

**ASSESSING AND TRAINING CARDIORESPIRATORY
FITNESS AFTER STROKE**

Dianne Marsden

MAppMgmt (Health), BAppSci (Physiotherapy)



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School of Medicine and Public Health

Faculty of Health

University of Newcastle

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SUPERVISORS

Associate Professor Neil Spratt

B Med Sci (Hons), B Med (Hons), PhD, FRACP

- Senior Staff Specialist Neurologist: John Hunter Hospital, Newcastle, NSW, Australia
- Associate Professor: School of Biomedical Science and Pharmacy, Faculty of Health and Medicine, University of Newcastle, Newcastle, NSW, Australia
- Career Development Fellow: National Health and Medical Research Council, Australia

Professor Robin Callister

PhD, MSc, BPharm

- Head of the Discipline of Human Physiology: School of Biomedical Sciences and Pharmacy, Faculty of Health and Medicine, University of Newcastle, Newcastle, NSW, Australia
- Leader of Exercise Science: Priority Research Centre in Physical Activity and Nutrition, University of Newcastle, Newcastle, NSW, Australia

Professor Christopher Levi

B Med Sci, MBBS (Hons), FRACP

- Senior Staff Neurologist: John Hunter Hospital, Newcastle, NSW, Australia
- Director of Clinical Research and Translation: Research, Innovation and Partnerships, Hunter New England Local Health District, NSW, Australia
- Conjoint Professor of Medicine (Neurology): University of Newcastle, Newcastle, NSW, Australia
- Practitioner Fellow: National Health and Medical Research Council, Australia

DECLARATIONS

STATEMENT OF ORIGINALITY

The thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968.

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I hereby certify that the work embodied in this thesis contains a published paper and scholarly works of which I am a joint author. I have included as part of the thesis a written statement, endorsed by my supervisor, attesting to my contribution to the joint publication and scholarly works.

Dianne Marsden

Date 13th November 2015

STATEMENT OF CONTRIBUTION

I, **Neil Spratt**, attest that Research Higher Degree candidate Dianne Marsden contributed significantly to the study design, data collection, data analysis and writing of the publication/ manuscripts entitled:

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She collaborated with her fellow authors from the University of Newcastle to undertake this work.

Signature of Supervisor:

Associate Professor Neil Spratt

Date: 13th November 2015

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ABSTRACT

Introduction: Cardiorespiratory fitness levels of people after stroke are low compared to non-stroke people of the same age and sex. Improving cardiorespiratory fitness has many potential health benefits for stroke survivors. Despite this, cardiorespiratory fitness is often overlooked in post-stroke management. Access to metropolitan-based services can be difficult for residents of regional and rural communities.

Aims: The aims of the project were to:

1. Identify the characteristics and to determine the effectiveness of interventions to improve cardiorespiratory fitness after stroke.
2. Compare cardiorespiratory responses and performance measures during three clinically-applicable exercise tests.
3. Examine the exercise intensity parameters achieved by stroke survivors during task-specific and ergometer workstation activities.
4. Explore the feasibility and efficacy of an individually-tailored home- and community-based exercise program to improve cardiorespiratory fitness in stroke survivors.

Methods: Characteristics of exercise interventions were investigated by systematic review. Change in cardiorespiratory fitness, measured by peak oxygen consumption (VO_{2peak}), was examined by meta-analysis. Community-dwelling stroke survivors were recruited. The primary outcome, oxygen consumption (VO_2) was assessed using a portable metabolic measurement system. Cardiorespiratory responses and performance measures were assessed on three exercise tests [Six-Minute Walk Test (6MWT), distance;

Shuttle Walk Test (SWT), number of shuttles; cycle progressive exercise test (cPXT), final workload]. VO_2 was recorded during an individualised circuit exercise session incorporating an interval training approach on 5-minute workstations (task-specific and ergometer activities). A pilot controlled trial of an individually-tailored exercise program was undertaken. Feasibility was measured by retention, participation and adverse events. Control and intervention groups both received usual care, and the intervention group undertook the 12-week program, including once-weekly telephone/email support. Cardiorespiratory fitness was assessed at baseline and 12 weeks.

Results: Aim 1: Twenty eight studies were included in the systematic review with 12 randomised controlled trials able to be included in the meta-analysis. Baseline fitness was low (8-23mL/kg/min). Interventions were typically centre-based, included an aerobic component and used three 30 to 60 minutes sessions per week at a prescribed intensity. Despite the modest dose of interventions, cardiorespiratory fitness improvement favoured intervention [increase in $\text{VO}_{2\text{peak}}$ of 2.27 mL/kg/min (95% CI: 1.58 to 2.95)]. Aim 2: There was no difference in $\text{VO}_{2\text{peak}}$ among the three exercise tests (range: 17.1- 18.1 mL/kg/min). Correlations between $\text{VO}_{2\text{peak}}$ and performance measures were high ($r=0.78, 0.73, 0.77$). Aim 3: Nine task-specific (eg walking, stairs, balance) and three ergometer (upright cycle, rower, treadmill) workstations were used. Participants exercised for at least 11 minutes on the circuit. Moderate or higher intensity was achieved for 78% of task-specific and 83% of ergometer workstations. Aim 4: All intervention participants reported undertaking their prescribed program. No adverse events occurred. $\text{VO}_{2\text{peak}}$ improved by 16%

more in the intervention group (1.17 ± 0.29 to 1.35 ± 0.33 L/min) than the control group (1.24 ± 0.23 to 1.24 ± 0.27 L/min) ($p=0.044$).

Conclusions: I have shown it is feasible to assess and train cardiorespiratory fitness using strategies applicable to most clinical settings. The 16% improvement in cardiorespiratory fitness observed in the home- and community-based program was similar to centre-based, resource-intensive programs. Performance measures of the 6MWT, SWT and cPXT may be clinically useful as proxies for cardiorespiratory fitness. An interval training approach using task-specific and ergometer activities appears a promising way to incorporate both cardiorespiratory fitness and functional training into post-stroke management. The studies provide preliminary data to inform the design of a future large, multicentre randomised controlled trial. This trial would test the effectiveness of the home- and community-based exercise intervention in improving cardiorespiratory fitness and functional recovery of stroke survivors living in metropolitan, regional and rural areas.

CHAPTER 1: STROKE AND CARDIORESPIRATORY FITNESS

This chapter provides an overview of stroke and cardiorespiratory fitness. It outlines why improving cardiorespiratory fitness may be an important component of post-stroke management.

1.1 Stroke and transient ischaemic attack

Stroke is defined by the World Health Organisation (WHO) 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” [1] (p 1-4).

There are two main types of stroke, ischaemic and haemorrhagic, which account for approximately 85% and 15% of strokes, respectively [2]. Ischaemic stroke results from inadequate blood flow to areas of the brain, often due to a clot [3,4]. The clot may be an embolism of cardiac origin, as a result of atrial fibrillation, or a thrombus formed within a diseased blood vessel, such as an artery affected by atherosclerosis [3,4]. A spontaneous bleed into the brain results in an intracerebral haemorrhage [3]. Both ischaemic and haemorrhagic stroke types result in part of the brain dying, which leads to a loss of brain function and impairments including compromised movement, thinking and communication [5]. Either stroke type may be fatal [5].

Transient ischaemic attack (TIA) was traditionally called a “mini stroke” and defined clinically by the presence of focal neurological symptoms lasting less than 24 hours [6]. However, with improvements in stroke imaging, it has been shown that up to a third of people with resolving symptoms lasting less than 24 hours have infarcts. This has led to a tissue-based definition of TIA: a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal

ischaemia, without acute infarction [6]. People who have suffered a stroke or TIA are at increased risk of a subsequent stroke [6] as well as myocardial infarction and cardiac death [7].

Stroke results in a number of primary and secondary impairments that can affect body functions and structure, activity levels and participation [8]. These are also influenced by environmental and personal factors [8]. Primary impairments include motor, sensory, language, perceptual, cognitive and behavioral changes. Secondary changes can include reduced fitness, altered mood, and musculoskeletal adaptations.

1.2 Stroke in Australia and in the Hunter Region

Stroke is a major cause of death and disability in Australia [9]. Approximately 50,000 strokes (new or recurrent) will occur in Australia in 2015 [9]. Stroke is a major cause of disability [5]; two-thirds of people surviving a stroke in Australia will have a disability that limits their capacity to undertake activities of daily living independently [10]. Stroke is also costly, with the total financial costs of stroke in Australia estimated to have been AU\$5 billion in 2012 [11].

Rates of stroke occurrence (attack rates) and case fatality have been examined in the Hunter Region, New South Wales, Australia, which is the location of the studies in this thesis [12]. This region has a mixed urban and rural population. Data from patients admitted with acute stroke over 13 years (1996 to 2008) to all 14 public hospitals in the region that admit acute stroke patients has been analysed. The results indicate a fall in stroke attack rates but stable case fatality despite an aging population [12]. The results highlight stroke is a major disease burden in the region.

1.3 Physical activity, exercise and cardiorespiratory fitness

The ability to perform physical activity depends on physical fitness, which has five key components: cardiorespiratory fitness, muscular endurance, muscular strength, body composition, and flexibility [13,14]. Cardiorespiratory fitness is a measure of how well the circulatory, respiratory and musculoskeletal systems work together to deliver oxygen, remove metabolic byproducts, and use oxygen to produce energy during physical activity [15]. Exercise, a specific form of physical activity, is planned, structured repetitive movement with the objective to maintain or improve physical fitness [13].

Physical activity can be undertaken at a range of intensities. These are often expressed in terms of metabolic equivalents (METs) or in percentages of maximal oxygen consumption (VO_{2max}), peak oxygen consumption (VO_{2peak}), maximal heart rate (HR_{max}) or heart rate reserve [14]. Oxygen consumption (VO_2) of approximately 3.5 mL/kg/min or one MET is utilised by an adult at rest [16]. Any increase in physical activity results in an increased demand for oxygen. Table 1-1 outlines the VO_2 and METs required to perform physical tasks at different levels of activity (intensities) [16]. These values are based on the results for healthy people and do not take into account any additional energy demands required by people with a disability, such as hemiparesis after stroke. The energy cost of walking for chronic stroke survivors with hemiparesis is approximately twice that of non-stroke subjects [17]. It has been reported that 15-18 mL/kg/min is the minimum VO_{2peak} required to meet the demands of independent living [18].

Table 1-1 Classification of physical activity based on exercise intensity

Energy Requirements- adapted from [16]				
	Male (based on 65kg)		Female (based on 55kg)	
Level	mLO ₂ /kg/min	METs	mLO ₂ /kg/min	METs
Light	6.1 - 15.2	1.6 - 3.9	5.4 - 12.5	1.2 - 2.7
Moderate	15.3 - 22.9	4.0 - 5.9	12.6 - 19.8	2.8 - 4.3
Heavy	19.9 - 27.1	6.0 - 7.9	19.9 - 27.1	4.4 - 5.9
Very Heavy	27.2 - 34.4	8.0 - 9.9	27.2 - 34.4	6.0 - 7.5
Unduly Heavy	≥ 34.5	≥ 10.0	≥ 34.5	≥ 7.6

As people age, their capacity to undertake aerobic exercise diminishes. Age-related changes in physiological responses to a bout of aerobic exercise include: a decrease in VO_{2 max} of 8-10% per decade in untrained or inactive populations; a more rapid increase in systolic blood pressure with exercise; less complete emptying of the left ventricle during strenuous exercise; and a reduced maximal heart rate (HR) of 1 beat/ minute per year of age, which is reflected in the calculation estimating maximal HR of 220 – age [19]. Table 1-2 summarises representative values of VO_{2max} and percentiles for men and women aged 50 to 79 years.

Table 1-2 VO_{2max} values for males and females aged 50-89 years

Percentile values for VO _{2 max} in mL/kg/min adapted from [14] p 85-89							
		Males			Females		
%	rating	50-59 years	60-69 years	70-79 years	50-59 years	60-69 years	70-79 years
95	superior	49.7	46.1	42.4	39.9	36.9	36.7
80	excellent	43.3	39.5	36.0	35.2	32.3	30.2
60	good	38.3	35.0	30.9	31.4	29.1	26.6
40	fair	35.2	31.4	28.0	28.7	26.6	23.8
20	poor	31.1	27.4	23.7	25.5	23.7	21.2
1	very poor	21.3	18.6	17.9	19.3	18.1	16.4
	Sample size (n=)	9102	2682	467	3103	1088	209
Normative values of VO _{2 max} adapted from [19]							
	mL/kg/min mean (SD)	36.7 (7.1)	33 (7.7)	29 (7.3)	29 (5.4)	27 (4.7)	27 (5.8)
	METs	10	9	8	8	8	8

1.4 Assessing cardiorespiratory fitness

Cardiorespiratory fitness testing has two main purposes: to assess a person's risk of adverse exercise-related events and to make recommendations about commencing, continuing or progressing an exercise program while minimising the risk of adverse events [14]. VO_{2max} is the accepted best measure of cardiorespiratory fitness [14]. It is measured via open circuit spirometry, during which the participant breathes through a low resistance valve, and ventilation and expired fractions of oxygen and carbon dioxide are recorded [14].

Normative values for VO_{2max} for older people are outlined in Table 1-2. Blood pressure, HR, ratings of perceived exertion, and workload are also often recorded to assess the participant's response to exercise [14]. A 12 lead ECG is often used for monitoring of HR and cardiac rhythms to identify any exercise-

induced abnormalities [20]. During progressive exercise tests there is a point at which the person shifts from aerobic to anaerobic metabolism, where lactate accumulates and fatigue develops more rapidly. This transition in metabolism is indicated by a respiratory exchange ratio (RER) of 0.85, after which the RER continues to increase reaching criteria $\text{RER} \geq 1.1$ as an indication of maximal effort being attained [7,21].

The most common modalities used to test cardiorespiratory fitness are motorised treadmills, cycle ergometers and field tests, such as the Six-Minute Walk Test (6MWT) [14,19]. Older participants without significant balance or gait disturbances are able to use a treadmill protocol, whereas for participants with gait or balance problems, cycle ergometry is preferred [19]. Cycle ergometer testing is often terminated due to local fatigue of the quadriceps muscles resulting in $\text{VO}_{2\text{max}}$ measurements 10-15% lower than those obtained on a treadmill [19].

Cardiorespiratory testing protocols can be either submaximal or maximal [19]. Submaximal protocols have a predetermined end point, often 70-85% heart rate reserve, 70-85% age-predicted maximum HR or 5 METs [14,19]. Indications a person has reached their maximal capacity include: achieving predicted maximal HR, $\text{RER} \geq 1.1$, a plateau of VO_2 or HR despite increasing workloads [22]. Both submaximal and maximal protocols are ceased if the participant demonstrates abnormal signs or symptoms, is unable to maintain the testing protocol or asks to stop [14,19].

1.5 Proposed mechanisms by which physical activity improves health

Participating in regular physical activity may result in chronic adaptations that provide health benefits through a number of biological mechanisms. These adaptations have been outlined by the American College of Sports Medicine [14] and in a review by Warburton et al [23] and include:

- central and peripheral changes resulting in increased maximal oxygen uptake [14]
- decreased blood pressure, HR, myocardial oxygen cost, and minute ventilation at a given absolute submaximal intensity [14]
- increased capillary density in skeletal muscle [14]
- increased exercise thresholds for the rise of lactate in the blood [14]
- reduced blood platelet adhesiveness and aggregation [14]
- reduced total and intra-abdominal body fat through increased energy expenditure [14]
- reduced blood pressure [23]
- enhanced lipid lipoprotein profiles through lowering triglyceride levels, increasing high-density lipoprotein cholesterol levels, and decreasing low-density lipoprotein to high-density lipoprotein ratios [23]
- improved insulin sensitivity and glucose homeostasis [23]
- improved coronary blood flow and cardiac function [23]

- reduced systemic inflammation [23], arterial inflammation by lowering homocysteine levels [24], and chronic inflammation by reducing mediators such as C-reactive protein [23]
- improved shear-stress-mediated endothelial function [23]
- improved psychological well-being by reduced stress, anxiety and/or depression [23].

As well as the long-term changes resulting from ongoing regular exercise, a single bout of exercise may also result in transient changes [25]. These include decreases in blood pressure that may last for 12 to 16 hours, reductions in triglyceride levels, increases in high density lipoprotein (HDL) cholesterol level, reductions in insulin resistance and improvements in glucose control [25]. These acute changes indicate the important role individual exercise sessions may have in providing health benefits.

1.6 Lack of physical activity as a stroke risk factor

Lack of physical activity is a modifiable risk factor for stroke. Other modifiable risk factors include: hypertension, diabetes mellitus, smoking, coronary heart disease, atrial fibrillation, hypercholesterolemia, a diet lacking in fruit and vegetables and obesity. Non-modifiable risk factors include age, gender and race. Increasing regular physical activity has the potential to reduce the risk of a first-ever or subsequent stroke.

Primary prevention of stroke

A low level of physical activity is an independent predictor of stroke risk [19]. Ten risk factors, including a lack of physical activity, combined to account for

88.1% (99% CI 82.3 to 92.2%) of stroke population attributable risk in the initial cohort of 3000 cases and 3000 controls in the world-wide INTERSTROKE trial [26]. This indicates almost all strokes could be prevented if these ten risk factors were eliminated. A lack of physical activity accounted for 28.5% (99% CI 14.4 to 48.5%) of the reported population attributable risk and was second only behind hypertension (34.6%, 99% CI 30.4 to 39.1%) [26]. In the INTERSTROKE study, being physically active was defined as being involved regularly in moderate or strenuous exercise four or more hours per week (ie at a level that has the potential to improve cardiorespiratory fitness). Lee et al in their meta-analysis of cohort and case-control studies identified an association between levels of physically activity and stroke risk for men and women [27]. Those who were highly and moderately active had 27% and 20% lower risk, respectively. These results demonstrate the potential for preventing a first-ever stroke by being more physically active.

In Australia physical inactivity is a leading contributor to the burden of disease and injury, second only to tobacco smoking [5]. In 2003 it accounted for 6.6% of the total disease burden, mainly due to its effects on cardiovascular disease [28]. In 2007-08, 63% of Australian adults had insufficient exercise, in terms of both the time spent exercising per week and the intensity of the exercise, to obtain health benefits [5].

Secondary prevention of stroke

Being physically active may be an important part of the life-style modification component of secondary prevention after stroke. Approximately one quarter of strokes are subsequent events [6]. It has not been determined through controlled trials whether participating in regular aerobic exercise reduces the

risk of subsequent stroke [6]. However studies examining the effects of aerobic exercise programs after stroke have shown potential health benefits that may reduce the risk of another stroke. The results from a systematic review with meta-analysis conducted by Pang et al in 2006 indicate aerobic exercise can improve cardiorespiratory fitness after stroke [29]. Other exercise interventions after stroke have been shown to reduce blood pressure [6,30] and weight [6], improve blood glucose levels [24], lipid profiles [24,30], and arterial function [31].

