The Measurement and Improvement of Fitness Post Stroke

Ashlee Kate Dunn

B ExSporSci (Hons)

The University of Newcastle, Australia

This thesis is submitted in fulfilment of the requirements for the award of

the degree of:

Doctorate of Philosophy (Human Physiology)

The University of Newcastle, Australia

October 2016
Statement of Originality

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__________________________________________
Name: Ashlee Kate Dunn
Date:

__________________________________________
Name: Prof Robin Callister
Date:
Supervisors

Primary Supervisor

Professor Robin Callister (35%)
Priority Research Centre for Physical Activity and Nutrition
School of Biomedical Sciences and Pharmacy
Faculty of Health and Medicine
University of Newcastle, Australia

Co-supervisors

Associate Professor Neil Spratt (30%)
Priority Research Centre for Translational Neuroscience and Mental Health
School of Medicine and Public Health
Faculty of Health and Medicine
University of Newcastle, Australia

Professor Paulette Van Vliet (35%)
Priority Research Centre for Translational Neuroscience and Mental Health
School of Health Sciences
Faculty of Health and Medicine
University of Newcastle, Australia
Publications, presentations and awards arising from this thesis

This thesis includes a number of chapters that have been published or submitted for publication. To date, four have been accepted or published (Chapters 3, 4, 6, 7) and two have been submitted and are currently under review (Chapters 5, 8). I have also presented research arising from this thesis at numerous conferences, as well as University and Hunter New England Health events. Throughout my candidature, I have received a number of awards and scholarships. The details of the aforementioned publications, presentations and awards are listed below.

Peer-reviewed Journal Articles:


2. **A Dunn, DL Marsden, P Van Vliet, NJ Sprat and R Callister.** Independently ambulant, community dwelling stroke survivors have reduced cardiorespiratory fitness, mobility and knee strength compared to an age- and gender-matched cohort. *Topics in Stroke Rehabilitation* (epub ahead of print)


4. **A Dunn, DL Marsden, P Van Vliet, NJ Sprat and R Callister.** Maintenance of cardiorespiratory fitness and walking endurance improvements at 12 months follow-up of an individually tailored home and community-based exercise program for stroke survivors. *Stroke Research and Treatment* (under review)


**Conference Presentations:**


4. DL Marsden, R Callister, **A Dunn**, CR Levi, NJ Spratt. How Fit is the Stroke


9. **A Dunn**, DL Marsden, P Van Vliet, NJ Spratt, R Callister. How do the shuttle walk test and the upright cycle test compare as measures of cardiorespiratory


Awards and Scholarships Arising from Thesis:

1. 2014: Finalist for Best Abstract at Be Active 2014 conference
2. 2013: Smart Strokes Most Controversial Abstract Award
4. Australian Postgraduate Award (APA) Scholarship
5. Emlyn and Jennie Thomas HMRI Postgraduate Medical Research Scholarship (top up)

Research Grants:

1. Hunter New England Allied Health Research Committee Research Grant: $3,000
2. John Hunter Hospital Charitable Trust: $18,000
3. National Stroke Foundation: $19,436
4. Hunter Medical Research Institute Grant: $25,000
Contributions to this Thesis

The central component of this thesis is the “How Fit is the Stroke Survivor? (HowFITSS? trial). The HowFITSS? pilot trial forms the basis of my thesis and PhD candidate Ms Di Marsden’s thesis. I have been significantly involved in all aspects of the project from conceptualisation of the trial to implementation and long term follow up of the intervention.

This included involvement and contributions towards:

- Writing and submitting grant applications for personnel and equipment
- Collaborating with Di Marsden to determine data sharing
- Writing and submitting of ethics applications and variations through both the University of Newcastle and Hunter New England Health District
- Selection of equipment and protocols
- Training of research assistants and internship students
- Participant recruitment, including both stroke and non-stroke individuals
- Management of participants throughout the trial including weekly contact support
- Developing training manuals for equipment used in the trial
- Data collection in the Human Performance Laboratory including setting up, calibrating and using equipment
- Management of equipment used in the trial including troubleshooting, maintenance and regular contact with company representatives
- Data management including extracting, organising, checking and data storage
• Statistical analysis
• Writing and editing manuscripts arising from this trial
• Presentation of findings from the HowFITSS? trial at conferences and community events

Further, I have indicated at the beginning of each chapter my contribution.
Acknowledgements

This thesis was written in loving memory of my grandma, Shirley Noonan, who passed away from a stroke. She was an amazing woman who showed unconditional love to us all, and is missed every single day. You will always be in my heart Gran.

This thesis would not have been possible without the support from some amazing people. Firstly, to my supervisors Prof Robin Callister, A/Prof Neil Spratt and Prof Paulette Van Vliet. I am privileged to have worked with such a brilliant team. Thank you for your mentorship, insight and guidance throughout my PhD journey.

To Robin, thank you for the hours spent in your office, for the many drafts you read and re-read and for your unwavering support. I could not have asked for a more dedicated supervisor. Your encouragement and guidance were very much appreciated and I cannot thank you enough for helping me through the past few years.

To the amazing and selfless Jennie Thomas. Thank you doesn’t seem enough. My PhD journey would not have been financially possible without your generous support. Thank you for the reassuring and encouraging emails, for showing me that life is amazing and much bigger than a PhD, and for the warm hugs. You are such an incredible person and I am very blessed to be part of the inspiring Jennie Thomas Family.

To my family; Mum, Dad, Jo and Max. Thank you for always being there for me and always encouraging me to do my best. To my Mum and Dad, thank you for your unconditional love you have always shown myself and Jo, no matter what we do in life we have always had your support and encouragement. Mum, your insight and
motivation, provided on most days throughout my PhD, will never be forgotten. Jo, thank you for always helping me to keep a work-life balance and for all the fun and laughter we shared. I couldn’t ask for a better and more understanding sister. To Kobe and Chloe, thank you for spending days at home helping me get through the months spent writing while everyone else was at work. I love you all.

To my amazing husband Matt. Thank you for living the PhD journey every day with me, for your patience and understanding, and for picking up the slack when I could not. You have been my rock, and have helped me make it through with a smile. Your love and support is forever appreciated, and I can’t see how I would have made it without you. I am looking forward to our lives together thesis free!

To my desk buddy Elroy Aguiar, thank you for your emotional and technical support. From your offers to get me lollies at Pinkies to showing me how to change my reference style in Endnote for the hundredth time, I have appreciated it all. To Carolyn Clark and Jovanka Stojanovski, thank you for being my at-work support network. Your kind and caring approach, alongside your listening ears and supportive words has made a tremendous difference. I am lucky to have such amazing colleagues.

To Di Marsden, thank you for the hours spent in the lab – we finally made it through! To the fantastic team of interns and research assistants who contributed to data collection and data extraction – namely Erin Nugent, Adriana Giles, Erika Brown, Brent Hull, Kate Beatty, Allison Baldwin and Jaeger Olden – I am forever grateful!
To the amazing statistician, Daniel Barker. Thank you for the countless meetings, for your patience and time spent explaining how I should handle data, why I should use certain syntax, and how to create a do file. You allowed me to complete my own statistics and learn skills that I’m sure I will use throughout my career.

Lastly, to our awesome volunteers who spent countless hours in the lab with us, I cannot thank you enough. Your selflessness and willingness to help others is a true testament to the amazing people you are. Thank you for your time, effort and generosity over the years of data collection. You are an inspiring group of people and I am forever grateful.
List of Common Abbreviations

Listed below are the common abbreviations used throughout this thesis. Additional abbreviations used in the main text are defined within chapters at first use.

10MWT – Ten Metre Walk Test
6MWT – Six Minute Walk Test
ACSM – American College of Sports Medicine
ATS – American Thoracic Society
BIA – Bioelectrical Impedance Analysis
BMI – Body Mass Index
cGXT – Cycle Graded Exercise Test
CRF – Cardiorespiratory Fitness
FAS – Fatigue Assessment Scale
HowFITSS? – How Fit is the Stroke Survivor? Program
HR – Heart Rate
HRR – Heart Rate Reserve
ICC – Intra-class Correlation
QoL – Quality of Life
RER – Respiratory Exchange Ratio
SD – Standard Deviation
SWT – Shuttle Walk Test
VE – Ventilation
VO\textsubscript{2} – Oxygen Consumption
**Thesis Abstract**

The increasing number of people surviving stroke and living in the community with fitness levels below that required to perform activities of daily living is a rising global concern. Previous research has identified the major benefits exercise can provide following stroke, including improvements in quality of life, community participation, addressing additional co-morbidities, as well as assisting in preventing secondary stroke. Previous exercise interventions have demonstrated a lack of i) individualised, tailored programs, ii) exercises that can be conducted at home or in the community, and iii) programs that focus on the improvement and maintenance of fitness over the long term.

Therefore, the central component and primary aim of this thesis was the development and long term evaluation of the How Fit is the Stroke Survivor? (*HowFITSS?*), an individually tailored, home and community based exercise program for stroke survivors.

However, secondary aims 1, 2 and 3 have been presented first. These aims investigate exercise testing in stroke and provide context for the *HowFITSS?* trial.

Prior to the development of the program, we investigated the feasibility of various tests of cardiorespiratory fitness (CRF) in stroke. Oxygen consumption (VO\textsubscript{2peak}) and performance measures were compared between the traditional graded cycle ergometer test (cGXT), the commonly used six-minute walk test (6MWT) and a new walking test of CRF, the Shuttle Walk Test (SWT). Results demonstrated that all three tests are indicators of CRF in stroke, with similar VO\textsubscript{2peak} (range: 17.08 - 18.09 mL.kg\textsuperscript{-1}.min\textsuperscript{-1}). All three tests were determined feasible, with all stroke survivors completing the
6MWT. One was unable to perform the SWT due to instability identified during the 6MWT and three could not perform the cGXT due to pre-existing lower limb arthritic conditions. Results from this sub-study informed the inclusion of all three tests as outcome measures for the long term evaluation of the HowFITSS? program.

Following baseline assessments, it was identified that there is a lack of reported data for independently ambulant, community dwelling stroke survivors. An age and gender matched comparison group were recruited and assessed using the same fitness tests as stroke survivors, including measures of fatigue, depression and quality of life. Despite the mild deficits evident in this stroke group, they significantly under performed on all fitness tests, including:

- **6MWT VO$_{2\text{peak}}$** (stroke group: $16.46\pm3.66\text{mL.kg}^{-1}\text{.min}^{-1}$; comparison group: $21.03\pm8.32\text{mL.kg}^{-1}\text{.min}^{-1}$)
- **6MWT distance (stroke group: 464±121m, comparison group: 606±129m)**
- **SWT VO$_{2\text{peak}}$** (stroke group: $17.44\pm4.94\text{mL.kg}^{-1}\text{.min}^{-1}$, comparison group: $23.11\pm9.48\text{mL.kg}^{-1}\text{.min}^{-1}$)
- **SWT distance (stroke group: 415±174m, comparison group: 651±236m)**
- **cGXT VO$_{2\text{peak}}$** (stroke: $17.0\pm6.3\text{mL.kg}^{-1}\text{.min}^{-1}$, comparison: $22.4\pm6.5\text{mL.kg}^{-1}\text{.min}^{-1}$)
- and **cGXT final workload (stroke: 118±32W, comparison: 157±42W)**

Stroke survivors also walked slower compared to the non-stroke group. These results further reinforced the need for an exercise intervention in stroke survivors even those with only mild to no motor deficits.
The primary aim of this thesis was to assess the long term effects of the 12-week How Fit is the Stroke Survivor? (HowFITSS?) exercise program on stroke survivors from pre-intervention to 12 month follow up. The HowFITSS? trial was therefore designed as a home and community based program with minimal therapist support. Results found improvements in CRF for the intervention group compared to the control group at 12 weeks. The control group were then provided with the intervention, and both groups followed up at 6 and 12 months. Therapist support was tapered to no communication from the 6 to 12 month time points. Stroke survivors significantly improved VO$_{2\text{peak}}$ and performance measures during the 6MWT (ES=0.75 $p=0.002$) and cGXT (ES=1.09 $p=<0.001$) from baseline to 12-months follow up, with non-significant but promising improvements on the SWT (ES=0.23 $p=0.251$). Similarly, quality of life, balance and walking speed significantly improved, with all measures of fitness maintained during the follow up period alone.

The HowFITSS? model shows promising results as a cost effective, feasible method for improving fitness in stroke survivors over the long term. Both research and clinical practice may benefit from employing the HowFITSS? model, in improving fitness, quality of life, fatigue and depressive symptoms in people after stroke. Further translational studies are required to investigate the HowFITSS? model in a health care setting, with wide dissemination to community dwelling stroke survivors.
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Chapter 1 – Thesis Introduction

1.1 Chapter overview

This chapter begins with an overview of the pathogenesis of stroke and statistics outlining the prevalence of stroke both in Australia and worldwide. A summary of the primary risk factors is presented, which are divided into non-modifiable and modifiable factors, one of which is physical activity. Secondary prevention of stroke is explored, with an emphasis on the evidence for exercise and secondary prevention. The chapter concludes with the primary and secondary aims of the thesis, followed by an outline of each of the remaining chapters.

1.2 Background and context

1.2.1 Stroke

Stroke is caused by the interruption of the blood supply to the brain, due to either a blood vessel blockage as a consequence of a clot (ischaemic stroke; 85% of cases) or a blood vessel leaking or rupturing (haemorrhagic stroke; 15% of cases)\(^1\). In the case of ischemia, this disruption deprives the affected area of the brain of oxygen and glucose which are essential for brain function. In haemorrhagic stroke, the physical (arterial pulsation) and chemical (iron) damage are the key mechanisms for injury. Consequently, this causes damage and eventual death of brain tissue. Depending on the location and the severity of the stroke, it has potential to result in numerous functional deficits\(^2\). The most common lesion site is the middle cerebral artery (MCA) branching from the internal carotid artery. The MCA feeds the frontal, temporal and parietal lobes,
with classic deficits including hemiplegia of the face and arm, sensory loss and hemianopia. It has been reported that prognostically important locations for stroke are the limbic and language areas in the left hemisphere, and visuospatial and motor regions in the right hemisphere\(^3\). Anterior and posterior cerebral artery strokes can cause lower extremity hemiplegia and weakness, and visual loss respectively. Vertebral-basilar strokes affect the cerebellar and brainstem, often resulting in serious consequences from impaired balance and coordination to death.

Stroke is one of the leading causes of adult disability and death in Australia and worldwide. Approximately 15 million people experience a stroke worldwide each year\(^4\), with 60,000 stroke events occurring annually in Australia\(^5\), equating to one every 10 minutes. A total of 375,800 Australians had experienced a stroke throughout their lifetime in 2009\(^1\) and this is estimated to explode to over 500,000 by 2017\(^6\). Stroke is a leading economic burden, reportedly costing the Australian economy $5 billion per year\(^7\) in 2012. Stroke accounted for 8,304 deaths in Australia in 2010, however this death rate has decreased by 71% since 1979. Consequently, a decrease in death rates translates to increasing numbers of stroke survivors living in the community who require high quality interventions, not only to address any functional limitations and improve quality of life, but also to prevent secondary stroke occurring.
1.2.2 Physical consequences of stroke

One in three stroke survivors will remain disabled as a consequence of a stroke\textsuperscript{1,8}. The physical consequences of stroke can be devastating, and can result in a variety of impairments including hemiparesis, compromised balance, muscle weakness, spasticity or sensory disturbances\textsuperscript{9}. Despite being discharged, half of all disabled stroke survivors living at home require assistance with activities of daily living, transport and mobility. Approximately one quarter of these people need help with self-care, meal preparation and cognitive or emotional tasks\textsuperscript{6}. Apart from decreased quality of life and loss of independence, this necessary assistance is a burden to family members and carers as well as the health care system. It is therefore understandable that the lasting effects of a major stroke are viewed as being worse than death by greater than 50\% of those who are at risk\textsuperscript{10}.

Upon discharge from hospital, 60-80\% of stroke survivors can walk independently, however they walk at speeds that are insufficient to function effectively in the community (<0.8m s\textsuperscript{-1})\textsuperscript{11}. It is estimated that only 7\% of people discharged from inpatient rehabilitation can manage steps and inclines or walk distances required for community ambulation\textsuperscript{12}. Many stroke survivors currently rate their quality of life as very poor as a consequence of the aforementioned outcomes\textsuperscript{13}.

1.3 Risk factors for stroke

The same factors implicated for primary prevention of stroke are also associated with secondary prevention. The following factors are therefore relevant to those who have already suffered a stroke.
1.3.1 Primary prevention: non-modifiable risk factors

Non-modifiable risk factors for stroke are those that you cannot change.

1.3.1.1 Age

Age and stroke are strongly correlated, with the risk of stroke doubling for each successive decade after 55 years of age\(^{10}\). Supporting this, the Framingham Study\(^ {14}\) reports a steady increase in stroke risk from 5.9% and 3.0% at 55-59 years of age to 22.3% and 23.9% at 80-84 years for males and females respectively. In 2010, 81% of all stroke deaths occurred in those aged 75 years and over\(^ 1\).

1.3.1.2 Gender

Females have a higher lifetime risk of stroke, as well as a higher post stroke mortality rate\(^ {15}\). This is thought to be due to the longer life expectancy of females, with age correlating negatively with clinical outcome\(^ {10}\). Reports from the Framingham Study\(^ {16}\) estimate that 1 in 5 women and 1 in 6 men who have not had a stroke by the age of 55 will have a stroke in their remaining lifetime. Although the biological explanations for this increased incidence in females is still unclear, there are suggestions that numerous variables may play a role, including the influence of oestrogen on the endothelium and vasculature, and risk factors applicable specifically to women including the use of oral contraceptives, pregnancy and hormone replacement therapy\(^ {10,16}\).

1.3.1.3 Race and ethnicity

Race and ethnicity can influence the risk of stroke. It is reported that Aboriginal and Torres Straight Islander people are 1.7 times more likely to have a stroke than non-Indigenous Australians\(^ 1\). It is thought that these differences may be explained by a
higher prevalence of stroke risk factors including hypertension, obesity, diabetes and smoking in this population\textsuperscript{17,18}.

1.3.1.4 Family history

For the past 30 years, there has been research conducted regarding evidence of a genetic predisposition to stroke. There are many aspects of genetic epidemiology of stroke that are still unclear, although it is known that both maternal and paternal history of stroke are strongly associated with increased stroke risk\textsuperscript{10,19}. Polymorphisms on chromosomes 5 and 6 may be associated with ischemic stroke in humans\textsuperscript{20-22}, and it is speculated that the following may predispose an individual to stroke:

Genetic:

1. Genetic heritability of primary stroke risk factors
2. Genetic heritability of susceptibility to the effects of risk factors

Non-genetic:

3. Familial culture, environment and lifestyle factors
4. Interaction between points 1, 2 and 3

Thus, although genetic predisposition to stroke is considered a non-modifiable risk factor, early intervention to improve lifestyle factors may reduce the risk of stroke despite genetic predisposition\textsuperscript{23}. 


1.3.2 Primary prevention: modifiable risk factors

1.3.2.1 Blood pressure

High blood pressure (hypertension) is the number one risk factor for stroke, with blood pressure levels proportional to stroke incidence\(^4\). A large case-control study, the INTERSTROKE trial\(^{24}\) demonstrated that self-reported history of hypertension or blood pressure \(>160/90\)mmHg accounts for 34.6% (99%CI 30.4 – 39.1) of population attributable risk of stroke. A worrying statistic is that greater than two thirds of people older than 65 years of age are hypertensive, translating to a large proportion of individuals who are at risk of stroke\(^{10}\). Antihypertensive therapy has been associated with a 35 – 44% reduction in the risk of stroke\(^{10}\), however, despite the efficacy of treatment and relatively easy monitoring procedures, it is estimated that there is a significant proportion of the population who are undiagnosed. Despite the treatment options of pharmacological therapy or lifestyle modification such as increasing physical activity and improving nutritional intake, only half of those diagnosed with hypertension are able to meet their target blood pressure reductions\(^{10}\).

1.3.2.2 Smoking

It is well established that smoking increases the risk of stroke\(^{10,25}\). The mechanisms responsible are thought to be both acute and chronic in nature. Apart from the immediate effects of smoking such as increasing heart rate, blood pressure and decreasing arterial distensibility\(^{26}\), smoking is also responsible for the formation and progression of atherosclerotic plaque and structural arterial wall damage\(^{25,27}\). In addition to increasing the risk of an ischemic stroke from this plaque build up, smoking is reported to triple the risk of cryptogenic stroke (a stroke which cannot be attributed to
any specific cause) among individuals with no evidence of cardiac or atherosclerotic burdens\(^ {27}\).

\subsubsection*{1.3.2.3 Overweight, obesity and type 2 diabetes}

People with Type 2 Diabetes are more than three times more susceptible to stroke than the general population\(^ {28}\). Similarly, obese individuals are at a higher risk of stroke; for each unit increase in body mass index (BMI), there is a reported 6\% increase in relative risk of stroke\(^ {23}\). Type 2 diabetics and obese individuals generally have an increased susceptibility to atherosclerosis as well as other risk factors including hypertension, abnormal blood lipids and atherogenic risk factors\(^ {10}\).

\subsubsection*{1.3.2.4 Physical activity}

Of the five risk factors that account for more than 80\% of the risk of stroke, lack of physical activity is second only to hypertension\(^ {24}\). It is reported that, in 2007-2008, 12 million (72\%) adult Australians were physically inactive\(^ 1\) (Section 1.5), and, in 2003, over 2,300 stroke deaths in Australia were attributable to physical inactivity\(^ {29}\).

A meta-analysis by Lee (2003)\(^ {30}\) suggests that moderately active individuals had a 20\% lower risk, and highly active individuals had a 27\% lower risk of stroke incidence or mortality than low-active individuals. The definition of low, moderate and high intensity exercise varied widely between studies, making conclusions difficult regarding exact amounts of exercise required. The mechanism by which physical activity provides protection against stroke may be due to a number of effects including lowering blood pressure, improving lipid profile and blood coagulation, reducing the risk of cardiovascular disease and diabetes, as well as lowering body fat\(^ {31}\).
1.4 Recurrent stroke and secondary prevention

One in six survivors of first-ever stroke have a secondary stroke within the next five years\(^6\). An Australian study by Hardie (2004)\(^{32}\) reported that 40% of recurrent stroke events were fatal within 30 days, equating to twice the 30-day case fatality of first ever stroke. It is therefore extremely important that all modifiable risk factors are addressed to minimise the risk of a secondary event. A modelling study by Hackam et al.\(^{33}\) highlights the potential for exercise as a strategy to reduce the risk of secondary stroke, stating that, in combination with dietary modification, aspirin, a statin and an antihypertensive agent, there is potential for a cumulative risk reduction of >80%. There is great potential for exercise in the role of secondary prevention, with additional benefits such as improved mood, lower blood pressure, greater strength and cardiovascular changes\(^{34-36}\).

1.5 Physical activity and fitness in stroke

It has been reported that of those who have experienced first-ever stroke, 77.1% did not accumulate at least 30 minutes of moderate-intensity physical activity on most days of the week, classifying them as being insufficiently active\(^6\). Similarly, when compared to age and gender matched controls, stroke survivors spend significantly more time sitting, and do significantly less physical activity, as measured using accelerometers\(^{37}\). Following stroke, hemiparesis, co-morbidities, disruptions to the cardiovascular, respiratory or neuromuscular systems can all greatly influence physical functioning and fitness\(^{38,39}\). Fear of falls due to instability, inefficient mobility, fatigue, and inability to ambulate in a community setting can all promote a sedentary lifestyle, resulting in further deconditioning of the body. Improving fitness in this population has potential to
Cardiorespiratory fitness (CRF) is a large component of fitness. It quantifies the ability of the heart, lungs, blood vessels and skeletal muscles to work together in order to deliver oxygen to and remove waste products from working muscle. It is acknowledged that there are other components to fitness, which will be examined in Chapter 2. For the purpose of this thesis, fitness refers to the following components: CRF, walking ability, leg strength, balance and body composition. The focus of this thesis will be on CRF.

1.6 Summary

With medical advances and improved patient care over the last 30 years, more individuals are surviving stroke, meaning there are a growing number of stroke survivors living in the community. These individuals may have a decreased quality of life and the inability to function properly in the community setting due to the residual physical effects of their stroke. It is not only important to intervene following stroke to improve functional capacity and everyday living, but also to potentially decrease the risk of a recurrent stroke. The risk of secondary stroke is six times higher than that of first ever stroke in the general population, and the 30-day case fatality is twice that of first ever stroke.
Chapter 1. Thesis Introduction

1.7 Primary and secondary aims

The development and implementation of the intervention for this thesis was performed in conjunction with PhD candidate Di Marsden (Hunter Stroke Service) in keeping with the rules and regulations of the University of Newcastle, Australia. As a result, the aims of the current study are in keeping with the overall HowFITSS? trial and Ms Di Marsden’s aims for her thesis.

1.7.1 Primary aim (Chapter 8)

Assess the long term follow up outcomes of the HowFITSS? exercise program at 6- and 12-months post intervention, when minimal to no support was provided by researchers.

Primary hypothesis

Stroke survivors who completed the HowFITSS? exercise program will maintain fitness levels over the long term post-intervention without support.

1.7.2 Secondary aim 1 (Chapter 3)

Systematically review and meta-analyse the current evidence regarding the 6MWT in stroke survivors to assess the impact of changing the walkway protocol.

Secondary hypothesis 1

Changing the walkway protocol may influence the distance achieved in stroke.
1.7.3 Secondary aim 2 (Chapter 5)

Compare the responses to the submaximal six-minute walk test, the graded shuttle walk test and cycle graded exercise test as measures of CRF in stroke survivors, and to compare the practicality of using these three tests as measures of CRF in stroke survivors.

Secondary hypothesis 2

The SWT will be an effective measure of CRF in stroke survivors.

1.7.4 Secondary aim 3 (Chapter 6)

Compare cardiorespiratory fitness, walking ability, knee strength and body composition in independently ambulant, community dwelling stroke survivors to healthy age- and gender-matched comparison participants.

Secondary hypothesis 3

Independently ambulant, community-dwelling stroke survivors will have lower fitness levels when compared to age and gender matched individuals.
1.8 Study design

The pilot study titled “How Fit is the Stroke Survivor?” (HowFITSS?) was a waitlist controlled trial, with ten stroke survivors in the intervention group and ten in the waitlist control group. Groups were block allocated due to restrictions in availability of the laboratory. The intervention group received the HowFITSS? program following the first assessment session. The waitlist control group attended two assessment sessions, three months apart without intervention. Following the second assessment, the group commenced the HowFITSS? program. Following the intervention period, both groups were invited to return for follow up assessments at 6 and 12 months post program initiation. Figure 1.2 represents the overall study design. A rolling recruitment strategy was required, therefore participants began the intervention at different times.

![Figure 1.2 Study design for the HowFITSS? pilot trial](image)

1.9 Context of this thesis

As a result of integrating the aims of the HowFITSS? intervention with PhD candidate Ms Marsden, two papers arose on which I am second author. A summary of these two papers has been included in this thesis to demonstrate the context of the manuscripts of which I am first author. The diagram below (Figure 1.3) displays the breakdown of the
project and the papers associated with each author. The work on which I am first author is represented as pink, and the second author papers are in green. This breakdown is in keeping with the rules and regulations of the University of Newcastle, Australia.

Figure 1.3 Breakdown of papers resulting from the HowFITSS? Trial
1.10 Thesis structure

This thesis is presented as a series of manuscripts that address the above aims. To date, two have been published and two are under review.

1.10.1 Chapter 2 – Literature review

This chapter presents a review of the current literature surrounding various components of fitness, with the primary focus being cardiorespiratory fitness. The review explores additional subsections of fitness including walking ability, leg strength, balance and body composition, each in the context of stroke and healthy populations. Further investigation reveals major findings and limitations in exercise prescription to improve cardiorespiratory fitness, from which the How Fit is the Stroke Survivor? (HowFITSS?) program is developed. This literature review was solely performed by the candidate, Ashlee Dunn, independent of Di Marsden’s work.

1.10.2 Chapter 3 – Systematic review of the 6MWT in the stroke literature and the impact of walkway length on distance achieved

This chapter presents the results of a systematic review with meta-analyses of stroke studies that incorporated the use of the 6MWT to determine the effects of deviation from the standard walkway protocol. A systematic search was conducted from inception to March 2014. Studies were eligible if they reported a baseline (intervention studies) or first instance (observational studies) measure for the 6MWT by stroke survivors who were any time post stroke. In total, 127 studies (participants $n = 6,012$) that met the
inclusion criteria, 64 were also suitable for meta-analysis. This systematic review has been published in the journal, *Stroke Research and Treatment* [42](#) (appendix 1).

1.10.3 Chapter 4 – Systematic review of exercise interventions for stroke survivors and the consequential impact on aerobic fitness

This chapter presents a summary of a systematic review with meta-analyses of studies that used an exercise intervention to improve cardiorespiratory fitness in stroke survivors. This systematic review has been published in the journal *Neurorehabilitation and Neural Repair* [43](#), with the full manuscript presented in appendix 2. A systematic search was conducted from inception to December 2011. Studies were eligible if they included an intervention with the potential to improve CRF, and peak oxygen consumption (VO$_{2peak}$) assessed pre-intervention and post-intervention via a progressive aerobic exercise test. In total, 28 studies were included, reporting results for 920 participants.

1.10.4 Chapter 5 – Comparison of three measures of CRF in stroke

This chapter presents an evaluation of the cardiorespiratory and performance responses to the 6MWT, SWT and cGXT in stroke survivors. Despite having multiple, clinically relevant advantages, this is the first paper to evaluate the SWT in stroke survivors as a possible test of CRF. The study describes the outcomes (VO$_{2peak}$, HR$_{peak}$, performance measures) achieved on the 6MWT, SWT and cGXT, and assesses the feasibility of all three tests. This study informed the use of the SWT in the *HowFITSS*? Trial (Chapter 7 and 8) This manuscript is currently under review in the journal *Physiotherapy Theory and Practice*. This study and manuscript were led by the candidate, Ms Ashlee Dunn.
1.10.5 Chapter 6 – Comparison of the fitness levels of independently ambulant, community dwelling stroke survivors to healthy age and gender matched comparisons

This chapter presents a published paper (appendix 3) focusing on the physical capacity and fitness of a sub-group of stroke survivors without disability. This group had not been investigated, as it was assumed that no exercise intervention was required. The manuscript explores the differences and similarities between the stroke group to age and gender matched healthy comparison participants. Both groups performed all assessments including body composition, leg strength, walking speed and tests of CRF (6MWT, SWT, cGXT). This study is the first to specifically investigate stroke survivors without hemiparetic gait and compare to them healthy individuals. This manuscript is published in the journal *Topics in Stroke Rehabilitation*. This study and manuscript were led by the candidate, Ms Ashlee Dunn.

1.10.6 Chapter 7 – Evaluation of the HowFITSS? controlled trial paper

This chapter presents a summary of the pre-post published findings from the HowFITSS? pilot trial, with the full manuscript presented in appendix 4. Twenty stroke survivors were assessed at baseline, with ten allocated to the intervention group and ten to the wait-list control group. The intervention group received the HowFITSS? program which was individually tailored, home and community based with weekly contact with a research clinician. The wait-list control received no program and no communication for the 12-week period. Following the 12 weeks, both groups were re-assessed and feasibility was determined.
1.10.7 Chapter 8 – Long term follow up paper

This chapter presents the long term follow up findings, as an extension of Chapter 7. Following the HowFITSS? pilot intervention, participants were re-assessed at 6 and 12 months post intervention initiation. During this period, contact with research staff was minimised, tapering to no contact during the 6-12 month phase. Retention was explored, as were reasons for program non-compliance. This is the first study to explore the long term efficacy of an individually tailored home and community based exercise program with a focus on increasing daily activity and reducing sitting time. This manuscript is currently under review in the journal Stroke Research and Treatment.

1.10.8 Chapter 9 – Thesis discussion

The purpose of this chapter is to synthesise and discuss the findings and implications of the HowFITSS? study based on the series of manuscripts presented in this thesis. The chapter acknowledges strengths and limitations to this body of work, and presents a series of evidence-based recommendations for future research and clinical practice. This chapter is entirely the work of the candidate, Ashlee Dunn.
Chapter 2 – Literature Review

2.1 Cardiorespiratory fitness

Cardiorespiratory fitness reflects the ability of a person to carry out large muscle, dynamic, moderate to high intensity exercise over a prolonged period of time\textsuperscript{44}. It has been reported that peak oxygen consumption (VO$_{2\text{peak}}$) values less than 20mL·kg$^{-1}$·min$^{-1}$ are associated with limited physical function when performing daily activities\textsuperscript{45}, and that values below 18mL·kg$^{-1}$·min$^{-1}$ for males and 15mL·kg$^{-1}$·min$^{-1}$ for females are related to loss of independence\textsuperscript{39}. For healthy individuals aged over 60 years, normal mean VO$_{2\text{peak}}$ is between 33±7.3mL·kg$^{-1}$·min$^{-1}$ and 27±4.7mL·kg$^{-1}$·min$^{-1}$ for males and females respectively\textsuperscript{46}. A recent systematic review by Smith (2012)\textsuperscript{39} reported the average VO$_{2\text{peak}}$ for stroke survivors to be extremely low, ranging from 8-22 mL·kg$^{-1}$·min$^{-1}$. This is well below the estimated levels achievable by their healthy age matched counterparts.

2.1.1 Assessing cardiorespiratory fitness

The gold standard for CRF assessment is a graded exercise test (GXT) with breath-by-breath measurements via open-circuit indirect calorimetry. A GXT reflects the person’s physiological capacity and response to exercise as reflected by peak oxygen uptake levels (VO$_{2\text{peak}}$), peak heart rate (HR$_{\text{peak}}$), ventilation (VE) and respiratory exchange ratio (RER)\textsuperscript{47}. A GXT typically requires a warm up period with low resistance, followed by progressive, uninterrupted exercise of increasing intensity for set time periods\textsuperscript{48} with a predefined end point either at maximal or submaximal level. Results from a GXT can provide valuable feedback, and can be used to inform specific prescription of exercise\textsuperscript{49},...
or to track changes in fitness over time. Current recommendations for stroke survivors indicate the use of an appropriate ergometer such as a treadmill or cycle\textsuperscript{50}. Often treadmill testing is contraindicated in this population due to compromised balance or other physical disability. It is therefore unsurprising that upright, semi-recumbent and recumbent cycles are the most common ergometers for GXTs in the stroke literature\textsuperscript{47}.

Characteristically, the equipment required for measurement of VO\textsubscript{2} is expensive for both purchase costs and maintenance, requires trained personnel to operate and is typically not available in the clinical rehabilitation setting\textsuperscript{47}. It is therefore recommended in the current guidelines that walking tests be used as proxy measures of CRF if ergometer testing is not practical or feasible\textsuperscript{50}. The most common functional walking test is the 6-minute walk test (6MWT), which was originally designed and developed in the 1960s for cardiovascular and respiratory disease populations\textsuperscript{51}. Over time, the test has been employed by clinicians for use in the stroke population. The 6MWT requires the individual to walk as far as possible over six minutes, shuttling back and forth along a 30m corridor. The 6MWT is self-paced, and is considered a submaximal test\textsuperscript{52,53} as the individual is not required to walk progressively faster over time. This is atypical of a cardiorespiratory fitness test in healthy adults, where progression is required to increase workload and elicit cardiorespiratory exhaustion. Standardised instructions for the 6MWT are provided by the American Thoracic Society (ATS)\textsuperscript{54}, although it has been identified that a substantial number of studies do not adhere to this protocol\textsuperscript{42}. Because space is an issue in clinical settings, a 30m, uninterrupted, straight walkway may be difficult to acquire.
An alternative walking test which has not been investigated in stroke is the shuttle walk test (SWT). The test was first described by Singh (1992) in an attempt to create a more standardised, progressive walking endurance test. Unlike the 6MWT, the SWT is a progressive, symptom-limited maximal test, which only requires 10m to perform. To date, the SWT has not been validated in the stroke population. A review by Parreira et al. identified 36 articles that used the SWT in other chronic disease populations, reporting several studies have compared the responses during the SWT, 6MWT and ergometer tests. The review concluded that the SWT is a valid and reliable test for assessment of maximal exercise capacity in chronic respiratory disease. It is noted that respiratory disease populations generally do not present with motor disability, and therefore investigation is required in stroke.

2.1.2 Cardiorespiratory fitness in stroke

Stroke survivors reportedly achieve a low VO$_{2\text{peak}}$, with the average ranging between 9.8 – 21.5mL$\cdot$kg$^{-1}$$\cdot$min$^{-1}$ on a cycle ergometer. Despite yielding a 5-10% higher VO$_{2\text{peak}}$, treadmill testing is less common, making up 32% of the testing modality in the current stroke literature. It has been suggested that when using a cycle ergometer, test termination can be significantly influenced by leg fatigue and knee pain, rather than cardiorespiratory limitation. Walking tests are therefore commonly used in stroke survivors due to the functionality and low cost.

The average distances achieved on the 6MWT for healthy males and females aged 70-79 years are 530m and 490m respectively. In comparison, the average 6MWT distance from multiple studies of stroke survivors was reported significantly lower at 247m. To date, there have been minimal studies measuring oxygen consumption during the
6MWT. In a study assessing the reliability of the CosmedK4b² portable metabolic cart in stroke\textsuperscript{61}, the average VO\textsubscript{2peak} was reported as 12.8±3.2mL.kg.min\textsuperscript{-1} and distance of 308±142m. The authors concluded that there is high reliability of portable metabolic monitoring in ‘overground’ walking in stroke survivors. Throughout the literature, VO\textsubscript{2peak} during the 6MWT has been reported ranging from 11.8±3.7mL.kg.min\textsuperscript{-1} \textsuperscript{62} to 23.8±1.8mL.kg.min\textsuperscript{-1} \textsuperscript{53}.

The Shuttle Walk Test (SWT) as described by Singh et al.\textsuperscript{55} is an incremental, externally paced walking test developed for respiratory disease populations. Only one study has investigated the SWT in stroke\textsuperscript{63} using a modified version of the protocol as described by Verschuren et al.\textsuperscript{64}. The protocol was a walk/run test designed for children with cerebral palsy, and included 23 stages lasting one minute each. The traditional SWT does not allow running, and has a total of 12 stages lasting one minute each. The van Bloemendaal et al.\textsuperscript{63} study also did not measure VO\textsubscript{2peak}, the gold standard measure of fitness.

2.2 Walking ability

It has been reported that 37% of the variance in walking speed can be explained by five independent variables: functional disability, aerobic endurance, leg strength, balance and cognitive impairment\textsuperscript{65}. At least four of the five variables can be trained or improved with physical rehabilitation. Through improving walking ability, there may be potential for improved CRF as the individual can walk faster or for longer periods of time in order to stress the cardiorespiratory system.
2.2.1 Assessing walking ability

Walking speed can be measured over a variety of distances, however the 10-metre walk test (10MWT) is most common throughout the clinical literature. The test requires participants to walk along a 14m walkway, with the middle 10m time recorded. The 10MWT correlates with other aspects of gait and recovery and is simple, quick and easy to administer.66.

2.2.2 Walking ability in stroke

Although hemiparesis is only present in about half of all stroke survivors67, it has been reported that 90% of stroke survivors walk with impaired coordination65. Following stroke, the number of functioning motor units is markedly reduced, possibly attributable to the degeneration of alpha motor neurons from decreased descending input68-70. Walking speed is a reliable and valid indicator of gait recovery66,71, deficit severity and a strong determinant of community mobility72-74. Ambulation speed has been categorised into household walker (<0.4m·s⁻¹), limited community walker (0.4-0.8m·s⁻¹) and full community walker (>0.8m·s⁻¹)75. A walking speed of 1.07-1.50m·s⁻¹ is required to be fast enough to function as a pedestrian in different contexts65,76. It has been documented in a meta-analysis of walking speed, that the average walking speed for healthy males and females aged 70-79 years is 1.26m·s⁻¹ and 1.13m·s⁻¹ respectively74,77, whereas the walking speed of ambulant stroke survivors is documented at only 0.53m·s⁻¹72. This is well below the required community ambulation speed and substantially slower than that of their age matched counterparts.

Energy requirements for hemiparetic gaits in stroke survivors are elevated by 55-100% compared to age matched controls78. Consequently, stroke survivors fatigue at a rate 2.5
Chapter 2. Literature Review

time faster than an age matched individual\textsuperscript{79}. In keeping with international standards, 40% of local stroke survivors discharged post thrombolysis had moderately severe to severe disability, and were unable to walk unassisted\textsuperscript{80}. Following discharge from rehabilitation in a different healthcare setting, only 7% of stroke survivors have sufficient capacity to ambulate outside of their own homes\textsuperscript{81}. Walking in the community requires the individual to be able to maintain walking activity for long periods of time, and it is extremely important for stroke survivors to be able to walk in the community. Community ambulation enables social and domestic participation as well as improving quality of life\textsuperscript{12}. In a sample of community dwelling stroke survivors one-year post stroke, compromised walking endurance was the greatest functional limitation and the only variable significantly associated with community reintegration\textsuperscript{82}. Decreased ambulatory endurance has a high risk of translating to physical inactivity and a sedentary lifestyle, further compromising mobility and increasing risk for secondary stroke.

2.3 Leg strength

Strength is defined as the ability to produce force or torque (the tendency of a force to rotate an object about an axis)\textsuperscript{83}. A common post-stroke outcome is accelerated muscular atrophy, resulting in significantly diminished leg strength. Alongside this, there may be primary impairment of upper motor neurons and secondary neuromuscular adaptations to denervation and disuse, which also contribute to loss of muscle strength\textsuperscript{84}. Leg strength affects numerous aspects of activity, in particular walking ability and falls risk.
2.3.1 Assessing leg strength

In healthy populations, leg strength is often measured using a one repetition maximum test, involving free weights or machine weights to determine the maximum weight that only one repetition can be successfully and safely performed. This testing is often not suitable or accurate for older populations including stroke survivors, due to the safety risk and pressure applied to joints during testing. A controlled method for testing leg strength that is more suitable in stroke is isokinetic leg dynamometry. The Humac Norm dynamometer is often used throughout the literature and has been found to be reliable in stroke for both extension and flexion in the paretic and non-paretic limb (test-retest ICC: 0.96-0.98)\(^7\).

2.3.2 Leg strength in stroke

Leg strength progressively declines with age at a rate of approximately 10% per decade\(^8\). Exercise can have a major impact on leg strength and motor control in stroke\(^8\)\. There are variable relationships between residual strength of the paretic knee extensors, walking speed and gait symmetry post-stroke\(^9\). Leg muscle weakness can result in a compensatory gait pattern, in which stronger muscles attempt to counter for the deficits by generating greater work than normally required\(^9\). This translates to inefficient gait, requiring much more energy to perform, and contributing to premature fatigue or pain.

Typically, the more affected leg is assigned the majority of leg strength rehabilitation. However, it has been found that the less affected limb may also demonstrate decreases in strength. Harris (2001)\(^9\) reported that quadriceps strength of the less affected leg decreased by 30% in the first seven days after stroke, and Prado-Medeiros (2012)\(^9\)
concluded that both the paretic and less affected limbs displayed weakness which correlated with physical function. This may be attributable to the 10% of cortical descending pathways that do not actually cross to the opposite side of the lesion\textsuperscript{69}. These findings strongly suggest that both the more affected and less affected limbs require assessment and training interventions following stroke.

2.4 Balance

Balance is a complex motor skill, requiring central processing of visual, vestibular and somatosensory information to activate skeletal muscle to appropriately produce posture, stance and locomotion activities\textsuperscript{90}. As previously mentioned, falls risk is associated with leg strength and ability to activate muscle\textsuperscript{91,92}. Balance affects many aspects of activity including walking, turning, negotiation of uneven ground and recovery from a balance disturbance.

2.4.1 Assessing balance

Balance can be quantified using a number of assessment tools. In the stroke population, these include the Berg Balance Scale (BBS)\textsuperscript{93}, Timed Up and Go (TUG)\textsuperscript{94} and the Functional Reach Test\textsuperscript{95}. The Step Test measures the balance on a single limb as well as requiring minimal time to complete. The Step Test has a high retest reliability in the stroke population (ICC > 0.88) and has been found to correlate with gait velocity\textsuperscript{96}. 
2.4.2 Balance in stroke

Poor balance can result in a fall. Stroke survivors are at an increased risk of falls due to possible asymmetric gait, affected vision and poor motor control. In mild to moderate stroke, the 6-month incidence of falls is reported to be 73%\textsuperscript{97}. The consequences of a fall can be serious, leading to readmission to hospital and further bed rest and deconditioning. Extreme fear of recurrent falls is often influential, which can cripple quality of life and social interactions. One study found that 44% of stroke survivors restricted their activity following a fall\textsuperscript{98} which can be a serious setback to rehabilitation, which can further decline balance ability. This potential downward spiral can severely negatively impact on balance.

2.5 Body composition and muscle mass

With age, there is a natural decline in muscle mass (sarcopenia) which may be accelerated following stroke due to reduced capacity to activate muscle, inactivity and metabolic changes as a consequence of the stroke\textsuperscript{99}. Loss of muscle mass is associated with osteoporosis, impaired glucose metabolism, cardiovascular deconditioning, and also the ability to walk and to look after oneself\textsuperscript{100}. It is important to measure muscle mass over time to understand the magnitude of sarcopenia, and to attempt to minimise muscle wastage over time.

2.5.1 Assessing body composition and muscle mass

Simple anthropometry measures often include height, weight, body mass index (BMI), and waist circumference. In order to gain an understanding of muscle mass, more
sophisticated equipment is required. The gold standard for body composition is dual-energy x-ray absorptiometry (DEXA). DEXA is a large, expensive piece of equipment, which must be housed in a radiation certified room. The scan requires trained personnel to operate and exposes the individual to low doses of ionising radiation, restricting the number of times the assessment can be performed. An alternative method of measuring muscle mass is bioelectrical impedance analysis (BIA). BIA involves a small electrical current running through the body, based on the principle that the resistance of the current is proportional to the amount of fat free mass\textsuperscript{101}. It is simple and time efficient to administer, and has been shown to be valid and reliable\textsuperscript{102}.

2.5.2 Body composition and muscle mass in stroke

Following stroke, significant structural and metabolic changes can occur in muscle\textsuperscript{103}. Initial immobility can lead to muscle weakness, and coupled with the residual gait deficits as a result of the stroke, often leads to decreased activity and greater disuse atrophy\textsuperscript{71}. Physical capacity is significantly influenced by muscle atrophy post-stroke\textsuperscript{71} with potential to increase muscle mass as part of rehabilitation. It has been shown that CT scans of stroke survivors’ paretic mid-thigh had 25% increased intramuscular fat and 20% decreased muscle area compared to the non-paretic thigh\textsuperscript{78}. A meta-analysis found stroke survivors have significantly less muscle mass in the affected limb compared to the less-affected limb, with muscle mass an independent determinant of VO\textsubscript{2peak}\textsuperscript{104}.
2.6 Other measures

2.6.1 Blood pressure

It is estimated that 50% of stroke survivors are hypertensive\textsuperscript{105}, therefore it is extremely important to monitor blood pressure at rest, during exercise and immediately post-exercise. According to the American College of Sports Medicine (ACSM), an indication to terminate testing is a blood pressure response of systolic $>250\text{mmHg}$ and diastolic $>115\text{mmHg}$.

2.6.2 Electrocardiograph (ECG)

Cardiac disease occurs in up to 75\% of stroke survivors\textsuperscript{106}, therefore there is an increased risk for adverse exertional cardiac events\textsuperscript{107}. One study previously reported 11.2\% of stroke survivors exhibited a clinically relevant abnormality during a GXT\textsuperscript{49}. It is recommended that stroke survivors be monitored by ECG for initial exercise testing\textsuperscript{107} so that any signs of ischemia (eg dynamic ST segment and T wave changes) or altered cardiac rhythm can be monitored in real time and used as criteria for exercise termination if required. It can also be used to assess whether exercising at higher intensities is safe for the individual.

2.6.3 Quality of life, fatigue and depression

2.6.3.1 Stroke and Aphasia Quality of Life (SAQoL)

Health related quality of life is often compromised following stroke. A quick, subjective assessment of the impact stroke has on an individual’s ability to lead a fulfilling life is the SAQoL. This questionnaire is an interview-administered self-report scale involving 53 questions that cover 12 sub-domains (self-care, mobility, upper-extremity function,
work, vision, language, thinking, personality, mood, energy and family and social roles). The SAQoL has been found to be acceptable, reliable (ICC: 0.96-0.98) and valid ($r = 0.26-0.70$) in the stroke population\textsuperscript{108,109}.

\subsection*{2.6.3.2 Fatigue Assessment Scale (FAS)}
Fatigue plagues a large proportion of stroke survivors\textsuperscript{110} and can affect their quality of life, as well as the amount of physical activity they can perform. To date, there is a gap in the current knowledge regarding the mechanisms for fatigue post stroke. One way to subjectively quantify fatigue levels is the 10-item FAS. The FAS has been found to have good internal consistency\textsuperscript{111} and, according to Mead (2007)\textsuperscript{112}, has the best retest reliability for fatigue scales in stroke survivors.

\subsection*{2.6.3.3 Patient Health Questionnaire 9-item (PHQ-9)}
Depression after stroke affects approximately one third of all survivors\textsuperscript{113,114} and is associated with increased morbidity and mortality following stroke\textsuperscript{115}. The PHQ-9 is designed to distinguish between major and minor depressive symptoms and it performs equally well in both the general and stroke populations\textsuperscript{115}. The PHQ-9 has been shown to be reliable (ICC=0.98), have good internally consistency (Cronbach’s $\alpha=0.79$) and moderate validity ($r=0.70$) in stroke\textsuperscript{116}.

\section*{2.7 Exercise prescription for improving cardiorespiratory fitness in stroke survivors}
Our recent meta-analysis\textsuperscript{43} of exercise interventions post stroke reported a 10-15\% improvement in CRF regardless of whether the intervention was purely aerobic or was a
general exercise intervention with an aerobic component (Figure 2.1). This evidence suggests that incorporating an aerobic component into post stroke rehabilitation is effective in improving fitness in stroke survivors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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<tbody>
<tr>
<td></td>
<td>VO_{peak}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(l/min)</td>
<td>(l/min)</td>
<td>(l/min)</td>
<td>(l/min)</td>
</tr>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Aeric</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Chu et al, 2004</td>
<td>21.2</td>
<td>2.3</td>
<td>7</td>
<td>17.6</td>
</tr>
<tr>
<td></td>
<td>4.7</td>
<td>5</td>
<td>2.4</td>
<td>3.60 (0.06, 6.10)</td>
</tr>
<tr>
<td>Ivey et al, 2007</td>
<td>15.7</td>
<td>5.7</td>
<td>36</td>
<td>14.4</td>
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<tr>
<td></td>
<td>5.4</td>
<td>20</td>
<td>4.5</td>
<td>1.30 (1.52, 4.52)</td>
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<tr>
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<td>16.6</td>
<td>6.4</td>
<td>39</td>
<td>12.8</td>
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<tr>
<td></td>
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<td>34</td>
<td>7.1</td>
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<td>37</td>
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<tr>
<td></td>
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<td>34</td>
<td>6.1</td>
<td>2.70 (0.38, 5.12)</td>
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<td>5.6</td>
<td>32</td>
<td>14.9</td>
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<tr>
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<td>5.9</td>
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<tr>
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<td>18</td>
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<td>950</td>
<td>40.0</td>
<td>2.60 (6.41, 7.70)</td>
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<tr>
<td>Mixed</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>3.3</td>
<td>44</td>
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<td></td>
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<td>40</td>
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<td>12.7</td>
</tr>
<tr>
<td></td>
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<td>4</td>
<td>11.8</td>
<td>3.60 (1.24, 5.94)</td>
</tr>
<tr>
<td>Lee et al, 2003 - cycle</td>
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<td>3.8</td>
<td>12</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
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<td>4</td>
<td>2.1</td>
<td>1.80 (0.23, 3.38)</td>
</tr>
<tr>
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<td>3.8</td>
<td>12</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
<td>4.3</td>
<td>4</td>
<td>2.1</td>
<td>0.60 (0.03, 5.12)</td>
</tr>
<tr>
<td>Parg et al, 2005</td>
<td>23.5</td>
<td>6.3</td>
<td>32</td>
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</tr>
<tr>
<td></td>
<td>4.5</td>
<td>31</td>
<td>8.3</td>
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</tr>
<tr>
<td></td>
<td>2.61</td>
<td>17</td>
<td>5.6</td>
<td>1.71 (0.05, 3.38)</td>
</tr>
<tr>
<td>Tuchet et al, 2001</td>
<td>11.95</td>
<td>2.1</td>
<td>7</td>
<td>9.12</td>
</tr>
<tr>
<td></td>
<td>2.3</td>
<td>3</td>
<td>7.8</td>
<td>3.43 (0.04, 6.22)</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>117</td>
<td>116</td>
<td>59.1</td>
<td>1.00 (0.05, 2.07)</td>
</tr>
</tbody>
</table>

Figure 2.1 Forest plot of aerobic versus mixed interventions in their improvement of VO_{peak} levels\textsuperscript{117}

According to Mead and van Wijck\textsuperscript{118}, exercise professionals must be able to provide exercise programs that 1) accommodate individual needs including disability level and co-morbidities, 2) are safe, 3) progress fitness gains, and 4) facilitate long term self-management of physical activity. Consideration of the World Health Organisation’s International Classification of Functioning, Disability and Health (ICF) is important when prescribing exercise in this population. This framework (Figure 2.2) can be used to identify and categorise measures of fitness that capture different aspects of the stroke survivor’s health and quality of life.
Following the decision of the exercise training modality to be prescribed, the intensity of training should be determined. Training the aerobic system requires the use of large muscle groups, which increases cardiac demand. Intensity of training is often determined through measurement of heart rate (HR). Following stroke, peak heart rate occurs at approximately 74-86% of age predicted $HR_{\text{max}}$\textsuperscript{120}, making exercise training based on heart rate response difficult. Heart rate reserve (HRR) determined using the Karvonen\textsuperscript{121} method may be more suitable, as it takes into account resting heart rate. The American College of Sports Medicine\textsuperscript{122} recommends an intensity of 60-90% of $HR_{\text{max}}$ for healthy individuals. In the stroke context, Billinger et al.\textsuperscript{120} have defined moderate intensity exercise as 40-59% HRR or 64-76% $HR_{\text{max}}$, whereas high intensity is 60-84% HRR or 77-93% $HR_{\text{max}}$. It has recently been suggested that interval training, which is defined as concentrated efforts of moderate to high intensity exercise alternated with bouts of recovery\textsuperscript{123}, may be a suitable method for training in stroke.
survivors. Interval training is designed to mitigate fatigue to allow the individual to exercise for the recommended 30 minutes to meet national guidelines.

Despite these recommendations, establishing exercise intensity based purely on HR has limitations in this population. Many stroke survivors have co-morbidities or are taking prescription medications that could interfere with HR. In this case, a rating of perceived exertion (RPE) scale could be used, however the individual must be familiar with ratings and be able to quantify difficulty of exercise. Given that the individual is familiarised with the scale prior to commencement of the program, RPE may be an appropriate method during moderate intensity exercise, with some limitations at high intensities (>80% VO$_{2\text{max}}$). To date, there is minimal reporting of the actual intensity achieved during exercise interventions, regardless of the method used to indicate intensity.

A recent systematic review of exercise interventions post stroke highlighted several gaps in the literature surrounding applicability, generalisability and long term maintenance. It is important to note that in a clinical setting there is often limited funding and equipment. Therefore, to make intervention appropriate for these settings, cost and time effectiveness must be justified. Currently, many programs require stroke survivors to travel to a centre several times per week. This is time intensive, and often not feasible, as stroke survivors can be prohibited from driving. Secondly, there is often a blanket program which is prescribed to all participants regardless of age, disability, likes or dislikes. Stroke survivors are a heterogeneous population and may be better suited to a tailored, individualised program. Thirdly, the programs do not focus on time outside of the face-to-face therapy hours. Independent of physical activity levels, there
Chapter 2. Literature Review

is a link between increased amounts of sitting time and cardiovascular disease morbidity and mortality\textsuperscript{129}, suggesting that being active during the hours outside of face-to-face therapy times is important. Currently, studies do not focus on these additional hours and do not highlight the importance of living an active lifestyle by making mindful changes to daily routine. This includes reducing sitting time, which is emerging as an important concept for clinical populations\textsuperscript{129}. Lastly, there is a lack of long term follow up after an exercise intervention period. Often, the stroke survivor is provided with an intensive, relatively short term exercise program without guidance or knowledge on how to maintain these improvements as they transition out of the program into a situation where the resources are no longer available to them. The development of the HowFITSS? exercise program was based on these gaps in the literature, with the goal to not only improve fitness but to maintain it over the long term with minimal resources.

1.8 Summary of Gaps in Knowledge

There are several gaps in the current knowledge surrounding CRF post stroke that have been identified throughout this review. Many of these have been used to inform this thesis. They include:

\textit{CRF Exercise Testing}

- Stroke survivors are a heterogeneous population and often require individual tailoring for both assessment and prescription of exercise. Guidelines suggest ergometer testing, which may not be feasible for a number of reasons:
  - Ergometers may not be available in all clinical settings
  - Ergometers may require too much space for some settings
  - Limitations to ergometer testing such as compromised balance on a treadmill or joint pain on a cycle
• Walking tests such as the 6MWT can be used as an alternative to ergometer testing. However, the challenges associated with this test include:
  o It requires 30m of uninterrupted, straight, flat corridor space (ATS standard) to compare the results to normative data
  o The test is a submaximal test and therefore relies on more assumptions to provide an indication of CRF

• The SWT is an amalgamation of the progressive nature of an ergometer test with the walking modality of the 6MWT. The SWT is yet to be investigated in stroke
  o Performance compared to age and gender matched controls is unknown in stroke

Prescription of Exercise in Stroke

• It has been shown that exercise programs with an aerobic component have the potential to improve CRF in stroke
• Interval training may be a strategy for mitigating fatigue to accumulate the required 30 minutes of exercise per day
• It is unclear whether HR is an adequate measure of intensity in stroke survivors
• Most current interventions require stroke survivors to travel to a centre to perform exercise training
• Blanket program approaches have commonly been used, without individualisation
• There is a lack of long term follow up after exercise interventions in stroke
• Emphasis on long term maintenance of exercise and an active lifestyle is absent
This thesis investigates both the assessment and prescription aspects of CRF, since the two components should be integrated in post stroke care. The core of this thesis is the development of the *HowFITSS?* program, based on the preliminary findings (Chapters 3-7) and the gaps in the literature as previously described. *HowFITSS?* was designed to address these limitations, and is further elaborated in Chapter 8 of this thesis.
Chapter 3 - Protocol variations and six-minute walk test performance in stroke survivors: a systematic review with meta-analysis

3.1 Preface

This chapter presents a published peer-reviewed manuscript, which investigated the use of the six-minute walk test in stroke survivors. This review informed the use of the test in the HowFITSS? trial and provided recommendations for reporting this test in future research publications. This manuscript has been published in the journal *Stroke Research and Treatment*.

