective options to combat rising incidence, case-fatality and excess mortality in countries that may urgently need support and attention. Much can be learned from countries that maintain stroke incidence, mortality and case-fatality rates at low levels relative to other countries, despite having similar demographic or socioeconomic circumstances. It is also important to ensure that what is learned from better performing countries is adapted for implementation in low performing countries, and that there are efforts made to routinely monitor changes over time. To ensure maximal use of the information, in the future, well-designed community-based stroke surveillance studies are needed to continue to be undertaken, which also abide by agreed standards in conducting and reporting these studies. As highlighted in Chapter 3, national clinical registries may be used to provide such estimates for stroke in lieu of community-based incidence studies. These registries, such as the AuSCR, can also be used to routinely monitor and assess the quality of care provided at acute stroke hospitals and subsequent patient

outcomes. However, establishing and running a comprehensive clinical quality disease registry is expensive, and require support from sectors, including government.

12.3 Summary of findings related to improving the quality of evidence-based care at hospitals (PART B)

Routinely collected data from a clinical registry, such as the AuSCR, is a driving force to changing hospital performance, and can be used in QI programs to help clinicians close the gaps in acute stroke care. In Chapter 5, data from the participating hospitals in QLD over a five year period were used to describe the influence of external facilitation to improve the quality of stroke care in hospitals by changing clinician behaviour. Gaps in stroke care were informed by data from the AuSCR and the Stroke Foundational National Audit program. The overall aim of Chapter 5 was to evaluate the influence of the process of external facilitation for QI at the hospital-level for improving acute stroke care within an Australian context.

The main findings of Chapter 5 were:

1. There was no significant difference in support time from external facilitators to hospitals that developed a comprehensive action plan vs simple or no action plan.
2. No statistically significant association between either the mode, or dosage of external facilitation and complexity of action plans developed.
3. Eight out of twelve hospitals selected all eight PoC for comprehensive action planning and there was an observed improvement in absolute change in only 4 PoCs.
4. It is unclear whether hospitals with more comprehensive plans were more motivated to change practice.

12.4 Future implications from improving quality of evidence-based care at hospitals (PART B)

A clear message from the implementation science literature is that information on care gaps alone does not change behaviour and active support or 'facilitation' in some form is required.[102] As described in the paper presented in Chapter 5, successful implementation of an action plan to reduce practice gaps is most likely when implementation processes are appropriately facilitated by either internal or external facilitators.[11]

To our knowledge, our study is the first to explore dosage of external facilitation in a complex multifaceted QI program in acute stroke care in Australia. The delivery of a complex multifaceted intervention to many sites required several different modes of contact, including email, face-to-face and telephone. In this study, the external facilitators provided support to hospital staff to ensure action plans were developed and implemented to change practice. Similarly, the authors of the 'Get With The Guidelines Stroke' program have evaluated the impact of facilitation on quality of care, which were shown to improve adherence to all primary performance measures.[167] In our study a small, but consistent, trend across all forms of delivery of facilitation indicated that a larger dose of external facilitation was associated with more indicators being targeted in action plans. However, in sites with more directed action plans targeting fewer indicators, it was demonstrated that much greater improvement in indicators could be achieved. A lack of definite dose-response is not evidence that external facilitation has no effect, but perhaps the content of facilitation provided is more important than the amount of time spent with facilitators. Unfortunately, I was also unable to comment further on the efficacy of the type of interventions provided since no data on the details of the specific support that was provided at each contact point was available. The pie chart, presented as Figure 1 in

the manuscript (page 103 of thesis) is a general description of the types of support provided by the external facilitator as reported by them. Further research is needed to unpack the role of external facilitation, and the processes involved as part of a multifaceted QI program that uses audit and feedback strategies. Future studies may also include a two-step process where the external facilitators first educate and identify the local barriers and enablers of the hospital, followed by a second meeting that is completely focussed on action planning.[168] In-depth data on the content of support provided must be collected to further understand key factors that play a role in changing clinician behaviour.

12.5 Summary of findings related to addressing the burden of anxiety or depression following stroke (PART C)

In Part B, I provided details of how audit, clinical registry, and hospital administrative data may be used to monitor the quality of stroke care provided in Australian hospitals and identify and help reduce disparities in stroke care, mortality and stroke reoccurrence in the community. In Part C, Chapters 6 and 7, I discussed how we can use data from the clinical registry linked with hospital administrative datasets to investigate potential areas for intervention to reduce practice gaps related to anxiety and depression. By combining these routinely collected datasets it was possible to assess a wider range of factors specific to reducing the burden of anxiety or depression following stroke. In Chapter 6, I described the processes involved to set up the final linked data set used for the analyses presented in Chapter 7.

The main results of Chapter 7 were:

1. Using the EQ-5D-3L, patients that reported having problems with anxiety or depression had a significantly poorer quality of life than those who reported having no issues with anxiety or depression.
2. The factors most strongly associated with post-stroke anxiety or depression were a prior diagnosis of anxiety or depression, dementia, being at home with support, and low socioeconomic advantage compared to high.
3. Acute stroke processes of care, routinely collected in AuSCR, were not independently associated with anxiety or depression.

To address an important limitation of study presented in Chapter 7, in Chapter 8, I undertook a study to assess the convergent validity, sensitivity and specificity of the EQ-5D-3L survey as a tool for screening anxiety or depression in people with stroke.

The preliminary findings were:

1. The EQ-5D-3L had a response rate of 70%.
2. A strong correlation and excellent AU-ROC was observed between the EQ-5D-3L anxiety or depression domain and either subscales of the HADS.
3. The sensitivity and specificity of the EQ-5D-3L anxiety or depression domain and comorbid anxiety or depression symptoms were 100% and 64%, respectively, with a moderate correlation.
4. The sensitivity and specificity of the EQ-5D-3L anxiety or depression domain for anxiety were 89% and 71%, respectively. Whereas, the sensitivity and specificity of the EQ-5D-3L anxiety or depression domain for depression were 85% and 79%, respectively.
5. Forty-three participants completed the additional questions based on the ICHOM survey (81% response rate).

In the next three chapters I focus on a potentially beneficial community-based MBI program. In Chapters 9 and 10, I conducted a scoping and systematic review with meta-analyses, respectively. This comprehensive search of the available evidence is important to understand the magnitude of the potential benefits of MBIs on stroke recovery. The specific aims were to: (i) synthesise the existing evidence of how yoga and tai chi may influence some of the modifiable risk factors for stroke and CVD, (ii) systematically evaluate published evidence on the effectiveness of yoga, on the physical function, mental health, and overall quality of life of survivors of stroke.

The major findings were:

1. Yoga and tai chi appear beneficial in moderating some of the highly prevalent risk factors for stroke, such as hypertension, diabetes and cholesterol.
2. The effectiveness of MBIs on reducing smoking and alcohol intake is not very well understood.
3. The underlying pathophysiological mechanisms of MBIs on the changes to risk factors of stroke are not clear.
4. Neuroimaging research on brain structure and neural connectivity, with MBIs as an intervention, is still in its infancy.
5. There is a need to further unpack these beneficial changes on the pathophysiological pathways leading to therapeutic changes to some of these highly modifiable risk factors for stroke.
6. Yoga may ameliorate state anxiety symptoms and depression in survivors of stroke. Interestingly, consistent but nonsignificant improvements were demonstrated for balance, trait anxiety, and overall quality of life.

Finally, in Chapter 11 a formative evaluation of the processes involved in developing a yoga-based MBI designed for survivors of stroke living in the community was described. The chapter is also used to highlight how 'co-design' is an important aspect of intervention development, where consumers contributed to the four stages of development that led to the final design of the program, which is now ready for testing in a clinical trial.

12.6 Future implications from addressing the burden of anxiety or depression following stroke (PART C)

I conducted one of the largest assessments of factors associated with self-reported anxiety or depression following acute stroke or TIA using registry data linked to hospital administrative datasets and the National Death Index (Chapter 7). Using the EQ-5D-3L, almost one in two AuSCR respondents reported having anxiety or depression at follow-up. Thus confirming the high prevalence of these disorders in survivors after being discharged into the community. I was unable to detect an association between the quality of care received in hospital and self-reported anxiety or depression following stroke. The lack of an independent association between the quality of acute stroke care received, and anxiety or depression following stroke suggests that quality and type of acute stroke care received does not independently impact on anxiety or depression following stroke in the same way as it appears to influence other types of post-stroke disabilities, such as quality of life or survival.[86] Future studies must assess if the development of anxiety or depression following stroke may be influenced by evidence-based mood management in acute care or in the period immediately post-discharge. The AuSCR does not collect information on quality of care provided during rehabilitation. Therefore, using linked data from the Australasian Rehabilitation Outcomes Centre and the AuSCR will allow

us to explore if anxiety or depression at 90-180 days is impacted on by the quality of care received in rehabilitation. Moreover, from the current linked dataset, we do not know if those with anxiety or depression are being well supported or prescribed and managed by appropriate medication or behavioural therapy. Therefore this gap could be answered by using linked data of AuSCR and hospital administrative datasets with the Pharmaceutical Benefits Scheme and the Medicare Benefits Schedule. This will allow us to tease out the impacts of adherence to medications, frequency of general practice visits and use of mental health plans on post-stroke problems with mood.

A major finding of this study is the identification of patient factors in those who were likely to report being moderately or severely anxious or depressed between 90 and 180 days following stroke or TIA, including stroke severity, socioeconomic status, and history of anxiety, depression or dementia prior to admission. This is in agreement with results of other studies where history of anxiety or depression or dementia was regularly highlighted as one of the strongest predictors of the development of anxiety or depression following stroke.[117] Further research is warranted to gain a better understanding of why those with a history of anxiety, depression or dementia are more likely to experience problems with anxiety or depression following stroke and the types of supports and interventions that are required to mitigate these consequences. Identification of those with prior mental health problems for early intervention and support may help reduce the prevalence of post-stroke anxiety or depression. It may be more important to target interventions during the early post-discharge period rather than the acute period. So perhaps more information is needed about the optimal timing of interventions for prevention and management of anxiety or depression, particularly during transition to home and integration back into the community. Considering the high prevalence of anxiety or depression, blanket screening, and screening of those at high risk at various time point during the transition period (e.g. while in hospital, early post-discharge and later post-discharge

period) may be beneficial. General practitioners may need to be more vigilant in follow up these registry patients with these risk factors. Psychosocial interventions for the promotion of mental health or providing social support to those from a low socioeconomic background may be beneficial.

The preliminary findings of the convergent validity study (Chapter 8) provides novel information regarding the usefulness of the EQ-5D-3L for population health research of initial clinical screening purposes (i.e. to identify possible 'sub-clinical symptoms'). Despite ongoing concerns regarding the use of generic quality of life measures for clinical decision making in mental health, such as the EQ-5D-3L, our findings lend some support for the potential use of the EQ-5D-3L for population screening purposes to report on the prevalence of conditions such as anxiety or depression, in the stroke population.

Based on the findings established from the extensive literature search presented in Chapters 9 and 10, MBIs seem beneficial in reducing the impacts of stroke, and may be a potential additional therapy to current strategies. To confirm the potential benefits of MBIs as an adjunct therapy for stroke recovery, large well-designed RCTs are needed and should include power calculations for sample size, comparison group, blinding assessments, are needed. Given the economic burden in health care, these trials should include clinical effectiveness and cost-effectiveness analyses. Understanding the potential risk reductions associated with MBIs are important for both researchers and practitioners to inform the choice of adjunct interventions and training programs implemented for those with high risk of recurrent stroke or other CVD.