Despite the potential benefits of being more active after stroke, it has been estimated that 77% of Australians who have suffered a stroke are sedentary or have low levels of physical activity [2]. Studies investigating strategies to engage stroke survivors in physical activity, including incorporating aerobic exercise into a healthy lifestyle may assist in reducing these numbers.

1.7 Cardiorespiratory fitness levels after stroke

The cardiorespiratory levels of stroke survivors are very low compared to people without stroke [60]. If fitness levels can be improved even marginally for people after stroke it could make a large difference to their independence and quality of life by providing a larger range of VO_2 in which to work [19]. The results from a systematic review indicated that mean $\text{VO}_{2\text{peak}}$ values ranged from 8 $\text{mLO}_2/\text{kg}/\text{min}$ for inpatients with acute stroke [61] to 22 $\text{mLO}_2/\text{kg}/\text{min}$ for chronic community-dwelling stroke survivors [62]. These $\text{VO}_{2\text{peak}}$ values equated to 26% and 87% respectively of the values of healthy age- and sex-matched people [60]. Most everyday physical activities are undertaken in light (3.5 to 10.4 $\text{mLO}_2/\text{kg}/\text{min}$) or moderate intensity (10.5 to 21.0 $\text{mLO}_2/\text{kg}/\text{min}$)

categories [14,63,64]. Consequently, healthy people can perform these activities of daily living comfortably, with reserve to spare, but for people with stroke these VO_2 requirements approach or reach their maximum capacities (VO_{2peak}). For stroke survivors this makes undertaking many everyday activities difficult to sustain for any length of time and more physically demanding activities almost impossible [7].

Over the past 20 years cardiorespiratory fitness testing and training after stroke has been a growing area of research. In 1995 Potempa et al were the first group to investigate the effect of an aerobic training program on improving cardiorespiratory fitness in stroke survivors by measuring maximal oxygen consumption during a cycle progressive exercise test. Since then researchers have investigated methods to assess and train cardiorespiratory fitness, the effects of fitness on body structure and function as well as on activity levels. A number of key groups have led the research. Macko et al described a treadmill screening and testing protocol in 1997 [32] which has been used in subsequent studies [33-42]. Studies undertaken by Billinger et al have included piloting the total body recumbent stepper as a testing modality [43-46]. Billinger et al authored the recent Physical Activity and Exercise Recommendations for Stroke Survivors [47]. Aerobic capacity and function after stroke has been investigated by Tang et al [24,48-50], Eng et al [22,29,51-54] and Mackay-Lyons et al [18,55-57]. Kuys et al [58,59] have investigated the cardiorespiratory stimulus provided in the rehabilitation setting.

Investigating the change in VO_{2peak} conferred by aerobic training approaches used with people after stroke can have a number of advantages. It may inform us on the effects of different training regimes after stroke. It might assist in

deciding what training strategies would be most beneficial depending on stroke deficits and time since stroke. It can also provide information for sample size calculations for future studies.

1.8 Possible factors contributing to reduced cardiorespiratory fitness after stroke

Reduced levels of physical activity and cardiorespiratory fitness after stroke are likely a consequence of the combined primary effects of the stroke, secondary post-stroke factors and co-existing factors.

Primary effects of stroke on function

The sensorimotor effects of stroke can include weakness, incoordination, spasticity, sensory-perceptual deficits and balance disturbances [65,66]. These can lead to reduced mobility, increased physiological costs due to reduced efficiency of movement, and decreased confidence to perform motor tasks independently [67].

Secondary effects on the three physiological systems that influence cardiorespiratory fitness

Musculoskeletal system

Stroke can result in the reduced ability to recruit motor units in the periphery known as paresis. This can subsequently lead to alterations in skeletal muscle, primarily but not solely in the affected limb/s. Changes may include:

- a change in muscle fibre types from Type 1 (slow twitch) to Type 2 (fast twitch), which are more fatigue-prone[15]
- increased reliance on anaerobic metabolism due to compromised capacity to use oxygen in muscle, in part due to the loss of Type I muscle fibres [65]

- increased intramuscular fat [15]
- reduced muscle capillary density in paretic leg muscles which can lead to increased glucose intolerance [15]
- an almost three-fold elevation in paretic leg muscles of the expression of tumor necrosis factor-alpha (TNF- α), an inflammatory cytokine implicated in both muscle atrophy and insulin resistance [15]
- disuse muscle atrophy leading to loss of lean muscle mass, particularly in large leg muscles, which negatively affects VO_{2peak} [15] as well as leg muscle strength on both the affected and unaffected sides [68,69]
- changes in muscle length and stiffness which may result in contractures [67].

Circulatory system

These may include:

- changes in the autonomic nervous system that may alter regulation of cardiac output and blood flow to skeletal muscles [15]
- impaired peripheral blood flow due to reductions in arterial diameter and blood flow velocity, particularly in a paretic limb [70].

Respiratory system

Respiratory function is usually only affected to a modest extent but can add to the overall dysfunction [65]. Dysfunction may be due to:

- the stroke itself, particularly brain stem strokes [15]
- weakened respiratory muscles (intercostal, abdominal and hemi-diaphragm) as a consequences of the stroke, leading to impaired breathing mechanics and eventual rib cage contractures [15,65]

- lifestyle factors such as smoking and inactivity [15,65]
- comorbidities including chronic obstructive pulmonary disease [15]

The large number of changes in skeletal muscle suggests that these may be the primary drivers of reduced cardiorespiratory fitness after stroke. If the above changes can be prevented, minimised or improved through exercise a stroke survivor's cardiorespiratory fitness level may also improve.

Personal and environmental barriers

Reasons that people who have had stroke do not participate in regular physical activity are varied and complex [71]. These need to be considered for each stroke survivor during exercise prescription to assist with compliance.

Participation in physical activity may be influenced by direct physical impairments caused by their stroke [72,73] or be subsequent to the stroke, such as fear of causing a recurrent stroke [72] or falling [73]. Some people may experience embarrassment [72,73], loss of confidence [73] or a lack of motivation [72]. For some it may be a lack of knowledge that physical activity is feasible and desirable [47] or of how and where to go about exercising [72]. Some people may believe that exercise is too difficult, boring, not interesting or would not improve their condition [73]. Depression and fatigue, common consequences of stroke, may also impact on stroke survivors' ability or desire to engage in physical activity [47]. Environment factors that may influence the uptake of exercise programs include access to transport [72], cost [72], and a perceived lack of support from health professionals [73] or family [47]. Access can also be an issue. This may be to resources to promote exercise and physical activity [67], including rehabilitation [72] and to exercise specialists to demonstrate and provide instruction in activities [47]. Identifying the barriers and enablers, and

developing strategies to overcome or utilise these, may be an important component of exercise prescription for stroke survivors.

1.9 Potential benefits of increasing physical activity and improving cardiorespiratory fitness for recovery post-stroke

Stroke is associated with a vicious cycle of inactivity, deconditioning and reduced cardiorespiratory fitness. Breaking this cycle can have many benefits for stroke survivors.

Improving mobility

Impaired mobility is a common and disabling effect of stroke. Improving mobility can make undertaking everyday activities easier or less fatiguing, and increase the potential for engaging in activities that are meaningful to the stroke survivor, such as “getting around” in their community. In systematic reviews with meta-analysis, aerobic exercise has been demonstrated to improve mobility after stroke including walking endurance [29,74-76] and fast gait speed [74,76]. The results for comfortable gait speed have been mixed with one review showing benefit [76] and two reviews indicating no effect [74,75].

Walking performance may provide useful proxy measures to assess cardiorespiratory fitness and changes in fitness. Proxy measures are required as VO_2 is not readily measured in most clinical settings.

Reducing the effects of sedentary behaviour

Incorporating physical activity programs into post-stroke management has the potential to reduce sedentary behaviour as well as improve cardiorespiratory fitness. People after stroke are often inactive, with approximately 20 hours of their day in sedentary behaviours [77,78]. This is three hours more than age- and sex-matched controls [77] and appears unchanged at 1, 6 and 12 months

after stroke [78]. This is a concern as evidence is emerging that sedentary behaviour appears to be independently associated with increased risk for cardiovascular and all-cause mortality in both men and women [79]. The association with the increased risk of death does not appear to be overcome by spending time undertaking moderate-to-vigorous intensity physical activity [79]. Stroke survivors are often sedentary for prolonged bouts. Alzahrani et al [80] observed that people after stroke spent similar amounts of time on their feet as age-matched controls (mean difference 36 minutes, 95% CI -27 to 99) but the frequency of the stroke survivors' activity counts were less (mean difference 4062 activity counts, 95% CI 1787 to 6337). The difference in activity between the groups was frequency rather than duration.

For people after stroke a whole-of-day approach to physical activity may be applicable [81]. Interventions that combine cardiorespiratory fitness training with strategies to reduce prolonged bouts of inactivity may be appropriate for stroke survivors in reducing their cardiovascular risk.

Preventing or minimising bone loss

Fractures, in particular hip fractures, post-stroke can have serious adverse consequences, including death [82]. Bone loss, in conjunction with falling after stroke, can contribute to an increased risk of fractures. There is currently limited evidence for the effects of being physically active on improving or maintaining bone mineral density and cortical thickness in people after stroke. Only three studies met the inclusion criteria for a recent systematic review of skeletal effects of physical activity after stroke [83]. All three studies included participants with chronic stroke. Effect sizes were small but favoured physical activity for lower limb bone health [83]. Minimising bone loss is important as

after stroke bone loss is pronounced, with reduced bone mineral density of up to 12% in the proximal femur and up to 24% in the paretic proximal humerus in people one year after stroke [83]. These values are much larger than healthy people aged over 60 years where the usual rate of bone loss is approximately 1% per year [83]. Physical activity interventions using weight-bearing exercise and strengthening the muscles around susceptible joints may assist in preventing bone loss [83]. Cardiorespiratory fitness training strategies can be designed to meet these criteria, and hence may provide bone-health benefits.

Enhancing neuroplasticity

Emerging evidence indicates that aerobic exercise has the potential to be a valuable intervention for enhancing neuroplasticity after stroke [84]. A systematic review in animal studies has identified aerobic exercise increases brain-derived neurotrophic factor (BDNF), insulin-like growth factor-I (IGF-I), nerve growth factor (NGF), synaptogenesis and dendritic branching after stroke [85]. The authors suggest, based on the animal models, that the first few months after stroke when the brain is most responsive is the ideal time to harness neuroplasticity [85]. In animal models BDNF appears to play a specific role in motor learning [84], which is often a key focus of post-stroke therapy. It appears important that the task practiced is novel and motor-challenging, rather than just simple repetition of a familiar activity [84]. Aerobic exercise may be an effective means to enhance BDNF levels, as exercise induces a cascade of events that leads to increased BDNF gene expression in multiple regions of the central nervous system [84]. It is therefore plausible that incorporating challenging, task-specific activity into an aerobic exercise program could not

only drive neuroplasticity but also take advantage of neuroplasticity to assist with motor recovery.

Improving cognitive performance including executive functions

As well as improving physical function, being physically active after stroke may also improve cognitive performance, including executive function. There is some evidence that increasing physical activity may improve cognitive performance, as identified by Cumming et al [86] in their systematic review with meta-analysis. The authors hypothesised that increasing arousal and wakefulness, possibly by increasing neurotransmitters, and reducing depressive symptoms were potential mechanisms whereby increasing physical activity may improve cognition [86]. There is emerging evidence that increasing physical activity can improve higher order cognitive processes (executive functions) [46,54]. The emerging evidence in stroke survivors reflects that of animal models where there is considerable evidence that exercise-induced increases in BDNF benefits cognitive function [84]. Improving physical activity may have the added benefit of improving the cognitive functional recovery of stroke survivors. This is important as cognitive deficits affect approximately two-thirds of stroke survivors [86].

Improving psychosocial functioning

Psychosocial factors may be an important component of the downward spiral of inactivity, deconditioning and reduced cardiorespiratory fitness. People with post-stroke fatigue (PSF) and/or depression may find it difficult to be physically active, which results in worsening fatigue, depression and health-related quality of life (HRQoL). Identifying strategies to improve the psychosocial health after stroke is important, as these issues are common among stroke survivors.

HRQoL is often reduced for people after stroke compared to those without stroke [87]. Depression affects approximately a third of stroke survivors, can occur at any time post-stroke and is related to reduced functional recovery and reduced social participation [52]. PSF is estimated to affect 30-68% of stroke survivors [88].

Despite PSF being common [88] and often one of the worse symptoms reported by stroke survivors [89] there is little evidence for effective management strategies, including the role of increasing physical activity. A systematic review found limited evidence for associations of post-stroke fatigue with cardiorespiratory fitness, physical activity levels, muscle strength and muscle mass, however only three small studies were included [88]. A more recent longitudinal study identified higher fatigue levels were associated with lower step counts at 1, 6 and 12 months after stroke ($p < 0.001$, 0.01 and 0.007 respectively), but the causal direction could not be determined [90]. It is plausible that increasing physical activity may improve cardiorespiratory fitness levels, thus shifting the submaximal VO_2 threshold. This means that at a given relative workload, VO_2 is reduced, which is less fatiguing. The mechanism of PSF is not known but it is likely to be a complicated interaction of physiological, psychosocial, behavioural and physical components [91]. Exploring the relationships between PSF and improving activity levels may provide some insight to the mechanism(s) and management of PSF.

A distinction to be aware of, and made, is between PSF and exertion fatigue, particularly when investigating physical activity and cardiorespiratory fitness after stroke. Exertion fatigue is commonly experienced after physical or mental effort and is acute in nature, with rapid onset, lasts a short time and with a quick

recovery period [45]. PSF is characterised by a persistent, chronic excessive lack of energy that is perceived by the individual to interfere with daily activities [91]. Tseng et al [45] identified VO_{2peak} as an independent predictor of exertion fatigue whereas depression was an independent predictor of PSF. The type of fatigue experienced by a stroke survivor undergoing physical activity interventions needs to be clarified, for example when determining reasons for stopping an exercise test or not participating in a program. This is so strategies to help to manage the type of fatigue can be implemented.

There appears to be a link between depression and physical activity after stroke. Higher levels of depressive symptoms have been shown to be negatively associated with the physical activity levels of community-dwelling stroke survivors, regardless of how the physical activity was measured: frequency of activity or duration of activity [80]. Structured exercise programs appear likely to be able to reduce depressive symptoms after stroke [52]. Overall, physical exercise resulted in less depressive symptoms over 13 studies involving 1022 patients (SMD = -0.13 [95% confidence interval (CI) = -0.26, -0.01], $I^2 = 6\%$, $p = 0.03$) with low heterogeneity [52]. To further explore the relationship between depression and cardiorespiratory fitness measures of depression could be routinely included in study designs.

1.10 Current recommendations for cardiorespiratory fitness, exercise and physical activity after stroke

There is a growing body of evidence to support incorporating physical activity and cardiorespiratory fitness training into management after stroke, as outlined above. The recently released “Physical Activity and Exercise Recommendations for Stroke Survivors” suggest that for stroke survivors beyond the early acute

phase, aerobic exercise should be incorporated into management [47].

Moderate intensity exercise, using large muscle activities for 20 to 60 minute sessions on 3 to 5 days per week is recommended [47]. There is currently little evidence that it is feasible for stroke survivors to achieve the recommended duration and exercise intensity, as measured by the gold standard of VO_2 .

Providing this evidence can inform clinicians and managers on possible strategies to assist in incorporating cardiorespiratory fitness training into post-stroke therapy.

1.11 Increasing the focus on cardiorespiratory fitness after stroke

The challenge for health services

In Australia access to post-stroke therapy, including therapy focused on increasing cardiorespiratory fitness after stroke, appears limited for many stroke survivors. The Australian National Stroke Audit Acute Services: Clinical Audit Report 2013 results indicate that of those surviving a stroke in Australia, 44% of people were discharged home from acute services, 31% went to inpatient rehabilitation and 8% went to residential aged care, and 12% awaited placement or other medical services [92]. Of the people discharged alive, 52% accessed some form of rehabilitation service: 72% of these as an inpatient, 13% as an outpatient and 15% in the community [92]. Of the 44% of people who were discharged directly home, only 31% subsequently had access to rehabilitation [92]. The median length of stay in acute care for a person discharged after stroke was 5 days [92]. These figures indicate that there is currently little opportunity for cardiorespiratory fitness to be incorporated routinely into post-stroke management for a large proportion of stroke survivors.

Following discharge from conventional therapy there are often few community-based services to promote regular physical activity after stroke [7]. With such little community support available, stroke survivors may live with the functional and cardiovascular health consequences of physical inactivity [7]. Resource-efficient, effective strategies to support community-dwelling stroke survivors to engage in physical activity and improve cardiorespiratory fitness need to be trialled to help to provide options for filling this gap in care.

The challenge for clinicians

Many clinicians currently have limited knowledge and experience in prescribing fitness programs for the diverse stroke population they manage [93]. Therapy after stroke usually prioritises the regaining of physical function to support independent living, with little or no focus on training cardiorespiratory fitness. People after stroke with significant weakness and loss of coordination need to regain sufficient use of large muscle groups before cardiorespiratory fitness can be a focus of therapy. However once this is achieved therapy targeting improving cardiorespiratory fitness may still be overlooked. Therapy sessions are often below the intensity and duration recommended to provide a cardiovascular challenge. Two studies identified that standing and walking, activities with the potential to provide sufficient stimulus, were undertaken for an average of only 22 [58] and 25 [59] minutes in a physiotherapy rehabilitation session. The sessions averaged an exercise intensity of 24% of heart rate reserve [58,59], which is at the lower end of the light intensity category [33]. Mackay-Lyons and Makrides observed only a small proportion of therapy session time was spent in an appropriate HR training zone: 2.8 minutes in physiotherapy and 0.7 minutes in occupational therapy which equated to 5%

and 3% of sessions respectively [55]. Resources to inform clinicians on developing and implementing exercise programs suitable for training cardiorespiratory fitness after stroke are emerging [47,94].

If cardiorespiratory fitness training is to be widely adopted as a routine component of post-stroke management then clinicians, stroke survivors and their carers require reassurance that it is safe to do. There can be a reluctance to push the intensity of training in the stroke population due to the fear of causing an adverse cardiovascular event or subsequent stroke. From the data synthesised in a Cochrane systematic review there is little to suggest fitness training results in adverse events in a stroke population [95]. Routine reporting of adverse events during studies that assess or train cardiorespiratory fitness will provide further information on the risks involved.

1.12 Conclusion

Stroke is a prevalent and disabling disease. Improving levels of physical activity has the potential to prevent first ever stroke and most likely subsequent events. Being physically active can provide health benefits, including addressing a number of contributing biological factors, both acutely and on a long-term basis. Physical activity has the potential to overcome a number of the adverse primary and secondary effects of stroke, particularly those affecting the musculoskeletal system as well as improving physical, cognitive and psychosocial function. Undertaking physical activity at a sufficient dose has the potential to improve cardiorespiratory fitness, thus providing a greater range of capacity to undertake everyday activities. The challenge is for clinicians and health services to adopt cardiorespiratory fitness training as part of usual post-stroke management. To

date this has often been overlooked in those requiring functional retraining and ignored in those with little or no mobility deficits. There is a need to better understand the role of exercise in generating improvements in cardiorespiratory fitness, determine methods to reliably assess cardiorespiratory fitness in the clinical setting, and identify strategies that are clinically-applicable and resource-efficient to assist in the inclusion of cardiorespiratory fitness into routine post-stroke management.