3.2 Citation


3.3 My contributions

I am the lead author on this paper, and contributed significantly from conception to final draft. I performed the search in conjunction with librarian Debbie Booth, of which I then determined include/exclude papers. I extracted all data, and worked with statisticians to produce the meta-analysis. I independently wrote the initial draft of the paper, and worked with co-authors to develop final drafts. I created the tables and figures, as well as liaising with the journal to finalise the publication.
3.4 Abstract

Objective: To investigate the use of the six-minute walk test (6MWT) for stroke survivors, including adherence to 6MWT protocol guidelines and distances achieved.

Methods: A systematic search was conducted from inception to March 2014. Included studies reported a baseline (intervention studies) or first instance (observational studies) measure for the 6MWT by stroke survivors who were any time post stroke.

Results: Of 127 studies (participants n = 6,012) that met the inclusion criteria, 64 were also suitable for meta-analysis. Only 25 studies made reference to the American Thoracic Society (ATS) standards for the 6MWT, and 28 reported using the protocol standard 30m walkway. Thirty-nine studies modified the protocol walkway, while 60 studies did not specify the walkway used. On average, stroke survivors walked 284±107m during the 6MWT, which is substantially less than healthy age matched individuals. The meta-analysis identified that changes to the ATS protocol walkway are associated with reductions in walking distances achieved.

Conclusion: The 6MWT is now widely used in stroke studies. The distances achieved by stroke patients indicate substantially compromised walking ability. Variations to the standard 30m walkway for the 6MWT are common and caution should be used when comparing the values achieved from studies using different walkway lengths.
3.5 Introduction

Compromised walking ability is a functional limitation significantly associated with poorer community integration following stroke and improving walking capacity and endurance is often a key goal of stroke rehabilitation. Functional walking tests, such as the 6MWT, were originally developed in the 1960s and used to assess people with cardiovascular and respiratory disease. More recently, the 6MWT has been used to characterise and monitor changes in walking capacity following stroke. The test is commonly used as a measure of walking endurance and is a significant predictor of community ambulation and integration in stroke survivors.

In 2002, the American Thoracic Society (ATS) published guidelines for the 6MWT with the objective of standardising the protocol to encourage further application of the 6MWT and allow direct comparisons among different studies and populations. The ATS guidelines include test indications and contraindications, safety measures, a step-by-step protocol, and provide assistance with clinical interpretation. Key components of the protocol include the test location, walkway length, measurements and instructions. According to the ATS protocol, the test should be performed on a flat, enclosed (indoor) walkway 30m in length. This protocol requires 180° turns at either end of the walkway and additional space for turning is required. The guidelines advise that shorter walkway lengths require more directional changes and can reduce the distances achieved. It is likely that the influence of directional changes may be amplified in the stroke population, who characteristically have impaired balance, asymmetrical gait patterns and altered responses for turn preparation. Conversely, reducing the number of directional changes may increase the distance achieved.
The aims of this systematic review were to synthesise the current literature that used the 6MWT and to investigate: (1) the extent of its use in stroke survivors; (2) the characteristics of the stroke survivor populations studied; (3) the adherence to the ATS standard protocol; (4) the distances achieved; and (5) the influences of protocol modification and factors such as age, gender, disability and time post-stroke on distances achieved.

3.6 Methods

The conduct and reporting of this review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement.

3.6.1 Search strategy and selection criteria

A systematic computer-based search was undertaken of the databases MEDLINE, CINAHL, EMBASE, PsycINFO, AMED, SPORTDiscus and COCHRANE from inception to 24th March 2014. The search strategy used for MEDLINE is outlined in Table 3.1 and was adapted to suit each database as required. Studies were deemed eligible if they were published in English, in peer-reviewed journals and included the distance walked during the 6MWT by stroke survivors during the baseline (intervention studies) or first instance (observational studies). The World Health Organisation defines stroke as “a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin” and must have been diagnosed clinically. Both ischemic and haemorrhagic stroke were included at any time post stroke. Studies reporting data from mixed neurological groups
that included people after stroke were excluded. Theses and articles published in abstract form only, including conference proceedings, were also excluded.

Table 3.1 Search strategy used for MEDLINE

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
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<td>1</td>
<td>Cerebrovascular Disorders.mp. or exp Cerebrovascular Disorders</td>
</tr>
<tr>
<td>2</td>
<td>Stroke.mp. or exp Stroke/</td>
</tr>
<tr>
<td>3</td>
<td>(cerebral or cerebellar or brainstem or vertebrobasilar).mp.</td>
</tr>
<tr>
<td>4</td>
<td>(infarct* or ischemia or thrombo* or embol*).mp.</td>
</tr>
<tr>
<td>5</td>
<td>3 and 4</td>
</tr>
<tr>
<td>6</td>
<td>(cerebral or brain or subarachnoid or intracerebral).mp.</td>
</tr>
<tr>
<td>7</td>
<td>(haemorrhage or haematoma or bleed* or haemorrhage or hematoma).mp.</td>
</tr>
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<td>9</td>
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<tr>
<td>10</td>
<td>6MWT</td>
</tr>
<tr>
<td>11</td>
<td>Six minute walk*</td>
</tr>
<tr>
<td>12</td>
<td>6 minute walk*</td>
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<td>10 or 11 or 12</td>
</tr>
<tr>
<td>14</td>
<td>9 and 13</td>
</tr>
</tbody>
</table>

3.6.2. Selection of studies

The author Ashlee Dunn identified and obtained abstracts from the relevant studies based on title, and classified each study as being a possible inclusion or definite exclusion according to the first inclusion criterion the study failed to meet. Studies were excluded if they were a subset from a larger study using the same participants, if the distance achieved on the 6MWT was not presented as text but rather a graph or chart or if the 6MWT distance was not reported. Full text versions of all possible inclusion studies were then retrieved and reviewed by the author Ashlee Dunn who classified them as ‘include’, ‘exclude’ or ‘unsure’. This process was then independently conducted by the second reviewer EN. For instances where there was uncertainty or disagreement between authors, a consensus decision was reached through discussion and the involvement of a third reviewer RC if necessary.
3.6.3 Data extraction and synthesis

Author Ashlee Dunn then extracted the following variables from included studies:

- Study characteristics: year published, participant numbers, gender ratio
- Participant characteristics: age, gender, time since stroke, disability score
- 6MWT: distance achieved, protocol used, assistance provided, assistive devices used, instructions given

3.6.4 Quantitative analysis of adherence to ATS protocol guidelines

To date, there is no standardised approach to assessing the quality of reporting of observational studies such as adherence to protocol guidelines. As this is a systematic review looking only at baseline values rather than interventions, assessment of conventional methodological study quality is not applicable. Therefore, for the purpose of this review, a unique two-point scale was designed. Points were awarded as follows: one point for describing the protocol used and one point for referring to the ATS standards for the 6MWT. Therefore, a study could score zero, one or two points unless it was published prior to the ATS standards [n=3] in which case it could only achieve a score of zero or one.

3.6.5 Meta-analysis

A meta-analysis was conducted to examine the influence of the 6MWT protocol variations, as well as age (continuous, years), gender (proportion of male participants in the study), physical disability score (converted to a continuous z-score), and time since stroke (continuous, months), on the distance walked. Studies were excluded from the meta-analysis if they did not perform the 6MWT indoors, on a flat walkway, with usual walking device, or if the walkway length was not described. Included studies were
pooled into three groups based on the walkway length used: <30m, =30m and >30m shuttles. Studies where the test was performed on an oval or rectangular track were pooled together to create a fourth “continuous walkway” group. The ATS standards state 30m or 100ft walkway, which converts to 30.5m. Any studies using a 30.5m walkway were therefore included in the =30m group. In studies that reported medians (IQR), the medians were used as means and IQRs were converted to SDs by dividing the reported IQRs by 1.35; these approaches assume symmetrical distributions. A random-effects meta-regression was conducted where the square of each study’s standard error was used as fixed values of the sampling variance. Statistical significance was accepted at the level of $\alpha \leq 0.05$. A second meta-regression was also conducted to examine the effects of age, gender, disability and time since stroke in only those studies that used the 30m walkway protocol.

3.7 Results

The search across seven databases yielded 1,717 citations from which 127 articles were identified for inclusion in the review. Figure 3.1 details the flow of studies and reasons for exclusion throughout the selection process. Table 3.3 summarises the study characteristics, participant characteristics and 6MWT results. Of the included studies the first paper to use the 6MWT in stroke survivors was reported in 1998. The use of the test has since increased rapidly, with 11 papers published from 2000 to 2004, 48 papers published from 2005 to 2009 and 67 papers published from 2010 onward. Most (98%) papers were published since the publication of the ATS guidelines in 2002.
Records identified through database searching (n = 1,717)

AMED = 70
CINAHL = 159
Cochrane = 518
EMBASE = 474
Medline = 361
PsycINFO = 47
SPORDiscus = 88

Duplicates removed (n = 646)

Records screened by title and abstract (n = 1,071)

Records excluded based on abstract (n = 885)

Full-text articles assessed for eligibility (n = 186)

Records excluded on full text (n = 59)
No data presented on 6MWT distance at baseline (n = 22)
Secondary analysis (n = 17)
Protocol, commentary, conference proceeding, case study or review (n = 13)
Full text not available in Australia (n = 2)
Full text not available in English (n = 3)
Not specifically Stroke (n = 2)

Studies included in qualitative analysis (n = 127)

Studies included in quantitative analysis (n = 64)

Records excluded from meta-analysis (n = 63)
No protocol described (n = 60)
Protocol not clinically applicable (n = 3)

Figure 3.1 PRISMA flow diagram
3.7.1 Participant characteristics

The 127 studies reported on a collective sample size of 6,012 participants, including 3,654 males (61%), 2,188 females (36%) and 170 (3%) not specified. The participant eligibility criteria reported in studies included the following: participants greater than 6 months post stroke [n=40 studies], no significant cognitive or communicative issues [n=85 studies], mild or no cardiovascular or pulmonary problems [n=66 studies], no orthopaedic or musculoskeletal problems or pain [n=57 studies], no other neurological conditions [n=42 studies], and able to meet a specified minimal or maximal walking speed either overground or on a treadmill [n=17 studies]. Only 77 studies reported being ambulant with or without assistance as an eligibility criteria, however a further nine studies reported a minimal walking speed and four studies report ability to walk on a treadmill as inclusion criteria. These criteria imply the ability to walk, even if it is not explicitly stated.

<table>
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<th>Estimate</th>
<th>StdErr</th>
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<th>tValue</th>
<th>Probt</th>
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<th>Upper CI</th>
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<td>1.7</td>
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<td>0.38</td>
<td>0.708</td>
<td>-2.7</td>
<td>4.0</td>
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<td>Proportion males</td>
<td>0.6</td>
<td>0.8</td>
<td>75</td>
<td>0.75</td>
<td>0.455</td>
<td>-1.0</td>
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<td>Time since stroke</td>
<td>0.5</td>
<td>0.4</td>
<td>75</td>
<td>1.16</td>
<td>0.251</td>
<td>-0.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Participant mean ages (SD) ranged from 45 (7) to 76 (13) years, and mean time since stroke varied from 11 (4) days to 8.5 (0.9) years. Thirteen studies did not specify time post stroke. Most studies included participants either within 6 months post stroke [n=32], 1-3 years [n=27] or more than 3 years post stroke [n=50], with much smaller numbers in the 6-12 month range [n=9]. A disability score was reported in only 58% of all studies. Of those that did report degree of disability, 12% reported the use of more than one scale. Common disability scales reported in these studies were the Fugl-
Chapter 3. Systematic Review 1

Meyer Assessment (FM) [n=24], Barthel Index (BI) [n=13], Functional Independence Measure (FIM) [n=12], Rivermead Mobility Index [n=10], Functional Ambulatory Category (FAC) [n=8], Chedoke McMaster [n=6], Motor Assessment Scale (MAS) [n=6] and the Motricity Index (MI) [n=3]. Other scales included the Walking Ability Questionnaire [n=1], Dynamic Gait Index (DGI) [n=1], the Late Life Function and Disability Instrument (LLFDI) [n=1] and the Modified Korean Barthel Index [n=2]. Sub-scale specific lower-limb measures were preferred in the meta-analysis, and these were available in the FM (motricity lower limb, lower extremity) [n=10], FIM (mobility, walking capacity, locomotion) [n=7], Chedoke McMaster (leg) [n=5] and MAS (walking) [n=3] only.
<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age (SD) years</th>
<th>Time since stroke (SD)</th>
<th>Number of Participants (male: female)</th>
<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards Protocol described Reporting score</th>
<th>Distance achieved (SD) meters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ada et al11 2003</td>
<td>I = 66 (11) C = 66 (11)</td>
<td>Months</td>
<td>I = 28 (17) C = 26 (20)</td>
<td>27 19.08</td>
<td>SA-SIP I = 12.1 (5.5) C = 15.2 (5.5)</td>
<td>ATS = NR (0) Walkway = NR (0) Total = 0</td>
</tr>
<tr>
<td>*Ali et al14 2009</td>
<td>67.56 (9.5)</td>
<td>Days</td>
<td>41.84 (26.08)</td>
<td>25 NR</td>
<td>FIM total 100.84 (12.43)</td>
<td>ATS = No (0) Walkway = continuous circuit of 50m circumference (1) Total = 1</td>
</tr>
<tr>
<td>*Allet et al146 2013</td>
<td>I = 57.97 (11.02) DO = 53.25 (10.53)</td>
<td>Months</td>
<td>I = 37.7 (31.7) DO = 26.25 (10.69)</td>
<td>44 30:14</td>
<td>SSAS I = 50.5 (37-74)x DO = 54.0 (37-73)x</td>
<td>ATS = No (0) Walkway = continuous square path 52m in total (1) Total = 1</td>
</tr>
<tr>
<td>Bassie et al14 2003</td>
<td>64.2#</td>
<td>Years</td>
<td>0.5 - 6</td>
<td>5 02.03</td>
<td>MAS 5.2</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
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<tr>
<td>*Billinger et al149 2012</td>
<td>61.2 (4.7)</td>
<td>Days</td>
<td>68.6 (40.1)</td>
<td>10 06:04</td>
<td>FM lower 27.4 (8.8)</td>
<td>ATS = Yes (1) Walkway = 100ft (30.48m) walkway (1) Total = 2</td>
</tr>
<tr>
<td>Blennerhassett et al150 2004</td>
<td>I1 = 56.3 (10.5) I2 = 53.9 (19.8)</td>
<td>Days</td>
<td>I1 = 50.1 (49.2) I2 = 36.0 (25.1)</td>
<td>30 17:13</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
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<tr>
<td>*Blennerhassett et al12 2012</td>
<td>66 (49.3 – 72.0)x</td>
<td>NR</td>
<td>30 20:10</td>
<td>NR</td>
<td>ATS = No (0) Walkway = continuous rectangular track 86m in total (1) Total = 1</td>
<td></td>
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<tr>
<td>Bowden et al151 2013</td>
<td>58.74 (12.97)</td>
<td>Months</td>
<td>22.70 (16.38)</td>
<td>27 19.08</td>
<td>FM 23.1 (4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
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<tr>
<td>Brock et al152 2011</td>
<td>I1 = 61.3 (13.0) I2 = 56.6 (15.8)</td>
<td>Days</td>
<td>I1 = 60.3 (24.0) I2 = 63.6 (23.9)</td>
<td>26 19.07</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 12.5m long including a purpose built ramp and step, and thin foam mats (1) Total = 1</td>
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<td>Study Year</td>
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<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described</td>
<td>Reporting score</td>
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<tr>
<td>Brogardh et al&lt;sup&gt;153&lt;/sup&gt; 2012</td>
<td>I = 61.3 (8.5) C = 63.9 (5.8)</td>
<td>Months I = 37.4 (31.8) C = 33.1 (29.2)</td>
<td>31 25.06</td>
<td>FIM I1 = 83.1 (3.1) I2 = 83.5 (3.2)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 305 (108) C = 393 (115)</td>
</tr>
<tr>
<td>Brogardh et al&lt;sup&gt;154&lt;/sup&gt; 2012</td>
<td>64 (NR)</td>
<td>Months 42 (30)</td>
<td>50 41.09</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>303 (130)</td>
</tr>
<tr>
<td>Byun et al&lt;sup&gt;155&lt;/sup&gt; 2011</td>
<td>58.9 (11.9)</td>
<td>Months 9.6 (4.5)</td>
<td>30 19.11</td>
<td>K-MBI 53.6 (24.1)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>104 (96.4)</td>
</tr>
<tr>
<td>Carda et al&lt;sup&gt;156&lt;/sup&gt; 2011</td>
<td>I1 = 62.2 (11.7) I2 = 64.5 (12.5) I3 = 59.6 (14.3)</td>
<td>Months I1 = 46.9 (41.3) I2 = 52.3 (43.8) I3 = 43.9 (39.6)</td>
<td>69 34.35</td>
<td>FAC I1 = 3.9 (0.9) I2 = 4.0 (0.8) I3 = 3.8 (0.6)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 176.2 (98.5) I2 = 191.7 (88.6) I3 = 195.7 (81)</td>
</tr>
<tr>
<td>Carda et al&lt;sup&gt;157&lt;/sup&gt; 2012</td>
<td>63.9 (10.5)</td>
<td>Days 1,273 (1,460)</td>
<td>62 43.19</td>
<td>FAC 3 (2 – 4)*</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>Without HFO = 146.1 (99.7) With HFO = 189 (94.9)</td>
</tr>
<tr>
<td>Carroll et al&lt;sup&gt;158&lt;/sup&gt; 2012</td>
<td>72.4 (12.3)</td>
<td>Days 12.5 (6.25 – 34)*</td>
<td>50 21.29</td>
<td>BI 100 (90-100) *</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>158.6 (129.2)</td>
</tr>
<tr>
<td>*Carvalho et al&lt;sup&gt;159&lt;/sup&gt; 2008</td>
<td>60 (4.1)</td>
<td>Months 62 (33)</td>
<td>34 24.10</td>
<td>FM lower 30 (13 – 34)*</td>
<td>ATS = Yes (1) Walkway = indoors and outdoors over a 30m course (1) Total = 2</td>
<td>In 365.2 (142.6) Out 373.6 (150.8)</td>
</tr>
<tr>
<td>*Carvalho et al&lt;sup&gt;160&lt;/sup&gt; 2013</td>
<td>59 (5.8)</td>
<td>Months 53 (36)</td>
<td>41 31.10</td>
<td>FM lower 28 (13 – 34)*</td>
<td>ATS = Yes (1) Walkway = 30m walkway (1) Total = 2</td>
<td>372 (139)</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
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<td>------------</td>
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<tr>
<td><em>Chanruengvanich et al</em> 2006</td>
<td>I = 62.83 (7.41) C = 63.18 (7.13)</td>
<td>NR</td>
<td>62:42</td>
<td>NR</td>
<td>ATS = No (0) Walkway = continuous rectangular path, total distance 30m (1) Total = 1</td>
<td>I = 391.99 (82.6) C = 341.6 (89.97)</td>
</tr>
<tr>
<td>Da Silva et al 2013</td>
<td>54 (9)</td>
<td>Years 7.8#</td>
<td>12:06</td>
<td>FM 163.3#</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td></td>
</tr>
<tr>
<td><em>Daly et al</em> 2006</td>
<td>I = 57.7 (11.9) C = 63.6 (10.4)</td>
<td>Years I = 3.6 (3.8) C = 3.3 (2.1)</td>
<td>29:22</td>
<td>FM knee flex subscale I = 4 (2)# C = 3 (2)#</td>
<td>ATS = No (0) Walkway = 30.5m walkway (1) Total = 1</td>
<td></td>
</tr>
<tr>
<td><em>Daly et al</em> 2011</td>
<td>I = 59 (NR) C = 62 (NR)</td>
<td>NR</td>
<td>44:32</td>
<td>FIM loco/mob I = 30 (2.75) C = 30 (8.50)</td>
<td>ATS = No (0) Walkway = 30.5m walkway (1) Total = 1</td>
<td></td>
</tr>
<tr>
<td><em>Danielsson et al</em> 2011</td>
<td>59.7 (8.1)</td>
<td>Years 8.5 (0.9)</td>
<td>31:22</td>
<td>FM lower 29 (12)#</td>
<td>ATS = Yes (1) Walkway = 30m walkway (1) Total = 2</td>
<td></td>
</tr>
<tr>
<td><em>Dean et al</em> 2001</td>
<td>62.7 (8.5)</td>
<td>NR</td>
<td>14:06</td>
<td>NR</td>
<td>ATS = No (Published prior to ATS) Walkway = 50m walkway (1) Total = 1</td>
<td></td>
</tr>
<tr>
<td>Donovan et al 2008</td>
<td>61.3 (11.1)</td>
<td>Months 46.5 (32.9)</td>
<td>30:21</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 3 environments: clinic (150m walkway), outdoors and in mall (1) Total = 1</td>
<td></td>
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<tr>
<td>Duncan et al 1998</td>
<td>I = 67.3 (8.6) C = 67.8 (7.2)</td>
<td>Days I = 66 (NR) C = 56 (NR)</td>
<td>20:NR</td>
<td>FM lower I = 21.7 (NR) C = 23.2 (NR)</td>
<td>ATS = No (Published prior to ATS) Walkway = NR (0) Total = 0</td>
<td></td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
</tr>
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<td>-------------------</td>
</tr>
</tbody>
</table>
| Duncan et al⑥7 2003 | I = 68.5 (9)  
C = 70.2 (11.4)  
D = 74.6 (9.8) | Days  
I = 77.5 (28.7)  
C = 73.5 (27.1)  
D = 84.0 (27.2) | 100  
FM lower  
i = 24.1 (0.7)  
C = 23.7 (3.5)  
D = 26.0 (2.9) | ATS = No (0)  
Walkway = NR (0)  
Total = 0 | |
| Duncan et al⑥8 2011 | I1 = 60.1 (12.3)  
I2 = 63.3 (12.5)  
I3 = 62.6 (13.3) | Days  
I1 = 84.1 (8.3)  
I2 = 64.2 (9.0)  
I3 = 62.9 (9.0) | 408  
FM leg  
i1 = 23.7 (6.7)  
i2 = 24.8 (5.4)  
i3 = 24.7 (5.3) | ATS = No (0)  
Walkway = NR (0)  
Total = 0 | |
| *Eng et al⑥1 2002 | 62.6 (8.5) | Years  
4.4 (3.0) | 25  
CM lower  
8.9 (2.4) | ATS = No (Published prior to ATS)  
Walkway = continuous 42m rectangular path (1)  
Total = 1 | 267.7 (89.7) |
| *Eng et al⑥6 2004 | 62.5 (8.6) | Years  
3.5 (2.0) | 12  
CM lower  
9.4 (2.5) | ATS = No (0)  
Walkway = continuous 42m rectangular path (1)  
Total = 1 | 378.3 (123.1) |
| *Flansbjer et al⑥0 2005 | M = 69 (7)  
F = 66 (5) | Months  
M = 16 (5)  
F = 18 (5) | 50  
NR | ATS = No (0)  
Walkway = 30m walkway (1)  
Total = 1 | T1 = 384 (132)  
T2 = 398 (136) |
| *Flansbjer et al⑥0 2008 | I = 61.5  
C = 60 (5) | Months  
I = 18.9 (7.9)  
C = 20.0 (11.6) | 24  
NR | ATS = No (0)  
Walkway = 30m walkway (1)  
Total = 1 | I = 228 (137)  
C = 234 (134) |
| *Forsberg et al⑥1 2013 | 68.1 (11.2) | Years  
4.6 (5.5) | 67  
RMI  
37 (35-39) | ATS = No (0)  
Walkway = 30m walkway (1)  
Total = 1 | 247 (160-342) |
| Fritz et al⑥3 2013 | I = 67.6 (8.3)  
C = 64.5 (10.1) | Years  
I = 2.5 (2.6)  
C = 3.6 (3.2) | 28  
FM  
i = 68.5 (21.7)  
C = 65.6 (18.0) | ATS = No (0)  
Walkway = NR (0)  
Total = 0 | I = 285.4 (158.7)  
C = 263.2 (178.5) |
<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age (SD) years</th>
<th>Time since stroke (SD)</th>
<th>Number of Participants (male: female)</th>
<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards</th>
<th>Protocol described</th>
<th>Reporting score</th>
<th>Distance achieved (SD) meters</th>
</tr>
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<tbody>
<tr>
<td><em>Fulk et al</em> 2008</td>
<td>66.3 (14.3)</td>
<td>Days 33.7 (17.8)</td>
<td>37</td>
<td>FIM loco 5 (2 – 7)</td>
<td>ATS = No (0)</td>
<td>Walkway = 150 feet (45.72m) at one site, 250 feet (76.20m) at another two sites (1) Total = 1</td>
<td></td>
<td>T1 = 144.2 (136.3) T2 = 160.9 (146.3)</td>
</tr>
<tr>
<td><em>Fulk et al</em> 2010</td>
<td>65.7 (11.9)</td>
<td>Months 42.1 (98.1)</td>
<td>19 NR</td>
<td>FIM lower 28.7 (5.7)</td>
<td>ATS = Yes (1)</td>
<td>Walkway = continuous oval course 30m in circumference (1) Total = 2</td>
<td></td>
<td>348.6 (144)</td>
</tr>
<tr>
<td>Geroin et al 2011</td>
<td>I1 = 63.6 (6.7) I2 = 63.3 (6.4) I3 = 61.1 (6.3)</td>
<td>Months 30</td>
<td>NR</td>
<td></td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0) Total = 0</td>
<td></td>
<td>I1 = 162.9 (52.1) I2 = 156.1 (62.9) I3 = 116.8 (75.2)</td>
</tr>
<tr>
<td>Gerrits et al 2009</td>
<td>54 (10)</td>
<td>Months 18</td>
<td>11:07</td>
<td>FAC 4.6 (SEM=0.1)</td>
<td>ATS = No (0)</td>
<td>Walkway = 50m walkway (1) Total = 1</td>
<td></td>
<td>186 (SEM=25.9)</td>
</tr>
<tr>
<td><em>Gjellesvik et al</em> 2012</td>
<td>48.9 (10.6)</td>
<td>Years 7.2 (7.5)</td>
<td>8</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = 50m walkway (1) Total = 1</td>
<td></td>
<td>474 (91)</td>
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<tr>
<td>Globas et al 2012</td>
<td>I = 68.6 (6.7) C = 68.7 (6.1)</td>
<td>Months 36</td>
<td>BI I = 91.7 (9.7) C = 88.3 (9.6)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0) Total = 0</td>
<td></td>
<td>I1 = 274.4 (113.0) C = 2612 (177.0)</td>
<td></td>
</tr>
<tr>
<td>Gordon et al 2013</td>
<td>I = 63.4 (9.4) C = 64.9 (11.1)</td>
<td>Months 128</td>
<td>BI I = 94.3 (8.1) C = 91.5 (9.7)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0) Total = 0</td>
<td></td>
<td>I1 = 247.1 (141.5) C = 228.0 (138.7)</td>
<td></td>
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<tr>
<td>Hidler et al 2009</td>
<td>I = 59.9 (11.3) C = 54.6 (9.4)</td>
<td>Days 63</td>
<td>RMI I = 9.5 (0.5) C = 11.3 (0.6)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0) Total = 0</td>
<td></td>
<td>I1 = 118.2 (13.2) C = 134.33 (14.1)*</td>
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<td>Hinson et al 2007</td>
<td>BI = 62 (8) Wh = 66 (9)</td>
<td>Months 118</td>
<td>NR</td>
<td></td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0) Total = 0</td>
<td></td>
<td>BI = 214 (108) Wh = 201 (123)</td>
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<tr>
<td>Study Year</td>
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<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
<td>Reporting score</td>
<td>Distance achieved (SD) meters</td>
</tr>
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<tr>
<td>Hoang et al 2012</td>
<td>64.6 (11.2)</td>
<td>Months 40 (42.2)</td>
<td>32 (21:11)</td>
<td>BI 89.7 (9.9)</td>
<td>ATS = No (0)</td>
<td>Walkway = continuous 123m circuit (1)</td>
<td>Total = 1</td>
<td>201.8 (110.5)</td>
</tr>
<tr>
<td>Hornby et al 2008</td>
<td>I1 = 57 (10) I2 = 57 (11)</td>
<td>Months I1 = 50 (51) I2 = 73 (87)</td>
<td>48 (30:18)</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>I1 = 170 (86) I2 = 170 (86)</td>
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<tr>
<td>Hwang et al 2013</td>
<td>1 = 54.6 (9.2) 2 = 54.9 (12.9)</td>
<td>Months 1 = 55.1 (18.8) 2 = 36.7 (19.0)</td>
<td>47 (27:20)</td>
<td>DGI 1 = 20.5 (2.7) 2 = 15.8 (4.8)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>1 = 392.4 (68.9) 2 = 268.6 (74.5)</td>
</tr>
<tr>
<td>*Iosia et al 2012</td>
<td>62.7 (14.7)</td>
<td>Days 101 (36)</td>
<td>12 (08:04)</td>
<td>BI 70 (50 – 88)</td>
<td>ATS = No (0)</td>
<td>Walkway = 20m walkway (1)</td>
<td>Total = 1</td>
<td>226 (111)</td>
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<td>Janssen et al 2008</td>
<td>I1 = 54.2 (10.7) I2 = 55.3 (10.4)</td>
<td>Months I1 = 12.3 (5.4) I2 = 15.3 (9.9)</td>
<td>12 (06:06)</td>
<td>FAC I1 = 4.5 (0.5) I2 = 4.7 (0.5)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>I1 = 160.3 (134.4) I2 = 187.3 (92.0)</td>
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<td>Jin et al 2012</td>
<td>I = 57 (6) C = 56 (7)</td>
<td>Months I = 18.5 (5.2) C = 17.9 (4.8)</td>
<td>133 (94:39)</td>
<td>RMI I = 10.3 (1.4) C = 10.2 (1.4)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>I = 212.0 (63.5) C = 212.2 (50.1)</td>
</tr>
<tr>
<td>*Kang et al 2012</td>
<td>I1 = 55.9 (6.5) I2 = 56.3 (7.6) C = 56.1 (7.8)</td>
<td>Months I1 = 14.1 (4.4) I2 = 13.5 (4.0) C = 15.1 (7.4)</td>
<td>30 (16:14)</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = continuous 50m track (1)</td>
<td>Total = 1</td>
<td>I1 = 240.3 (20.9) I2 = 237.7 (25.4) C = 239.1 (22.0)</td>
</tr>
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<td>Kelley et al 2013</td>
<td>65.75 (9.48)</td>
<td>Years 2.87 (NR)</td>
<td>20 (13:07)</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>51.61 (26.15)</td>
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<tr>
<td>Study Year</td>
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<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
<td>Reporting score</td>
<td>Distance achieved (SD) meters</td>
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<tr>
<td><em>Kelly et al</em> 2003</td>
<td>66 (48 – 73)*</td>
<td>Days 30 (19 – 39)*</td>
<td>17 13.04 NR</td>
<td>ATS = No (0) Walkway = 20m walkway (1) Total = 1</td>
<td><strong>301.8 (202.8 – 384.9)</strong></td>
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<tr>
<td><em>Kim et al</em> 2014</td>
<td>62.2 (11.7)</td>
<td>Days 32.6 (24.7)</td>
<td>55 37.18 KM-BI 74 (17.6)</td>
<td>ATS = No (0) Walkway = 50m walkway (1) Total = 1</td>
<td><strong>262.8 (120.7)</strong></td>
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<tr>
<td><em>Kuding et al</em> 2009</td>
<td>57.6 (11.0)</td>
<td>Months 45.4 (42.8)</td>
<td>26 14:12 NR</td>
<td>ATS = No (0) Walkway = 100 foot walkway (1) Total = 1</td>
<td><strong>202.4 (134.3)</strong></td>
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<td>Kluding et al 2011</td>
<td>63.7 (9.1)</td>
<td>Months 50.4 (37.9)</td>
<td>9 05.04 FM 87.7 (29.1)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td><strong>760 (696.3)</strong></td>
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<tr>
<td>Kuys et al 2011</td>
<td>I = 63 (14) C = 72 (17)</td>
<td>Days I = 52 (32) C = 49 (30)</td>
<td>30 12:18 Modified BI I = 76 (18) C = 80 (9)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 177 (130) C = 219 (147)</td>
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<td>Lam et al 2010</td>
<td>66.8 (SEM=1.1)</td>
<td>Months 59.0 (SEM=9.28)</td>
<td>52 34.18 NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td><strong>253.25 (SEM=19.38)</strong></td>
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<td><em>Langhammer et al</em> 2006</td>
<td>74 (NR)</td>
<td>NR</td>
<td>57 31.26 MAS walk 3.5 (2.5)</td>
<td>ATS = No (0) Walkway = 85m walkway (1) Total = 1</td>
<td><strong>234 (208)</strong></td>
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<td><em>Langhammer et al</em> 2008</td>
<td>I1 = 76.0 (12.7) I2 = 72.0 (13.6)</td>
<td>NR</td>
<td>75 43:32 BI I1 = 56.6 (38.9) I2 = 66.0 (39.0)</td>
<td>ATS = No (0) Walkway = 185m walkway in hospital and different institutions including patients’ homes or outdoors (1) Total = 1</td>
<td>I1 = 187.9 (211.1) I2 = 221.5 (197.8)</td>
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<td>Study Year</td>
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<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described Reporting score</td>
<td>Distance achieved (SD) meters</td>
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<td>Langhammer et al194 2010</td>
<td>74.0 (13.3) I1 = 74.0 (13.3) I2 = 75.0 (10.4)</td>
<td>Days I1 = 419 (1,034) I2 = 349 (820)</td>
<td>39 I1 = 16:23</td>
<td>MAS I3 I1 = 5.4 (NR) I2 = 5.3 (NR)</td>
<td>ATS = No (0) Walkway = 85m walkway (1) Total = 1</td>
<td>I1 = 277.7 (139.9) I2 = 299.4 (159.3)</td>
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<td>Lee et al195 2005</td>
<td>69 (11)</td>
<td>Months 43 (32)</td>
<td>11 09:02</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>324.4 (173.1)</td>
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<td>Lee et al196 2008</td>
<td>67.2 (10.6) I1 = 67.2 (10.6) I2 = 62.9 (9.3) I3 = 60.5 (10.6) C = 65.3 (6.0)</td>
<td>Months I1 = 52.4 (2.2) I2 = 44.2 (63.9) I3 = 63.2 (40.5) C = 65.5 (42.3)</td>
<td>48 28:20</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 249.3 (158.3) I2 = 239.8 (141.0) I3 = 266.0 (123.5) C = 273.2 (162.1)</td>
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<td>Lord et al197 2008</td>
<td>64.2 (14.8) I1 = 64.2 (14.8) I2 = 60.7 (17.6)</td>
<td>Days I1 = 83.1 (29.8) I2 = 80.3 (33.0)</td>
<td>30 18:12</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 125.1 (71.0) I2 = 142.3 (69.4)</td>
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<td>*Mackay-Lyons et al198 2013</td>
<td>61.5 (15.4) I1 = 61.5 (15.4) I2 = 59.0 (12.7)</td>
<td>Days I1 = 23.3 (5.7) I2 = 23.1 (4.4)</td>
<td>30 29:21</td>
<td>CM I1 = 4.8 (1.5) I2 = 4.9 (1.2)</td>
<td>ATS = Yes (1) Walkway = continuous 100m walkway (1) Total = 2</td>
<td>I1 = 188.7 (82.3) I2 = 195.5 (77.7)</td>
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<td>Macko et al199 2005</td>
<td>63.0 (10) I = 63.0 (10) C = 64.0 (8.8)</td>
<td>Months I = 35 (29) C = 39 (59)</td>
<td>61 43:18</td>
<td>RMI I = 11.3 (0.4) C = 11.7 (0.4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 232.0 (23.3) C = 258.5 (33.2)</td>
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<tr>
<td>Macko et al200 2008</td>
<td>70 (1.7)</td>
<td>Months 56 (19)</td>
<td>20 09:11</td>
<td>BI 74.8 (4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>T1 = 116 (15) T2 = 113 (14)</td>
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<td>*Maeda et al201 2009</td>
<td>45 (7)</td>
<td>Months 19 (9)</td>
<td>18 15:03</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 30m walkway (1) Total = 1</td>
<td>AFO = 174 (77) W/O AFO = 140 (69)</td>
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</table>
| Marsden et al 2010 | I = 70.0 (9.0)  
C = 73.1 (9.3) | Months  
I = 37.2 (26.7)  
C = 39.0 (23.6) | 25  
NR | 19.06 | ATS = No (0)  
Walkway = 20m walkway (1)  
Total = 1 | I = 301.6 (121.5)  
C = 349.1 (124.2) |
| Mayo et al 2013 | I1 = 67.7 (14.4)  
I2 = 67.8 (12.3) | Days  
I1 = 265.4 (131.8)  
I2 = 252.0 (165.3) | 87  
NR | 60.27 | ATS = No (0)  
Walkway = NR (0)  
Total = 0 | I1 = 323.4 (19.5)  
I2 = 321.6 (17.1) |
| Mehrholz et al 2006 | 54# | Weeks  
Range 3-12 | 6  
FAC | 05:01 | NR | ATS = No (0)  
Walkway = NR (0)  
Total = 0 |
| Mehrholz et al 2007 | 62.8 (10.2) | Days  
30.6 (15.5) | 55  
RMI | 40:15 | 2.51 (1.62) | ATS = No (0)  
Walkway = NR (0)  
Total = 0 |
| Michael et al 2009 | 71 (NR) | Years  
7.5 (NR) | 10  
NR | 07:03 | NR | ATS = No (0)  
Walkway = 100 feet (30.48m) walkway (1)  
Total = 1 |
| Mikitsch et al 2013 | I = 58 (11)  
C = 57 (12) | Months  
I = 9.8 (19.1)  
C = 9.1 (20.8) | 40  
BI | 25:15 | I = 55 (45-80)x  
C = 53 (45-75)x | ATS = Yes (1)  
Walkway = NR (0)  
Total = 1 |
| Morello et al 2011 | 67 (12.3) | Months  
3.9 (1.6) | 63  
NR | 43:20 | NR | ATS = No (0)  
Walkway = 15m walkway (1)  
Total = 1 |
| Mudge et al 2009 | I = 76 (38 – 89)x  
C = 71 (44 – 86)x | Years  
I = 3.33 (0.6 – 13.3)x  
C = 5.8 (0.5 – 18.7)x | 58  
RMI | 32:26 | I = 14 (6.1 – 15)x  
C = 13.5 (9 – 15)x | ATS = No (0)  
Walkway = NR (0)  
Total = 0 |
| Mudge et al 2009 | 67.4 (12.5) | Months  
66 (61) | 49  
RMI | 29:20 | 13 (6 – 15)x | ATS = No (0)  
Walkway = NR (0)  
Total = 0 |
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<td>Muren et al 2008</td>
<td>58 (9)</td>
<td>Months</td>
<td>60 (27)</td>
<td>30</td>
<td>NR</td>
<td>ATS = Yes (1) Walkway = 30m walkway (1) Total = 2</td>
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<td>Murtezani et al 2009</td>
<td>49.8 (17.4)</td>
<td>NR</td>
<td>44</td>
<td>26:18</td>
<td>BI 68 (20.5)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
</tr>
<tr>
<td>*Ng et al 2005</td>
<td>61.1 (6.8)</td>
<td>Years</td>
<td>5.6 (3.3)</td>
<td>11</td>
<td>06:05</td>
<td>NR</td>
</tr>
<tr>
<td>*Ng et al 2009</td>
<td>I1 = 56.5 (8.2)</td>
<td>I2 = 57.8 (7.3)</td>
<td>I3 = 56.9 (8.6)</td>
<td>C = 56.5 (8.0)</td>
<td>Years</td>
<td>I1 = 4.9 (3.9)</td>
</tr>
<tr>
<td>*Ng et al 2011</td>
<td>58.5 (6.1)</td>
<td>Years</td>
<td>7.0 (6.5)</td>
<td>26</td>
<td>13:13</td>
<td>NR</td>
</tr>
<tr>
<td>*Ng et al 2012</td>
<td>57.4 (7.8)</td>
<td>Years</td>
<td>5.2 (3.7)</td>
<td>62</td>
<td>51:11</td>
<td>NR</td>
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<tr>
<td>Nolan et al 2009</td>
<td>53.44 (11.50)</td>
<td>Months</td>
<td>54.89 (36.98)</td>
<td>18</td>
<td>14:04</td>
<td>NR</td>
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<tr>
<td>*Olawale et al 2011</td>
<td>I1 = 56.8 (6.4)</td>
<td>I2 = 56.8 (8.3)</td>
<td>C = 57.2 (5.9)</td>
<td>Months</td>
<td>I1 = 10.2 (6.9)</td>
<td>I2 = 10.7 (6.8)</td>
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<td>Study Year</td>
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<td>Referenced ATS standards</td>
<td>Protocol described</td>
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</table>
| Ouellette et al\textsuperscript{217} 2004 | I = 65.8 (2.5)  
C = 66.1 (2.1) | Months  
I = 31.8 (3.3)  
C = 25.6 (4.0) | 42 | LLFDI  
I = 52.7 (2.3)  
C = 55.6 (2.2) | ATS = No (0)  
Walkway = NR (0) | Total = 0 |  | I = 217.1 (30.5)  
C = 2210 (34.0) |  |
| *Outermans et al\textsuperscript{218} 2010 | I1 = 56.8 (8.6)  
I2 = 56.3 (8.6) | Days  
I1 = 22.5 (8.2)  
I2 = 23.5 (7.8) | 43 | NR | ATS = Yes (1)  
Walkway = 50m walkway (1) | Total = 2 |  | I = 459.8 (145.8)  
C = 4010 (131.5) |  |
| *Ovando et al\textsuperscript{219} 2011 | 53 (17) | Months 18 (11) | 8 | FM  
C = 25 (4.5) | ATS = No (0)  
Walkway = 30m walkway (1) | Total = 1 |  | 400.9 (136.0) |  |
| Pang et al\textsuperscript{220} 2005 | I = 65.8 (9.1)  
C = 64.7 (8.4) | Years  
I = 5.2 (5.0)  
C = 5.1 (3.6) | 63 | NR | ATS = Yes (1)  
Walkway = NR (0) | Total = 1 |  | I = 328.1 (143.5)  
C = 304.1 (123.8) |  |
| *Park et al\textsuperscript{221} 2011 | I = 59.38 (8.46)  
C = 56.92 (7.79) | Months  
I = 28.08 (12.59)  
C = 28.87 (17.96) | 25 | WAQ  
I = 46.38 (10.38)  
C = 48.75 (10.15) | ATS = No (0)  
Walkway = 20m walkway (1) | Total = 1 |  | I = 166.23 (58.20)  
C = 151.83 (69.95) |  |
| *Patterson et al\textsuperscript{222} 2007 | 64 (10) | Months 48 (99) | 74 | NR | ATS = No (0)  
Walkway = 30.5m walkway (1) | Total = 1 |  | 216 (120) |  |
| *Patterson et al\textsuperscript{223} 2008 | 64 (8) | Months 20.55 (94.0) | 39 | NR | ATS = No (0)  
Walkway = 30.5m walkway (1) | Total = 1 |  | 227 (105) |  |
| *Peurala et al\textsuperscript{224} 2005 | I = 63.3 (8.9)  
I2 = 51.2 (7.9)  
I3 = 52.3 (6.8) | Years  
I1 = 2.6 (2.4)  
I2 = 2.4 (2.6)  
I3 = 4.0 (5.8) | 45 | FIM  
I1 = 99.2 (12.8)  
I2 = 106.9 (10)  
I3 = 100.7 (11.4) | ATS = No (0)  
Walkway = 54m walkway (1) | Total = 1 |  | I = 127.1 (87.2)  
C = 152.3 (89.6)  
\( \Theta = 152.3 (89.6) \) |  |

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<th>Age (SD) years</th>
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<th>Referenced ATS standards</th>
<th>Protocol described</th>
<th>Reporting score</th>
<th>Distance achieved (SD) meters</th>
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<td><em>Pohl et al</em> 2002</td>
<td>72.1 (10.2)</td>
<td>Days 73.3 (26.8)</td>
<td>72:40:32</td>
<td>FM lower 24 (3.8)</td>
<td>ATS = No (0) Walkway = 100 feet (30.48m) walkway (1) Total = 1</td>
<td>215.8 (91.6)</td>
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<td>Polise et al 2013</td>
<td>56.4 (12.5)</td>
<td>Months 64.8 (53.6)</td>
<td>98:54:44</td>
<td>NR</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
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<td><em>Pradon et al</em> 2013</td>
<td>53.3 (13.7)</td>
<td>Months 16 (8)</td>
<td>24:12:12</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 30m walkway (1) Total = 1</td>
<td>273.8 (73.4)</td>
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<td>Rabadi et al 2008</td>
<td>66.5 (9.8)</td>
<td>Years 2.9 (2.4)</td>
<td>40:13:27</td>
<td>NR</td>
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<td>Rand et al 2009</td>
<td>63 (1)</td>
<td>Months 39 (7)</td>
<td>70:39:31</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>633 (49)</td>
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<td>Ryan et al 2011</td>
<td>62.8 (10.3)</td>
<td>Days I = 215 (8.7) C = 19.7 (16.8)</td>
<td>44:35.09</td>
<td>CM I = 4.2 (1.1) C = 4.1 (1)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 190 (176) C = 270 (236)</td>
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<td>Ryan et al 2011</td>
<td>71.1 (9.7)</td>
<td>Years 2.0 (1.1)</td>
<td>16:14.02</td>
<td>CM leg 5 (1.4)</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
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<td><em>Salbach et al</em> 2004</td>
<td>71.1 (9.7)</td>
<td>Days I = 239 (83) I2 = 217 (73)</td>
<td>91:56:35</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 20m walkway (1) Total = 1</td>
<td>I = 209 (126) I2 = 204 (131)</td>
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<td>Salbach et al 2014</td>
<td>71.1 (9.7)</td>
<td>Years 2.0 (1.1)</td>
<td>16:14.02</td>
<td>CM leg 5 (1.4)</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>254.9 (180.9)</td>
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<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described Reporting score</td>
<td>Distance achieved (SD) meters</td>
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<td>*Schmid et al²³¹ 2012</td>
<td>64.06 (8.78)</td>
<td>Months 52.00 (42.14)</td>
<td>77:56:19</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 30m walkway (1) Total = 1</td>
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<td>Severinsen et al²³² 2011</td>
<td>68 (9)</td>
<td>Months 18 (6)</td>
<td>48:35:13</td>
<td>FM 68 (25)</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>291 (71)</td>
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<td>*Sibley et al²³³ 2008</td>
<td>68 (12)</td>
<td>Days 52.4 (13.6)</td>
<td>26:16:10</td>
<td>FIM 107.1 (10.2)</td>
<td>ATS = Yes (1) Walkway = 30m walkway (1) Total = 2</td>
<td>343.6 (107.3)</td>
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<tr>
<td>Simpson et al²³⁴ 2011</td>
<td>67.6 (9.9)</td>
<td>NR</td>
<td>80:56:22</td>
<td>NR</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>275.9 (141.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Singh et al²³⁵ 2013</td>
<td>I = 65.4 (8.8) C = 67.0 (8.4)</td>
<td>Months I = 40.5 (41.8) C = 34.3 (23.6)</td>
<td>28:16:12</td>
<td>BI I = 87.00 (15.45) C = 92.31 (12.69)</td>
<td>ATS = No (0) Walkway = 30m walkway (1) Total = 1</td>
<td>I = 162.40 (78.97) C = 209.92 (176.53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stookey et al²³¹ 2013</td>
<td>61.2 (8.4)</td>
<td>NR</td>
<td>23:11:12</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>T1 = 278 (123.2) T2 = 307.7 (142.0) T3 = 305.1 (138.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Stookey et al²³⁶ 2014</td>
<td>61.5 (9.8)</td>
<td>NR</td>
<td>43:30:13</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 100ft (30.48m) walkway (1) Total = 1</td>
<td>242 (115)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Stuart et al²³² 2009</td>
<td>I = 66.8 (1.4) C = 70.0 (1.7)</td>
<td>Years I = 4.2 (8.8) C = 3.5 (9.5)</td>
<td>78:54:24</td>
<td>BI I = 79.5 (2.6) C = 85.4 (2.0)</td>
<td>ATS = No (0) Walkway = 10m walkway (1) Total = 1</td>
<td>I = 184.0 (11.8) C = 194.4 (9.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
<td>Reporting score</td>
<td>Distance achieved (SD) meters</td>
</tr>
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<td>------------</td>
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</tr>
<tr>
<td><em>Sullivan et al</em> 2007</td>
<td>11 = 60.6 (13.7) I2 = 63.4 (8.8) I3 = 58.2 (15.2) I4 = 61.4 (11.2)</td>
<td>Months</td>
<td>80</td>
<td>FM lower I1 = 24.5 (5.5) I2 = 24.4 (4.5) I3 = 24.2 (4.0) I4 = 22.1 (9.3)</td>
<td>ATS = No (0)</td>
<td>Walkway = continuous, 18m oval walkway (1)</td>
<td>Total = 1</td>
<td>I1 = 189.3 (99.9) I2 = 170.0 (115.2) I3 = 187.8 (99.9) I4 = 190.0 (135.4)</td>
</tr>
<tr>
<td><em>Tang et al</em> 2006</td>
<td>64.6 (14.4)</td>
<td>Days</td>
<td>36</td>
<td>CM 5.1 (1)</td>
<td>ATS = Yes (1)</td>
<td>Walkway = 30m walkway (1)</td>
<td>Total = 2</td>
<td>341.6 (107.9)</td>
</tr>
<tr>
<td><em>Tseng et al</em> 2009</td>
<td>I = 64.7 (SEM = 3.6) C = 65.7 (SEM = 2.3)</td>
<td>Days</td>
<td>36</td>
<td>FIM I = 84.0 (SEM = 4.1) C = 83.9 (SEM = 4.2)</td>
<td>ATS = Yes (1)</td>
<td>Walkway = 30m walkway (1)</td>
<td>Total = 2</td>
<td>I = 207.0 (46.6) C = 198.9 (40.2)</td>
</tr>
<tr>
<td>Tanne et al 2008</td>
<td>I = 61 (10) C = 58 (5)</td>
<td>Days</td>
<td>48</td>
<td>FIM I = 123 (5) C = 122 (5)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>I = 444 (90) C = 438 (101)</td>
</tr>
<tr>
<td>Toledano-Zarhi et al 2011</td>
<td>I = 65 (10) C = 65 (12)</td>
<td>Days</td>
<td>28</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>I = 415.9 (172.5) C = 459.3 (116.3)</td>
</tr>
<tr>
<td><em>Tseng et al</em> 2009</td>
<td>56.8 (11.8)</td>
<td>Months</td>
<td>9</td>
<td>FM 79.4 (32.8)</td>
<td>ATS = No (0)</td>
<td>Walkway = 100 feet (30.48m) walkway (1)</td>
<td>Total = 1</td>
<td>295.5 (171.4)</td>
</tr>
<tr>
<td><em>van Bloemendaal et al</em> 2012</td>
<td>58.8 (9.8)</td>
<td>Months</td>
<td>75</td>
<td>NR</td>
<td>ATS = Yes (1)</td>
<td>Walkway = 30m walkway (1)</td>
<td>Total = 2</td>
<td>472.5 (156.1)</td>
</tr>
<tr>
<td>van de Port et al 2012</td>
<td>I = 56 (10) C = 58 (10)</td>
<td>Days</td>
<td>250</td>
<td>RMI I = 12.67 (1.58) C = 12.35 (2.00)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
<td>I = 339 (120) C = 306 (135)</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described</td>
<td>Reporting score</td>
<td>Distance achieved (SD) meters</td>
<td></td>
</tr>
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<td>------------</td>
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<td>----------------------------</td>
<td></td>
</tr>
<tr>
<td><em>Verheijde et al</em> 2013</td>
<td>70 (13)</td>
<td>Days 52 (87)</td>
<td>43</td>
<td>LEFS 33 (18)</td>
<td>ATS = Yes (1) Walkway = 33m walkway(1) Total = 2</td>
<td></td>
<td>240 (130)</td>
<td></td>
</tr>
<tr>
<td><em>Verma et al</em> 2011</td>
<td>I = 53.27 (8.53) C = 55.07 (8.80)</td>
<td>Weeks 6.3 (3.2)</td>
<td>30</td>
<td>BI I = 60 (9.82) C = 53 (16.98)</td>
<td>ATS = Yes (1) Walkway = 50m walkway (1) Total = 2</td>
<td></td>
<td>I = 115.2 (43.30) C = 96.67 (94.23)</td>
<td></td>
</tr>
<tr>
<td><em>Westlake et al</em> 2009</td>
<td>I1 = 58.6 (16.9) I2 = 55.1 (13.6)</td>
<td>Months I1 = 43.8 (26.8) I2 = 36.8 (20.3)</td>
<td>16</td>
<td>FM lower I1 = 23.0 (4.3) I2 = 21.4 (5.1)</td>
<td>ATS = No (0) Walkway = 39m walkway (1) Total = 1</td>
<td></td>
<td>I1 = 267.3 (187.2) I2 = 234.3 (141.2)</td>
<td></td>
</tr>
<tr>
<td>Wevers et al* 2011</td>
<td>60.7 (10.9)</td>
<td>Days 266 (38)</td>
<td>27</td>
<td>NR</td>
<td>ATS = No (0) Walkway = outdoor 30m walkway (1) Total = 1</td>
<td></td>
<td>1 = 408 (132) 2 = 417 (139) 3 = 413 (127) 4 = 422 (132)</td>
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</tr>
<tr>
<td>White et al* 2013</td>
<td>65.76 (11.01)</td>
<td>Years 2.11 (1.76)</td>
<td>21</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td></td>
<td>377.82 (176.19)</td>
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</tr>
<tr>
<td>Wing et al* 2008</td>
<td>60.2 (14.1)</td>
<td>Months 40.9 (29.1)</td>
<td>35</td>
<td>FM motor 31.8 (SEM=3.2)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
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<td>228.6 (SEM=22.3)</td>
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</tr>
<tr>
<td><em>Yang et al</em> 2009</td>
<td>I = 56.8 (10.2) C = 60.0 (10.4)</td>
<td>Months I = 62.7 (27.4) C = 64.0 (40.4)</td>
<td>48</td>
<td>NR</td>
<td>ATS = Yes (1) Walkway = 25m walkway (1) Total = 2</td>
<td></td>
<td>I = 352.3 (71.7) C = 350.0 (79.6)</td>
<td></td>
</tr>
<tr>
<td><em>Yang et al</em> 2014</td>
<td>I1 = 63.9 (10.5) I2 = 54.5 (8.0)</td>
<td>Months I1 = 11.1 (8.1) I2 = 11.1 (9.7)</td>
<td>30</td>
<td>BI I1 = 17.4 (2.2) I2 = 16.5 (3.8)</td>
<td>ATS = No (0) Walkway = 10m walkway (1) Total = 1</td>
<td></td>
<td>I1 = 216.4 (107.4) I2 = 193.1 (127.3)</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of Participants (male: female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described Reporting score</td>
<td>Distance achieved (SD) meters</td>
<td></td>
</tr>
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<td>-----------------------</td>
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<td>--------------------------------------</td>
<td>-----------------------------</td>
<td>-------------------------------------------------------------</td>
<td>-----------------------------</td>
<td></td>
</tr>
<tr>
<td>Yiu et al252</td>
<td>2012</td>
<td>67.41 (10.13)</td>
<td>Days 96.9 (69.0)</td>
<td>98</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>267.65 (139.53)</td>
<td></td>
</tr>
<tr>
<td>*Zalewski et al253</td>
<td>2011</td>
<td>71.3 (9.5)</td>
<td>NR</td>
<td>17</td>
<td>NR</td>
<td>ATS = No (0) Walkway = continuous 200m track (1) Total = 1</td>
<td>258.5 (146.0)</td>
<td></td>
</tr>
<tr>
<td>Zedlitz et al254</td>
<td>2012</td>
<td>61 = 54.8 (9.1)</td>
<td>Years I1 = 4.4 (4.2), I2 = 4.3 (3.9)</td>
<td>83</td>
<td>MI I1 = 90.2 (15.0), I2 = 90.1 (12.1)</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>438 (123), I2 = 437 (107)</td>
<td></td>
</tr>
</tbody>
</table>

*= included in meta-analysis, ^= converted from feet to meters, #= calculated from individual data, x= median (IQR), AFO = Ankle-Foot Orthoses, ATS=American Thoracic Society, BI=Barthel Index, C=control, CM=Chedoke-McMaster, DGI = Dynamic Gait Index, DO = Drop Out, FAC=Functional Ambulation Category, FIM=Functional Independence Measure, FM=Fugyl-Meyer, HFO = Hip Flexor Orthoses, I=intervention, K-MBI=Korean Modified-Barthel Index, LEFS = Lower Extremity Functional Scale, LLFDI = Late-life Function and Disability Instrument, MAS=Motor Assessment Scale, MI=Motricity Index, NR=Not reported, SA-SIP=Stroke Adapted Sickness Impact Profile, SEM=Standard Error of the Mean, SIAS = Stroke Impairment Assessment Set, WAQ=Walking Ability Questionnaire.