Finally, in Chapter 11, in a bid to conduct a future RCT to assess the impacts of MBI on stroke recovery, the formative evaluation of the development of an MBI program was presented. This has important implications for stroke recovery research and practice, as it provides information about an approach that could be adopted for rehabilitative programs for other populations with

chronic disabilities. Engagement of stakeholders in the planning, adaptation and modification of the intervention and research protocols was reliant on their early involvement in the project. Effective implementation of this program is key to delivering the most robust evidence about the efficacy of a yoga-based MBI in survivors of stroke, where the consequences of stroke remains of great concern. This new program will be subsequently evaluated in future clinical trials planned within Australia, and potentially in collaboration with experts from other countries.

12.7 Concluding remarks

In summary, this thesis has covered strategies to improve stroke care and outcomes at a hospital and community-level. A series of studies, with varying study designs, were presented as papers or traditional chapters, and provided a better understanding of the impact of stroke around the world, and potential strategies to identify and reduce evidence-to-practice gaps in acute stroke care. The evidence from this thesis could also help inform policy and practice decisions on how to better support survivors of stroke with anxiety and depression in hospital, and the early period following stroke, and strategies to reduce these consequences when in the community.

References

1. Feigin VL, Abajobir AA, Abate KH, Abd-Allah F, Abdulle AM, Abera SF, et al. Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet Neurology. 2017;16(11):877-97.

2. Deloitte Access Economics. The economic impact of stroke in Australia.Sydney: Deloitte Access Economics. 2013.

3. Andrew NE, Kilkenny M, Naylor R, Purvis T, Lalor E, Moloczij N, et al. Understanding long-term unmet needs in Australian survivors of stroke. International Journal of Stroke. 2014;9:106-12.

4. Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-Year Risk of First Recurrent Stroke and Disability After First-Ever Stroke in the Perth Community Stroke Study. Stroke. 2004;35:731-5.

5. Coutts SB, Hill MD, Campos CR, Choi YB, Subramaniam S, Kosior JC, et al. Recurrent events in transient ischemic attack and minor stroke: what events are happening and to which patients? Stroke. 2008;39(9):2461-6.

6. Feng W, M. HH, Adams RJ. Risk of recurrent stroke, myocardial infarction, or death in hospitalized stroke patients. Neurology. 2010;74(7):588-93.

7. Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne, Australia.

8. Cadilhac DA, Lannin NA, Kim J, Anderson CS, Andrew N, Kilkenny M, et al.; The Australian Stroke Clinical Registry Annual Report 2016. The Florey Institute of Neuroscience and Mental Health; December 2017, Report No 8 , 53 pages.

9. Sturm JW, Davis SM, O'Sullivan JG, Vedadhaghi ME, Donnan GA. The Avoid Stroke as Soon as Possible (ASAP) general practice stroke audit. The Medical Journal of Australia. 2002;176(7):312-6.

10. Cadilhac DA, Carter RC, Thrift AG, Dewey HM. Why invest in a national public health program for stroke?: An example using Australian data to estimate the potential benefits and cost implications. Health Policy. 2007;83(2–3):287-94.

11. Gozdzik A. Applying the PARiHS framework in a knowledge dissemination initiative. CANNT Journal 2013;23(2):48-50.

12. Stetler CB, Legro MW, Rycroft-Malone J, Bowman C, Curran G, Guihan M, et al. Role of "external facilitation" in implementation of research findings: a qualitative evaluation of facilitation experiences in the Veterans Health Administration. Implementation Science. 2006;1:23.

13. Squires JE, Sullivan K, Eccles MP, Worswick J, Grimshaw JM. Are multifaceted interventions more effective than single-component interventions in changing health-care professionals' behaviours? An overview of systematic reviews. Implementation Science. 2014;9:152. doi: 10.1186/s13012-014-0152-6

14. Cadilhac DA, Andrew NE, Lannin NA, Middleton S, Levi CR, Dewey HM, et al. Quality of Acute Care and Long-Term Quality of Life and Survival. Stroke. 2017;48(4):1026-32.

15. Lincoln NB, Brinkmann N, Cunningham S, Dejaeger E, De Weerdt W, Jenni W, et al. Anxiety and depression after stroke: a 5 year follow-up. Disability and Rehabilitation. 2013;35(2):140-5.

16. National Stroke Foundation. National Stroke Audit Acute Services. Report 2017. Melbourne, Vic: National Stroke Foundation; 2017.

17. Stroke Foundation. National Stroke Audit – Rehabilitation Services Report 2016.

18. Eriksson M, Asplund K, Glader E-L, Norrving B, Stegmayr B, Terént A, et al. Self-Reported Depression and Use of Antidepressants After Stroke: A National Survey. Stroke. 2004;35(4):936-41.

19. Hosseini SA, Fallahpour M, Sayadi M, Gharib M, Haghgoo H. The impact of mental practice on stroke patients' postural balance. Journal of the Neurological Sciences. 2012;322(1–2):263-7.

20. Kutlubaev MA, Hackett ML. Part II: predictors of depression after stroke and impact of depression on stroke outcome: an updated systematic review of observational studies. International Journal of Stroke. 2014;9(8):1026-36.

21. Lerdal A, Gay CL. Fatigue in the acute phase after first stroke predicts poorer physical health 18 months later. Neurology. 2013;81(18):1581-7.

22. Staub F, Carota A. Depression and fatigue after stroke. In: M. Barnes BD, & J. Bogousslavsky, editor. Recovery after stroke. Cambridge: Cambridge University Press; 2005.

23. Hofmann SG, Sawyer AT, Witt AA, Oh D. The Effect of Mindfulness-Based Therapy on Anxiety and Depression: A Meta-Analytic Review. Journal of Consulting and Clinical Psychology. 2010;78(2):169-83.

24. Kirkwood G, Rampes H, Tuffrey V, Richardson J, Pilkington K. Yoga for anxiety: a systematic review of the research evidence. British Journal of Sports Medicine. 2005;39(12):884-91.

25. Lakkireddy D, Atkins D, Pillarisetti J, Ryschon K, Bommana S, Drisko J, et al. Effect of Yoga on Arrhythmia Burden, Anxiety, Depression, and Quality of Life in Paroxysmal Atrial Fibrillation. Journal of the American College of Cardiology. 2013;61(11):1177-82.

26. Smith C, Hancock H, Blake-Mortimer J, Eckert K. A randomised comparative trial of yoga and relaxation to reduce stress and anxiety. Complementary Therapies in Medicine. 2007;15:77-83.

27. Tsai JC, Wang WH, Chan P, Lin LJ, Wang CH, Tomlinson B, et al. The beneficial effects of Tai Chi Chuan on blood pressure and lipid profile and anxiety status in a randomized controlled trial. Journal of Alternative and Complementary Medicine 2003;9(5):747-54.

28. Lawrence M, Booth J, Mercer S, Crawford E. A systematic review of the benefits of mindfulness-based interventions following transient ischemic attack and stroke. International Journal of Stroke. 2013;8:465-74.

29. Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO Collaborative Study. Bulletin of the World Health Organization. 1980;58(1):113-30.

30. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An Updated Definition of Stroke for the 21st Century: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2013;44(7):2064-89.

31. Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Hennerici MG. Classification of stroke subtypes. Cerebrovascular Diseases. 2009;27(5):493-501.

32. Karamanakos PN, von Und Zu Fraunberg M, Bendel S, Huttunen T, Kurki M, Hernesniemi J, et al. Risk factors for three phases of 12-month mortality in 1657 patients from a defined population after acute aneurysmal subarachnoid hemorrhage. World Neurosurgery. 2012;78(6):631-9.

33. Hildebrand M, Brewer M, Wolf T. The Impact of Mild Stroke on Participation in Physical Fitness Activities. Stroke Research and Treatment. 2012;2012:548682.

34. Cumming TB, Blomstrand C, Skoog I, Linden T. The High Prevalence of Anxiety Disorders After Stroke. The American Journal of Geriatric Psychiatry.24(2):154-60.

35. Morrison V, Pollard B, Johnston M, MacWalter R. Anxiety and depression 3 years following stroke: Demographic, clinical, and psychological predictors. Journal of Psychosomatic Research. 2005;59(4):209-13.

36. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke. The Oxfordshire Community Stroke Project. Stroke. 1994;25(2):333-7.

37. Dhamoon MS, Sciacca RR, Rundek T, Sacco RL, Elkind MS. Recurrent stroke and cardiac risks after first ischemic stroke: the Northern Manhattan Study. Neurology. 2006;66(5):641-6.

38. Petty GW, Brown RD, Jr., Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Survival and recurrence after first cerebral infarction: a population-based study in Rochester, Minnesota, 1975 through 1989. Neurology. 1998;50(1):208-16.

39. Cadilhac DA, Kilkenny MF, Johnson R, Wilkinson B, Amatya B, Lalor E. The Know Your Numbers (KYN) Program 2008 to 2010: Impact on Knowledge and Health Promotion Behavior among Participants. International Journal of Stroke. 2013;10(1):110-6.

40. Bernhardt J, Hayward KS, Kwakkel G, Ward NS, Wolf SL, Borschmann K, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: The Stroke Recovery and Rehabilitation Roundtable taskforce. International Journal of Stroke. 2017;12(5):444-50.

41. Billinger SA, Arena R, Bernhardt J, Eng JJ, Franklin BA, Johnson CM, et al. Physical Activity and Exercise Recommendations for Stroke Survivors: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2014;45(8):2532-53.

42. Gordon LA, Morrison EY, McGrowder DA, Young R, Fraser YT, Zamora EM, et al. Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes. BMC Complementary and Alternative Medicine. 2008;8:21.

43. Donohue JM, Pincus HA. Reducing the Societal Burden of Depression. PharmacoEconomics. 2007;25(1):7-24.

44. World Health Organization [Available from: http://www.who.int/topics/risk_factors/en/.

45. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. The Lancet. 2016;388(10046):761-75.

46. Lee KK, Miller MR, Shah ASV. Air Pollution and Stroke. Journal of Stroke. 2018;20(1):2-11.

47. Sacco RL. Risk factors and outcomes for ischemic stroke. Neurology. 1995;45(2 Suppl 1):S10-4.

48. Lai SM, Alter M, Friday G, Sobel E. A multifactorial analysis of risk factors for recurrence of ischemic stroke. Stroke. 1994;25(5):958.

49. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: The jnc 7 report. JAMA. 2003;289(19):2560-71.

50. Qureshi AI, Ezzeddine MA, Nasar A, Suri MF, Kirmani JF, Hussein HM, et al. Prevalence of elevated blood pressure in 563,704 adult patients with stroke presenting to the ED in the United States. The American Journal of Emergency Medicine. 2007;25(1):32-8.

51. Arboix A. Cardiovascular risk factors for acute stroke: Risk profiles in the different subtypes of ischemic stroke. World Journal of Clinical Cases. 2015;3(5):418-29.

52. Yu JG, Zhou RR, Cai GJ. From hypertension to stroke: mechanisms and potential prevention strategies. CNS Neuroscience & Therapeutics. 2011;17(5):577-84.

53. NCD Risk Factor Collaboration (NCD-RisC). Effects of diabetes definition on global surveillance of diabetes prevalence and diagnosis: a pooled analysis of 96 population-based studies with 331 288 participants. The Lancet Diabetes & Endocrinology. 2015;3(8):624-37.

54. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414:782.

55. Colagiuri S, Walker AE. Using An Economic Model Of Diabetes To Evaluate Prevention And Care Strategies In Australia. Health Affairs. 2008;27(1):256-68.

56. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375(9733):2215-22.

57. Berthet K, Neal B, Chalmers J, Macmahon S, Bousser MG, Colman S, et al. Reductions in the risks of recurrent stroke in patients with and without diabetes: The PROGRESS Trial. Blood Pressure. 2004;13(1):7-13.

58. American Diabetes Association. Pancreas and Islet Transplantation in Type 1 Diabetes. Diabetes Care. 2006;29(4):935.

59. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: Epidemiology, pathophysiology, and management. JAMA. 2002;287(19):2570-81.