1.13 References

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CHAPTER 2: AIMS AND HYPOTHESES

The overarching aim of this project was to examine strategies to assess and train cardiorespiratory fitness in people after stroke. I was particularly focused on examining strategies that could be used in metropolitan, regional or rural settings using minimal equipment and personnel.

2.1 Aims and Hypotheses

The aims and hypotheses of the studies in this thesis are:

Aim 1 (Chapter 4).

- a. To determine the effectiveness of exercise interventions in improving the cardiorespiratory fitness of people after stroke.
- b. To identify the characteristics of participants and interventions studied to date to help inform future strategies to improve cardiorespiratory fitness of people after stroke.

Hypothesis 1

- a. Exercise interventions with an aerobic component can improve cardiorespiratory fitness after stroke

Aim 2 (Chapter 5)

- a. To investigate and compare cardiorespiratory responses and performance measures during three clinically-applicable exercise tests.
- b. To assess the feasibility of using the Shuttle Walk Test (SWT) in stroke survivors compared to the Six-Minute Walk Test (6MWT) and cycle progressive exercise test (cPXT).

Hypothesis 2

- a. For community-dwelling, independently-ambulant stroke survivors, the distance walked during the 6MWT, the number of shuttles completed during the SWT, and the final workload achieved during the cPXT all correlate strongly with peak oxygen consumption (Chapter 5).
- b. For community-dwelling, independently-ambulant stroke survivors, the SWT is a feasible clinical walking test to assess cardiorespiratory fitness compared to the 6MWT and cPXT.

Aim 3 (Chapter 6).

- a. To examine the exercise intensity parameters achieved by stroke survivors during task-specific and ergometer workstation activities using an interval training approach.
- b. To determine whether people after stroke can use a circuit of the above workstations to accumulate a dose of exercise that may be sufficient to produce cardiovascular benefits.
- c. To determine whether interval training on a circuit of workstations is a safe and feasible cardiorespiratory fitness training approach for people after stroke.

Hypothesis 3

- a. Applying interval training principles to task-specific and ergometer workstations enables stroke survivors to exercise at an intensity sufficient to improve cardiorespiratory fitness

- b. Interval training on a circuit of workstations is a safe and feasible cardiorespiratory fitness training approach for people after stroke

Aim 4 (Chapter 7)

- a. To determine the feasibility and preliminary efficacy of an individually tailored home- and community-based exercise program to improve cardiorespiratory fitness in stroke survivors.
- b. To examine the effects of the above program on performance measures, fatigue, depression and health-related quality of life.

Hypothesis 4

- a. An individually tailored home- and community-based exercise program is a feasible and effective cardiorespiratory training approach for people after stroke (Chapter 7)
- b. The program will lead to improved performance measures and levels of fatigue, depression and health-related quality of life.

The results from these pilot studies will be used to inform the design of a future larger, multicentre randomised controlled trial.

2.2 Structure of the project

To address Aim 1, a systematic review with meta-analysis (Chapter 4) was undertaken. The results of this investigation helped to inform the design of the pilot intervention project: How Fit Is the Stroke Survivor? (HowFITSS?) (Chapter 7). Data collected at baseline from the HowFITSS? cohort of participants were used to answer Aims 2 and 3 (Chapters 5 and 6). Following completion of the baseline measures, a controlled trial of a 12-week intervention was undertaken to answer Aim 4 (Chapter 7). The individually-tailored circuit of workstations trialled in Chapter 6 provided an opportunity for participants to practise activities that were included in their home- and community-based program in a supervised environment.

CHAPTER 3: METHODS FOR THE HOW FIT IS THE STROKE SURVIVOR? (HowFITSS?) PROJECT

The methods used in the HowFITSS? project are outlined below. Most of the assessments and measures used are described in detail in the submitted manuscripts (Chapters 5 to 7).

3.1 Setting

This project was undertaken in the Hunter Region, New South Wales, Australia.

This is a well-defined geographic location of 29,200 square kilometres encompassing 11 local government areas, two of which are metropolitan and nine are predominantly regional/ rural [1]. It has a population of 696,449 of which 55% live in the two metropolitan local government areas [1]. There are 14 public Hunter New England Local Health District hospitals in the region that admit acute stroke patients, including two tertiary referral hospitals (one with a thrombolysis service), one rural referral hospital, six district hospitals and six community hospitals/ multipurpose services. The stroke attack rates for the Hunter population aged 20 years and above decreased consistently from 129 to 106 stroke events per 100,000 population (WHO age-standardised) between 1996 to 2008 [2]. Pre-hospital and early notification systems have been established to enable rapid access to the thrombolytic centre. All of the non-thrombolytic services are bypassed for people who are deemed potentially eligible for thrombolysis [3,4].

Data were collected in the Human Performance Laboratory in the Health and Physical Education Building (HPE) at the University of Newcastle, Callaghan Campus.

3.2 Ethics and Clinical Trial Registration

The project was approved by the Hunter New England Human Ethics Committee (11/04/20/4.04) and the University of Newcastle Human Research Ethics Committee (H-2011-0172). It was conducted in compliance with the Australian National Health and Medical Research Council guidelines [5]. It was registered with the Australian New Zealand Clinical Trials Registry, ANZCTR Trial ID: ACTRN12614000134628.

All participants provided informed written consent to participate. Participants gave written consent for the use of photographs.

3.3 Participants

A convenience sample of 23 community-dwelling stroke survivors aged ≥ 18 years old, who were within one year of their most recent stroke and able to follow basic commands was recruited. This was achieved through clinician referral from inpatient units, outpatient clinics and community-based services of the Hunter New England Local Health District. Key exclusion criteria were: unable to attend the centre for the assessment sessions, pregnancy, and determined medically unfit to participate by a medical practitioner. Absolute and relative contraindications to exercise testing [6] were provided on the Medical Clearance form completed by the medical practitioner.

Of the 23 participants, 10 were in the intervention group, 10 in the control group and 3 in an “own exercise” group. These latter three consented to baseline assessments including the circuit of workstations session, but did not wish to participate in the intervention component. They were already undertaking their

own exercise programs. Data from all participants were included in the study in Chapter 4, intervention and “own exercise” group participants in Chapter 5 and intervention and control group participants in Chapter 6.

The project was designed to enable stroke survivors to participate regardless of where they lived in the Hunter region. We recruited 14 participants who lived in metropolitan areas, 4 from in regional and 5 from rural areas. The median distance travelled from home to the centre was 18 kilometres with a range of range of 2 to 147 kilometres.

Participants were provided with an appointment schedule document prior to their first assessment. This outlined appointment times and dates, the assessment room location, contact telephone details for the researchers and instructions on what to do the day before and day of assessment (Appendix). A map of the campus highlighting the location of HPE building was provided.

3.4 Outcome measures and cardiorespiratory fitness assessment procedures

Participant characteristics

Functional Ambulation Category (FAC)

The FAC is a six-level categorical scale that can be used to rate walking ability. Scores range from 0 (non-functional ambulation) where a person cannot ambulate, ambulates in parallel bars only, or requires supervision or physical assistance from more than one person to ambulate safely outside of parallel bars to 5 (ambulator- independent) where a person can ambulate independently

on non-level and level surfaces, stairs, and inclines [7]. It is a simple to use, quick visual measurement of walking that has excellent reliability, good concurrent and predictive validity, and good responsiveness in people after stroke [8].

Modified Rankin Scale (mRS)

The mRS is a valid and clinically relevant instrument for assessing recovery from stroke [9]. The scale consists of seven well-defined and easily understood grades that describe global disability. Scores range from 0 no symptoms at all to 6 which is death [9].

Body Mass Index (BMI):

BMI was calculated by: $\text{mass (kg)} / [\text{height (m)}]^2$ ie kg/ m²

Three exercise tests

Upright cycle progressive exercise test (cPXT or GXT)

The protocol used was based on recommendations for cardiorespiratory exercise testing in the elderly using cycle ergometry [10]: These included: familiarising the participant with the testing equipment; providing a warm up of one to two minutes, aiming for test duration of eight to 12 minutes; and starting at a low resistance and using modest, equal increments in work for both physiological and psychological purposes. The final workload, test duration and reasons for stopping were recorded.

Six-Minute Walk Test (6MWT)

This was conducted in the corridor of the HPE building using guideline recommendations [11] except a 20-metre walkway was used due to limited corridor length. Distance walked was recorded.

The Shuttle Walk Test (SWT)

The use of this exercise test with a stroke population was a novel component of this project. Tests were conducted using the protocol [12] and associated audio recording (Department of Respiratory Medicine, Glenfield Hospital NHS Trust, Leicester, UK). The number of shuttles completed was recorded.

During both walking tests participants were allowed to use, if needed, their usual walking device and any ankle-foot orthosis.

Procedures for assessing cardiorespiratory measures

A novel component of HowFITSS? was the assessment of both oxygen consumption (VO_2) and heart rate (HR) during the three clinically-applicable exercise tests (Chapters 5-7) and during the circuit of task-specific and ergometer activity workstations (Chapter 6).

The selection of workstations for each participant was based on activities they wished to incorporate into their home- and community-based exercise program. The activities were practised via a circuit of 5-minute workstations in the controlled laboratory setting during which exercise intensity parameters were measured.

We used a portable metabolic measurement system to assess VO_2 (Cosmed K4b2, Italy) (Figure 3-1 A and B) and a 12-lead wireless electrocardiogram device to record HR and rhythm (Cosmed Quark T12, Italy) (Figure 3-1 C). Data were transmitted wirelessly to a laptop where it was monitored for safety (Figure 3-1 D) during the exercise tests (Figure 3-1 D-F) and workstations (Figure 3-1 G-L).

Other physical performance measures

Step Test

This was used to assess balance. The test was carried out as per Hill et al using a 7.5 cm step and a 15 second trial for each leg [13]. In summary participants were required to place the foot of the leg being tested wholly onto the step, then return it fully to the floor (completed step) repeatedly and as fast as possible. Only completed steps were counted. The researcher supervised the participant. No hands-on support was provided unless the participant lost balance and required assistance. At this point the test was ceased and only completed steps were counted. The researchers demonstrated the test and the participant practiced a few steps with each foot for familiarisation. It is a reliable and valid measure in the stroke population [13].

The 10m Walk Test

This was used to assess each participant's fast and self-selected walking speed [14].

Psychosocial measures

As fatigue, depression and decreased health-related quality of life are adverse results of stroke that have the potential to be improved by increasing cardiorespiratory fitness they were assessed. The following validated questionnaires were used.

Fatigue Assessment Scale (FAS)

This was used to assess each participant's fatigue levels [15]. The questionnaire is comprised of 10 statements about symptoms of fatigue that are answered on a 5-point scale of: (1) Never, (2) Sometimes, (3) Regularly, (4)

Often and (5) Always. Therefore a minimum score (representing no fatigue) is 10 and a maximum is 50. An evaluation of fatigue scales after stroke identified the FAS as having high face-validity and the best test-retest reliability of the tools assessed [16].

Stroke and Aphasia Quality of Life (SAQoL-39)

This questionnaire was used to assess self-reported health-related quality of life [17]. The tool has 2 response formats, both based on a 5-point scale: (1) could not do it at all to (5) no trouble at all, and (1) definitely yes to (5) definitely no. The overall score and four subdomain scores [physical (17 items), communication (7 items), psychological (11 items) and energy (4 items)] can range from 1 to 5, with higher scores indicating better health-related quality of life. The overall score is calculated by summing the item scores and dividing by 39. Subdomain scores are calculated by summing the relevant item scores and dividing by the number of items. The SAQoL-39 was chosen as it is an acceptable, reliable, and valid measure of stroke-specific health-related quality of life that can be used for people with aphasia [17].

Patient Health Questionnaire (PHQ-9)

This was used to assess depression [18]. The nine-symptom checklist asks about symptoms experienced over the last two weeks. Responses are given on a 4-point scale of: (0) Not at all, (1) Several days, (2) More than half the days, (3) Nearly every day. The maximum possible score is 27. Cut scores for severity have been published; 5-9 = minimal symptoms, 10-14 = minor depression, 15-19 = moderately severe depression, and >20 = severe depression [19]. The PHQ-9 has been reported as having high specificity in stroke survivors [18,20].

Figure 3-1 Assessing cardiorespiratory fitness using the Cosmed systems



3.5 Appendix



THE UNIVERSITY OF
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AUSTRALIA

HowFITSS?



Health
Hunter New England
Local Health District

Appointment Schedule

How Fit is the Stroke Survivor- Part 2 Testing Fitness

Version 3 – 09/ 08/ 13

Dr Neil Spratt
C/- Neurology Unit
John Hunter Hospital
Locked Bag 1
Hunter Region Mail Centre
NSW 2310

Name: _____

If you are **unable to make** the appointment please **ring** Di Marsden on
[REDACTED] or on the day [REDACTED]

Each Session is held at the Fitness Labs at the University of Newcastle- see map over.

Part A

Session 1: Fitness Assessment		Session 2: Fitness Assessment	
Date	Time	Date	Time

Part B (if applicable)

Session 3: Exercise Assessment		Session 4: Fitness Assessment		Session 5: Fitness-Assessment	
Date	Time	Date	Time	Date	Time

The sessions are held in the Health and Physical Education Building, next door to the Forum, in room HPE 2.08



THE UNIVERSITY OF
NEWCASTLE
AUSTRALIA

HowFITSS?

What to do the



Health
Hunter New England
Local Health District

day before and day of assessment

- Please don't eat, drink alcohol or caffeine drinks, smoke or use other tobacco products within 3 hours of testing.
- Drink ample fluids over the 24 hour period preceding the test to ensure normal hydration before testing.
- It is good to be rested for the assessment so please avoid significant exertion or exercise on the day of the assessment.
- Assessments may be tiring. For appointments at the University of Newcastle you may wish to have someone accompany you to the assessment to take you home afterward.



What to wear

- Clothing should permit freedom of movement Please wear a loose short sleeve shirt such as a t-shirt.
- Walking or running shoes should be worn.

What to bring

- Please wear or bring any orthoses you wear such as a foot drop splint.
- Please bring your usual walking aid if you use one.
- Please bring a list of your medications, including how much and how often you take them to the assessment. Please report the last actual dose taken. As an alternative, you may wish to bring your medications with you for the researchers to record.
- *Continue your medication regimen on their usual schedule.*

Chief Investigator:
Investigators:

Dr Neil Spratt
Ms Di Marsden
Prof Christopher Levi
Prof Robin Callister
Ms Ashlee Dunn

HNE LHD/ UoN
HNE LHD/ UoN
HNE LHD/ UoN
UoN
UoN

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Ph

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CHAPTER 4: CHARACTERISTICS OF EXERCISE TRAINING INTERVENTIONS TO IMPROVE CARDIORESPIRATORY FITNESS AFTER STROKE: A SYSTEMATIC REVIEW WITH META-ANALYSIS

4.1 Details

Authors and affiliations

DL Marsden MAppMgmt (Health)^{1 2 3}, A Dunn BExSpSci(Hon)^{1 2}, R Callister PhD^{1 2}, CR Levi FRACP^{1 2 3} and NJ Spratt FRACP, PhD^{1 2 3}

1. University of Newcastle, Callaghan, New South Wales, Australia
2. Hunter Medical Research Institute, New Lambton Heights, New South Wales, Australia
3. Hunter New England Local Health District, New Lambton Heights, New South Wales, Australia

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Key words

Stroke, cardiorespiratory fitness, oxygen consumption, aerobic, systematic review, meta-analysis

4.2 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: peer-reviewed articles published in English, adult stroke survivors, an intervention with the potential to improve cardiorespiratory fitness, and peak oxygen consumption (VO_{2peak}) assessed pre and post-intervention 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 VO_{2peak} values were low (8-23ml/kg/min). Meta-analysis of the 12 randomised controlled trials demonstrated overall improvements in VO_{2peak} of 2.27 (95% CI: 1.58,2.95) mL/kg/min post-intervention. A similar 10-15% improvement occurred with both aerobic and mixed interventions, and in shorter (≤ 3 months) and longer (> 3 months) length programs. Only one study calculated total dose received and only one included long term follow-up.

Conclusions: The results demonstrate interventions with an aerobic component can improve cardiorespiratory fitness post-stroke. 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 longer-term; and whether improved fitness results in better function and reduced risk of subsequent cardiovascular events.

4.3 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%CI: 14.4-48.5%) of stroke population-attributable risk, second only to hypertension (34.6%: 30.4-39.1%) [2]. Adults who are highly or moderately active have 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 values ranging from 8 to 22 mL/kg/min, which equates to 26-87% 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, as activities of daily living become too fatiguing [8]. Stroke guidelines recommend cardiorespiratory fitness training after stroke [9-12]; however, this is rarely implemented as regaining physical function is a primary focus. Many clinicians have limited experience with cardiorespiratory fitness testing or exercise prescription after stroke [13].

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 peak oxygen consumption (VO_{2peak}) achieved during progressive aerobic exercise testing using open circuit spirometry.

Subgroup analyses were planned to investigate factors hypothesised to influence effectiveness of the interventions. By synthesising the data available regarding characteristics of studies, participants (gender, age, time post-stroke) and interventions (type, dose, training setting, group/individual program, risks, satisfaction, effect maintenance) our aim was also to inform clinicians on strategies to improve cardiorespiratory fitness of people post-stroke.

4.4 Methods

The conduct and reporting of this review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14] and the Consolidated Standards of Reporting Trials (CONSORT) [15] statements.

Eligibility criteria

A systematic search was undertaken of MEDLINE, CINAHL, EMBASE, PsycINFO, AMED, SPORTDiscus and COCHRANE databases from their inception to 27 December 2011. Terms used for the MEDLINE search are listed in Table 3-1. These were adapted as required to suit each database searched. Inclusion criteria were: people aged 18 years and over at any time post-stroke or TIA; controlled and non-controlled 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 pre and post intervention; and an exercise intervention used which had the potential to improve cardiorespiratory fitness. Theses and papers published in abstract form only, including conference proceedings, were excluded.

Table 4-1 Search strategy used for MEDLINE

1	((cardiovascular or cardiorespiratory or aerobic* or exercise) and (fit* or condition* or capacit*)).mp.
2	Cerebrovascular Disorders.mp. or exp Cerebrovascular Disorders
3	Stroke.mp. or exp Stroke/
4	(cerebral or cerebellar or brainstem or vertebrobasilar).mp.
5	(infarct* or ischemia or thrombo* or embol*).mp.
6	4 and 5
7	(cerebral or brain or subarachnoid or intracerebral).mp.
8	(haemorrhage or haematoma or bleed* or hemorrhage or hematoma).mp.
9	7 and 8
10	(Transient Ischemic Attack or Transient Ischaemic Attack).mp.
11	2 or 3 or 6 or 9 or 10
12	(Physical Therap* Modalit* or Physical Fit* or fit* train* or Exercise therap*).mp.
13	((aerobic or fit*) and train*).mp.
14	rehabilitation.mp. or exp Rehabilitation/
15	therapeutic exercis*.mp.
16	12 or 13 or 14 or 15
17	1 and 11 and 16

Study selection

After duplicates were removed author DM sorted the search results by title and abstract into “include” and “exclude” and author AD reviewed for agreement.