Table 3.3 Description of included studies
3.7.2 Context of the 6MWT

A variety of terms were used to describe the purpose of the 6MWT, with common descriptors being a test of endurance [n=26], capacity [n=22], function [n=21], performance [n=6] and ability [n=5]. Twenty-four studies did not report the purpose of conducting the 6MWT in their study. On several occasions the test was performed in a different context or for a different purpose to that described in the ATS guidelines. The 6MWT was performed: to induce fatigue; over a variety of obstacles such as foam mats and purpose built ramps; and in non-standard locations such as outdoors including suburban streets or shopping centres. Walking distances achieved in outdoor locations ranged from 175±67m to 463±84m, with participants walking 234±66.5m in the shopping centre. Stroke survivors in two intervention groups who walked over foam mats and purpose built ramps walked 102.6±64.5m and 78.5±61.3m.

3.7.3 Assistance and instructions provided

Assistance provided to participants during the 6MWT was reported in 24 studies, with most of these studies indicating no assistance or minor assistance required. The single point cane was the most commonly used assistive device [n=426] used during the 6MWT. Other devices used included the walker [n=106], quad cane [n=77] and crutch [n=5]. A total of 251 stroke survivors used an ankle foot orthosis (AFO) during the test. Reporting use of a “usual device” without specifying the device used was prevalent [n=310 participants].

Only 44% of studies reported the instructions provided to participants for the 6MWT with variations evident between studies. The most common phrase used was to “cover
as much distance as possible” [n=20 studies], followed by “walk as far as you can” [n=16]. Five studies specified walking at a fast pace in their instructions, and eight studies instructed participants to walk at a comfortable speed. Encouragement was provided in 10 studies, and no encouragement or verbal feedback was given in 14 studies.

3.7.4 Quantitative analysis of adherence to ATS protocol guidelines

Including the three studies published prior to the ATS standards, 49 of the 127 studies received a zero score, indicating they did not mention the ATS guidelines and did not describe a protocol for the test including walkway length or course design. Sixty-three studies received a score of one indicating that these studies either referenced the ATS standard, or provided details on the walkway length used. Of these, 53 received the one point for reporting the walkway length or course design, while only ten received the one point for referencing the ATS guidelines. Only 15 studies scored two points, with only nine of these reporting a reference to the ATS guidelines and complying with them by using a 30m walkway.

3.7.5 Modifications to the 6MWT protocol walkway length

Only 25 of the 127 studies made a reference to the ATS guidelines for the 6MWT, with only nine of these clearly reporting the use of a 30m walkway. Although referencing the ATS standards, six studies modified the protocol with variations including the use of a 25m walkway250, a 33m walkway244, a 50m walkway218,245, a 100m walkway198 and a 30m oval course174. Overall, 67 studies provided a description of the walkway whereas 60 studies did not provide any description of the length or shape of the walkway used. Of those providing a description, 27 reported using an indoor 30m walkway in
accordance with the guidelines while 10 used shorter walkway lengths, 14 used longer walkways lengths, and 14 used continuous walkways. Straight walkway lengths varied from 10m\textsuperscript{237} to 85m\textsuperscript{143,193,194}.

### Table 3.4 Meta-regression coefficients for 30m protocol sub-group

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimate</th>
<th>StdErr</th>
<th>DF</th>
<th>tValue</th>
<th>Probt</th>
<th>Lower CI</th>
<th>Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-2.4</td>
<td>3.3</td>
<td>25</td>
<td>-0.72</td>
<td>0.479</td>
<td>-9.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Proportion males</td>
<td>0.4</td>
<td>1.4</td>
<td>25</td>
<td>0.30</td>
<td>0.768</td>
<td>-2.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Time since stroke</td>
<td>-0.1</td>
<td>0.7</td>
<td>25</td>
<td>-0.12</td>
<td>0.909</td>
<td>-1.5</td>
<td>1.4</td>
</tr>
</tbody>
</table>

#### 3.7.6 Distances achieved using the 6MWT in stroke survivors

Sixty-four studies were included in the meta-analysis. The pooled distance walked across these 64 studies was 247.3m (SE=9.09). Heterogeneity was high with a tau (tau squared represents between study variance) of 84.9m. We explored whether this heterogeneity was due to track type. Stroke survivors achieved a distance of 285m (95% CI, 252-318 m) on a 30m track. A significantly greater distance was achieved using the 30m walkway compared to protocols with longer (231m, 95%CI 189, 272, p=0.048) or continuous (213m, 95%CI 171, 255, p=0.010) walkways; there was no significant difference between the 30m walkway and shorter (242m 95%CI 199, 286, p=0.122) walkway lengths. Of the 60 studies that did not provide a description of the walkway used, an average distance of 246±117m was reported. Differences in distributions of age, gender or time since stroke did not have a significant influence on distance walked. Disability scores were only available on 74 (58%) studies, and therefore could not be included in the analysis.
Figure 3.2 Distances achieved (point estimate, 95%CI) during the 6MWT based on walkway protocol used

The regression analysis conducted in the 46 studies reporting use of the 30m walkway found that none of the variables, i.e. age (p=0.479), gender (p=0.768) or time post-stroke (p=0.909), were significantly associated with distance achieved on the 6MWT in stroke survivors (Table 3.4). Disability scores were only available on 12 (12/46, 26%) of these studies and therefore were not included in this analysis.

3.8 Discussion

This review has identified that the 6MWT is now in widespread use to assess aspects of walking-related performance in stroke survivor studies. Many of the study populations had to meet strict eligibility criteria including able to meet a minimal walking speed and no co-morbidities, and therefore may only be selectively representative of stroke survivors. Many stroke survivors would not be able to meet the criteria for these studies, making a bias towards more well recovered, non-disabled, otherwise healthier
participants. However, even in this selected population, the distances achieved on the 6MWT indicate substantial walking limitations in people after stroke. Overall, both the reporting of, and adherence to, the ATS guidelines for the 6MWT regarding the walkway length could be improved. Similarly, reporting of the instructions given prior to testing, as well as any assistance provided to participants during the test requires attention in future publications. Alterations to the ATS protocol walkway, including shortening or extending the walkway length or using a continuous track are more common than adhering to the 30m-walkway length. Consequently, a set of guidelines has been developed for future reporting of the 6MWT (Table 3.5). The findings from the meta-analysis were that the distance achieved during the 6MWT was associated with variations to the walkway length, but not in the manner one would predict. These findings have implications for the comparison of the values achieved using the 6MWT in different studies of stroke survivors.

The introduction of the ATS guidelines in 2002 was aimed at providing a protocol for consistency between studies. Of the 127 studies included in this review, 39 described a modified protocol whereas 60 studies did not specify the walkway length or walking course design. Of the 15 studies that received a reporting score of two, only nine reported both the ATS guidelines and used a 30m walkway length in accordance with the guidelines: the remaining six studies referenced the ATS guidelines but reported using a modified track. Consequently, although the ATS guidelines may be referenced in a report, it cannot be assumed that there was adherence to the guidelines. Protocol modification was more common than compliance with the 30m ATS standards, but no studies reported a reason for changing the protocol. Although there may be factors that necessitate or justify protocol changes, these reasons remain unreported. It is
understandable that in a setting where space is limited, there may be no other option than to use a walkway distance of less than 30m. Reasons for lengthening the walkway are less clear. One explanation is that if space greater than 30m in length is available, then a reason to extend the walkway length above the standard would be to decrease the effects of turning for stroke survivors in whom turning and balance ability may be compromised. We anticipated that the reduced turning requirements on the extended walkways and continuous tracks would result in longer distances being achieved than on the standard 30m walkway. The results of the meta-analysis show the opposite, with these protocols resulting in shorter 6MWT distances. One possible explanation for these types of protocol changes would be to accommodate reduced turning abilities and more severe disability of participants in these studies, which may also explain the reduced walk distances achieved.

The main impact of varying the 6MWT track length or design is the extent of turning required throughout the test. Turning requires the integration of multiple sensory systems and utilises vestibular, visual and proprioceptive information to appropriately move the body in space. Stroke survivors often experience difficulty during turning, possibly as a result of altered sensory, motor and biomechanical systems. This results in a differing orientation and sequencing of movements during turning compared to healthy controls, which requires more time to complete. Stroke survivors may take almost twice as many steps and twice as much time to complete a 180° turn compared to age matched controls. Similarly, two studies have reported significantly slower 180° turning times during the Timed Up and Go (TUG) in stroke with a similar finding by van Herk (1998) who demonstrated that the time taken to walk 10m straight versus 5m with return in stroke survivors was different, with the 5m track with
return requiring significantly more time to complete (p < 0.001). When comparing stroke survivors’ performances on the 6MWT over 10, 20 and 30m tracks, Ng et al. (2011) quantified the increased number of turns associated with shortening the track and reported a significantly shorter distance achieved during the 10m protocol, with the 30m protocol reporting the longest distance walked. This is contradictory to the findings in this review, however when looking at percent difference there is some commonality.

In the study by Ng et al., there is a reported reduction in distances achieved of 5% (20m compared to 30m) to 15% (10m compared to 30m). The results from the current meta-analysis suggest a reduction of 15% when comparing the <30m protocol to the 30m walkway length. Although this was not statistically significant, it is consistent with the magnitude of compromise found in the study by Ng et al. who measured the same population over multiple walkway lengths and could therefore make a direct comparison.

Another important finding from Ng et al. was that turning direction did not influence 6MWT distance independent of walkway length. The effects of turning direction on TUG times were also investigated in two other studies. Faria et al. also found no difference in TUG times. In contrast Heung et al. found a significantly faster TUG time when turning towards the paretic side. There appears to be an expectation that turning towards the affected side would result in slower speeds and therefore decreased 6MWT distance, however as demonstrated in the literature, this may not be the case. Generally, the studies in this review did not specify the directions turned and therefore could not be analysed. It is noted however, that in the clinical setting it is usually at the discretion of the individual performing the test as to which direction they turn during the 6MWT.
Our findings highlight the substantial effects of stroke on walking speed. Stroke survivors achieved an average distance of 285m (95%CI 252, 318) on a standard 30m track, whereas healthy older individuals >60 years achieve an average 6MWT distance of 499m (95%CI 480, 519). The extent of the performance compromise on the 6MWT is striking, particularly when the studies in this review are largely reporting on a highly selected, high performing cohort of independently ambulant stroke survivors. When considering these distances achieved, it is important to also acknowledge any assistive devices used throughout the 6MWT. Overall, 948 stroke survivors used a walking aid, and 251 walked with an AFO. Allet et al. found that stroke survivors walked approximately 15m further during the 6MWT using a simple cane with an ergonomic handgrip than when walking with a 4-point cane or Nordic stick. This area requires further investigation and should be considered when interpreting data.

Of the variables age, gender and time post-stroke, none had a significant effect on the distances achieved. This is likely because meta-regression was performed using summary level data for each study, rather than individual patient data that would have more power to tease out heterogeneity. In healthy adults, the variables age and gender have been suggested as sources of variability on distances achieved. Unfortunately, the effect of disability on distance walked could not be discerned in this review due to the large number of different disability scales used to describe stroke populations, the lack of consistency of scales between studies, and the under-reporting of mobility related disability. An attempt to use an alternative measure of motor function, such as 10m walking speed or balance was also unsuccessful, as few of the studies in the meta-analysis reported on these measures.
The instructions provided to stroke survivors differ between studies, potentially impacting on the perceived goal of the 6MWT. In the current analysis, five studies reported wording to walk at a “fast” pace, while nine studies instructed participants to walk at a “comfortable” pace. According to the ATS guidelines, instructions should be informing the participant to walk “as far as possible for 6 minutes” with no mention of walking speed. The guidelines also provide standard encouragement wording to use. Of those studies that reported on the encouragement given throughout the test, 42% provided encouragement and 58% provided no verbal encouragement or feedback. The guidelines specify that the 6MWT should be performed indoors, however several studies reported using the 6MWT in different environments such as outdoors\textsuperscript{145,242,243} including suburban streets and in shopping centres\textsuperscript{244}. Although these trials were excluded from the meta-analysis, the exact implications of performing the 6MWT in different locations are unclear. Carvahlo et al.\textsuperscript{76} directly compared distances achieved indoors and outdoors, concluding that stroke survivors in Group B (self-selected walking speed $\geq 0.8\text{m.s}^{-1}$) achieved a greater distance in the outdoor setting, whereas for those in Group A (self-selected walking speed $<0.8\text{m.s}^{-1}$) there was no difference. It has also been suggested that gait parameters do not differ in stroke survivors when walking in different environments\textsuperscript{244}. This is another factor that should be considered when interpreting the results reported from the 6MWT.
### Table 3.5 Checklist for reporting of the 6MWT

<table>
<thead>
<tr>
<th>Checklist for reporting of the 6MWT</th>
<th>Check</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. a) Acknowledge awareness of the ATS standards by referencing</td>
<td></td>
</tr>
<tr>
<td>b) Report walkway length even if 30m</td>
<td></td>
</tr>
<tr>
<td>c) If deviating from ATS standards, describe changes (walkway length, course layout, location) and explain reason</td>
<td></td>
</tr>
<tr>
<td>2. a) Describe the instructions given prior to the test</td>
<td></td>
</tr>
<tr>
<td>b) Describe any encouragement provided during the test</td>
<td></td>
</tr>
<tr>
<td>3. Report the number and type of assistive devices used</td>
<td></td>
</tr>
<tr>
<td>4. Report any assistance or support provided to participants</td>
<td></td>
</tr>
<tr>
<td>5. a) Report the demographics of the population including disability level</td>
<td></td>
</tr>
<tr>
<td>c) Report clearly the inclusion and exclusion criteria</td>
<td></td>
</tr>
</tbody>
</table>
This review highlights the need for future researchers to be mindful in reporting their implementation of the 6MWT by describing the walkway used and rationales for deviations from the 30m walkway or other aspects of the protocol. To assist future researchers we have developed a checklist of items for unambiguous reporting of the use of the 6MWT (Table 3.5). We acknowledge that changing the protocol may be necessary in some settings due to space restrictions. If the primary purpose of the test is to compare performances pre-post intervention then consistency is the main requirement between tests. Each setting may require their own documented protocol in order to maintain consistency between measurement times and test supervisors. The effects of level of disability on 6MWT performance could not be readily discerned due to the large number of different disability scales used, with many of these providing little indication of mobility impairment. Similarly, the extent of assistance provided, as well as the instructions given to the participants, requires attention in future studies. It can be concluded from the review that by changing the protocol researchers are limiting the ability to compare results between studies in stroke as well as other clinical populations. There is a lack of comprehensive reporting of the 6MWT protocol, which needs to be addressed in future research publications.
Chapter 4 – Characteristics of exercise training interventions to improve cardiorespiratory fitness after stroke: a systematic review with meta-analysis

4.1 Preface

This chapter presents a summary of a published peer-reviewed manuscript (appendix 2), which describes and analyses current exercise training interventions in the stroke literature.

As second author on this paper, I had significant contributions in initial literature searches to inform the question, creating the search strategy, data checking, running the meta-analysis and creating the forest plot, as well as editing the manuscript. This review highlighted the gaps and the requirements for the HowFITSS? trial, and is therefore included in this thesis. This manuscript has been published in the journal *Neurorehabilitation and Neural Repair*.

4.2 Citation

4.3 Background

Following stroke, there is minimal evidence for the benefit of physical activity to prevent subsequent stroke or improve longitudinal cardiovascular health outcomes. It is therefore troubling that an estimated 77% of stroke survivors are sedentary or have low levels of physical activity. Cardiorespiratory fitness after stroke has been reported to be very low, with VO$_{2peak}$ values ranging from 8-22 mL·kg$^{-1}$·min$^{-1}$, which equates to 26% to 87% of gender and aged matched healthy individuals. Stroke guidelines recommend cardiorespiratory fitness training after stroke; however, this is rarely implemented due to the primary focus on regaining physical function. Many therapists have limited experience with assessing CRF or prescription of exercise after stroke.

4.4 Objective

The aim of this systematic review with meta-analysis was to determine the effectiveness of exercise interventions to improve cardiorespiratory fitness after stroke. The primary outcome was change in CRF, as measured by the gold standard of VO$_{2peak}$. By synthesizing the data available regarding characteristics of studies, participants (gender, age, and time post stroke), and interventions (type, dose, training setting, group/individual program, risks, satisfaction, and effect maintenance), our aim was also to inform therapists on strategies to improve cardiorespiratory fitness of people post stroke.
4.5 Methods

A systematic search was undertaken of MEDLINE, CINAHL, EMBASE, PsycINFO, AMED, SPORTDiscus, and COCHRANE databases from their inception to December 27, 2011. Key inclusion criteria were the following: peer-reviewed articles published in English, adult stroke survivors, an intervention with the potential to improve cardiorespiratory fitness, and VO$_{2\text{peak}}$ assessed pre- and post-intervention by a graded aerobic exercise test. Statistical analysis was undertaken using RevMan5. Meta-analyses were planned to compare change in the primary outcome VO$_{2\text{peak}}$ in RCTs that used an intervention group and a control group with no intervention, sham training, or an intervention that would be unlikely to have an aerobic training effect.

4.6 Results

From 3209 citations identified, 28 studies were included, reporting results on 920 participants (male=437 [47.5%], female=313 [34.0%], not specified=170 [18.5%]). Mean ages ranged from 53 (no SD provided) to 71 (range=61-79) years. The mean time since stroke ranged from 14.3 (SD: 6.1) days to 7.5 (range=4-20) years, with the following distribution: within 1 month (n=3); 2 to 3 months (n=2); 1 to 3 years (n=7) and greater than 3 years (n=9).

Of the 28 studies that met the eligibility criteria, 16 used aerobic training$^{126,185,192,199,240,265-275}$ (treadmill n=8, cycle n=6, deep-water exercise n=1, cycle and recumbent stepper n=1), 11 used a mixed intervention$^{167,190,196,205,220,276-281}$ (an aerobic component in conjunction with usual care, strength, balance, and/or endurance activities), and one$^{282}$ used knee flexion/extension isokinetic training of the paretic leg,
aimed at improving CRF. Program length ranged from 2 to 3 weeks to 6 months, with 12 studies being between 3 and 6 months in length. Session durations ranged from 20 to 90 minutes, with most training lasting 30 to 60 minutes (n=23). Frequency of sessions ranged from 2 to 5 times/wk, with most (n=22) training 3 times/wk. Only one study reported the proportion of prescribed dose achieved (63±28%)\textsuperscript{281}. Interventions were undertaken in outpatient rehabilitation settings (n=6), inpatient settings (n=4), university centers (n=6), community centers (n=2), at both a community center and at home (n=2), and at home (n=1). Seven studies did not specify but appeared center based.

Meta-analysis of the 12 randomized controlled trials demonstrated overall improvements in VO\textsubscript{peak} of 2.27 (95%CI=1.58, 2.95) mL\textsuperscript{-1}kg\textsuperscript{-1}min\textsuperscript{-1} post-intervention. A similar 10% to 15% improvement occurred with both aerobic and mixed interventions and in shorter (≤3 months) and longer (>3 months) length programs. Only one included long term follow up.

### 4.7 Conclusions

This review highlights that interventions that are aerobic or have an aerobic component can improve fitness by approximately 10% to 15%, even with modest doses of exercise. Further investigation is required to determine effectiveness in those with greater impairment and co-morbidities, optimal timing and dose of intervention, whether improvements can be maintained in the longer term, and whether improved fitness results in better function and reduced risk of subsequent cardiovascular events.
Chapter 5 – Evaluation of three measures of cardiorespiratory fitness in independently ambulant stroke survivors

5.1 Preface

This chapter presents a peer-reviewed manuscript that is currently under review and awaiting decision. The manuscript investigates the use the Shuttle Walk Test in stroke survivors against two well established tests of cardiorespiratory fitness. This manuscript is currently under review in the journal *Physiotherapy Research and Practice*.

5.2 Citation

*A Dunn, DL Marsden, D Barker, P Van Vliet, NJ Spratt and R Callister. Evaluation of three measures of cardiorespiratory fitness in independently ambulant stroke survivors, Physiotherapy Research and Practice (under review)*

5.3 My Contribution

As first author, I led the paper from conception to publication. This included development of the assessment sessions, gaining funding for equipment, equipment training, leading and conducting assessments on stroke survivors, paperwork and document control, data entry and data extraction, data analysis and writing and editing the manuscript.
5.4 Abstract
Measuring cardiorespiratory fitness (CRF) in the stroke population is challenging. Currently, the recommended method is a graded exercise test (GXT) on an ergometer such as a treadmill or cycle, which may not always be feasible. We investigated whether walking tests such as the six-minute walk test (6MWT) and the shuttle walk test (SWT) may also be appropriate indicators of CRF in the stroke population. Twenty-three independently ambulant stroke survivors (11 males, age 61.5 ± 18.4 years) within one-year post stroke performed the 6MWT, SWT and cycle GXT, during which peak oxygen consumption (VO$_{2peak}$), and heart rate (HR$_{peak}$) were recorded. Results showed that there were no differences (p>0.05) in mean VO$_{2peak}$ among the three tests (min-max: 17.08 - 18.09mL.kg$^{-1}$.min$^{-1}$). HR$_{peak}$ was significantly (p=0.005) lower during the 6MWT. Correlations between VO$_{2peak}$ and performance measures were high in all three tests (6MWT VO$_{2peak}$ and distance: r=0.78, SWT VO$_{2peak}$ and shuttles: r=0.73, cycle GXT VO$_{2peak}$ and workload: r=0.77). All three tests elicited similar peak cardiorespiratory responses in ambulant stroke survivors and were feasible. The performance measures may be clinically useful as proxy measures of CRF.

5.5 Introduction
Cardiorespiratory fitness (CRF) is a measure of the combined functional status of the respiratory, cardiovascular and skeletal muscle systems$^{283}$. Limitations in any of these body systems will decrease CRF and lead to deconditioning in the other body systems. CRF is influenced by a number of factors (eg age, gender, medical conditions), particularly the capacity to perform or engagement in regular physical activity. The importance of CRF is often ignored from a clinical perspective, but low CRF is strongly
associated with increased morbidity and mortality, and improvements in CRF are associated with decreased risk of mortality from all causes and cardiovascular disease\textsuperscript{283}. Following stroke there are multiple biological, physical and psychological consequences that reinforce a sedentary lifestyle and contribute to low CRF\textsuperscript{38,284}. As more than half of all stroke survivors are inactive\textsuperscript{58}, increasing regular exercise and improving CRF levels are important goals for post stroke management\textsuperscript{50}, and can assist in improving performance of activities of daily living, community integration\textsuperscript{145,162}, and quality of life\textsuperscript{285}.

Accurate and clinically feasible methods to assess CRF levels in stroke survivors are important to determine an individual’s exercise capacity, for guiding prescription of an exercise program that is appropriate and safe, and for monitoring the effectiveness and health benefits of programs. CRF can be determined directly, whereby peak oxygen consumption (VO\textsubscript{2peak}) is measured during a graded exercise test (GXT) on an ergometer\textsuperscript{57} or indirectly (proxy measures) where CRF is estimated from test performance measures. Direct measures are more precise and therefore used in research, however they are not usually feasible due to cost, space or other resource needs in clinical settings\textsuperscript{283}. CRF can be evaluated using maximal or submaximal exercise tests, but the extent to which particular tests are effective in different clinical populations needs to be established\textsuperscript{189}.

The American Stroke Association Scientific Statement recommends a GXT using an ergometer such as a treadmill or cycle for assessing CRF in stroke survivors\textsuperscript{50}, however treadmill testing after stroke may require expensive harness systems for safety and cycling may be an unfamiliar activity, which can be challenging for stroke survivors. As
an alternative, the guidelines suggest the use of a walking test. Walking tests have multiple advantages as walking is the most popular exercise modality for middle-aged and older adults\textsuperscript{286}, and is often used as an outcome measure in stroke rehabilitation due to familiarity, functionality, simplicity and low cost. Also, if exercise testing is to be used prescriptively, the testing modality should be the same as that during training\textsuperscript{57}. Currently, there are two types of walking tests available in the clinical setting: walking distance covered in a predefined time or walking at a progressively increased, externally set pace. The six-minute walk test (6MWT)\textsuperscript{136} is commonly used in stroke to assess walking ability\textsuperscript{42}, and requires the individual to walk back and forth along a fixed-length (standard 30m) walkway covering as much distance as possible in six minutes. The 6MWT is classified as a submaximal test for CRF assessment by being self-paced, and the requirement for an uninterrupted, straight, flat 30m walkway is a limitation as this is often not readily available in clinical settings. The Shuttle Walk Test (SWT) developed by Singh et al.\textsuperscript{55} is an externally paced, graded walking test on a 10m course. The SWT has an advantage in that it is a GXT with the speed the individual must walk increasing to keep in time with audio signals. To date, the SWT has not been evaluated in stroke survivors as a possible test of CRF. Despite the multiple advantages of these tests, both the 6MWT and SWT can be limited by walking speed. Therefore, the aims of this study were to compare the responses to the submaximal 6MWT, the graded SWT and cycle GXT as measures of CRF in stroke survivors, and to compare the practicality of using these three tests as measures of CRF in stroke survivors.
5.6 Methods

5.6.1 Participants

Participants were assessed at baseline as part of a controlled exercise intervention study\(^{117}\) (ANZCTR Trial ID: ACTRN12614000134628). Recruitment of stroke survivors was undertaken with the purpose of evaluating eligibility for the *HowFITSS?* Study. This was conducted through clinician referral and by approaching eligible participants in the inpatient setting. All participants were discharged prior to testing. Individuals were eligible if they: 1) had experienced a clinically diagnosed stroke (ischemic or haemorrhagic) in the past 12 months, 2) were able to follow a two-step command, 3) were not pregnant, and 4) had no contraindications to exercise as deemed by the referring clinician. Individuals were also required to be able to visit the University of Newcastle Human Performance Laboratory. All participants provided written informed consent. This research was approved by the Hunter New England Human Ethics Committee (11/04/20/4.04) and University of Newcastle Human Research Ethics Committee (H-2011-0172).

5.6.2 Data Collection

Testing was conducted over one or two sessions depending on the laboratory space availability. To reflect rehabilitation setting practices, between tests participants rested until HR returned to their pre-exercise value and they felt sufficiently recovered to continue. Cardiorespiratory measurements were undertaken throughout all three tests using a portable system. Demographic data including age, gender, time since stroke, medications and comorbidities were determined from medical history.
5.6.2.1 Cardiorespiratory Measurement

A portable open-circuit spirometry system (K4b², COSMED®, Italy) was used to collect breath-by-breath data throughout the three tests. The time delay from the mask to the unit was corrected for, as were barometric pressure and humidity. The system was powered by a portable battery pack that was harnessed onto the participant’s back, and together the equipment weighed less than 1kg. Calibration of time delay, the turbine, and gas analysers were performed to manufacturer’s specifications prior to each testing session. Metabolic variables including oxygen consumption (VO₂), minute ventilation (VE) and the respiratory exchange ratio (RER) were recorded and averaged over 30s epochs. The VO₂peak and HRpeak data were extracted as the highest average 30s epoch values recorded during each test. To minimise the overestimation of VE and RER, the same method was employed excluding the last epoch in which recovery may have begun. The electrocardiograph was monitored continuously in each participant using a portable 12-lead system (Quark T12, COSMED®, Italy). This was used to derive heart rate (HR) data.

5.6.2.2 Six-Minute Walk Test

The 6MWT was conducted in accordance with the American Thoracic Society Guidelines (2002)¹³⁶ using a modified walkway. The test was performed indoors over a straight, uninterrupted corridor 20m in length identified by tape on the floor. The walkway length of 20m is shorter than the ATS standard 30m course, however 30m was not feasible due to space restrictions⁴². Participants were instructed to walk as far as possible in the 6-minute time frame, turning in a standard manner, as concisely as possible over a line indicated by tape on the floor. Standardised verbal encouragement was given at one-minute intervals throughout the test. It has been reported that wearing
the Cosmed K4b² portable system does not interfere with the reliability of the 6MWT in stroke survivors.  

5.6.2.3 Incremental Shuttle Walk Test  
As originally reported by Singh (1992), participants walked shuttles between markers spaced 9m apart, which created a 10m course that included turning around the markers. The test requires the individual to walk for as many shuttles as possible at increasing speeds dictated by an audio CD (Department of Respiratory Medicine, Glenfield Hospital NHS Trust, Leicester, UK). Participants were instructed not to jog or run. The test begins at 0.50m.s⁻¹ and increases by 0.17m.s⁻¹ every minute. Following 12 levels, the final speed required is 2.37m.s⁻¹. The test was terminated of the participant’s own volition or when the participant was unable to reach within 0.5m of the marker at the time of the audio signal. No verbal feedback or encouragement was given during the test.

5.6.2.4 Upright Cycle Graded Exercise Test  
An upright cycle ergometer is currently recommended and is the most common modality for CRF exercise testing in the stroke literature. The majority of the sample population were not suitable for testing on a treadmill due to unfamiliarity with the activity and lack of confidence, balance issues and the absence of a body weight support safety harness system in the laboratory. Participants pedalled on an upright mechanically braked cycle ergometer (818E, Monark, Sweden), which is affordable and widely available in Australian clinics. Participants commenced pedalling at 50 or 60rpm with no resistance for one minute, followed by increases in resistance providing 25W increments every minute until test termination. This workload was chosen as
Chapter 5. Evaluation of Measures of CRF

increments less than 25W are difficult to adjust on a non-electronically braked ergometer, with the ACSM’s Resources for Clinical Exercise Physiology\textsuperscript{288} suggesting a test duration between 4-12 minutes, rather than a particular set workload increment. Once the test was stopped, participants were encouraged to complete a cool-down on the cycle. Prior to testing, the Karvonen Formula\textsuperscript{121} was used to calculate 85% of heart rate reserve (85\%HRR = [(220 – age) – resting HR) x 0.85] + resting HR). It has been reported previously that the Karvonen Formula is appropriate for patients who are taking varying doses of beta-blockers\textsuperscript{289}. Attaining 85\%HRR was then used as a safety test termination criterion consistent with safety precautions often employed in a clinical setting when a doctor is not present. Other termination criteria were the inability to maintain cadence, volitional fatigue, abnormal cardiac responses to exercise or failure of equipment\textsuperscript{122}.

5.6.3 Outcome Measures

The primary cardiorespiratory outcome measure was peak oxygen consumption (VO\textsubscript{2peak}) relative to body weight. Secondary cardiorespiratory outcomes included peak heart rate (HR\textsubscript{peak}), peak minute ventilation (VE\textsubscript{peak}) and peak respiratory exchange ratio (RER). Performance measures were recorded for each test. These were: total distance walked on the 6MWT, the total number of shuttles walked during the SWT (out of a possible 102), and the final workload achieved at test termination on the cycle GXT. Practicability was assessed by the number of participants who could complete each test.

5.6.4 Walking Speed

The 10m Walk Test (10mWT)\textsuperscript{131} was used to measure self-selected and fast walking speeds. Participants walked along a 14m walkway, with the middle 10m time recorded.
Three trials were performed at each speed, with the average time taken and converted to m's⁻¹.

### 5.7 Statistical Analysis

Data were analyzed using Stata Statistical Software 11.0 (Statacorp. 2011). A linear mixed model with random intercept was used to compare the physiological responses on the three tests. This was chosen to adjust for repeated testing of individuals, as well as including information from those participants who were unable to complete all three tests under the missing at random (MAR) assumption²⁹⁰. The model was adjusted for the use of arthritis medication as a proxy of lower limb pain, as well as the reporting of pre-existing lower limb conditions, which precluded some participants from undertaking the cycle test. Results were presented as mean ± standard deviation unless otherwise stated. Bland-Altman plots of the difference in VO₂peak between two tests (6MWT v cycle GXT, SWT v cycle GXT and 6MWT v SWT) against the VO₂peak achieved on the cycle GXT and SWT for each participant²⁹¹ provide a visualisation of systematic variations around the zero line, indicating possible heteroscedasticity²⁹². Effect sizes were calculated using Cohen’s d with an effect size (ES) <0.2 categorised as small, 0.2 to 0.5 as medium, 0.5 to 0.8 as large and >0.8 as very large²⁹³. The level of association between VO₂peak and outcome measure achieved, VO₂peak and HRpeak on each test as well as walking speed and outcome variables were assessed using the correlation spreadsheet provided by Hopkins (2001)²⁹⁴. Correlations were interpreted as reported by Eng et al.¹⁶⁹ with a coefficient of 0.90 to 1.00 categorized as very high, 0.70 to 0.89 as high, 0.50 to 0.69 as moderate and 0.26 to 0.49 as low.
5.8 Results

Characteristics of the 23 participants (n=11 males) are summarized in Table 5.1. There were no significant differences between relative VO$_{2\text{peak}}$ during the 6MWT, SWT, and cycle GXT. Compared to the SWT, the respiratory exchange ratio was significantly higher during the cycle GXT (p=0.003, ES=0.58) and HR$_{\text{peak}}$ was significantly lower during the 6MWT (p=0.005, ES=0.46). All other variables were not significantly different between tests (p>0.05, small to medium ES). Participants achieved an average of 68%, 75% and 76% of predicted maximal heart rate (calculated as 206.9 – (0.67 x age)) during the 6MWT, SWT and cycle GXT respectively. The response patterns during the three tests are displayed in Figure 5.1.

Distance walked during the 6MWT was 460±115m and ranged from 202m to 623m, with males walking 461±134m (67% of predicted distance$^{296}$) and females walking 456±100m (78% of predicted distance$^{296}$) (Table 5.2). The average number of shuttles and distance achieved on the SWT were 40±18 shuttles and 400±180m respectively, with distances ranging from 120 – 660m. The average power output reached on the cycle GXT was 115±33W, with a range from 50 – 175W. Only three of the 20 stroke survivors who performed the cycle GXT were unable to reach 100W during this test.
### Table 5.1 Participant characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.5 ± 18.4 (23.2-84.3)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (48)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (52)</td>
</tr>
<tr>
<td>Months post-stroke</td>
<td>3.7 ± 3.2 (1-16)</td>
</tr>
<tr>
<td>Body Mass Index (kg m²)</td>
<td>27.7 ± 5.9 (20.4-43.3)</td>
</tr>
<tr>
<td>Type of stroke, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>23 (100)</td>
</tr>
<tr>
<td>Co-morbidities, n (%)</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6 (26)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>4 (17)</td>
</tr>
<tr>
<td>COPD</td>
<td>1 (4)</td>
</tr>
<tr>
<td>CVD</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (17)</td>
</tr>
<tr>
<td>PVD</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Medications, n (%)</td>
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</tr>
<tr>
<td>β-blockers</td>
<td>8 (35)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>5 (22)</td>
</tr>
<tr>
<td>Functional Ambulatory Category, n (%)</td>
<td></td>
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<tr>
<td>6</td>
<td>22 (96)</td>
</tr>
<tr>
<td>5</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Modified Rankin Score, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2 (9)</td>
</tr>
<tr>
<td>2</td>
<td>16 (70)</td>
</tr>
<tr>
<td>3</td>
<td>4 (17)</td>
</tr>
<tr>
<td>1</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Self-selected walking speed</td>
<td>1.2 ± 0.3 (0.6-1.6)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACE: angiotensin-converting enzyme, COPD: Chronic Obstructive Pulmonary Disease, CVD: Cardiovascular Disease, n: number, PVD: Peripheral Vascular Disease,
Figure 5.1 Mean $VO_2$ (A), HR (B), VE (C) in each 20% increment of test time for the Shuttle Walk Test (SWT), Six-Minute Walk Test (6MWT) and Cycle Graded Exercise Test.
Correlations between VO$_{2peak}$ and outcome measure were high in all three tests (Table 5.3) (6MWT VO$_{2peak}$ and distance: \( r=0.78 \), SWT VO$_{2peak}$ and shuttles: \( r=0.73 \), cycle GXT VO$_{2peak}$ and workload: \( r=0.77 \)). There were low correlations between HR$_{peak}$ and VO$_{2peak}$ for each test (6MWT: \( r=0.28 \), SWT \( r=0.44 \), cycle GXT: \( r=0.30 \)). Self-selected walking speed showed small, moderate and large correlations with VO$_{2peak}$ and the performance measure for each test (6MWT VO$_2$=0.52, distance=0.84; SWT VO$_2$=0.48, shuttles=0.80; cGXT VO$_2$=0.52, workload/kg$^{-1}=0.65$) with higher correlations with fast walking speed (6MWT VO$_2$=0.71, distance=0.83; SWT VO$_2$=0.69, shuttles=0.84; cGXT VO$_2$=0.72, workload/kg$^{-1}=0.69$). In those with lower VO$_{2peak}$ values, there was very little difference in the values obtained on the different tests (Figure 5.2) whereas there is an indication of heteroscedasticity for the 6MWT compared to the cycle GXT and the SWT with greater discrepancy between the tests at higher VO$_{2peak}$ values. This pattern is not evident between the SWT and cycle GXT. In those with VO$_{2peak}$ values greater than 20 mL.kg$^{-1}$.min$^{-1}$ values on the SWT and cycle GXT were usually higher than those on the 6MWT. Similarly, it was observed that those who achieved higher values on all three tests tend to have a fast walking speed greater than 2.0m.s$^{-1}$. 
Table 5.2 Peak cardiorespiratory and performance responses to the SWT, 6MWT and cycle GXT

<table>
<thead>
<tr>
<th>Variable</th>
<th>6MWT</th>
<th>SWT</th>
<th>Cycle GXT</th>
<th>6MWT v SWT</th>
<th>6MWT v cycle</th>
<th>SWT v cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Effect Size</td>
<td>Effect Size</td>
<td>Effect Size</td>
</tr>
<tr>
<td>VO$_{2}$peak (mL·kg$^{-1}$·min$^{-1}$)</td>
<td>17.08 ± 4.29</td>
<td>18.09 ± 5.43</td>
<td>17.82 ± 6.17</td>
<td>0.21$^a$</td>
<td>0.14</td>
<td>0.05</td>
</tr>
<tr>
<td>HR$_{peak}$ (beats·min$^{-1}$)</td>
<td>115 ± 20</td>
<td>124 ± 21</td>
<td>128 ± 25</td>
<td>0.46$^a$</td>
<td>0.61$^b$</td>
<td>0.19</td>
</tr>
<tr>
<td>VE$_{peak}$ (L·min$^{-1}$)</td>
<td>46 ± 11</td>
<td>47 ± 15</td>
<td>50 ± 19</td>
<td>0.10</td>
<td>0.25$^a$</td>
<td>0.14</td>
</tr>
<tr>
<td>RER</td>
<td>0.99 ± 0.12</td>
<td>0.97 ± 0.14</td>
<td>1.06 ± 0.14</td>
<td>0.13</td>
<td>0.51$^b$</td>
<td>0.58$^b$</td>
</tr>
<tr>
<td>Peak performance</td>
<td>460 ± 115m</td>
<td>40 ± 18 shuttles</td>
<td>115 ± 33W</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VO$_{2}$peak and peak performance correlation</td>
<td>0.78$^b$</td>
<td>0.73$^b$</td>
<td>0.77$^b$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VO$<em>{2}$peak and HR$</em>{peak}$ correlation</td>
<td>0.28</td>
<td>0.44</td>
<td>0.30</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Abbreviations: $^a$medium effect size; $^b$large effect size; VO$_{2}$peak, peak oxygen consumption; HR$_{peak}$, peak heart rate; VE$_{peak}$, minute ventilation; RER, respiratory exchange ratio; 6MWT, Six-minute Walk Test; SWT, Shuttle Walk Test; GXT, graded exercise test
Table 5.3 Intra-class correlations between measures during the 6MWT, SWT and cycle GXT

<table>
<thead>
<tr>
<th>Variable</th>
<th>6MWT v SWT</th>
<th>6MWT v cycle</th>
<th>SWT v cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO$_{2\text{peak}}$ (mL·kg$^{-1}$·min$^{-1}$)</td>
<td>ICC 0.87b 90%CI 0.75, 0.94</td>
<td>ICC 0.83b 90%CI 0.65, 0.92</td>
<td>ICC 0.83b 90%CI 0.64, 0.92</td>
</tr>
<tr>
<td>RER</td>
<td>0.68 0.42, 0.83</td>
<td>0.22 -0.17, 0.56</td>
<td>0.45 0.08, 0.72</td>
</tr>
<tr>
<td>VE$_{\text{peak}}$ (L·min$^{-1}$)</td>
<td>0.86b 0.72, 0.93</td>
<td>0.57 0.24, 0.78</td>
<td>0.68 0.39, 0.84</td>
</tr>
<tr>
<td>HR$_{\text{peak}}$ (beats·min$^{-1}$)</td>
<td>0.67 0.39, 0.84</td>
<td>0.74b 0.50, 0.88</td>
<td>0.57 0.23, 0.78</td>
</tr>
<tr>
<td>Peak performance</td>
<td>0.93b 0.86, 0.97</td>
<td>0.57 0.24, 0.79</td>
<td>0.62 0.29, 0.82</td>
</tr>
</tbody>
</table>

Abbreviations: VO$_{2\text{peak}}$, peak oxygen consumption; HR$_{\text{peak}}$, peak heart rate; VE$_{\text{peak}}$, minute ventilation; RER, respiratory exchange ratio; 6MWT, Six-minute Walk Test; SWT, Shuttle Walk Test; GXT, graded exercise test
Figure 5.2 The differences in peak oxygen consumption ($VO_2\text{peak}$) achieved on the Cycle Graded Exercise Test – Six-Minute Walk Test (6MWT) and Cycle Graded Exercise Test – Shuttle Walk Test (SWT), plotted against the mean $VO_2\text{peak}$ for the Cycle Graded Exercise Test.
Chapter 5. Evaluation of Measures of CRF

Of the 23 participants, three could not perform the cycle GXT due to pre-existing lower limb arthritic conditions (knee=2, hip=1), which did not restrict their walking ability, but precluded them from cycling without pain. One participant did not perform the SWT due to balance issues when turning, identified during the 6MWT. Only five of the 20 participants who performed the cycle GXT stopped this test as a result of their HR reaching the predetermined cut off of 85%HRR. Other reasons for stopping during the cycle GXT were leg fatigue [n=6], lower limb pain [n=3], shortness of breath [n=2], both leg fatigue and shortness of breath [n=2], ECG changes (right bundle-branch block) [n=1] and poor ECG signal [n=1]. No significant adverse events occurred during any of the testing sessions. No participants had facial palsy or facial hair, which may contribute to leakage around the facemask during assessment of oxygen consumption.

5.9 Discussion

All three tests provided a similar indication of CRF and were generally well tolerated in independently ambulant stroke survivors. Strong correlations indicate that performance measures on each test may be useful as proxies for VO\textsubscript{2peak} in any setting where VO\textsubscript{2} measurement is not practical. Each test has advantages and disadvantages, and may be more appropriate depending on the individual’s ability and the space or resources available.

This is the first study to compare oxygen consumption measured during the 6MWT, SWT and cycle GXT in stroke survivors. The Bland-Altman plots for the 6MWT v cycle GXT and 6MWT v SWT indicated the higher the VO\textsubscript{2peak} achieved, the larger the discrepancy between the tests. This discrepancy for higher achievers may be due to a ceiling effect of the 6MWT, indicating limitations for a self-paced walking test in
functionally independent stroke survivors. This was not the case for the SWT, and due to the incremental nature of the test, may provide a greater stimulus to achieve a higher VO$_{2\text{peak}}$. Generally, those who achieved a VO$_{2\text{peak}}$ above 20mL·kg$^{-1}$·min$^{-1}$ were able to achieve a fast walking speed of greater than 2.0m·s$^{-1}$ over 10m. In keeping with this finding, there were high correlations between faster walking speeds during the 10MWT and performance measures for the 6MWT, SWT and cGXT. Future studies should consider investigating fast walking over 10m as a criterion for test selection in stroke. High correlations were also found between VO$_{2\text{peak}}$ and performance measure in all three tests, demonstrating that the 6MWT, SWT and cycle GXT are valid tools for assessing and monitoring CRF in ambulatory stroke survivors. Due to the equipment expenses, time, and need for trained personnel associated with assessing oxygen consumption, metabolic measurement systems are not often available in clinical settings, therefore the use of a proxy measure of VO$_{2\text{peak}}$ is justified. The relationship between VO$_{2\text{peak}}$ and number of shuttles walked has not been explored for the SWT in stroke. It has been reported in other chronic disease populations, with correlations ranging from moderate ($r=0.67$) in patients with operable lung cancer, to very high ($r=0.95$) in adult patients with cystic fibrosis. Most of these correlations are slightly higher than reported in the current study, possibly because those populations typically do not have motor disability similar to that observed as a result of stroke. There were low associations between VO$_{2\text{peak}}$ and HR$_{\text{peak}}$, suggesting that heart rate may have limitations as a criterion for peak exercise intensity in stroke survivors. Clinical doses of beta-blockers may reduce heart rate by 30-35% during maximal exercise, with eight participants in the current study taking beta-blockers, and five taking ACE inhibitors at the time of assessment.
When comparing the other physiological variables, a significantly lower HR was recorded during the 6MWT. The weak relationship between HR_{peak} and VO_{2peak} indicates limitations to HR measurements in this population, where cardiac medications are prevalent, and autonomic disturbances may be present. The respiratory exchange ratio was significantly higher during the cycle GXT, which is most likely attributable to the unaccustomed use of the leg muscles to perform the work and a greater production of lactic acid requiring respiratory buffering. Interestingly, almost 40% of participants terminated the cycle GXT prematurely due to leg fatigue or lower limb pain, indicating that a cycling GXT may not be the optimal choice of test for CRF in an ambulatory stroke population due to unfamiliarity with cycling or non-stroke related arthritic pain prevalent in older age groups. It is acknowledged that we are comparing two different modes of exercise, however it was deemed unsafe to allow exercise testing on a treadmill due to the lack of a safety harness system in the laboratory. Cycle testing has also been reported as the most commonly used mode of exercise testing in stroke, and is often available in clinical settings.

The SWT has only recently been considered and suggested for investigation in stroke survivors and has potential for use as a test of CRF. Only one previous study has investigated the use of the SWT in stroke. Unlike the current study, Bloemendaal et al. used a modified version of the protocol as described by Verschuren et al., which is a walk/run test designed for children with cerebral palsy. Cardiorespiratory variables were not recorded during the Bloemendaal et al. study and therefore cannot be compared to the current results. While few studies have examined the use of the SWT in stroke populations, numerous studies have compared the 6MWT and cycle GXT. The majority examined correlations between cycle GXT...
VO\textsubscript{2peak} and 6MWT distance, with no VO\textsubscript{2} measures during the 6MWT. Similarly to our study, Salbach et al.\textsuperscript{62} used the Cosmed K4b\textsuperscript{2} portable metabolic system to measure the cardiorespiratory response during the 6MWT and a cycle GXT. They reported a significantly higher VO\textsubscript{2peak} during the cycle GXT (13.8±3.3mL.kg.min\textsuperscript{-1}) than the 6MWT (11.8±3.7mL.kg.min\textsuperscript{-1}, p=0.032). The cycle protocol used by Salbach et al. had less intense progressions (5, 10 or 15W increments) compared to the current study (25W increments). They reported VO\textsubscript{2peak}, HR\textsubscript{peak} and VE\textsubscript{peak} well below the values obtained in our study, which may in part be explained by the longer time post stroke and older cohort, as well as a shorter mean 6MWT distance reported in the study by Salbach et al. This should be considered in the interpretation of both reports.

Although the 6MWT is often used as a walking test in the current stroke literature\textsuperscript{42}, the SWT is much less common. It has been studied extensively in cardiac and respiratory populations\textsuperscript{56}, for whom the test was designed. In other disease populations, the SWT has been used as a tool for exercise prescription\textsuperscript{304}, for the assessment of ambulatory oxygen\textsuperscript{305}, for detecting changes in exercise performance following pharmacological bronchodilation\textsuperscript{306}, as a valid measure of exercise capacity in adults with cystic fibrosis\textsuperscript{298}, after coronary bypass surgery\textsuperscript{307} and in chronic heart failure patients\textsuperscript{308-310}. A review by Parreira et al.\textsuperscript{56} identified 36 articles that used the SWT in other chronic disease populations, reporting several studies have compared the responses during the SWT, 6MWT and ergometer tests. The review concluded that the SWT is a valid and reliable test for assessment of maximal exercise capacity in chronic respiratory disease. Given the results in other chronic disease populations, the SWT warrants further investigation as a clinical and research tool in the ambulant stroke population.
All three tests were generally well tolerated by this cohort of independently ambulant stroke survivors. All participants were able to complete the 6MWT without rest, however in well recovered individuals, the test seemed to be limited by walking speed rather than CRF. One stroke survivor was unable to attempt the SWT due to balance issues identified during the 6MWT. Balance may be challenged during the SWT, as the track is much shorter than that during the 6MWT, resulting in an increased requirement for turning. The external pacing of the SWT also necessitates fast walking. In stroke survivors who can safely walk at a fast pace and turn on the spot competently, the SWT may be appropriate. Unlike the 6MWT, the SWT requires the individual to walk at progressively faster speeds to keep up with the audio signal. This progressive nature is similar to that of a traditional GXT. The cycle GXT was the most unfamiliar activity in this population, and in older stroke survivors, comorbid arthritis of the knee was a barrier. The cycle GXT protocol used in this study was submaximal, however most individuals terminated testing due to leg fatigue. By using a cycle ergometer, there are no issues with balance or falls. It should be noted however, that stroke survivors with compromised balance or range of motion may have difficulty getting onto a cycle ergometer and may require assistance. Overall, the three tests provide an indication of CRF and each test has advantages.

5.9.1 Study Limitations

This study is the first to directly measure and evaluate cardiorespiratory variables during the 6MWT, SWT and cycle GXT in stroke survivors. There are several limitations to this study, which need to be considered when interpreting the findings. Due to technical difficulties, there were three participants for whom the HR data did not record during the 6MWT. There were also three participants who could not undertake
the cycle GXT. Therefore, the random effects model was used to address the inclusion of these participants in the analysis, under the missing at random assumption\textsuperscript{290}. The sample of stroke survivors in this study had relatively little disability, and does not account for individuals with stroke with greater level of disability. Therefore, these results may not be relevant to non-ambulant stroke patients.

5.10 Conclusion

The results indicate that all three tests are good indicators of CRF and are generally well tolerated in independently ambulant stroke survivors. If walking ability is not compromised by balance or motor control problems, then a walking based test is recommended for CRF assessment in ambulatory stroke survivors, at least in countries such as Australia where cycling is not a common activity. The SWT is recommended for higher performing walkers, whereas both the SWT and 6MWT are suitable for those with slower walking ability. For stroke survivors with higher risks of falling (eg due to compromised balance), cycle based testing is recommended, acknowledging that the test may be stopped prematurely for those with joint problems or for whom cycling is an unfamiliar activity. Further studies are needed to identify the most appropriate tests of CRF for stroke populations who are non-ambulatory.
Chapter 6 - Independently ambulant, community dwelling stroke survivors have reduced cardiorespiratory fitness, mobility and knee strength compared to an age- and gender-matched cohort

6.1 Preface

This chapter presents a sub-study that compares the performances of independently ambulant, community dwelling stroke survivors, to age and gender matched comparisons on a number of fitness tests. There is currently a lack of normative data on the SWT in stroke, and no data available on the fitness levels of stroke survivors without disability. This manuscript has been published in the journal *Topics in Stroke Rehabilitation* (appendix 3).

6.2 Citation

*A Dunn, DL Marsden, P Van Vliet, NJ Sprat and R Callister. Independently ambulant, community dwelling stroke survivors have reduced cardiorespiratory fitness, mobility and knee strength compared to an age- and gender-matched cohort. Topics in Stroke Rehabilitation (epub ahead of print)*
6.3 My Contribution

As first author, I led the paper from conception to publication. This included development of the assessment sessions, gaining funding for equipment, equipment training, leading and conducting the assessments stroke survivors, paperwork and document control, data entry and data extraction, data analysis and writing and editing the manuscript.

6.4 Abstract

**Background:** Most exercise interventions for stroke survivors are designed for those who have substantial motor and functional disabilities. There remains a group of well-recovered stroke survivors who have yet to be investigated in terms of their physical capacity and fitness levels.

**Objective:** To assess and compare the physical capacities of independently ambulant, community dwelling stroke survivors to age- and gender-matched comparison participants.

**Methods:** Data were obtained from 17 stroke survivors participating in the HowFITSS? Trial, all with Functional Ambulatory Category of ≥4 and a self-selected walking speed ≥0.8m’s⁻¹. An additional 17 healthy control participants were recruited. Cardiorespiratory fitness (CRF) was measured using oxygen consumption (VO$_{2\text{peak}}$), and additional measures of walking speed (m’s⁻¹), leg strength and body composition were also assessed. Differences between groups were assessed by matched-pairs t-tests. Effect sizes were calculated using Cohen’s $d$.

**Results:** There were no significant differences in age, BMI, muscle mass or body fat between groups (p≥0.05). Peak VO$_2$ was lower in the stroke group for the shuttle walk
test (p=0.037) and progressive cycle test (p=0.019), as were all CRF test performance measures (p<0.05). Stroke survivors walked significantly (p<0.001) slower at both self-selected and fast speeds. Effect sizes of group differences for all leg strength variables were medium to large, with peak torque lower in the stroke group for all trials.

**Conclusions:** Despite being independently ambulant and community dwelling, the CRF, walking speed and leg strength of this group were reduced compared to non-stroke comparison participants. These patients may benefit from undertaking targeted exercise programs.

### 6.5 Introduction

It is estimated that of the 75% of people who survive a first stroke, 25% are left with minor disability and 40% a moderate-severe disability. Consequently, most exercise interventions for stroke survivors are designed for those who have substantial motor and functional disabilities, with the primary goal to improve performance of activities of daily living (ADLs). In contrast, little attention has been paid to comparatively well-recovered stroke survivors who return to independent, community living, and it is unclear whether they have physical fitness deficits that would benefit from exercise programs.

Numerous studies have assessed the fitness levels of stroke survivors, and cardiorespiratory fitness (CRF) and leg strength are consistently lower, ranging from 26% to 75% of that achieved by a non-stroke comparison group. Also, stroke survivors may have a higher energy cost of walking than comparison groups. Previous studies included a range of stroke-related disability levels. Consequently, it is unclear whether deficits in CRF, walking speed and leg strength are present in well-
Chapter 6. Fitness levels in stroke survivors against comparisons

recovered stroke survivors, and if present, the extent and variation in these deficits. Many of these studies were conducted in older populations, where comorbidities may contribute to deficits in physical fitness and performance. Inclusion of younger participants may provide new insights regarding the type and magnitude of deficits and whether specific exercise programs should be recommended. In those studies that compared data from stroke survivors to a control group, differences in the age or gender of the groups\textsuperscript{312}, even if controlled for in statistical analyses, may influence interpretation. Also, many studies focus on one or two fitness characteristics, which limits our understanding of fitness levels across a range of fitness parameters in the same population. Consequently there is a need to specifically investigate well-recovered stroke survivors to inform exercise program recommendations for this group.

The aim of this study was to compare cardiorespiratory fitness, walking ability, knee strength and body composition in independently ambulant, community dwelling stroke survivors to healthy age- and gender-matched comparison participants.

6.6 Methods

6.6.1 Participants

Data were obtained from stroke participants assessed at baseline as part of a controlled exercise intervention study\textsuperscript{117} (ANZCTR Trial ID: ACTRN12614000134628). Sample size was based on that suggested to detect the minimal detectable change (difference) for the Six-Minute Walk Test (6MWT) between groups\textsuperscript{314}. All testing was conducted by an experienced Exercise Scientist (AD) and Neurological Physiotherapist (DM) with support from trained research assistants. Inclusion criteria were: 1) had experienced a clinically diagnosed stroke (ischemic or haemorrhagic) in the past 12 months, 2) FAC ≥
4 with a self-selected walking speed of \( \geq 0.8 \text{m/s}^{-1} \), 3) no use of a walking aid, 4) able to follow a two-step command, 5) were not pregnant, and 6) had no contraindications to exercise as deemed by the referring medical officer. Seventeen healthy age- and gender-matched comparison participants were recruited using word of mouth and flyers posted around the University campus. Eligibility criteria for this group were: 1) no history of stroke or transient ischemic attack (TIA), 2) matched the age (within 5 years) and gender of a stroke participant, and 3) no contraindications to exercise testing. All participants were screened using the Exercise and Sport Science Australia Pre-Exercise Screening Questionnaire\(^{315}\), and medical clearance was obtained from their family/general physician when required. Participants were asked to refrain from vigorous physical activity for 24 hours prior to testing\(^{316}\).

Demographic data including age, gender, time since stroke, medications, past and current physical activity, and comorbidities were determined from medical history. Although none of the stroke survivors were regarded as having any current disability associated with one side of the body, side “more affected” was determined either by the side reported as more affected at the time of stroke onset or from clinical notes made at time of admission, with the “less affected” side the opposite. Ten of the 17 stroke survivors were more affected on their dominant right side. The remaining participants were more affected on their non-dominant side (5 left, 2 right). Level of physical activity was calculated semi-quantitatively using information reported during the screening process and interview. Activity levels were defined according to the International Physical Activity Questionnaire (IPAQ)\(^{317,318}\) categorical score and categorised as low, moderate or high levels. All participants provided written informed consent. This research was approved by the Hunter New England Human Ethics
Committee (11/04/20/4.04) and University of Newcastle Human Research Ethics Committee (H-2011-0172). None of the authors have any conflict of interest in the submission of this manuscript.

6.6.2 Cardiorespiratory Fitness

Oxygen consumption (VO$_2$) was recorded throughout three aerobic fitness tests: Six-minute Walk Test (6MWT), Incremental Shuttle Walk Test (SWT), Upright Cycle Graded Test (cGXT), using a portable open-circuit spirometry system (K4b$^2$, COSMED, Italy). Calibration of time delay, the turbine, and gas analysers were performed to manufacturer’s specifications prior to each testing session. Heart rate (HR) was measured by 12-lead electrocardiography (Quark T12, COSMED, Italy), which was continuously monitored prior to, during and post exercise for all participants. All variables were averaged over 30s epochs, with peak oxygen consumption (VO$_{2\text{peak}}$) and HR (HR$_{\text{peak}}$) determined as the highest epoch value during the test.

6.6.3 Six-Minute Walk Test

The 6MWT was conducted in accordance with the American Thoracic Society Guidelines (2002)$^{136}$ using a 20m walkway due to space restrictions$^{42}$. The endurance test was performed indoors over a straight, uninterrupted corridor. Participants were instructed to walk as far as possible in the 6-minute time frame. Standardised verbal encouragement was given at one-minute intervals throughout the test. The total distance achieved was recorded. It has been reported that wearing the Cosmed K4b$^2$ portable system does not interfere with the reliability of the 6MWT in stroke survivors$^{287}$. 