60. Klop B, Elte JWF, Castro Cabezas M. Dyslipidemia in Obesity: Mechanisms and Potential Targets. Nutrients. 2013;5(4):1218-40.

61. Nelson RH. Hyperlipidemia as a Risk Factor for Cardiovascular Disease. Primary care. 2013;40(1):195-211.

62. Yaghi S, Elkind MSV. Lipids and Cerebrovascular Disease: Research and Practice. Stroke. 2015;46(11):3322-8.

63. Zhang X, Patel A, Horibe H, Wu Z, Barzi F, Rodgers A, et al. Cholesterol, coronary heart disease, and stroke in the Asia Pacific region. International Journal of Epidemiology. 2003;32(4):563-72.

64. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22(8):983-8.

65. Andrew NE, Thrift AG, Cadilhac DA. The Prevalence, Impact and Economic Implications of Atrial Fibrillation in Stroke: What Progress Has Been Made? Neuroepidemiology. 2013;40(4):227-39.

66. Lambiase MJ, Kubzansky LD, Thurston RC. Prospective Study of Anxiety and Incident Stroke. Stroke. 2014;45(2):438-43.

67. Barlinn K, Kepplinger J, Puetz V, Illigens BM, Bodechtel U, Siepmann T. Exploring the risk-factor association between depression and incident stroke: a systematic review and meta-analysis. Neuropsychiatric Disease and Treatment. 2015;11:1-14.

68. Yuan HW, Wang CX, Zhang N, Bai Y, Shi YZ, Zhou Y, et al. Poststroke Depression and Risk of Recurrent Stroke at 1 Year in a Chinese Cohort Study. PLoS ONE. 2012;7(10):e46906.

69. Shah RS, Cole JW. Smoking and stroke: the more you smoke the more you stroke. Expert Review of Cardiovascular Therapy. 2010;8(7):917-32.

70. Asplund K, Karvanen J, Giampaoli S, Jousilahti P, Niemela M, Broda G, et al. Relative risks for stroke by age, sex, and population based on follow-up of 18 European populations in the MORGAM Project. Stroke. 2009;40(7):2319-26.

71. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. Journal of the American College of Cardiology. 2004;43(10):1731-7.

72. Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, Mohapatra S, et al. Alcohol consumption and the risk of morbidity and mortality for different stroke types--a systematic review and meta-analysis. BMC Public Health. 2010;10:258.

73. Medeiros F, Casanova Mde A, Fraulob JC, Trindade M. How can diet influence the risk of stroke? International Journal of Hypertension. 2012;2012:763507.

74. Houston MC. Nutraceuticals, Vitamins, Antioxidants, and Minerals in the Prevention and Treatment of Hypertension. Progress in Cardiovascular Diseases. 2005;47(6):396-449.

75. Reinholdsson M, Palstam A, Sunnerhagen KS. Prestroke physical activity could influence acute stroke severity (part of PAPSIGOT). Neurology. 2018;91(16):e1461-e7.

76. Gordon NF, Gulanick M, Costa F, Fletcher G, Franklin BA, Roth EJ, et al. Physical activity and exercise recommendations for stroke survivors: an American Heart Association scientific statement from the Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention; the Council on Cardiovascular Nursing; the Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council. Stroke. 2004;35(5):1230-40.

77. Kroll ME, Green J, Beral V, Sudlow CL, Brown A, Kirichek O, et al. Adiposity and ischemic and hemorrhagic stroke: Prospective study in women and meta-analysis. Neurology. 2016;87(14):1473-81.

78. Kurth T, Gaziano JM, Berger K, Kase CS, Rexrode KM, Cook NR, et al. Body mass index and the risk of stroke in men. Archives of Internal Medicine. 2002;162(22):2557-62.

79. Strazzullo P, D'Elia L, Cairella G, Garbagnati F, Cappuccio FP, Scalfi L. Excess body weight and incidence of stroke: meta-analysis of prospective studies with 2 million participants. Stroke. 2010;41(5):e418-26.

80. Ndumele CE, Matsushita K, Lazo M, Bello N, Blumenthal RS, Gerstenblith G, et al. Obesity and Subtypes of Incident Cardiovascular Disease. Journal of the American Heart Association. 2016;5(8).

81. Thrift AG, Cadilhac DA, Thayabaranathan T, Howard G, Howard VJ, Rothwell PM, et al. Global stroke statistics. International Journal of Stroke. 2014;9:6-18.

82. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet. 2014;383(9913):245-54.

83. Cadilhac DA, Kim J, Lannin NA, Kapral MK, Schwamm LH, Dennis MS, et al. National stroke registries for monitoring and improving the quality of hospital care: A systematic review. International Journal of Stroke. 2016;11(1):28-40.

84. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. The Lancet. 2010;376(9735):112-23.

85. Cadilhac DA, Ibrahim J, Pearce DC, Ogden KJ, McNeill J, Davis SM, et al. Multicenter comparison of processes of care between Stroke Units and conventional care wards in Australia. Stroke. 2004;35(5):1035-40.

86. Cadilhac DA, Pearce DC, Levi CR, Donnan GA. Improvements in the quality of care and health outcomes with new stroke care units following implementation of a clinician-led, health system redesign programme in New South Wales, Australia. Quality and Safety in Health Care. 2008;17(5):329-33.

87. The European Stroke Organisation Executive Committee. & The E. S. O. Writing Committee. Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack. 2008. Report No.: 1015-9770 Contract No.: 5.

88. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2018;49(3):e46-e110.

89. National Acute Stroke Services Framework 2011.

90. Australian Commission on Safety and Quality in Health Care. Acute Stroke Clinical Care Standard. Sydney: ACSQHC, 2015.

91. National Health and Medical Research Council. NHMRC levels of evidence and grades for recommendations for guideline developers. Canberra: National Health and Medical Research Council; 2009 Available from: https://www.mja.com.au/sites/default/files/NHMRC.levels.of.evidence.2008-09.pdf.

92. Cadilhac DA, Lannin NA, Anderson CS, Levi CR, Faux S, Price C, et al. Protocol and pilot data for establishing the Australian Stroke Clinical Registry. International Journal of Stroke. 2010;5(3):217-26.

93. Begg SJ, Vos T, Barker B, Stanley L, Lopez AD. Burden of disease and injury in Australia in the new millennium: measuring health loss from diseases, injuries and risk factors. The Medical Journal of Australia. 2008;188(1):36-40.

94. National Stroke Foundation. National Stroke Audit Clinical Report Acute Services 2009. Melbourne, Vic: National Stroke Foundation; 2009.

95. National Stroke Foundation. National Stroke Audit Clinical Report Acute Services 2011 Melbourne, Vic: National Stroke Foundation; 2011.

96. National Stroke Foundation. National Stroke Audit Acute Services. Organisational Survey Report 2011. Melbourne, Vic: National Stroke Foundation; 2011.

97. Purvis T, Kilkenny MF, Middleton S, Cadilhac DA. Influence of stroke coordinators on delivery of acute stroke care and hospital outcomes: An observational study. International Journal of Stroke. 2017;13(6):585-91.

98. Busingye D, Kilkenny MF, Purvis T, Kim J, Middleton S, Campbell BCV, et al. Is length of time in a stroke unit associated with better outcomes for patients with stroke in Australia? An observational study. BMJ Open. 2018;8(11):e022536. doi: 10.1136/bmjopen-2018-.

99. National Stroke Foundation. National Stroke Audit Acute Services. Organisational Survey Report 2013. Melbourne, Vic: National Stroke Foundation; 2013.

100. ; Australian Institute of Health and Welfare 2003. Public hospital establishments National Minimum Data Set. National Health Data Dictionary. Version 12. AIHW Cat. No. HWI 60. Canberra: Australian Institute of Health and Welfare.

101. O'Malley KJ, Cook KF, Price MD, Wildes KR, Hurdle JF, Ashton CM. Measuring Diagnoses: ICD Code Accuracy. Health Services Research. 2005;40(5):1620-39.

102. Grimshaw JM, Eccles MP, Walker AE, Thomas RE. Changing physicians' behavior: What works and thoughts on getting more things to work. Journal of Continuing Education in the Health Professions. 2002;22(4):237-43.

103. Grimshaw J, Eccles M, Tetroe J. Implementing clinical guidelines: Current evidence and future implications. Journal of Continuing Education in the Health Professions. 2004;24(S1):S31-S7.

104. Grimshaw JM, Eccles MP, Lavis JN, Hill SJ, Squires JE. Knowledge translation of research findings. Implementation Science. 2012;7(1):1-17.

105. Murphy P, Smith D, Vislosky M, Tripputi M, Cumbler E, Blakie J, et al. The impact of a statewide stroke quality improvement program: Colorado Stroke Alliance and Colorado Stroke Registry. The Journal of Neuroscience Nursing. 2011;43(5):246-52.

106. Grau AJ, Eicke M, Biegler MK, Faldum A, Bamberg C, Haass A, et al. Quality monitoring of acute stroke care in Rhineland-Palatinate, Germany, 2001-2006. Stroke. 2010;41(7):1495-500.

107. Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. Health technology assessment. 2004;8(6):1-72.

108. Cadilhac DA, Andrew NE, Kilkenny MF, Hill K, Grabsch B, Lannin NA, et al. Improving quality and outcomes of stroke care in hospitals: Protocol and statistical analysis plan for the Stroke123 implementation study. International Journal of Stroke. 2018;13(1):96-106.

109. Rycroft-Malone J. The PARIHS framework--a framework for guiding the implementation of evidence-based practice. Journal of Nursing Care Quality. 2004;19(4):297-304.

110. Speroff T, O'Connor GT. Study Designs for PDSA Quality Improvement Research. Quality Management in Healthcare. 2004;13(1):17-32.

111. Kitson AL, Rycroft-Malone J, Harvey G, McCormack B, Seers K, Titchen A. Evaluating the successful implementation of evidence into practice using the PARiHS framework: theoretical and practical challenges. Implementation Science. 2008;3:1-.

112. Harvey G, Loftus-Hills A, Rycroft-Malone J, Titchen A, Kitson A, McCormack B, et al. Getting evidence into practice: the role and function of facilitation. Journal of Advanced Nursing. 2002;37(6):577-88.

113. Hughes RG. Advances in Patient Safety Tools and Strategies for Quality Improvement and Patient Safety. In: Hughes RG, editor. Patient Safety and Quality: An Evidence-Based Handbook for Nurses. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008.

114. Andrew NE, Sundararajan V, Thrift AG, Kilkenny MF, Katzenellenbogen J, Flack F, et al. Addressing the challenges of cross-jurisdictional data linkage between a national clinical quality registry and government-held health data. The Australian and New Zealand Journal of Public Health. 2016;40(5):436-42.

115. Hunger M, Sabariego C, Stollenwerk B, xf, rn, Cieza A, et al. Validity, reliability and responsiveness of the EQ-5D in German stroke patients undergoing rehabilitation. Quality of Life Research. 2012;21(7):1205-16.

116. Pinto EB, Maso I, Vilela RNR, Santos LC, Oliveira-Filho J. Validation of the EuroQol quality of life questionnaire on stroke victims. Arquivos de Neuro-Psiquiatria. 2011;69:320-3.

117. Ayerbe L, Ayis S, Wolfe CDA, Rudd AG. Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. The British Journal of Psychiatry. 2013;202(1):14-21.

118. Clemens S, Begum N, Harper C, Whitty JA, Scuffham PA. A comparison of EQ-5D-3L population norms in Queensland, Australia, estimated using utility value sets from Australia, the UK and USA. Quality of Life Research. 2014;23(8):2375-81.

119. Hinz A, Kohlmann T, Stobel-Richter Y, Zenger M, Brahler E. The quality of life questionnaire EQ-5D-5L: psychometric properties and normative values for the general German population. Quality of Life Research. 2014;23(2):443-7.