The full text for all included papers were obtained and reviewed by authors DM 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 papers was also undertaken.

Data items and extraction

Data from the included papers were extracted into Excel 2007 ^a by DM and checked by AD, and included:

- 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
- VO_{2peak} : testing method, results pre and post intervention in mL/kg/min.

Study quality/ risk of bias

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

Synthesis of results

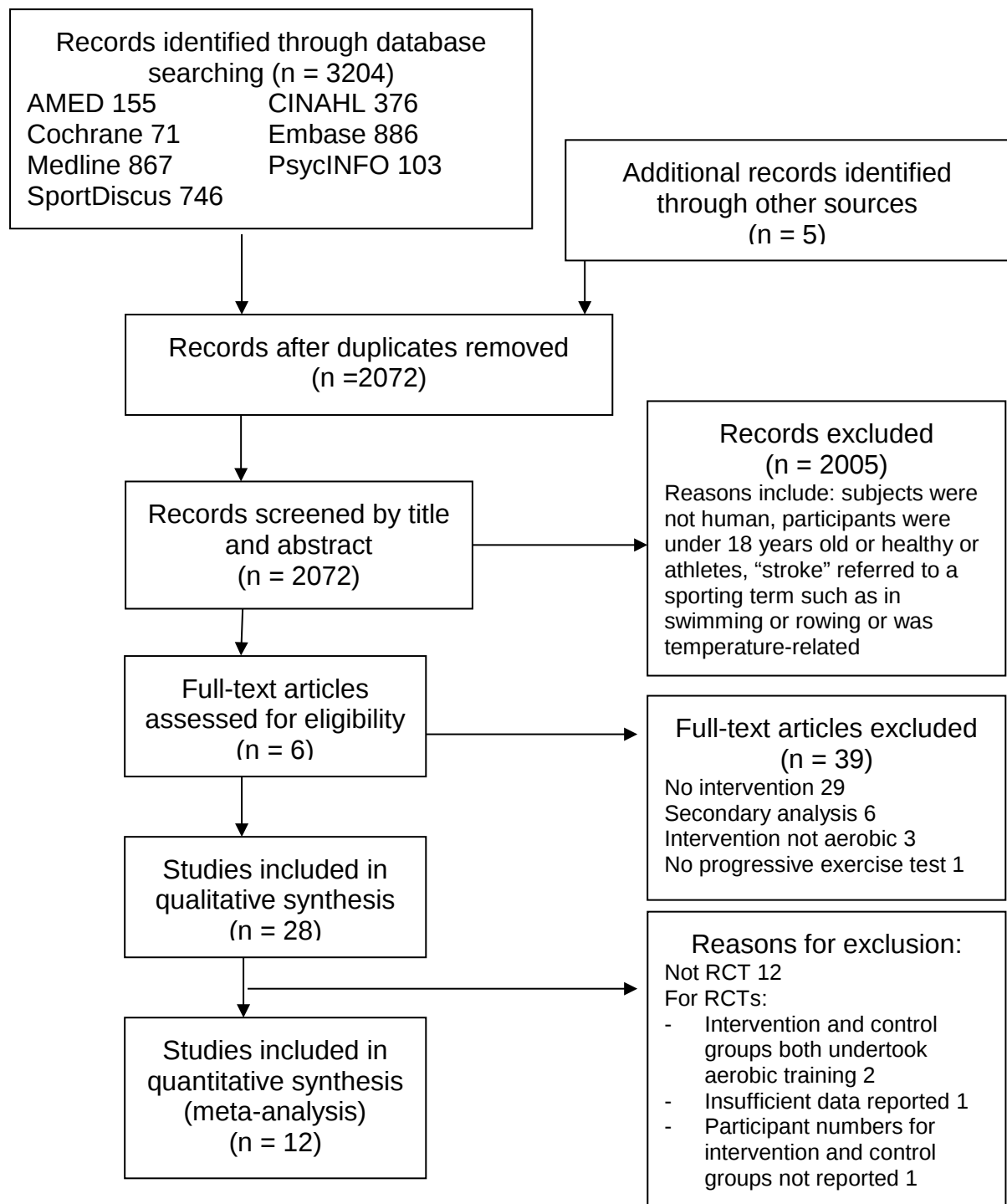
Statistical analysis was undertaken using RevMan5 ^c. Meta-analyses were planned to compare change in the primary outcome, VO_{2peak} in RCTs that used an intervention group and a control group with no intervention, sham training or an intervention that would be unlikely to have an aerobic training effect. 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” [16] (moderate

intensity for at least 30 minutes/day on most days of the week). As VO_{2peak} data are continuous, a random effects analysis model was used with mean difference at post-intervention as the effect measure, with 95% CI. Standard errors were converted to standard deviations [17]. Post measures for one study [18] were not reported so were calculated by adding the change score to the baseline score and using the baseline standard deviations. For Lee et al. [19] where more than one intervention was compared to a shared control group, the total number of control participant numbers were split evenly between the intervention groups with the means and standard deviations left unchanged [17]. Statistical heterogeneity was measured using the Chi^2 , Tau^2 and I^2 tests.

4.5 Results

Figure 4-1 outlines the flow of papers, including reasons for exclusion. From 3209 citations, 28 studies were included.

Figure 4-1 PRISMA Flow Diagram



Characteristics of studies

The study characteristics are summarised in Table 4-2. There were 16 RCTs, 1 controlled trial with matched participants and 10 non-controlled trials using pre-post testing of the cohort. The remaining study [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 paper, as the United States arm [21] was included independently. All studies were published since 2000 except one (1995 [22]). The studies were undertaken in 9 countries, predominantly in North America (USA [n=16], Canada [n=4]). Study inclusion/exclusion criteria often included: more than 5 months post-stroke [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]. Eight studies required participants to pass a treadmill [n=6] or cycle [n=2] screening test.

The 28 studies enrolled 1090 participants [males=337 (30.9%), females=191 (17.5%), not specified=552 (52.6%)] and reported results on 920 participants [males=437 (47.5%), females=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. Main reasons for attrition included: medical conditions unrelated to study (39.9%), “non-compliance” (22.1%), “medical reason or non-compliance” (14.1%), transport/scheduling issues (6.1%), another stroke (3.1%), and a fall with hip fracture (3.1%).

Table 4-2 Characteristics of the studies grouped by training type, then listed by time since stroke

Study Year Country	Study design <i>Location</i> Group or Individual?	Inclusion/ exclusion criteria	Age (SD) years	Time since stroke (SD)	Number of Participants (male: female)	Attrition
Aerobic						
Tang et al [23] 2009 Canada	Matched controlled <i>Inpt</i> nr- appears indiv	<3 mths post stroke; walk > 5m independently; CMSA leg score 3-6 NO: CI ACSMG; msk impairments or pain to prevent pedalling	I= 64.7 (3.6) C= 65.7 (2.3)	Days: I= 19.1 (3.8), C= 14.9 (2.3)	Enrolled= 57 Matched pairs reported= 18 I= 18 (11:7), C= 18 (11:7)	I= 0 (0%) C= 0 (0%)
Murakami et al [24] 2002 Japan	Non-controlled pre-post measures <i>Inpt rehab</i> nr- appears indiv	Mild to mod hemiparesis ,ambulatory, independent indoors- walking or wheelchair	55 (13)	Days 76 (65)	Results= 29 (23:6)	nr
Calmels et al [25] 2011 France	Non controlled pre- post measures <i>Outpt rehab</i> nr- appears indiv	Age 18-70; >3 mths and <2 yrs post stroke; participating in rehab, independent ambulator; stable clinical and medical management; MMSE>23 NO: uncontrolled respiratory, metabolic, immune, infectious or inflammatory disorders	53.7 (8.6)	Mths 12.1 (7.52)	Enrolled= 16 (13:3) Results= 14 (12:2)	2 (13%)
Janssen et al [26] 2008 Netherlands	RCT <i>Outpt rehab</i> nr- appears indiv	Age 18-70; >5 mths post stroke; leg hemiparesis; able to cycle and to tolerate electrical stimulation with no CI NO: severe cognitive, communication, perceptual, sensory problems preventing understanding or following instructions; other neurological or psychiatric problems so can't follow program	I= 54.2 (10.7) C= 55.3 (10.4)	Mths I= 12.3 (5.4) C= 18.3 (9.9)	Enrolled= 16 Results: I= 6 (3: 3); C= 6 (3:3)	I= 2 (25%) C= 2 (25%)
Moore et al [27] 2010 USA	RCT with cross-over <i>nr- appears centre</i> nr- appears indiv	Hemiparesis >6 mths duration; attending physical therapy, unilateral supratentorial stroke; walk 10m 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	Age: 53 (17)	Mths 18 (11)	Enrolled=30 Results= 20 (14:6)	10 (33%)
Macko et al [28] 2001 USA	Non-controlled pre- post measures <i>Research centre</i> Indiv initial bouts then 1:5 supervised	Age >50; >6 mths post index ischaemic stroke; mild to mod hemiparetic gait; not already doing aerobic X; walk >0.2m/s on treadmill NO: CI ACSMG; HF, unstable angina, PAD, aphasia, dementia, major depression, other medical conditions precluding X	67 (8)	Mths 28 (26)	Enrolled= 23 (19:4) Results= 19	4 (17%)
Macko et al [29] 2005 USA	RCT <i>nr- appears centre</i> nr- appears indiv	Age >45; >6 mths post stroke; hemiparetic gait; pass screening treadmill test NO: HF, unstable angina, PAD, aphasia, dementia, major depression, other medical conditions precluding X	I= 63 (10) C= 64 (8)	Mths I= 35 (29) C= 39 (59)	Enrolled= 61 I= 32 (22: 10), C= 29 (21:8) Results: I= 25, C= 20	I= 7 (22%) C= 9 (31%)
Chu et al [30] 2004 Canada	RCT <i>Community facility</i> Group	>1 yr post first-ever stroke; unilateral weakness; independent walker; medically stable; able pedal to raise HR to 60% max NO: significant msk probs; previous MI	I= 61.9 (9.4) C= 63.4 (8.4)	Yrs I= 3.0 (2.0) C= 4.2 (2.1)	Enrolled: I= 7 (6:1), C= 6 (5:1) Results: I= 7 (6:1), C= 5 (5:0)	I= 0 (0%) C= 1 (17%)

Study Year Country	Study design Location Group or Individual?	Inclusion/ exclusion criteria	Age (SD) years	Time since stroke (SD)	Number of Participants (male: female)	Attrition
Quaney et al [31] 2009 USA	RCT <i>I- laboratory</i> <i>C- home</i> nr- appears indiv	>6 mths post first-ever ischaemic stroke; hemiparesis; MMSE>23 incl correct 3 step command; adequate cardiac function for the protocol; not performing more than 20min aerobic X 3/wk NO: large daily alcohol intake; serious medical, other neurological diseases	I= 64.10 (12.30) C= 58.96 (14.68)	Yrs: I= 4.62 (3.21) C= 5.11 (3.53)	Enrolled= 40 Results: I= 19 (10:9), C= 19 (7:12)	I= 1 (5%) C= 1 (5%)
Lam et al [20] 2010 Germany	Post hoc analysis <i>nr- appears centre</i> nr- unclear	>6 mths post first-ever ischaemic stroke; not already performing aerobic X >20mins/ day and >once/ wk; walk >0.1 m/s on treadmill for >3 mins NO: CI ASCMG; HF; angina; PAD; aphasia; dementia; depression; other neurological diseases	68.6 (SEM= 1.1)	Mths: 58.34 (SEM= 8.77)	Results= 32 (26:6)	nr
Luft et al [21] 2008 USA	RCT <i>nr- appears centre</i> nr- appears indiv	Age >45; ≥6 mths post first ever ischaemic stroke; hemiparetic gait; completed sub-acute rehab; pass screening treadmill test NO: CI to fMRI; HF; angina; PAD; major depression; major aphasia; dementia; major neurological, orthopaedic, medical or chronic pain	I= 63.2 (8.7) C= 63.6 (10.0)	Mths (IQR) I= 62.5 (36.0- 88.9) C= 44.6 (18.8- 70.5)	Enrolled= 113 Results: I= 37 (19:18), C= 43 (14:20)	I= 20 (35%) C= 22 (39%)
Ivey et al [32] 2010 USA	RCT <i>nr- appears centre</i> nr- appears indiv	>6 mths post stroke; completed therapy; mild /mod hemiparetic gait; ambulatory NO: history vascular surgery, vascular disorders of leg or PAD	I= 62 (8) C= 60 (8)	nr	Enrolled: I= 39, C= 41 Results: I= 18:11, C= 11:13	I= 10 (26%) C= 17 (41%)
Ivey et al [33] 2007 USA	RCT <i>Outpt</i> nr- appears indiv	Age >45; >6 mths post ischaemic 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	I= 63 (9) C= 62 (10)	nr	Enrolled= 69 Results: I= 26 (13:13), C= 20 (13:7)	I= 9 (26%) C= 14 (41%)
Potempa et al [22] 1995 USA	RCT <i>Laboratory</i> nr- appears indiv	Age 21-77; >6 mths post stroke; 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	Range= 43-72	nr	Results: I= 19 (8:11), C= 23 (15:8)	nr
Rimmer et al [34] 2009 USA	Pre-post measures, cluster assigned <i>Outpt rehab</i> nr- appears group	Age ≥18; >6 mths post stroke; independent ambulator; MMSE≥ 16	I int= 55.7 (12.6) I dur= 59.4 (7.1) C= 63.7 (9.1)	nr	Enrolled: I int= 18 (6:12), I dur= 19 (8:11), C= 18 (8:10) Results: I int= 14, I dur= 14, C= 13	I int= 4 (22%) I dur= 5 (26%) C= 5 (28%)
Yang et al [35] 2007 Taiwan	Non-controlled pre- post measures <i>nr- appears centre</i> nr- appears indiv	<1 yr post stroke; mild- mod hemiparetic gait; history of chronic artery disease NO: regular aerobic X	64.13 (7.58)	nr	Results= 15 (9:6)	0 (0%)
Mixed						
Teixeira da Cunha Filho et al [36] 2001 USA	RCT <i>Inpt</i> nr- appears indiv	<6 wks post stroke; significant gait deficit (0-2 on FAC); MMSE≥ 21, able to: stand up with/without assistance, take at least 1 step with/ without assistance	I= 57.83 (5.56) C= 59.67 (13.58)	Days I= 15.67 (7.66) C= 14.33 (6.06)	Enrolled: I= 7 (7:0), C= 8 (8:0) Results :I= 6 (6:0), C=6 (6:0)	I= 1 (14%) C= 2 (25%)
Letombe et al [37] 2010 France	RCT <i>Inpt rehab</i> nr- appears indiv	Hemiplegia; stable clinical state; well balance medication treatment NO: memory or cognitive disorders; neglect; unstable brain lesions	I= 59.1 (9.4) C= 60.6 (8.2)	Days I= 20 (2) C= 21 (3)	Results: I= 9 (5:4), C= 9 (6:3)	nr

Study Year Country	Study design Location Group or Individual?	Inclusion/ exclusion criteria	Age (SD) years	Time since stroke (SD)	Number of Participants (male: female)	Attrition
Duncan et al [18] 2003 USA	RCT <i>Home</i> Indiv	Age >50; 30-150 days post stroke with mild-mod deficits; community-dwelling; ambulate 25 feet indep; MMSE>15 NO: serious cardiac conditions; angina; cardiomyopathy; aortic stenosis; PE; O ₂ dependence; severe wt bearing pain	I= 68.5 (9) C= 70.2 (11.4)	Days I= 77.5 (28.7) C= 73.5 (27.1)	Enrolled: I=50, C=50 Results: I= 44 (23:21), C= 48 (27:21)	I= 6 (12%) C= 2 (4%)
Sunnerhagen et al [38] 2007 Sweden	Non-controlled pre-post measures <i>Rehab centre</i> Group	>6 mths post first stroke; hemiparetic; not currently receiving rehab; independent walker 30m with/without walking aid NO: interfering co-morbidities incl heart or joint problems; medically stable	53 (range= 40-68))	Mths 16 (range= 9-35)	Results= 21: 0 VO ₂ results paretic= 17: 0 Non-paretic= 18: 0	nr
Tang et al [39] 2010 Canada	Non-controlled repeated measures <i>Community facility & home</i> Group & indiv	>3 mths post stroke; walk > 10m independently; marked leg spasticity and weakness NO: CI to max X testing; significant pain, msk, cognitive or behavioural issues that would limit testing or program participation	64.5 (12.2)	Mths 30 (27.3)	Enrolled= 43 (30:13) Results=38 Results VO ₂ = 32	2 (5%) before & 3 (7%) after I commenced
Lee et al [19] 2008 Australia	RCT <i>University</i> nr- appears indiv	Age ≥45; ≥3 mths post stroke; unilateral hemiparesis of leg; community-dwelling; self-selected walking speed between 0.15-1.4 m/s NO: CI ACSMG; contractures; severe cognitive deficits	I both= 60.5 (10.6) I PRT= 62.9 (9.3) I cyc= 67.2 (10.6) C= 65.3 (6.0)	Mths I both= 63.2 (40.5) I PRT= 44.2 (63.9) I cyc= 52.4 (2.2) C= 65.8 (42.3)	Enrolled: I both= 13, I PRT= 13, I cyc= 14, C= 12 Results: I both= 12 (8:4), I PRT= 12 (8:4), I cyc= 12 (6:6), C= 12 (6:6)	I both= 1 (8%) I PRT= 1 (8%) I cyc= 2 (14%) C= 0 (0%)
Kluding et al [40] 2011 USA	Non-controlled pre-post measures <i>University</i> nr-appears indiv	>6 mths post stroke; able to sit- stand, walk 30 feet independently; MMSE>22; non-smoker; 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	63.7 (9.1)	Mths 50.4 (37.9)	Enrolled= 11 Results= 9 (5:4)	2 (18%)
Pang et al [41] 2005 Canada	RCT <i>Community facility</i> Group	Age> 50; ≥1 yr or more post single stroke; living at home; walk >10m independently NO: serious cardiac disease; uncontrolled HT; pain on walking; neurological conditions in addition to stroke; other disease that would prevent participation; pedal > 60 rev/min and raise HR to 60% max; MMSE>22	I= 65.8 (9.1) C= 64.7 (8.4)	Years I= 5.2 (5.0) C= 5.1 (3.6)	Enrolled= 63 Results: I= 19:13, C= 18:13	I= 2 (6%) C= 1 (3%)
Michael et al [42] 2009 USA	Non-controlled pre- post measures <i>Community facility & home</i> Group & indiv	Ischaemic stroke; mild- mod hemiparetic gait; walk on treadmill NO: HF; unstable angina; PAD; major depression; major aphasia; dementia; major neurological, orthopaedic, medical or chronic pain that would preclude participation	71 (range= 61-79)	Yrs 7.5 (range 4-20)	Enrolled= 10 (7:3) Results= 7	3 (30%)
Carr et al [43] 2003 USA	RCT <i>Outpt rehab</i> nr- appears indiv	>6 mths post stroke NO: severe cognitive deficits; abnormal heart conditions; uncontrolled BP	Range 30-82	nr	Enrolled= 22:18	nr
Rimmer et al [44] 2000 USA	RCT <i>University</i> Group	Age 30-70; >6 mths post stroke; walk >50 feet independently; reside within 1hr commute of intervention site	Overall= 53.17(8.28)	nr	Enrolled & results=35 (9:26) I= 18, C=17	I= 0 (0%) C= 0 (0%)

Study Year Country	Study design <i>Location</i> Group or Individual?	Inclusion/ exclusion criteria	Age (SD) years	Time since stroke (SD)	Number of Participants (male: female)	Attrition
<i>Knee flexion/extension isokinetic training</i>						
Billinger et al [45] 2010 USA	Non-controlled pre- post measures <i>nr- appears centre</i> nr but appears indiv	> 6 mths post stroke; hemiparesis; sit to stand with minimal assist; walk 10m independently; mild to mod stroke deficits; F/E knee at least 35deg ROM against gravity; no new or severe cardiopulmonary conditions; non-smoker; no diabetes; PVD, current therapy	60.6 (14.5)	Mths 69.1 (82.2)	Enrolled & Results= 12 (5:7)	0 (0%)

ACSMG= American College of Sports Medicine Guidelines BP= blood pressure C= control group CI= contra-indications CMSA= Chedoke-McMasters Stroke Assessment CV= cardiovascular cyc= cycle deg= 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 &PRT int= intensity IQR= interquartile range LL= lower limb max= maximal MI= myocardial Infarction mins= minutes MMSE= Mini-Mental State Examination mod= moderate m/s= metres per second msk= musculoskeletal mths= months nr= not reported O₂= oxygen Outpt= outpatient PAD= peripheral artery disease PE= pulmonary embolism PRT= progressive resistance training RCT= randomised 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 yr=year

Study quality

Criteria ratings for 15 of the 16 included RCTs could be extracted from PEDro ^c (Table 4-3). Letombe et al. [37] 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 subjects or blinded therapists and only three undertook intention-to-treat analysis. Fourteen of the 15 rated studies were similar for VO_{2peak} at baseline for the intervention and control groups. Only four reported sample size calculations.