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6.6.4 Incremental Shuttle Walk Test

As originally reported by Singh (1992)\textsuperscript{55}, participants walked shuttles between two markers spaced 9m apart, creating a 10m course that included turning around the markers. The test requires the individual to walk for as many shuttles as possible at increasing speeds dictated by an audio CD (Department of Respiratory Medicine, Glenfield Hospital NHS Trust, Leicester, UK). Participants were instructed not to jog or run. The test begins at 0.50m.s\textsuperscript{-1} and increases by 0.17m.s\textsuperscript{-1} every minute. The test was terminated of the participants own volition or when the participant was unable to reach within 0.5m of the marker at the time of the audio signal. The final completed shuttle was recorded.

6.6.5 Upright Cycle Graded Exercise Test

A graded exercise test was performed on an upright cycle ergometer. Participants pedalled on an upright cycle (818E, Monark, Sweden) at a rate of 50 or 60 rpm, with workloads increasing in 25 W increments per minute starting from 0 W until test termination. The Karvonen Formula\textsuperscript{121} was used to calculate 85% of heart rate reserve (85\%HRR = [(220 – age) – resting HR] x 0.85] + resting HR), which was used as a safety test-termination criterion. Other termination criteria were the inability to maintain cadence, volitional fatigue, failure of equipment or abnormal cardiac responses to exercise\textsuperscript{122}. Participants were encouraged to complete a cool-down on completion of the test.

6.6.6 Walking Speed

The 10 m Walk Test (10mWT)\textsuperscript{131} was used to assess both self-selected and fast walking speeds. Participants were required to walk along a 14m walkway, with the middle 10m
timed and recorded. Three trials were performed for each test, with the average taken and converted to m s$^{-1}$.

6.6.7 Isometric and Isokinetic Leg Strength

The HUMAC-NORM (CSMi Solutions, USA) isokinetic dynamometer was used to measure muscle torque of knee extensors and flexors in both limbs. Participants were positioned with a back angle of 85 degrees and the popliteal fossa of the involved side resting against the edge of the seat. To minimise body movement, an adjustable seatbelt was applied across the waist and upper torso, with an additional Velcro strap securing the thigh. The lateral femoral condyle of the involved knee was aligned with the rotational axis of the dynamometer. The distal aspect of the tibial attachment was positioned just proximal to the medial malleolus.

The test protocol involved three maximal isometric extension trials, three maximal isometric flexion trials, and three maximal isokinetic flexion and extension trials each involving three repetitions at 60° s$^{-1}$. It has been suggested that stroke survivors have difficulty generating faster movements$^{319}$, therefore a slow speed of 60° s$^{-1}$ was used. Each isometric trial was preceded by a 30s rest period. Both legs were assessed, with the right limb consistently tested first. Verbal encouragement and coaching were provided throughout the test. Maximum peak torque (Nm) was extracted from the best isometric and isokinetic trials. Data were categorised according to side more affected for the stroke group, and the mean of both limbs for the comparison group$^{320}$, as there was no difference between limbs for the latter group.
Chapter 6. Fitness levels in stroke survivors against comparisons

6.6.8 Body Composition

Body composition was assessed using bioelectrical impedance analysis (InBody 720 Biospace, Korea) to measure body fat (%), muscle mass (kg) and lean mass (kg).\(^{321}\)

6.6.9 Statistical Analysis

Data were analysed using Stata Statistical Software 11.0 (Statacorp. 2011). Comparisons of demographic and clinical data were assessed by matched pairs (between group) t-tests, with significance set at p<0.05. All data were tested for normality using Shapiro-Wilks statistics. Missing data excluded both participants in the pair. Results are presented as mean ± standard deviation unless otherwise stated. Effect sizes were calculated using Cohen’s d with an effect size (ES) <0.2 categorised as small, 0.2 to 0.5 as medium, 0.5 to 0.8 as large and >0.8 as very large.\(^{293}\) In order to represent the performance of the stroke group compared to the comparison group, the mean results of the stroke group were calculated as a percentage of the mean results of the comparison group, whose values were designated as 100%.

6.7 Results

Characteristics of the 34 participants (n=17 stroke, 53% males) are summarised in Table 6.1. All stroke survivors were classified in FAC 5, with one exception (FAC 4). The majority of participants (n=11) were classed as 1 on the Modified Rankin Scale, with two participants 0, and four as 2. All participants walked at a self-selected speed of $\geq 0.9 \text{m/s}^1$, classing them as community ambulators.\(^{322}\) There was an even balance in gender both within groups and between groups, with reported comorbidities reasonably similar between groups. There were no significant differences in age, height, weight,
muscle mass or body fat (Table 6.2) between groups (p>0.05). No significant adverse events occurred during testing. In the stroke group, eight participants were categorised as having low activity, six were in the moderate activity category, and three in the high activity category. Physical activity levels of the comparison group were three in the low activity category, ten performed moderate activity, and four high activity.

Table 6.1 Participant characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Stroke (n=17)</th>
<th>Comparison (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.7 ± 16.5</td>
<td>58.6 ± 16.1</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (53)</td>
<td>9 (53)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (47)</td>
<td>8 (47)</td>
</tr>
<tr>
<td>Months post-stroke</td>
<td>3.5 ± 3.6</td>
<td>-</td>
</tr>
<tr>
<td>Body Mass Index (kg m⁻²)</td>
<td>27.7 ± 6.1</td>
<td>25.9 ± 4.8</td>
</tr>
<tr>
<td>Co-morbidities, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>0 (0)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (22)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>4 (22)</td>
<td>3 (17)</td>
</tr>
<tr>
<td>COPD</td>
<td>1 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>CVD</td>
<td>1 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (17)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>PVD</td>
<td>1 (6)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Medications, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>8 (44)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>4 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Functional Ambulatory Category, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>16 (94)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>Modified Rankin Scale, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2 (12)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11 (65)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (24)</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation or counts (percentages). Abbreviations: n: number, COPD: Chronic Obstructive Pulmonary Disease, CVD: Cardiovascular Disease, PVD: Peripheral Vascular Disease, ACE: angiotensin-converting enzyme.
Figure 6.1 Stroke group results as a percentage of comparison group results (designated as 100%) for A) VO$_{2\text{peak}}$, HR$_{\text{peak}}$ and performance on cardiorespiratory fitness tests, and B) peak torque achieved for more affected and less affected limbs.
Chapter 6. Fitness levels in stroke survivors against comparisons

Outcome variables from each test are presented in Table 6.2. During the three CRF exercise tests, VO$_2$peak, HR$_{peak}$ and performance outcomes were lower in the stroke group with large to very large effect size differences in VO$_2$peak and very large differences in performance outcomes between the groups. Stroke survivors had mean VO$_2$peak values that were 75.5% to 78.3% of those of the comparison group (Figure 6.1). The mean difference between groups in 6MWT distance (142m) exceeded the reported minimal detectable change (MDC) for stroke (50m), as did walking speed (10mWT MDC 0.10m s$^{-1}$; difference between groups: self-selected 0.3m s$^{-1}$, fast 0.5m s$^{-1}$)$^{314}$ and the SWT MDC reported in COPD (SWT MDC: 47.5m; difference: 236m)$^{323}$.

Of the 15 stroke survivors who performed the cGXT, only two terminated testing due to their HR reaching the predetermined 85% HRR limit compared to 13 of the 15 in the comparison group. The remaining two non-stroke participants stopped due to leg fatigue, as did six in the stroke group. Other reasons for stroke survivors stopping included shortness of breath (n=4), knee pain (n=2), ECG changes (n=1) and a poor ECG signal (n=1). Knee pain prevented two stroke survivors from performing the cycle GXT, and one stroke survivor from performing knee strength testing.

There were very large effect sizes for walking speed differences, with the stroke group walking substantially slower at both self-selected and fast walking speeds. Leg strength of the stroke group was lower for all isometric and isokinetic trials, with medium to large effect sizes equating to 78% to 89% of the comparison group (Figure 6.1). There was a trend towards a greater discrepancy in strength between groups for the isokinetic trials. Body composition was similar between groups.
Table 6.2 Outcome measures for stroke and comparison groups, including between group differences

<table>
<thead>
<tr>
<th>Test</th>
<th>Stroke (n=17)</th>
<th>Comparison (n=17)</th>
<th>Effect Size</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWT (n=34)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO(_{2})peak (mL kg(^{-1}) min(^{-1}))</td>
<td>16.46 ± 3.66</td>
<td>21.03 ± 8.32</td>
<td>0.71(^b)</td>
<td>0.06(^*)</td>
</tr>
<tr>
<td>HR(_{\text{peak}}) (beats min(^{-1}))</td>
<td>115 ± 21</td>
<td>124 ± 23</td>
<td>0.39(^a)</td>
<td>0.22</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>464 ± 121</td>
<td>606 ± 129</td>
<td>1.14(^c)</td>
<td>&gt;0.01(*)</td>
</tr>
<tr>
<td>SWT (n=34)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO(_{2})peak (mL kg(^{-1}) min(^{-1}))</td>
<td>17.44 ± 4.94</td>
<td>23.11 ± 9.48</td>
<td>0.75(^b)</td>
<td>0.04(*)</td>
</tr>
<tr>
<td>HR(_{\text{peak}}) (beats min(^{-1}))</td>
<td>125 ± 21</td>
<td>135 ± 29</td>
<td>0.34(^a)</td>
<td>0.21</td>
</tr>
<tr>
<td>Shuttle distance (m)</td>
<td>415 ± 174</td>
<td>651 ± 236</td>
<td>1.14(^c)</td>
<td>&gt;0.01(*)</td>
</tr>
<tr>
<td>Cycle GXT (n=30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO(_{2})peak (mL kg(^{-1}) min(^{-1}))</td>
<td>17.0 ± 6.3</td>
<td>22.4 ± 6.5</td>
<td>0.84(^c)</td>
<td>0.02(*)</td>
</tr>
<tr>
<td>HR(_{\text{peak}}) (beats min(^{-1}))</td>
<td>128 ± 26</td>
<td>146 ± 17.0</td>
<td>0.83(^c)</td>
<td>0.01(*)</td>
</tr>
<tr>
<td>Final workload (W)</td>
<td>118 ± 32</td>
<td>157 ± 42</td>
<td>1.06(^c)</td>
<td>0.01(*)</td>
</tr>
<tr>
<td>Walking Speed (n=34)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-selected (m s(^{-1}))</td>
<td>1.2 ± 0.3</td>
<td>1.5 ± 0.1</td>
<td>1.03(^c)</td>
<td>&gt;0.01(*)</td>
</tr>
<tr>
<td>Fast (m s(^{-1}))</td>
<td>1.7 ± 0.4</td>
<td>2.2 ± 0.5</td>
<td>1.04(^c)</td>
<td>&gt;0.01(*)</td>
</tr>
<tr>
<td>Knee Strength (n=32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isometric Peak Torque</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 140.7 ± 59.1</td>
<td>158.2 ± 49.5</td>
<td>0.32(^a)</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>L: 136.9 ± 44.0</td>
<td>164.9 ± 44.0</td>
<td>0.45(^a)</td>
<td>0.10(*)</td>
<td></td>
</tr>
<tr>
<td>Flexion (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 74.6 ± 34.2</td>
<td>84.5 ± 28.9</td>
<td>0.31(^a)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>L: 75.4 ± 26.3</td>
<td>86.4 ± 26.3</td>
<td>0.33(^a)</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Isokinetic Peak Torque</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 94.2 ± 43.1</td>
<td>118.1 ± 46.6</td>
<td>0.53(^b)</td>
<td>0.06(*)</td>
<td></td>
</tr>
<tr>
<td>L: 97.6 ± 39.0</td>
<td>110.7 ± 40.0</td>
<td>0.48(^a)</td>
<td>0.07(*)</td>
<td></td>
</tr>
<tr>
<td>Flexion (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 66.6 ± 33.9</td>
<td>82.2 ± 32.9</td>
<td>0.47(^a)</td>
<td>0.10(*)</td>
<td></td>
</tr>
<tr>
<td>L: 64.3 ± 26.0</td>
<td>82.1 ± 26.0</td>
<td>0.60(^b)</td>
<td>0.03(*)</td>
<td></td>
</tr>
<tr>
<td>Body composition (n=26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>32.0 ± 10.0</td>
<td>34.4 ± 9.0</td>
<td>0.08</td>
<td>0.53</td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td>28.4 ± 5.5</td>
<td>28.1 ± 5.9</td>
<td>0.05</td>
<td>0.86</td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 8.0 ± 1.6</td>
<td>7.7 ± 1.6</td>
<td>0.14</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>L: 7.9 ± 1.5</td>
<td>7.9 ± 1.5</td>
<td>0.13</td>
<td>0.56</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: 6MWT: Six-Minute Walk Test, SWT: Shuttle Walk Test, GXT: Graded Exercise Test, HR\(_{\text{peak}}\): peak heart rate, A: more affected, L: less-affected, VO\(_{2}\)peak: peak oxygen consumption. Effect sizes refer to mean between group differences \(^a\) medium effect size, \(^b\) large effect size, \(^c\) very large effect size, P-values refer to between group differences, \(*\) p<0.05
6.8 Discussion

Despite being independently ambulant, with evidence of very good functional recovery following stroke, there were still deficits in the stroke group for CRF, walking speed and leg strength. Across this variety of fitness tests, these stroke survivors underperformed compared to the age- and gender-matched group. Reasons for these significant differences between groups are speculative, with reported changes in muscle fibre recruitment and composition, respiratory function and autonomic control of cardiac functions after stroke possible factors. Although exercise programs for stroke are usually focused on improving ability to perform ADLs and increasing quality of life, exercise after stroke is also important to improve CRF, increase muscle strength, reduce depressive symptoms, and prevent complications associated with inactivity, as well as to decrease the likelihood of secondary stroke. Therefore, there are important health benefits from exercise programs for stroke survivors who are functionally independent and with little to no functional limitations. The very low fitness levels found in this group, along with the known high risk for secondary stroke, suggest that this group would be a very good target for future exercise intervention studies.

This is the first study to specifically assess the fitness levels of independently ambulant stroke survivors across a range of tests. Our findings are in line with the previously reported comparisons between stroke survivors with a range of disabilities and non-stroke groups. Using a recumbent cycle ergometer, Tomczak et al. assessed ten hemiparetic stroke survivors, reporting an average VO$_{2peak}$ of 16.0mL.kg$^{-1}$.min$^{-1}$, 57% of that achieved by the control group. A similar VO$_{2peak}$ using a cycle ergometer test was
reported by Fujitani et al.\textsuperscript{327}; hemiplegic stroke survivors achieved a VO$_{2\text{peak}}$ of 17.7mL kg$^{-1}$ min$^{-1}$ at baseline, 79\% of that achieved by healthy subjects aged 55-64 years. This is similar to the current study, with stroke survivors achieving a VO$_{2\text{peak}}$ 76\% of the comparison group for the cGXT. Previously, no studies have compared oxygen consumption on the SWT and 6MWT in stroke to comparison groups. Despite being independently ambulant in the community, and having minimal differences in leg strength between the affected and less affected sides, the stroke group were unable to sustain walking at high speeds during the 6MWT and SWT. The difference in distance achieved between groups was larger for the SWT, where the pace is set externally. Differences in HR$_{\text{peak}}$ between groups were moderate for the walking tests, but very large for the cGXT. These walking tests may not have been sufficiently challenging for some of the non-clinical participants, and greater differences between groups may have been observed if these participants were allowed to run. Similarly, if it were not for the predetermined HRR limit on the cGXT protocol that most of the comparative participants reached, this discrepancy may have been larger. The difference in HR is reflected in the reasons for test termination, with most stroke survivors stopping the test for musculoskeletal related reasons, particularly leg fatigue.

Knee strength in stroke survivors has been compared to healthy individuals in several studies\textsuperscript{312,328-330}. The reported mean strength of approximately 50\% in stroke compared to control participants is lower than the ~20\% deficits found between our groups. Also, the previous studies used hand-held dynamometry and therefore only isometric measurements were obtained. The Humac Norm dynamometer in the current study provided both isometric and isokinetic measurements. Our stroke group displayed weakness in the isometric and isokinetic trials on both the affected and less-affected
sides. These findings support the recommendation that training should not just focus on the side of greater neurological deficit. These results, together with the large discrepancy between groups on the final workload of the cGXT indicate deficits in both muscle strength and endurance. Strength training is currently recommended post stroke to increase the ability to perform activities of daily living, as well as reducing cardiac demands. Specific muscle endurance training may also be beneficial to allow more extensive challenging of the cardiorespiratory system. Alternatively, interval training may be advantageous to challenge the cardiorespiratory system without prematurely fatiguing the neuromuscular system.

This is the first study to comprehensively assess the fitness levels of well recovered stroke survivors. It is also one of few studies that have included a non-stroke, individually age- and gender-matched comparison group. A recent systematic review on cardiorespiratory fitness after stroke found only two of the 41 included studies directly assessed comparative healthy age- and gender-matched participants. The inclusion of this comparison group was particularly important for identifying leg strength deficits, as in these stroke participants the usual method of using the less affected side as a control would not have identified any deficits. The current study also employed the gold standard measurement of CRF, oxygen consumption, in a portable manner to allow for assessment during overground walking during the 6MWT and SWT.

The results from this study are particularly striking considering the relatively young age of this sample population. This study included one stroke survivor aged just 23 years, one 32 years and three aged 40-50 years, all considerably younger than the average age
Chapter 6. Fitness levels in stroke survivors against comparisons

of participants involved in studies assessing fitness in stroke of 53 to 71 years\textsuperscript{39}. These fitness deficits are therefore not just applicable to older populations, and it is important that younger independently ambulant stroke survivors also be considered for targeted exercise programs. Also, it often assumed that stroke survivors were inactive prior to the stroke event, and it is impossible to retrospectively assess fitness levels. While this assumption may be generally true, there are exceptions. Anecdotally, this group were motivated to return to prior activities including training at the gym and running. Therefore, although it cannot be said definitively that stroke is the cause of reduced fitness in stroke survivors it is likely that the reduced fitness levels in this group are at least partly due to the stroke event.

This study has limitations. The relatively small sample size meant it was not possible to control for comorbidities. It is important for future studies to consider comorbidities and their potential effects on fitness levels. Also, additional functional impairment assessments and data on the site and size of the stroke lesion to better describe the study population may have improved the interpretation and generalizability of the findings. Additionally, with multiple statistical comparisons there is a risk for Type I error, which should be considered when interpreting results; consequently the effect sizes may be more important for interpretation. Lastly, there was a difference in self-reported physical activity levels between the groups, which may reflect the reduced physical capacity of participants or contributed to their reduced fitness.

6.9 Conclusion

Well-recovered, independently ambulant stroke survivors had lower cardiorespiratory fitness, walking speeds and leg strength compared to the healthy age- and gender-
matched comparison group. In regard to the assumption that well recovered, independently ambulant stroke survivors do not require specific exercise interventions, the current study suggests the contrary. Although the goal may not be to regain function, exercise can provide a myriad of benefits, including the potential to decrease the risk of secondary stroke. Further research into programs specifically for well-recovered stroke survivors is warranted.
Chapter 7 – A program of home and community based physical activity can improve the cardiorespiratory fitness and walking endurance of stroke survivors

7.1 Preface

This chapter presents a summary of a published manuscript (appendix 4), which investigated the feasibility and short-term (3-months) efficacy of an individually tailored home and community based pilot exercise program (How Fit is the Stroke Survivor? (HowFITSS?) Trial).

7.2 Citation


7.3 My Contribution

As second author on this paper, I had significant contributions to the paper from conception to publication. This included development of the assessment sessions, gaining funding for equipment, equipment training, leading and conducting the assessments on stroke survivors, providing weekly support to participants during the
intervention period, paperwork and document control, data entry and data extraction, data analysis and editing the manuscript.

7.4 An introduction to the HowFITSS? pilot exercise program

Development of the HowFITSS? pilot intervention was based on findings from previous chapters of this thesis. The HowFITSS? program included several unique and practical components, which were designed to be translatable to the current Australian health care system. These include:

- *Individualisation*: The program was tailored to the individual. This meant taking into account previous exercise history, current exercise, likes and dislikes, equipment available at home, gyms or community programs close to home as well as age and ability. Partners or carers present at the session were also included in the planning and development of the program.

- *The HowFITSS? Exercise Manual*: Each participant received the HowFITSS? Exercise Manual (appendix 15) to complement the program. The manual included information on the importance of exercise, safety during exercise, different types of exercise (eg aerobic vs resistance training), examples of simple exercises and also how to overcome barriers to exercise. The manual was based on the Australian Government’s Choose Health: Be Active Physical Activity Guide for Older Australians booklet. Each manual contained a core set of exercises, which were based on previous research\(^\text{150,201,205,220,280,332,333}\), in addition to other activities. All exercises could be completed at home with minimal to no equipment. A ‘progress’ option was also included to describe how to increase the intensity of the exercise once the basic exercise was mastered.
Progression of exercise was based on the stroke survivors’ perception of effort, as well as time spent performing the exercises.

- **Emphasis on reducing sedentary time:** All stroke survivors in the HowFITSS? trial were encouraged to break up prolonged sitting whenever possible. Participants were advised to get up and move every hour, progressing to every half hour, progressing to completing short bouts of exercise in each break.

- **Emphasis on increasing every day physical activity:** The HowFITSS? program was not just about structured exercise. As part of a more holistic and plausible long term program, we encouraged participants to chose the active option whenever possible; for example, taking stairs instead of the lift and walking to the shops instead of driving.

- **Participant support:** Support was provided through phone calls and emails on a weekly basis during the intervention period by an Exercise Scientist (Ashlee Dunn). Support decreased to once a fortnight during the post intervention to 3-month follow up assessment, and once every six weeks afterwards. This made participants accountable for their exercise, gave them some motivation to continue moving and gave the Exercise Scientist an opportunity to check on their health status.

- **Long term follow up:** Unlike most exercise programs in the stroke literature, the HowFITSS? trial included a long term follow up 12-months after the exercise program was delivered (see Chapter 8). The assessments were used to evaluate long term adherence and benefits of the program.
7.5 Objective

To determine the feasibility of the HowFITSS? individually tailored home and community based exercise program to improve cardiorespiratory fitness (CRF) and walking endurance in stroke survivors.

7.6 Methods

A pilot controlled trial was undertaken to investigate the effects of a 12-week exercise intervention on community dwelling stroke survivors (ANZCTR Trial ID: ACTRN12614000134628). Twenty independently ambulant, community dwelling stroke survivors were recruited and block allocated (intervention=10, control=10). Both groups received usual care, with the intervention group additionally undertaking a 12-week, individually tailored, home and community based exercise program, including once-weekly telephone/email support. Clinicians were blinded to group allocation (details are available in appendix 4). Assessments were conducted at baseline and 12 weeks. Follow up assessments were conducted at 6 and 12 months (Chapter 8). Feasibility was determined by retention, program participation, and adverse events. Efficacy measures included change in cardiorespiratory fitness (CRF) through measuring oxygen consumption (VO_{2peak}) and performance measures during the Shuttle Walk Test (SWT), Six-Minute Walk Test (6MWT) and Cycle Graded Exercise Test (cGXT).

7.7 Results

All participants completed the study with no adverse events. All intervention participants reported undertaking their prescribed program. 6MWT VO_{2peak} improved
by 16% more in the intervention group (1.17±0.29 to 1.35±0.33 L·min⁻¹) than the control group (1.24±0.23 to 1.24±0.27 L·min⁻¹) (p=0.044). There were trends to improvement in the SWT [0.14 L·min⁻¹ (95% CI: -0.04 to 0.32)] and cGXT [0.20 L·min⁻¹ (95% CI: -0.04 to 0.43)]. 6MWT distance improved by 66.5±63.8m (16%) in the intervention group compared to 14.5±38.5m (3%) in the control group (p=0.049). There were no statistically significant differences between the groups for changes in fatigue, depression, or health-related quality of life.

7.8 Conclusion
The HowFITSS? program appears to be a feasible model for independently ambulant stroke survivors. The program requires few health resources, and is suitable in most community settings. The 16% improvement in CRF is similar to that achieved in centre-based resource-intensive program. This study demonstrates a promising, resource-efficient intervention to improve the fitness of community dwelling stroke survivors.
Chapter 8 – Cardiorespiratory fitness and walking endurance improvements at 12 months follow-up of an individually tailored home and community-based exercise program for stroke survivors

8.1 Preface

This chapter presents the results from the long-term (12 months) follow up of the HowFITSS? trial. This manuscript is currently under review in the journal Stroke Research and Treatment.

8.2 Citation

A Dunn, DL Marsden, D Barker, P Van Vliet, NJ Sprat and R Callister. Cardiorespiratory fitness and walking endurance improvements at 12 months follow-up of an individually tailored home and community-based exercise program for stroke survivors, Stroke Research and Treatment (under review)

8.3 My Contribution

As first author, I led the paper from conception to publication. My role included leading the study for the follow up period, conducting all of the assessment sessions, paperwork and document control, data entry and data extraction, data analysis and writing and editing the manuscript.
8.4 Abstract

This study evaluated the immediate and longer-term effects of an individually tailored, home- and community-based exercise program with ongoing remote support in stroke survivors on cardiorespiratory fitness (CRF), ambulation and health-related quality of life (HRQoL). Twenty stroke survivors completed the 12-week HowFITSS? exercise program aimed at increasing CRF and daily physical activity. Support was provided by phone calls and email (which decreased in frequency over the 12 months). Participants were assessed at baseline, then at 3, 6 and 12 months after initiation of the intervention. CRF (VO$_{2\text{peak}}$) was evaluated using a portable metabolic cart during the six-minute walk test (6MWT), Shuttle Walk Test (SWT) and cycle graded exercise test (cGXT). Walking speed, balance, body composition, fatigue, depression and HRQoL were also measured. CRF improved significantly from pre-intervention to 12-month follow up on the 6MWT (Effect Size, ES=0.87 p=0.002) and cGXT (ES=0.60 p<0.001), with more modest improvements on the SWT (ES=0.52 p=0.251). From baseline to 12-months, significant within-participant improvements were found for self-selected walking speed, balance and HRQoL. Performances on the remaining tests were maintained over the post-intervention period. There may be health benefits of providing stroke survivors with an exercise intervention with long-term support that encourages increased regular physical activity.

8.5 Introduction

The most recent exercise guidelines for stroke$^{50}$ recommend that stroke rehabilitation be designed to facilitate the development and maintenance of an active lifestyle, and to increase or maintain improvements in physical function, including cardiorespiratory
fitness (CRF). There is good evidence that short-term exercise programs can improve CRF\textsuperscript{43} and other aspects of physical performance, especially in supervised exercise programs. It is less clear if these benefits are maintained once the formal program, and likely access to the resources provided during the intervention period, end. To date, there has been little reporting of the maintenance of fitness improvements following exercise interventions after stroke.

There is potential for significant advantages of exercising over the long term, including prevention of complications associated with inactivity, increased independence and community participation\textsuperscript{162} as well as decreased likelihood of secondary stroke\textsuperscript{39,40}. Stroke survivors spend significantly more time sitting than non-stroke controls\textsuperscript{334}, which places them at greater risk of lifestyle diseases including diabetes and cardiac complications\textsuperscript{335}. In addition, two recent systematic reviews have reported that CRF in stroke survivors is low\textsuperscript{39,43}, with levels barely reaching those required for activities of daily living\textsuperscript{46}. There is a heightened risk of recurrent stroke consequential of a sedentary lifestyle and prevalent co-morbidities. Strategies to not only increase fitness but also maintain these improvements over time may be very important for ensuring independence and health-related quality of life (HRQoL), while decreasing mortality over the long term.

In the HowFITSS? controlled trial\textsuperscript{117}, we showed that a 12-week individually tailored home and community based exercise program improved CRF by 11-15\%, depending on the assessment method used, in the intervention group compared to the control group. The intervention provided an individually tailored exercise program aimed at increasing CRF and promoted a long-term active lifestyle. The aim of the current investigation was
to evaluate the longer-term effects, up to 12 months, of the HowFITSS? exercise program in a cohort of stroke survivors.

8.6 Methods

8.6.1 Study Design

The current analysis is a longitudinal cohort study. Independently ambulant, community dwelling stroke survivors were assessed at baseline then participated in the HowFITSS? intervention. Remote support was provided during the 12-week intervention and subsequent nine months. Participants were reassessed post intervention (3 months) and at 6 and 12 months. This research was approved by the Hunter New England Human Ethics Committee (11/04/20/4.04) and University of Newcastle Human Research Ethics Committee (H-2011-0172).

8.6.2 Participants

Participants had been recruited to a controlled trial that has been reported in detail elsewhere\textsuperscript{117} (ANZCTR Trial ID: ACTRN12614000134628). Stroke survivors in the intervention group (n=10) received the 12-week program immediately while those in the control group (n=10) were wait listed for 12 weeks then received the 12-week intervention. Participants were included who: 1) had experienced a clinically diagnosed stroke (ischemic or haemorrhagic) in the past 12 months, 2) were able to follow a two-step command, 3) were not pregnant, 4) had no contraindications to exercise as deemed by the referring clinician, and 5) were able to attend the centre for assessments. All participants received medical clearance prior to commencement of the exercise program. All participants provided written informed consent.
8.6.3 Intervention

The *HowFITSS?* intervention was an individually tailored, home and community based program, with the overall goals of increasing physical activity and fitness. The program included a manual provided to each participant, which reinforced the verbal information provided by an experienced Exercise Scientist (AD) and Neurological Physiotherapist (DM). The program consisted of a core set of exercises (e.g., fast walking, squats, sit to stand) informed by previous research plus individualised activities based on the participants’ previous exercise history and activities they enjoyed or wanted to resume. This included both exercise and activities of daily living that would increase heart rate.

Weekly support was provided via emails or phone calls by author AD, and consisted of checking how the participant was going with exercise, providing additional advice, encouragement, support, accountability, and motivation to continue. For the 3 months following the 12-week intervention participants received fortnightly communication via email or telephone. Between the 6 and 12-month assessments, these communications decreased to once every six weeks. Participants were encouraged to progress the intensity and duration of physical activity, and increase the variety of activities, throughout the 12 months.

8.6.4 Participant characteristics

Demographic data including age, gender, time since stroke, blood pressure medications, co-morbidities, Functional Ambulatory Category (FAC) and modified Rankin Scale (mRS) were determined from medical history provided by the GP or by interview. Average level of physical activity over each time period was calculated semi-
quantitatively using information reported during the screening process and interview. Activity levels at baseline were defined according to the International Physical Activity Questionnaire (IPAQ) categorical score and categorised as low, moderate or high levels.

8.6.5. Assessments

All assessments were conducted at the University of Newcastle Human Performance Laboratory. The test order and methods, including standardised instructions, were consistent across all assessment sessions. A description of these assessments has been reported elsewhere\textsuperscript{117}.

8.6.6 Outcome Measures

The primary outcome measure was change in CRF measured by relative VO\textsubscript{2peak} (mL·kg\textsuperscript{-1}·min\textsuperscript{-1}) from pre-intervention to 12 months follow up. This was assessed during the 6MWT, SWT and cGXT. Secondary outcome measures included changes in all other variables from pre-intervention to 12 months, as well as changes in all variables from 3-6, 6-12, and 3-12 months.

8.6.7 Cardiorespiratory fitness assessments

- **Six Minute Walk Test (6MWT)** was conducted in accordance with the American Thoracic Society Guidelines\textsuperscript{136} using a modified walkway length of 20m due to space restrictions in the testing centre. Participants were instructed to walk as far as possible during the six-minute time frame by shuttling back and forth along the marked corridor. Standardised verbal encouragement but no physical support was provided during the test\textsuperscript{42}. Participants were allowed to use assistive devices if required.
- **Incremental Shuttle Walk Test (SWT)** was conducted in accordance with Sing et al.\(^{55}\) and required participants to walk shuttles between two markers placed 9m apart. An audio CD dictated the speed required for each level, beginning at 0.50m.s\(^{-1}\) and increases by 0.17m.s\(^{-1}\) every minute. Participants were instructed not to run. The test was terminated when the participant could not reach within 0.5m of the marker at the time of the audio signal. No verbal or physical encouragement was provided throughout the test.

- **Cycle Graded Exercise Test (cGXT)** was performed on an upright ergometer (818E, Monark, Sweden) with the participant cycling at a cadence of 50 or 60rpm. The protocol began at 0W and increased by 25W each minute through increased resistance. The test was terminated; 1) upon the individual’s request, 2) according to ACSM guidelines for exercise testing\(^{122}\), 3) the participant could not maintain cadence, or 4) if 85% of the predetermined heart rate reserve (85%HRR = \([(220 – \text{age}) – \text{resting HR} \times 0.85] + \text{resting HR})\(^{121}\) was reached.

During the 6MWT, SWT and cGXT, a portable open-circuit spirometer (K4b\(^2\), COSMED, Italy) and 12-lead electrocardiograph (Quark T12, COSMED, Italy) were used to measure metabolic variables indicative of fitness including oxygen consumption (VO\(_2\)), heart rate (HR), ventilation (VE) and respiratory exchange ratio RER. Calibrations were performed in accordance with manufacturer’s specifications prior to each testing session, with corrections made for time delay from the mask to the unit, barometric pressure and humidity. The system locked into a harness, which sat high up on the participant’s chest. Power was derived from a battery pack and transmitted to the computer by telemetry. Altogether, the equipment weighed less than 1kg, and has been shown to not interfere with the reliability of the 6MWT in stroke survivors\(^{287}\).
Performances on the three CRF tests were also recorded: 6MWT distance (m), SWT shuttles (n), and cGXT peak workload (W).

### 8.6.8 Secondary assessments

- **10-metre walk test (10mWT)**\(^{131}\) was used to measure self-selected and fast walking speeds. Participants walked along a 14m walkway, with the time taken to walk the middle 10m recorded. Three trials were performed at each speed. The average time for each condition was converted to m/s.

- **Step Test**\(^{96}\) was used to assess balance. Participants stepped one leg at a time, repetitively up and down a 7.5cm step for a 15 second period. The number of steps completed over the 15 second period was recorded.

- **Body Composition**\(^{321}\) was assessed using bioelectrical impedance analysis (InBody 720 Biospace, Korea) to measure body fat (%), muscle mass (kg) and lean mass (kg).

- **Fatigue Assessment Scale (FAS)**\(^{337}\), **Patient Health Questionnaire (PHQ-9)**\(^{115}\) and **Stroke and Aphasia Quality of Life (SAQoL-39)**\(^{109}\) questionnaires were used to assess fatigue, depression and HRQoL, respectively. Higher scores on the FAS and PHQ-9 represent worse fatigue and depression, and lower scores on the SAQoL-39 represent worse HRQoL.

### 8.6.9 Statistical Analysis

Data were analyzed using Stata Statistical Software 11.0 (Statacorp. 2011). All outcome measures were found to be normally distributed (Shapiro-Wilks statistic), therefore parametric analyses were applied. Analyses were conducted on the principle of
intention to treat, therefore a linear mixed model with random intercept was used to compare the outcome measures over the multiple time points. This modelling approach was chosen to adjust for the repeated testing of individuals, as well as to include information from those participants who were unable to complete all tests under the missing at random assumption. Associations between missing data and all variables were assessed using t-tests with significance set at p<0.002 as determined by Bonferroni adjustment. No significant associations were found, therefore no covariate adjustments were included in the model. Significance level was set at 5%, with results presented as mean ± standard deviation unless otherwise stated. Effect sizes (ES) were categorised by: <0.2 as small, 0.2 to 0.5 as medium, 0.5 to 0.8 as large and >0.8 as very large. The unadjusted odds ratio of the ability to attend follow up at 12 months based on participant age (<55 years, ≥55 years) was also calculated.

8.7 Results

Participant characteristics are presented in Table 8.1. Participants ranged in age from 23 to 84 years. There were slightly more females than males, and there were more females in those less than 60 years of age. Time since stroke ranged from one to 16 months. Most participants had a Functional Ambulation Category score of 5 indicating independent ambulation on all surfaces. Modified Rankin Scale scores ranged from 0 (no symptoms) to 3 (moderate disability) with most participants scoring 1 (no significant disability). During follow-up assessment sessions, participants reported keeping physically active over the 9-month post-intervention period by doing gym classes, outdoor activities such as gardening, walking and running, home-based exercises provided in the HowFITSS? manual, keeping active at work and generally reducing sedentary time.
One participant was unable to attend any of the three follow up time points due to long standing severe knee pain. Fifteen of the 19 participants at 3 months attended the 6-month follow up; the other four were unable to be assessed due to advice from cardiologists [n=2], recent surgery [n=1], and unable to be contacted [n=1]. At the 12-month assessment, 13 participants were assessed. None of those who were unable to attend the 6-month time point could return for the 12-month assessment. Of the original 20 participants, the reasons for inability to attend the 12-month assessment were due to advice from cardiologists [n=1], extreme stroke-related fatigue [n=1], severe hip pain [n=1], severe knee pain [n=1], kidney problems precluding exercise [n=1] and one was unable to be contacted. One participant who was unable to attend the 6-month time point on the advice from a cardiologist also could not attend the 12-month assessment after experiencing a secondary stroke, which did not occur during exercise.
Table 8.1 Participant characteristics at baseline (n=20). Data are mean ± SD or number (percentage).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.1 ± 19.2</td>
</tr>
<tr>
<td>Gender, n (%) male</td>
<td>8 (42)</td>
</tr>
<tr>
<td>Body Mass Index (kg m²)</td>
<td>27.6 ± 5.9</td>
</tr>
<tr>
<td>Months post stroke</td>
<td>5.3 ± 3.5</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (21)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>3 (16)</td>
</tr>
<tr>
<td>Cardiac - RBBB</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Cardiac - PFO</td>
<td>1 (5)</td>
</tr>
<tr>
<td>COPD</td>
<td>1 (5)</td>
</tr>
<tr>
<td>CVD</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (21)</td>
</tr>
<tr>
<td>PVD</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Blood pressure Medications, n (%)</td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>8 (42)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>4 (21)</td>
</tr>
<tr>
<td>Functional Ambulatory Category, n (%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>18 (90)</td>
</tr>
<tr>
<td>4</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Modified Rankin Scale, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (5)</td>
</tr>
<tr>
<td>1</td>
<td>15 (75)</td>
</tr>
<tr>
<td>2</td>
<td>3 (15)</td>
</tr>
<tr>
<td>3</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation or counts (percentages).
Abbreviations: n: number, COPD: Chronic Obstructive Pulmonary Disease, CVD: Cardiovascular Disease, PVD: Peripheral Vascular Disease, ACE: angiotensin-converting enzyme
The average age of those stroke survivors who did not come back for assessments for health reasons was 68.8 ± 10.6 years compared to 55.8 ± 21.5 years for those who did attend. Everyone under the age of 50 years (n=7) was able to return and complete follow up assessments. Those less than 55 years of age had 5.1 times the odds of returning to follow up assessments compared to those above the age of 55 years. There was only one reported adverse event, with one participant experiencing a fall while performing fast walking in the home setting; this occurred between the end of the intervention and the 6-month follow up. The individual required a medical check-up, with no injuries apart from bruising occurring as a consequence of the fall.

Improvements in CRF and associated performance measures varied among the three tests used and over the 12 months (Tables 8.2 and 8.3). The largest improvements in VO$_{2peak}$ based on effect sizes over the 12 months were seen using the 6MWT, followed by the cGXT and SWT. Most of the improvement in 6MWT VO$_{2peak}$ and distance walked was achieved during the first 3 months, with smaller improvement in walking endurance in the subsequent 3 months, then maintenance of these improvements over the following 6 months. Improvements on the SWT were smaller than those on the 6MWT both initially and over the 12 months (Tables 8.2 and 8.3). On the SWT increases in VO$_{2peak}$ were slightly larger in the latter 9 months than during the 3-month intervention period. Improvements in the number of shuttles completed were substantial during the first 3 months and continued throughout the following 9 months. The pattern of improvements on the cycle GXT was quite different to those on the 6MWT and SWT. There was little change over the course of the first 3 months but substantial improvements in both VO$_{2peak}$ and the maximum workload attained over the following 9 months.
There was a very large improvement in self-selected walking speed at 12 months; it improved significantly during the first 3 months, with further improvement during the following 3 months and these improvements were maintained at 12 months (Tables 8.2 and 8.3). Fast walking speed did not change during the first 3 months but improved by 5.9% during the following 3 months and this improvement was maintained at 12 months. Balance as assessed by the Step Test improved significantly during the first 3 months and continued to improve over the subsequent 9 months resulting in large improvements over the 12 months.

Changes in the measures assessed by questionnaire were variable (Tables 8.2 and 8.3). Small but non-significant improvements in the FAS were observed at 12 months with most of the improvement obtained during the first 3 months. Improvements on the PHQ-9 were modest, with the average score moving from a mild depression range to the normal range by 6 months post program initiation. Small significant improvements were observed on the SAQoL at 12 months.
Table 8.2 Mean and SD of outcomes measures at four time points over 12 months for those who attended each time point.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline n=20</th>
<th>3 months n=19</th>
<th>6 months n=15</th>
<th>12 months n=13</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6MWT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$VO_{2peak}$ (mL·kg$^{-1}$·min$^{-1}$)</td>
<td>15.62 (3.31)</td>
<td>17.75 (3.80)</td>
<td>18.42 (5.16)</td>
<td>18.84 (4.28)</td>
</tr>
<tr>
<td>$VO_{2peak}$ (L·min$^{-1}$)</td>
<td>1.20 (0.27)</td>
<td>1.33 (0.29)</td>
<td>1.37 (0.38)</td>
<td>1.43 (0.39)</td>
</tr>
<tr>
<td>$HR_{peak}$ (bt.min$^{-1}$)</td>
<td>117 (23)</td>
<td>121 (18)</td>
<td>127 (15)</td>
<td>129 (22)</td>
</tr>
<tr>
<td>VE (L·min$^{-1}$)</td>
<td>44.0 (11.7)</td>
<td>49.7 (15.0)</td>
<td>55.4 (14.0)</td>
<td>51.9 (11.6)</td>
</tr>
<tr>
<td>RER</td>
<td>1.04 (0.14)</td>
<td>1.04 (0.11)</td>
<td>1.11 (0.16)</td>
<td>1.01 (0.11)</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>449 (114)</td>
<td>509 (87)</td>
<td>550 (77)</td>
<td>538 (78)</td>
</tr>
<tr>
<td><strong>SWT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$VO_{2peak}$ (mL·kg$^{-1}$·min$^{-1}$)</td>
<td>16.79 (4.56)</td>
<td>17.81 (4.28)</td>
<td>19.07 (5.47)</td>
<td>19.24 (5.02)</td>
</tr>
<tr>
<td>$VO_{2peak}$ (L·min$^{-1}$)</td>
<td>1.26 (0.31)</td>
<td>1.34 (0.33)</td>
<td>1.43 (0.42)</td>
<td>1.46 (0.43)</td>
</tr>
<tr>
<td>$HR_{peak}$ (bt.min$^{-1}$)</td>
<td>124 (25)</td>
<td>126 (22)</td>
<td>136 (21)</td>
<td>140 (25)</td>
</tr>
<tr>
<td>VE (L·min$^{-1}$)</td>
<td>44.0 (14.9)</td>
<td>47.9 (14.9)</td>
<td>53.7 (16.3)</td>
<td>52.8 (16.2)</td>
</tr>
<tr>
<td>RER</td>
<td>0.99 (0.14)</td>
<td>0.98 (0.10)</td>
<td>1.00 (0.11)</td>
<td>1.00 (0.11)</td>
</tr>
<tr>
<td>Shuttles (n)</td>
<td>38 (17)</td>
<td>44 (17)</td>
<td>48 (16)</td>
<td>51 (18)</td>
</tr>
<tr>
<td><strong>cGXT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$VO_{2peak}$ (mL·kg$^{-1}$·min$^{-1}$)</td>
<td>16.10 (4.75)</td>
<td>16.79 (4.87)</td>
<td>17.65 (7.67)</td>
<td>19.17 (5.67)</td>
</tr>
<tr>
<td>$VO_{2peak}$ (L·min$^{-1}$)</td>
<td>1.22 (0.29)</td>
<td>1.26 (0.35)</td>
<td>1.33 (0.51)</td>
<td>1.40 (0.36)</td>
</tr>
<tr>
<td>$HR_{peak}$ (bt.min$^{-1}$)</td>
<td>126 (25)</td>
<td>130 (22)</td>
<td>141 (23)</td>
<td>140 (22)</td>
</tr>
<tr>
<td>VE (L·min$^{-1}$)</td>
<td>43.9 (15.4)</td>
<td>46.0 (17.7)</td>
<td>52.3 (18.1)</td>
<td>50.9 (18.6)</td>
</tr>
<tr>
<td>RER</td>
<td>1.08 (0.14)</td>
<td>1.05 (0.15)</td>
<td>1.11 (0.12)</td>
<td>1.09 (0.12)</td>
</tr>
<tr>
<td>Max WL (W)</td>
<td>108 (32)</td>
<td>109 (38)</td>
<td>119 (50)</td>
<td>127 (39)</td>
</tr>
<tr>
<td><strong>Walking speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-selected (m·s$^{-1}$)</td>
<td>1.2 (0.3)</td>
<td>1.3 (0.2)</td>
<td>1.4 (0.2)</td>
<td>1.4 (0.2)</td>
</tr>
<tr>
<td>Fast (m·s$^{-1}$)</td>
<td>1.7 (0.4)</td>
<td>1.7 (0.3)</td>
<td>1.8 (0.3)</td>
<td>1.8 (0.3)</td>
</tr>
<tr>
<td><strong>Balance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step test (R)</td>
<td>16 (4)</td>
<td>18 (4)</td>
<td>19 (4)</td>
<td>19 (3)</td>
</tr>
<tr>
<td>Step test (L)</td>
<td>16 (5)</td>
<td>17 (4)</td>
<td>18 (4)</td>
<td>19 (3)</td>
</tr>
<tr>
<td><strong>Body Composition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.0 (19.7)</td>
<td>78.3 (18.0)</td>
<td>78.2 (18.7)</td>
<td>79.8 (21.0)</td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td>26.8 (7.2)</td>
<td>29.6 (7.2)</td>
<td>28.8 (8.0)</td>
<td>28.8 (8.6)</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>36.2 (8.5)</td>
<td>31.6 (8.9)</td>
<td>33.1 (9.8)</td>
<td>35.4 (9.4)</td>
</tr>
<tr>
<td><strong>Questionnaires</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>FAS score (possible range 10 to 50)</td>
<td>24 (6)</td>
<td>22 (6)</td>
<td>22 (9)</td>
<td>21 (9)</td>
</tr>
<tr>
<td>PHQ-9 score (total out of 27)</td>
<td>6 (5)</td>
<td>5 (4)</td>
<td>4 (4)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>SAQoL mean score (total out of 5)</td>
<td>4.3 (0.5)</td>
<td>4.1 (0.5)</td>
<td>4.3 (0.6)</td>
<td>4.4 (0.5)</td>
</tr>
</tbody>
</table>
Abbreviations: $\text{VO}_2\text{peak}$, peak oxygen consumption; $\text{HR}_\text{peak}$, peak heart rate; $\text{VE}$, minute ventilation; $\text{RER}$, respiratory exchange ratio; $\text{Max WL}$, maximum workload; $\text{R}$, right; $\text{L}$, left; $\text{6MWT}$, Six-minute Walk Test; $\text{SWT}$, Shuttle Walk Test; $\text{cGXT}$, cycle graded exercise test; $\text{FAS}$, Fatigue Assessment Scale; $\text{PHQ-9}$, Patient Health Questionnaire; $\text{SAQoL}$, Stroke and Aphasia Quality of Life
<table>
<thead>
<tr>
<th>Variable</th>
<th>Change 0-3mo (p-value)</th>
<th>Effect size 0-3mo</th>
<th>Change 3-6mo (p-value)</th>
<th>Effect size 3-6mo</th>
<th>Change 6-12mo (p-value)</th>
<th>Effect size 6-12mo</th>
<th>Change 0-12mo (p-value)</th>
<th>Effect size 0-12mo</th>
<th>Change 3-12mo (p-value)</th>
<th>Effect size 3-12mo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body Composition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>0.663</td>
<td>0.04</td>
<td>-0.9</td>
<td>0.184</td>
<td>0.01</td>
<td>-0.1</td>
<td>0.336</td>
<td>0.08</td>
<td>2.0</td>
<td>0.925</td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td>0.059</td>
<td>0.39</td>
<td>10.4</td>
<td>0.616</td>
<td>0.10</td>
<td>-2.7</td>
<td>0.871</td>
<td>&gt;0.01</td>
<td>0.0</td>
<td>0.345</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>0.152</td>
<td>0.54</td>
<td>-12.7</td>
<td>0.386</td>
<td>0.16</td>
<td>4.7</td>
<td>0.212</td>
<td>0.24</td>
<td>6.9</td>
<td>0.613</td>
</tr>
<tr>
<td><strong>6MWT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2peak (mL·kg⁻¹·min⁻¹)</td>
<td>0.002*</td>
<td>0.60</td>
<td>13.6</td>
<td>0.667</td>
<td>0.15</td>
<td>3.8</td>
<td>0.596</td>
<td>0.09</td>
<td>2.3</td>
<td>0.002*</td>
</tr>
<tr>
<td>HRpeak (bt·min⁻¹)</td>
<td>0.04*</td>
<td>0.46</td>
<td>10.8</td>
<td>0.886</td>
<td>0.12</td>
<td>3.0</td>
<td>0.284</td>
<td>0.17</td>
<td>4.4</td>
<td>0.002*</td>
</tr>
<tr>
<td>VE (L·min⁻¹)</td>
<td>0.516</td>
<td>0.20</td>
<td>3.4</td>
<td>0.113</td>
<td>0.50</td>
<td>5.0</td>
<td>0.822</td>
<td>0.12</td>
<td>1.6</td>
<td>0.026*</td>
</tr>
<tr>
<td>RQ</td>
<td>0.009</td>
<td>0.43</td>
<td>12.9</td>
<td>0.031*</td>
<td>0.39</td>
<td>11.5</td>
<td>0.040*</td>
<td>0.27</td>
<td>-6.3</td>
<td>0.130</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>&gt;0.001*</td>
<td>0.59</td>
<td>13.4</td>
<td>0.007*</td>
<td>0.49</td>
<td>8.1</td>
<td>0.040*</td>
<td>0.15</td>
<td>-2.2</td>
<td>0.005*</td>
</tr>
<tr>
<td><strong>SWT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2peak (mL·kg⁻¹·min⁻¹)</td>
<td>0.274</td>
<td>0.23</td>
<td>6.1</td>
<td>0.505</td>
<td>0.26</td>
<td>7.1</td>
<td>0.931</td>
<td>0.03</td>
<td>0.9</td>
<td>0.251</td>
</tr>
<tr>
<td>HRpeak (bt·min⁻¹)</td>
<td>0.225</td>
<td>0.24</td>
<td>6.3</td>
<td>0.608</td>
<td>0.23</td>
<td>6.7</td>
<td>0.907</td>
<td>0.09</td>
<td>2.1</td>
<td>0.318</td>
</tr>
<tr>
<td>VE (L·min⁻¹)</td>
<td>0.953</td>
<td>0.06</td>
<td>1.6</td>
<td>0.090</td>
<td>0.59</td>
<td>7.9</td>
<td>0.413</td>
<td>0.21</td>
<td>2.9</td>
<td>0.114</td>
</tr>
<tr>
<td>RQ</td>
<td>0.133</td>
<td>0.26</td>
<td>8.9</td>
<td>0.156</td>
<td>0.37</td>
<td>12.1</td>
<td>0.826</td>
<td>0.06</td>
<td>-1.7</td>
<td>0.065</td>
</tr>
<tr>
<td>Shuttles (n)</td>
<td>0.722</td>
<td>0.13</td>
<td>-1.0</td>
<td>0.773</td>
<td>0.21</td>
<td>2.0</td>
<td>0.928</td>
<td>0.04</td>
<td>0.0</td>
<td>0.537</td>
</tr>
<tr>
<td><strong>GXT</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2peak (mL·kg⁻¹·min⁻¹)</td>
<td>0.648</td>
<td>0.14</td>
<td>4.3</td>
<td>0.648</td>
<td>0.14</td>
<td>5.1</td>
<td>0.456</td>
<td>0.22</td>
<td>8.6</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>HRpeak (bt·min⁻¹)</td>
<td>0.743</td>
<td>0.13</td>
<td>3.3</td>
<td>0.771</td>
<td>0.16</td>
<td>5.6</td>
<td>0.501</td>
<td>0.15</td>
<td>5.3</td>
<td>0.001*</td>
</tr>
<tr>
<td>VE (L·min⁻¹)</td>
<td>0.752</td>
<td>0.09</td>
<td>3.2</td>
<td>0.030*</td>
<td>0.61</td>
<td>8.5</td>
<td>0.007*</td>
<td>0.06</td>
<td>-0.7</td>
<td>0.471</td>
</tr>
<tr>
<td>RQ</td>
<td>0.688</td>
<td>0.12</td>
<td>4.8</td>
<td>0.410</td>
<td>0.35</td>
<td>13.7</td>
<td>0.960</td>
<td>0.07</td>
<td>-2.7</td>
<td>0.245</td>
</tr>
<tr>
<td>Max WL (W)</td>
<td>0.609</td>
<td>0.18</td>
<td>-2.8</td>
<td>0.201</td>
<td>0.44</td>
<td>5.7</td>
<td>0.586</td>
<td>0.20</td>
<td>-1.8</td>
<td>0.304</td>
</tr>
<tr>
<td>Walking speed</td>
<td>0.689</td>
<td>0.03</td>
<td>0.1</td>
<td>0.957</td>
<td>0.23</td>
<td>9.2</td>
<td>0.193</td>
<td>0.18</td>
<td>6.7</td>
<td>0.001*</td>
</tr>
</tbody>
</table>
Table 8.3. Changes in outcome measures over the 12 months. P-values based on intention to treat mixed model analysis, effect sizes and percent changes based on those who attended each time point.

<table>
<thead>
<tr>
<th>Measure</th>
<th>p-value</th>
<th>Effect Size</th>
<th>Percent Change</th>
<th>p-value</th>
<th>Effect Size</th>
<th>Percent Change</th>
<th>p-value</th>
<th>Effect Size</th>
<th>Percent Change</th>
<th>p-value</th>
<th>Effect Size</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-selected (m·s⁻¹)</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fast (m·s⁻¹)</td>
<td>0.019*</td>
<td>0.33</td>
<td>8.3</td>
<td>0.227</td>
<td>0.51</td>
<td>7.7</td>
<td>0.968</td>
<td>0.11</td>
<td>0.0</td>
<td>0.001*</td>
<td>0.84c</td>
<td>16.7</td>
</tr>
<tr>
<td><strong>Balance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Step test (R)</td>
<td>0.003*</td>
<td>0.42</td>
<td>12.5</td>
<td>0.094</td>
<td>0.40</td>
<td>5.6</td>
<td>0.617</td>
<td>0.17</td>
<td>0.0</td>
<td>0.013*</td>
<td>0.68b</td>
<td>18.8</td>
</tr>
<tr>
<td>Step test (L)</td>
<td>&gt;0.001*</td>
<td>0.36</td>
<td>6.3</td>
<td>0.675</td>
<td>0.26</td>
<td>5.9</td>
<td>0.194</td>
<td>0.12</td>
<td>5.6</td>
<td>&lt;0.001*</td>
<td>0.76b</td>
<td>18.8</td>
</tr>
<tr>
<td><strong>Questionnaires</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>FAS score</td>
<td>0.081</td>
<td>0.39</td>
<td>-8.3</td>
<td>0.409</td>
<td>0.10</td>
<td>0.0</td>
<td>0.293</td>
<td>0.10</td>
<td>-4.5</td>
<td>0.556</td>
<td>0.33a</td>
<td>-12.5</td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td>0.372</td>
<td>0.23</td>
<td>-16.7</td>
<td>0.045*</td>
<td>0.41</td>
<td>-20.0</td>
<td>0.142</td>
<td>0.17</td>
<td>0.0</td>
<td>0.443</td>
<td>0.07</td>
<td>-33.3</td>
</tr>
<tr>
<td>SAQoL mean score</td>
<td>0.105</td>
<td>0.26</td>
<td>-4.7</td>
<td>0.035*</td>
<td>0.36</td>
<td>4.9</td>
<td>0.129</td>
<td>0.16</td>
<td>2.3</td>
<td>&lt;0.001*</td>
<td>0.29</td>
<td>2.3</td>
</tr>
</tbody>
</table>

**Abbreviations:** *p<0.05; ₋medium effect size; ₊large effect size; ₊very large effect size; f/u, follow up; VO₂peak, peak oxygen consumption; HRₚeak, peak heart rate; VE, minute ventilation; RQ, respiratory quotient; Max WL, maximum workload; R, right; L, left; 6MWT, Six-minute Walk Test; SWT, Shuttle Walk Test; cGXT, cycle graded exercise test; FAS, Fatigue Assessment Scale; PHQ-9, Patient Health Questionnaire; SAQoL, Stroke and Aphasia Quality of Life
8.8 Discussion

This study investigated the long-term effects of a 12-week home and community based exercise intervention with long-term support in independently ambulant stroke survivors over 12 months. The results indicate that the HowFITSS? model may be an effective intervention to support independently ambulant stroke survivors improve their function long term. Despite minimal support during the follow up period, there was continued improvement or maintenance of CRF, walking speed and balance, as well as improvements in fatigue, mood and HRQoL. Fitness improvements after stroke may continue to occur over a prolonged period with regular exercise and the time course of improvement in particular fitness measures may reflect the specificity of the activities undertaken. Health issues, primarily not related to stroke, did impact negatively on the ability of some participants to attend assessments over the longer term.