120. Konig HH, Bernert S, Angermeyer MC, Matschinger H, Martinez M, Vilagut G, et al. Comparison of population health status in six european countries: results of a representative survey using the EQ-5D questionnaire. Medical Care. 2009;47(2):255-61.

121. McCaffrey N, Kaambwa B, Currow DC, Ratcliffe J. Health-related quality of life measured using the EQ-5D–5L: South Australian population norms. Health and Quality of Life Outcomes. 2016;14:133.

122. Saarni SI, Harkanen T, Sintonen H, Suvisaari J, Koskinen S, Aromaa A, et al. The impact of 29 chronic conditions on health-related quality of life: a general population survey in Finland using 15D and EQ-5D. Quality of Life Research. 2006;15(8):1403-14.

123. Shiroiwa T, Fukuda T, Ikeda S, Igarashi A, Noto S, Saito S, et al. Japanese population norms for preference-based measures: EQ-5D-3L, EQ-5D-5L, and SF-6D. Quality of Life Research. 2016;25:707-19.

124. Andrew NE, Kilkenny MF, Lannin NA, Cadilhac DA. Is health-related quality of life between 90 and 180 days following stroke associated with long-term unmet needs? Quality of Life Research. 2016;25(8):2053-62.

125. Jorgensen TS, Turesson C, Kapetanovic M, Englund M, Turkiewicz A, Christensen R, et al. EQ-5D utility, response and drug survival in rheumatoid arthritis patients on biologic monotherapy: A prospective observational study of patients registered in the south Swedish SSATG registry. PLoS One. 2017;12(2):e0169946.

126. Kim S-H, Jo M-W, Lee J-W, Lee H-J, Kim JK. Validity and reliability of EQ-5D-3L for breast cancer patients in Korea. Health and Quality of Life Outcomes. 2015;13:203.

127. Chen P, Lin K-C, Liing R-J, Wu C-Y, Chen C-L, Chang K-C. Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. Quality of Life Research. 2016;25(6):1585-96.

128. Carlson KD, Herdman AO. Understanding the Impact of Convergent Validity on Research Results. Organizational Research Methods. 2010;15(1):17-32.

129. Szende A, Devlin N, Oppe M. EQ-5D Value Sets : Inventory, Comparative Review and User Guide. Dordrecht: Springer; 2007.

130. Payakachat N, Ali MM, Tilford JM. Can The EQ-5D Detect Meaningful Change? A Systematic Review. PharmacoEconomics. 2015;33(11):1137-54.

131. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. Journal of Psychosomatic Research. 2002;52(2):69-77.

132. Aben I, Verhey F, Lousberg R, Lodder J, Honig A. Validity of the Beck Depression Inventory, Hospital Anxiety and Depression Scale, SCL-90, and Hamilton Depression Rating Scale as Screening Instruments for Depression in Stroke Patients. Psychosomatics. 2002;43(5):386-93.

133. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatrica Scandinavica. 1983;67(6):361-70.

134. Kruithof N, Van Cleef MHM, Rasquin SMC, Bovend'Eerdt TJH. Screening Poststroke Fatigue; Feasibility and Validation of an Instrument for the Screening of Poststroke Fatigue throughout the Rehabilitation Process. Journal of Stroke and Cerebrovascular Diseases. 2016;25(1):188-96.

135. Trippolini MA, Dijkstra PU, Geertzen JHB, Reneman MF. Construct Validity of Functional Capacity Evaluation in Patients with Whiplash-Associated Disorders. Journal of Occupational Rehabilitation. 2015;25(3):481-92.

136. Sagen U, Vik TG, Moum T, Mørland T, Finset A, Dammen T. Screening for anxiety and depression after stroke: Comparison of the Hospital Anxiety and Depression Scale and the Montgomery and Åsberg Depression Rating Scale. Journal of Psychosomatic Research. 2009;67(4):325-32.

137. Prisnie JC, Fiest KM, Coutts SB, Patten SB, Atta CAM, Blaikie L, et al. Validating screening tools for depression in stroke and transient ischemic attack patients. The International Journal of Psychiatry in Medicine. 2016;51(3):262-77.

138. Salinas J, Sprinkhuizen SM, Ackerson T, Bernhardt J, Davie C, George MG, et al. An International Standard Set of Patient-Centered Outcome Measures After Stroke. Stroke. 2016;47(1):180-6.

139. International Consortium for Health Outcomes Measurement (ICHOM) [Available from: www.ichom.org.

140. Jutte JE, Needham DM, Pfoh ER, Bienvenu OJ. Psychometric evaluation of the Hospital Anxiety and Depression Scale 3 months after acute lung injury. Journal of Critical Care. 2015;30(4):793-8.

141. Collins MM, Corcoran P, Perry IJ. Anxiety and depression symptoms in patients with diabetes. Diabetic Medicine. 2009;26(2):153-61.

142. Pattanaphesaj J, Thavorncharoensap M. Measurement properties of the EQ-5D-5L compared to EQ-5D-3L in the Thai diabetes patients. Health and Quality of Life Outcomes. 2015;13(1):14.

143. Zou KH, O'Malley AJ, Mauri L. Receiver-operating characteristic analysis for evaluating diagnostic tests and predictive models. Circulation. 2007;115(5):654-7.

144. Mandrekar JN. Receiver Operating Characteristic Curve in Diagnostic Test Assessment. Journal of Thoracic Oncology. 2010;5(9):1315-6.

145. Supina AL, Johnson JA, Patten SB, Williams JV, Maxwell CJ. The usefulness of the EQ-5D in differentiating among persons with major depressive episode and anxiety. Quality of Life Research. 2007;16(5):749-54.

146. Strik JJMH, Honig A, Lousberg R, Denollet J. Sensitivity and Specificity of Observer and Self-Report Questionnaires in Major and Minor Depression Following Myocardial Infarction. Psychosomatics. 2001;42(5):423-8.

147. Chisholm D, Healey A, Knapp M. QALYs and mental health care. Social Psychiatry and Psychiatric Epidemiology. 1997;32(2):68-75.

148. Buffart LM, van Uffelen JGZ, Riphagen II, Brug J, van Mechelen W, Brown WJ, et al. Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. BMC Cancer. 2012;12:559-.

149. Hagins M, States R, Selfe T, Innes K. Effectiveness of Yoga for Hypertension: Systematic Review and Meta-Analysis. Evidence-Based Complementary and Alternative Medicine. 2013;2013:13.

150. Kwong JSW, Lau HLC, Yeung F, Chau PH, Woo J. Yoga for secondary prevention of coronary heart disease. Cochrane Database of Systematic Reviews. 2015;Issue 6. Art. No.: CD009506. DOI: 10.1002/14651858.CD009506.pub3.

151. McDermott KA, Rao MR, Nagarathna R, Murphy EJ, Burke A, Nagendra RH, et al. A yoga intervention for type 2 diabetes risk reduction: A pilot randomized controlled trial. BMC Complementary and Alternative medicine. 2014;14.

152. Lazaridou A, Philbrook P, Tzika AA. Yoga and Mindfulness as Therapeutic Interventions for Stroke Rehabiliation: A Systematic Review. Evidence-Based Complementary and Alternative Medicine. 2013;2013(1-9).

153. Lynton H, Kligler B, Shiflett S. Yoga in stroke rehabiliation: a systematic review and results of a pilot study. Topics in Stroke Rehabilitation. 2007;14(4):1-8.

154. Lawrence M, Celestino Junior FT, Matozinho HHS, Govan L, Booth J, Beecher J. Yoga for stroke rehabilitation. Cochrane Database of Systematic Reviews. 2017:12. Art. No: CD011483. doi: 10.1002/14651858.CD011483.pub2.

155. van Teijlingen E, Hundley V. The importance of pilot studies. Nursing standard (Royal College of Nursing (Great Britain) : 1987). 2002;16(40):33-6.

156. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655.

157. Hedberg JG. Education design research – Edited by J van den Akker. British Journal of Educational Technology. 2008;39(3):559-60.

158. Stetler CB, Legro MW, Wallace CM, Bowman C, Guihan M, Hagedorn H, et al. The role of formative evaluation in implementation research and the QUERI experience. Journal of General Internal Medicine. 2006;21 Suppl 2:S1-8.

159. Malinowski P. Neural mechanisms of attentional control in mindfulness meditation. Frontiers in Neuroscience. 2013;7(8).

160. Garrett R, Immink MA, Hillier S. Becoming connected: the lived experience of yoga participation after stroke. Disability and Rehabilitation. 2011;33((25-26)):2404-15.

161. Immink MA, Hillier S, Petkov J. Randomised Controlled Trial of Yoga for Chronic Poststroke Hemiparesis: Motor Function, Mental Health, and Quality of Life Outcomes. Topics in Stroke Rehabilitation. 2014;21(3):256-71.

162. Holkup PA, Tripp-Reimer T, Salois EM, Weinert C. Community-based Participatory Research: An Approach to Intervention Research With a Native American Community. ANS Advances in Nursing Science. 2004;27(3):162-75.

163. Johnson-Frey SH. Stimulation through simulation? Motor imagery and functional reorganization in hemiplegic stroke patients. Brain and Cognition. 2004;55(2):328-31.

164. Cadilhac DA, Fisher R, Bernhardt J. How to do health services research in stroke: A focus on performance measurement and quality improvement. International Journal of Stroke. 2018;13(2):166-74.

165. Filipe A, Renedo A, Marston C. The co-production of what? Knowledge, values, and social relations in health care. PLoS biology. 2017;15(5):e2001403.

166. Thayabaranathan T, Andrew NE, Immink MA, Hillier S, Stevens P, Stolwyk R, et al. Determining the potential benefits of yoga in chronic stroke care: a systematic review and meta-analysis. Topics in Stroke Rehabilitation. 2017;24(4):279-287.

167. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, et al. Get With the Guidelines–Stroke Is Associated With Sustained Improvement in Care for Patients Hospitalized With Acute Stroke or Transient Ischemic Attack. Circulation. 2009;119(1):107.

168. Cadilhac DA, Andrew NE, Stroil Salama E, Hill K, Middleton S, Horton E, et al. Improving discharge care: the potential of a new organisational intervention to improve discharge after hospitalisation for acute stroke, a controlled before–after pilot study. BMJ Open. 2017;7(8).

Appendices

Australian Stroke Clinical Registry

This questionnaire will help us understand how you have been feeling in the past week. Please choose the option with "✓" that is closest to how you have been feeling. You do not have to think too much to answer: your immediate feeling is best.

1. I feel tense or 'wound up':

- Most of the time ☐
- A lot of the time ☐
- From time to time, occasionally ☐
- Not at all ☐

2. I get sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

3. Worrying thoughts go through my mind:

- A great deal of the time ☐
- A lot of the time ☐
- From time to time, but not too often ☐
- Only occasionally ☐

4. I can sit at ease and feel relaxed

- Definitely ☐
- Usually ☐
- Not often ☐
- Not at all ☐

5. I get a sort of frightened feeling like 'butterflies' in the stomach:

- Not at all ☐
- Occasionally ☐
- Quite often ☐
- Very often ☐

6. I feel restless as I have to be on the move:

- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

7. I get sudden feelings of panic:

- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

8. I still enjoy the things I used to enjoy:

- Definitely as much ☐
- Not quite so much ☐
- Only a little ☐
- Hardly at all ☐

9. I can laugh and see the funny side of things:

- As much as I always could ☐
- Not quite so much now ☐
- Definitely not so much now ☐
- Not at all ☐

10. I feel cheerful:

- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

11. I feel as if I am slowed down:

- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

12. I have lost interest in my appearance:

- Definitely ☐
- I don't take as much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

13. I look forward with enjoyment to things:

- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

14. I can enjoy a good book or radio or TV program:

- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

15. In general, how do you rate your ability to think?

- Excellent ☐
- Very good ☐
- Good ☐
- Fair ☐
- Poor ☐

16. In the past 7 days, how would you rate your fatigue:

- None ☐
- Mild ☐
- Moderate ☐
- Severe ☐
- Very severe ☐

17. In general, please rate how well you carry out your social activities and roles. *(This includes activities at home, work, community, and responsibilities as a parent, child, friend, etc)*

- Excellent ☐
- Very good ☐
- Good ☐
- Fair ☐
- Poor ☐

18. Do you have any problems with communication or understanding?

No ☐ Yes ☐

19. Do you need a tube for feeding?

No ☐ Yes ☐

20. Do you take any medication/s for anxiety or depression?

No ☐ Yes ☐

Thank you for taking the time to fill out this questionnaire. Please return this form, along with the Follow-up form to the AuSCR office using the replied paid envelope.