Participant characteristics

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

Table 4-3 Methods quality scores for RCTs

Study	Scores from PEDRO Database												Additional quality scores	
	1) random allocation	2) concealed allocation	3) baseline comparability	4) blind subjects	5) blind therapists	6) blind assessors	7) adequate follow-up	8) intention-to-treat analysis	9) between-group comparisons	10) point estimates & variability	Score [10]	Eligibility criteria for participants	VO _{2peak} Equivalent at baseline	Power calculation
<u>Aerobic</u>														
Janssen et al [26]	Y	N	Y	N	N	N	N	N	Y	Y	4	Y	Y	N
Moore et al [27]	Y	Y	Y	N	N	N	N	N	Y	Y	5	N	Y	Y
Macko et al [29]	Y	N	Y	N	N	Y	N	N	Y	Y	5	Y	Y	N
Chu et al [30]	Y	N	Y	N	N	Y	Y	N	Y	Y	6	Y	Y	N
Quaney et al [31]	Y	N	Y	N	N	Y	Y	N	Y	Y	6	Y	Y	N
Luft et al [21]	Y	N	Y	N	N	Y	N	N	Y	Y	5	Y	Y*	N
Ivey et al [32]	Y	N	Y	N	N	N	N	N	Y	Y	4	Y	Y	N
Ivey et al [33]	Y	N	Y	N	N	N	N	N	Y	Y	4	Y	Y	N
Potempa et al [22]	Y	N	Y	N	N	N	Y	N	Y	Y	5	N	N*	Y
<u>Mixed</u>														
Teixeira da Cunha Filho et al [36]	Y	N	Y	N	N	N	N	N	Y	Y	4	Y	Y*	N
Duncan et al [18]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	Y	Y	Y
Lee et al [19]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	Y	Y	N
Pang et al [41]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	Y	Y	Y
Carr et al [43]	Y	N	Y	N	N	N	N	N	N	Y	3	N	Y*	N
Rimmer et al [44]	Y	N	Y	N	N	N	N	N	Y	Y	4	Y	Y*	N
Total score for criteria /15	15	4	15	0	0	7	6	3	14	15		12	13	4

Letombe- no scores at time of report Y=Yes N=No *= presumed, based on mean (SD)

Interventions

The testing methods and intervention characteristics are summarised in Table 4-4.

a. Type

Of the 28 studies that met the search criteria, 16 [20-35] used aerobic training [treadmill n=8; cycle n=6; deep water exercise n=1; cycle and recumbent stepper n=1], 11 [18,19,36-44] used a mixed intervention [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.

b. Dose prescribed

All studies reported program length and planned intervention frequency and duration. Program length ranged from 2-3 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 30 to 60 minutes [n=23]. Frequency of sessions ranged from 2 to 5 times/week with most [n=22] training 3 times/week. Planned intensity was reported in 25 studies. Intensity was often calculated from baseline exercise testing and included % heart rate reserve (HRR) [n=11] and % power output [n=6]. Rating of perceived exertion was used as an adjunct measure in five studies. No study provided details regarding instructions to participants about trying to undertake further exercise outside of intervention sessions.

c. Dose delivered

Although training parameters were described, there was limited reporting of whether they were 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 [28,29] reported progressions over 6 months in session duration, %HRR, treadmill velocity and incline. Another study [41] 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 40-50% HRR while other progressed to 70-80%. Only one study reported the proportion of prescribed dose achieved ($63\pm 28\%$) [39].

d. Training settings and individual/ group program

Interventions were undertaken in outpatient rehabilitation settings [n=6], inpatient settings [n=4], university centres [n=6], community centres [n=2], at both a community centre and at home [n=2], and at home. Seven studies did not specify but appeared centre-based. The majority of centre-based interventions appeared to be provided on an individual basis [n=18], 5 were group, 1 was initially individual and progressed to group and 1 was unclear if individual or group. The two programs with centre and home interventions were carried out as a supervised group at the centre 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 [40], while another chose the method they

thought best suited the participant [39]. Twenty-seven of the 28 studies used maximal protocols. The remaining study [31] used a "metabolic stress test" but did not specify the test type or equipment used. Baseline $\text{VO}_{2\text{peak}}$ 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 four studies had mean baseline $\text{VO}_{2\text{peak}}$ measures above 18 mL/kg/min.

Adverse events/ effect maintenance/ participant satisfaction

Adverse events were not reported in 17 studies, 8 reported having no events during testing or training [18,26,28-30,32,40,45] and 3 reported events including: 5 low impact falls by 4 participants with no injuries in the intervention group [41]; 2 temporary musculoskeletal problems managed by altering the exercise regime, with the programs completed without interruption [39]; 2 events during testing, a mild seizure and a drop in blood pressure, and one following an exercise session where the participant became dizzy and mildly incoherent but went on to complete the program [44]. No studies described instructions or a program to continue exercise after the completion of the intervention. Only one study undertook post-program follow-up measures [31]. They showed a statistically significant difference between groups on completion of their 8 week intervention ($p=0.04$) but no difference 8 weeks later at follow-up ($p=0.4$). Only one study reported participant satisfaction [39].

Outcomes

Table 4-4 summarises the $\text{VO}_{2\text{peak}}$ results pre- and post-intervention.

Meta-analyses of RCTs

Twelve of the 16 RCTs contained data suitable for inclusion in the meta-analyses (Figure 4-1). The overall mean difference was 2.27 (95%CI: 1.58,

2.95) mL/kg/min and favoured interventions to improve VO_{2peak} . This equated to a 10-15% improvement from baseline. The studies were statistically homogeneous [$\tau^2=0.00$, $\chi^2= 6.92$, $I^2= 0\%$]. In the subgroup analyses, benefit was observed in aerobic and mixed interventions, which were almost equally effective (Figure 4-2) as were programs ≤ 3 months and >3 months in length (Figure 4-3). The “time since stroke” meta-analysis was not undertaken due to insufficient data for comparison, with only two studies [18,36] conducted within 3 months and the remaining studies more than 12 months post-stroke. 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 ($p<0.05$) increases ranging from 10% [28] to 27.4% [20]. Of the 4 mixed intervention non-RCT trials, 2 showed statistically significant increases, of 9% and 16%, respectively [39,42]. The isokinetic training of the paretic leg intervention produced no significant improvement ($p=0.413$); however this program was only 4 weeks long [45].

Table 4-4 Intervention description, testing mode and results

Studies are- grouped by training type, then listed by time since stroke.

Study	Intervention	Program length	Duration (mins)	Frequency (/ wk)	Intensity	Sessions completed	VO ₂ testing method	Baseline (T1) VO _{2peak} ml/kg/min (SD)	Program end (T2) VO _{2peak} ml/kg/min (SD)	Reported change	Calculated % change from Baseline
Aerobic											
Tang et al [23]	I= conventional inpt rehab + cycle erg C= conventional inpt rehab	4-5 wks	I= 30 cycle additional	Rehab=5 Cycle= 3	50-70% PO at VO _{2peak} RPE 4-6/10	9.2 ± 0.7 sessions= 90.5% ± 1.5 %	Recumbent cycle erg	I= 11.6 (0.7 SEM) C= 11.2 (0.5 SEM)	I= 13.1 (0.9 SEM) C= 12.1 (0.8 SEM)	T1 to T2 I= 12.6 (5.3)% C= 8.3 (4.5)%	I= 13 C= 8 I-C= 5
Murakami et al [24]	Conventional rehab + adapted cycle erg	8 wks	20- cycle	5	30-50% PO from initial test	nr	Cycle erg	16.3 (4.4)	18.1 (5.5)	T1-2 16% ↑, p< 0.005	11
Calmels et al [25]	Interval training adapted cycle erg	2 mths	30	3	40-80% max PO	nr	Cycle erg	18.5 (3.7)	21.3 (6.1)	T1 to T2 14.84% p=0.04	15
Janssen et al [26]	I= cycle erg with ES C= cycle erg	6 wks	25-30	2	nr	nr	Recumbent cycle erg	I= 1.0 (0.3) L/min C= 1.0 (0.3) L/min	I= 1.1 (0.3) L/min C= 1.2 (0.3) L/min	Grp by time GLM= 0.758	I= 10 C= 20 I-C= - 10
Moore et al [27]	I= High intensity stepping on treadmill with to 40% partial BWS C= waiting for intervention	4 wks	nr	2 to 5	80-85% HRmax or Borg RPE = 17	nr	Treadmill	I= 17 (3.2) C= 16 (5.4)	I= 18 (5.4) C= 16 (7.1)	No change Time effects= 0.57	I= 6 C= 0
Macko et al [28]	Treadmill	6 mths	40	3	40→60% HRR	88%	Treadmill	15.2 (3.0)	16.7 (4.3)	10% p<0.05	10
Macko et al [29]	I= treadmill X C= 35 min stretching, 5 min low int walking (30-40% HRR)	6 mths	40	3	40→70% HRR	I= 84% C= 77%	Treadmill	I= 14.9 (0.9 SEM) C= 14.7 (1 SEM)	I= 17.3 (1 SEM) C= 14.9 (1 SEM)	Grp by time p= 0.018	I= 16 C= 1 I-C= 15
Chu et al [30]	I= chest deep water X with a focus on leg X C= arm & hand X- seated	8 wks	60	3	50-80% HRR	I= 157/168 (93%) C= 111/120 (93%)	Cycle erg	I= 17.3 (3.0) C= 17.1 (3.2)	I= 21.2 (2.3) C= 17.6 (4.7)	T1 to T2 I= 22% p<0.05	I= 23 C= 3 I-C= 20
Quaney et al [31]	I= cycle erg C= unsupervised prog of stretching at home	8 wks	45	3	40→70% HRmax	nr	nr	I= 14.76 (4.23) C= 14.67 (5.42)	I= 15.47 (5.13) C= 14.39 (4.99)	Between grp Post: p= 0.04 Retention: p= 0.4	I= 5 C= -2 I-C= 7
Lam et al [20]	Treadmill	3 mths	40	3	40→80% HRR	nr	Treadmill	20.188 (1.167 SEM)	Absolute change= 5.066 (0.720 SEM)	Relative change = 0.274 (0.041 SEM)	25
Luft et al [21]	I= treadmill X C= stretching	6 mths	40	3	40→60% HRR	I= 89% C= 85%	Treadmill	I= 12.9 (†11.5 to 14.3) C= 12.9 (†11.5 to 14.4)	I= 15.2 (†13.5 to 16.8) C= 12.5 (†10.7 to 14.2)	Grp by time p=0.001	I= 18 C= -3 I-C= 21
Ivey et al [32]	I= treadmill X C= supervised active & passive stretching of upper and lower body	6 mths	40	3	40→70% HRR	nr	Treadmill	I= 14.1 (4.0) C= 13.5 (3.6)	I= 16.6 (5.64) C= 12.8 (3.9)	T1 to T2 I=18% C= -4%	I= 18 C= -5 I-C= 23

Study	Intervention	Program length	Duration (mins)	Frequency (/ wk)	Intensity	Sessions completed	VO ₂ testing method	Baseline (T1) VO _{2peak} ml/kg/min (SD)	Program end (T2) VO _{2peak} ml/kg/min (SD)	Reported change	Calculated % change from Baseline
Ivey et al [33]	I= treadmill X C= stretching	6 mths	40	3	40→70% HRR	nr	Treadmill	I= 13.7 (0.9 SEM) C= 14.8(0.9 SEM)	I= 15.7 (1.1 SEM) C= 14.4 (1 SEM)	Grp by time T1-2: p= 0.002	I= 15 C= -3 I-C= 18
Potempa et al [22]	I= cycle erg C= passive ROM X	10wks	30	3	30%→ highest level attainable of max PO	nr	Cycle erg	I= 16.6 (1 SEM) C= 15.1 (1 SEM)	I= 18.8 (1.1 SEM) C= 15.2 (0.9 SEM)	Within I grp: p< 0.0001	I= 13 C= 1 I-C= 12
Rimmer et al [34]	I int & I dur = cycle erg, recumbent stepper C= conventional rehab including gait training, balance, strength, ROM X	14 wks	I int= 30 I dur= 30→60 C= 60 incl 30 gait & balance	All= 3	I int= HRR 40→69% I dur= <50% HRR C= nr	nr however missed sessions were made up the following week	Cycle erg	I int= 15.06 (7.4) I dur= 13.27 (3.6) C= 12.57 (4.2)	I int= 15.71 (7.6) I dur= 14.02 (3.9) C= 12.22 (3.6)	T1 to T2 Within grp I int p= 0.239 I dur p=0.279 C p= 0.467	I int= 4 I dur= 6 C= -3
Yang et al [35]	Treadmill	12 wks	50	3	40→60% HRR	nr	Treadmill	11.24 (2.42)	14.06 (3.19)	T1 to T2 P<0.01	25
<i>Mixed</i>											
Teixeira da Cunha Filho et al [36]	I= regular rehab + treadmill with BWS C= regular rehab	2-3 wks	Usual care +20mins: I= treadmill C= gait training	5	speed ↑ BWS ↓ as able	nr	Cycle erg	I= 8.57 (2.09) C= 8.02 (2.05)	I= 11.55 (2.76) C= 8.12 (2.3)	Between grp: T1 to T2 p= 0.039	I= 35 C= 1 I-C= 34
Letombe et al [37]	I= usual inpt care + semi-recumbent cycle, stretching, additional physical X incl treadmill, stepper, balance, isokinetic strength, UL, games C= usual inpt care	5 wks	I= 40-60 mins additional	4	70-80% PO	nr	1 legged test on cycle erg	I= 11.13 (4.6) C= nr (graph only)	I= 19.44 (4.59) C= = nr (graph only)	T1 to T2 I= 20.33% p <0.05 C= 8%	I= 20% C= 8% I-C= 12%
Duncan et al [18]	I= endurance on cycle, strength , balance, UL functional use, ROM C= usual home service as prescribed by physician & visit by research staff every 2 wks	12-14 wks	I= 90mins with up to 30mins on bike	3	nr	I= 33.4 ± 2.3 C= 8.7 (5.3) PT, 10.4 (7.1) OT	Cycle erg	I= 11.7 (3.3) C= 11.2 (2.9)	nr	T1 to T2 ml/kg/min I= 1.05 (0.23 SE) C= 0.06 (0.23 SE) Between grp= 0.99 (0.33 SE) p< 0.01	I= 9 C= 0 I-C= 9
Sunnerhagen et al [38]	PRT- 5 station circuit incl 2 functional X stations	8 wks	45	3	nr	nr	Cycle erg with 1 leg tested at a time	Paretic= 12.4 (4.7) Non-paretic= 13.9 (4.3)	Paretic= 15.7 (7.2) Non-paretic= 15.8 (6.0)	T1 to T2 Paretic: p< 0.01 Non-paretic: ns	Paretic= 27 Non= 14 Difference= 13