The current study shows promising results, including substantial improvements in VO_{2peak}, performance measures, walking speed, balance and HRQoL up to 12 months after a simple, individually tailored, home and community based exercise program. Few studies have included long term follow up from exercise interventions after stroke\textsuperscript{58,339}, however the available studies suggest that benefits gained during exercise interventions are often lost at follow up\textsuperscript{11,268,340}. Unlike our model, these studies did not include ongoing support. It has been previously demonstrated that professional support is a key influence on exercise behaviour in stroke survivors and people with disabilities\textsuperscript{341,342} and should be considered in future exercise trials. Strong relationships have been found between HRQoL and motor function, balance, gait and independence in activities of daily living after stroke\textsuperscript{143}. It is speculated that an exercise program that encourages the
use of functional and enjoyable activities may be more likely to be sustained and therefore provide benefits that are valued by the participants.

A key goal of the HowFITSS? intervention was to provide a non-clinic-based exercise program that was sufficiently challenging to improve CRF. Compromised walking capacity may limit the capacity to challenge the cardiorespiratory system, particularly for home-based exercise programs. A feature of the HowFITSS? program was to encourage participants to walk faster and for longer. The program was effective in increasing both self-selected and fast walking speeds, but particularly self-selected speed (17% faster at 12 months), and walking endurance (20% further) as indicated by performance on the 6MWT. Although the improvements in fast walking speed were modest (6%), the percentage of fast walking speed that participants now selected for self-paced walking increased from 70% at baseline to 78% at 12 months. These improvements may have been necessary precursors to increase CRF. The immediate CRF improvements following the HowFITSS? program were most evident in the 6MWT, which is dependent on the participant’s capacity for a sustained walking speed over the six minute time frame. Over the 3-6 month follow-up period, the progressive SWT showed the greatest CRF improvement. This is also the timeframe over which fast walking speed increased. This improvement in fast walking speed likely enabled the improved performance and CRF demonstrated on the SWT, which requires participants to walk progressively faster. The pattern for progression was different again in the cGXT. As cycling was not included in the HowFITSS? program, unless chosen specifically by a participant (n=2 in this study), the principle of exercise specificity suggests it may be harder to achieve improvements in the cGXT with a home-based program. Small but consistent improvements were seen both during the program and
over the short-term follow-up in cGXT VO$_{2peak}$ and maximum workload, with the greatest improvements seen over the 6-12 month follow up period. Although not assessed in this study, the improvements in cGXT performance may be the result of increased leg strength and endurance. These speculated gains took longer to develop and become evident as an outcome measure, suggesting that although a formal exercise program may be complete at 3 or 6 months, there is great potential for further improvements that may develop across various time frames depending on the outcome measure.

Balance was the other measure that improved substantially (19%) over the 12 months. This improvement could be due to specific exercise recommendations or adaptions as a consequence of faster walking or more extensive physical activity. Notably only one fall was reported, which did not result in serious injury. It is possible that the significant improvements in balance and self-selected walking speed seen in the current study may have resulted in greater confidence in walking. It is speculated that this could have resulted in an increase in HRQoL, as well as the trend toward improved depressive scores. Body composition changes were modest and inconsistent. Initially participants gained muscle and lost body fat, and while much of the muscle gain was retained at 12 months, most of the lost body fat had been regained. It has been previously reported that lean mass is associated with VO$_{2peak}$ ($r=0.60$)\textsuperscript{71} and has a direct effect on an individual’s ability to perform physical activity\textsuperscript{100}. It is speculated this improvement and maintenance of muscle mass may have had implications for walking ability and cycle ergometer performance in this stroke cohort.
Chapter 8. Long term Follow up of HowFITSS? Pilot

There are several possible reasons why the HowFITSS? model resulted in these long term benefits. The program is unique in the holistic, lifestyle approach to exercise maintenance. Participants were encouraged to keep active in every day living, for example by taking stairs instead of the lift, carrying groceries and parking further away to increase walking. It has been suggested that incorporating physical activity into everyday life may better enable stroke survivors to maintain participation in exercise\(^{340}\). The exercise intervention emphasised the importance of not only increasing physical activity and exercise, but also reducing sitting time. Stroke survivors have been shown to sit for significantly longer periods of time compared to controls\(^{334}\). Breaking up sitting time in obese individuals has been shown to lower blood pressure\(^{343}\) and reduce thrombotic risks\(^{344}\) which are both important factors for reducing risk of secondary stroke. We also suggested activities specific to the participant and their likes or dislikes, and investigated past history of activity, what their goals were and what types of activities they might like to try\(^{50}\). Where possible, the spouse or carer of the stroke survivor was invited to attend the assessment sessions where exercise education and counselling were provided. This allowed for the spouse or carer to understand why exercise was important, and to hopefully translate that understanding to greater support for exercise continuation in the home environment.

8.8.1 Strengths and Limitations

To the best of our knowledge, this is the first study to assess CRF using the measurement of oxygen consumption during the 6MWT, SWT and cGXT at 6 and 12-months post exercise intervention in stroke. The results are promising, with all three tests of CRF showing improvements over time. The difference in time course of responsiveness suggests careful consideration needs to be given to the particular tool
used for CRF assessment over a specific time frame. Unlike most exercise stroke trials, the current study used broad inclusion criteria to better reflect a typical cohort and improve the generalisability of the findings. This allowed stroke survivors with multiple comorbidities to participate providing medical clearance was obtained. Co-morbidities are prevalent in stroke survivors, with a previous study reporting that 75% had hypertension, 37% had ischemic heart disease and 24% had diabetes. In the current study comorbidities had an impact on participant retention over the long term, with 25% unable to attend at 6-months and 35% at 12-months follow up. One stroke survivor had a secondary stroke, with the rest unable to attend due to conditions such as cardiac problems, including atrial fibrillation, and arthritis resulting in severe knee or hip pain. Over half of those on beta-blockers were unable to complete the 12-month assessments. It may be harder for those on beta-blockers to be physically active, or the prescription of beta-blockers may indicate more problematic disease or co-morbidities. Future research studies should consider recruiting larger sample sizes to take into account the drop out rates associated with this population over time, as previously suggested.

Comorbidities increase with age and it is noted that all stroke survivors under the age of 50 years (n=7) were able to attend all time points, and complete all assessments. It appears that the sustainability of an exercise intervention and the potential for long term benefits is much greater in a younger population, in this case in those less than 55 years, who were over five times more likely to be able to attend follow up than those older than 55 years of age. There may be considerable potential for benefits in younger stroke survivors, who may have a greater capacity to engage in challenging exercise and a long period of time over which to benefit. Assessors were not blinded in this study, however all test procedures and instructions were standardised and fitness assessments were
objectively measured. It would have been advantageous to include the use of physical activity monitors to assess physical activity levels over the duration of the study.

8.9 Conclusion

The current study indicates that there are long term benefits of providing stroke survivors with the HowFITSS? individually tailored, home and community based exercise program with ongoing long term support. By focusing on more than just improving CRF by including living an active lifestyle, stroke survivors showed significantly improved quality of life. Further research investigating the long-term effects of exercise interventions of this nature is required in larger scale trials.
Chapter 9 – Thesis Discussion

9.1 Overview

The aims of this thesis were to:

1) systematically review and meta-analyse the current evidence regarding the 6MWT in stroke survivors to assess the impact of changing the walkway protocol;

2) compare the responses to the submaximal six-minute walk test, the graded shuttle walk test and cycle graded exercise test as measures of CRF in stroke survivors, and to compare the practicality of using these three tests as measures of CRF in stroke survivors;

3) compare cardiorespiratory fitness, walking ability, knee strength and body composition in independently ambulant, community dwelling stroke survivors to healthy age- and gender-matched comparison participants and

4) assess the long term follow up outcomes of the HowFITSS? exercise program at 6 and 12 months post intervention, when minimal to no support was provided by researchers. The findings have been discussed in detail in the previous chapters. This chapter will focus on the overall aims of the thesis, summarise the findings of the chapters relating to fitness assessment in stroke, development of the HowFITSS? program as well as discussing the future of this model of intervention. The implications for future research and for practice will also be discussed in each section below. This chapter is organised in order of presentation in this thesis.
9.2 Secondary aim 1

Systematically review and meta-analyse the current evidence regarding the 6MWT in stroke survivors to assess the impact of changing the walkway protocol.

A systematic review was conducted to synthesise all reported results from the 6MWT in stroke survivors, in order to inform the use of a modified version of the 6MWT as an outcome measure of the HowFITSS? trial. Only 27 of the studies (21%) described adhered to the ATS standards and used a 30m walkway. Extending, shortening or using a continuous track was common, and had a significant impact on distance achieved. This is assumed to be due to the extent of turning required.

9.2.1 Additional studies

Since the publication of this chapter in early 2015, no additional studies assessing the impact of changing walkway length have been conducted in stroke. However, there have been several studies investigating the modification of the 6MWT in other chronic diseases and healthy populations. New Technical Standards\textsuperscript{347} were released from the European Respiratory Society and the American Thoracic Society, within the context of chronic respiratory disease. These standards acknowledge that track layout and length may affect performance, particularly when very short tracks are used. The authors suggest keeping the track layout and length constant between tests on the same individual, which is in keeping with the current study. Interestingly, similar results have been found in healthy older and younger individuals when the 6MWT protocol has been adjusted\textsuperscript{348}. Despite no gait deficits or disease, these differences are thought to be due to turning and gait speed strategy. The study concluded that, when increasing gait
interruptions such as turning, accelerating, decelerating, there is an increase in spatial gait variability, which has been linked to an increased risk of falls. It can be assumed that this response may be amplified in stroke, where gait and spatial awareness can be compromised.

Emerging studies have assessed the 6MWT in the home setting, which can have implications on track layout options. A study in COPD patients aimed to compare the distances achieved during the 6MWT on a standard 30m track in a clinical setting, to testing in the home environment\textsuperscript{349}. Results demonstrated that the 6MWT performed at home resulted in shorter distances achieved, presumably due to the shorter track lengths available in the home setting, and therefore the increased number of turns required. In contrast, a recent study conducted in chronic heart failure patients assessed the development and validation of a self-administered 6MWT smartphone application\textsuperscript{350}. This allowed patients to perform the 6MWT in a home setting without the therapist present. This test however, does not require a pre-measured course, and is therefore not recorded. Future studies employing this technology, particularly in stroke, may consider entering the course length into the data collected by the application.

\textit{9.2.2 Implications and future considerations in research and practice}

This review highlighted the large number of studies that modify the 6MWT protocol, and the implications in doing so. Based on results from meta-analysis, we suggested that comparisons of distances achieved between studies that report using different walkway lengths or shapes is not recommended. Similarly, pooling data to develop normative reference values may not be accurate when protocols are heterogeneous within this pooling.
Modifying the walkway length is common in the clinical setting. This is understandable, as 30m of uninterrupted, straight, flat corridor is not readily available in many settings.

The implications for practicing clinicians and researchers are:

- It is important not to compare results on a modified walkway to those on a standard 30m track
- If modifying a walkway, keep this consistent over time
- Make a note on the results clearly stating the walkway used
- Do not compare the result to normative data from 6MWT results on different walkway lengths and layouts
- If reporting the data, include other information about the test as listed in the checklist

Due to space restrictions in the testing facility for the HowFITSS? trial, the walkway required modification to a length of 20m. This review allowed us to understand the implications in modifying the walkway length in stroke, and informed the results in the context of other studies using 20m walkways.

### 9.2.3 Systematic review of exercise interventions after stroke

The chapter presented a summary of the published systematic review conducted to inform the structure of the HowFITSS? intervention. This review highlighted several major gaps in the current literature, which require addressing in future research. Firstly, the majority of interventions were delivered in a centre-based environment, with therapists working one-on-one with participants. While this approach shows promising
results, it is also resource intensive (facility hire, staff wages, time required, travel for participants). Similarly, most programs took a blanket approach, and applied to everyone despite differences in age, gender, likes and dislikes, and exercise goals. Future trials to test the effectiveness of individualised and potentially cost-effective interventions would be warranted. Secondly, there is often a lack of focus on maintaining fitness improvements post-intervention, with minimal studies assessing long term follow up of fitness. Lastly, the majority of studies requires participants to meet rigorous inclusion criteria. This required exclusion of stroke survivors with co-morbidities, and therefore may not be generalisable to the entire stroke population.

Following the publication of this review, the American Heart Association and American Stroke Association updated the physical activity guidelines for stroke in 2014\textsuperscript{50}. The updated guidelines suggest home based exercise programs be employed by future research trials in stroke. Emerging studies have been identified using tele-health in the home setting, with the aim to improve a variety of functional outcomes\textsuperscript{351-355}. However, most studies required gaming or virtual reality equipment, or lengthy training periods from a nurse or physiotherapist.

9.3 Secondary aim 2

*Compare the responses to the submaximal six-minute walk test, the graded shuttle walk test and cycle graded exercise test as measures of CRF in stroke survivors, and to compare the practicality of using these three tests as measures of CRF in stroke survivors*
During the development of the *HowFITSS?* program, it was important to consider the outcome measures used to assess the effectiveness of the program. We wanted to choose accurate, feasible and clinically relevant exercise tests. Chapter 5 presented a study that evaluated three tests of CRF in stroke survivors, including the SWT. There were no significant differences in VO$_{2\text{peak}}$ between the 6MWT, SWT and cGXT, and all tests were well tolerated by most participants. Strong correlations between outcome measures and VO$_{2\text{peak}}$ on each of the three tests of CRF suggest that performance measures may be valid indicators for fitness in this population. The performance measures could therefore be used as indicators of fitness in clinical settings. Heart rate was poorly correlated with peak oxygen consumption, and may have limitations in its use as a criterion measure of exercise intensity in stroke. The SWT has been largely unexplored in stroke, but shows potential for future use in exercise testing. There is potential particularly for stroke survivors with higher performance levels, indicated by the lack of heteroscedasticity between the SWT and cycle GXT.

### 9.3.1 Implications and Future Considerations in Research and Practice

These analyses demonstrated that all three tests are feasible indicators of CRF in stroke survivors with mild to moderate deficits. Several studies have investigated the use of the 6MWT and cycle GXT in stroke$^{82,159,169,239,242,302,303}$, with only one study using a modified version of the SWT$^{63}$. Following the promising findings in the current study, future stroke research may consider the use of the SWT as a walking test of CRF. The SWT has potential for indicating baseline fitness levels, assessing the effectiveness of interventions or for exercise prescription. It is suggested that further research be conducted to evaluate:

- The use of the SWT in stroke survivors living with disability
• The sensitivity of the SWT over time, whether it is a good indicator of changes in fitness levels following an exercise intervention
• A reliability study in a larger population of stroke survivors, with multiple measures taken over a number of days
• The use of the SWT in the acute setting such as a rehabilitation ward
• The potential use of the SWT with multiple stroke survivors at once

This study highlights that the 6MWT, SWT and cycle GXT are appropriate indicators of CRF in stroke survivors. In clinics where it is often difficult to obtain flat, uninterrupted, straight corridor space, the SWT has the advantage of requiring only 10m to perform, compared to the 30m optimal for the 6MWT. Minimal equipment is required to perform testing, and is portable should the test require relocating. As is current practice in some respiratory populations\(^56\), the SWT has potential in stroke survivors as a test of CRF in both the clinical and research setting.

9.4 Secondary aim 3

Compare cardiorespiratory fitness, walking ability, knee strength and body composition in independently ambulant, community dwelling stroke survivors to healthy age- and gender-matched comparison participants

The sample population who consented to the \textit{HowFITSS?} program were quite well-recovered, with only one participant showing a clear hemiparetic gait. This made interpretation of the results from previous chapters difficult to compare to broader stroke populations who often have motor and functional disabilities. It was therefore imperative we compared this group to age and gender matched non-stroke individuals,
which has not previously been reported. Matched pairs analysis demonstrated the stroke group performed significantly poorly on all tests, including significantly lower VO$_{2}$peak and performance measures on the 6MWT, SWT and cycle GXT. Interestingly, only two of the 15 stroke survivors who completed the cycle GXT reached the predetermined cut off point of 85%HRR. The remaining 13 predominantly stopped due to musculoskeletal reasons, suggesting that the limiting factor for this group may be compromised muscular performance rather than cardiorespiratory limitation.

The stroke group performed worse on a number of secondary outcomes, including leg strength, self-selected and fast walking speeds, despite similar muscle mass between groups. Often, the side without neurological deficit is not trained in rehabilitation as it is assumed to be normal or not requiring intervention. This study however, found deficits in both the more and less affected legs compared to non-stroke comparisons. There is an implication for strength training both sides of the body regardless of deficit. The stroke group also reported worse fatigue and depressive scores despite living fully functional, independent lives in the community.

9.4.1 Implications and Future Considerations in Research and Practice

This study demonstrated that despite no apparent functional gait deficits due to hemiparesis, the CRF, leg strength and walking speed of this group are significantly impaired compared to non-stroke comparisons. Currently data are lacking in this sub group of stroke survivors, suggesting more research is required. Future trials might investigate exercise interventions targeted at this group, with follow up over time.
Over one third of all stroke survivors are non-disabled, therefore there are significant implications for practice, including:

- Stroke survivors who are independently ambulant may experience further benefits from exercise interventions, including reducing risk of recurrent stroke.
- Simple exercise tests, such as the 6MWT or SWT to indicate CRF levels, should be administered to those who are community dwelling and independently ambulant.
- The composition of an appropriate exercise program for this group, which is easily available in the community setting is suggested.
- Despite no functional deficits, independently ambulant stroke survivors may require education on the other benefits of exercise including decreased risk of secondary stroke.

9.5 Primary aim

Assess the long term follow up outcomes of the HowFITSS? exercise program at 6- and 12-months post intervention, when minimal to no support was provided by researchers.

It has been previously recommended that exercise programs post stroke facilitate long term compliance through maintenance of active lifestyle\textsuperscript{50}. Exercise over the long term has numerous benefits, including independence and quality of life, as well as decreased mortality and likelihood of secondary stroke\textsuperscript{39,40}. However, there is minimal evidence surrounding the transition from an intensive exercise intervention to an independent, active life in the community.
In Chapter 7, I have presented a summary of our study assessing the short-term feasibility and efficacy of the HowFITSS? pilot exercise program (appendix 4). Group-by-time differences favoured the intervention group significantly for 6MWT VO$_{2peak}$ and distance achieved (primary outcome), with non-significant trends in improvement for the SWT and cGXT also. The results from this study suggest that home based, individualised interventions that require minimal therapist time are feasible, safe and capable of improving CRF in stroke over the short-term.

Chapter 8 presented the outcomes from follow-up assessments at both 6- and 12-months post exercise intervention, when minimal therapist support was provided. VO$_{2peak}$ and performance measures across all CRF tests improved from pre-intervention levels, with statistically significant improvements in the 6MWT and cGXT. Significant improvements were seen in walking speed, balance and quality of life, with maintenance of performance on all other outcome variables. Non-stroke related co-morbidities were responsible for the majority of missed assessments, with only 65% retention rate at the 12-months follow-up visit.

There are several aspects of the HowFITSS? program that may have contributed to the success in maintenance of fitness:

- A holistic lifestyle approach encouraging physical activity and decreasing sedentary, sitting time
- Tailoring the intervention to the individual so participants were performing exercises they enjoyed
- Exercises were home and community based, with no travel required
• A program handbook was provided, giving simple education regarding exercise after stroke
• Initial weekly contact from an exercise scientist (current PhD candidate), providing encouragement, motivation and feedback
• Partners and carers were encouraged to be involved in the assessment sessions

9.5.1 Implications and future considerations in research and practice

Through this thesis, we have demonstrated that the HowFITSS? home and community based program is a feasible method for improving CRF in ambulant, community dwelling stroke survivors. Based on the findings in the previous chapters, as well as the experienced gained throughout this trial, there are several recommendations for future research considerations, including:

• This is one of few studies to investigate the long term effectiveness of an individually tailored, home and community based exercise program in stroke survivors. Future studies should consider even longer-term follow up (for example 5 years).
• The current study was a follow up of a wait-list controlled trial. To assess the changes in CRF over time without an exercise intervention, randomised controlled trials with long term follow up prior to providing the control group with the program may be warranted.
• Larger sample sizes would further strengthen the evidence for this program, particularly due to high attrition rates relating to multiple co-morbidities.
• Investigators of long term follow up trials may consider the use of alternative tests of CRF, such as the SWT. The SWT is currently used in other clinical
populations due to the progressive nature of the test, and the minimal space required which may also be advantageous in stroke.

- The current study did not use objective monitors to quantify physical activity levels throughout the intervention. Use of accelerometers such as the ActivPal or Actigraph may add strength to future exercise trials by providing objective physical activity data.

- The trial was designed to be cost effective through decreasing therapist time, travel and equipment costs. To strengthen research for future implementation in health care settings, consideration of a cost analysis and cost savings may be of benefit.

- Future research is required as to the feasibility of translation and implementation of the HowFITSS? model into a program that can be provided to stroke survivors across the health care system. This includes analysis of therapist uptake, delivery, adherence and patient satisfaction.

Home and community based, individually tailored exercise programs, such as the HowFITSS? program, have great potential to improve the functional abilities, community participation and QoL of community dwelling, ambulant stroke survivors even after the intervention has ceased. This program has significant implications for practice, and has potential to complement or even replace the traditional model of one-on-one delivery. Through encouraging an active lifestyle, the HowFITSS? program is a feasible model for adherence over time. The time and cost effectiveness may be an advantage in the Australian health care system, and requires economic analysis. With the introduction and dissemination of tele-health technology, the HowFITSS? program
has greater potential to be delivered to participants at home to increase adherence while minimising therapist travel time or patient travel time.

9.5.2 Future directions for HowFITSS?

With the increased use of technology, there is potential in the future to create a HowFITSS? App. for computers, smartphones or tablets to complement the program. Previous research has reported that the use of tablets in stroke rehabilitation is feasible and acceptable, and may also make the activity programs available to those in outer suburbs and rural areas. Such an App. could add to the program in a variety of ways by the possible inclusion of some, or all, of the following:

- Instructional videos that demonstrate the activities/exercises, as well as giving options on increasing the intensity of the exercise.
- A database of exercises categorised by type.
- A communication tool to video call with the therapist. This would allow the therapist to check the patient’s technique, see the set-up of the home environment and provide motivational support.
- Digital activity diary, in which the individual could record and export physical activity completed.
- A reminder to exercise if no activity has been logged for the day. This could be received by SMS, email or through an application notification.
- Appointment reminders and a calendar to schedule in exercise.
- Questionnaires for feedback to the program.
- An online community forum for stroke survivors to connect with others who have experienced a stroke and are improving their fitness levels.
• An online blog/social media platform providing additional information on new and upcoming exercise events in the community, as well as updates on emerging research in the field.

• An in-App. option to perform the 6MWT as a self-administered, at home test following which the results could be sent to the therapist to assess changes in fitness over time.

9.6 Concluding Remarks

Exercise post stroke can provide additional benefits to traditional rehabilitation, including improved mood, increased endurance and potential prevention of secondary stroke. Most of the current evidence is obtained from studies based on intensive face-to-face interventions, which are costly and have limited feasibility over the long term. There is a significant need for feasible, clinically applicable exercise programs that can be completed at home or in the community by stroke survivors over the long term without significant time required from a therapist. This thesis thoroughly explored the current literature and developed systematic reviews, investigated various modes for exercise testing in stroke and performed assessments on non-stroke individuals to compare results. These data informed the HowFITSS? model, which contributes to the field in a unique, and novel intervention. The HowFITSS? individualised, home and community based program demonstrated promising results in the current cohort. Based on the findings from this thesis, there is great potential for the HowFITSS? program to be administered on a larger scale in the health care setting to stroke survivors in both rural and metropolitan areas.
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Chapter 11. Appendices

Appendix 1. Published manuscript of Chapter 3
Review Article

Protocol Variations and Six-Minute Walk Test Performance in Stroke Survivors: A Systematic Review with Meta-Analysis


1 University of Newcastle, Callaghan, NSW 2308, Australia
2 Hunter Medical Research Institute, New Lambton Heights, NSW 2305, Australia
3 Hunter New England Local Health District, New Lambton Heights, NSW 2305, Australia

Correspondence should be addressed to A. Dunn; ashlee.dunn@uon.edu.au

Received 30 September 2014; Revised 18 December 2014; Accepted 18 December 2014

Academic Editor: Graeme Hankey

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Objective. To investigate the use of the six-minute walk test (6MWT) for stroke survivors, including adherence to 6MWT protocol guidelines and distances achieved.

Methods. A systematic search was conducted from inception to March 2014. Included studies reported a baseline (intervention studies) or first instance (observational studies) measure for the 6MWT performed by stroke survivors regardless of time after stroke.

Results. Of 127 studies (participants \( n = 6,012 \)) that met the inclusion criteria, 64 were also suitable for meta-analysis. Only 25 studies made reference to the American Thoracic Society (ATS) standards for the 6MWT, and 28 reported using the protocol standard 30m walkway. Thirty-nine studies modified the protocol walkway, while 60 studies did not specify the walkway used. On average, stroke survivors walked \( 284 \pm 107 \) m during the 6MWT, which is substantially less than healthy age-matched individuals. The meta-analysis identified that changes to the ATS protocol walkway are associated with reductions in walking distances achieved.

Conclusion. The 6MWT is now widely used in stroke studies. The distances achieved by stroke patients indicate substantially compromised walking ability. Variations to the standard 30 m walkway for the 6MWT are common and caution should be used when comparing the values achieved from studies using different walkway lengths.

1. Introduction

Compromised walking ability is a functional limitation significantly associated with poorer community integration following stroke [1] and improving walking capacity and endurance is often a key goal of stroke rehabilitation [2–5]. Functional walking tests, such as the 6MWT, were originally developed in the 1960s and used to assess people with cardiovascular and respiratory disease [6, 7]. More recently, the 6MWT has been used to characterise and monitor changes in walking capacity following stroke. The test is commonly used as a measure of walking endurance and is a significant predictor of community ambulation and integration in stroke survivors [8].

In 2002, the American Thoracic Society (ATS) published guidelines for the 6MWT [9] with the objective of standardising the protocol to encourage further application of the 6MWT and allow direct comparisons among different studies and populations. The ATS guidelines include test indications and contraindications, safety measures, and a step-by-step protocol and provide assistance with clinical interpretation. Key components of the protocol include the test location, walkway length, measurements, and instructions. According to the ATS protocol, the test should be performed on a flat, enclosed (indoor) walkway 30 m in length. This protocol requires \( 180^\circ \) turns at either end of the walkway and additional space for turning is required. The guidelines advise that shorter walkway lengths require more directional changes and can reduce the distances achieved [9]. It is likely that the influence of directional changes may be amplified in the stroke population, who characteristically have impaired balance, asymmetrical gait patterns, and altered responses for turn preparation [8, 10, 11]. Conversely, reducing the number of directional changes may increase the distance achieved [12].
The aims of this systematic review were to synthesise the current literature that used the 6MWT and to investigate (1) the extent of its use in stroke survivors; (2) the characteristics of the stroke survivor populations studied; (3) the adherence to the ATS standard protocol; (4) the distances achieved; and (5) the influences of protocol modification and factors such as age, gender, disability, and time after stroke on distances achieved.

2. Methods

The conduct and reporting of this review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) statement [13].

2.1. Search Strategy and Selection Criteria. A systematic computer-based search was undertaken of the databases MEDLINE, CINAHL, EMBASE, PsycINFO, AMED, SPORT-Discus, and COCHRANE from inception to 24th of March, 2014. The search strategy used for MEDLINE is outlined in Table 1 and was adapted to suit each database as required. Studies were deemed eligible if they were published in English, in peer-reviewed journals, and included the distance walked during the 6MWT by stroke survivors during the baseline (intervention studies) or first instance (observational studies). The World Health Organisation [14] defines stroke as "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin" and must have been diagnosed clinically. Both ischemic and hemorrhagic stroke were included at any time after stroke. Studies reporting data from mixed neurological groups that included people after stroke were excluded. Theses and articles published in abstract form only, including conference proceedings, were also excluded.

2.2. Selection of Studies. The author A. Dunn identified and obtained abstracts from the relevant studies based on title and classified each study as being a possible inclusion or definite exclusion according to the first inclusion criterion the study failed to meet. Studies were excluded if they were a subset from a larger study using the same participants, if the distance achieved on the 6MWT was not presented as text but rather a graph or chart, or if the 6MWT distance was not reported. Full-text versions of all possible inclusion studies were then retrieved and reviewed by the author A. Dunn who classified them as “include,” “exclude,” or “unsure.” This process was then independently conducted by the second reviewer E. Nugent. For instances where there was uncertainty or disagreement between authors, a consensus decision was reached through discussion and the involvement of a third reviewer, R. Callister, if necessary.

2.3. Data Extraction and Synthesis. Author A. Dunn then extracted the following variables from included studies:

(i) study characteristics: year published, participant numbers, and gender ratio;
(ii) participant characteristics: age, gender, time since stroke, and disability score;
(iii) 6MWT: distance achieved, protocol used, assistance provided, assistive devices used, and instructions given.

2.4. Quantitative Analysis of Adherence to ATS Protocol Guidelines. To date, there is no standardised approach to assessing the quality of reporting of observational studies such as adherence to protocol guidelines. As this is a systematic review looking only at baseline values rather than interventions, assessment of conventional methodological study quality is not applicable. Therefore, for the purpose of this review, a unique two-point scale was designed. Points were awarded as follows: one point for describing the protocol used and one point for referring to the ATS standards for the 6MWT. Therefore, a study could score zero, one, or two points unless it was published prior to the ATS standards (n = 3) in which case it could only achieve a score of zero or one.

2.5. Meta-Analysis. A meta-analysis was conducted to examine the influence of the 6MWT protocol variations, as well as age (continuous, years), gender (proportion of male participants in the study), physical disability score (converted to a continuous z-score), and time since stroke (continuous, months), on the distance walked. Studies were excluded from the meta-analysis if they did not perform the 6MWT indoors, on a flat walkway, with usual walking device, or if the walkway length was not described. Included studies were pooled into three groups based on the walkway length used: <30 m, =30 m, and >30 m shuttles. Studies where the test was performed on an oval or rectangular track were pooled together to create a fourth “continuous walkway” group. The ATS standards state 30 m or 100 ft walkway, which converts
to 30.5 m. Any studies using a 30.5 m walkway were therefore included in the =30 m group. In studies that reported medians (IQRs), the medians were used as means and IQRs were converted to SDs by dividing the reported IQRs by 1.35; these approaches assume symmetrical distributions. A random-effects meta-regression was conducted where the square of each study’s standard error was used as fixed values of the sampling variance. Statistical significance was accepted at the level of $\alpha \leq 0.05$. A second meta-regression was also conducted to examine the effects of age, gender, disability, and time since stroke in only those studies that used the 30 m walkway protocol.

**3. Results**

The search across seven databases yielded 1,717 citations from which 127 articles were identified for inclusion in the review. Figure 1 details the flow of studies and reasons for exclusion throughout the selection process. Table 2 summarises the study characteristics, participant characteristics, and 6MWT results. Of the included studies the first paper to use the 6MWT in stroke survivors was reported in 1998 [39]. The use of the test has since increased rapidly, with 11 papers published from 2000 to 2004, 48 papers published from 2005 to 2009, and 67 papers published from 2010 onward. Most (98%) papers were published since the publication of the ATS guidelines in 2002.

3.1. Participant Characteristics. The 127 studies reported on a collective sample size of 6,012 participants, including 3,654 males (61%), 2,188 females (36%), and 170 (3%) not specified. The participant eligibility criteria reported in studies included the following: participants greater than 6 months after stroke ($n = 40$ studies), no significant cognitive or communicative issues ($n = 85$ studies), mild or no cardiovascular or pulmonary problems ($n = 66$ studies), no orthopaedic or musculoskeletal problems or pain ($n = 57$ studies), no other neurological conditions ($n = 42$ studies), and participants able to meet a specified minimal or maximal walking speed either overground or on a treadmill ($n = 17$ studies). Only 77 studies reported being ambulant with or without assistance as eligibility criteria; however a further nine studies reported a minimal walking speed and four studies report ability to...
<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age (SD) years</th>
<th>Time since stroke (SD)</th>
<th>Number of participants (male : female)</th>
<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards Protocol described Reporting score</th>
<th>Distance achieved (SD) meters</th>
</tr>
</thead>
<tbody>
<tr>
<td>*All et al. [16] 2009</td>
<td>6756 (9.5)</td>
<td>Days</td>
<td>41.84 (26.08)</td>
<td>25 NR</td>
<td>FIM total 100.84 (12.43)</td>
<td>ATS = No (0) Walkway = continuous circuit of 50 m circumference using 4 pt. cane = 101.4 (54.08)</td>
</tr>
<tr>
<td>*Bat cho et al. [17] 2013</td>
<td>I = 57.97 (11.02) DO = 53.25 (10.53)</td>
<td>Months</td>
<td>I = 37.7 (31.7) DO = 26.25 (10.69)</td>
<td>44 : 30 : 14</td>
<td>SIAS I = 56.5 (37–74)² DO = 54.0 (37–73)²</td>
<td>ATS = No (0) Walkway = continuous square path 52 m in total using Nordic stick = 98.04 (51.28)</td>
</tr>
<tr>
<td>Bassile et al. [18] 2003</td>
<td>64.2³</td>
<td>Years</td>
<td>0.5–6</td>
<td>5 : 02 : 03</td>
<td>MAS 5.2</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
</tr>
<tr>
<td>*Billinger et al. [9] 2012</td>
<td>61.2 (4.7)</td>
<td>Days</td>
<td>68.6 (40.1)</td>
<td>10 : 06 : 04</td>
<td>FM lower 27.4 (8.8)</td>
<td>ATS = Yes (1) Walkway = 100 ft (30.48 m) walkway (1) Total = 2</td>
</tr>
<tr>
<td>Blennerhassett and Dite [20] 2004</td>
<td>I1 = 56.3 (10.5) I2 = 53.9 (19.8)</td>
<td>Days</td>
<td>I1 = 50.1 (49.2) I2 = 36.0 (25.1)</td>
<td>30 : 17 : 13</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
</tr>
<tr>
<td>*Blen nerhassett et al. [21] 2012</td>
<td>66 (49.3–72.0)³</td>
<td>NR</td>
<td>30 : 20 : 10</td>
<td>NR</td>
<td></td>
<td>ATS = No (0) Walkway = continuous rectangular track 86 m in total (1) Total = 1</td>
</tr>
<tr>
<td>Bowden et al. [22] 2013</td>
<td>58.74 (12.97)</td>
<td>Months</td>
<td>22.70 (16.38)</td>
<td>27 : 19 : 08</td>
<td>FM 23.1 (4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
</tr>
<tr>
<td>Brock et al. [23] 2011</td>
<td>I1 = 61.3 (13.0) I2 = 56.6 (15.8)</td>
<td>Days</td>
<td>I1 = 60.3 (24.0) I2 = 63.6 (25.9)</td>
<td>26 : 19 : 07</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 12.5 m long including a purpose built ramp and step and thin foam mats (1) Total = 1</td>
</tr>
</tbody>
</table>

² SIAS = 36.5 (30.7–42.3)³
³ FM lower = 27.4 (4.0)²
⁴ SIAS = 36.5 (30.7–42.3)³
⁵ FM lower = 27.4 (4.0)²
⁶ SIAS = 36.5 (30.7–42.3)³
⁷ FM lower = 27.4 (4.0)²
⁸ SIAS = 36.5 (30.7–42.3)³
⁹ FM lower = 27.4 (4.0)²
¹⁰ SIAS = 36.5 (30.7–42.3)³
¹¹ FM lower = 27.4 (4.0)²
¹² SIAS = 36.5 (30.7–42.3)³
¹³ FM lower = 27.4 (4.0)²
¹⁴ SIAS = 36.5 (30.7–42.3)³
¹⁵ FM lower = 27.4 (4.0)²
¹⁶ SIAS = 36.5 (30.7–42.3)³
¹⁷ FM lower = 27.4 (4.0)²
¹⁸ SIAS = 36.5 (30.7–42.3)³
¹⁹ FM lower = 27.4 (4.0)²
²⁰ SIAS = 36.5 (30.7–42.3)³
²¹ FM lower = 27.4 (4.0)²
²² SIAS = 36.5 (30.7–42.3)³
²³ FM lower = 27.4 (4.0)²
²⁴ SIAS = 36.5 (30.7–42.3)³
²⁵ FM lower = 27.4 (4.0)²
²⁶ SIAS = 36.5 (30.7–42.3)³
²⁷ FM lower = 27.4 (4.0)²
²⁸ SIAS = 36.5 (30.7–42.3)³
²⁹ FM lower = 27.4 (4.0)²
³⁰ SIAS = 36.5 (30.7–42.3)³
³¹ FM lower = 27.4 (4.0)²

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age (SD) years</th>
<th>Time since stroke (SD)</th>
<th>Number of participants (male:female)</th>
<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards Protocol described Reporting score</th>
<th>Distance achieved (SD) meters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brogårdh et al. [24] 2012</td>
<td>I = 61.3 (8.5) C = 63.9 (5.8)</td>
<td>Months</td>
<td>31 25 : 06</td>
<td>I = 83.1 (3.1) I2 = 83.5 (3.2)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 305 (108) C = 393 (115)</td>
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<tr>
<td>Brogårdh et al. [25] 2012</td>
<td>64 (NR)</td>
<td>Months</td>
<td>50 41 : 09</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>303 (130)</td>
</tr>
<tr>
<td>Byun et al. [26] 2011</td>
<td>58.9 (11.9)</td>
<td>Months</td>
<td>30 19 : 11</td>
<td>K-MBI 53.6 (24.1)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>104 (96.4)</td>
</tr>
<tr>
<td>Carda et al. [27] 2011</td>
<td>I1 = 62.2 (11.7) I2 = 64.5 (12.5) I3 = 59.6 (14.3)</td>
<td>Months</td>
<td>69 34 : 35</td>
<td>FAC I1 = 3.9 (0.9) I2 = 4.0 (0.8) I3 = 3.8 (0.6)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 176.2 (98.5) I2 = 191.7 (98.6) I3 = 195.7 (81)</td>
</tr>
<tr>
<td>Carda et al. [28] 2012</td>
<td>63.9 (10.5)</td>
<td>Days</td>
<td>62 43 : 19</td>
<td>FAC 3 (2–4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td></td>
</tr>
<tr>
<td>Carroll et al. [29] 2012</td>
<td>72.4 (12.3)</td>
<td>Days</td>
<td>50 21 : 29</td>
<td>BI 100 (90–100)</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>158.6 (129.2)</td>
</tr>
<tr>
<td>*Carvalho et al. [30] 2008</td>
<td>60 (4.1)</td>
<td>Months</td>
<td>34 24 : 10</td>
<td>FM lower 30 (13–34)</td>
<td>ATS = Yes (1) Walkway = indoors and outdoors over a 30 m course (1) Total = 2</td>
<td>In 365.2 (142.6) Out 373.6 (150.8)</td>
</tr>
<tr>
<td>*Carvalho et al. [31] 2013</td>
<td>59 (5.8)</td>
<td>Months</td>
<td>41 31 : 10</td>
<td>FM lower 28 (13–34)</td>
<td>ATS = Yes (1) Walkway = 30 m walkway (1) Total = 2</td>
<td>372 (139)</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of participants (male : female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Distance achieved (SD) meters</td>
</tr>
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</tr>
<tr>
<td>Chanruengvanich et al. [32] 2006</td>
<td>I = 62.83 (7.41) C = 63.18 (7.13)</td>
<td>NR</td>
<td>62 : 42</td>
<td>NR</td>
<td>ATS = No (0) Walkway = continuous rectangular path, total distance 30 m (1) Total = 1</td>
<td>I = 391.99 (82.6) C = 341.6 (89.97)</td>
</tr>
<tr>
<td>Da Silva et al. [33] 2013</td>
<td>54 (9) Years 78</td>
<td>12 : 06</td>
<td>FM 163.3</td>
<td>ATS = Yes (1) Walkway = NR (0) Total = 1</td>
<td>274.2</td>
<td></td>
</tr>
<tr>
<td>Daly et al. [34] 2006</td>
<td>I = 57.7 (11.9) C = 63.6 (10.4)</td>
<td>Years I = 3.6 (3.8) C = 3.3 (2.1)</td>
<td>29 : 22</td>
<td>FM knee flex subscale I = 4 (2) C = 3 (2)</td>
<td>ATS = No (0) Walkway = 30.5 m walkway (1) Total = 1</td>
<td>1 = 186.6 (75.6) C = 128.3 (83.8)</td>
</tr>
<tr>
<td>Daly et al. [35] 2011</td>
<td>I = 59 (NR) C = 62 (NR)</td>
<td>NR</td>
<td>44 : 32</td>
<td>FIM loco/mob I = 30 (2.75) C = 30 (8.50)</td>
<td>ATS = Yes (1) Walkway = 30.5 m walkway (1) Total = 2</td>
<td>352 (136)</td>
</tr>
<tr>
<td>Danielsson et al. [36] 2011</td>
<td>59.7 (8.1) Years 8.5 (0.9)</td>
<td>31 : 22</td>
<td>FM lower 29 (12)</td>
<td>ATS = No (0) Walkway = 50 m walkway (1) Total = 1</td>
<td>1 = 261.5 (128.4)</td>
<td></td>
</tr>
<tr>
<td>Dean et al. [37] 2001</td>
<td>62.7 (8.5)</td>
<td>NR</td>
<td>14 : 08</td>
<td>NR</td>
<td>ATS = No (published prior to ATS) Walkway = 50 m walkway (1) Total = 1</td>
<td></td>
</tr>
<tr>
<td>Donovan et al. [38] 2008</td>
<td>61.3 (11.1) Months 46.5 (32.9)</td>
<td>30 : 21</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 3 environments: Clinic = 244.4 (66.4) clinic (150 m walkway), outdoors and in mall (1) Total = 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duncan et al. [39] 1998</td>
<td>I = 673 (9.6) C = 678 (7.2)</td>
<td>Days I = 66 (NR) C = 56 (NR)</td>
<td>20</td>
<td>FM lower I = 21.7 (NR) C = 23.2 (NR)</td>
<td>ATS = No (published prior to ATS) Walkway = NR (0) Total = 0</td>
<td>I = 149.66 (NR)</td>
</tr>
</tbody>
</table>

Table 2: Continued.
### Table 2: Continued.

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age (SD) years</th>
<th>Time since stroke (SD)</th>
<th>Number of participants (male : female)</th>
<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards Protocol described</th>
<th>Reporting score</th>
<th>Distance achieved (SD) meters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duncan et al. [40] 2003</td>
<td>I = 68.5 (9) C = 70.2 (11.4) D = 74.6 (9.8)</td>
<td>Days I = 77.5 (28.7) C = 73.5 (27.2) D = 84.0 (27.2)</td>
<td>100</td>
<td>FM lower I = 24.1 (3.7) C = 23.7 (3.5) D = 26.0 (2.9)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td></td>
<td>I = 238.0 (103.9) C = 215.6 (94.8) D = 244.1 (88.6)</td>
</tr>
<tr>
<td>Duncan et al. [41] 2011</td>
<td>I1 = 60.1 (12.3) I2 = 63.3 (12.5) I3 = 62.6 (13.3)</td>
<td>Days I1 = 64.1 (8.3) I2 = 64.2 (9.0) I3 = 62.9 (8.0)</td>
<td>408</td>
<td>FM leg I1 = 23.7 (6.7) I2 = 24.8 (6.4) I3 = 24.7 (6.3)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td></td>
<td>I1 = 124.1 (77.5) I2 = 125.7 (81.8) I3 = 126.3 (75.0)</td>
</tr>
<tr>
<td>*Eng et al. [42] 2002</td>
<td>62.6 (8.5)</td>
<td>Years 4.4 (3.0)</td>
<td>25</td>
<td>CM lower 8.9 (2.4)</td>
<td>ATS = No (published prior to ATS) Walkway = continuous 42 m rectangular path (1) Total = 1</td>
<td></td>
<td>267.7 (89.7)</td>
</tr>
<tr>
<td>*Eng et al. [43] 2004</td>
<td>62.5 (8.6)</td>
<td>Years 3.5 (2.0)</td>
<td>12</td>
<td>CM lower 9.4 (2.5)</td>
<td>ATS = No (0) Walkway = continuous 42 m rectangular path (1) Total = 1</td>
<td></td>
<td>378.3 (123.1)</td>
</tr>
<tr>
<td>*Flansbjer et al. [4] 2005</td>
<td>M = 59 (7) F = 58 (5)</td>
<td>Months M = 16 (5) F = 18 (5)</td>
<td>50</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 30 m walkway (1) Total = 1</td>
<td>T1 = 384 (132) T2 = 398 (136)</td>
<td></td>
</tr>
<tr>
<td>*Flansbjer et al. [44] 2008</td>
<td>I = 61 (5) C = 60 (5)</td>
<td>Months I = 18.9 (7.9) C = 20.0 (11.6)</td>
<td>24</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 30 m walkway (1) Total = 1</td>
<td>I = 228 (137) C = 234 (134)</td>
<td></td>
</tr>
<tr>
<td>*Forsberg and Nilsagård [45] 2013</td>
<td>68.1 (11.2)</td>
<td>Years 4.6 (5.5)</td>
<td>67</td>
<td>RMI 37 (35–39)</td>
<td>ATS = No (0) Walkway = 30 m walkway (1) Total = 1</td>
<td></td>
<td>247 (160–342)</td>
</tr>
<tr>
<td>Fritz et al. [46] 2013</td>
<td>I = 67.6 (9.3) C = 64.5 (10.1)</td>
<td>Years I = 2.5 (2.6) C = 3.6 (3.2)</td>
<td>28</td>
<td>FM I = 68.5 (21.7) C = 65.6 (18.0)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td></td>
<td>I = 285.4 (158.7) C = 263.2 (178.5)</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of participants (male : female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
<td>Reporting score</td>
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</tr>
<tr>
<td>*Fulk et al. [47] 2008</td>
<td>66.3 (14.3)</td>
<td>Days 33.7 (17.8)</td>
<td>37 (20:17)</td>
<td>FIM loco 5 (2–7)</td>
<td>ATS = No (0)</td>
<td>Walkway = 150 feet (45.72 m) at one site, 250 feet (76.20 m) at another two sites (1)</td>
<td>Total = 1</td>
</tr>
<tr>
<td>*Fulk et al. [48] 2010</td>
<td>65.7 (11.9)</td>
<td>Months 42.1 (36.1)</td>
<td>19</td>
<td>NR</td>
<td>FM lower 28.7 (5.7)</td>
<td>ATS = Yes (1)</td>
<td>Walkway = continuous oval course 30 m in circumference (1)</td>
</tr>
<tr>
<td>Geroin et al. [49] 2011</td>
<td>I1 = 63.6 (6.7) I2 = 63.3 (6.4) I3 = 61.1 (6.3)</td>
<td>Months I1 = 25.7 (6.0) I2 = 26.7 (5.1) I3 = 26.9 (5.8)</td>
<td>30</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>Gerrits et al. [50] 2009</td>
<td>54 (10)</td>
<td>Months 22 (18)</td>
<td>18</td>
<td>NR</td>
<td>FAC 4.6 (SEM = 0.1)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
</tr>
<tr>
<td>*Gjellesvik et al. [51] 2012</td>
<td>48.9 (10.6)</td>
<td>Years 72 (7.5)</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = 50 m walkway (1)</td>
</tr>
<tr>
<td>Globas et al. [52] 2012</td>
<td>I = 68.6 (6.7) C = 68.7 (6.1)</td>
<td>Months I = 60.2 (46.6) C = 70.0 (67.4)</td>
<td>36</td>
<td>BI I = 91.7 (9.7) C = 88.3 (9.6)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>Gordon et al. [53] 2013</td>
<td>I = 63.4 (9.4) C = 64.9 (11.1)</td>
<td>Months I = 12.8 (3.6) C = 11.8 (3.6)</td>
<td>128</td>
<td>BI I = 94.3 (8.1) C = 91.5 (9.7)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>Hidler et al. [54] 2009</td>
<td>I = 59.9 (11.3) C = 54.6 (9.4)</td>
<td>Days I = 110.9 (62.5) C = 138.9 (60.9)</td>
<td>63</td>
<td>RMI I = 9.5 (0.5) C = 11.3 (0.6)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>Hinson et al. [55] 2007</td>
<td>Bl = 62 (8) Wh = 66 (9)</td>
<td>Months Bl = 47 (57) Wh = 44 (54)</td>
<td>118</td>
<td>NR</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of participants (male : female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described Reporting score</td>
<td>Distance achieved (SD) meters</td>
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</tr>
<tr>
<td>*Hoang et al. [56] 2012</td>
<td>64.6 (11.2)</td>
<td>Months 40 (42.2)</td>
<td>32 21 : 11</td>
<td>BI 89.7 (9.9)</td>
<td>ATS = No (0) Walkway = continuous 123 m circuit (1) Total = 1</td>
<td>201.8 (110.5)</td>
<td></td>
</tr>
<tr>
<td>Hornby et al. [57] 2008</td>
<td>I1 = 57 (10) I2 = 57 (11)</td>
<td>Months I1 = 50 (51) I2 = 73 (87)</td>
<td>48 30 : 18</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 170 (86) I2 = 170 (86)</td>
<td></td>
</tr>
<tr>
<td>Hwang et al. [58] 2013</td>
<td>I = 54.6 (9.2) 2 = 54.9 (12.9)</td>
<td>Months 1 = 35.1 (18.8) 2 = 36.7 (19.0)</td>
<td>47 27 : 20</td>
<td>DGI 1 = 20.5 (2.7) 2 = 15.8 (4.8)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>1 = 392.4 (68.9) 2 = 268.6 (74.5)</td>
<td></td>
</tr>
<tr>
<td>*Iosa et al. [59] 2012</td>
<td>62.7 (14.7)</td>
<td>Days 101 (36)</td>
<td>12 08 : 04</td>
<td>BI 70 (50–88)*</td>
<td>ATS = No (0) Walkway = 20 m walkway (1) Total = 1</td>
<td>226 (111)</td>
<td></td>
</tr>
<tr>
<td>Janssen et al. [60] 2008</td>
<td>I1 = 54.2 (10.7) I2 = 55.3 (10.4)</td>
<td>Months I1 = 12.3 (5.4) I2 = 18.3 (9.9)</td>
<td>12 06 : 06</td>
<td>FAC I1 = 4.5 (0.5) I2 = 4.7 (0.5)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 160.3 (134.4) I2 = 187.3 (92.0)</td>
<td></td>
</tr>
<tr>
<td>Jin et al. [61] 2012</td>
<td>I = 57 (6) C = 56 (7)</td>
<td>Months I = 18.5 (5.2) C = 17.9 (4.8)</td>
<td>133 94 : 39</td>
<td>RMI I = 10.3 (1.4) C = 10.2 (1.4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 212.0 (63.5) C = 212.2 (50.1)</td>
<td></td>
</tr>
<tr>
<td>*Kang et al. [62] 2012</td>
<td>I1 = 55.9 (6.5) I2 = 56.3 (7.6) C = 56.1 (7.8)</td>
<td>Months I1 = 14.1 (4.4) I2 = 13.5 (4.0) C = 13.1 (7.4)</td>
<td>30 16 : 14</td>
<td>NR</td>
<td>ATS = No (0) Walkway = continuous 50 m track (1) Total = 1</td>
<td>I1 = 240.3 (20.9) I2 = 237.7 (25.4) C = 239.1 (22.0)</td>
<td></td>
</tr>
<tr>
<td>Kelley et al. [63] 2013</td>
<td>65.75 (9.48)</td>
<td>Years 2.87 (NR)</td>
<td>20 13 : 07</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>51.61 (26.15)</td>
<td></td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of participants (male : female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Protocol described</td>
<td>Reporting score</td>
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</tr>
<tr>
<td>*Kelly et al. [1] 2003</td>
<td>66 (48–73)x</td>
<td>Days 30 (19–39)x</td>
<td>17 13 : 04</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = 20 m walkway (1)</td>
<td>Total = 1</td>
</tr>
<tr>
<td>*Kim et al. [64] 2014</td>
<td>62.2 (11.7)</td>
<td>Days 32.6 (24.7)</td>
<td>55 37 : 18</td>
<td>KM-BI 74 (176)</td>
<td>ATS = No (0)</td>
<td>Walkway = 50 m walkway (1)</td>
<td>Total = 1</td>
</tr>
<tr>
<td>*Kling and Gajewski [65] 2009</td>
<td>57.6 (11.0)</td>
<td>Months 45.4 (42.8)</td>
<td>26 14 : 12</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = 100 feet (30.48 m) walkway (1)</td>
<td>Total = 1</td>
</tr>
<tr>
<td>Khuding et al. [66] 2011</td>
<td>63.7 (9.1)</td>
<td>Months 50.4 (37.9)</td>
<td>9 05 : 04</td>
<td>FM 87.7 (29.1)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>Kuys et al. [67] 2011</td>
<td>I = 63 (14) C = 72 (17)</td>
<td>Days 1 = 52 (32) C = 49 (30)</td>
<td>30 12 : 18</td>
<td>Modified BI I = 76 (18) C = 80 (9)</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>Lam et al. [68] 2010</td>
<td>66.8 (SEM = 1.1)</td>
<td>Months 59.0 (SEM = 9.28)</td>
<td>52 34 : 18</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>Total = 0</td>
</tr>
<tr>
<td>*Langhammer et al. [69] 2006</td>
<td>74 (NR)</td>
<td>NR</td>
<td>57 31 : 26</td>
<td>MAS walk 3.5 (2.5)</td>
<td>ATS = No (0)</td>
<td>Walkway = 85 m walkway (1)</td>
<td>Total = 1</td>
</tr>
<tr>
<td>*Langhammer et al. [70] 2008</td>
<td>I1 = 76.0 (12.7) I2 = 72.0 (13.6)</td>
<td>NR</td>
<td>75 43 : 32</td>
<td>BI I1 = 56.6 (38.9) I2 = 66.0 (39.0)</td>
<td>ATS = No (0)</td>
<td>Walkway = 85 m walkway in hospital and different institutions including patients’ homes or outdoors (1)</td>
<td>Total = 1</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of participants (male:female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards</td>
<td>Distance achieved (SD) meters</td>
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</tr>
<tr>
<td>*Langhammer and Stanghelle [71] 2010</td>
<td>I1 = 74.0 (13.3) I2 = 75.0 (10.4)</td>
<td>Days</td>
<td>I = 49 (1,034) I2 = 349 (820)</td>
<td>MAS i3 I1 = 5.4 (NR) I2 = 5.3 (NR)</td>
<td>ATS = No (0) Walkway = 85 m walkway (1) Total = 1</td>
<td>I1 = 277.7 (139.9) I2 = 299.4 (159.3)</td>
<td></td>
</tr>
<tr>
<td>Lee et al. [72] 2005</td>
<td>69 (11)</td>
<td>Months 43 (32)</td>
<td>II 09 : 02</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>324.4 (173.1)</td>
<td></td>
</tr>
<tr>
<td>Lee et al. [73] 2008</td>
<td>I1 = 672 (10.6) I2 = 62.9 (9.3) I3 = 60.5 (10.6) C = 65.3 (6.0)</td>
<td>Months I1 = 52.4 (2.2) I2 = 44.2 (63.9) I3 = 63.2 (40.5) C = 65.8 (42.3)</td>
<td>48 28 : 20</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 249.3 (158.3) I2 = 239.8 (141.0) I3 = 266.0 (123.5) C = 273.2 (162.1)</td>
<td></td>
</tr>
<tr>
<td>Lord et al. [74] 2008</td>
<td>I1 = 64.2 (14.8) I2 = 60.7 (176)</td>
<td>Days I1 = 83.1 (29.8) I2 = 80.3 (33.0)</td>
<td>30 18 : 12</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 125.1 (71.0) I2 = 142.3 (89.4)</td>
<td></td>
</tr>
<tr>
<td>*MacKay-Lyons et al. [75] 2013</td>
<td>I1 = 61.5 (15.4) I2 = 59.0 (12.7)</td>
<td>Days I1 = 23.3 (5.7) I2 = 23.1 (4.4)</td>
<td>50 29 : 21</td>
<td>CM I1 = 4.8 (1.5) I2 = 4.9 (1.2)</td>
<td>ATS = Yes (1) Walkway = continuous 100 m walkway (1) Total = 2</td>
<td>I1 = 188.7 (82.3) I2 = 195.5 (77.7) I3 = 273.2 (162.1)</td>
<td></td>
</tr>
<tr>
<td>Macko et al. [76] 2005</td>
<td>I = 63 (10) C = 64 (8)</td>
<td>Months I1 = 35 (29) C = 39 (59)</td>
<td>61 43 : 18</td>
<td>RMI I1 = II.3 (0.4) C = II.7 (0.4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 232.0 (22.3) C = 258.5 (33.2)</td>
<td></td>
</tr>
<tr>
<td>Macko et al. [77] 2008</td>
<td>70 (1.7)</td>
<td>Months 56 (19)</td>
<td>20 09 : II</td>
<td>BI 74.8 (4)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>T1 = 116 (15) T2 = 113 (14)</td>
<td></td>
</tr>
<tr>
<td>*Maeda et al. [78] 2009</td>
<td>45 (7)</td>
<td>Months 19 (9)</td>
<td>18 15 : 03</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 30 m walkway (1) Total = 1</td>
<td>AFO = 174 (77) W/O AFO = 140 (69)</td>
<td></td>
</tr>
<tr>
<td>Study Year</td>
<td>Age (SD) years</td>
<td>Time since stroke (SD)</td>
<td>Number of participants (male : female)</td>
<td>Disability scale Score (SD)</td>
<td>Referenced ATS standards Protocol described</td>
<td>Distance achieved (SD) meters</td>
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</tr>
<tr>
<td>*Marsden et al. [79] 2010</td>
<td>I = 70.0 (9.0) C = 73.1 (9.3) Months</td>
<td>I = 37.2 (26.7) C = 39.0 (23.6)</td>
<td>25 : 19 : 06</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 20 m walkway (1)</td>
<td>301.6 (121.5) C = 349.1 (124.2)</td>
<td></td>
</tr>
<tr>
<td>Mayo et al. [80] 2013</td>
<td>I1 = 67.7 (14.4) I2 = 67.8 (12.3) Days</td>
<td>I1 = 265.4 (131.8) I2 = 252.0 (165.3)</td>
<td>87 : 60 : 27</td>
<td>NR</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I1 = 323.4 (19.5) I2 = 321.6 (17.1)</td>
<td></td>
</tr>
<tr>
<td>Mehrholz et al. [81] 2006</td>
<td>54* Weeks Range: 3–12</td>
<td>6 : 05 : 01</td>
<td>FAC 2 (0)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>96.7 (33.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mehrholz et al. [82] 2007</td>
<td>62.8 (10.2) Days</td>
<td>30.6 (15.5)</td>
<td>55 : 40 : 15</td>
<td>RMI 2.51 (1.62)</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>15.9 (34.3)</td>
<td></td>
</tr>
<tr>
<td>*Michael et al. [83] 2009</td>
<td>71 (NR) Years 75 (NR)</td>
<td>10 : 07 : 03</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 100 feet (30.48 m walkway (1) Total = 1</td>
<td>256 (33.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Moriello et al. [85] 2011</td>
<td>67 (12.3) Months</td>
<td>3.9 (1.6)</td>
<td>63 : 43 : 20</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 15 m walkway (1) Total = 1</td>
<td>277 (136)</td>
<td></td>
</tr>
<tr>
<td>Mudge et al. [86] 2009</td>
<td>I = 76 (39–89)x C = 71 (44–86)x Years</td>
<td>I = 3.33 (0.6–13.3)x C = 5.8 (0.5–18.7)x</td>
<td>58 : 32 : 26</td>
<td>RMI I = 14 (6.1–15)x C = 13.5 (9–15)x</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>I = 263 (110) C = 201 (99)</td>
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<td>Mudge and Stott [87] 2009</td>
<td>67.4 (12.5) Months</td>
<td>66 (61)</td>
<td>49 : 29 : 20</td>
<td>RMI 13 (6–15)x</td>
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<td>*Muren et al. [88] 2008</td>
<td>58 (9)</td>
<td>Months 60 (27)</td>
<td>30 : 17</td>
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<td>ATS = Yes (1) Walkway = 30 m walkway (1) Total = 2</td>
<td>353 (137)</td>
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<td>Murtezani et al. [89] 2009</td>
<td>49.8 (17.4)</td>
<td>NR</td>
<td>44 : 26</td>
<td>BI (68 (20.5))</td>
<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>336.6 (82.2)</td>
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<td>*Ng and Hui-Chan [90] 2005</td>
<td>61.1 (6.8)</td>
<td>Years 5.6 (3.3)</td>
<td>II 06 : 05</td>
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<td>*Ng and Hui-Chan [91] 2009</td>
<td>I1 = 56.5 (8.2) I2 = 57.8 (7.3) I3 = 56.9 (8.6) C = 55.5 (8.0)</td>
<td>Years I1 = 4.9 (3.9) I2 = 4.7 (2.8) I3 = 4.3 (3.8) C = 5.0 (3.0)</td>
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<td>NR</td>
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<td>58.5 (6.1)</td>
<td>Years 7.0 (6.5)</td>
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<td>NR</td>
<td>ATS = No (0) Walkway = performed on 10, 20, and 30 m walkways turning towards affected and nonaffected sides separately (1) Total = 1</td>
<td>227.32 (79.07)</td>
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<td>57.4 (7.8)</td>
<td>Years 5.2 (3.7)</td>
<td>62 : 51</td>
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<td>Nolan et al. [93] 2009</td>
<td>53.44 (11.50)</td>
<td>Months 54.89 (36.98)</td>
<td>18 : 14</td>
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<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
<td>252.2 (95.31)</td>
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<td>*Olawale et al. [94] 2011</td>
<td>II = 56.8 (6.4) I2 = 56.8 (8.3) C = 572 (5.9)</td>
<td>Months II = 10.2 (6.9) I2 = 10.7 (6.8) C = 10.3 (5.9)</td>
<td>60 : 34</td>
<td>NR</td>
<td>ATS = No (0) Walkway = 15 × 10 m rectangular course (1) Total = 1</td>
<td>111.43 (50.96)</td>
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* indication refers to the study where the data was collected.
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<th>Study Year</th>
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<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards</th>
<th>Distance achieved (SD) meters</th>
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<td>Ouellette et al. [95] 2004</td>
<td>I = 65.8 (2.5) C = 66.1 (2.1)</td>
<td>Months I = 31.8 (3.3) C = 25.6 (4.0)</td>
<td>42 28:14</td>
<td>LLFDI I = 52.7 (2.3) C = 55.6 (2.2)</td>
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<td>I1 = 56.8 (8.6) I2 = 56.3 (8.6)</td>
<td>Days I1 = 22.5 (8.2) I2 = 23.5 (7.8)</td>
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<td>53 (17)</td>
<td>Months 18 (11) 8 06 : 02</td>
<td>FM 25 (4.5)</td>
<td>ATS = No (0) Walkway = 30 m walkway (1) Total = 1</td>
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<td>Pang et al. [98] 2005</td>
<td>I = 65.8 (9.1) C = 64.7 (8.4)</td>
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<td>63 37 : 26</td>
<td>NR</td>
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<td>I = 328.1 (143.5) C = 304.1 (123.8)</td>
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<td>*Park et al. [99] 2011</td>
<td>I = 59.38 (8.46) C = 56.92 (7.79)</td>
<td>Months I = 28.08 (12.59) C = 28.67 (17.96)</td>
<td>25 12:13</td>
<td>WAQ I = 46.38 (10.38) C = 48.75 (10.15)</td>
<td>ATS = No (0) Walkway = 20 m walkway (1) Total = 1</td>
<td>I = 166.23 (58.29) C = 151.83 (69.95)</td>
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<td>*Patterson et al. [100] 2007</td>
<td>64 (10)</td>
<td>Months 48 (59) 74 43 : 31</td>
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<td>64 (8)</td>
<td>Months 20.55 (64.0) 39 25 : 14</td>
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<td>*Peurala et al. [102] 2005</td>
<td>I1 = 53.3 (8.9) I2 = 51.2 (7.9) I3 = 52.3 (6.8)</td>
<td>Years I1 = 2.6 (2.4) I2 = 2.4 (2.6) I3 = 4.0 (5.8)</td>
<td>45 37 : 08</td>
<td>FIM I1 = 99.2 (12.8) I2 = 106.9 (10) I3 = 107.0 (11.4)</td>
<td>ATS = No (0) Walkway = 54 m walkway (1) Total = 1</td>
<td>I1 = 127.1 (87.2) I2 = 152.3 (89.6) I3 = 111.8 (57.3)</td>
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<td>Referred ATS standards Reporting score</td>
<td>Distance achieved (SD) meters</td>
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<td>*Pohl et al. [12] 2002</td>
<td>72.1 (10.2)</td>
<td>Days 73.3 (26.8)</td>
<td>72 40 : 32</td>
<td>FM lower 24 (3.8)</td>
<td>ATS = No (0) Walkway = 100 feet (30.48 m) walkway (1) Total = 1</td>
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<td>Polese et al. [103] 2013</td>
<td>56.4 (12.5)</td>
<td>Months 64.8 (53.6)</td>
<td>98 54 : 44</td>
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<td>*Pradon et al. [104] 2013</td>
<td>53.3 (13.7)</td>
<td>Months 16 (8)</td>
<td>24 12 : 12</td>
<td>NR</td>
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<td>Rabadi et al. [105] 2008</td>
<td>I1 = 75.00 (10.58) I2 = 73.58 (13.02)</td>
<td>Days I1 = 16.36 (15.70) I2 = 14.10 (11.23)</td>
<td>I16 68 : 48</td>
<td>FIM motor I1 = 25.93 (12.41) I2 = 25.93 (11.78)</td>
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<td>I1 = 26.69 (48.77) I2 = 29.16 (38.56)</td>
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<td>Rand et al. [106] 2009</td>
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<td>40 13 : 27</td>
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<td>Ryan et al. [107] 2011</td>
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<td>Months 39 (7)</td>
<td>70 39 : 31</td>
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<td>ATS = No (0) Walkway = NR (0) Total = 0</td>
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<td>Ryan et al. [108] 2011</td>
<td>I = 62.8 (10.3) C = 60.7 (12.8)</td>
<td>Days I = 21.5 (8.7) C = 19.7 (16.8)</td>
<td>44 35 : 09</td>
<td>CM I = 4.2 (1.1) C = 4.1 (1)</td>
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<td>I = 190 (176) C = 270 (236)</td>
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<td>*Salbach et al. [109] 2004</td>
<td>I1 = 71 (12) I2 = 73 (8)</td>
<td>Days I1 = 239 (83) I2 = 217 (73)</td>
<td>91 56 : 35</td>
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<td>ATS = No (0) Walkway = 20 m walkway (1) Total = 1</td>
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<td>16 14 : 02</td>
<td>CM leg 5 (1.4)</td>
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<td>*Schmid et al. [111] 2012</td>
<td>64.06 (8.78)</td>
<td>Months 52.00 (42.14)</td>
<td>77 58:19</td>
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<td>Severinsen et al. [112] 2011</td>
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<td>Months 18 (6)</td>
<td>48 35:13</td>
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<td>*Sibley et al. [113] 2008</td>
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<td>Days 52.4 (13.6)</td>
<td>26 16:10</td>
<td>FIM 107.1 (10.2)</td>
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<td>Simpson et al. [114] 2011</td>
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<td>80 58:22</td>
<td>NR</td>
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<td>*Singh et al. [115] 2013</td>
<td>I = 65.4 (9.8) C = 670 (8.4)</td>
<td>Months I = 40.5 (41.8) C = 34.9 (23.6)</td>
<td>28 16:12</td>
<td>BI I = 87.00 (15.45) C = 92.31 (12.69)</td>
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<td>23 11:12</td>
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<td>*Stuart et al. [118] 2009</td>
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<td>78 54:24</td>
<td>BI I = 79.5 (2.6) C = 85.4 (2.0)</td>
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<td>Sullivan et al. [119] 2007</td>
<td>I1 = 60.6 (13.7) I2 = 63.4 (8.6) I3 = 58.2 (15.2) I4 = 61.4 (11.2)</td>
<td>Months I1 = 27.5 (16.1) I2 = 28.4 (19.0) I3 = 23.1 (15.0) I4 = 20.7 (14.4)</td>
<td>80 I1 = 24.5 (5.5) I2 = 24.4 (4.5) I3 = 24.2 (4.0) I4 = 22.1 (6.3)</td>
<td>FM lower I1 = 24.5 (5.5) I2 = 24.4 (4.5) I3 = 24.2 (4.0) I4 = 22.1 (6.3)</td>
<td>ATS = No (0) Walkway = continuous, 18 m oval walkway (1) Total = 1</td>
<td>I1 = 189.3 (99.9) I2 = 170.0 (115.2) I3 = 187.6 (99.9) I4 = 190.0 (135.4)</td>
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<td>64.6 (14.4)</td>
<td>Days 50.3 (17) 36</td>
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<td>I = 64.7 (SEM = 3.6) C = 65.7 (SEM = 2.3)</td>
<td>Days I = 191 (SEM = 3.8) C = 149 (SEM = 2.3) 36</td>
<td>NR</td>
<td>FIM I1 = 84.0 (SEM = 4.1) I2 = 83.9 (SEM = 4.2)</td>
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<td>I1 = 207.0 (46.6) C = 198.9 (40.2)</td>
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<td>I = 61 (10) C = 58 (5)</td>
<td>Days I = 65 (37) I = 93 (60) 48</td>
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<td>FIM I1 = 123 (5) I = 122 (5)</td>
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<td>I1 = 444 (90) C = 438 (101)</td>
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<td>Toledano-Zarh et al. [123] 2011</td>
<td>I = 65 (8) C = 65 (12)</td>
<td>Days I = 11 (5) C = 11 (4) 28</td>
<td>21 : 07</td>
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<td>I = 56 (10) C = 58 (10)</td>
<td>Days I = 91 (42) C = 103 (51) 250</td>
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<td>RMI I1 = 12.67 (1.58) I2 = 12.67 (1.58)</td>
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<td>Days 52 (87)</td>
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<td>LEFS 33 (18)</td>
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<tr>
<td>Verma et al. [128] 2011</td>
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<td>Weeks 6.3 (3.2)</td>
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<td>BI I = 60 (9.82)</td>
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<tr>
<td>Westlake and Patten [129] 2009</td>
<td></td>
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<td>I1 = 43.8 (26.8)  I2 = 36.8 (20.3)</td>
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<td>FM lower I1 = 23.0 (4.3)  I2 = 21.4 (5.1)</td>
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<td>Days 266 (38)</td>
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<td>White et al. [131] 2013</td>
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<td>Years 2.11 (1.76)</td>
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<td>Wing et al. [132] 2008</td>
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<tr>
<td>Yang et al. [133] 2006</td>
<td></td>
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<td>Months</td>
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<td>Yang et al. [134] 2014</td>
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<td>I1 = 11.1 (8.1)  I2 = 11.1 (9.7)</td>
<td>30</td>
<td>BI I1 = 17.4 (2.2)  I2 = 16.5 (3.8)</td>
</tr>
</tbody>
</table>
Table 2: Continued.