<Patient name>	*<Date of mail out>*	*<Patient Record Number>*

FOLLOW-UP FORM

AuSCR Australian Stroke Clinical Registry

Please complete the form:
- Neatly and legibly
- Write in **black ink** and press firmly
- Each question must be completed
- Place ☑ in appropriate boxes

Please return this form to AuSCR office using the reply paid envelope:
AuSCR, Public Health,
Florey Institute of Neuroscience and Mental Health
245 Burgundy Street, Heidelberg, VIC, 3084

Personal details:
(only complete <u>if your personal details have changed</u> since you were last in hospital)

Title ☐☐☐☐☐☐☐☐☐☐☐☐

First Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Last Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Address type ☐ Home ☐ Business ☐ Other

Street Address ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Suburb ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Post Code ☐☐☐☐ State ☐☐☐

Country ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Phone Number ☐☐☐☐☐☐☐☐☐☐ Mobile Number ☐☐☐☐☐☐☐☐☐☐

Medicare No ☐☐☐☐☐☐☐☐☐☐

Date of Birth ☐☐/☐☐/☐☐☐☐ (dd/mm/yyyy)

Gender ☐ Male ☐ Female ☐ Intersex or indeterminate

Please confirm if you are of Aboriginal and/or Torres Strait Islander origin?
- ☐ Aboriginal but not Torres Strait Islander origin
- ☐ Torres Strait Islander but not Aboriginal origin
- ☐ Both Aboriginal and Torres Strait Islander origin
- ☐ Neither Aboriginal nor Torres Strait Islander origin
- ☐ Indigenous not otherwise described

Follow- up Questions

1. Where are you staying at present?

- ☐ Hospital
- ☐ Home with care supports (e.g. assistance from family, council services etc)
- ☐ Rehabilitation (inpatient)
- ☐ Home without care supports
- ☐ Hostel Care
- ☐ Transitional care service
- ☐ Nursing Home
- ☐ Other _____

2. Do you live on your own?

☐ Yes, I live entirely on my own ☐ No, I live with others

3. Since you were in hospital for your stroke *<date inserted by AuSCR office>***, have you had another stroke?**

☐ Yes ☐ No

4. Since you were in hospital for your stroke, have you been readmitted to hospital?

☐ Yes ☐ No

If Yes, what was the reason for your admission?_____

Date of re-admission ☐☐/☐☐/☐☐☐☐ (dd/mm/yyyy)

5. Which of these sentences best describes your level of disability today? *(Tick one box only).*

☐ ***0 = NO SYMPTOMS AT ALL***

☐ ***1 = NO SIGNIFICANT DISABILITY DESPITE SYMPTOMS***
able to carry out all usual duties and activities

☐ ***2 = SLIGHT DISABILITY***
unable to carry out all previous activities, but able to look after own affairs without assistance

☐ ***3 = MODERATE DISABILITY***
requiring some help, but able to walk without assistance

☐ ***4 = MODERATELY SEVERE DISABILITY***
unable to walk without assistance, and unable attend to own bodily needs without assistance

☐ ***5 = SEVERE DISABILITY***
bedridden, incontinent, and requiring constant nursing care and attention

By placing a tick <u>in one box in each group</u> below, please indicate which statements best describe your own health state today.

6. Mobility

Thinking about your health today, which of the following statements best describes your mobility?

☐ I have no problems in walking about
☐ I have some problems in walking about
☐ I am confined to bed

7. Self-care

Thinking about your health today, which of the following statements best describes your self-care?

☐ I have no problems with self-care
☐ I have some problems washing or dressing myself
☐ I am unable to wash or dress myself

8. Usual activity

Thinking about your health today, which of the following statements best describes your usual activities such as work, study, housework, family or leisure activities?

☐ I have no problems with performing my usual activities
☐ I have some problems with performing my usual activities
☐ I am unable to perform my usual activities.

9. Pain/discomfort

Thinking about your health today, which of the following statements best describes any pain or discomfort you may be experiencing?

☐ I have no pain or discomfort
☐ I have moderate pain or discomfort
☐ I have extreme pain or discomfort

10. Anxiety/depression

Thinking about your health today, which of the following statements best describes any anxiety and depression you may be experiencing?

☐ I am not anxious or depressed
☐ I am moderately anxious or depressed
☐ I am extremely anxious or depressed

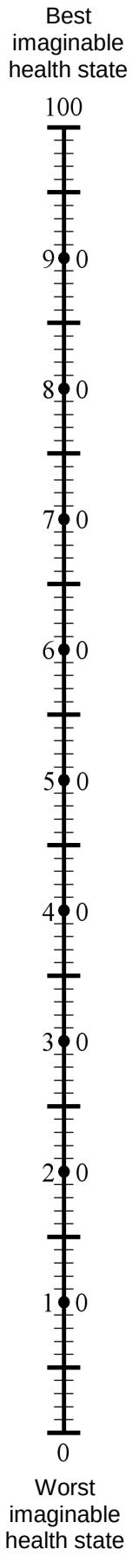
11. Health State

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion.

Please do this by drawing a line from the box below to whichever **point** on the scale indicates how good or bad your health state is today.

Your own health state today



12. Would you like to receive an information package from the Stroke Foundation about stroke and support services?

☐ Yes ☐ No

13. Would you be willing to be contacted in the future to hear about possible stroke research projects that you may be eligible for?

☐ Yes ☐ No

Form completed by: ☐ Self ☐ Other (please complete below)

Name: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ **Signature:** _____

Relationship to Patient: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Date: ☐☐/☐☐/☐☐☐☐ **Contact Number:** ☐☐☐☐☐☐☐☐☐☐

Additional Comments:

THIS IS THE END OF THE QUESTIONNAIRE. THANK YOU FOR YOUR TIME.

Please return to the AuSCR office using the reply paid envelope enclosed.

AuSCR
Australian Stroke Clinical Registry

TITLE FIRST NAME SURNAME
555 XXXXXXXX STREET
SUBURB QLD XXXX

Day Month 2018

Dear TITLE SURNAME,

The Australian Stroke Clinical Registry (AuSCR) and HOSPITAL NAME have a continuing interest in knowing about the recovery of patients with stroke or transient ischaemic attack (TIA). This information forms an essential part of our efforts to improve hospital care and outcomes for these conditions.

Completing the enclosed, brief questionnaire is voluntary, but we would very much appreciate receiving information about where you are living and how you are presently managing since returning from hospital.

If you are unable to complete the questionnaire yourself, we suggest that you might obtain the assistance of a relative, friend or carer, in order to provide us with as much information as possible. If you are a relative, friend or carer of the intended recipient of this letter, and in the event that they are now deceased, we respectfully ask that you inform us of their date of death. In this circumstance, no further contact will then be made by our office.

Please complete all the questions in the form provided and return it to the AuSCR Office. A reply paid envelope is enclosed for your convenience. If we do not receive your completed questionnaire within four weeks we may send another to you, or your next of kin, as a reminder.

Thank you for taking the time to complete this questionnaire. We hope that the responses will help us with our goal to improve stroke care across Australia. Please direct questions or concerns to the AuSCR office on freecall 1800 673 053 or admin@auscr.com.au.

Yours sincerely,

[redacted]

Associate Professor Dominique Cadilhac
AuSCR Data Custodian

Office Use Only
Patient Record ID: 70911

AuSCR OFFICE

Public Health, Stroke Division, Florey Institute of Neuroscience and Mental Health
245 Burgundy Street Heidelberg Victoria 3084 Australia
Free Call 1800 673 053 | www.auscr.com.au | admin@auscr.com.au

[TITLE] [FIRST NAME] [SURNAME]
[ADRESS]
[ADDRESS]

[DAY] [DATE] [YEAR]

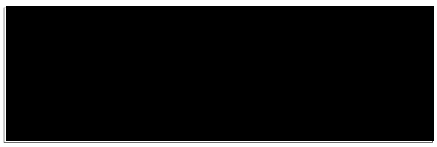
Dear [TITLE] [SURNAME],

For a time-limited period we are requesting an additional survey to be completed so that we can obtain a better understanding of the long-term effects of stroke in relation to problems with mood. This project will also assist us to identify whether we need to update the questions we routinely gather for the AuSCR to identify conditions such as anxiety, depression, or fatigue after stroke.

Completing this additional survey is optional, but encouraged. Please take the time to read the material before you decide whether to participate.

Please return all forms, whether completed or not in the enclosed replied paid envelope.

Yours sincerely,



Professor Dominique Cadilhac
AuSCR Data Custodian

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Office Use Only
Patient Record ID: XXXXX

Appendix E

Example search strategy

PubMed

((((((((((((((((((randomized controlled trial) OR RCT) OR before after study) OR pre post intervention) OR random allocation) OR control group*) OR active control) OR clinical trial) OR blinding) OR placebo) OR treatment) OR intervention))))) AND (((human) AND patients) NOT animals)) AND ((((((((((((((((exercise) OR hatha) OR ashtanga) OR bikram) OR iyengar) OR kripalu) OR kundalini) OR sivananda) OR vinyasa) OR bhakti) OR karma) OR yama) OR niyama) OR asana*) OR pranayama) OR pratyahara) OR dharana) OR dhyana)) AND (((((((((Yoga) OR mind body therapies) OR breathing exercises) OR meditation) OR relaxation therapy) OR mindfulness) OR mindfulness therapy) OR mindfulness based interventions) OR tai chi) OR taichi) OR attention)) AND ((((((((((((((cerebrovascular disorders) OR basal ganglia cerebrovascular disease) OR (brain ischemia OR brain ischaemia)) OR carotid artery diseases) OR intracranial arterial diseases) OR intracranial arteriovenous malformations) OR (intracranial hemorrhages OR intracranial haemorrhages)) OR stroke) OR brain infarction) OR vasospasm) OR post stroke) OR cerebrovasc*) OR brain vasc*) OR cerebral vasc*) OR cva*) OR subarachnoid) AND (((exercise) OR exercises) OR usual care))) AND ((((((fatigue) OR depression) OR depress*) OR anxiety) OR mental health) OR "quality of life"))))))

Appendix F

Yoga program for stroke

Example excerpts from the final program manual

Summary

- People living with stroke experience a range of challenges beyond physical impairments including anxiety, depression and fatigue, which reduce participation and quality of life
- Currently, there are few proven approaches to help survivors of stroke tackle these challenges
- Mindfulness-based interventions are promising approaches for improving cognition and mood in older adults and in people with disability including those who have experienced stroke
- We have developed a 12 week community-based program for survivors of stroke that is based on yoga
- In yoga, movement is used to focus attention as part of developing mindfulness.
- The mindful movement practices, or movement-based embodied contemplative practices, are accessible for people with different levels of ability
- Therefore, we believe the active ingredient for supporting survivors of stroke to experience greater wellbeing after stroke is through developing mindfulness
- To avoid drop-outs participants discuss their impairment restrictions with yoga teachers prior to commencing classes. That is, before starting a group class for the first time, participants should meet with a teacher who will explain the program, reassure the participant and clarify anything that is unclear and explain that there are various options/adaptations possible that are relevant to their circumstances.
- The yoga program is designed to be complementary to treatment or care plans that are already in place
- All of the practices can be completed from a chair position although some might prefer to use other base positions, if required.
- Since safety and avoiding injury is paramount to the experience of participating in the yoga program, alternate strategies and practice variations are recommended and may include closing the eyes to imagine performing the practices on the affected side or performing modified balance tasks.