Study	Intervention	Program length	Duration (mins)	Frequency (/ wk)	Intensity	Sessions completed	VO ₂ testing method	Baseline (T1) VO _{2peak} ml/kg/min (SD)	Program end (T2) VO _{2peak} ml/kg/min (SD)	Reported change	Calculated % change from Baseline
Tang et al [39]	Centre 90min incl education, aerobic and resistance training. Aerobic included walking, recumbent and upright bike Home: aerobic & resistance training	6 mths	30-60 mins aerobic	5x: 1@ centre 4@ home	60-80% HRR, 11-14/ 20 RPE	83.5 ± 11.5 % classes attended Median 4 aerobic session/ wk	36- recumbent cycle erg, 6- cycle erg, 1 treadmill	-3/12= 13.6 (4.1) Baseline= 14.8 (4.8)	16.2 (5.1)	-3/12 to baseline p= 0.301 Baseline to 6/12 p= 0.046	9
Lee et al [19]	I= both= recumbent cycle and PRT I= cyc= recumbent cycle, sham PRT I= PRT= sham recumbent cycle, PRT C= sham recumbent cycle & sham PRT	10-12 wks	60 min in total 30 min ea cycle and PRT	3	HR at 50→70% VO _{2peak} RPE	nr	Cycle erg	I both 14.4 (3.1) I cyc= 13.0(4.5) I PRT= 14.0 (3.3) C= 13.5 (3.5)	I both= 16.6 (5.2) I cyc= 14.5 (3.9) I PRT= 13.5 (3.8) C= 12.7 (4.3)	Compare to C- T1 to T2 ml/kg/min (range) I both= 3 (0.3-5.6) p=0.03, I cyc= 2.5 (1.9- 4.9) p= 0.002, I PRT= 0.5 (-1.0-2) p=0.51	I both= 15 I cyc= 12 I PRT= -4 C= -6
Kluding et al [40]	TBRS & lower limb muscle strengthening	12 wks	60 (30 mins aerobic)	3	HR at 50% peak VO ₂ , 11-14/20 RPE	Minimum 75%	TBRS & cycle- highest value reported	13.9 (4.5)	15.2 (4.3)	1.4 (2.4) p= 0.06	9
Pang et al [41]	I= fitness & mobility X prog C= seated upper extremity prog	19 wks	60	3	40→80% HRR	I= 81.4% C= 80.4 %	Cycle erg	I= 22.5 (5.2) C= 21.5 (4.3)	I= 24.5 (5.3) C= 21.8 (4.5)	T1 to T2 I= 2.0 (0.8-3.1) C= 0.3 (-0.08- 1.4) p=0.03	I= 9 C= 1 I-C= 8
Michael et al [42]	Progressive adaptive physical activity model: functional mobility, sit to stand, trunk stability, balance	6 mths	60	3 at centre, home prog on alternate days	nr	73%	Treadmill	15.3 (4.1)	17.5 (4.6)	15% p= 0.03	14
Carr et al [43]	I=upper & lower limb body erg, flexibility plus 8 strength training exercises C= upper and lower limb body erg, flexibility	16 wks	20→40 aerobic	3	C= 40→70% peak PO	nr	Recumbent cycle erg	I= 15.1 (5.1) C= 11.9 (4.0)	I= 17.9(5.6) C= 12.3 (3.7)	I= significance value nr C= ns	I= 19 C= 3 I-C= 16
Rimmer et al [44]	I= aerobic on own choice of equipment, strength/ endurance/ flexibility C= lag control for intervention	12 wks	60 (30 CV endur)	3	Target rate based on value when RER= 1	I= 93%	Cycle erg	I= 13.34 (4.22) C= 14.13 (2.96)	I= 14.43 (4.03) C= 12.69 (2.61)	nr- graph only	I= 8 C= -10 I-C= 18

Study	Intervention	Program length	Duration (mins)	Frequency (/ wk)	Intensity	Sessions completed	VO ₂ testing method	Baseline (T1) VO _{2peak} ml/kg/min (SD)	Program end (T2) VO _{2peak} ml/kg/min (SD)	Reported change	Calculated % change from Baseline
<i>Knee flexion/extension isokinetic training</i>											
Billinger et al [45]	Isokinetic knee F/E on Biodex for paretic limb	4 wks	60-90	3	60-70% HR max	7 completed 12/12, 5 completed 11/12 sessions	TBRS	19.3 (6.9)	19.0 (7.5)	p=0.413	-2

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 &PRT Inpt= inpatient int= intensity L/min= litres/minute max= maximal mins= minutes mths= months ns= non-significant 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 VO_{2peak}= peak oxygen consumption wks= weeks X = exercise "x% →y%"= progressed from x% to y% "x% -y%"= ranged from x% to y% @= at ↓= decrease ↑= increase †= range

Figure 4-2 Intervention type

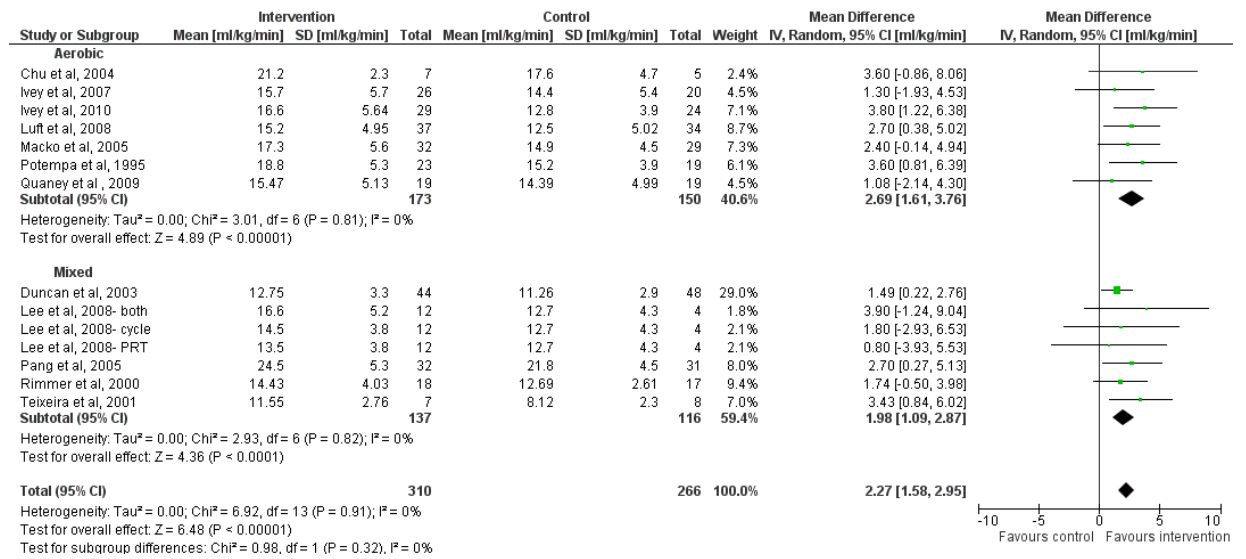
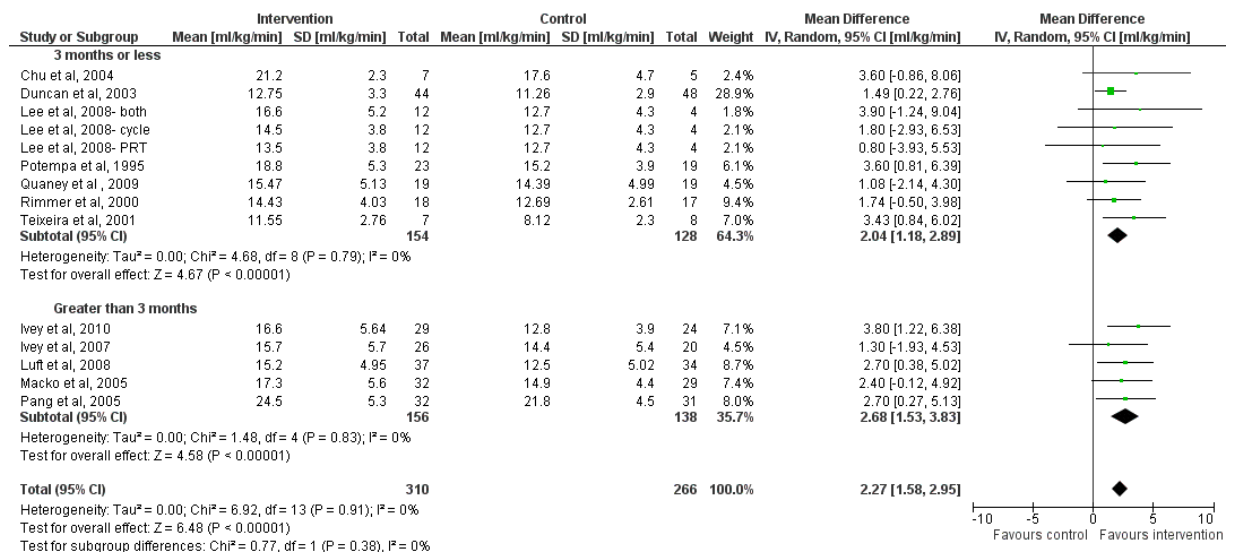


Figure 4-3 Program length



4.6 Discussion

Significant benefit with cardiorespiratory training

This review highlights that interventions that are aerobic or have an aerobic component can improve fitness by approximately 10-15%, even with modest doses of exercise. The observed improvement of 2.27 ml/kg/min (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 (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 resulted in improvements of approximately 10-15% VO_{2peak} . This finding is similar to the review by Shephard of aerobic training responses in the healthy elderly where gains in VO_{2peak} with training ranged from 12.9% in short term (8-10 weeks), 14.1% in medium term (12-18 weeks) and 16.9% for longer term (24-52 weeks) programs [8]. Cardiorespiratory training appears to be beneficial for people at any time, from weeks to many years, post-stroke. The results also appear to indicate a key factor in improving cardiorespiratory fitness is to incorporate aerobic activity, with the exact intervention appearing 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 $\text{VO}_{2\text{peak}}$ levels in all but 4 studies were below the 18mL/kg/min suggested as being a minimum required for independent living [8] and all studies showing baseline values well below normative data for an elderly population (29 ± 7.3 and 27 ± 5.8 mL/kg/min for healthy males and females, aged 70-79 years, respectively [47]). This is despite the studies typically including highly selected participants: ambulatory with limited co-morbidities. It is very likely 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 recognised 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 post-stroke.

Exercise dose, intensity and timing

“Dose” of exercise is governed by frequency (per week), duration (per session) and intensity (and for how long this is maintained within a session). Data in healthy populations indicate that exercise intensity is a key variable to maintain and improve cardiorespiratory fitness [46]. One study in our review compared two trials with similar interventions and found higher intensity was the only training variable that predicted better gains in cardiorespiratory fitness [20]. However, as highlighted by Pang et al. [41], the ability of participants to increase intensity varies, with the maximum achieved after 19 weeks of training ranging from unchanged from the initial 40-50% HRR up to 70-80% HRR. This intensity was maintained for 15 minutes compared to the recommended 30

minutes. Studies in the healthy elderly have reported greater improvements with higher intensity [8]; however lower intensities may be effective in untrained populations [48]. 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 one calculated the proportion of prescribed dose achieved ($63\pm 28\%$) [39].

Timing after stroke may also be a key factor, particularly in any contribution cardiorespiratory fitness training may make to functional recovery. Surprisingly, only five studies were within three months after stroke. This should be a key time for preventing cardiorespiratory deconditioning and promoting brain reorganisation, both of which require meaningful and challenging physical activity [49]. Inpatient environments have the potential to routinely incorporate cardiorespiratory fitness training into their programs; however, they are consistently identified as settings deprived of activity post-stroke [50,51]. One systematic review indicated that only 32.8 minutes (60%) of inpatient physiotherapy sessions was spent being active [52]. 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 [53,54].

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 centre programs [n=4]. A number of interventions appeared quite resource-intensive; 19 used one-to-one supervision, and 14 were greater than 3 months (Table 4-4). A review of physical activity programs for older adults identified health benefits and improved function were gained through both centre and home-based programs [55]. The home-based programs had better adherence, particularly in the long term [55]. Redesign of services to include cardiorespiratory fitness training within existing budgets may be more likely to be generalisable, rather than relying on service enhancements. One study redesigned their inpatient program to compare 20 minutes of treadmill training to the usual 20 minutes of standard gait training [36]. The therapy time was unchanged. Two studies used a combined centre and home program which may be a feasible way to assist stroke survivors be active on most days of the week [39,42]. Redesign may occur through the use of groups including circuit classes, as inpatient, outpatient and community-based programs [56]. Participation in groups has the advantage of increased ratio of group leader to participants [56] and the added benefits of social interaction and peer motivation [57].

Comparison to 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 interventions were predominantly highly supervised, centre-based programs trialled in cognitively-intact participants with mild to moderate disease [58]. Reviews of the effect of exercise-based rehabilitation on coronary heart disease [59] and heart failure [60] highlighted the 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 [60]. However in this population it does not reduce all-cause mortality nor could a minimum dose of exercise be recommended due to the variation in programs [60]. Following exercise there was no reduction in recurrent myocardial infarction or revascularisation 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 homogenous indicating 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 four 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 “non-compliance”, though this term was not explained. Studies were conducted in people with

mild-moderate deficits therefore there is limited generalisability of the results to those with greater stroke deficits or multiple co-morbidities.

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 $\text{VO}_{2\text{peak}}$ is measured in mL/kg/min it is influenced by change in weight, which may occur over time. Future studies should report both in litres/minute 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 [60]. 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 to 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 [58,59]. 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 centre-based, supervised treatment sessions rather than assisting participants adopt 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 generalisable interventions that are able to be delivered within existing budgets. Investigation is also required into strategies to engender long-term behaviour change and maintain improvements post-program. Larger-scale studies including outcomes for functional improvement, recurrent stroke, cardiovascular events, death or dependence, would help to confirm likely additional benefits of exercise post-stroke, and enhance clinical uptake. Studies are required to determine whether improved levels of cardiorespiratory fitness can also be obtained in those with greater impairments post-stroke, for older and younger patients, and those with significant co-morbidities as well as the importance of timing of the intervention post-stroke.

4.7 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 %VO_{2peak} 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 suggests that such training programs should be incorporated into routine post-stroke care.

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Conflict of Interest

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Resources

- Excel 2007, Microsoft Corporation
- Review Manager (RevMan) [Computer program]. Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011
- PEDro (Physiotherapy Evidence Database) <http://www.pedro.org.au/>

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CHAPTER 5: EVALUATION OF THREE MEASURES OF CARDIORESPIRATORY FITNESS IN STROKE SURVIVORS

5.1 Details

Authors and affiliations

Ashlee Dunn BExSpSci(Hon)^{a,b}, Dianne L Marsden MAppMgnt(Health)^{a,b,c},

Daniel Barker BMath^a, Paulette Van Vliet PhD^{a,b}, Neil J Spratt FRACP, PhD^{a,b,c}

Robin Callister PhD^{a,b}

a) University of Newcastle, Callaghan, New South Wales, Australia

b) Hunter Medical Research Institute, New Lambton Heights, New South
Wales, Australia

c) Hunter New England Local Health District, New Lambton Heights, New
South Wales, Australia

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Key words

Stroke, cardiopulmonary exercise test, six-minute walk, shuttle walk, cycle ergometer, graded exercise test, aerobic fitness, oxygen consumption, rehabilitation, assessment

Abbreviations

6MWT: Six-Minute Walk Test

CRF: cardiorespiratory fitness

GXT: graded exercise test

HR: heart rate

HRR: heart rate reserve

RER: respiratory exchange ratio

SWT: Shuttle Walk Test

VO_{2peak}: peak oxygen consumption

VE: minute ventilation

Clinical Trials Registration

ANZCTR Trial ID: ACTRN12614000134628 “How Fit is the Stroke Survivor?”

5.2 Abstract

Measuring cardiorespiratory fitness (CRF) in the stroke population is challenging. Currently, the suggested 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 in VO_{2peak} among the three tests (range: 17.08 - 18.09 mL.kg⁻¹.min⁻¹). HR_{peak} was significantly lower during the 6MWT ($p=0.005$). 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 proxies for change in fitness over time.

5.3 Introduction

Following stroke there are multiple biological, physical and psychological consequences that reinforce a sedentary lifestyle and contribute to low cardiorespiratory fitness (CRF) [1] [1]. It has been estimated that 77% of Australians who have suffered a stroke are sedentary or have low levels of physical activity [2]. Increasing exercise and improving CRF levels are important goals for post-stroke management, and can assist in improving performance of activities of daily living, community integration [3,4], and quality of life. Accurate and clinically feasible methods to assess CRF levels in stroke survivors are important to determine an individual's exercise capacity, and are useful in guiding prescription of an appropriate exercise regime. The gold standard for assessing CRF in healthy individuals is a graded exercise test (GXT) using gas analysis to assess peak oxygen consumption (VO_{2peak}) [5]. The American Stroke Association Scientific Statement recommends a GXT using an ergometer such as a treadmill or cycle for assessing CRF in stroke survivors [6]. However, due to the complex myriad of effects after stroke, maximal ergometer testing is not always appropriate for stroke survivors. Under these circumstances, 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 [7], and is often used as an outcome measure in stroke rehabilitation due to familiarity, functionality, simplicity and low cost. 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) [8] is commonly used in stroke [9], requiring the individual to walk back and forth a fixed-length walkway (standard 30m) to cover as much distance as possible in a

six-minute time frame. The Shuttle Walk Test (SWT) developed by Singh et al. [10] is an externally paced, graded walking test on a 10m course. Unlike the 6MWT, the SWT reflects a GXT by incrementally increasing the speed the individual must walk to keep in time with audio signals. To date, the SWT has not been evaluated in stroke survivors as a possible test of CRF. The aims of this study were to 1) evaluate the cardiorespiratory and performance responses during these three tests and 2) assess the feasibility of using the SWT test in stroke survivors compared to the 6MWT and cycle GXT.

5.4 Methods

Participants

Participants were assessed at baseline as part of an ongoing controlled exercise intervention study [How Fit is the Stroke Survivor? (*HowFITSS?*) trial ANZCTR Trial ID: ACTRN12614000134628]. Recruitment of stroke survivors was undertaken 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).

Procedures

Following feedback from a small pilot sample of stroke survivors, it was noted that the cycle GXT was particularly fatiguing on the legs. Testing order was therefore kept consistent between participants, performing the cycle GXT last to minimise the effects of leg fatigue associated with cycling. To reflect rehabilitation 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 co-morbidities were determined from medical history provided by the GP or by interview.

Cardiorespiratory Measurement

A portable open-circuit spirometry system (K4b², COSMED^a, 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 (VO_2), minute ventilation (VE) and the respiratory exchange ratio (RER) were recorded and averaged over 30s epochs. The $\text{VO}_{2\text{peak}}$ and HR_{peak} data were extracted as the highest average 30s epoch values recorded during the 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^a, Italy). This was used to derive heart rate (HR) data.

Six-Minute Walk Test

The 6MWT was conducted in accordance with the American Thoracic Society Guidelines (2002) [8] 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 restrictions [9]. 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. It has been reported that wearing the Cosmed K4b² portable system does not interfere with the reliability of the 6MWT in stroke survivors [11].

Incremental Shuttle Walk Test

As originally reported by Singh (1992) [10], 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^b, Glenfield Hospital NHS Trust, Leicester, UK). Participants were instructed not to jog or run. The test begins at $0.50\text{m}\cdot\text{s}^{-1}$ and increases by $0.17\text{m}\cdot\text{s}^{-1}$ every minute. Following 12 levels, the final speed required is $2.37\text{m}\cdot\text{s}^{-1}$. 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. No verbal feedback or encouragement was given during the test.

Upright Cycle Graded Exercise Test

An upright cycle ergometer is currently recommended and the most common modality for exercise testing in the stroke literature [12]. The majority of the sample population were not suitable for testing on a treadmill due to unfamiliarity with the activity, balance issues and the absence of a body weight support safety harness system in the laboratory. A submaximal cycle GXT was used to reflect the safety precaution often employed in a clinical setting when a doctor is not present. The protocol began with the participant pedalling on an upright cycle (818E, Monark^c, Sweden) at a rate of 50 or 60rpm. An initial workload of 0W for one minute was used, followed by increases in resistance of 25W increments every minute until test termination. Once the test was stopped, participants were encouraged to complete a cool-down on the cycle. Prior to testing, the Karvonen Formula [13] was used to calculate 85% of heart rate reserve ($85\%HRR = [(220 - \text{age}) - \text{resting HR}] \times 0.85 + \text{resting HR}$). This was then 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 [14].