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age (SD) years</th>
<th>Time since stroke (SD)</th>
<th>Number of participants (male : female)</th>
<th>Disability scale Score (SD)</th>
<th>Referenced ATS standards</th>
<th>Protocol described</th>
<th>Reporting score</th>
<th>Distance achieved (SD) meters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yiu et al. [135] 2012</td>
<td>67.41 (10.13)</td>
<td>Days 96.9 (69.0)</td>
<td>98 : 27</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = NR (0)</td>
<td>267.65 (139.53)</td>
<td></td>
</tr>
<tr>
<td>Zalewski and Dvorak [136] 2011</td>
<td>71.3 (9.5)</td>
<td>NR</td>
<td>17 : 03</td>
<td>NR</td>
<td>ATS = No (0)</td>
<td>Walkway = continuous 200 m track (1)</td>
<td>258.5 (146.0)</td>
<td></td>
</tr>
<tr>
<td>Zedlitz et al. [137] 2012</td>
<td>54.8 (9.1)</td>
<td>I1 = 4.4 (4.2)</td>
<td>83</td>
<td>MI</td>
<td>ATS = Yes (1)</td>
<td>Walkway = NR (0)</td>
<td>I1 = 438 (123)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>55.6 (8.8)</td>
<td>I2 = 3.3 (3.9)</td>
<td>43 : 40</td>
<td>90.1 (12.1)</td>
<td></td>
<td></td>
<td>I2 = 437 (107)</td>
<td></td>
</tr>
</tbody>
</table>

*Included in meta-analysis; † converted from feet to meters; ‡ calculated from individual data; § median (IQR); AFO = ankle-foot orthoses; ATS = American Thoracic Society; BI = Barthel Index; C = control; CM = Chedoke-McMaster; DGI = Dynamic Gait Index; DO = Drop Out group; FAC = Functional Ambulation Category; FIM = Functional Independence Measure; FM = Fugl-Meyer; HFO = hip flexor orthoses; I = intervention; K-MBI = Korean Modified-Barthel Index; LEFS = Lower Extremity Functional Scale; LLFDI = Late-Life Function and Disability Instrument; MAS = Motor Assessment Scale; MI = Motricity Index; NR = not reported; SA-SIP = Stroke Adapted Sickness Impact Profile; SEM = Standard Error of the Mean; SIAS = Stroke Impairment Assessment Set; WAQ = Walking Ability Questionnaire.
walk on a treadmill as inclusion criteria. These criteria imply the ability to walk, even if it is not explicitly stated.

Participant mean ages (SD) ranged from 45 (7) [78] to 76 (13) [70] years, and mean time since stroke varied from 11 (4) days [123] to 8.5 (0.9) years [36]. Thirteen studies did not specify time after stroke. Most studies included participants either within 6 months after stroke (n = 32), or 1-3 years (n = 27) or more than 3 years after stroke (n = 50), with much smaller numbers in the 6-12-month range (n = 9). A disability score was reported in only 58% of all studies. Of those that did report degree of disability, 12% reported the use of more than one scale. Common disability scales reported in these studies were the Fugl-Meyer Assessment (FM) (n = 24), Barthel Index (BI) (n = 13), Functional Independence Measure (FIM) (n = 12), Rivermead Mobility Index (n = 10), Functional Ambulatory Category (FAC) (n = 8), Chedoke McMaster (n = 6), Motor Assessment Scale (MAS) (n = 6), and the Motricity Index (MI) (n = 3). Other scales included the Walking Ability Questionnaire (n = 1), Dynamic Gait Index (DGI) (n = 1), the Late-Life Function and Disability Instrument (LLFDI) (n = 1), and the Modified Korean Barthel Index (n = 2). Subscale specific lower-limb measures were preferred in the meta-analysis, and these were available in the FM (motricity lower limb, lower extremity) (n = 10), FIM (mobility, walking capacity, and locomotion) (n = 7), Chedoke McMaster (leg) (n = 5), and MAS (walking) (n = 3) only.

3.2. Context of the 6MWT. A variety of terms were used to describe the purpose of the 6MWT, with common descriptors being a test of endurance (n = 26), capacity (n = 22), function (n = 21), performance (n = 6), and ability (n = 5). Twenty-four studies did not report the purpose of conducting the 6MWT in their study. On several occasions the test was performed in a different context or for a different purpose to that described in the ATS guidelines. The 6MWT was performed: to induce fatigue [124]; over a variety of obstacles such as foam mats and purpose built ramps [23]; and in nonstandard locations such as outdoors [30, 130, 138] including suburban streets or shopping centres [38]. Walking distances achieved in outdoor locations ranged from 175 ± 67 m to 463 ± 84 m [36], with participants walking 234 ± 66.5 m in the shopping centre [127]. Stroke survivors in two intervention groups who walked over foam mats and purpose built ramps [10] walked 102.6 ± 64.5 m and 78.5 ± 61.3 m.

3.3. Assistance and Instructions Provided. Assistance provided to participants during the 6MWT was reported in 24 studies, with most of these studies indicating no assistance or minor assistance required. The single point cane was the most commonly used assistive device (n = 426) used during the 6MWT. Other devices used included the walker (n = 106), quad cane (n = 77), and crutch (n = 5). A total of 251 stroke survivors used an ankle-foot orthosis (AFO) during the test. Reporting use of a “usual device” without specifying the device used was prevalent (n = 310 participants).

Only 44% of studies reported the instructions provided to participants for the 6MWT with variations evident between studies. The most common phrase used was to “cover as much distance as possible” (n = 20 studies), followed by “walk as far as you can” (n = 16). Five studies specified walking at a fast pace in their instructions, and eight studies instructed participants to walk at a comfortable speed. Encouragement was provided in 10 studies, and no encouragement or verbal feedback was given in 14 studies.

3.4. Quantitative Analysis of Adherence to ATS Protocol Guidelines. Including the three studies published prior to the ATS standards, 49 of the 127 studies received a zero score, indicating that they did not mention the ATS guidelines and did not describe a protocol for the test including walkway length or course design. Sixty-three studies received a score of one indicating that these studies either referenced the ATS standard or provided details on the walkway length used. Of these, 53 received one point for reporting the walkway length or course design, while only ten received one point for referencing the ATS guidelines. Only 15 studies scored two points, with only nine of these reporting a reference to the ATS guidelines and complying with them by using a 30 m walkway.

3.5. Modifications to the 6MWT Protocol Walkway Length. Only 25 of the 127 studies made a reference to the ATS guidelines for the 6MWT, with only nine of these clearly reporting the use of a 30 m walkway. Although referencing the ATS standards, six studies modified the protocol with variations including the use of a 25 m walkway [133], a 33 m walkway [127], a 50 m walkway [96, 128], a 100 m walkway [75], and a 30 m oval course [48]. Overall, 67 studies provided a description of the walkway whereas 60 studies did not provide any description of the length or shape of the walkway used. Of those providing a description, 27 reported using an indoor 30 m walkway in accordance with the guidelines while 10 used shorter walkway lengths, 14 used longer walkways, and 14 used continuous walkways. Straight walkway lengths varied from 10 m [118] to 85 m [69–71].

3.6. Distances Achieved Using the 6MWT in Stroke Survivors. Sixty-four studies were included in the meta-analysis. The pooled distance walked across these 64 studies was 247.3 m (SE = 9.09). Heterogeneity was high with a tau (tau squared represents between study variance) of 84.9 m. We explored whether this heterogeneity was due to track type. Stroke survivors achieved a distance of 285 m (95% CI, 252–318 m) on a 30 m track. A significantly greater distance was achieved using the 30 m walkway compared to protocols with longer (231 m, 95% CI 189, 272, P = 0.048) or continuous (213 m, 95% CI 171, 255, P = 0.010) walkways (Figure 2); there was no significant difference between the 30 m walkway and shorter (242 m 95% CI 199, 286, P = 0.122) walkway lengths. Of the 60 studies that did not provide a description of the walkway used, an average distance of 246 ± 117 m was reported. Differences in distributions of age, gender, or time since stroke did not have a significant influence on distance walked (Table 3). Disability scores were only available on 74 (58%) studies and therefore could not be included in the analysis.
Disability scores were only available on 12 (12/46, 26%) of distance achieved on the 6MWT in stroke survivors (Table 4). The findings from the meta-analysis were that the has been developed for future reporting of the 6MWT to the 30m walkway length. Consequently, a set of guidelines for the 6MWT regarding the walkway length could be improved. Similarly, reporting use of the 30m walkway found that none of the variables, that is, age, gender, or time after stroke, were significantly associated with distance achieved on the 6MWT in stroke survivors (Table 4). Disability scores were only available on 12 (12/46, 26%) of these studies and therefore were not included in this analysis.

### Table 3: Meta-regression coefficients for all studies.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimate</th>
<th>Std. Err.</th>
<th>DF</th>
<th>t value</th>
<th>Probt</th>
<th>Lower CI</th>
<th>Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.6</td>
<td>1.7</td>
<td>75</td>
<td>0.38</td>
<td>0.708</td>
<td>−2.7</td>
<td>4.0</td>
</tr>
<tr>
<td>Proportion males</td>
<td>0.6</td>
<td>0.8</td>
<td>75</td>
<td>0.75</td>
<td>0.455</td>
<td>−1.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Time since stroke</td>
<td>0.5</td>
<td>0.4</td>
<td>75</td>
<td>1.16</td>
<td>0.251</td>
<td>−0.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

The regression analysis conducted in the 46 studies reporting use of the 30m walkway found that none of the variables, that is, age, gender, or time after stroke, were significantly associated with distance achieved on the 6MWT in stroke survivors. Disability scores were only available on 12 (12/46, 26%) of these studies and therefore were not included in this analysis.

### 4. Discussion

This review has identified that the 6MWT is now in widespread use to assess aspects of walking-related performance in stroke survivor studies. Many of the study populations had to meet strict eligibility criteria including being able to meet a minimal walking speed and no comorbidities and therefore may only be selectively representative of stroke survivors. Many stroke survivors would not be able to meet the criteria for these studies, making a bias towards more well recovered, nondisabled, otherwise healthier participants. However, even in this selected population, the distances achieved on the 6MWT indicate substantial walking limitations in people after stroke. Overall, both the reporting of and adherence to the ATS guidelines for the 6MWT regarding the walkway length could be improved. Similarly, reporting of the instructions given prior to testing, as well as any assistance provided to participants during the test, requires attention in future publications. Alterations to the ATS protocol walkway, including shortening or extending the walkway length or using a continuous track, are more common than adhering to the 30m walkway length. Consequently, a set of guidelines has been developed for future reporting of the 6MWT (Table 5). The findings from the meta-analysis were that the distance achieved during the 6MWT was associated with variations to the walkway length, but not in the manner one would predict. These findings have implications for the comparison of the values achieved using the 6MWT in different studies of stroke survivors.

The introduction of the ATS guidelines in 2002 was aimed at providing a protocol for consistency between studies. Of the 127 studies included in this review, 39 described a modified protocol whereas 60 studies did not specify the walkway length or walking course design. Of the 15 studies that received a reporting score of two, only nine reported both the ATS guidelines and used a 30m walkway length in accordance with the guidelines: the remaining six studies referenced the ATS guidelines but reported using a modified track. Consequently, although the ATS guidelines may be referenced in a report, it cannot be assumed that there was adherence to the guidelines. Protocol modification was more common than compliance with the 30m ATS standards, but no studies reported a reason for changing the protocol. Although there may be factors that necessitate or justify protocol changes, these reasons remain unreported. It is understandable that, in a setting where space is limited, there may be no other option than to use a walkway distance of less than 30m. Reasons for lengthening the walkway are less clear. One explanation is that if space greater than 30m in length is available, then a reason to extend the walkway length above the standard would be to decrease the effects of turning for stroke survivors in whom turning and balance ability may be compromised. We anticipated that the reduced turning requirements on the extended walkways and continuous tracks would result in longer distances being achieved than on the standard 30m walkway. The results of the meta-analysis show the opposite, with these protocols resulting in shorter 6MWT distances. One possible explanation for these types of protocol changes would be to accommodate reduced turning abilities and more severe disability of participants in these studies, which may also explain the reduced walk distances achieved.

The main impact of varying the 6MWT track length or design is the extent of turning required throughout the test. Turning requires the integration of multiple sensory systems and utilizes vestibular, visual, and proprioceptive information to appropriately move the body in space. Stroke survivors often experience difficulty during turning, possibly as a result of altered sensory, motor, and biomechanical systems. This results in a differing orientation and sequencing of movements during turning compared to healthy controls. Turning may take almost twice as many steps and twice as much time to complete a 180° turn compared to age-matched controls. Similarly, two studies have reported significantly slower 180°

![Figure 2: Distances achieved (point estimate, 95% CI) during the 6MWT based on walkway protocol used.](image-url)
Table 4: Meta-regression coefficients for 30 m protocol subgroup.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimate</th>
<th>Std. Err.</th>
<th>DF</th>
<th>t value</th>
<th>Probt</th>
<th>Lower CI</th>
<th>Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−2.4</td>
<td>3.3</td>
<td>25</td>
<td>−0.72</td>
<td>0.479</td>
<td>−9.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Proportion males</td>
<td>0.4</td>
<td>1.4</td>
<td>25</td>
<td>0.30</td>
<td>0.768</td>
<td>−2.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Time since stroke</td>
<td>−0.1</td>
<td>0.7</td>
<td>25</td>
<td>−0.12</td>
<td>0.909</td>
<td>−1.5</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Table 5: Checklist for reporting of the 6MWT.

<table>
<thead>
<tr>
<th>Checklist for reporting of the 6MWT</th>
<th>Check</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>(a) Acknowledge awareness of the ATS standards by referencing</td>
<td>□</td>
</tr>
<tr>
<td>(b) Report walkway length even if it is 30 m</td>
<td>□</td>
</tr>
<tr>
<td>(c) If deviating from ATS standards, describe changes (walkway length, course layout, and location) and explain reason</td>
<td>□</td>
</tr>
<tr>
<td>(2)</td>
<td></td>
</tr>
<tr>
<td>(a) Describe the instructions given prior to the test</td>
<td>□</td>
</tr>
<tr>
<td>(b) Describe any encouragement provided during the test</td>
<td>□</td>
</tr>
<tr>
<td>(3) Report the number and type of assistive devices used</td>
<td>□</td>
</tr>
<tr>
<td>(4) Report any assistance or support provided to participants</td>
<td>□</td>
</tr>
<tr>
<td>(5)</td>
<td></td>
</tr>
<tr>
<td>(a) Report the demographics of the population including disability level</td>
<td>□</td>
</tr>
<tr>
<td>(b) Report clearly the inclusion and exclusion criteria</td>
<td>□</td>
</tr>
</tbody>
</table>

turning times during the Timed Up and Go (TUG) in stroke [10, 141] with a similar finding by van Herk et al. (1998) [5] who demonstrated that the time taken to walk 10 m straight versus 5 m with return in stroke survivors was different, with the 5 m track with return requiring significantly more time to complete (\( P < 0.001 \)). When comparing stroke survivors’ performances on the 6MWT over 10, 20, and 30 m tracks, Ng et al. (2011) [8] quantified the increased number of turns associated with shortening the track and reported a significantly shorter distance achieved during the 10 m protocol, with the 30 m protocol reporting the longest distance walked. This is contradictory to the findings in this review; however when looking at percent difference there is some commonality. In the study by Ng et al., there is a reported reduction in distances achieved of 5% (20 m compared to 30 m) to 15% (10 m compared to 30 m). The results from the current meta-analysis suggest a reduction of 15% when comparing the <30 m protocol to the 30 m walkway length. Although this was not statistically significant, it is consistent with the magnitude of compromise found in the study by Ng et al. who measured the same population over multiple walkway lengths and could therefore make a direct comparison.

Another important finding from Ng et al. was that turning direction did not influence 6MWT distance independent of walkway length. The effects of turning direction on TUG times were also investigated in two other studies. Faria et al. [141] also found no difference in TUG times. In contrast Heung and Ng [142] found a significantly faster TUG time when turning towards the paretic side. There appears to be an expectation that turning towards the affected side would result in slower speeds and therefore decreased 6MWT distance; however as demonstrated in the literature, this may not be the case. Generally, the studies in this review did not specify the directions turned and therefore could not be analysed. It is noted however that in the clinical setting it is usually at the discretion of the individual performing the test as to which direction they turn during the 6MWT.

Our findings highlight the substantial effects of stroke on walking speed. Stroke survivors achieved an average distance of 285 m (95% CI 252, 318) on a standard 30 m track, whereas healthy older individuals >60 years achieve an average 6MWT distance of 499 m (95% CI 480, 519) [143]. The extent of the performance compromise on the 6MWT is striking, particularly when the studies in this review are largely reporting on a highly selected, high performing cohort of independently ambulant stroke survivors. When considering these distances achieved, it is important to also acknowledge any assistive devices used throughout the 6MWT. Overall, 948 stroke survivors used a walking aid, and 251 walked with an AFO. Allet et al. [16] found that stroke survivors walked approximately 15 m further during the 6MWT using a simple cane with an ergonomic handgrip than when walking with a 4-point cane or Nordic stick. This area requires further investigation and should be considered when interpreting data.

Of the variables age, gender, and time after stroke, none had a significant effect on the distances achieved. This is likely because meta-regression was performed using summary level data for each study, rather than individual patient data that would have more power to tease out heterogeneity. In healthy adults, the variables age and gender have been suggested as sources of variability on distances achieved [9].

Unfortunately, the effect of disability on distance walked could not be discerned in this review due to the large number of different disability scales used to describe stroke
populations, the lack of consistency of scales between studies, and the underreporting of mobility related disability. An attempt to use an alternative measure of motor function, such as 10 m walking speed or balance, was also unsuccessful, as few of the studies in the meta-analysis reported on these measures.

The instructions provided to stroke survivors differ between studies, potentially impacting on the perceived goal of the 6MWT. In the current analysis, five studies reported wording to walk at a “fast” pace, while nine studies instructed participants to walk at a “comfortable” pace. According to the ATS guidelines, instructions should be informing the participant to walk “as far as possible for 6 minutes” with no mention of walking speed. The guidelines also provide standard encouragement wording to use. Of those studies that reported on the encouragement given throughout the test, 42% provided encouragement and 58% provided no verbal encouragement or feedback. The guidelines specify that the 6MWT should be performed indoors; however several studies reported using the 6MWT in different environments such as outdoors [36, 124, 126] including suburban streets and in shopping centres [127]. Although these trials were excluded from the meta-analysis, the exact implications of performing the 6MWT in different locations are unclear.

Carvalho et al. [138] directly compared distance achieved indoors and outdoors, concluding that stroke survivors in Group B (self-selected walking speed \( \geq 0.8 \text{ m s}^{-1} \)) achieved a greater distance in the outdoor setting, whereas for those in Group A (self-selected walking speed \( < 0.8 \text{ m s}^{-1} \)) there was no difference. It has also been suggested that gait parameters do not differ in stroke survivors when walking in different environments [127]. This is another factor that should be considered when interpreting the results reported from the 6MWT.

This review highlights the need for future researchers to be mindful in reporting their implementation of the 6MWT by describing the walkway used and rationales for deviations from the 30 m walkway or other aspects of the protocol. To assist future researchers we have developed a checklist of items for unambiguous reporting of the use of the 6MWT (Table 5). We acknowledge that changing the protocol may be necessary in some settings due to space restrictions. If the primary purpose of the test is to compare performances pre-post intervention then consistency is the main requirement between tests. Each setting may require their own documented protocol in order to maintain consistency between measurement times and test supervisors. The effects of level of disability on 6MWT performance could not be readily discerned due to the large number of different disability scales used, with many of these providing little indication of mobility impairment. Similarly, the extent of assistance provided, as well as the instructions given to the participants, requires attention in future studies. It can be concluded from the review that by changing the protocol researchers are limiting the ability to compare results between studies in stroke as well as other clinical populations. There is a lack of comprehensive reporting of the 6MWT protocol, which needs to be addressed in future research publications.

Conflict of Interests

D. L. Marsden was an author on paper [79], which was an included paper in the review.

Acknowledgments

The authors would like to acknowledge Debbie Booth (Faculty of Health and Medicine librarian, University of Newcastle) for her assistance with the search, and Dr. Christopher Oldmeadow (Clinical Research Design, Information Technology (CReDITSS), Hunter Medical Research Institute) for his statistical support.

References


[99] H.-J. Park, D.-W. Oh, S.-Y. Kim, and J.-D. Choi, "Effectiveness of community-based ambulation training for walking function..."


Appendix 2: Published manuscript of Chapter 4
Characteristics of Exercise Training Interventions to Improve Cardiorespiratory Fitness After Stroke: A Systematic Review With Meta-analysis

Dianne L. Marsden, MAppMgnt¹,²,³, Ashlee Dunn, BExSpSci(Hon)¹,², Robin Callister, PhD¹,², Christopher R. Levi, MD¹,²,³, and Neil J. Spratt, MD, PhD¹,²,³

Abstract
Background. Cardiorespiratory fitness is low after stroke. Improving fitness has the potential to improve function and reduce secondary cardiovascular events. Objective. This review with meta-analysis aims to identify characteristics and determine the effectiveness of interventions to improve cardiorespiratory fitness after stroke. Methods. A systematic search and review with meta-analysis was undertaken. Key inclusion criteria were the following: peer-reviewed articles published in English, adult stroke survivors, an intervention with the potential to improve cardiorespiratory fitness, and peak oxygen consumption (VO₂peak) assessed preintervention and postintervention via a progressive aerobic exercise test. Results. From 3209 citations identified, 28 studies were included, reporting results for 920 participants. Studies typically included chronic, ambulant participants with mild to moderate deficits; used an aerobic or mixed (with an aerobic component) intervention; and prescribed 3 sessions per week for 30 to 60 minutes per session at a given intensity. Baseline VO₂peak values were low (8-23 mL/kg/min). Meta-analysis of the 12 randomized controlled trials demonstrated overall improvements in VO₂peak of 2.27 (95% confidence interval = 1.58, 2.95) mL/kg/min postintervention. A similar 10% to 15% improvement occurred with both aerobic and mixed interventions and in shorter (<3 months) and longer (>3 months) length programs. Only 1 study calculated total dose received and only 1 included long-term follow-up. Conclusions. The results demonstrate that interventions with an aerobic component can improve cardiorespiratory fitness poststroke. Further investigation is required to determine effectiveness in those with greater impairment and comorbidities, optimal timing and dose of intervention, whether improvements can be maintained in the longer term, and whether improved fitness results in better function and reduced risk of subsequent cardiovascular events.

Keywords
stroke, cardiorespiratory fitness, oxygen consumption, aerobic, systematic review, meta-analysis

Introduction
In primary prevention, level of physical activity is an independent predictor of stroke risk.¹,² Lack of physical activity accounts for 28.5% (99% confidence interval [CI] = 14.4%-48.5%) of stroke population-attributable risk, second only to hypertension (34.6%, 99% CI = 30.4%-39.1%).³ Adults who are highly or moderately active have an approximately 25% lower stroke risk.¹ Following stroke, evidence is scant for the benefit of physical activity to reduce death, dependence, or disability; prevent subsequent stroke; or improve longitudinal cardiovascular health outcomes.³⁻⁵ However, given the benefits of exercise in primary prevention, there is a very high probability that it is also beneficial in secondary prevention. It is therefore concerning that an estimated 77% of stroke survivors are sedentary or have low levels of physical activity.⁶ Cardiorespiratory fitness after stroke is very low, with peak oxygen consumption (VO₂peak) values ranging from 8 to 22 mL/kg/min, which equates to 26% to 87% of gender- and aged-matched healthy individuals.⁷ Levels below 15 and 18 mL/kg/min for women and men,
respectively, can lead to loss of independence because activities of daily living become too fatiguing. Stroke guidelines recommend cardiorespiratory fitness training after stroke; however, this is rarely implemented because regaining physical function is a primary focus. Many clinicians have limited experience with cardiorespiratory fitness testing or exercise prescription after stroke.

The aim of this systematic review with meta-analysis was to determine the effectiveness of exercise interventions to improve cardiorespiratory fitness after stroke. The primary outcome was change in cardiorespiratory fitness, as measured by the gold standard of VO2peak achieved during progressive aerobic exercise testing using open-circuit spirometry. Subgroup analyses were planned to investigate factors hypothesized to influence effectiveness of the interventions. By synthesizing the data available regarding characteristics of studies, participants (gender, age, and time poststroke), and interventions (type, dose, training setting, group/individual program, risks, satisfaction, and effect maintenance), our aim was also to inform clinicians on strategies to improve cardiorespiratory fitness of people poststroke.

Methods

The conduct and reporting of this review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) and the Consolidated Standards of Reporting Trials (CONSORT) statements.

Eligibility Criteria

A systematic search was undertaken of MEDLINE, CINAHL, EMBASE, PsycINFO, AMED, SPORTDiscus, and COCHRANE databases from their inception to December 27, 2011. Terms used for the MEDLINE search are listed in Table 1. These were adapted as required to suit each database searched. Inclusion criteria were the following: people aged 18 years and over at any time poststroke or post–transient ischemic attack; controlled and noncontrolled trials published in a peer-reviewed, English language journal and containing primary data; peak or maximal oxygen consumption assessed using open-circuit spirometry via a progressive aerobic exercise test preintervention and postintervention; and an exercise intervention used that had the potential to improve cardiorespiratory fitness. Theses and articles published in abstract form only, including conference proceedings, were excluded.

Study Selection

After duplicates were removed author DLM sorted the search results by title and abstract into “include” and “exclude,” and author AD reviewed for agreement. The full text for all included articles were obtained and reviewed by authors DLM and AD for a final decision, with any discrepancies discussed and a consensus agreed. Author RC was consulted if further clarification was required. Hand searching of articles identified in the reference lists of included articles was also undertaken.

Data Items and Extraction

Data from the included articles were extracted into Excel 2007 by DLM and checked by AD and included the following:

- Study characteristics: study design, country, year published, inclusion and exclusion criteria, participant numbers, including gender ratio, attrition, quality
- Participant characteristics: age, time since stroke
- Interventions: type, dose (program length, session duration, frequency and intensity), advice regarding exercise outside of intervention, training setting, group/individual program, risks/adverse events, satisfaction, effect maintenance
- VO2peak: testing method, results preintervention and postintervention in mL/kg/min

Table 1. Search Strategy Used for MEDLINE.

<table>
<thead>
<tr>
<th>Number</th>
<th>Search Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>((cardiovascular or cardiorespiratory or aerobic* or exercise) and (fit* or condition* or capacit*)).mp.</td>
</tr>
<tr>
<td>2</td>
<td>Cerebrovascular Disorders.mp. or exp Cerebrovascular Disorders</td>
</tr>
<tr>
<td>3</td>
<td>Stroke.mp. or exp Stroke/</td>
</tr>
<tr>
<td>4</td>
<td>(cerebral or cerebellar or brainstem or vertebrobasilar).mp.</td>
</tr>
<tr>
<td>5</td>
<td>(infarct* or ischemia or thrombo* or embol*).mp.</td>
</tr>
<tr>
<td>6</td>
<td>4 and 5</td>
</tr>
<tr>
<td>7</td>
<td>(cerebral or brain or subarachnoid or intracerebral).mp.</td>
</tr>
<tr>
<td>8</td>
<td>(haemorrhage or haematoma or bleed* or hemorrhage or hematoma).mp.</td>
</tr>
<tr>
<td>9</td>
<td>7 and 8</td>
</tr>
<tr>
<td>10</td>
<td>(Transient Ischemic Attack or Transient Ischaemic Attack).mp.</td>
</tr>
<tr>
<td>11</td>
<td>2 or 3 or 6 or 9 or 10</td>
</tr>
<tr>
<td>12</td>
<td>(Physical Therap* Modalit* or Physical Fit* or fit* train* or Exercise Therap*).mp.</td>
</tr>
<tr>
<td>13</td>
<td>((aerobic or fit*) and train*).mp.</td>
</tr>
<tr>
<td>14</td>
<td>rehabilitation.mp. or exp Rehabilitation/</td>
</tr>
<tr>
<td>15</td>
<td>therapeutic exerc*.mp.</td>
</tr>
<tr>
<td>16</td>
<td>12 or 13 or 14 or 15</td>
</tr>
</tbody>
</table>

**Study Quality and Risk of Bias**

The Physiotherapy Evidence Database (PEDro) independently assesses studies against 10 criteria for quality. Ratings for the randomized controlled trials (RCTs) included in this review were extracted from PEDro and categorized by score: excellent (9-10), good (6-8), fair (4-5), and poor (<4). Quality was also evaluated by VO\textsubscript{2peak} equivalence at baseline and the inclusion of sample size calculations.

**Synthesis of Results**

Statistical analysis was undertaken using RevMan5.\textsuperscript{1} Meta-analyses were planned to compare change in the primary outcome—VO\textsubscript{2peak} in RCTs that used an intervention group and a control group with no intervention, sham training, or an intervention that would be unlikely to have an aerobic training effect. Four analyses with subgroups were planned: intervention type, time since stroke (≤3 months, >3 and ≤12 months, >12 months), program length (≤3 months, >3 months), and “met exercise recommendations for older adults”\textsuperscript{16} (moderate intensity for at least 30 min/d on most days of the week). Because VO\textsubscript{2peak} data are continuous, a random-effects analysis model was used with mean difference at postintervention as the effect measure, with 95% CI. Standard errors were converted to standard deviations (SDs).\textsuperscript{17} Post measures for 1 study\textsuperscript{18} were not reported and so were calculated by adding the change score to the baseline score and using the baseline SDs. For Lee et al\textsuperscript{19} where more than 1 intervention was compared with a shared control group, the total number of control participant numbers were split evenly between the intervention groups, with the means and SDs left unchanged.\textsuperscript{17} Statistical heterogeneity was measured using the $\chi^2$, $\tau^2$, and $I^2$ tests.

**Results**

Figure 1 outlines the flow of articles, including reasons for exclusion. From 3209 citations, 28 studies were included.

**Characteristics of Studies**

The study characteristics are summarized in Table 2. There were 16 RCTs, 1 controlled trial with matched participants, and 10 noncontrolled trials using pre-post testing of the cohort. The remaining study\textsuperscript{20} undertook a post hoc pre-post analysis of the intervention groups of 2 RCTs. Only data from the German arm was extracted from this article because the United States arm\textsuperscript{21} was included independently. All studies were published since 2000 except 1 (Potempa et al,\textsuperscript{22} 1995). The studies were undertaken in 9 countries, predominantly in North America (the United States [n = 16] and Canada [n = 4]). Study inclusion/exclusion criteria often included the following: more than 5 months poststroke (n = 18), mild to moderate stroke deficits (n = 10), independently ambulant (n = 21), mild or no cardiovascular/cardiopulmonary history (n = 19), no significant cognitive or communication issues (n = 12), no other major neurological condition (n = 7), and no major musculoskeletal problems or pain (n = 10). Also, 8 studies required participants to pass a treadmill (n = 6) or cycle (n = 2) screening test.

The 28 studies enrolled 1090 participants (male = 337 [30.9%], female = 191 [17.5%], not specified = 552 [52.6%]) and reported results on 920 participants (male = 437 [47.5%], female = 313 [34.0%], not specified = 170 [18.5%]). Attrition rates were reported in 22 studies and ranged from 0% (n = 5) to 41% of the control group in 2 studies. The main reasons for attrition included medical conditions unrelated to the study (39.9%), “noncompliance” (22.1%), “medical reason or noncompliance” (14.1%), transport/scheduling issues (6.1%), another stroke (3.1%), and a fall with hip fracture (3.1%).

**Study Quality**

Criteria ratings for 15 of the 16 included RCTs could be extracted from PEDro\textsuperscript{3} (Table 3). Letombe et al\textsuperscript{23} was being rated at the time of this report. The ratings were: good (n = 5), fair (n = 9), and poor (n = 1). These 15 RCTs were all determined to have point estimates and variability, random allocation, and baseline comparability. No study had blinded participants or blinded therapists, and only 3 undertook intention-to-treat analysis. Of the 15 rated studies, 14 were similar for VO\textsubscript{2peak} at baseline for the intervention and control groups. Only 4 reported sample size calculations.

**Participant Characteristics**

The participant characteristics are outlined in Table 2. Mean ages ranged from 53 (no SD provided) to 71 (range = 61-79) years. The mean time since stroke ranged from 14.3 (6.1) days to 7.5 (range = 4-20) years, with the following distribution: within 1 month (n = 3); 2 to 3 months (n = 2); 1 to 3 years (n = 7) and greater than 3 years (n = 9). There were 7 studies that provided no details on time since stroke; however, 6 of these had inclusion criteria of more than 6 months, and for 1 study, it was greater than 12 months.

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\textsuperscript{2}Resource: PEDro (Physiotherapy Evidence Database) http://www.pedro.org.au/
**Interventions**

The testing methods and intervention characteristics are summarized in Table 4.

**Type.** Of the 28 studies that met the search criteria, 16 used aerobic training\(^{20-22,24-36}\) (treadmill, \(n = 8\); cycle, \(n = 6\); deep-water exercise, \(n = 1\); cycle and recumbent stepper, \(n = 1\)), 11 used a mixed intervention\(^{18,19,23,37-44}\) (an aerobic component in conjunction with usual care, strength, balance, and/or endurance activities), and one\(^{45}\) used knee flexion/extension isokinetic training of the paretic leg, aimed at improving cardiorespiratory fitness.

**Dose prescribed.** All studies reported program length and planned intervention frequency and duration. Program length ranged from 2 to 3 weeks to 6 months, with 12 studies being between 3 and 6 months in length. Session durations ranged from 20 to 90 minutes, with most training lasting 30 to 60 minutes (\(n = 23\)). Frequency of sessions ranged from 2 to 5 times/wk, with most (\(n = 22\)) training 3 times/wk. Planned intensity was reported in 25 studies. Intensity was often calculated from baseline exercise testing and included percentage heart rate reserve (HRR; \(n = 11\)) and percentage power output (\(n = 6\)). Rating of perceived exertion was used as an adjunct measure in 5 studies. No study provided details regarding instructions to participants about trying to undertake further exercise outside of intervention sessions.

**Dose delivered.** Although training parameters were described, there was limited reporting of whether they were
Table 2. Characteristics of the Studies, Grouped By Training Type and Listed by Time Since Stroke.

<table>
<thead>
<tr>
<th>Study, Year, Country</th>
<th>Study Design, Location; Group or Individual?</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Age (SD), years</th>
<th>Time Since Stroke (SD)</th>
<th>Number of Participants (Male, Female)</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aerobic</strong></td>
<td></td>
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</tr>
<tr>
<td>Tang et al. 2009, Canada</td>
<td>Matched controlled, Inpt: nr, appears indiv</td>
<td>&lt;3 Months poststroke; walk &gt;5 m independently; CMSA leg score 3-6. NO: Conin ACSMG; msk impairments, or pain to prevent pedaling</td>
<td>I = 64.7 (3.6), C = 65.7 (2.3)</td>
<td>Days, I = 19.1 (3.8), C = 14.9 (2.3)</td>
<td>Enrolled = 57; Matched pairs reported = 18, I = 18 (11.7), C = 18 (11.7)</td>
<td>1 = 0 (0%), C = 0 (0%)</td>
</tr>
<tr>
<td>Murakami et al. 2002, Japan</td>
<td>Noncontrolled pre-post measures, Inpt rehab; nr, appears indiv</td>
<td>Mild to mod hemiparesis; ambulatory; independent indoors walking or wheelchair</td>
<td>I = 55 (13)</td>
<td>Days, 76 (65)</td>
<td>Results = 29 (23:6)</td>
<td>nr</td>
</tr>
<tr>
<td>Calmes et al. 2011, France</td>
<td>Noncontrolled pre-post measures, Outpt rehab; nr, appears indiv</td>
<td>Age 18-70; &gt;3 months and &lt;2 years poststroke; participating in rehab; independent ambulator; stable clinical and medical management; MMSE &gt; 23. NO: uncontrolled respiratory, metabolic, immune, infectious, or inflammatory disorders</td>
<td>I = 53.7 (13), C = 55.3 (10.4)</td>
<td>Months, I = 12.3 (5.4), C = 18.3 (9.9)</td>
<td>Enrolled = 16; Results: I = 6 (3:3), C = 6 (3:3)</td>
<td>1 = 2 (25%), C = 2 (25%)</td>
</tr>
<tr>
<td>Moore et al. 2010, United States</td>
<td>RCT with cross-over, nr, appears center; nr, appears indiv</td>
<td>Hemiparesis &gt;6 months duration; attending physical therapy; unilateral supratentorial stroke; walk 10 m independently at self-selected speed ≤0.9 m/s; stated goal to improve walking ability; able to adhere to study requirements. NO: LL contractures; significant osteoporosis; CV instability; history of peripheral or central nervous system injury; cognitive or communication impairment</td>
<td>Age, 53 (17)</td>
<td>Months, 18 (11)</td>
<td>Enrolled = 30; Results = 20 (14:6)</td>
<td>10 (33%)</td>
</tr>
<tr>
<td>Macko et al. 2001, United States</td>
<td>Noncontrolled pre-post measures, research center; Indiv initial bouts then 1:5 supervised</td>
<td>Age &gt;50; &gt;6 months post–index ischemic stroke; mild to mod hemiparetic gait; not already doing aerobic X; walk &gt;0.2 m/s on treadmill. NO: ACSMG; HF; unstable angina; PAD; aphasia; dementia; major depression; other medical conditions precluding X</td>
<td>I = 67 (8)</td>
<td>Months, 28 (26)</td>
<td>Enrolled = 23 (19:4); Results = 19</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Macko et al. 2005, United States</td>
<td>RCT, nr, appears indiv</td>
<td>Age &gt;45; &gt;6 months poststroke; hemiparetic gait; pass screening treadmill test. NO: HF; unstable angina; PAD; aphasia; dementia; major depression; other medical conditions precluding X</td>
<td>I = 63 (10), C = 64 (8)</td>
<td>Months, I = 35 (29), C = 39 (21:8)</td>
<td>Enrolled = 61, I = 32 (22:10), C = 29 (21:8); Results: I = 25, C = 20 (17:1)</td>
<td>1 = 7 (22%), C = 9 (31%)</td>
</tr>
<tr>
<td>Chu et al. 2004, Canada</td>
<td>RCT, community facility, group</td>
<td>Age &gt;1 Year post–first-ever stroke; unilateral weakness; independent walker; medically stable; able to pedal to raise HR to 60% max. NO: significant msk probs, previous MI</td>
<td>I = 61.9 (9.4), C = 63.4 (8.4)</td>
<td>Years, I = 30 (2.0), C = 42.2 (2.1)</td>
<td>Enrolled = 17 (6:1), C = 6 (5:1); Results: I = 7 (6:1), C = 5 (5:0)</td>
<td>1 = 0 (0%), C = 1 (17%)</td>
</tr>
<tr>
<td>Quaney et al. 2009, United States</td>
<td>RCT, laboratory, C—home; nr, appears indiv</td>
<td>&gt;6 Months post–first-ever ischemic stroke; hemiparesis; MMSE &gt;23 incl correct 3-step command; adequate cardiac function for the protocol; not performing more than 20 minutes aerobic X 3 times/wk. NO: large daily alcohol intake; serious medical; other neurological diseases</td>
<td>I = 64.10 (12.30), C = 58.96 (14.68)</td>
<td>Years, I = 462 (12:1), C = 5.11 (3.53)</td>
<td>Enrolled = 40; Results: I = 19 (10:9), C = 19 (7:12)</td>
<td>1 = 1 (5%), C = 1 (5%)</td>
</tr>
<tr>
<td>Lam et al. 2010, Germany</td>
<td>Post hoc analysis, nr, appears center; nr, unclear</td>
<td>&gt;6 Months post–first-ever ischemic stroke; not already performing aerobic X &gt;20 min/d and &gt;once/wk; walk &gt;0.1 m/s on treadmill for &gt;3 minutes. NO: Conin ACSMG; HF, angina; PAD; aphasia; dementia; depression; other neurological diseases</td>
<td>68.6 (SEM = 1.1)</td>
<td>Months, 58.34 (SEM = 8.77)</td>
<td>Results = 32 (26:6)</td>
<td>nr</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Study, Year, Country</th>
<th>Study Design, Location; Group or Individual?</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Age (SD), years</th>
<th>Time Since Stroke (SD)</th>
<th>Number of Participants (Male, Female)</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luft et al, 2008, United States</td>
<td>RCT, nr, appears center; indiv</td>
<td>Age &gt;45; ≥6 months post-first-ever ischemic stroke; hemiparetic gait; completed subacute rehab; pass screening treadmill test. NO: Confin to (MRI); HF; angina; PAD; major depression; major aphasia; dementia; major neurological, orthopedic, medical, or chronic pain</td>
<td>I = 63.2 (8.7), C = 63.6 (10.0)</td>
<td>Months (IQR), I = 62.3 (26.0-80.9), C = 44.6 (18.8-70.5)</td>
<td>Enrolled: I = 113; Results: I = 20 (35%), C = 22 (39%)</td>
<td></td>
</tr>
<tr>
<td>Ivey et al, 2010, United States</td>
<td>RCT, nr, appears center; indiv</td>
<td>≥6 Months poststroke; completed therapy; mild/mod hemiparetic gait; ambulatory. NO: history of vascular surgery, vascular disorders of leg, or PAD</td>
<td>I = 62.8 (8), C = 60 (8)</td>
<td>nr</td>
<td>Enrolled: I = 39, C = 41; Results: I = 18, C = 17</td>
<td></td>
</tr>
<tr>
<td>Ivey et al, 2007, United States</td>
<td>RCT, Outpt; indiv</td>
<td>Age &gt;45; ≥6 months postischemic stroke; complete oral glucose tolerance test; completed therapy; mild/mod hemiparetic gait; ambulatory; follow 2-point command; pass screening treadmill test. NO: HF; diabetes; dementia; major depression; PAD</td>
<td>I = 63 (9), C = 62 (10)</td>
<td>nr</td>
<td>Enrolled = 69; Results: I = 26 (13:13), C = 20 (13:7)</td>
<td></td>
</tr>
<tr>
<td>Potempa et al, 1995, United States</td>
<td>RCT, laboratory; indiv</td>
<td>Age 21-77; ≥6 months poststroke; medically stable; completed rehab. NO: disorder precluding or confounding max X test measurements; unstable cardiac disease; uncontrolled HT, PVD, pulmonary disease, renal, or hepatic failure; cancer; diabetes requiring insulin therapy</td>
<td>Range = 43-72</td>
<td>nr</td>
<td>Results: I = 19 (8:11), C = 23 (15:8)</td>
<td></td>
</tr>
<tr>
<td>Rimmer et al, 2009, United States</td>
<td>Pre-post measures, cluster assigned, Outpt rehab; indiv</td>
<td>Age ≥18; ≥6 months poststroke; independent ambulator; MMSE ≥16</td>
<td>I int = 55.7 (12.6), I dur = 59.4 (7.1), C = 63.7 (9.1)</td>
<td>nr</td>
<td>Enrolled: I int = 18 (6:12), I dur = 19 (8:11), C = 18 (8:10); Results: I int = 14, I dur = 14, C = 13</td>
<td></td>
</tr>
<tr>
<td>Yang et al, 2007, Taiwan</td>
<td>Noncontrolled pre-post measures; indiv</td>
<td>&lt;1 Year poststroke; mild-moderate hemiparetic gait; history of chronic artery disease. NO: regular aerobic X</td>
<td>64.13 (7.58)</td>
<td>nr</td>
<td>Results = 15 (9:6)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Mixed**

<table>
<thead>
<tr>
<th>Study, Year, Country</th>
<th>Study Design, Location; Group or Individual?</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Age (SD), years</th>
<th>Time Since Stroke (SD)</th>
<th>Number of Participants (Male, Female)</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teixeira da Cunha Filho et al, 2001, United States</td>
<td>RCT, Inpt; indiv</td>
<td>&lt;6 Weeks poststroke; significant gait deficit (0-2 on FAC); MMSE ≥21; able to: stand up with/without assistance, take at least 1 step without assistance</td>
<td>I = 57.83 (5.56), C = 59.67 (13.58)</td>
<td>Days, I = 15.67 (7.6), C = 14.33 (6.06)</td>
<td>Enrolled: I = 7 (70), C = 8 (80); Results: I = 6 (60), C = 6 (60)</td>
<td>I = 1 (14%), C = 2 (25%)</td>
</tr>
<tr>
<td>Letombe et al, 2010, France</td>
<td>RCT, Inpt rehab; indiv</td>
<td>Hemiparesis; stable clinical state; well balance medication treatment. NO: memory or cognitive disorders; neglect; unstable brain lesions</td>
<td>I = 59.1 (9.4), C = 60.6 (8.2)</td>
<td>Days, I = 20 (2), C = 21 (3)</td>
<td>Results: I = 9 (5:4), C = 9 (6:3)</td>
<td>nr</td>
</tr>
<tr>
<td>Duncan et al, 2003, United States</td>
<td>RCT, home; indiv</td>
<td>Age ≥50; 30-150 days poststroke with mild-moderate deficits; community dwelling; ambulate 25 feet indep; MMSE &gt;15. NO: serious cardiac conditions; angina, cardiomyopathy; aortic stenosis; PE; O2 dependence; severe wt-bearing pain</td>
<td>I = 68.5 (9), C = 702 (11.4)</td>
<td>Days, I = 77.5 (38.7), C = 73.5 (27.1)</td>
<td>Enrolled: I = 50, C = 50; Results: I = 44 (23:21), C = 48 (27:21)</td>
<td>I = 6 (12%), C = 2 (4%)</td>
</tr>
<tr>
<td>Surnerhagen et al, 2007, Sweden</td>
<td>Noncontrolled pre-post measures, rehab center; group</td>
<td>≥6 months post-first stroke; hemiparetic; medically stable not currently receiving rehab; independent walker 30 m with/without walking aid; no interfering comorbidities incl heart or joint problems; medically stable</td>
<td>53 (range = 40-68)</td>
<td>Months, 16 (range = 9-35)</td>
<td>Results: paretic = 17; nonparetic = 18</td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Study, Year, Country</th>
<th>Study Design, Location; Group or Individual?</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Age (SD), years</th>
<th>Time Since Stroke (SD)</th>
<th>Number of Participants (Male, Female)</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tang et al. 2010, Canada</td>
<td>Noncontrolled repeated-measures, community facility and home; group and indiv</td>
<td>&gt;3 Months poststroke; walk &gt;10 m independently; marked leg spasticity and weakness. NO: ConIn to max X testing; significant pain, msk, cognitive, or behavioral issues that would limit testing or program participation</td>
<td>64.5 (12.2)</td>
<td>Months, 30 (27.3)</td>
<td>Enrolled = 43 (30:13); results = 38 results</td>
<td>2 (5%) before and 3 (7%) after commenced</td>
</tr>
<tr>
<td>Lee et al. 2008, Australia</td>
<td>RCT; university; nr, appears indiv</td>
<td>Age &gt;245; ≥3 months poststroke; unilateral hemiparesis of leg; community dwelling; self-selected walking speed between 0.15 and 1.4 m/s. NO: Conln ACSMG; contractures; severe cognitive deficits</td>
<td>60.5 (10.6)</td>
<td>I both = 60.5 (10.6), I PRT = 66.5 (10.6)</td>
<td>Enrolled: I both = 13, l PRT = 13, I cyc = 14</td>
<td>1 both = 1 (8%), 1 PRT = 1 (8%), 1 cyc = 2 (14%), C = 0 (0%)</td>
</tr>
<tr>
<td>Kuding et al. 2011, United States</td>
<td>Noncontrolled pre-post measures, university; nr, appears indiv</td>
<td>&gt;6 Months poststroke; able to sit, to stand; walk, 30 feet independently; MMSE &gt;22; nonsmoker; not receiving therapy. NO: recent chest discomfort, HF, MI, or heart surgery in past 3/12; arrhythmia; cardiomyopathy; aortic stenosis; PE; msk that would limit X; other neurological conditions than stroke</td>
<td>63.7 (9.1)</td>
<td>Months 50.4 (37.9)</td>
<td>Enrolled = 11; Results = 9 (5.4)</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Pang et al. 2005, Canada</td>
<td>RCT, community facility; group</td>
<td>Age &gt;50; &gt;1 year or more post-stroke; living at home; walk &gt;10 m independently. NO: serious cardiac disease; uncontrolled HT; pain on walking; neurological conditions in addition to stroke; other disease that would prevent participation; pedal &gt;60 rev/min and raise HR to ≥60% max; MMSE &gt;22</td>
<td>65.8 (9.1), C = 64.7 (8.4)</td>
<td>Years, 1 = 5.2 (5.0), C = 5.1 (3.6)</td>
<td>Enrolled = 63; Results: 1 = 19.13, C = 18.13</td>
<td>1 = 2 (6%), C = 1 (3%)</td>
</tr>
<tr>
<td>Michael et al. 2009, United States</td>
<td>Noncontrolled pre-post measures, community facility and home; group and indiv</td>
<td>Ischemic stroke; mild-mod hemiparetic gait; walk on treadmill. NO: HF: unstable angina; PAD: major depression; major aphasia; dementia; major neurological, orthopedic, medical, or chronic pain that would preclude participation</td>
<td>71 (range = 61-79)</td>
<td>Years, 7.5 (range = 4-20)</td>
<td>Enrolled = 10 (7-3); Results = 7</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Carr et al. 2003, United States</td>
<td>RCT, Outpt rehab; nr, appears indiv</td>
<td>&gt;6 Months poststroke. NO: severe cognitive deficits; abnormal heart conditions; uncontrolled BP</td>
<td>Range 30-82</td>
<td>nr</td>
<td>Enrolled = 22:18</td>
<td>nr</td>
</tr>
<tr>
<td>Rimmer et al. 2000, United States</td>
<td>RCT, university; group</td>
<td>Age 30-70; &gt;6 months poststroke; walk &gt;50 feet independently; reside within 1 hour commute of intervention site</td>
<td>Overall = 53.17 (8.28)</td>
<td>nr</td>
<td>Enrolled and results = 35 (9.26), 1 = 18, C = 17</td>
<td>1 = 0 (0%), C = 0 (0%)</td>
</tr>
<tr>
<td>Knee flexion/extension isokinetic training</td>
<td>Billinger et al. 2010, United States</td>
<td>Noncontrolled pre-post measures, nr, appears center; nr but appears indiv</td>
<td>&gt;6 months poststroke; hemiparesis; sit to stand with minimal assistance; walk &gt;10 m independently; mild to mod stroke deficits; F/E knee at least 35° ROM against gravity. NO: new or severe cardiopulmonary conditions; non-smoker diabetes; PVD; current therapy</td>
<td>60.6 (14.5)</td>
<td>Months, 69.1 (82.2)</td>
<td>Enrolled and results = 12 (5.7)</td>
</tr>
</tbody>
</table>

Abbreviations: ACSMG, American College of Sports Medicine Guidelines; BP, blood pressure; C, control group; Conln, contraindications; CMSA, Chedoke-McMasters Stroke Assessment; CV, cardiovascular; cyc, cycle; °, degrees; dur, duration; E, extension; F, flexion; FAC, Functional Ambulatory Classification; fMRI, functional magnetic resonance imaging; Grp, group; HF, heart failure; HR, heart rate; HT, hypertension; incl, including; indiv, individual; Inpt, inpatient; I, intervention group; I both, received both cycle and PR; int, intensity; IQR, interquartile range; LL, lower limb; max, maximal MI, myocardial Infarction MMSE, Mini-Mental State Examination mod, moderate msk, musculoskeletal; nr, not reported; O2, oxygen; Outpt, outpatient; PAD, peripheral artery disease; PE, pulmonary embolism; PR, progressive resistance training; RCT, randomized controlled trial; rehab, rehabilitation; revs/min, revolutions/minute; ROM, range of motion; SD, standard deviation; SEM, standard error of the mean; wks, weeks; wt, weight; X, exercise.
### Table 3. Quality Scores for the Methods Used in RCTs.