Introduction

Stroke is a leading cause of death and disability in Australia. Survivors of stroke often experience problems with physical and mental health following stroke. The goal of yoga for survivors of stroke is to reduce adverse outcomes and subsequently the risk of new cardiovascular events. The foundation for the new program is based on pilot clinical trials of yoga for stroke led by Dr Maarten Immink and Professor Susan Hillier at the University of South Australia with the most recent trial based on a small research project awarded by the Stroke Foundation in 2009.[1] The positive results from the pilot trials in terms of quality of life and emotional well-being,[1-3] add to an emerging body of evidence indicating a promising place for yoga in long-term care for survivors of stroke.[4] Subsequently, through a collaboration with Prof Cadilhac and other experts we have come together to further develop an effective program using yoga as an option to support survivors of stroke in the community.

1.0 Background literature

People living with stroke experience a range of challenges beyond physical impairments including anxiety, depression and fatigue, which reduce participation and quality of life. This is further compounded by the risk of further cardiovascular events. Currently, there are few proven approaches to help survivors of stroke tackle these challenges and achieve improvements in outcomes. Below we provide information to describe the condition of stroke and why yoga might be of benefit.

1.1 Understanding stroke and its impacts

Pathologically, stroke is caused by an interruption of the blood supply to the brain, usually due to a blockage caused by a clot (ischaemic stroke) or ruptured blood vessel (haemorrhagic stroke) (see Figure 1).[5] This causes inadequate supply of oxygen and nutrients, and inadequate removal of metabolic waste products, in vital parts of the brain. Consequently, the brain cells in the proximate area die and those in the neighbouring areas are affected by both the decreased blood flow and secondary factors arising from cellular dysfunction, resulting in loss of brain function.[6] Transient ischaemic attacks (TIAs) are defined as cerebrovascular events without evidence of pathology on brain imaging.[7] These can be precursor 'warning' events prior to a full stroke.

All strokes are different so for some people the effects may be relatively minor and may not last long, while others may be left with more serious long term problems, depending on the location and size of stroke. Survivors of stroke may experience problems with movement and balance when there is muscle weakness or paralysis, loss of sensation and/or hyperactive muscles, all of which can affect mobility and body balance.[8] This usually happens on one side of body and can also cause a lot of pain and discomfort. Other consequences of stroke include problems with vision, swallowing, controlling bladder and bowels and excessive tiredness or fatigue.[9,10] Some survivors also have difficulties with speech and language after stroke. It is also very common to find that their short-term memory and concentration is affected by stroke, but it can also affect other thinking processes as well, such as problem-solving, planning and finding their way around.[11] Stroke has a major emotional impact, which can lead to problems like depression and anxiety.[12] In recent years, there is a better understanding of how strokes can be prevented and treated. Since the major causes of stroke are well known, this has helped clinicians to provide patients with medications and suggest lifestyle changes as part of treatment strategies. Since time to recovery is critical, prompt treatment of patients experiencing stroke saves lives, reduces disability and improves long-term recovery.[13]

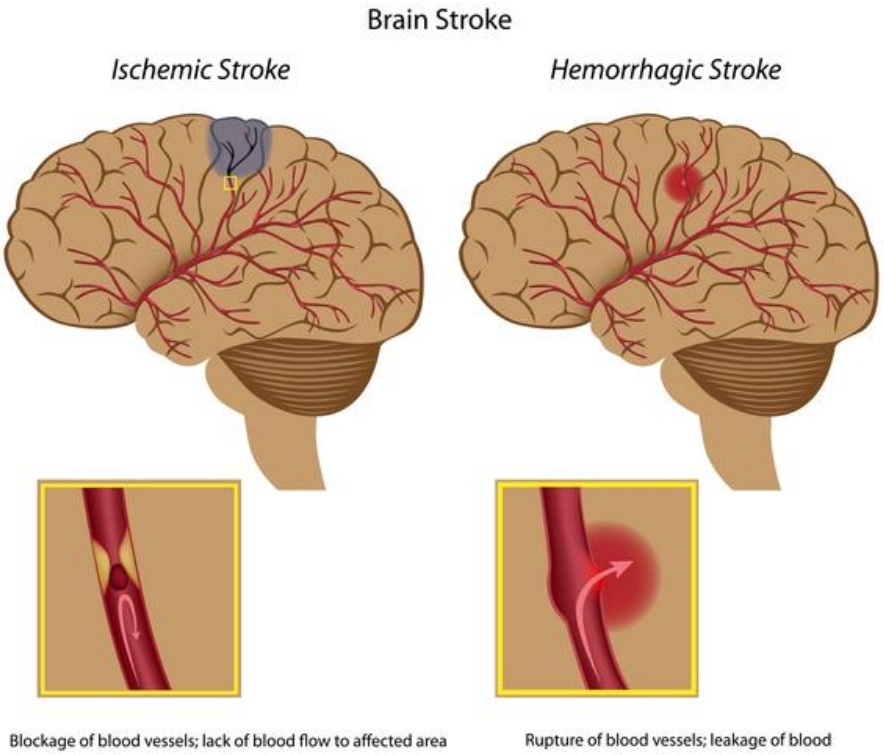


Figure 1. Major types of stroke

1.2 Risk factors that are known to cause stroke

There are many risk factors associated with stroke. These can be categorised into modifiable, and non-modifiable factors. Some risk factors that can be treated or modified include smoking, hypertension, high cholesterol, obesity, physical inactivity, diabetes, poor diets, and excessive intake of alcohol. [14] On the other hand, risk factors such as age, gender, ethnicity, family history, and socio-economic position are known as non-modifiable and cannot be changed. Individuals experiencing more than one of these risk factors are at much greater risk of experiencing stroke.

The causal chain and the complexities of stroke risk are reflected in Figure 2 below:

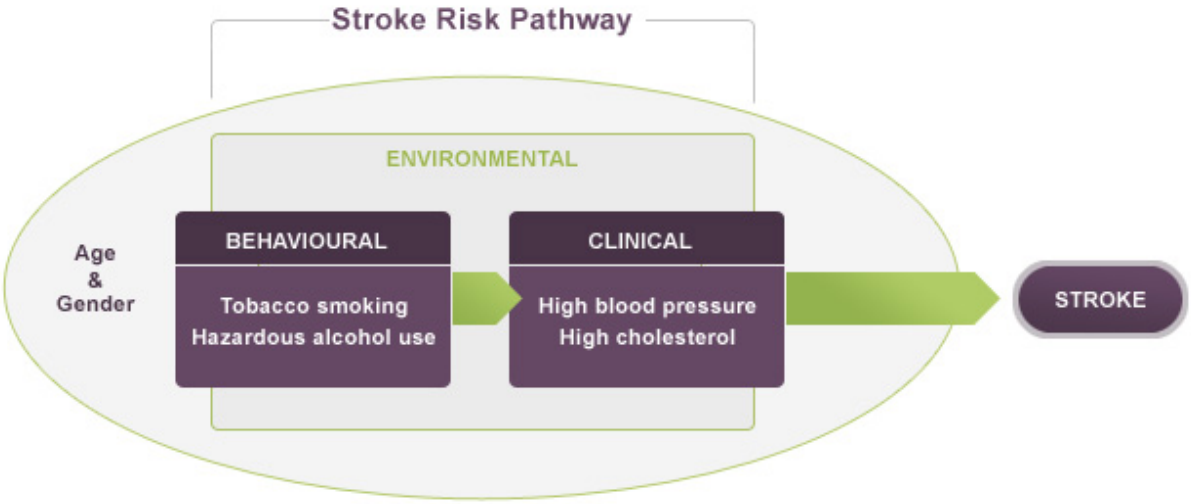


Figure 2. Risk pathway for stroke and example of risk factors

3.2.3 Mindfulness meditation

The program includes a set of meditation practices that implement a progressive approach to working to direct attention on purpose to the present moment with the quality of openness, acceptance and non-judgement. As such, the meditation practices support the cultivation of mindfulness, which emphasises purposeful, open and accepting use of attention.

The meditation practices will be progressed in terms of the duration of the practice as well as the object of attention focus. Like posture and deep controlled breathing, meditation practices progress from paying attention to various experiences in the body to more subtle experiences associated with breathing, thoughts and mental activity.

3.4 Importance of consistency in program delivery

The program is a standardised yoga program specifically designed for survivors of stroke. Standardisation of the program is important to ensure consistency so that all participants receive a very high quality yoga program that is evidence-based, and if found effective, could be replicated for other, similar, chronic illnesses to produce the same benefits. The clinical research aspect of the program also relies on participants completing a yoga program that is consistent across delivery sites in terms of the practices and the method of teaching the program. To ensure consistency, teachers are expected to only deliver the set of practices established for the program and to use the examples of class plans provided as a guide for weekly classes, allowing for progression over a 12 week time period (see Section 5).

An important aspect of consistency is the level of engagement the survivor has with the yoga practices in the program. This engagement is in terms of duration of yoga practice in each session, as well as the frequency of sessions. The duration for yoga practice is suggested in class plans and so the teacher's adherence to the class plans will ensure some level of consistency in time spent on the yoga practices for the class. All group classes must be 60-70 minutes long.

As yoga provides benefits based on the regularity of yoga practice, it is important that the teachers provide encouragement and reminders about the importance of regularly attending the yoga classes, as well as completing daily home practice on days that classes are not attended. Teachers should also encourage participants to record home practice in the log book which will be used to assess the overall dosage of the program, as well as the feasibility and acceptability of the home component.

3.8 Carer involvement

In principle, carers can be involved in the yoga classes and may be present at the pre-commencement meeting. The primary teacher will need to monitor the dynamics between the carer and survivor of stroke to ensure this is not opposing the aim of the class, or the program. The guiding principle though is that the carer should not interfere with the survivor or the groups' participation. In addition, the presence of the carer should not present a source of distraction for the stroke survivor. Where a carer would like to join the class, these expectations should be clearly explained to both the carer and the stroke survivor, and both should agree before the carer commences participation in classes. They should also agree to recourse should any issues arise, which could include asking the carer to not participate in future classes. If such a situation arises each participant and/or carer should have a short interview with the Primary teacher, and the reason/s must be noted.

4.0 Yoga Practices

4.1 Movements & Postures

4.1.1 Base Positions

Purpose of Base Positions: To position the body to allow one to participate in the practices comfortably, and with stability, therefore allowing one to focus on the nature of their practice and capacity to participate. Selecting the appropriate base position depends not only on the type of practice that will be performed, but also on one's own unique needs in terms of strength, balance and posture as well as the variation of the practice they choose to complete. Suitable base pose may change from practice to practice and develop over time. Important to listen to the body and allow time to find the best position.

4.1.2 Sitting in a Chair

Aim: For many, sitting in a chair as a base position provides a comfortable and stable body position from which to participate in the practices. All of the practices can be completed from a chair position although some might prefer to use other base positions, if required.

The sitting in a chair base position is recommended for the breathing techniques and meditation practices.

Key instruction points: Ensure that the chair is stable and comfortably positioned. Chairs with arm supports might interfere with some of the practices that involve arm movements. The seat height should allow the feet to rest on the floor.

The seated posture should be comfortable, and as best as possible, the torso should be upright (i.e. not slouching forward). Bringing the buttocks toward the back of the chair seat often helps to provide support an upright posture.

Practice variations: If required, instead of a chair, a wheelchair or other mobility device could be used that allows for sitting. Ensure that the wheelchair or mobility device is sufficiently stable for movement from a seated position and that the device will not move or roll whilst seated. Participants should be reminded to put wheel brakes on, as required.