Outcome measures

The primary cardiorespiratory outcome measure was peak oxygen consumption ($VO_{2\text{peak}}$). Secondary cardiorespiratory outcomes included peak heart rate (HR_{peak}), peak minute ventilation (VE_{peak}) and peak respiratory exchange ratio (RER). Performance measures were also 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. Feasibility was assessed by the number of participants who could complete each test.

Statistical analysis

Data were analysed 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, with the SWT used as the reference group. 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) assumption [15]. The model 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 $\pm$ standard deviation unless otherwise stated. The level of association between the VO_{2peak} and outcome measure achieved, and VO_{2peak} and HR_{peak} on each test were assessed using the correlation spread sheet provided by Hopkins (2001) [16]. Correlations were interpreted as reported by Eng et al [17] 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.

5.5 Results

Characteristics of the 23 participants (n=11 males) are summarized in Table 5-

1. 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 affect their walking ability, but precluded them from cycling without pain. One did not

perform the SWT due to balance issues when turning, identified during the 6MWT. 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 included 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]. Participants achieved an average of 68%, 75% and 76% of predicted maximal heart rate (calculated as $206.9 - (0.67 \times \text{age})$) during the 6MWT, SWT and cycle GXT respectively. No significant adverse events occurred during any of the testing sessions.

Table 5-1 Participant characteristics

Characteristics	Value
Age (years)	61.5 ± 18.4 (23.2-84.3)
Gender, n (%)	
Male	11 (48)
Female	12 (52)
Months post-stroke	3.7 ± 3.2 (1-16)
Body Mass Index (kg·m ²)	27.7 ± 5.9 (20.4-43.3)
Type of stroke, n (%)	
Ischemic	23 (100)
Co-morbidities, n (%)	
Atrial fibrillation	6 (26)
Arthritis	4 (17)
COPD	1 (4)
CVD	2 (9)
Diabetes	4 (17)
PVD	1 (4)
Medications, n (%)	
β-blockers	8 (35)
ACE inhibitors	5 (22)
Functional Ambulatory Category, n (%)	
5	22 (96)
4	1 (4)
Modified Rankin Score, n (%)	
0	2 (9)
1	16 (70)
2	4 (17)
3	1 (4)
<i>Abbreviations: n: number, SD: standard deviation, ACE: angiotensin-converting enzyme</i>	

The cardiorespiratory responses to the 6MWT, SWT and cycle GXT are shown in Table 5-2. There were no significant differences between relative $\text{VO}_{2\text{peak}}$ during the 6MWT, SWT, and cycle GXT. The response pattern during the three tests is displayed in Figure 5-1. Compared to the SWT, the respiratory exchange ratio was significantly higher during the cycle GXT ($p=0.003$) and HR was significantly lower during the 6MWT ($p=0.005$). Distance walked during the 6MWT was $460\pm115\text{m}$ and ranged from 202m to 623m, with males walking $461\pm134\text{m}$ (67% of predicted distance [18]) and females walking $456\pm100\text{m}$ (78% of predicted distance [18]). The average number of shuttles and distance achieved on the SWT were 40 ± 18 shuttles and $400\pm180\text{m}$ respectively, with distances ranging from 120 – 660m. The average power output reached on the cycle GXT was $115\pm33\text{W}$, 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. Correlations between $\text{VO}_{2\text{peak}}$ and outcome measure were high in all three tests (6MWT $\text{VO}_{2\text{peak}}$ and distance: $r=0.78$, SWT $\text{VO}_{2\text{peak}}$ and shuttles: $r=0.73$, cycle GXT $\text{VO}_{2\text{peak}}$ and workload: $r=0.77$). There were low correlations between HR_{peak} and $\text{VO}_{2\text{peak}}$ for each test (6MWT: $r=0.28$, SWT $r=0.44$, cycle GXT: $r=0.30$). In those with lower $\text{VO}_{2\text{peak}}$ values, there was very little difference in the values obtained on the different tests. In those with $\text{VO}_{2\text{peak}}$ values greater than $20 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ values on the SWT and cycle GXT were usually higher than those on the 6MWT.

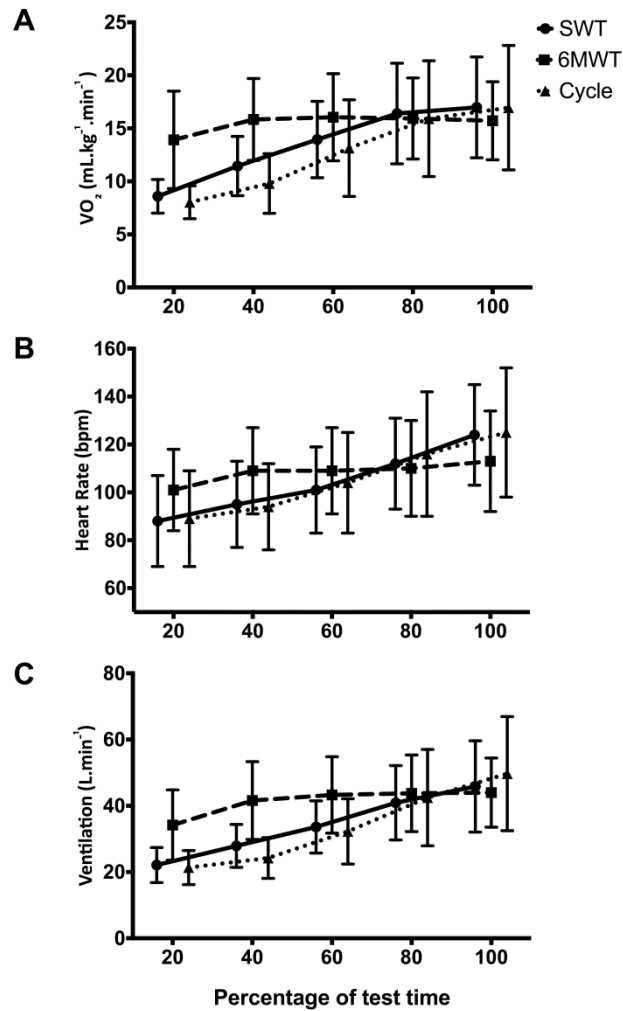
Table 5-2 Peak cardiorespiratory and performance responses to the SWT, 6MWT and cycle GXT

Variable	6MWT	SWT	Cycle GXT	SWT v 6MWT	SWT v cycle	SWT v 6MWT		SWT v cycle		6MWT v cycle	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	P-Value	P-Value	ICC	90%CI	ICC	90%CI	ICC	90%CI
VO _{2peak} (mL·kg ⁻¹ ·min ⁻¹)	17.08 $\pm$ 4.29	18.09 $\pm$ 5.43	17.82 $\pm$ 6.17	0.182	0.250	0.87 ^b	0.75, 0.94	0.83 ^b	0.64, 0.92	0.83 ^b	0.65, 0.92
RER	0.99 $\pm$ 0.12	0.97 $\pm$ 0.14	1.06 $\pm$ 0.14	0.515	0.003 ^a	0.68	0.42, 0.83	0.45	0.08, 0.72	0.22	-0.17, 0.56
VE _{peak} (L·min ⁻¹)	46 $\pm$ 11	47 $\pm$ 15	50 $\pm$ 19	0.579	0.578	0.86 ^b	0.72, 0.93	0.68	0.39, 0.84	0.57	0.24, 0.78
HR _{peak} (beats·min ⁻¹)	115 $\pm$ 20	124 $\pm$ 21	128 $\pm$ 25	0.005 ^a	0.564	0.67	0.39, 0.84	0.57	0.23, 0.78	0.74 ^b	0.50, 0.88
Peak performance	460 $\pm$ 115m	40 $\pm$ 18 shuttles	115 $\pm$ 33W			0.93 ^b	0.86, 0.97	0.62	0.29, 0.82	0.57	0.24, 0.79
VO _{2peak} and peak performance correlation	0.78 ^b	0.73 ^b	0.77 ^b								
VO _{2peak} and HR _{peak} correlation	0.28	0.44	0.30								

^asignificant difference $p < 0.05$ compared to the cycle GXT; ^bhigh correlation $r > 0.70$

Abbreviations: 6MWT: Six-Minute Walk Test, 90%CI: 90 percent confidence interval, GXT: graded exercise test, HR_{peak}: peak heart rate, ICC: intraclass correlation coefficient, RER: respiratory exchange ratio, SD: standard deviation, SWT: Shuttle Walk Test, VE_{peak}: peak ventilation, VO_{2peak}: peak oxygen consumption, W: Watts

Figure 5-1 Mean VO_2 (A), HR (B), VE (C) in each 20% increment of test time for the SWT, 6MWT and cycle GXT



5.6 Discussion

Our study aimed to evaluate the 6MWT, SWT and cycle GXT as measures of CRF, and to assess the feasibility of each in the stroke population. The findings indicate that all three tests are feasible in ambulatory stroke survivors, although the cycle GXT was the least practical due to lower limb arthritic pain. The current study shows that the walking tests were well tolerated, and elicited statistically similar VO_{2peak} results to the cycle GXT. The findings demonstrate that the performance measures may be useful as proxies for VO_{2peak} in any setting where VO_2 monitoring is not practical. The SWT is a good indicator of CRF and functional capacity in stroke survivors.

This is the first study to directly measure oxygen consumption during the 6MWT, SWT and cycle GXT in stroke survivors. There were low associations between VO_{2peak} and HR_{peak} , suggesting that heart rate may have limitations as a criterion for peak exercise intensity in stroke survivors, and may be due to medications, such as beta-blockers (n=8 participants) or ACE inhibitors (n=5 participants), that are prevalent in the stroke population. High correlations were found between VO_{2peak} and performance measure in all three tests, demonstrating that the 6MWT, SWT and cycle GXT are valid tools for predicting VO_{2peak} in stroke survivors. Due to the equipment expenses, time, and need for trained personnel associated with assessing oxygen consumption, the use of a proxy measure of VO_{2peak} is favourable in the clinical setting. The relationship between VO_{2peak} 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 ($r=0.67$) [19] in patients with operable lung cancer, to very high ($r=0.95$) [20] in adult patients with cystic fibrosis. Most of

these correlations are slightly higher than reported in the current study, possibly because these populations typically do not result in physical disability similar to that observed as a result of stroke.

When comparing the other physiological variables, a significantly lower HR was recorded during the 6MWT possibly because self-paced tests are typically not limited by cardiovascular factors and are technically submaximal in nature [21]. In our study all three test modalities resulted in mean respiratory exchange ratios <1.1 , indicating a submaximal effort was achieved [22]. The respiratory exchange ratio was significantly higher during the cycle GXT, which is most likely attributable to the reliance on the leg muscles to perform the work.

Interestingly, almost 40% of participants terminated the cycle GXT prematurely due to leg fatigue or lower limb pain, indicating that cycling may not be appropriate due to unfamiliarity to 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 [12], and is often available in clinical settings.

The SWT has only recently been considered and suggested for investigation in stroke survivors [23] and has potential for use as a test of CRF. Despite a range of cognitive abilities, all participants understood the SWT and were able to follow instructions given. Only one previous study has investigated the use of the SWT in stroke [24]. Unlike the current study, Bloemendaal et al. [24] used a modified version of the protocol as described by Verschuren et al. [25], 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 [17,26-31]. The majority examined correlations between cycle GXT VO_{2peak} and 6MWT distance, with no VO_2 measures during the 6MWT. Similarly to our study, Salbach et al. [23] used the Cosmed K4b² portable metabolic system to measure the cardiorespiratory response during the 6MWT and a cycle GXT. They reported a significantly higher VO_{2peak} during the cycle GXT ($13.8 \pm 3.3 \text{ mL.kg.min}^{-1}$) than the 6MWT ($11.8 \pm 3.7 \text{ mL.kg.min}^{-1}$, $p=0.032$). The cycle protocol used in the study by Salbach had less intense progressions (5, 10 or 15W increments) compared to the current study (25W increments). They reported VO_{2peak} , HR_{peak} and VE_{peak} well below the values obtained in our study, which may suggest that our sample population were a less disabled group following their stroke. 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 [9], the SWT is much less common. It has been studied extensively in cardiac and respiratory populations [32], for whom the test was designed. In other disease populations, the SWT has been used as a tool for exercise prescription [33], for the assessment of ambulatory oxygen [34], for detecting changes in exercise performance following pharmacological bronchodilation [35], as a valid measure of exercise capacity in adults with cystic fibrosis [20], after coronary bypass surgery [36] and in chronic heart failure patients [37-39]. A review by Parreira et al. [32] 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.

Study limitations

This study is the first to directly measure and evaluate cardiorespiratory variables during the 6MWT, SWT and cycle GXT in stroke survivors. However, 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. The use of a 20m 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 30m walkway. 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 (MAR) assumption [15]. Peak values for the GXT may be underestimated for the 5 participants who were stopped from continuing the exercise test when they reached 85% of age-predicted HRR. The sample of stroke survivors in this study had relatively little disability, and does not account for more disabled stroke patients. Therefore, these results are unlikely to be relevant to non-ambulant stroke patients.

5.7 Conclusion

Our results indicate that all three tests are good indicators of CRF, and are well tolerated in independently ambulant stroke survivors. The cycle GXT was unable to be performed by participants with lower limb conditions not associated with stroke. Peak cardiorespiratory responses were similar between the walking tests and the cycle GXT, and strong relationships were found between VO_{2peak} and performance measures. These findings suggest that each test is a good indicator of CRF in stroke survivors. The performance measures could be used as indicators of fitness in clinical settings. The SWT was previously largely unexplored in the stroke population, and has many features that make it suitable for use for clinical testing.

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138a Louisa Road, Birchgrove NSW 2041 AUSTRALIA

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Conflict of interest

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

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CHAPTER 6: APPLYING INTERVAL TRAINING PRINCIPLES TO TASK-SPECIFIC AND ERGOMETER WORKSTATIONS ENABLES STROKE SURVIVORS TO EXERCISE AT AN INTENSITY SUFFICIENT TO IMPROVE CARDIORESPIRATORY FITNESS

6.1 Details

Authors and affiliations

Dianne Lesley Marsden ^{1 2 3}, Ashlee Dunn ^{1 3}, Robin Callister ^{1 3}, Patrick McElduff ¹, Christopher Royce Levi ^{1 2 3}, Neil James Spratt ^{1 2 3}

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

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6.2 Abstract

Purpose: To examine the exercise intensity (level and patterns) achieved by stroke survivors when performing task-specific and ergometer activities using an interval training approach.

Methods: Thirteen independently ambulant participants within one year of most recent stroke were assessed (females=54%; median age=65.6 years, IQR=23.9). Participants undertook task-specific and ergometer activities via 5-minute workstations while wearing a portable metabolic system. Physical activity was accumulated using an individually-tailored circuit of up to seven workstations. The average oxygen consumption (VO_2) during each 30-second epoch was recorded. $\text{VO}_2 \geq 10.5 \text{ mL/kg/min}$ was categorised as $\geq$ moderate intensity.

Results: Circuits were individualised using nine task-specific (eg walking, stairs, balance) and three ergometer (upright cycle, rower, treadmill) workstations. Participants exercised at moderate or higher intensity for the majority of the duration of each workstation [task-specific: 369/472 epochs (78%), ergometer: 170/204 epochs (83%)]. All participants completed at least 11 minutes physical activity per exercise session. No serious adverse events occurred.

Conclusions: Applying interval training principles to a circuit of task-specific and ergometer workstations enabled ambulant participants to exercise at an intensity and for a duration that can improve cardiorespiratory fitness. The training approach appears feasible, safe and a promising way to incorporate both cardiorespiratory fitness and functional training into post-stroke management.

6.3 Introduction

It is well established that stroke survivors have very low levels of cardiorespiratory fitness (CRF) [1,2]. Consequently, undertaking everyday activities can require them to operate at or near their maximum CRF capacity [3]. CRF levels early after stroke appear to be predictive of functional recovery [4].

Engaging in exercise training after stroke has the potential to improve CRF. Even modest amounts of regular aerobic exercise can improve CRF by 10-15% after stroke [1]. This gain may lead to improved ability to perform activities of daily living by decreasing the relative intensity of these activities and increasing exercise endurance [5]. Increasing activity levels after stroke can also improve walking (speed, tolerance and independence) and balance [6], prevent or reduce depressive symptoms [7], and influence neuroplasticity, which can aid motor recovery [8]. Fatigue is a significant, distressing and common sequela of stroke [9]. Although there is limited evidence available regarding the associations between regular exercise, fitness and fatigue in people after stroke, it is likely that exercise training will have a positive impact on fatigue [9].

Regular exercise may also reduce the risk of recurrent stroke or cardiac events after stroke by lowering blood pressure, reducing weight, increasing glucose tolerance, improving lipid levels and reducing arterial inflammation [5]. Despite the potential benefits of exercise, it is estimated that over three quarters of people after stroke are sedentary or have low levels of physical activity [10].

At least 30 minutes of moderate intensity exercise most days of the week is recommended in physical activity and exercise guidelines post-stroke and for older people [5,11]. It can be performed in one session or accumulated in bouts

of 10 to 15 minutes duration [5,11]. Despite these recommendations, CRF training is often overlooked in post-stroke management, with the focus being on functional retraining [5]. Optimal exercise strategies to improve CRF after stroke have yet to be identified [12]; however, the inclusion of some aerobic conditioning component in exercise programs appears to be key to achieving improved fitness, with the specific program being less important [1].

Traditionally, aerobic conditioning via continuous training at a moderate intensity has been recommended post-stroke [13]. Interval training, designed to mitigate fatigue by alternating short bursts of high intensity exercise with short recovery periods (rest or low intensity exercise), is a plausible alternate strategy for people after stroke [12,14,15]. Meta-analyses of interval training in healthy [16] and clinical populations [17,18] have shown it to be effective in improving CRF, and evidence for interval training in a stroke population is emerging [19-23]. In contrast, circuit training using workstations involving task-specific and ergometer activities has been investigated over many years including inpatient, outpatient and community settings [24-33]. The focus of these circuit studies have largely been functional recovery and with the exception of Pang et al [28], they have not reported the intensity of exercise achieved.

The aims of this pilot study were to:

1. examine the exercise intensity parameters (oxygen consumption and heart rate: patterns over time, mean and peak values) achieved by stroke survivors during task-specific and ergometer workstation activities when utilising an interval training approach compared to standard exercise fitness tests

2. determine whether people after stroke can use a circuit of the above workstations to accumulate exercise
3. determine whether interval training on a circuit of workstations is a safe and feasible CRF training approach for people after stroke.

6.4 Methods

Study design

Community-dwelling stroke survivors were recruited for a pilot controlled trial of an exercise intervention to improve cardiorespiratory fitness [“How Fit is the Stroke Survivor?” (HowFITSS?) trial (ANZCTR Trial ID: ACTRN12614000134628)]. This study examines data at baseline from the HowFITSS? trial. The study was conducted in the Human Performance Laboratory at the University of Newcastle. 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 National Health and Medical Research Council guidelines [34].