<table>
<thead>
<tr>
<th>Study</th>
<th>Random Allocation</th>
<th>Concealed Allocation</th>
<th>Baseline Comparability</th>
<th>Blinded Subjects</th>
<th>Blinded Therapists</th>
<th>Adequate Follow-up</th>
<th>Intention-to-Treat Analysis</th>
<th>Between-Group Comparisons</th>
<th>Point Estimates and Variability Score (/10)</th>
<th>Eligibility Criteria for Participants</th>
<th>VO₂peak Equivalent at Baseline</th>
<th>Power Calculation</th>
</tr>
</thead>
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Abbreviations: Y, yes; N, no; SD, standard deviation.

¹Letombe, no scores at time of report.

²Presumed, based on mean (SD).
achieved. Adherence to training frequency was the most reported (n = 11), with all reporting greater than 72% of sessions attended. There was limited reporting of progression of parameters. Two studies reported progressions over 6 months in session duration, percentage HRR, treadmill velocity, and incline. Another study reported target and achieved HR and duration for which target HR was sustained. They planned to progress the target HR zone; however, some participants could not progress past the initial 40% to 50% HRR, whereas other progressed to 70% to 80%. Only 1 study reported the proportion of prescribed dose achieved (63 ± 28%).

**Training settings and individual/group program.** Interventions were undertaken in outpatient rehabilitation settings (n = 6), inpatient settings (n = 4), university centers (n = 6), community centers (n = 2), at both a community center and at home (n = 2), and at home (n = 1); 7 studies did not specify but appeared center based. The majority of center-based interventions appeared to be provided on an individual basis (n = 18); 5 were group interventions, 1 was initially individual and progressed to group interventions, and it was unclear if 1 was an individual or a group intervention. The 2 programs with center and home interventions were carried out as a supervised group at the center and unsupervised individually at home. The home-only program used a supervised, individual approach.

**Testing**

A single ergometer modality was used to undertake progressive aerobic exercise tests in 25 studies. One study used 2 modalities, with the highest value obtained used for each patient, whereas another chose the method that they thought best suited the participant. Of the 28 studies, 27 used maximal protocols. The remaining study used a “metabolic stress test” but did not specify the test type or equipment used. Baseline VO$_{2peak}$ in the studies ranged from 8.0 ± 2.1 to 22.5 ± 5.2 mL/kg/min, with a median of 14 mL/kg/min. Only 4 studies had mean baseline VO$_{2peak}$ measures above 18 mL/kg/min.

**Adverse Events, Effect Maintenance, and Participant Satisfaction**

Adverse events were not reported in 17 studies; 8 reported having no events during testing or training and 1 following an exercise session where the participant became dizzy and mildly incoherent but went on to complete the program. No studies described instructions or a program to continue exercise after the completion of the intervention. Only 1 study undertook postprogram follow-up measures. They showed a statistically significant difference between groups on completion of their 8-week intervention ($P = .04$) but no difference 8 weeks later at follow-up ($P = .4$). Only 1 study reported participant satisfaction.

**Outcomes**

Table 4 summarizes the VO$_{2peak}$ results preintervention and postintervention.

**Meta-analyses of RCTs**

Of the 16 RCTs, 12 contained data suitable for inclusion in the meta-analyses (Figure 1). The overall mean difference was 2.27 (95% CI = 1.58, 2.95) mL/kg/min and favored interventions to improve VO$_{2peak}$. This equated to a 10% to 15% improvement from baseline. The studies were statistically homogeneous ($\chi^2 = 0.00; \chi^2 = 6.92; I^2 = 0\%$). In the subgroup analyses, benefit was observed in aerobic and mixed interventions, which were almost equally effective (Figure 2), as were programs ≤3 months and >3 months in length (Figure 3). The “time since stroke” meta-analysis was not undertaken because of insufficient data for comparison, with only 2 studies conducted within 3 months and the remaining studies, more than 12 months poststroke. No study protocol dose “met recommendations for older adults,” so this subgroup analysis was not undertaken.

**Non-RCT Studies**

Improvements in VO$_{2peak}$ in the non-RCT trials occurred in 5 of the 6 aerobic trials, with significant ($P < .05$) increases ranging from 10% to 27.4%. Of the 4 mixed-intervention non-RCT trials, 2 showed statistically significant increases of 9% and 16%, respectively. The isokinetic training of the paretic leg intervention produced no significant improvement ($P = .413$); however, this program was only 4 weeks long.

**Discussion**

**Significant Benefit With Cardiorespiratory Training**

This review highlights the fact that interventions that are aerobic or have an aerobic component can improve fitness by approximately 10% to 15%, even with modest doses of exercise. The observed improvement of 2.27 mL/kg/min...
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Program Length</th>
<th>Duration (minutes)</th>
<th>Frequency (weeks)</th>
<th>Intensity</th>
<th>Sessions Completed</th>
<th>VO₂ peak Method</th>
<th>Baseline (T1), mL/kg/min (SD)</th>
<th>Program end (T2), VO₂ peak m/L/kg/min (SD)</th>
<th>Reported Change</th>
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<td><strong>Aerobic</strong></td>
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<tr>
<td>Tang et al²⁸</td>
<td>I  =  conventional inpt rehab + Cycle erg, C = Conventional inpt rehab</td>
<td>4.5</td>
<td>1 = 30 cycle</td>
<td>5</td>
<td>50%-70% PO at</td>
<td>9.2 ± 0.7</td>
<td>Recumbent cycle</td>
<td>I  = 11.6 (0.7 SEM), C  = 11.2 (0.5 SEM)</td>
<td>I  = 13.1 (0.9 SEM), C  = 12.1 (0.8 SEM)</td>
<td>T 1  to  T2, I  = 12.6 (5.3 SEM), C  = 8.3 (4.5%)</td>
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<td>VO₂ peak RPE</td>
<td>sessions = 90.5%</td>
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<td>4-6 out of 10</td>
<td>1.5%</td>
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<tr>
<td>Murakami et al²⁸</td>
<td>Conventional rehab + Adapted cycle erg</td>
<td>8 Weeks</td>
<td>20, cycle</td>
<td>5</td>
<td>30%-50% PO</td>
<td>nr</td>
<td>Cycle erg</td>
<td>I  = 16.3 (4.4'), C  = 18.1 (5.5)</td>
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<td>T 1  = 16%, P  &lt; .005</td>
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<td>from initial test</td>
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<td>Calmesi et al²⁹</td>
<td>Interval training adapted cycle erg</td>
<td>2 Months</td>
<td>30</td>
<td>3</td>
<td>40%-80% max PO</td>
<td>nr</td>
<td>Cycle erg</td>
<td>I  = 18.5 (3.7)</td>
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<td>T 1  to  T2, 14.94% P  &lt; .04</td>
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<td>Janssen et al²⁴</td>
<td>I  =  cycle erg with ES, C = cycle erg</td>
<td>6 Weeks</td>
<td>25-30</td>
<td>2</td>
<td>nr</td>
<td>Recumbent cycle</td>
<td>I  = 1.0 (0.3) L/</td>
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<td>erg</td>
<td>min, C  = 1.0 (3.0) L/min, C  = 1.2 (0.3) L/min</td>
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<tr>
<td>Moore et al³⁶</td>
<td>I  =  High-intensity stepping on treadmill with to 40% partial BWS, C = Waiting for intervention</td>
<td>4 Weeks</td>
<td>nr</td>
<td>2 to 5</td>
<td>80-85% HRmax or Borg RPE = 17</td>
<td>nr</td>
<td>Treadmill</td>
<td>I  = 17 (3.2), C  = 16 (6.4)</td>
<td>I  = 18 (5.4), C  = 16 (7.1)</td>
<td>No change time effects = 0.57</td>
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<tr>
<td>Macko et al³⁴</td>
<td>Treadmill</td>
<td>6 Months</td>
<td>40</td>
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<td>40%-60% HRR</td>
<td>88%</td>
<td>Treadmill</td>
<td>I  = 152 (3.0)</td>
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<td>10% P  &lt; .05</td>
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<tr>
<td>Macko et al³⁵</td>
<td>I  =  treadmill X, C = 35 minutes stretching, 5 minutes low-int walking (30%-40% HRR)</td>
<td>6 Months</td>
<td>40</td>
<td>3</td>
<td>40%-70% HRR</td>
<td>84%, C  = 77%</td>
<td>Treadmill</td>
<td>I  = 14.9 (0.9 SEM), C  = 14.7 (1 SEM)</td>
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<td>P  &lt; .001</td>
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<td>Chu et al³⁶</td>
<td>I  =  Chest-deep water X, with a focus on leg X, C = Arm and hand X, seated</td>
<td>8 Weeks</td>
<td>60</td>
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<td>50%-80% HRR</td>
<td>157/168 (93%), C  = 11 1/120 (93%)</td>
<td>Cycle erg</td>
<td>I  = 17.3 (3.0), C  = 17.1 (3.2)</td>
<td>I  = 212 (2.3), C  = 17.6 (4.7)</td>
<td>T 1  to  T2, I  = 22%, P  &lt; .05</td>
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<td>Quaney et al³⁷</td>
<td>I  =  Cycle erg, C = Unsupervised prog of stretching at home</td>
<td>8 Weeks</td>
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<td>40%-70% HRmax</td>
<td>nr</td>
<td>nr</td>
<td>I  = 14.76 (4.23), C  = 14.67 (5.42)</td>
<td>I  = 15.47 (5.13), C  = 14.39 (4.99)</td>
<td>Between grp, Post  P  = .04, Retention: P  = 4</td>
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<td>Lam et al³⁵</td>
<td>Treadmill</td>
<td>3 Months</td>
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<td>40%-80% HRR</td>
<td>nr</td>
<td>Treadmill</td>
<td>20.188 (1.167 SEM)</td>
<td>Absolute change = 5.066 (0.720 SEM)</td>
<td>Relative change = 0.274 (0.041 SEM)</td>
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<tr>
<td>Luft et al³¹</td>
<td>I  =  Treadmill X, C = Stretching</td>
<td>6 Months</td>
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<td>3</td>
<td>40%-60% HRR</td>
<td>89%, C  = 85%</td>
<td>Treadmill</td>
<td>I  = 12.9 (11.5 to 14.3), C  = 12.9 (11.5 to 14.4')</td>
<td>I  = 152 (13.5 to 16.8'), C  = 125 (10.7 to 14.7)</td>
<td>Grp by time, P  &lt; .001</td>
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<tr>
<td>Ivey et al³⁸</td>
<td>I  =  Treadmill X, C = Supervised active and passive stretching of upper and lower body</td>
<td>6 Months</td>
<td>40</td>
<td>3</td>
<td>40%-70% HRR</td>
<td>nr</td>
<td>Treadmill</td>
<td>I  = 14.1 (40), C  = 13.5 (3.6)</td>
<td>I  = 16.6 (5.64), C  = 128 (3.9)</td>
<td>T 1  to  T2, I  = 18%, C  = -4%</td>
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<td>Ivey et al³⁹</td>
<td>I  =  Treadmill X, C = Stretching</td>
<td>6 Months</td>
<td>40</td>
<td>3</td>
<td>40%-70% HRR</td>
<td>nr</td>
<td>Treadmill</td>
<td>I  = 13.7 (0.9 SEM), C  = 14.8 (0.9 SEM)</td>
<td>I  = 15.7 (1.1 SEM), C  = 14.4 (1 SEM)</td>
<td>Grp by time T1-2, P  &lt; .002</td>
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<tr>
<td>Potempa et al³²</td>
<td>I  =  Cycle erg, C = Passive ROM X</td>
<td>10 Weeks</td>
<td>30</td>
<td>3</td>
<td>30%-highest</td>
<td>nr</td>
<td>Cycle erg</td>
<td>I  = 18.8 (1.1 SEM), C  = 15.1 (0.6 SEM)</td>
<td>I  = 18.8 (1.1 SEM), C  = 15.2 (0.9 SEM)</td>
<td>Within I grp, P  &lt; .001</td>
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<td>level attainable of max PO</td>
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(continued)
### Table 4. (continued)

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<th>Study</th>
<th>Intervention</th>
<th>Program Length</th>
<th>Duration (minutes)</th>
<th>Frequency (/week)</th>
<th>Intensity</th>
<th>Sessions Completed</th>
<th>VO₂ Testing Method</th>
<th>Baseline (T1), VO₂peak mL/kg/min (SD)</th>
<th>Program end (T2), VO₂peak mL/kg/min (SD)</th>
<th>Reported Change</th>
<th>Calculated Percentage Change From Baseline</th>
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<tbody>
<tr>
<td>Rimmer et al11</td>
<td>I int and I dur = Cycle erg, recumbent stepper; C = Conventional rehab, including gait training, balance, strength, ROM X</td>
<td>14 Weeks</td>
<td>I int = 30, I dur = 60, C = 60</td>
<td>I = All, 3</td>
<td>HRR, 40% ~ 69%, I dur = 50% HRR, C = nr</td>
<td>Cycle erg</td>
<td>I int = 15.06 (7.4), I dur = 13.27 (3.6), C = 12.57 (4.2)</td>
<td>I to T2 within grp, I int P = .239, I dur P = .279, C P = .467</td>
<td>I int = 4, I dur = 6, C = -3</td>
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<td>Yang et al12</td>
<td>Treadmill</td>
<td>12 Weeks</td>
<td>I = 50</td>
<td>3</td>
<td>40% ~ 60% HRR</td>
<td>Treadmill</td>
<td>I int = 11.24 (2.42), I dur = 14.06 (3.19)</td>
<td>T1 to T2 P &lt; .01</td>
<td>25</td>
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<tr>
<td>Teixeira da Cunha Filho et al13</td>
<td>I = Regular rehab + treadmill, with BWS; C = Regular rehab</td>
<td>2-3 Weeks</td>
<td>Usual care + 20 minutes: I = treadmill, C = Gait training</td>
<td>5</td>
<td>speed ↑ BWS ↓ as able</td>
<td>Cycle erg</td>
<td>I = 8.57 (2.09), C = 8.02 (2.05)</td>
<td>I = 11.55 (2.76), C = 8.12 (2.3)</td>
<td>Between grp: T1 to T2 P = .039</td>
<td>I = 35, C = 1, I - C = 34</td>
<td></td>
</tr>
<tr>
<td>Letombe et al14</td>
<td>I = Usual inst care + semirecumbent cycle, stretching, additional physical X incl treadmill, stepper, balance, isokinetic strength, UL games; C = Usual inst care</td>
<td>5 Weeks</td>
<td>I = 40-60 Minutes additional</td>
<td>4</td>
<td>70%-80% PO</td>
<td>1-Legged test on cycle erg</td>
<td>I = 11.13 (4.6), C = nr (graph only)</td>
<td>I = 19.44 (4.59), C = nr (graph only)</td>
<td>T1 to T2, I = 20.33%, C = 8%, I - C = 12%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duncan et al15</td>
<td>I = Endurance on cycle, strength, balance, UL functional use, ROM; C = Usual home service as prescribed by physician and visit by research staff every 2 weeks</td>
<td>12-14 Weeks</td>
<td>I = 90 Minutes with up to 30 minutes on bike</td>
<td>3</td>
<td>nr</td>
<td>Cycle erg</td>
<td>I = 33.4 ± 2.3, C = 8.7 (5.3), PT, 10.4 (7.1) OT</td>
<td>Cycle erg</td>
<td>I = 11.7 (3.3), C = 11.2 (2.9)</td>
<td>T1 to T2 mL/kg/min, I = 1.05 (0.23 SE), C = 0.06 (0.22 SE), between grp = 0.99 (0.33 SE), P &lt; .01</td>
<td>I = 9, C = 0, I - C = 9</td>
</tr>
<tr>
<td>Sunnerhagen et al16</td>
<td>PRT, 5-station circuit incl 2 functional X stations</td>
<td>8 Weeks</td>
<td>I = 45</td>
<td>3</td>
<td>nr</td>
<td>Cycle erg</td>
<td>I = 12.4 (4.7), Paretic = 12.4 (4.7), nonparetic = 13.9 (4.3)</td>
<td>Paretic = 15.7 (7.2), nonparetic = 15.8 (6.0)</td>
<td>T1 to T2, paretic P &lt; .01, nonparetic ns</td>
<td>Paretic = 27, nonparetic = 14, difference = 13</td>
<td></td>
</tr>
<tr>
<td>Tang et al17</td>
<td>Center: 90 minutes incl education, aerobic and resistance training, aerobic included walking, recumbent and upright bike; Home: aerobic and resistance training</td>
<td>6 Months</td>
<td>I = 30-60 Minutes aerobic</td>
<td>5×1 at center 4 at home</td>
<td>60%-80% HRR, 11-14 out of 20 RPE</td>
<td>Recumbent cycle erg; 6, cycle erg, I treadmill</td>
<td>36, 11-14 out of 20 RPE</td>
<td>-3/12 = 13.6 (4.1), Baseline = 14.8 (4.8)</td>
<td>16.2 (5.1)</td>
<td>-3/12 to baseline, P = .301; baseline to 6/12, P = .046</td>
<td>9</td>
</tr>
</tbody>
</table>
Table 4. (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Program Length</th>
<th>Duration (minutes)</th>
<th>Frequency (weeks)</th>
<th>Intensity</th>
<th>Sessions Completed</th>
<th>VO2 Peaks Tested Method</th>
<th>Baseline (T1), VO2peak mL/kg/min (SD)</th>
<th>Program end (T2), VO2peak mL/kg/min (SD)</th>
<th>Calculated Percentage Change From Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al&lt;sup&gt;19&lt;/sup&gt;</td>
<td>I both = Recumbent cycle and PRT; I cyc = Recumbent cycle; sham PRT; I PRT =</td>
<td>10-12 Weeks</td>
<td>60 Minutes in total 30 minutes ex cycle and PRT</td>
<td>3</td>
<td>HR at 50%−70% VO2peak, RPE</td>
<td>nr</td>
<td>Cycle erg</td>
<td>I both = 14.4 (3.1), I cyc = 13.0 (4.5), I PRT = 14.0 (3.3), C = 13.5 (3.5)</td>
<td>I both = 16.6 (5.2), I cyc = 14.5 (3.9), I PRT = 13.5 (3.8), C = 12.7 (4.3)</td>
<td>Compare to C, T1 to T2 mL/kg/min (range), I both = 3 (0.3-5.6), P = 0.3; I cyc = 2.5 (1.9-4.9), P = 0.002; I PRT = 0.5 (−1.0 to 2), P = .51</td>
</tr>
<tr>
<td>Kluding et al&lt;sup&gt;5&lt;/sup&gt;</td>
<td>TBRS and lower-limb muscle strengthening</td>
<td>12 Weeks</td>
<td>60 (30 minutes aerobic)</td>
<td>3</td>
<td>HR at 50% peak VO2, 11-14 out of 20 RPE</td>
<td>Minimum 75%</td>
<td>TBRS and cycle-highest value reported</td>
<td>I = 13.9 (4.5), C = 13.5 (3.8), I = 2.5 (−1.0 to 2), P = .03</td>
<td>I = 13.0 (3.8), C = 12.7 (4.3)</td>
<td>I = 9.2; I cyc = 2.5 (1.9-4.9), P = 0.002; I PRT = 0.5 (−1.0 to 2), P = .51</td>
</tr>
<tr>
<td>Pang et al&lt;sup&gt;38&lt;/sup&gt;</td>
<td>I = Fitness and mobility X prog; C = Seated upper extremity prog</td>
<td>19 Weeks</td>
<td>60</td>
<td>3</td>
<td>40%−80% HRR</td>
<td>I = 81.4%, C = 80.4%</td>
<td>Cycle erg</td>
<td>I = 22.5 (5.2), C = 21.5 (4.3)</td>
<td>I = 24.5 (5.3), C = 21.8 (4.5)</td>
<td>I = 9.2; I cyc = 2.5 (1.9-4.9), P = 0.002; I PRT = 0.5 (−1.0 to 2), P = .51</td>
</tr>
<tr>
<td>Michael et al&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Progressive adaptive physical activity model; functional mobility, sit to stand, trunk stability, balance</td>
<td>6 Months</td>
<td>60</td>
<td>at center, home prog on alternate days</td>
<td>nr</td>
<td>73%</td>
<td>Treadmill</td>
<td>I = 153 (4.1)</td>
<td>I = 157 (4.6)</td>
<td>I = 9.2; I cyc = 2.5 (1.9-4.9), P = 0.002; I PRT = 0.5 (−1.0 to 2), P = .51</td>
</tr>
<tr>
<td>Carr et al&lt;sup&gt;45&lt;/sup&gt;</td>
<td>I = Upper and lower-limb body erg, flexibility plus 8 strength-training exercises; C = Upper- and lower-limb body erg, flexibility</td>
<td>16 Weeks</td>
<td>20 to 40</td>
<td>3</td>
<td>C = 40%−70% peak PO</td>
<td>nr</td>
<td>Recumbent cycle erg</td>
<td>I = 15.1 (5.1), C = 11.9 (4.0)</td>
<td>I = 17.9 (5.6), C = 12.3 (3.7)</td>
<td>I = 9; C = 3, I − C = 16</td>
</tr>
<tr>
<td>Rimmer et al&lt;sup&gt;39&lt;/sup&gt;</td>
<td>I = Aerobic on own choice of equipment, strength/endurance/flexibility; C = Lag control for intervention</td>
<td>12 Weeks</td>
<td>60 (30 CV endur)</td>
<td>3</td>
<td>Target rate based on value when RER = 1</td>
<td>I = 93%</td>
<td>Cycle erg</td>
<td>I = 13.34 (4.22), C = 14.13 (2.96)</td>
<td>I = 14.43 (4.03), C = 12.69 (2.61)</td>
<td>I = 8, C = 10, I − C = 18</td>
</tr>
</tbody>
</table>

Knee flexion/extension isokinetic training

| Billinger et al<sup>40</sup> | Isokinetic knee F/E on Biodex for paretic limb | 4 Weeks       | 60-90               | 3                 | 60%−70% HR max | 7 Completed 12/12, 5 completed 11/12 sessions | TBRS 193 (6.9) | I = 93%; I cyc = 2.5 (1.9-4.9), P = 0.002; I PRT = 0.5 (−1.0 to 2), P = .51 | I = 9.2; I cyc = 2.5 (1.9-4.9), P = 0.002; I PRT = 0.5 (−1.0 to 2), P = .51 | I = 9, C = 1, I − C = 8 |

Abbreviations: BWS, body-weight support; C, control group; CV, cardiovascular; dur, duration; endur, endurance; erg, ergometer; ES, electrical stimulation; E, extension; F, flexion; GLM, general linear model analysis; Grp, group; HR, heart rate; HRR, heart rate reserve; incl, including; I, intervention group; I both, received both cycle and PRT; Inpt, inpatient; int, intensity; max, maximal; ns, nonsignificant; OT, occupational therapy; PO, power output; prog, program; PRT, progressive resistance training; PT, physiotherapy; rehab, rehabilitation; RER, respiratory exchange ratio; ROM, range of motion; RPE, rate of perceived exertion; nr, not reported; SD, standard deviation; SEM, standard error of the mean; T1 to T2, baseline to end of program; TBRS, total body recumbent stepper; UL, upper limb; VO2peak, peak oxygen consumption; X, exercise; x%−y%, progressed from x% to y%; x% ↑y%, ranged from x% to y%; ↓, decrease; ↑, increase.

<sup>a</sup>Studies are grouped by training type, then listed by time since stroke.

<sup>b</sup>Range.
(95% CI = 1.58, 2.95) in the meta-analysis of 12 RCTs in this review provides further confirmation of the positive effect of cardiorespiratory training, with a result similar to the 2.14 (95% CI = 0.50, 3.78) mL/kg/min observed in the recent Cochrane review based on 4 studies.4 The dose protocols of the studies included in the meta-analysis were relatively modest, with none meeting the recommendation of 30 minutes of moderate-intensity physical activity most days of the week.46 Despite this, they were still effective in generating improvements. The subgroup analysis identified programs of less than and greater than 3 months in length, both resulting in improvements of approximately 10% to
15% VO_{peak}. This finding is similar to the review by Shephard of aerobic training responses in the healthy elderly, where gains in VO_{peak} with training ranged from 12.9% for the short-term (8-10 weeks), 14.1% for the medium-term (12-18 weeks), and 16.9% for longer-term (24-52 weeks) programs. Cardiorespiratory training appears to be beneficial for people at any time, from weeks to many years post-stroke. The results also appear to indicate that a key factor in improving cardiorespiratory fitness is to incorporate aerobic activity, with the exact intervention appearing to be less important. A larger dose of these programs or different interventions may lead to greater improvements in cardiorespiratory fitness levels after stroke.

Very Low Levels of Baseline Fitness

The very low levels of baseline cardiorespiratory fitness of stroke survivors are highlighted in this review. Baseline VO_{peak} levels in all but 4 studies were below the 18 mL/kg/min suggested as being a minimum required for independent living, and all studies showed baseline values well below normative data for an elderly population (29 ± 7.3 and 27 ± 5.8 mL/kg/min for healthy men and women, aged 70-79 years, respectively). This is despite the studies typically including highly selected participants: ambulatory with limited comorbidities. It is very likely that fitness levels in the general stroke population are even lower. Many stroke survivors are likely to be limited in day-to-day activities by their cardiorespiratory fitness. This is in addition to any disability caused by the more widely recognized major physical impairments of stroke, including muscle weakness, poor balance, loss of coordination, and spasticity. The results highlight the large room for improvement in cardiorespiratory fitness poststroke.

Exercise Dose, Intensity, and Timing

“For this very unfit population, commencement of training at a lower intensity level with progression as tolerated is likely to be required. The dose of exercise required to maintain or enhance cardiorespiratory fitness after stroke remains unclear. Although frequency, duration, and intensity levels were prescribed in the majority of the studies, only 1 calculated the proportion of prescribed dose achieved (63% ± 28%).

Timing after stroke may also be a key factor, particularly in any contribution cardiorespiratory fitness training may make to functional recovery. Surprisingly, only 5 studies were within 3 months after stroke. This should be a key time for preventing cardiorespiratory deconditioning and promoting brain reorganization, both of which require meaningful and challenging physical activity. Inpatient environments have the potential to routinely incorporate cardiorespiratory fitness training into their programs; however, they are consistently identified as settings deprived of activity poststroke. One systematic review indicated that only 32.8 minutes (60%) of inpatient physiotherapy sessions was spent being active. Other studies have shown that little or no time during inpatient physiotherapy sessions was spent in a HR range that would be expected to improve cardiorespiratory fitness.”

Mode of Delivery of Interventions

Given the current health economic climate, interventions designed to increase cardiorespiratory fitness need to be resource-efficient as well as effective. Only a few of the studies in this review used group programs (n = 5), unsupervised home interventions (n = 2) or community center programs (n = 4). A number of interventions appeared quite resource intensive; 19 used 1-to-1 supervision, and 14 were greater than 3 months (Table 4). A review of physical activity programs for older adults identified health benefits and improved function that were gained through both center- and home-based programs. The home-based programs had better adherence, particularly in the long term. Redesign of services to include cardiorespiratory fitness training within existing budgets may be more likely to be generalizable, rather than relying on service enhancements. One study redesigned their inpatient program to compare 20 minutes of treadmill training with the usual 20 minutes of standard gait training. The therapy time was unchanged. Two studies used a combined center and home program, which may be a feasible way to assist stroke survivors to be active on most days of the week. Redesign may occur through the use of groups, including circuit classes, as inpatient, outpatient, and community-based programs. Participation in groups has the advantage of increased ratio of group leader to participants and the added benefits of social interaction and peer motivation.
Comparison With Other Chronic Diseases

A number of the issues identified above are common to other chronic diseases. A recent review of exercise and Parkinson’s disease identified that interventions were predominantly highly supervised, center-based programs, trialled in cognitively intact participants with mild-to-moderate disease. Reviews of the effect of exercise-based rehabilitation on coronary heart disease and heart failure highlighted the fact that participants were predominantly middle-aged men with low and low to moderate risk, respectively. Exercise interventions may improve health-related quality of life and improve exercise capacity without increased risk of death in heart failure patients. However, in this population, it does not reduce all-cause mortality, nor could a minimum dose of exercise be recommended because of the variation in programs. Following exercise, there was no reduction in recurrent myocardial infarction or revascularization for coronary heart disease participants. However, for those followed up for more than 12 months, there was a reduction in all-cause and cardiac mortality. Further investigation in stroke is required to investigate the very important health-related quality of life, secondary prevention, and mortality outcomes.

Strengths and Limitations

The use of the PRISMA and CONSORT statements guided the unbiased conducting of the review with meta-analysis. The meta-analysis was statistically homogeneous, indicating that like studies were being compared, had reasonable participant numbers, and provided a more robust estimate of likely benefit than the individual studies alone. There were some unavoidable limitations. Only studies published in English were included. There are relatively few RCTs in the field, and not all could be included in the meta-analysis. Study quality of the RCTs included in the meta-analysis was variable, with ratings of good (n = 5) and fair (n = 7). Only 4 of the studies used an intention-to-treat analysis, with most reporting data only for those who completed the program. This, combined with high attrition rates in some studies, may introduce considerable bias. Attrition rates, when reported, varied from 0% to 41%, and the main reasons provided were medical problems not related to the program and noncompliance, although this term was not explained. Studies were conducted in people with mild to moderate deficits; therefore, there is limited generalizability of the results to those with greater stroke deficits or multiple comorbidities.

Suggestions for Reporting in Future Studies

To improve the understanding of the effects of training on cardiorespiratory fitness, it would be useful for studies to consistently report several data items. As VO\textsubscript{2peak} is measured in mL/kg/min it is influenced by change in weight, which may occur over time. Future studies should report both in L/min for absolute change and mL/kg/min to give an indication of cardiorespiratory fitness level. Although dose was prescribed, it was difficult to ascertain the dose that was delivered. This has also been identified as an issue in heart failure interventions. To gain a better understanding of the stimulus required for benefit, studies should quantify the proportion of dose achieved in terms of sessions attended, intensity, and duration of the sessions. Reporting of the progression of parameters would also provide insight into effects of training on stroke survivors’ endurance and exercise tolerance. Few adverse events were reported during testing or training, and the majority were minor. Lack of reporting on the presence or absence of adverse events and reasons for attrition is common with exercise interventions in other chronic disease populations. All studies should report these to help inform the risks versus benefits of training. This may inform tailoring interventions for the heterogeneous stroke population.

Implications for Future Research

Despite the positive results highlighted in this review, many questions are yet to be answered. Further investigation is required into what actual dose, as opposed to prescribed dose, of aerobic activity is adequate to gain the benefit demonstrated and what is required in an intervention, in terms of aerobic training programs and dose, to obtain even greater improvements. Most studies undertook very traditional center-based, supervised treatment sessions rather than assisting participants in adopting cardiorespiratory fitness training as part of a “lifestyle change” for a chronic disease. The results of this analysis suggest that inclusion of any aerobic exercise is far more important than the specific program; therefore, future studies should focus on broadly generalizable interventions that are able to be delivered within existing budgets. Investigation is also required into strategies to engender longer term behavior change and maintain improvements postprogram. Larger-scale studies, including outcomes for functional improvement, recurrent stroke, cardiovascular events, death, or dependence, would help confirm likely additional benefits of exercise poststroke and enhance clinical uptake. Studies are required to determine whether improved levels of cardiorespiratory fitness can also be obtained in those with greater impairments poststroke, for older and younger patients, and those with significant comorbidities as well as to determine the importance of timing of the intervention poststroke.

Conclusion

This study provides clear evidence that important cardiorespiratory fitness benefits can be obtained from training,
whether aerobic or mixed with an aerobic component. Training can increase cardiorespiratory fitness in people with mild-moderate impairment after stroke, reducing the percentage VO$_{2\,\text{peak}}$ at which people have to work to undertake everyday tasks. Cardiorespiratory fitness is a relatively new area of stroke research and requires further investigation to inform practice. This review provides strong evidence that exercise training is feasible and effective in at least a subset of people after stroke, and given the available evidence in other related diseases, it suggests that such training programs should be incorporated into routine post-stroke care.

Acknowledgments

We would like to acknowledge Debbie Booth (Faculty Librarian—Health, University of Newcastle) for assistance with the systematic search and Patrick McElduff (Associate Professor of Biostatistics, University of Newcastle) for advice on the meta-analyses.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: DL Marsden is supported by the Heart Foundation and the University of Newcastle through the provision of a postgraduate scholarship and by the Hunter Stroke Service. Her research is supported through grants from the National Stroke Foundation, John Hunter Hospital Charitable Trust, and the Hunter New England Allied Health Research Committee Research Grants. A Dunn is supported by the University of Newcastle through the provision of an Australian Post-Graduate Award scholarship. CR Levi is a National Health and Medical Research Council Practitioner Fellow and Senior Staff Specialist Neurologist, Hunter New England Local Health District. NJ Spratt was supported by a health professional research fellowship from the National Health and Medical Research Council and by the Greater Building Society/Hunter Medical Research Institute.

References


Appendix 3: Published manuscript of Chapter 6
Independently ambulant, community-dwelling stroke survivors have reduced cardiorespiratory fitness, mobility and knee strength compared to an age- and gender-matched cohort

Ashlee Dunn¹,², Dianne L. Marsden¹,²,³, Paulette Van Vliet¹,², Neil J. Spratt¹,²,³, Robin Callister¹,²

¹Priority Research Centre for Physical Activity and Nutrition, University of Newcastle, Callaghan, New South Wales, Australia, ²Hunter Medical Research Institute, New Lambton Heights, New South Wales, Australia, ³Hunter New England Local Health District, New Lambton Heights, New South Wales, Australia

Background: Most exercise interventions for stroke survivors are designed for those who have substantial motor and functional disabilities. There remains a group of well-recovered stroke survivors who have yet to be investigated in terms of their physical capacity and fitness levels.

Objective: To assess and compare the physical capacities of independently ambulant, community-dwelling stroke survivors to age- and gender-matched comparison participants.

Methods: Data were obtained from 17 stroke survivors participating in the How FITSS? Trial, all with functional ambulatory category of ≥4 and a self-selected walking speed ≥0.8 m s⁻¹. An additional 17 healthy control participants were recruited. Cardiorespiratory fitness (CRF) was measured using oxygen consumption (VO₂peak), and additional measures of walking speed (m s⁻¹), leg strength and body composition were also assessed. Differences between groups were assessed by matched pairs t-tests. Effect sizes were calculated using Cohen’s d.

Results: There were no significant differences in age, BMI, muscle mass or body fat between groups (p > 0.05). Peak VO₂ was lower in the stroke group for the shuttle walk test (p = 0.037) and progressive cycle test (p = 0.019), as were all CRF test performance measures (p < 0.05). Stroke survivors walked significantly (p < 0.001) slower at both self-selected and fast speeds. Effect sizes of group differences for all leg strength variables were medium to large, with peak torque lower in the stroke group for all trials.

Conclusions: Despite being independently ambulant and community dwelling, the CRF, walking speed and leg strength of this group were reduced compared to non-stroke comparison participants. These patients may benefit from undertaking targeted exercise programmes.

Keywords: stroke, cardiopulmonary exercise test, six-minute walk, shuttle walk, cycle ergometer, physical capacity, oxygen consumption, rehabilitation

Introduction

It is estimated that among the 75% of people who survive first stroke, 25% are left with minor disability and 40% a moderate–severe disability.¹ Consequently, most exercise interventions for stroke survivors are designed for those who have substantial motor and functional disabilities, with the primary goal to improve performance of activities of daily living (ADLs). In contrast, little attention has been paid to comparatively well-recovered stroke survivors who return to independent, community living, and it is unclear whether they have physical fitness deficits that would benefit from exercise programmes.

Numerous studies have assessed the fitness levels of stroke survivors, and cardiorespiratory fitness (CRF)²,³ and leg strength⁴ are consistently lower, ranging from 26 to 75% achieved by a non-stroke comparison group. Also, stroke survivors may have a higher energy cost of walking than comparison groups.⁵ Previous studies included a range of stroke-related disability levels. Consequently, it is unclear whether deficits in CRF, walking speed and leg strength are present in well-recovered stroke survivors, and if present, the extent and variation in these deficits. Many of these studies were conducted in older populations, where comorbidities may contribute to deficits in...
physical fitness and performance. Inclusion of younger participants may provide new insights regarding the type and magnitude of deficits, and whether specific exercise programs should be recommended. In those studies that compared data from stroke survivors to a control group, differences in the age or gender of the groups, even if controlled for in statistical analyses, may influence interpretation. In addition, many studies focus on one or two fitness characteristics, which limits our understanding of fitness levels across a range of fitness parameters in the same population. Consequently, there is a need to specifically investigate well-recovered stroke survivors to inform exercise programme recommendations for this group.

The aim of this study was to compare CRF, walking ability, knee strength and body composition in independently ambulant, community-dwelling stroke survivors to healthy age- and gender-matched comparison participants.

Methods
Participants
Data were obtained from stroke participants assessed at baseline as part of a controlled exercise intervention study (ANZCTR Trial ID: ACTRN12614000134628). Sample size was based on that suggested to detect the minimal detectable change (MDC) (difference) for the six-minute walk test (6MWT) between groups. All testing was conducted by an experienced exercise scientist (AD) and neurological physiotherapist (DM) with support from trained research assistants. Inclusion criteria were: (1) had experienced a clinically diagnosed stroke (ischemic or haemorrhagic) in the past 12 months, (2) FAC ≥ 4 with a self-selected walking speed of ≥0.8 m s⁻¹, (3) no use of a walking aid, (4) able to follow a two-step command, (5) were not pregnant, and (6) had no contraindications to exercise as deemed by the referred medical officer. Seventeen healthy age- and gender-matched comparison participants were recruited using word of mouth and flyers posted around the University campus. Eligibility criteria for this group were: (1) no history of stroke or transient ischemic attack, (2) matched the age (within 5 years) and gender of a stroke participant, and (3) no contraindications to exercise testing. All participants were screened using the Exercise and Sport Science Australia Pre-Exercise Screening Questionnaire, and medical clearance was obtained from their family/general physician when required. Participants were asked to refrain from vigorous physical activity for 24 h prior to testing.

Demographic data including age, gender, time since stroke, medications, past and current physical activity, and comorbidities were determined from medical history. Although none of the stroke survivors were regarded as having any current disability associated with one side of the body, Side ‘more affected’ was determined either by the side reported as more affected at the time of stroke onset, or from clinical notes made at the time of admission, with the ‘less affected’ side the opposite. Ten of the 17 stroke survivors were more affected on their dominant right side. The remaining participants were more affected on their non-dominant side (five left and two right). Level of physical activity was calculated semi-quantitatively using information reported during the screening process and interview. Activity levels were defined according to the International Physical Activity Questionnaire (IPAQ) categorical score and categorised as low, moderate or high levels. All participants were provided written informed consent. This research was approved by the Hunter New England Human Ethics Committee (11/04/20/4.04) and University of Newcastle Human Research Ethics Committee (H-2011-0172). None of the authors have any conflict of interest in the submission of this manuscript.

Cardiorespiratory fitness
Oxygen consumption (VO₂) was recorded throughout three aerobic fitness tests: six-minute walk test (6MWT), incremental shuttle walk test (SWT), and using a portable open-circuit spirometry system (K4b², COSMED, Italy). Calibration of time delay, the turbine, and gas analysers was performed to manufacturer’s specifications prior to each testing session. Heart rate (HR) was measured by 12-lead electrocardiography (Quark T12, COSMED, Italy), which was continuously monitored prior to, during and post exercise for all participants. All variables were averaged over 30s epochs, with peak oxygen consumption (VO₂peak) and HR (HRpeak) determined as the highest epoch value during the test.

Six-minute walk test
The 6MWT was conducted in accordance with the American Thoracic Society Guidelines (2002) using a 20 m walkway due to space restrictions. The endurance test was performed indoors over a straight, uninterrupted corridor. Participants were instructed to walk as far as possible in the 6-min time frame. Standardised verbal encouragement was given at one-minute intervals throughout the test. The total distance achieved was recorded. It has been reported that wearing the Cosmed K4b² portable system does not interfere with the reliability of the 6MWT in stroke survivors.

Incremental shuttle walk test
As originally reported by Singh et al., participants walked shuttles between two markers spaced 9 m apart, creating a 10 m course that included turning around the markers. The test requires the individual to walk for as many shuttles...
as possible at increasing speeds dictated by an audio CD (Department of Respiratory Medicine, Glenfield Hospital NHS Trust, Leicester, UK). Participants were instructed not to jog or run. The test begins at 0.50 m s\(^{-1}\) and increases by 0.17 m s\(^{-1}\) every minute. The test was terminated of the participants own volition or when the participant was unable to reach within 0.5 m of the marker at the time of the audio signal. The final completed shuttle was recorded.

**Upright cycle graded exercise test**

A graded exercise test was performed on an upright cycle ergometer. Participants pedalled on an upright cycle (818E, Monark, Sweden) at a rate of 50 or 60 rpm, with workloads increasing in 25 W increments per minute starting from 0 W until test termination. The Karvonen Formula\(^\text{16}\) was used to calculate 85% of heart rate reserve (85%HRR = [(220 − age) − resting HR] × 0.85) + resting HR), which was used as a safety test-termination criterion. Other termination criteria were the inability to maintain cadence, volitional fatigue, and failure of equipment or abnormal cardiac responses to exercise.\(^\text{9}\) Participants were encouraged to complete a cool-down on completion of the test.

**Walking speed**

The 10-m Walk Test (10 mWT)\(^\text{17}\) was used to assess both self-selected and fast walking speeds. Participants were required to walk along a 14 m walkway, with the middle 10 m timed and recorded. Three trials were performed for each test, with the average taken and converted to m s\(^{-1}\).

**Isometric and isokinetic leg strength**

The HUMAC-NORM (CSMi Solutions, USA) isokinetic dynamometer was used to measure muscle torque of knee extensors and flexors in both limbs. Participants were positioned with a back angle of 85° and the popliteal fossa of the involved side resting against the edge of the seat. To minimise body movement, an adjustable seatbelt was applied across the waist and upper torso, with an additional Velcro strap securing the thigh. The lateral femoral condyle of the involved knee was aligned with the rotational axis of the dynamometer. The distal aspect of the tibial attachment was positioned just proximal to the medial malleolus.

The test protocol involved three maximal isometric extension trials, three maximal isometric flexion trials, and three maximal isokinetic flexion and extension trials each involving three repetitions at 60° s\(^{-1}\). It has been suggested that stroke survivors have difficulty in generating faster movements,\(^\text{18}\) therefore a slow speed of 60° s\(^{-1}\) was used. Each isometric trial was preceded by a 30s rest period. Both legs were assessed, with the right limb consistently being tested first. Verbal encouragement and coaching were provided throughout the test. Maximum peak torque (Nm) was extracted from the best isometric and isokinetic trials. Data were categorised according to more affected side for the stroke group, and the mean of both limbs for the comparison group,\(^\text{19}\) as there was no difference between limbs for the latter group.

**Body composition**

Body composition was assessed using bioelectrical impedance analysis (InBody 720 Biospace, Korea) to measure body fat (%), muscle mass (kg) and lean mass (kg).\(^\text{20}\)

**Statistical analysis**

Data were analysed using Stata Statistical Software 11.0 (Statacorp. 2011). Comparisons of demographic and clinical data were assessed by matched pairs (between group) t-tests, with significance set to \(p < 0.05\). All data were tested for normality using Shapiro–Wilks statistics. Missing data excluded both participants in the pair. Results are presented as mean ± standard deviation unless otherwise stated. Effect sizes were calculated using Cohen’s \(d\) with an effect size (ES)<0.2 categorised as small, 0.2–0.5 as medium, 0.5–0.8 as large and >0.8 as very large.\(^\text{21}\) In order to represent the performance of the stroke group compared to the comparison group, the mean results of the stroke group were calculated as a percentage of the mean results of the comparison group, whose values were designated as 100%.

**Results**

Characteristics of the 34 participants (\(n = 17\) stroke, 53% males) are summarised in Table 1. All stroke survivors were classified in FAC 5, with one exception (FAC 4). The majority of participants (\(n = 11\)) were classed as one on the modified Rankin Scale, with two participants zero, and four as two. All participants walked at a self-selected speed of ≥0.9 m s\(^{-1}\), classing them as community ambulators.\(^\text{22}\) There was an even balance in gender both within groups and between groups, with reported comorbidities reasonably similar between groups. There were no significant differences in age, height, weight, muscle mass or body fat (Table 2) between groups (\(p > 0.05\)). No significant adverse events occurred during testing. In the stroke group, eight participants were categorised as low activity, six were in the moderate activity category, and three in the high activity category. Physical activity levels of the comparison group were three in the low activity category, ten in moderate activity, and four in high activity.

Outcome variables from each test are presented in Table 2. During the three CRF exercise tests, VO\(_{2}\)\(_{\text{peak}}\), HR\(_{\text{peak}}\) and performance outcomes were lower in the stroke group with large to very large effect size differences in
Table 1 Participant characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Stroke (n=17)</th>
<th>Comparison (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.7 ± 16.5</td>
<td>58.6 ± 16.1</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (53)</td>
<td>9 (53)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (47)</td>
<td>8 (47)</td>
</tr>
<tr>
<td>Months post-stroke (n)</td>
<td>3.5 ± 3.6</td>
<td>–</td>
</tr>
<tr>
<td>Bod mass index (kg m(^{-2}))</td>
<td>27.7 ± 6.1</td>
<td>25.9 ± 4.8</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>0 (0)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (22)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>4 (22)</td>
<td>3 (17)</td>
</tr>
<tr>
<td>COPD</td>
<td>1 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>CVD</td>
<td>1 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (17)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>PVD</td>
<td>1 (6)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Medications, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>8 (44)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>4 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Functional ambulatory category, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>16 (94)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>Modified ranking scale, n (%)</td>
<td>2 (12)</td>
<td>11 (65)</td>
</tr>
<tr>
<td>0</td>
<td>2 (12)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11 (65)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (24)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Data are mean ± standard deviation or counts (percentages).

Abbreviations: n: number, COPD: chronic obstructive pulmonary disease, CVD: cardiovascular disease, PVD: peripheral vascular disease, ACE: angiotensin-converting enzyme.

VO\(_{\text{peak}}\) and very large differences in performance outcomes between the groups. Stroke survivors had mean VO\(_{\text{peak}}\) values that were 75.5–78.3% of those of the comparison group (Figure 1). The mean difference between groups in 6MWT distance (142 m) exceeded the reported MDC for stroke (50 m), as did walking speed (10 mWT MDC 0.10 m s\(^{-1}\); difference between groups: self-selected 0.3 m s\(^{-1}\), fast 0.5 m s\(^{-1}\)) and the SWT MDC reported in COPD (SWT MDC: 47.5 m; difference: 236 m).

Of the 15 stroke survivors who performed the cGXT, only two terminated testing due to their HR reaching the predetermined 85% HRR limit compared to 13 of the 15 in the comparison group. The remaining two non-stroke participants stopped due to leg fatigue, as did six in the stroke group. Other reasons for stroke survivors’ termination included shortness of breath (n = 4), knee pain (n = 2), ECG changes (n = 1) and a poor ECG signal (n = 1). Knee pain prevented two stroke survivors from performing the cycle GXT, and one stroke survivor from performing knee strength testing.

There were very large effect sizes for walking speed differences, with the stroke group walking substantially slower at both self-selected and fast walking speeds. Leg strength of the stroke group was lower for all isometric and isokinetic trials, with medium to large effect sizes equating to 78–89% of the comparison group (Figure 1). There was a trend towards a greater discrepancy in strength between groups for the isokinetic trials. Body composition was similar between groups.

**Discussion**

Despite being independently ambulant, with evidence of very good functional recovery following stroke, there were still deficits in the stroke group for CRF, walking speed and leg strength. Across this variety of fitness tests, these stroke survivors underperformed compared to the age- and gender-matched group. Reasons for these significant differences between groups are speculative, with reported changes in muscle fibre recruitment and composition,23 respiratory function25 and autonomic control of cardiac functions4 after stroke possible factors. Although exercise programmes for stroke are usually focused on improving ability to perform ADLs and increasing quality of life,26–28 exercise after stroke is also important to improve CRF, increase muscle strength, reduce depressive symptoms29 and prevent complications associated with inactivity, as well as to decrease the likelihood of secondary stroke.2,30 Therefore, there are important health benefits from exercise programmes for stroke survivors who are functionally independent and with little to no functional limitations.29 The very low fitness levels found in this group, along with the known high risk for secondary stroke, suggest that this group would be a very good target for future exercise intervention studies.