Other base position options, which will be described next, include: Sitting on the Floor, Standing, and Laying on the Floor.

4.1.3 Sitting on the Floor

Aim: The sitting on the floor base position can provide a good level of stability for completing some of the practices but this base position has some requirements and might present challenges for some participants.

The sitting on the floor base position requires sufficient space to sit with the legs straight and also this base position requires a floor covering that provides some cushioning such as carpeting or a yoga mat. This position might also require some wall space to lean the body against to support the torso.

Challenges with the sitting on the floor base position include the mobility demands associated with getting down on to the floor and then getting up from the floor. Sitting on the floor also presents more challenge in keeping the body balanced and the torso in an upright

position while seated and also while doing any of the movements or postures. Finally, it can be more challenging to keep a comfortable seated position while sitting on the floor.

Key instruction points: Suggestions for safety transitioning between base positions are provided in the following pages for coming down to the floor and then back up again. The guiding principles for deciding whether or not to use the sitting on the floor base position are 1) ensuring that emphasis is placed on being comfortable; and 2) working well within one's own limits or unique needs. Participants should be empowered to use devices to support their posture and comfort in this base position (e.g. blocks, blankets, bolsters, cushion). The teacher's aide should circulate around the room to ensure appropriate use of the support devices by correcting postures and provide comfort.

The torso should be balanced and upright, not slouching, while sitting on the floor and including when joint specific movements are completed in this base position. It is possible to have knees slightly bent for the sake of comfort. A folded blanket or thin cushion can be placed under the buttocks to support achieving an upright seated position. When seated for joint specific movements involving the lower limbs, it is possible to place the hands on the floor beside or slightly behind the torso to support the torso.

Practice variations

Sitting with the back against the wall can provide a good level of support for the torso in the sitting on the floor base position.

If it is comfortable, it is possible to sit with the legs crossed for joint specific movements involving the upper limbs, as well as breathing techniques and meditation. If sitting crossed-legged, check that the legs will not fall asleep or become uncomfortable during the time allocated for a particular practice.

4.1.4 Standing

Aim: The standing base position can be used for the standing movements and balancing postures. This will help strengthen postural muscles. However, the standing base position does require one to have sufficient balance and muscle control and the individual should feel comfortable and stable in this position.

Key instruction points: One should choose a distance between their feet where they feel comfortable and balanced. Having the feet close together reduces the base of support and can make balance more challenging. For many, having the feet about hip-width apart is a good distance although other distances are fine. When standing, make sure knees are slightly bend, grounding through the feet, feeling a connection through the tripod under the foot (from heel to base of the little toe to the ball of the big toe and back to heel) to the support underneath. This grounding feeling can also be obtained from a seated position especially if participants are able to come a bit forward in their seat.

The torso should be upright as best as possible in the standing base position and one should avoid a stiff or unnatural position. Not having too many visual distractions can help maintain balance. Some use an unmoving visual target (like a point on the wall or the floor) to gaze upon to help balance. Participants should be instructed to do this. Also if the participant is standing on a yoga mat it might be better to encourage move to the bare floor to provide more stability.

Practice variations

Participants with hemiparesis (paralysis or weakness of one side of the body due to stroke). may find this pose challenging and should only work within their capacity to ensure they do not fall over or have a leg collapse.

To help support the standing base position, one might consider placing one or both hands on a wall, on the back of a chair or using an assistive device. With these, ensure that the wall, chair or device will not impede any planned movement and that one will be comfortable and stable whilst standing.

Should one feel uncomfortable or unstable in the standing base position, it is possible to take the time to use a wall or chair for support or to adopt the sitting in a chair base position before continuing with their practices.

Other alternate strategies may include closing the eyes to imagine performing the practices on the affected side or balance tasks. Take care if closing the eyes in standing – have a support nearby if not already holding onto something.

4.1.5 Laying On the Floor

Aim: The laying on the floor base position can be used to practice the cycling lower limb movement, breathing techniques, meditation or as a rest position between any of the body movements or postures.

Laying on the floor can be a comfortable position that allows muscles to relax and some might find that this base position helps them keep focused on their breathing techniques and meditation. However, as this position is similar to the position used for sleeping, it is possible to become sleepy, drowsy or actually fall asleep especially since fatigue can be common in survivors for stroke. Therefore, one of the requirements of using the laying on the floor base position is ensure that one will remain awake and alert. This base position also requires sufficient space to lay on the floor and having some cushioning under the body such as clean carpeting or a yoga mat. For meditation/relaxation on the floor it can be beneficial to come into a constructive rest pose, which include the support under the head as well as a folded blanket under the front part of the foot, heel remaining on the mat and also the use bolster at the back on knees.

Challenges with the laying on the floor base position include the mobility demands associated with getting down on to the floor and then getting up from the floor. Teachers need to keep participants active in their practice of mindfulness to avoid falling asleep.

4.2.8 Elbow Bending

Aim: To slowly bend and extend the elbow while directing attention to elbow movement and sensations associated with elbow movement.

Suggested base positions: Sitting in a chair or sitting on the floor

Key instruction points: The practice involves slowly alternating between bending and extending the elbow. The elbows bend such that the tips of the fingers touch the shoulders or such that the fingers move toward the shoulders. The elbows extend by moving the fingers away from the shoulders such that the upper and lower arms are level or to a point that the elbow feels comfortably extended.

From the seated position, the arms are raised in front to shoulder height such that they are parallel to the floor. The hands are turned such that the palms face up. The hands, arms and shoulders are encouraged to stay relaxed during the elbow movement.

Check that the raising of the arms does not cause slumping or unnecessary rounding of the back. Also, that the shoulders are not hunched up towards the ears or that there is tension and discomfort in the neck or shoulder region. If raising of the arms is not suitable or appropriate, elbow bending can be practiced such that the arms are lowered and the back of the hands rest on the lap when the elbows are extended.

If there is difficulty in bending one elbow, the other hand can be used to support and help move the forearm as the elbow bends and extends.

If appropriate for the individual, it is possible to practice elbow bending with the arms raised to the sides at shoulder height thus opening the chest. In this position, again the palms of the hand face up to start the movement.

The elbow should not be overextended such that this creates strain or discomfort. Individuals differ with respect to the amount that their elbows extend naturally and so only extend the elbows as much as is comfortable and feels suitable.

Aim to keep the movement at the elbow steady and flowing. One elbow may move more than the other, one elbow might move more smoothly than the other, it might be more difficult to control movement in one elbow as compared to the other or one arm might need support from the other to allow elbow movement. Even with these challenges, encourage participants to practice as best as possible and while ensuring the movement is comfortable and that there is no straining. Mentally, encourage an attitude of accepting how the wrists move while keeping an open attitude to experiencing the movement in the wrists.

Slow movement with elbow bending will establish a richer experience of the practice and allow participants to more fully incorporate attention into the movement. Intention allows one

to keep the attitude of purposefully choosing to move the elbows and at the same time choosing to pay full attention to the experience of bending and extending the elbows.

Practice variations

Elbow bending with arms lowered: This variation can be used when there is difficulty or discomfort in keeping the arms raised at shoulder level. First, place the back of the hands on the lap. Then slowly move one or both hands towards the shoulders as the elbows bend. If needed, it is possible to practice with one arm raised and the other arm lowered. Lowering of the arms with elbow bending can be used when the shoulders and arms need to rest before continuing the elbow movement with the arms raised.

Elbow bending with the lower arm support by the other hand: If needed, elbow bending can be done such that the movement is supported by having the opposite hand supporting the moving arm at the forearm or wrist. Ensure that elbow bending is completed also in the arm of the hand that supported the movement.

Single or double elbow bending: Elbow bending can be done one elbow at a time or with both elbows at the same time. Single elbow bending allows focus and effort of control to be directed on the movement in one elbow at a time. This can reduce attention demands and can also be beneficial to concentrate on the control of movement in one elbow. Double elbow bending challenges attention to follow two moving elbows at the same time and also encourages movement coordination between the elbows. Double elbow bending can be done such that they move together in a synchronised or mirrored fashion. As best as possible, move the elbows together such that the hands reach the shoulders at the same time and are lowered back to the lap at the same time. The elbows can also move opposite to one another such that one elbow is bending while the other is extending. Here, aim to coordinate the movement such that as one hand touches the shoulder, the other is lowered at the same time to the lap and so on. Coordination of double elbow bending in an asynchronous fashion is more challenging than double elbow bending in a synchronous fashion.

Imagery of elbow bending: Imagery can be used when for whatever reason it is not possible to practice with actual movement. To use imagery ensure a rich experience of the imagined movement is created and maintain a good level of focused attention on the generated imagery of the movement.
Close the eyes to visualise one or both elbows bending and extending feeling into the created imagery as if the movement is actually occurring.

Working with attention:
Preliminary – Watch one or both elbows bend and extend. Keep the eyes directed to purposefully observe the elbow movement. If the eyes are distracted away from watching elbow movement, use intention to bring the eyes back to watching the movement. The eyes may need to be redirected back to watching elbow movement several times. To watch both elbows at the same time, softly gaze at a point between the elbows such that the movement of the elbows is observed with peripheral vision. Alternatively, if moving both elbows, watch one elbow move for some time before slowly moving visual focus to the other elbow.

Intermediate – While slowly bending and extending the elbows, purposefully place attention on as many sensations as possible coming from the elbows and possibly in the forearms and upper arms. Experiencing as many sensations as possible with the movement can be assisted by closing the eyes. It that is not suitable, it is fine to keep the eyes open while watching the elbow move and feeling into the sensations of the elbow movement at the same time.

Progressive – Coordinate natural breathing with elbow bending. Work towards creating an engaged state of attention where the breath and elbow movement are closely linked. For example, breathing in comfortably as the elbow extends and slowly breathing out as the elbow bends. Conversely, breathe in as the elbow bends and breathe out as the elbow extends. Aim to coordinate the breath such that as each stage of elbow movement is completed simultaneously as each stage of inhalation or exhalation is completed. For example, as exhalation finishes the hands at the same time touch the shoulders and the elbow completes bending. If double elbow bending is being done in an opposite, asynchronous, fashion, the breath is coordinated to the opposing movement in each elbow. For example, breathe in as left hand is brought towards the shoulder and the right hand is lowered to the lap then breather out as the left hand is lowered to the lap and the right hand is brought towards the shoulder and so on.

4.4 Upper Limb Movements

4.4.1 Rowing

Aims:

- To slowly perform a rowing movement with one or both arms.
- To progressively develop capacity in directing attention to upper limb movement in the shoulders and elbows, the sensations associated with upper limb movement and the coordination of the natural breath with the rowing movement and sensations.

Suggested base positions: Sitting on the floor or sitting in a chair

Key instruction points: The practice involves using the arms to perform a rowing movement as if rowing a boat in a forwards and backwards direction. Rowing can be done with both arms or if needed, it can be done with a single arm or a single arm that is being supported or moved by the opposite arm. Rowing can be performed with some forward and backward movement of the torso along with the upper limb movement.

However, to focus the movement into the upper limbs and avoid unnecessary compensation with trunk movement, the trunk can be kept mostly still as rowing is limited to movement in the shoulders and elbows. The degree of rowing movement with the upper limb can be explored so long as larger movements do not cause straining or discomfort.

Setting up for the practice:

Sitting on the floor - Sit the body on the floor with the legs extended in front of the body. To support the body in this position, sit with a cushion under the buttocks and/or slightly bend the knees. Place the soles of the feet hip width apart

The starting position is with the hands being placed just below the chest as if holding on to two oars of a boat.

Sitting in a chair - Sit the body on a chair ensure comfort and stability. If some trunk movement is desired, ensure sitting away from the back of the chair slightly.

The starting position is with the hands being placed just below the chest as if holding on to two oars of a boat.