This is the first study to specifically assess the fitness levels of independently ambulant stroke survivors across a range of tests. Our findings are in line with the previously reported comparisons between stroke survivors with a range of disabilities and non-stroke groups. Using a recumbent cycle ergometer, Tomczak et al.31 assessed ten hemiparetic stroke survivors, reporting an average VO\(_{\text{peak}}\) of 16.0 mL kg\(^{-1}\) min\(^{-1}\), 57% of that achieved by the control group. A similar VO\(_{\text{peak}}\) using a cycle ergometer test was reported by Fujitani et al.32; hemiplegic stroke survivors achieved a VO\(_{\text{peak}}\) of 17.7 mL kg\(^{-1}\) min\(^{-1}\) at baseline, 79% of that achieved by healthy subjects aged 55–64 years. This is similar to the current study, with stroke survivors achieving a VO\(_{\text{peak}}\) 76% of the comparison group for the cGXT. Previously, no studies have compared oxygen consumption on the SWT and 6MWT in stroke to comparison groups. Despite being independently ambulant in the community, and having minimal differences in leg strength between the affected and less affected sides, the stroke group was unable to sustain walking at high speeds during the 6MWT and SWT. The difference in distance achieved between groups was larger for the SWT, where the pace was set externally. Differences in HR\(_{\text{peak}}\) between groups were moderate for the walking tests, but very large for the cGXT. These walking tests may not have
Dunn et al. Independently ambulant stroke survivors have reduced fitness

the recommendation that training should not just focus on the greater side of neurological deficit. These results, together with the large discrepancy between groups on the final workload of the cGXT indicate deficits in both muscle strength and endurance. Strength training is currently recommended post stroke to increase the ability to perform ADL, as well as to reducing cardiac demands.29 Specific muscle endurance training may also be beneficial to allow more extensive challenging of the cardiorespiratory system. Alternatively, interval training may be advantageous to challenge the cardiorespiratory system without prematurely exhausting the neuromuscular system.36–38

This is the first study to comprehensively assess the fitness levels of well-recovered stroke survivors. It is also one of the few studies that have included a non-stroke group, individually age- and gender-matched comparison group. A recent systematic review2 on CRF after stroke found only 2 of the 41 included studies that directly assessed comparative healthy age- and gender-matched participants.31,12 The inclusion of this comparison group was particularly important for identifying leg strength

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### Table 2 Outcome measures for stroke and comparison groups with between group differences represented by effect sizes and p values

<table>
<thead>
<tr>
<th>Test</th>
<th>Stroke (n=17)</th>
<th>Comparison (n=17)</th>
<th>Effect size</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6MWT (n=34)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO$_{2\text{peak}}$ (mL kg$^{-1}$ min$^{-1}$)</td>
<td>16.46 ± 3.66</td>
<td>21.03 ± 8.32</td>
<td>0.71$^b$</td>
<td>0.068</td>
</tr>
<tr>
<td>HR$_{\text{peak}}$ (beats min$^{-1}$)</td>
<td>115 ± 21</td>
<td>124 ± 23</td>
<td>0.39$^a$</td>
<td>0.219</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>464 ± 121</td>
<td>606 ± 129</td>
<td>1.14$^c$</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>SWT (n=34)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO$_{2\text{peak}}$ (mL kg$^{-1}$ min$^{-1}$)</td>
<td>17.44 ± 4.94</td>
<td>23.11 ± 9.48</td>
<td>0.75$^b$</td>
<td>0.037*</td>
</tr>
<tr>
<td>HR$_{\text{peak}}$ (beats min$^{-1}$)</td>
<td>125 ± 21</td>
<td>135 ± 29</td>
<td>0.34$^a$</td>
<td>0.207</td>
</tr>
<tr>
<td>Shuttle distance (m)</td>
<td>415 ± 174</td>
<td>651 ± 236</td>
<td>1.14$^c$</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>Cycle GXT (n=30)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO$_{2\text{peak}}$ (mL kg$^{-1}$ min$^{-1}$)</td>
<td>17.0 ± 6.3</td>
<td>22.4 ± 6.5</td>
<td>0.84$^b$</td>
<td>0.019*</td>
</tr>
<tr>
<td>HR$_{\text{peak}}$ (beats min$^{-1}$)</td>
<td>128 ± 26</td>
<td>146 ± 17</td>
<td>0.83$^b$</td>
<td>0.011*</td>
</tr>
<tr>
<td>Final workload (W)</td>
<td>118 ± 32</td>
<td>157 ± 42</td>
<td>1.06$^c$</td>
<td>0.009*</td>
</tr>
<tr>
<td><strong>Walking speed (n=34)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-selected (m s$^{-1}$)</td>
<td>1.2 ± 0.3</td>
<td>1.5 ± 0.1</td>
<td>1.03$^c$</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Fast (m s$^{-1}$)</td>
<td>1.7 ± 0.4</td>
<td>2.2 ± 0.5</td>
<td>1.04$^c$</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>Knee strength (n=32)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isometric peak torque</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 140.7 ± 59.1</td>
<td>158.2 ± 49.5</td>
<td>0.32$^b$</td>
<td>0.212</td>
<td></td>
</tr>
<tr>
<td>L: 136.9 ± 44.0</td>
<td></td>
<td>0.45$^b$</td>
<td>0.098</td>
<td></td>
</tr>
<tr>
<td>Flexion (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 74.6 ± 34.2</td>
<td>84.5 ± 28.9</td>
<td>0.31$^b$</td>
<td>0.179</td>
<td></td>
</tr>
<tr>
<td>L: 75.4 ± 26.3</td>
<td></td>
<td>0.33$^b$</td>
<td>0.215</td>
<td></td>
</tr>
<tr>
<td>Isokinetic peak torque</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Extension (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 94.2 ± 43.1</td>
<td>118.1 ± 46.6</td>
<td>0.53$^b$</td>
<td>0.060</td>
<td></td>
</tr>
<tr>
<td>L: 97.6 ± 39.0</td>
<td></td>
<td>0.48$^b$</td>
<td>0.071</td>
<td></td>
</tr>
<tr>
<td>Flexion (Nm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 66.6 ± 33.9</td>
<td>82.2 ± 32.9</td>
<td>0.47$^b$</td>
<td>0.095</td>
<td></td>
</tr>
<tr>
<td>L: 64.3 ± 26.0</td>
<td></td>
<td>0.60$^b$</td>
<td>0.027*</td>
<td></td>
</tr>
<tr>
<td><strong>Body composition (n=26)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body fat (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32.0 ± 10.0</td>
<td>34.4 ± 9.0</td>
<td>0.08</td>
<td>0.531</td>
<td></td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28.4 ± 5.5</td>
<td>28.1 ± 5.9</td>
<td>0.05</td>
<td>0.864</td>
<td></td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: 8.0 ± 1.6</td>
<td>7.7 ± 1.6</td>
<td>0.14</td>
<td>0.563</td>
<td></td>
</tr>
<tr>
<td>L: 7.9 ± 1.5</td>
<td></td>
<td>0.13</td>
<td>0.563</td>
<td></td>
</tr>
</tbody>
</table>

Notes: Effect sizes refer to mean between group differences *medium effect size, large effect size, very large effect size, p-values refer to between group differences, $^*p < 0.05$. Abbreviations: 6MWT: six-minute walk test, SWT: shuttle walk test, GXT: graded exercise test, HR$_{\text{peak}}$: peak heart rate, A: more affected, L: less-affected, VO$_{2\text{peak}}$: peak oxygen consumption.
Therefore, although it cannot be said definitively that stroke is the cause of reduced fitness in stroke survivors, it is likely that the reduced fitness levels in this group are at least partly due to the stroke event.

This study has limitations. The relatively small sample size meant it was not possible to control for comorbidities. It is important for future studies to consider comorbidities and their potential effects on fitness levels. Also, additional functional impairment assessments and data on the site and size of the stroke lesion to better describe the study population may have improved the interpretation and generalisability of the findings. Additionally, with multiple statistical comparisons, there is a risk for Type I error, which should be considered when interpreting results; consequently, the effect sizes may be more important for interpretation. Lastly, there was a difference in self-reported physical activity levels between the groups, which may reflect the reduced physical capacity of participants or contributed to their reduced fitness.

**Conclusion**

Well-recovered, independently ambulant stroke survivors had lower CRF, walking speeds and leg strength compared to the healthy age- and gender-matched comparison group. With regard to the assumption that well recovered, independently ambulant stroke survivors do not require specific exercise interventions, the current study suggests the contrary. Although the goal may not be to regain function, exercise provides a myriad of benefits, including the potential to decrease the risk of secondary stroke. Further research into programmes, specifically for well-recovered stroke survivors is warranted.

**Adherence to ethics and reporting requirements**

All participants provided written and informed consent. This research was approved by the Hunter New England Human Ethics Committee (11/04/20/4.04) and University of Newcastle Human Research Ethics Committee (H-2011-0172).

**Clinical Trials registration number**

ANZCTR Trial ID: ACTRN12614000134628 ‘How Fit is the Stroke Survivor?’

**Conflicts of interest**

None of the authors have any conflict of interest in the submission of this manuscript.

**Funding**

This research is supported by small project grants from the: National Stroke Foundation, John Hunter Hospital Charitable Trust, Hunter New England Allied Health Deficits, as in these stroke participants the usual method of using the less-affected side as a control would not have identified any deficits. The current study also employed the gold standard measurement of CRF, oxygen consumption, in a portable manner to allow for assessment during overground walking during the 6MWT and SWT.

The results from this study are particularly striking considering the relatively young age of this sample population. This study included one stroke survivor aged just 23, one 32 and three aged 40–50, all considerably younger than the average age of participants involved in studies assessing fitness in stroke of 53–71 years. These fitness deficits are therefore not just applicable to older populations, and it is important that younger independently ambulant stroke survivors also are considered for targeted exercise programmes. Also, it often assumed that stroke survivors were inactive prior to the stroke event, and it is impossible to retrospectively assess fitness levels. While this assumption may be generally true, there are exceptions. Anecdotally, this group was motivated to return to prior activities including training at the gym and running.
Research Committee and Hunter Medical Research Institute: Estate of the late Stephen James Fairfax Award [HMRI 13-55]. This funding has in no way influenced how the study was conducted. AD was supported by the University of Newcastle through an Australian Postgraduate Award (APA) Scholarship and HMRI through Emily and Jennie Thomas Postgraduate Medical Research funding. DLM was supported by the Heart Foundation and University of Newcastle through the provision of a postgraduate scholarship and by the Hunter Stroke Service. PvV was supported by an Australian Research Council Future Fellowship [grant number FT100100439]. NJS was supported by a Career Development Fellowship [grant number APP1035465] from the Australian National Health and Medical Research Council.

**ORCID**

Dianne L. Marsden [ORCID: http://orcid.org/0000-0002-6943-8428]

**References**


Appendix 4: Published manuscript of Chapter 7
A Home- and Community-Based Physical Activity Program Can Improve the Cardiorespiratory Fitness and Walking Capacity of Stroke Survivors

Dianne Lesley Marsden, BAppSci(Physiotherapy), MApMgmt(Health), PhD,*†‡
Ashlee Dunn, BExSpSci(Hon),§‖ Robin Callister, BPharm, MSc, PhD,§‖
Patick McElduff, BMath, PhD,¶
Christopher Royce Levi, MBBS, BMedSci, FRACP, FAHMS,‡**†† and
Neil James Spratt, FRACP, PhD‡‡‡§§

Background: The cardiorespiratory fitness of stroke survivors is low. Center-based exercise programs that include an aerobic component have been shown to improve poststroke cardiorespiratory fitness. This pilot study aims to determine the feasibility, safety, and preliminary efficacy of an individually tailored home- and community-based exercise program to improve cardiorespiratory fitness and walking capacity in stroke survivors.

Methods: Independently ambulant, community-dwelling stroke survivors were recruited. The control (n = 10) and intervention (n = 10) groups both received usual care. In addition, the intervention group undertook a 12-week, individually tailored, home- and community-based exercise program, including once-weekly telephone or e-mail support. Assessments were conducted at baseline and at 12 weeks. Feasibility was determined by retention and program participation, and safety by adverse events. Efficacy measures included change in cardiorespiratory...
fitness (peak oxygen consumption \( [\text{VO}_{2\text{peak}}] \)) and distance walked during the Six-Minute Walk Test (6MWT). Analysis of covariance was used for data analysis. Results: All participants completed the study with no adverse events. All intervention participants reported undertaking their prescribed program. \( \text{VO}_{2\text{peak}} \) improved more in the intervention group (1.17 ± 0.29 L/min to 1.35 ± 0.33 L/min) than the control group (1.24 ± 0.23 L/min to 1.24 ± 0.33 L/min, between-group difference = 0.18 L/min, 95% confidence interval [CI]: 0.01-0.36). Distance walked improved more in the intervention group (287 ± 123 m to 494 ± 67 m) compared to the control group (456 ± 101 m to 470 ± 106 m, between-group difference = 45 m, 95% CI: 3.90). Conclusions: Our individually tailored approach with once-weekly telephone or e-mail support was feasible and effective in selected stroke survivors. The 16% greater improvement in \( \text{VO}_{2\text{peak}} \) during the 6MWT achieved in the intervention versus control group is comparable to improvements attained in supervised, center-based programs. Key Words: Stroke—cardiorespiratory fitness—exercise—home program—walking capacity.

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Introduction

The cardiorespiratory fitness of stroke survivors is low\(^1,2\) with peak oxygen consumption (\( \text{VO}_{2\text{peak}} \)) values ranging from 26% to 87% of those of healthy age- and gender-matched individuals.\(^3\) It has been estimated that over three quarters of people after stroke have low levels of physical activity or are sedentary.\(^1\) Stroke survivors spend a large proportion of their day (median = 19.5 hours, 81%) in sedentary behaviors, often accumulated via prolonged bouts of inactivity (median = 1.7 hours).\(^4\) Stroke survivors spend 4 hours more per day in sedentary behavior than age-, sex-, and body mass index-matched healthy volunteers.\(^5\) Low levels of cardiorespiratory fitness and physical activity and high levels of sedentary time can reduce the ability to perform activities of daily living and may contribute to an increased risk for recurrent stroke and other cardiometabolic diseases.\(^6\)

Exercise programs that include an aerobic component have been shown to improve cardiorespiratory fitness,\(^1,7-9\) walking speed\(^8,9\) and walking endurance.\(^8,10\) Even modest amounts of aerobic training can improve cardiorespiratory fitness by 10%-15%.\(^1\) Of the 28 studies included in a recent systematic review, 25 used multiple sessions of center-based supervised training each week\(^1\); 2 studies used once-weekly center-based supervised sessions in conjunction with a home program; and 1 study used a one-on-one therapist-supervised home program.\(^1\) For safety reasons supervised cardiorespiratory fitness training programs may be required for stroke survivors with significant impairments or multiple comorbidities.

Programs providing ongoing support with little or no face-to-face supervision may offer a safe and effective alternative. Such programs may address the unmet needs of more independent stroke survivors and can provide an option for health services where limited, if any, community-based therapy services are available. Recent audit data indicate that 44% of stroke survivors were discharged directly home from the acute setting, with only 31% subsequently accessing rehabilitation.\(^11\) Although these people might have minimal mobility issues, they may benefit from ongoing interventions to maintain or improve their cardiorespiratory fitness and to reduce their sedentary behavior. The need for studies of home-based programs with intermittent supervision has been recognized in a recent review, particularly to provide evidence for therapies that may help stroke survivors who live away from major centers.\(^12\)

Individualizing exercise programs to suit each person’s ability is particularly pertinent to stroke survivors, given the heterogeneity of abilities in this population due to the effects of stroke and the wide age range over which stroke occurs. Individual tailoring also allows participants to engage in activities that are of interest to them.\(^13\)

The aims of the present pilot study were to determine the feasibility, safety, and preliminary efficacy of an individually tailored, home- and community-based exercise program to improve cardiorespiratory fitness in stroke survivors. The effects on performance measures, fatigue, depression, and health-related quality of life were also investigated to guide the design of a future larger, randomized controlled trial.

Materials and Methods

Study Design

A pilot controlled trial was undertaken to investigate the effects of a 12-week exercise intervention on community-dwelling stroke survivors (“How Fit is the Stroke Survivor?” [HowFITSS?] trial ANZCTR Trial ID: ACTRN1261400134628). Participants in both the control and intervention groups received usual care, and the intervention group also undertook the HowFITSS? exercise program. All participants were assessed at baseline and at 12 weeks.

Ethics Statement

The Hunter New England (11/04/20/4.04) and the University of Newcastle (H-2011-0172) Human Research Ethics Committees approved the study, which was conducted...
in compliance with the Australian National Health and Medical Research Council guidelines. All participants provided informed written consent.

**Participants**

A convenience sample of 20 stroke survivors aged 18 years old or above, who were within 1 year of their most recent stroke and able to follow basic commands, were recruited via clinician referral. Clinicians were blinded to group allocation. Key exclusion criteria were inability to attend the center for testing, pregnancy, and being determined as medically unfit to participate by a medical practitioner. Absolute and relative contraindications to fitness testing were provided on the medical clearance form used in the study. Data were collected in the Human Performance Laboratory at the University of Newcastle, Australia. Due to time limitations for access to the Human Performance Laboratory, a block design was required. Hence, by necessity, this was a controlled but not randomized trial; the first 10 participants recruited were assigned to the intervention group with the next 10 assigned to the control group.

**Assessments**

Assessments were undertaken in sessions conducted over 1 or 2 days, depending on each participant’s preference. Participant demographics (age, sex, country of birth, resides in a metropolitan, regional or rural location) and characteristics (stroke type, time since last stroke, number of strokes, side affected, thrombolysis with tPA, body mass index, current modified Rankin Scale score, and Functional Ambulation Category) were recorded. Assessors (authors D.M. and A.D.) were not blinded to group allocation. Standardized instructions were provided to participants for each test.

**Feasibility** was assessed by retention (number returning for 12-week assessments) and participation in the exercise program (intervention group, self-report) or other physical activities (both groups, self-report). At baseline, all participants were interviewed using a semistructured approach by author D.M. about their usual physical activity frequency, duration, and type, and about sedentary behavior. At the 12-week follow-up appointment, the participants were interviewed on their activity levels and the types of activities undertaken over the preceding 12 weeks. For the intervention group participants, the interview included their use of the prescribed program activities. Also, during their weekly phone calls or e-mails, the participants in the intervention group were asked about the activities they had been undertaking in the preceding week. Assessments of adherence to the exercise program and changes in physical activity levels were based on these self-reports.

**Safety** was assessed by the occurrence of any adverse events during assessments (documented) or the intervention period (self-report). Adverse events included falls and cardiac, respiratory, or new neurological abnormalities; recurrent events; hospitalization; and musculoskeletal pain that did not settle within an hour of stopping exercise.

**Cardiorespiratory fitness** was assessed using 3 tests. Standardized instructions were provided to the participants for each test.

1. The Six-Minute Walk Test (6MWT) was performed in accordance with the American Thoracic Society standards, with the exception of a 20-m straight walkway used due to limited space. Standardized instructions and encouragement were provided according to the guidelines and no physical assistance or support was provided. Distance walked was recorded.

2. The Shuttle Walk Test (SWT) required participants to walk back and forth between markers spaced 9 m apart (shuttles). Speeds were dictated by an audio CD (Glenfield Hospital NHS Trust, Leicester, UK) and increased each minute. The test was terminated when the participant was unable to reach within .5 m of the marker at the time of the audio signal. Standardized instructions for the test were used, including providing no encouragement during the test. If the participants were less than .5 m away from the cone when the beep sounded, feedback was provided that they were not going fast enough and needed to try to walk faster. The total number of shuttles walked was recorded.

3. The Cycle Progressive Exercise Test (cPXT) was performed on an upright cycle (818E Monark, Sweden). Participants cycled for 2-3 minutes for familiarization and to identify their preferred cadence (50 or 60 revolutions per minute) for the test. After a brief rest (2-3 minutes), the participant started pedaling and the test commenced once they reached their predetermined cadence. The workload resistance was adjusted each minute. The test commenced at a power output of 0 W with stepped increases in power output of 25 W each minute. Feedback was provided regarding participants’ maintenance of cadence. The final power output and duration of the test were recorded.

During each of these tests, cardiorespiratory fitness was measured by $\text{VO}_{2\text{peak}}$. The respiratory exchange ratio ($R$ value) was used as an index of participant effort. Oxygen consumption and $R$ values were recorded throughout each test using a portable metabolic system (K4b2; Cosmed, Rome, Italy). Heart rate (HR) was recorded via the Quinton T12, Cosmed), which was monitored throughout each test by author A.D., who is experienced in conducting exercise tests. Conservative criteria were adopted to stop a test when any rhythm that was not normal appeared. A copy of the ECG was sent to
The health benefits of Patient Health Questionnaire (PHQ-9) resting heart rate reserve (HRR) during the cPXT, calculated using the Karvonen formula of 85% HRR = [(220 – age) – resting HR] × .85 + resting HR. As HR is not usually monitored during the 6MWT or SWT in clinical settings, it was not used to set end criteria for these tests. Blood pressure was measured before and after each fitness test as a safety precaution. Reasons for stopping were recorded.

Other assessments included the following:

The 10-m Walk Test was used to assess fast and self-selected walking speeds. The time taken to walk the middle 10 m of a 14-m walkway was recorded. Three trials were performed for each speed. The average of the three trials was calculated then converted to velocity (in meter per second).

The Step Test was used to assess dynamic standing balance using the protocol outlined by Hill et al. It involved stepping 1 foot on, then off, a 7.5-cm step as quickly as possible in a 15-second period. Both legs were tested.

The Fatigue Assessment Scale (FAS), Patient Health Questionnaire (PHQ-9), and the Stroke and Aphasia Quality of Life-39 (SAQoL-39) questionnaire were used to assess fatigue, depression, and health-related quality of life, respectively. Higher scores represented worse levels of fatigue and depression, whereas lower scores indicated worse health-related quality of life.

The primary measure used to assess change in cardiorespiratory fitness was absolute VO2peak (in liter per minute) as relative VO2peak (in milliliter per kilogram per minute) is affected by any change in weight over time. Changes in VO2peak during the 6MWT, SWT, and cPXT were all examined to determine whether sensitivity to change differed among these tests.

Changes in other cardiorespiratory fitness measures (relative VO2peak R value, and HR during the 6MWT, cPXT, and SWT), performance measures (6MWT distance [in meter], cPXT maximum workload [in watt] and duration [in seconds], number of shuttles completed during the SWT, fast and self-selected walking speed [in meter per second], and number of steps during step test), and fatigue, depression, and health-related quality of life scores were examined.

Intervention

Following their baseline assessments, all participants continued to receive usual care. In addition, the intervention group received a 12-week individually tailored home- and community-based exercise program. Programs were devised through consultation between the participant and 2 experienced clinicians: a neurological physiotherapist (author D.M.) and exercise scientist (author A.D.), who were independent of the usual-care therapists. Carers who were present at the session were included in the discussion and planning. The intervention was designed so that it could be applied in most settings: metropolitan, regional, or rural.

The intervention aimed to increase daily physical activity and reduce sedentary time, using a whole-day approach to being more active. The health benefits of regular ongoing physical activity, including undertaking activity at a level that has the potential to improve cardiorespiratory fitness, were discussed. The potential benefits for preventing subsequent stroke were highlighted. Strategies to overcome any perceived barriers to being active were also considered. The individually tailored programs were based on participant preferences for activities, including any prestroke activity the participants wished to resume or work toward resuming, their physical capacity to undertake specific activities, and access to resources in their home and community, including pools, gyms, exercise classes, and therapy programs. An exercise manual was provided that included written information to reinforce the verbal information provided on exercising safely and overcoming barriers. The exercise manual contained a core home-exercise program, based on previously reported programs. This consisted of task-specific exercises that participants could use as part of their intervention (see Appendix 1), and information on how to progress these exercises over time. The participants were strongly encouraged to exercise at a level with the potential to improve cardiorespiratory fitness by meeting the exercise recommendations of accruing at least 30 min/day of moderate intensity physical activity on most days of the week. They were encouraged to undertake activities using large muscle groups. The concepts of interval training and accruing activity in 10- to 15-minute bouts were included in the discussion. Progressing the duration of the higher-intensity intervals and reducing the duration of the low-intensity intervals were discussed. Low-intensity intervals were encouraged to be active rather than complete rest.

Following the development of the individually tailored program, each participant practiced his or her chosen activities using interval training on a circuit of 5-minute task-specific and ergometer workstations under supervision. This single bout of supervised exercise was designed to build confidence and to provide participants with the experience of applying interval training to the various activities practiced. This single bout of exercise program was conducted at the Human Performance Laboratory at the University of Newcastle.

Ongoing contact during the 12 weeks was provided by 1 researcher (author A.D.) via weekly e-mail or telephone.
HOME EXERCISE TO IMPROVE POSTSTROKE FITNESS

calls. The support was tailored to each participant’s specific requirements, which included some or all of the following: checking adherence to regular activity, providing encouragement and strategies to overcome barriers, and any additional advice required as to how to progress their exercise program. The content of the support was developed in consultation with authors A.D., D.M., and R.C. (Professor of Clinical Exercise Physiology). If any medical issues were raised during the support sessions, A.D. discussed with author N.S. (Senior Staff Specialist Neurologist) for advice and possible referral back to the treating doctor if appropriate. After the initial consultation, no further face-to-face contact was provided with the exception of any participant with concerns about attending community-based facilities for the first time after stroke. These people were offered the option of having one of the research team accompany them to their initial exercise session.

Usual care consisted of any required medical or therapy appointments. Two people in each group were enrolled in outpatient physiotherapy at the time they commenced the 12-week period. All others had been discharged from ongoing therapy. Control participants were asked to continue their routine activities during the 12 weeks. These participants were not provided with any information from the research team about increasing physical activity, did not undertake the interval-training practice session, and the only contact initiated by the research team was a phone call to confirm their booking for the 12-week assessment session. The medical clearance form completed by each participant’s medical practitioner outlined that the stroke survivor would be undergoing fitness testing and a 12-week exercise program, but did not specify when the program would start.

Statistical Methods

Baseline characteristics are summarized as means and standard deviations for continuous data, and numbers and percentages for categorical data. Differences between groups in baseline characteristics were tested using a t-test for continuous data and Fisher’s exact test for categorical data.

The efficacy of the intervention was tested using analysis of covariance by fitting a linear regression model to the data with the outcome in the model being the outcome of interest at 12 weeks and the only predictor variable being their group (intervention or control). We included all of the data that were available for the analysis. The coefficient of the group variable is a measure of the treatment effect and can be interpreted as the difference between the groups at follow-up adjusted for baseline. Changes in means for each outcome were determined for each group. Between-group differences were determined by absolute difference and the difference in percent change from baseline between the 2 groups. For any missing data for items in the FAS, PHQ-9, or SAQoL, substitution was based on the mean of the other scores. As this was a pilot study, scatter plots illustrating data distribution and changes were used in addition to summary statistics. Analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC) and Stata V13 (StataCorp LP, College Station, TX).

Results

Demographic and other characteristic data for the intervention and control groups at baseline were compared and are summarized in Table 1. There were no statistically significant differences between the groups. All participants had suffered an ischemic stroke and all were independently ambulant. Three intervention participants used a walking stick for the 6MWT at baseline; no participant required a walking aid for the follow-up 6MWT assessment. Reasons for each participant stopping the cPXT are outlined in Appendix 2.

Feasibility and Safety

The target of 20 participants was reached and all participants attended the assessments at 12 weeks. No serious adverse events were observed during testing or reported by participants in either group or over the 12-week period. During baseline data collection, 1 intervention group participant had intermittent right bundle branch block on ECG and was referred to his general practitioner for investigation. A researcher (author D.M.) accompanied 2 intervention group participants to their first visit to a community exercise program and participated in the exercise session with them.

Based on interview self-reports, the intervention participants reported being physically active more than the control group participants over the 12-week period. All of the intervention group participants reported that they undertook their individualized exercise program. Seven of the 10 (70%) participants reported being active for at least 30 minutes on most days of the week; one reported being active for 20 minutes or more on most days of the week. The other 2 participants reported that they were more active than before they commenced the program, including breaking up long periods of sitting.

Participants undertook a variety of community and home-based activities: walking (n = 7), running (n = 2), boot camp (n = 1), aqua-aerobics (n = 2), ergometers (n = 2), weights (n = 1), aerobics class (n = 1); and the individualized home-exercise program in their manual (n = 5). Two participants continued with outpatient physiotherapy 1-2 times per week. One person commenced Masterstroke, which is a 9-week secondary prevention group program run by health professionals that included 1 hour of exercise in each twice-a-week session. Three people returned to leisure activities they participated in before their stroke including lawn bowls, horse riding, and dancing. These activities contributed to the accumulated physical activity levels of each participant across the 12 weeks and highlight the
achievement of these particular participants’ objectives regarding physical activity.

Of the control group participants, one self-reported increasing community-based activities including walking; one self-reported increasing, by a small amount, his or her home duties and walking; and five self-reported that they maintained their current levels of activity with only one of these reporting being active most days of the week. Three participants self-reported they had been less active, mainly due to health issues not related to their stroke. Three people received physiotherapy at some stage during the 12 weeks: two attended outpatient therapy and one was admitted for 2 weeks to a rehabilitation unit for inpatient therapy.

Appendix 2 shows the data for individual participants for the 6MWT and cPXT. There were some missing data from the exercise tests. Reasons for missing data were 2 intervention and 2 control group participants were unable to undertake the cPXT due to pre-existing arthritic limitations (knee n = 3, hip n = 1); 1 control group participant was excluded from the 12-week cPXT because his resting HR was at 85% HRR, and 1 control group participant did not perform the SWT due to a mobility safety issue, poor balance when turning, which was identified during the 6MWT. Baseline cardiorespiratory fitness data for 1 participant were missing due to equipment problems resulting in physiologically impossible values. HR data were missing for 3 intervention group participants during the 6MWT due to data from the ECG unit not being recorded on the laptop.

### Intervention Efficacy

There was a .18 L/min (95% confidence interval [CI]: .01-.36) greater improvement in VO₂peak on the 6MWT in intervention participants than in controls (Table 2). There were trends to improvement in the SWT (.14 L/min [95% CI: −.04 to .32]) and cPXT (.20 L/min [95% CI: −.04 to .43]). Enhancing the plausibility of the 6MWT result, a very strong concordance emerged between the effect size estimate for VO₂peak and performance measures for each of the 3 fitness tests. All 3 tests indicated 11%-15% greater benefit in the intervention group compared to the control group (Table 2). Figure 1 shows the changes for individual participants for selected cardiorespiratory fitness and performance measures and for the questionnaires. The intervention group improved 1.5 and 1.3 steps more (P < .05) than the control group for the right and left legs, respectively, in the step test. There were no statistically significant differences between the groups for changes in fatigue, depression, or health-related quality of life (Table 2).

### Discussion

Our 12-week program of home- and community-based exercise was feasible for participants to undertake and was effective in improving cardiorespiratory fitness. The improvements were of a similar magnitude to those identified in meta-analyses of exercise to improve cardiorespiratory fitness after stroke.1,9 There were no serious

<table>
<thead>
<tr>
<th>Table 1. Participant demographics and characteristics</th>
</tr>
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<tbody>
<tr>
<td><strong>Characteristic</strong></td>
</tr>
<tr>
<td>Sex</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
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<tr>
<td>Location of home</td>
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<td></td>
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<td></td>
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<tr>
<td>Country of birth</td>
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<td></td>
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<td>Time since stroke (months)</td>
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<tr>
<td>Number of strokes</td>
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<td></td>
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<td></td>
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<tr>
<td>Modified Rankin Scale</td>
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<td></td>
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<tr>
<td>Side affected by stroke</td>
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<tr>
<td>Thrombolysis with tPA</td>
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<tr>
<td>Functional Ambulation Category</td>
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</tbody>
</table>

Abbreviations: SD, standard deviation; tPA, tissue plasminogen activator.
<table>
<thead>
<tr>
<th>Test and outcome measure</th>
<th>Intervention</th>
<th>Control</th>
<th>Between-group difference</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>12 weeks</td>
<td>Change</td>
</tr>
<tr>
<td><strong>6MWT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO_{peak} absolute (L/min)</td>
<td>1.17 (.29)</td>
<td>1.35 (.33)</td>
<td>.18 (.20)</td>
</tr>
<tr>
<td>VO_{peak} relative (mL/kg/min)</td>
<td>16.0 (3.7)</td>
<td>18.6 (4.4)</td>
<td>2.6 (2.6)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>109 (18)</td>
<td>113 (12)</td>
<td>4 (21)‡</td>
</tr>
<tr>
<td>R value</td>
<td>.99 (.13)</td>
<td>1.01 (.09)</td>
<td>.02 (.16)</td>
</tr>
<tr>
<td><strong>Distance (m)</strong></td>
<td>427.0 (123.0)</td>
<td>493.5 (89.6)</td>
<td>66.5 (63.8)</td>
</tr>
<tr>
<td><strong>SWT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO_{peak} absolute (L/min)</td>
<td>1.22 (.30)</td>
<td>1.36 (.40)</td>
<td>.14 (.21)</td>
</tr>
<tr>
<td>VO_{peak} relative (mL/kg/min)</td>
<td>16.9 (4.8)</td>
<td>18.7 (5.0)</td>
<td>1.8 (3.0)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>114 (16)</td>
<td>116 (19)</td>
<td>2 (22)‡</td>
</tr>
<tr>
<td>R value</td>
<td>1.02 (.17)</td>
<td>.92 (.07)</td>
<td>−.10 (.20)</td>
</tr>
<tr>
<td>Shutlles (count)</td>
<td>36.3 (17.0)</td>
<td>43.2 (17.7)</td>
<td>6.9 (7.5)</td>
</tr>
<tr>
<td>cPXT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO_{peak} absolute (L/min)</td>
<td>1.26 (.36)</td>
<td>1.35 (.42)</td>
<td>.10 (.22)†</td>
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<tr>
<td>VO_{peak} relative (mL/kg/min)</td>
<td>17.3 (5.0)</td>
<td>18.9 (5.0)</td>
<td>1.6 (3.1)†</td>
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<td>Heart rate (beats/min)</td>
<td>127 (25)</td>
<td>125 (24)</td>
<td>−2 (24)†</td>
</tr>
<tr>
<td>R value</td>
<td>1.11 (.17)</td>
<td>1.05 (.20)</td>
<td>−.06 (.29)†</td>
</tr>
<tr>
<td>Duration (s)</td>
<td>303.8 (76.0)</td>
<td>318.8 (86.3)</td>
<td>15.0 (62.1)†</td>
</tr>
<tr>
<td>Workload (W)</td>
<td>100.0 (29.9)</td>
<td>109.4 (35.2)</td>
<td>9.4 (29.7)†</td>
</tr>
<tr>
<td><strong>Step test (15 s)</strong></td>
<td></td>
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<tr>
<td>Steps right</td>
<td>14.7 (5.1)</td>
<td>17.2 (3.9)</td>
<td>2.5 (2.1)</td>
</tr>
<tr>
<td>Steps left</td>
<td>14.6 (5.4)</td>
<td>16.5 (4.6)</td>
<td>1.9 (1.6)</td>
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<tr>
<td><strong>10-min walk test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast (m/s)</td>
<td>1.7 (.5)</td>
<td>1.7 (.3)</td>
<td>.0 (.3)</td>
</tr>
<tr>
<td>Self-selected speed (m/s)</td>
<td>1.2 (.3)</td>
<td>1.3 (.2)</td>
<td>−.1 (.1)</td>
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<tr>
<td>Fatigue Assessment Scale</td>
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<tr>
<td>Score (possible range 10 to 50)</td>
<td>26.2 (5.6)</td>
<td>21.8 (3.8)</td>
<td>−4.5 (4.9)</td>
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<tr>
<td>PHQ-9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score (total out of 27)</td>
<td>8.1 (5.7)</td>
<td>5.7 (3.4)</td>
<td>−2.4 (4.1)</td>
</tr>
<tr>
<td>SAQoL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean score (total out of 5)</td>
<td>4.1 (.5)</td>
<td>4.1 (.4)</td>
<td>−.1 (.5)</td>
</tr>
</tbody>
</table>

Abbreviations: 6MWT, Six-Minute Walk Test; CI, confidence interval; cPXT, Cycle Progressive Exercise Test; PHQ-9, Patient Health Questionnaire; SAQoL-39, Stroke and Aphasia Quality of Life-39; SD, standard deviation; SWT, Shuttle Walk Test; VO_{peak}, peak oxygen consumption.

For change scores: the number of participants included in the analysis = 10 except where

*n = 9.
†n = 8.
‡n = 7.
§n = 6.
Figure 1. Changes for individual participants for selected cardiorespiratory fitness and performance and questionnaire measures. Abbreviations: 6MWT, Six-Minute Walk Test; cPXT, Cycle Progressive Exercise Test; PHQ-9, Patient Health Questionnaire; SAQoL-39, Stroke and Aphasia Quality of Life-39; SWT, Shuttle Walk Test.
adverse events and no withdrawals. The intervention design enabled stroke survivors from regional and rural, as well as metropolitan communities, to participate. Our results highlight that many of the barriers perceived by clinicians to incorporating aerobic training into neurorehabilitation, including concerns for patient safety, patients’ inability to participate, and lack of resources, 40 can be overcome. It should be noted, however, that participants were self-selected, and all were independently ambulant.

Our intervention appears a feasible method for incorporating cardiorespiratory fitness training into poststroke management. All intervention group participants self-reported increasing their levels of physical activity and reducing sedentary time, with the majority also meeting exercise recommendations for the frequency and duration of exercise. 6,36 Our intervention did not require regular travel or attendance at a specific venue, which can be a barrier to participation. 40 Importantly, there was no requirement for regular therapist supervision, which most would regard as a major cost saving, yet short periodic ongoing professional support 41 was provided by phone or e-mail.

The improvement in VO$_{2peak}$ we observed is comparable to that previously achieved in more resource-intensive programs. 1 These programs typically used a single modality, such as a treadmill or cycle ergometer, for training, 1 which may limit who can participate and the appeal of the program. Also, these programs required participants to attend a center at least once a week to undertake the intervention or for clinicians to undertake home visits several times per week. 1 Resources for providing treatment once people are discharged back to the community after stroke are often very limited. Our results indicate that an intervention that requires minimal face-to-face contact may be sufficient for improving the cardiorespiratory fitness levels of independently ambulant stroke survivors.

An important feature of the exercise program may have been the single session of supervised interval training performed over a circuit of different activities following baseline testing. Most participants reported that they were more confident to exercise after undertaking this session. The participants reported feeling reassured that they could exercise safely for a reasonable period of time (all performed for at least 10 minutes) and intensity using activities that they had identified they were interested in. The session gave the participants an experience of interval training (41 m), 40 cardiorespiratory fitness training involving walking (47 m), 9 and mixed training involving walking (31 m). 6 However, this change was only half of that seen with more intensive cardiovascular conditioning (111 m). 10 In our study, 7 of 10 (70%) participants in the intervention group used walking as an activity compared to 2 of 10 (20%) participants in the control group. The use of walking as an exercise activity is a likely driver of the increased walking distance observed in the intervention group and has clear potential benefits for community participation. This raises the possibility that the improvements in 6MWT are reflective of improved walking ability, rather than a true indication of improved cardiorespiratory fitness. While the mean magnitude of change in absolute VO$_{2peak}$ was slightly higher for the cPXT than the 6MWT, there were fewer participants for the cPXT. This loss of statistical power is the likely explanation for the lack of significant difference for cPXT, rather than a physiological difference between the cPXT and the 6MWT.

The improvements we saw in walking distance but not in self-selected walking speed are consistent with the meta-analysis of Mehta et al., 15 who examined cardiovascular conditioning after stroke. At baseline, our cohort would already be considered community ambulators, with a self-selected walking speed greater than 0.8 m/s. 46 Walking speed was similar to healthy people aged 60-69 years (men 1.3 m/s, women 1.2 m/s). 50,51 Interestingly, participants were able to maintain their fast walking speed, measured over 10 m, to complete a 1-minute stage during the SWT. The ability to “get out and about” in the community is considered very important by stroke survivors, 46 and can reduce isolation and dependence while increasing social participation and physical activity. 57 The change we observed was similar to those reported in meta-analyses investigating the impact on walking distance of gait-orientated training (41 m), 40 cardiorespiratory fitness training involving walking (47 m), 9 and mixed training involving walking (31 m). 6 However, this change was only half of that seen with more intensive cardiovascular conditioning (111 m). 10 In our study, 7 of 10 (70%) participants in the intervention group used walking as an activity compared to 2 of 10 (20%) participants in the control group. The use of walking as an exercise activity is a likely driver of the increased walking distance observed in the intervention group and has clear potential benefits for community participation. This raises the possibility that the improvements in 6MWT are reflective of improved walking ability, rather than a true indication of improved cardiorespiratory fitness. While the mean magnitude of change in absolute VO$_{2peak}$ was slightly higher for the cPXT than the 6MWT, there were fewer participants for the cPXT. This loss of statistical power is the likely explanation for the lack of significant difference for cPXT, rather than a physiological difference between the cPXT and the 6MWT.
When examining the individual patient data, it is clear that many of the control group participants’ fitness appeared to deteriorate (Fig 1). Eighty percent of participants in the intervention group improved their 6MWT VO$_{2peak}$ whereas 78% of the control group participants had a lower VO$_{2peak}$ during the 6MWT after 12 weeks (Fig 1, A). Participants who performed the worst in the intervention group at baseline for 6MWT distance, fast walking speed, fatigue, depression, and health-related quality of life appeared to make the greatest improvements (Fig 1, B, E-G). This finding suggests that such a program may particularly benefit those with the most to gain.

**Strengths and Limitations**

A major strength of the present study was the individually tailored, home- and community-based program that enabled stroke survivors to participate, regardless of where they lived. Forty-four percent of participants lived in regional or rural communities. People from these communities are often unable to participate in clinical studies and programs that require them to travel to center-based interventions in metropolitan settings.

The point estimates for VO$_2$ (peak and change) were very similar across the 3 fitness tests we used. The lack of statistically significant difference for the SWT and cPXT may be due to the inadequate power of the study or greater variability between participants. The $R$ values achieved at the end of each test showed no group-by-time interaction between the intervention and control groups, suggesting that there were no differences in effort or intensity attained.$^{32}$

There were some limitations with our fitness tests. The $R$ values achieved during our tests indicate they were submaximal.$^{33,34}$ Peak values for the cPXT may be underestimated for the participants who were stopped from continuing the exercise test when they reached 85% of age-predicted HRR. The use of a 20-m walkway during the 6MWT could have affected the VO$_{2peak}$ values achieved. Participants may have had to slow down more often to make the larger number of turns that were required compared to testing on a 30-m walkway. Although fitness tests may not always elicit a stroke survivor’s actual VO$_{2peak}$, the use of a standardized testing procedure allows for repetition over time to measure for change.

The study was limited by the small number of self-selected participants and was not a randomized controlled trial. For the present pilot study, there was no blinding of assessors to group allocation. However, standardized tests and instructions were used. We relied on self-report to assess the exercise dose received throughout the 12 weeks and the changes in activity during the program. The accuracy of this information is limited by the participants’ recall and their ability to quantify their physical activity levels. Future studies would benefit from direct measures of activity via activity monitors and interviews conducted by blinded assessors using standardized interview schedules. The challenge of measuring exercise dose accurately in the real world has been recognized, as has the potential for emerging, low-cost wearable technology in measuring activity over time at home.$^{12}$ The use of this technology would need to be considered for a larger trial.

**Conclusion**

The results of the present pilot study show that a home- and community-based program to increase physical activity and reduce sedentary time is feasible and that it can result in improved cardiorespiratory fitness. Improving physical activity and cardiorespiratory fitness levels can provide multiple health benefits to stroke survivors. The present study demonstrates a promising intervention to improve the physical activity levels of community-dwelling stroke survivors and warrants further investigation in a large multicenter, randomized trial using wearable technology to examine dose–response relationships.

**Acknowledgments:** We would like to thank our participants for volunteering their time and the carers who accompanied them to the sessions; the Hunter New England Local Health District staff, who assisted with recruitment; David Paul, who set up the electronic data entry forms; Amelia Tomkins and Lucy Murtha, who assisted with formatting the figures; and the research assistants, who assisted with data collection and entry.

**Appendix 1. Summary of Activities Included in the Home-Exercise Manual**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Equipment</th>
<th>Description</th>
<th>Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sit to stand</td>
<td>Chair with or without arm rests</td>
<td>Sit to stand, aiming to increase speed reduce upper limb</td>
<td>↑ speed, number of repetitions</td>
</tr>
<tr>
<td>Fast/self-selected paced walking</td>
<td>Track (e.g., hallway, length of driveway, between telegraph poles)</td>
<td>Self-selected pace</td>
<td>↓ use of arm rests, seat height</td>
</tr>
<tr>
<td>Balance</td>
<td>Line on floor</td>
<td>Standing feet together, standing on 1 leg, eyes open eyes closed, walking along line (normal step length or heel–toe)</td>
<td>↑ walking or jogging speed</td>
</tr>
</tbody>
</table>

(continued on next page)
Appendix 1. (continued)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Equipment</th>
<th>Description</th>
<th>Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step</td>
<td>Block between 5 and 25 cm high</td>
<td>Up and over forwards, Up and over sideways, Stepping up forward and down backwards, Use table/bench if required</td>
<td>↓ use of table/bench, ↑ speed, Add in arm activities, Start at a lower height and gradually build up, ↑ depth of squat, Hold arms out in front</td>
</tr>
<tr>
<td>Squat</td>
<td>Chair or bench</td>
<td>Perform squat, Start with small range of movement, Use bench or chair for balance if required</td>
<td>↑ speed and number of repetitions, Add in the use of a squat</td>
</tr>
<tr>
<td>Side stepping</td>
<td>Table or bench</td>
<td>Sidestep around the table to both left and right sides, Hold onto table/bench for balance if required</td>
<td>Take wider steps, Add in a squat</td>
</tr>
<tr>
<td></td>
<td>around a table</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High knee walking</td>
<td>Track (e.g., hallway)</td>
<td>March on the spot, March up and down a walkway, Start with a small range of movement, Hold onto table/bench for balance if required</td>
<td>↑ speed and number of repetitions, Add in simultaneous arm activities</td>
</tr>
<tr>
<td>Leg side raises</td>
<td>Chair or bench</td>
<td>Hip abduction—left and right, Hold onto chair/bench for balance if required</td>
<td>↑ range of motion, Add weight around ankle</td>
</tr>
</tbody>
</table>

Legend: ↑, increase; ↓, decrease.

Appendix 2. Data for Individual Participants for the 6MWT and cPXT (Absolute VO$_{2peak}$ and Performance Measures)

<table>
<thead>
<tr>
<th>Participant</th>
<th>Six-Minute Walk Test</th>
<th>Cycle Progressive Exercise Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absolute VO$_{2peak}$ (L/min)</td>
<td>Distance walked (m)</td>
</tr>
<tr>
<td></td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Intervention group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.074</td>
<td>1.390</td>
</tr>
<tr>
<td>2</td>
<td>.804</td>
<td>1.045</td>
</tr>
<tr>
<td>3</td>
<td>1.309</td>
<td>1.387</td>
</tr>
<tr>
<td>4</td>
<td>.972</td>
<td>1.322</td>
</tr>
<tr>
<td>5</td>
<td>1.313</td>
<td>1.768</td>
</tr>
<tr>
<td>6</td>
<td>.981</td>
<td>.998</td>
</tr>
<tr>
<td>7</td>
<td>1.763</td>
<td>1.817</td>
</tr>
<tr>
<td>8</td>
<td>1.418</td>
<td>1.392</td>
</tr>
<tr>
<td>9</td>
<td>1.156</td>
<td>1.590</td>
</tr>
<tr>
<td>10</td>
<td>.891</td>
<td>.788</td>
</tr>
</tbody>
</table>

Control group | | | | | |
| 1           | 1.002 | .967 | .034 | 338 | 301 | 37 | Unable to do test | | |
| 2           | 1.278 | 1.208 | .070 | 489 | 491 | 2 | Unable to do test | | |
| 3           | 1.445 | 1.299 | .146 | 360 | 381 | 21 | Unable to do test | | |
| 4           | .919 | 1.112 | .192 | 433 | 423 | 10 | Unable to do test | | |
| 5           | 1.051 | 1.006 | .045 | 600 | 619 | 19 | Unable to do test | | |
| 6           | 1.385 | 1.371 | .014 | 520 | 481 | 39 | Unable to do test | | |
| 7           | 1.229 | 1.229 | – | 593 | 609 | 16 | Unable to do test | | | (continued on next page)
Appendix 2. (continued)

<table>
<thead>
<tr>
<th>Participant</th>
<th>Six-Minute Walk Test</th>
<th>Cycle Progressive Exercise Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absolute VO_{2peak} (L/min)</td>
<td>Distance walked (m)</td>
</tr>
<tr>
<td></td>
<td>12 weeks</td>
<td>Change</td>
</tr>
<tr>
<td>8</td>
<td>1.388</td>
<td>1.303</td>
</tr>
<tr>
<td>9</td>
<td>1.605</td>
<td>1.858</td>
</tr>
<tr>
<td>10</td>
<td>1.096</td>
<td>1.021</td>
</tr>
</tbody>
</table>

Abbreviations: abnorm, abnormality; ECG, electrocardiogram; Equip, no data due to equipment issues; HRR, reaching 85% heart rate reserve; →RBBB^, subsequently diagnosed with right bundle branch block; SOB, shortness of breath.

References


HOME EXERCISE TO IMPROVE POSTSTROKE FITNESS

Appendix 5. Hunter New England Ethics Approval
Appendix 6: University of Newcastle Ethics Approval
Appendix 7: ANZCTR Approval
Appendix 8: Information Statement for Stroke Group
What is the study about?
Researchers from Hunter Stroke Service (Hunter New England Health) and the University of Newcastle are studying what tests best measure the fitness and ways to improve fitness of people who have had a Transient Ischaemic Attack (TIA) or ischaemic stroke. As someone who has had a stroke or TIA in the Newcastle region, our research group, led by Dr Neil Spratt, would like to ask you to take part.

What would you have to do?
There are 2 parts to this study. You may choose to participate in Part A or both Parts A and B.

Part A: If you agree to take part you will need to:
1. Have a research team member ask you some questions about yourself, complete some questionnaires about your health including about your mood and activity levels and review your medical record to see what sort of stroke you had.
2. Attend 2 sessions over about 3 weeks at the University of Newcastle fitness lab. Each session will take about 2 hours. At these you will need to:
   a. Do tests each time of your fitness level. The tests are done on 2 different types of exercise bikes (Photo 1), with arm pedals and 2 walking tests.
   b. Have recordings taken of your height, weight, blood pressure, breathing and heart (this will include a wearing a testing unit with mask-photo 2), pulse, body fat (photo 3), leg strength (photo 4) grip strength, walking ability, blood lactate by a finger prick test (optional) and energy used (photo 5).
3. Wear an armband used to measure energy (photo 5) for a week at home between the two sessions. The armband is comfortable, small, lightweight and can be worn under normal clothing.

Part B: This involves a 12 week exercise program to improve your fitness. The first week will be at the university with the researchers. At this session we will come up with an exercise program that would suit you, your choice of exercise and location. We will test your breathing and heart responses on exercise equipment using the same method as during Part A. You will be asked to do your exercise program for 12 weeks with testing after 6 weeks and 12 weeks at the University. The exercise sessions may include instruction and support from the research team, along with contact to see how you are going. This will be by a method of your choice including phone or email
<table>
<thead>
<tr>
<th>1 Exercise Bikes</th>
<th>2 Testing Unit</th>
<th>3 Body fat test</th>
<th>4 Leg strength</th>
<th>5 Activity Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Exercise Bikes" /></td>
<td><img src="image2.png" alt="Testing Unit" /></td>
<td><img src="image3.png" alt="Body fat test" /></td>
<td><img src="image4.png" alt="Leg strength" /></td>
<td><img src="image5.png" alt="Activity Monitor" /></td>
</tr>
</tbody>
</table>

2 Testing Unit: The testing unit has:

- A face mask held on by soft bands around the head
- Straps that go over your shoulders and around your chest
- The recording unit
- Tubes that connect everything to the recording unit
- You can talk and breath easily when wearing the mask

5 Activity Monitor: The activity monitor is about the size of a matchbox and is held in place by a Velcro armband. There is minimal discomfort to wear it.
If you agree to participate you and your carer (if required) will be asked to sign a consent form. There is \textbf{no cost} in taking part. \textbf{Funding} is available to assist with your transport costs for testing.

**What choice do you have?**

Taking part in this research is \textbf{entirely your choice}. Whether or not you decide to take part, \textbf{your decision will not disadvantage you} in any way.

You can \textbf{withdraw} from the study at \textbf{any time} and \textbf{do not have to give any reason} for withdrawing. If you decide to withdraw, all information relating to you will be withdrawn from the study results.

**What are the risks and benefits?**

As the study involves fitness tests and exercise there is some risk of having a health event. This will be minimised by your doctor clearing you to participate.

During each session you will be closely supervised by research team members.

You may not benefit from participating in this study.

**How will your privacy be protected?**

All the information you give will be accessed, used and stored in accordance with Commonwealth Privacy Laws and the \textit{NSW Health Records and Information Privacy Act 2002}, be treated confidentially and only available to the researchers. During and after the project it will be stored in a locked cabinet in the research office and on a password-protected file.

**How will the information collected be used?**

All the information from all the participants in this study will be examined together. You will \textbf{not be} able to be identified. Results will contribute to Ms Marsden’s doctoral thesis (PhD) and may be published in scientific journals, reported and discussed at meetings/conferences. \textbf{Your name will not be used at any time}. If you chose, a letter outlining your results can be sent to you after completion of your 3rd assessment and copies of any papers published about this study.
Questions or further information?
If you need any more information you can contact research team members Di Marsden or Neil Spratt whose numbers are listed below.
Thank you for considering the invitation to take part in this research project.

Yours sincerely,

Dr Neil Spratt  
Student Supervisor

Prof Christopher Levi  
Student Supervisor

Ms Di Marsden  
PhD Student

Ms Ashlee Dunn  
PhD Student

The researchers responsible for this study are:

<table>
<thead>
<tr>
<th>Chief Investigator</th>
<th>Ms Di Marsden</th>
<th>HNEH/ UoN</th>
<th>Ph 4922 3380</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigators:</td>
<td>Ms Ashlee Dunn</td>
<td>UoN</td>
<td>Ph 4042 0281</td>
</tr>
<tr>
<td></td>
<td>Prof Robin Callister</td>
<td>UoN</td>
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<tr>
<td></td>
<td>Ms Louise Jordan</td>
<td>HNEH</td>
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This project has been approved by the Hunter New England Human Research Ethics Committee of Hunter New England Health, Reference 11/04/20/4.04. Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to Dr Nicole Gerrand, Manager Research Ethics and Governance, Hunter New England Local Health Network Locked Bag 1, New Lambton NSW 2305, telephone (02) 4921 4950, email Nicole.Gerrand@hnehealth.nsw.gov.au

This project has been made possible though funding by the Heart Foundation, National Stroke Foundation and the John Hunter Hospital Charitable Trust. This funding has not influenced the study in any way.
Appendix 9: Information Statement for Non-stroke Group
What is the study about?
Researchers from Hunter Stroke Service (Hunter New England Health) and the University of Newcastle are studying what tests best measure the fitness of people who have had a Transient Ischaemic Attack (TIA) or ischaemic stroke. We are also testing people who have not had a stroke or heart problems to compare the results of the two groups. Our research group, led by Dr Neil Spratt, would like to ask you to take part in this section of our research.

What would you have to do?
If you agree to take part you will need to:

1. Have a research team member ask you some questions about yourself and your past medical history and complete some questionnaires about your health, including your mood.

2. Attend 2 sessions over about 3 weeks at the University of Newcastle fitness lab. Each session will take about 2 hours. At these you will need to:
   a. Do tests each time of your fitness level. The tests are done on 2 different types of exercise bikes (Photo 1), with arm pedals and 2 walking tests.
   b. Have recordings taken of your height, weight, blood pressure, breathing and heart (this will include a wearing a testing unit with mask-photo 2), pulse, body fat (photo 3), leg strength (photo 4) grip strength, walking ability, blood lactate by a finger prick test (optional) and energy used (photo 5).

3. Wear an armband used to measure energy (photo 5) for a week at home between the two sessions. The armband is comfortable, small, lightweight and can be worn under normal clothing.
<table>
<thead>
<tr>
<th>1 Exercise Bikes</th>
<th>2 Testing Unit</th>
<th>The testing unit has:</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td>- A face mask held on by soft bands around the head</td>
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<tr>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td>- You can talk and breath easily when wearing the mask</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>3 Body fat test</th>
<th>4 Leg strength</th>
<th>5 Activity Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3.png" alt="Image" /></td>
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If you agree to participate you will be asked to sign a consent form. There is no cost in taking part. Funding is available to assist with your transport costs for testing.

**What choice do you have?**

Taking part in this research is entirely your choice. Whether or not you decide to take part, your decision will not disadvantage you in any way. You can withdraw from the study at any time and do not have to give any reason for withdrawing. If you decide to withdraw, all information relating to you will be withdrawn from the study results.

**What are the risks and benefits?**

As the study involves fitness tests and exercise there is some risk of having a health event. This will be minimised by your doctor clearing you to participate. During each session you will be closely supervised by research team members. You may not benefit from participating in this study

**How will your privacy be protected?**

All the information you give will be accessed, used and stored in accordance with Commonwealth Privacy Laws and the *NSW Health Records and Information Privacy Act 2002*, be treated confidentially and only available to the researchers. During and after the project it will be stored in a locked cabinet in the research office and on a password-protected file.

**How will the information collected be used?**

All the information from all the participants in this study will be examined together. You will not be able to be identified. Results will contribute to Ms Marsden's and Miss Dunn's doctoral thesis (PhD) and may be published in scientific journals, reported and discussed at meetings/conferences. Your name will not be used at any time. If you chose, a letter outlining your results can be sent to you after completion of your assessment and copies of any papers published about this study.
Questions or further information?

If you need any more information you can contact research team members Di Marsden, Ashlee Dunn or Neil Spratt whose numbers are listed below.

Thank you for considering the invitation to take part in this research project.

Yours sincerely,

Dr Neil Spratt                  Prof Christopher Levi            Ms Di Marsden             Ms Ashlee Dunn
Student Supervisor            Student Supervisor            PhD Student              PhD Student

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<td>Ph 4921 6171</td>
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This project has been made possible though funding by the Heart Foundation, National Stroke Foundation and the John Hunter Hospital Charitable Trust. This funding has not influenced the study in any way.
Appendix 10: Medical Clearance Form for Stroke Group
Appendix 11: ESSA Pre-exercise Screening Questionnaire for Non-stroke Group
Appendix 12: Medical Clearance Form for Non-stroke Group
Appendix 13: Participant Consent Form for Stroke Group
Appendix 14: Participant Consent Form for Non-stroke Group
Appendix 16: HowFITSS? Demographics Recording Sheet for Stroke Group
Appendix 17: Assessment Recording Sheet for Stroke Group
Appendix 18: Follow-up HowFITSS? Assessment Recording Sheet for Stroke Group
Appendix 19: HowFITSS? Assessment Recording Sheet for Non-stroke Group
Appendix 20: Fatigue Assessment Scale (FAS) Questionnaire for Stroke and Non-stroke Group
Appendix 21: Patient Health Questionnaire (PHQ-9) for Stroke and Non-stroke Group
Appendix 22: Stroke and Aphasia Quality of Life (SAQoL) Questionnaire for Stroke Group
Appendix 23: The Short Form 12 Health Survey Questionnaire (SF-12)
Appendix 24: Statement of Contribution Chapter 3

I attest that Research Higher Degree candidate Ashlee Dunn contributed substantially in terms of study concept and design, data collection, analysis, and preparation of the following manuscript:

Reference:


Signature: _________________________

Professor Robin Callister (Primary Supervisor)

Date: ________________
Appendix 25: Statement of Contribution Chapter 4

I attest that Research Higher Degree candidate Ashlee Dunn contributed substantially in terms of study concept and design, data collection, analysis, and preparation of the following manuscript:


Signature: _________________________

Professor Robin Callister (Primary Supervisor)

Date: ________________
Appendices

Appendix 26: Statement of Contribution Chapter 5

I attest that Research Higher Degree candidate Ashlee Dunn contributed substantially in terms of study concept and design, data collection, analysis, and preparation of the following manuscript:


Signature: _________________________

Professor Robin Callister (Primary Supervisor)

Date: ________________
Appendix 27: Statement of Contribution Chapter 6

I attest that Research Higher Degree candidate Ashlee Dunn contributed substantially in terms of study concept and design, data collection, analysis, and preparation of the following manuscript:

Reference: A Dunn, DL Marsden, P Van Vliet, NJ Sprat and R Callister. Independently ambulant, community dwelling stroke survivors have reduced cardiorespiratory fitness, mobility and knee strength compared to an age and gender matched cohort, Topics in Stroke Rehabilitation (epub ahead of print)

Signature: ______________________

Professor Robin Callister (Primary Supervisor)

Date: ______________
Appendix 28: Statement of Contribution Chapter 7

I attest that Research Higher Degree candidate Ashlee Dunn contributed substantially in terms of study concept and design, data collection, analysis, and preparation of the following manuscript:


Signature: ______________________

Professor Robin Callister (Primary Supervisor)

Date: _______________
Appendix 29: Statement of Contribution Chapter 8

I attest that Research Higher Degree candidate Ashlee Dunn contributed substantially in terms of study concept and design, data collection, analysis, and preparation of the following manuscript:

Reference: A Dunn, DL Marsden, D Barker, P Van Vliet, NJ Sprat and R Callister. Cardiorespiratory fitness and walking endurance improvements at 12 months follow-up of an individually tailored home and community-based exercise program for stroke survivors, Stroke Research and Treatment (under review)

Signature: __________________________

Professor Robin Callister (Primary Supervisor)

Date: ________________