Movement:
Forward rowing:
From the starting position, bring both hands up as the arms straighten. Next, with the arms straightened, lower the hands down. Then, draw the hands back towards the body. Continue rowing in a forward direction for a suitable number of repetitions.


Backward rowing:
From the starting position, push both hands slightly down and away from the body as the arms straighten. Next, with the arms straightened, raise the hands up and above. Then, bend the elbows as the hands lower towards the chest. Continue rowing in a backward direction for a suitable number of repetitions.

Practice variations

Single-arm rowing: This variation can be used for rowing if movement in one shoulder is not suitable or appropriate. While one arm is rowing forwards and backwards, the other arm can rest on the lap or in the starting position.
Single-arm rowing with support: This variation can be used to assist an arm to perform the rowing movement. Grasp the hand, wrist or forearm of the arm that will row with the opposite hand. Use the opposite arm to support or move the rowing arm in a forward or backward direction.
Mental imagery of rowing: This variation can be used to create an experience of rowing in an arm when movement in one shoulder is not suitable or appropriate. Encourage participants to close their mentally create an image and experience of the arm rowing in a forward or backward direction. This imagery can be done with an arm as the other arm physically performs rowing or the other arm rests. Imagery can also be used for both arms moving together.

Working with attention:
Preliminary – Maintain attention on the rowing movement in one or both arms. Movement to attend to can include the hand moving through space, the movement at the elbow joint, movement in the shoulder, movement in the shoulder blade and if the trunk is moving, movement in the trunk and waist. Use visual gaze to watch the rowing movement in one or both arms. To watch both arms simultaneously, gaze at point in between the arms and watch arm movement with peripheral vision. Another option to watch both arms rowing, is to move vision slowly from one arm to the other.

Intermediate – Along with attention to rowing movement, also place attention on the sensations occurring at each moment of rowing. These sensations might arise from the elbow or shoulder joints. Other sensations might arise from muscles causing the movement or stretching with the movement or the skin providing sensation during movement. The trunk might have sensations associated with keeping it still or moving with the arms.

Progressive – To link the breath with rowing, breathe in slowly as the hands are raised above the body and breathe out as the hands are lowered. This can be done when rowing in either forward or backward directions with one or both arms.
If this is not comfortable, try some other way to link the breath to the rowing movement in order to maintain a good level of attention on the simultaneous occurrence of breathing, movement and the sensations of movement. If linking the breath to movement becomes uncomfortable, stop this linking and use the intermediate stage of attention while rowing.

4.6.3 Palms to the Sky

Aims:

- To slowly raise the arms above the head to stretch the arms and sides of the body.
- To maintain stability in a standing or sitting position while raising the arms.
- To progressively develop capacity in purposefully paying attention to movement in the arms and stability in the body, the sensations associated with coordinated movement of the arms and stabilising the body and the coordination of the natural breath with arm movement and body stability

Suggested base positions: Standing or sitting in a chair

Key instruction points: The degree of movement in the shoulders and arms should not exceed one's limits for comfort and flexibility. The body should be stable in the standing position while the arms are raised and lowered. If this is not suitable, then hand lifts should be practiced while standing against a wall or while seated in a chair.
Care should be taken to not create strain or discomfort in the hands, wrists or forearms in attempting to get the palms to face up when raising the arms. If there is discomfort, the hands do not need to be turned so that the palms face up. If practicing while standing creates any discomfort such as dizziness or light headedness, then move to a sitting position to continue or stop the practice.

Setting up for the practice:
Standing - Establish a standing position with good posture. Separate the legs such that the feet are close together or if more balance is needed, separate the feet to about hip width distance. For the starting position, place the hands with interlaced the fingers on the top of the head with the palms facing up.

Sitting – Sit with good posture and the feet resting on the floor. For the starting position, place the hands with interlaced the fingers on the top of the head with the palms facing up.

Movement:
From the starting position, keep the fingers interlaced as both hands are raised above the head. Raise the hands as if pushing the palms towards the sky. Keep looking forward, do not look up at the hands. When the arms are lengthened allow then the back of the hands to slowly lower to the top of the head to continue. If it is suitable, the hands be kept above the head for a moment or two to stretch the arms and sides of the body before lowering the hands to the head. Continue to push the palms up and then lower to the top of the head, with an upwards stretch. If the arms get tired or the hands become uncomfortable, ask the participants to take a break by releasing the hands down to the sides before continuing.

Practice variations

Standing palms to the sky with wall support. To increase standing stability during this practice, stand with the back leaning slightly against a wall.
Single arm palms to the sky with or without support from the other hand. If needed, palms to the sky can be practiced with one arm either in a standing or sitting position. Support or movement assistance can be provided from the opposite arm.

Working with attention:
Preliminary – Maintain attention on the movement at shoulders and elbows and the arm as a whole as the palms of the hands are pushed up and then lowered. As the arms and the joints of the arms move, also pay attention to the stability within the arms and the stability in the torso and legs to enable movement of the shoulders. If standing, notice small movements in the lower legs that help maintain balance. If standing or sitting, notice small movements in the trunk or the body that allow the movement to take place. Keep the eyes softly gazing on a stationary object in front to help keep the body stable during the movement.

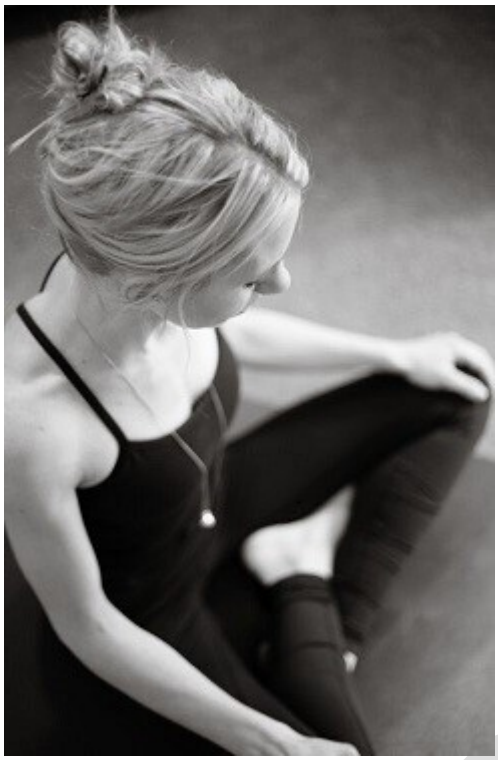
Intermediate – Along with movement in the arms during palms to the sky, direct attention to the sensations associated with the practice. These sensations can arise from movement in shoulder or elbow joints or the sensation of the hands with fingers interlaced or the sensation

of stretching the arms up and the relaxing them to lower the hands. Sensations can also be associated with body regions which are kept still or which are associated with stability in the body.

Progressive – Link the breath to hand lifts such that as the palms are pushed up, there is a slow breath in and as the back of the hands are lowered to the top of the head, there is a slow control breath out. Have a sense that the in breath is pushing the palms up and the out breath is allowing them to lower gently. By paying attention to the breath with the movement feel the movement become steadier and the body more stable. Work to coordinate the breath and movement. That is, as the in breath finishes the palms are pushed up as high as is comfortable and as the out breath finishes the back of the hands are returning to the top of the head. If breathing becomes uncomfortable, encourage participants to let go of trying to link breath and movement and use the intermediate stage of attention control.

7.0 Background to models used as demonstrators

Emma Gee



I'm Emma Gee & I survived a stroke at the young age of 24 years. As a full-time therapist who surreally worked with stroke survivors in their own rehabilitation & as an avid long-distance runner, to be ten years later living within a disabled body & feeling so trapped is something I never imagined.

After years trying to return to the 'old Em' & resume my past exercise routines, I have now accepted what I can't change & in beginning yoga have changed what I could. My practice was initially just another form of trying to fix me, but now it's a daily means of ensuring I can sustain my wellbeing & live a balanced life.

Unable to tolerate any medication, yoga has become my sole medication – both physically in managing my nerve pain & emotionally by helping me reflect, refuel & feel grounded. Whilst my regular practice in a studio with other yogis provides me with such a welcoming, accepting & encouraging community, the mindfulness that I've practiced off my mat is priceless.

Whether I'm travelling for work, grappling with nerve pain or trying to move past a seeming impossible roadblock in my day, the yogic mindset serves me. I'm definitely not a 'typical' yogi – I walk with a walking frame, need to modify all poses & need to hold onto a nearby objects to balance. But I have learnt, "that it's NOT what happens to you that matters, it's how you choose to deal with it!"

Excerpt from Reinventing Emma: Chapter 38: Life Now p 236
"Yoga is another opportunity to reflect on, which I have incorporated into my everyday life. Through yoga I can absorb all that I've done and at the same time calm my mind, like stilling a shaken-up glass snow dome and letting the white snowflakes settle. Afterwards I feel grounded, anchored and balanced...."

Mark Simcocks

My mother's father was an original ANZAC, losing his right arm at Gallipoli. He died at 39 from a stroke. My father's father, a public servant in Papua New Guinea, died at 41 from a stroke. My father, a union official, had his stroke at 52, and died at 65 from another stroke.

Ingrained with my parent's philosophy, of living life and "look after those that cannot look after themselves and look after those they leave behind, you never know when you're going to join them".

I was struck down with a stroke at 46, on 1st of March 2001, at 2:15 pm, leaving me with hemiplegia and hemianopia; unable to feel or recognise my left side. My critical care assessment was not good and deemed not suitable for rehabilitation. However, I was fixated on going to Royal Talbot. Four nurses, including the charge nurse at the stroke unit were members of our recreation business. The charge nurse understood my plight to get into Talbot and actively contacted them four times a day. Finally, I was admitted on psychological grounds.

At Talbot, the physio who was assigned to my case was an ex-client of our business and thought I might prefer to another physio. My reply was, "Could they get me out quicker?" I was told "we can tell you what to do but only you can do it, only you can make you better." I stayed with Marize.

I was offered an hour of physio per day. I stayed an extra half hour. This was then gradually increased by half hour intervals until I was had to leave when the therapists went home at 5 pm. 12 weeks after admittance to Talbot, in my first week of walking. Passing the nurses' station, I met the assessing doctor, my wife I pointed out the fact that I was upright and the response was, "I am so glad I am sitting down as there is no way I thought anything like this could have been possible."

Being science trained, I have treated my situation as an experiment to document. I have made myself available to student nurses, doctors, therapists and researchers, who experimented, monitored and reviewed my progress. My participation has provided insight and knowledge to professionals about people who are going through the same experience as I. By continuing to participate, I feel I am carrying forward the philosophy my parents gave to me. I know I have improved my family's future and hopefully improved the treatment outcomes and lives of those that have yet to join the group we know as "stroke survivors".

I have had, and continue to have, a fortunate life.

Marlene Lee

When I was 34 years old, I was enjoying 5 years of marriage, working in the financial industry, travelling, socialising with friends and doing everything to enjoy life.

But everything came to a stop when I was diagnosed with an AVM (arteriovenous malformation) in my brain and underwent neurosurgery that took 11 1/2 hours.

I came out with a stroke that affected the whole right side of my body and my speech.

I did not realise that the stroke would change my whole life thereafter.

I went through denial, questioning, frustrations, feeling sorry for myself, anger and finally the acceptance of my physical limitations.

Twenty years later, I am a proud mother of a 12-year-old daughter who makes me appreciate life every day and wanting to do everything a mother would for her child.

As I try my best to be the best mum for my daughter, I realise that I had to find time for myself.

Thanks to my good friend Kate, who is a yoga teacher, I was encourage to join her class and since then I have never looked back.

Doing yoga has helped me to put time aside for myself and doing the yoga moves to the best of my limited physical ability.

Yoga has not only helped me physically, but also helped me to regain my serenity, ability to relax and most of all, to be with myself in mind, body and spirit.