Participants

A convenience sample of 13 participants aged ≥ 18 years, who were within one year of their most recent stroke and able to follow basic commands, was investigated. Participants were recruited via clinician referral and by approaching inpatients recovering from stroke who were admitted to the local tertiary referral hospital. Key exclusion criteria were: unable to attend the centre for testing, pregnancy, and determined medically unfit to participate by a medical practitioner. Absolute and relative contraindications to exercise testing

[35] were provided on the Medical Clearance form used in the study. All participants provided informed written consent.

Data collection

Baseline data were collected during two assessment sessions, with sessions one week apart, except for one rural participant who requested all assessments to be done on the same day to minimise his travel. Participant demographics and characteristics (Body Mass Index, current modified Rankin Scale [36], Functional Ambulation Category [37]) were recorded. The following exercise tests were undertaken: the Six-Minute Walk Test [38] (6MWT), cycle progressive exercise test (cPXT), and Shuttle Walk Test (SWT) [39]. For the purpose of this study only the 6MWT and cPXT data were used for comparisons. The SWT has been used extensively in other clinical populations but is new to post-stroke CRF assessment. The feasibility of the SWT in a stroke population will be described elsewhere (manuscript submitted).

6MWT: This was undertaken as per guidelines [38], including using a flat, enclosed walkway with 180 degree turns at either end of the walkway with space for turning and providing standardised instructions and encouragement. A 20m walkway length was used due to limited space. The assessor remained at the start point. For one participant an additional researcher stood at the other end to supervise turning, to ensure safety due to identified balance issues on turning.

cPXT on an upright cycle (818E Monark, Sweden): Each participant cycled for a short period for familiarisation and to identify their preferred cadence (50 or 60 revolutions per minute) for the cPXT. After a brief rest, the participant started

pedalling, and the test commenced once they reached their predetermined cadence. The workload resistance started at 0 Watts with stepped incremental increases in workload of 25 Watts each minute until a test end criterion was met.

Circuit of workstations: Following completion of all of the baseline assessments, the “HowFITSS?” trial exercise intervention was planned with each participant. The “HowFITSS?” trial intervention consisted of a 12 week home- and community-based program individually-tailored to the abilities, interests and access to resources of each participant. It included strategies to increase physical activity and to reduce sedentary time [40]. Participants selected activities they wished to incorporate into their program which were then practised in a controlled laboratory setting during which exercise intensity parameters were measured. This paper reports on the exercise intensity parameters achieved during these practice sessions compared to exercise tests at baseline.

The practice of exercise activities was undertaken on a circuit of 5-minute workstations. Workstation selections were customised to each participant. There was no standardised program but many common workstations, including task-specific (eg fast/usual paced walking, stairs, step, balance) and ergometer (eg upright cycle, rower) activities were used (appendix). Training on all workstations was interval-based, except for endurance walking where the intensity was self-paced. The intervals involved alternating higher and lower intensity activity, with no rest periods. Intensity was altered by changing the speed while performing the same activity eg walking, rower, cycle, step or alternating a more intense activity with a less intense activity eg stairs

alternated with walking on the spot. Interval length, for both the higher and lower intensity activity was individualised for each participant on each workstation based on their capacity. Intervals ranged from 5 to 60 seconds.

We wanted to explore if whether people after stroke can accumulate exercise using a circuit of workstations. A goal of 30 minutes of exercise for the whole session was set in order to limit fatigue and physical demands on each participant. Six participants planned and practised their exercise program immediately after completing all assessments (ie the same visit) and seven returned the following week to undertake this component. The number of workstation bouts planned for each participant therefore depended on the number of exercise tests that had been undertaken that day [ie no tests: 6 workstation bouts (n=7); 1 test: 5 workstation bouts (n=5); 3 tests: 3 workstation bouts (n=1)]. Each exercise test was considered to have contributed 5 minutes of exercise.

Cardiorespiratory measures: During the 6MWT, cPXT and workstation circuit a portable metabolic system (Cosmed K4b2, Italy) and a 12 lead wireless electrocardiogram (ECG) device (Cosmed Quark T12, Italy) were used to monitor VO_2 and HR respectively. The metabolic system consisted of a soft rubber mask connected to a light-weight (less than 1kg) device worn with a harness, with the measuring unit on the chest and the battery pack on the back. The ECG unit was worn on a belt around the waist. Calibration was undertaken before each assessment session as per manufacturer's instructions. Data were transmitted wirelessly to a laptop. HR and breath-by-breath VO_2 data were averaged over 30 second epochs by the Cosmed software and the data exported to CSV spreadsheets.

Instruction to, and supervision of, participants during the exercise tests and workstation circuit was undertaken by an experienced neurological physiotherapist (author DM). Cardiorespiratory measures were collected as follows. During each exercise test and on each workstation the participant was questioned on how they were managing with the activity and observed for breathlessness, ability to hold a conversation, flushing or pallor, and diaphoresis. No heart rate (HR) information was available to the participant or physiotherapist. Oxygen consumption (VO_2), HR and cardiac rhythms were monitored by an exercise scientist experienced in exercise testing (author AD). End criteria for both the exercise testing and workstations included the participant's own volition and any concern with cardiac rhythm or participant wellbeing. Inability to maintain cadence or reaching 85% Heart Rate Reserve (HRR) were other criteria used for the cPXT. Reasons for stopping the cPXT, 6MWT or a workstation and any adverse events during an assessment session were recorded. A recovery period, usually 10-15 minutes, was provided between each of the fitness tests and commencement of the circuit, but there were no recovery periods between the workstations on the circuit.

Outcome measures

Oxygen consumption is the gold standard to measure exercise intensity, however HR is a more clinically-applicable measure; hence recordings for both are reported. To enable comparisons among participants VO_2 data relative to body weight were used (mL/kg/minute) and HR data were converted to a % of age-predicted maximal HR ($\%\text{HR}_{\text{max}}$) where age-predicted $\text{HR}_{\text{max}} = 206.9 - (0.67 \times \text{age})$ [41]. The time spent exercising on each exercise test and workstation was recorded.

Exercise intensities were categorised as: very low (<5.6 mL/kg/min, $<40\%$ HR_{max}), light (≥ 5.6 and <10.5 mL/kg/min, ≥ 40 and $<55\%$ HR_{max}), moderate (≥ 10.5 and <21 mL/kg/min, $55 \geq 55$ and $<70\%$ HR_{max}), vigorous (≥ 21 and <31.5 mL/kg/min, ≥ 70 and $<90\%$ HR_{max}) and high (≥ 31.5 mL/kg/min, $\geq 90\%$ HR_{max}) [42].

Aim 1- To explore and compare exercise intensity, four methods were used:

Exercise intensity patterns during each workstation and exercise test (Figure 6-1)- the average VO_2 during each 30 second epoch was used to investigate the pattern of oxygen consumption by each participant on each workstation and exercise test they undertook. Where only one or two participants undertook a workstation the data was collated on the one figure (Figure 6-1G).

Comparison of exercise intensity between each workstation and the 6MWT (Figure 6-2)- to compare exercise intensities on different workstations and the 6MWT, the average oxygen consumption (VO_{2mean}) and average % of age-predicted HR_{max} were determined. As the circuit was undertaken without rest between workstations we recognised we needed to allow for a period of physiological adaptation to each station, which can be seen in Figure 6-1.

Cardiorespiratory responses during the 6MWT have been shown to rise rapidly during the first two minutes after which they are maintained for the remainder of the test [43], which is reflected in Figure 6-1H. To allow for this only data from minutes 2 to 6 of the 6MWT and minutes 2 to 5 for each workstation were averaged. The data from any workstation bout that was terminated within two minutes was excluded from this analysis. Data from the cPXT were also excluded, as it is a progressive test, which can be seen in Figure 6-1I and averaging intensity would not be appropriate.

Time spent in HR-based exercise intensity categories (Figure 6-3)-: The time spent in each exercise intensity category during the 6MWT, cPXT and circuit was calculated.

Peak intensity: The peak HR (HR_{peak}) and VO_2 (VO_{2peak}) (30 second epoch mean) achieved on the 6MWT, cPXT and during the circuit of workstations were recorded for each participant (Table 6-1).

Aim 2- the ability of participants to accumulate exercise was explored in two ways:

Examining the time spent on the circuit of consecutive workstations (Figure 6-3 C). The workstations used by each participant are described in the last column of Table 6-1.

Determining the proportion of participants able to accumulate at least 30 minutes of exercise at an average of a moderate HR intensity (ie $\geq 55\% HR_{max}$) during a single assessment session (Figure 6-4). Average intensity was defined as the mean $\%HR_{max}$ maintained during the circuit and any included exercise tests. The workstations and any included exercise test are listed in the order they were performed in the last column of Table 6-1.

Aim 3- Safety and feasibility:

The circuit was deemed safe if no serious adverse events occurred. The use of a circuit of workstations was deemed feasible if the participant was able to complete at least two workstations without rest (a 10 minute bout of exercise).

Statistical analysis

All statistical analyses were undertaken using Stata 11/ IC for Windows (StataCorp LP, USA). Descriptive statistics were used to analyse the data [proportions and medians (IQR)].

6.5 Results

Characteristics of the 13 participants are shown in Table 6-1. All had suffered an ischaemic stroke. VO_{2peak} , HR_{peak} and duration achieved on the 6MWT, cPXT, and during the circuit are shown in Table 6-1. As all recruited participants were independently ambulant, all completed the 6MWT, with no rest periods or assistance required. HR data were missing for three participants during the 6MWT due to data from the ECG unit not being recorded on the laptop. Two participants were unable to undertake the cPXT due to pre-existing arthritic limitations (knee n=1, hip n=1).

All participants attempted the workstation circuit. Nine task-specific and three ergometer workstations were used (see Appendix). All participants completed two or more 5-minute workstation bouts during the circuit; the workstations used for each participant are shown in Table 6-1. Forty-five task-specific and 18 ergometer-based activity bouts were attempted. Of these 63 bouts, 59 (94%) were performed for 5 minutes. Regarding the other four bouts, one participant (13) disliked the step station and transitioned to an alternative activity, and three participants (1, 8, 10) terminated the circuit after 23, 12.5 and 11 minutes respectively. Participant 10 completed less than 2 minutes of exercise on the step and these data were excluded from the average intensity analyses.

Reasons for stopping the circuit and cPXT are summarised in Table 6-1. No serious adverse events, including dangerous arrhythmias, musculoskeletal injury or falls, occurred during any of the exercise tests or circuit. One participant experienced knee pain during the cPXT but this settled quickly once the test ceased.

Table 6-1 Participant demographics and characteristics; performance and cardiorespiratory measures during the 6MWT, cPXT and circuit of workstations

No	Demographics			Characteristics			6MWT			Cycle PXT				Circuit of Workstations (does not include any test data)				Circuit workstations and any exercise tests contributing to ≥ 30 minutes (in the order they were performed)
	Sex/ Age	Mths since stroke	Side affected/ strokes	mRS	BMI	FAC	Dist	VO _{2peak}	HR _{peak}	Dur	VO _{2peak}	HR _{peak}	Reason stop	Dur	VO _{2peak}	HR _{peak}	Reason stop	
1*	F/ 69.4	2.6	Left/ 1	1	40.5	4	294	11.0	missing	UTA: pre-existing arthritic limitations- knee				21	12.5	96	fatigue	fast/ sit-stand/ step/ balance/ stairs
2	M/ 76.3	4.3	Both/ 3	2	28.7	5	537	20.9	133	6	22.1	126	85% HRR	37	19.6	137	Nil	fast/ rower/ balance/ cycle/ step/ balance/ stairs
3*	M/ 80.5	2.7	Left/ 1	1	20.5	5	202#	13.6	missing	UTA: pre-existing arthritic limitations- hip				26	14.7	87	Nil	endurance/ balance/ sit-stand/ fast/ stairs
4	F/ 23.5	8.3	Left/ 1	3	23.1	5	406	19.5	missing	6	21.8	161	leg fatigue	32.5	25.2	174	Nil	Endurance/ stairs/ cycle/ fast/ rower/ step
5*+	F/ 65.6	13.7	Right/ 1	1	27.0	5	455	14.8	93	5	13.4	106	leg fatigue, SOB	30	17.7	123	Nil	Rower/ fast/ aerobic/ step/ cycle/ balance
6	F/ 23.1	16.0	Right/ 1	1	21.1	5	598	20.2	129	7.5	25.5	171	knee pain	31	31.0	170	Nil	treadmill x2/ balance/ cycle/ rower/ balance
7*+	F/ 71.2	1.3	Neither/ 1	2	30.8	5	330#	11.7	121	5	11.6	124	leg fatigue, SOB	26	11.4	115	Nil	rower/ fast/ cycle/ balance/ step
8*	M/ 42.2	1.1	Neither/ 1	1	43.2	5	428	12.7	99	5.5	11.8	117	Interference on ECG, SOB	12.5	12.2	133	fatigue, SOB	SWT [‡] / fast/ step/ stairs
9*	M/ 64.0	1.0	Right/ 2	0	23.6	5	591	22.9	88	8	27.4	103	leg fatigue	20	25.6	158	Nil	SWT [‡] / cycle/ balance/ step/ fast
10	F/ 51.1	3.7	Left/ 1	1	24.4	5	524	20.5	118	5.5	19.4	119	SOB	11	18.6	121	unable to tolerate mask	6MWT [‡] / cycle/ balance/ step
11*+	M/ 62.4	3.4	Right/ 2	1	23.8	5	552	19.1	79	5.5	22.8	102	ECG abnormality → RBBB [^]	15.5	28.1	124	Nil	6MWT [‡] / SWT [‡] / cPXT [‡] / balance/ rower/ treadmill
12+	M/ 75.0	3.9	Right/ 1	1	24.5	5	623	22.8	132	7.5	24.4	133	85% HRR	26.5	24.4	137	Nil	6MWT [‡] / cycle/ balance/ step/ rower/ fast
13	F/ 84.2	2.9	Right/ 1	1	20.4	5	481	19.7	122	3.5	15.4	112	leg fatigue, SOB	20	19.6	125	Nil	6MWT [‡] / bowls/ fast/ balance/ step/ outdoor
Median/ IQR	65.6/ 23.9	3.4/ 1.7			24.4/ 5.5	5/ 0	481/ 146	19.5/ 6.9	120/ 36	5.5/ 2.5	21.8/ 11	119/ 27		26/ 10	19.6/ 10.5	125/ 16		

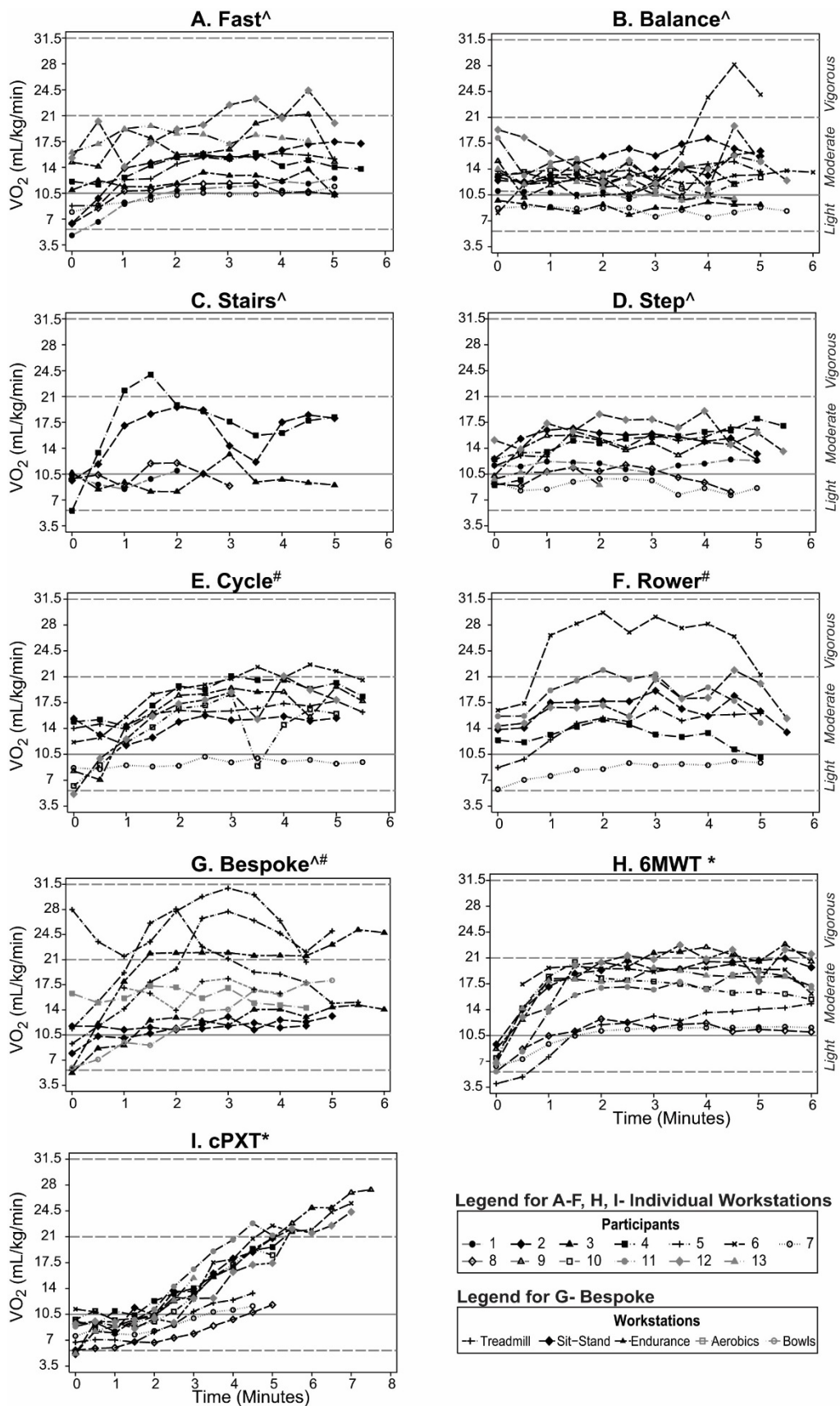
Legend: *= prescribed beta blockers; += prescribed ACE inhibitors; # used walking stick; ‡ exercise test not included in figure 3c calculations → RBBB[^] = subsequently diagnosed with right bundle branch block; No= participant number; mths= months; mRS= modified Rankin Score; BMI= Body Mass Index; FAC= Functional Ambulation Category; Dist= distance walked (metres); VO_{2peak}= peak oxygen consumption (mL/kg/min); HR_{peak}= peak HR (beats per minute); Dur= duration; reason stop= reason for stopping; M= male; F= female; UTA= unable to attempt; HRR= heart rate reserve; SOB= shortness of breath; ECG= electrocardiogram; 6MWT= Six-Minute Walk Test; cPXT= cycle progressive exercise test.

The patterns of exercise intensity are shown in Figure 6-1: workstations (1A to 1G), 6MWT (1H) and cPXT (1I). Each workstation is shown separately except for those with one to three practice bouts, which have been combined in the Bespoke Figure 6-1G. The figures highlight the variability between exercise tests and workstations as well as between the participants. Of the 986 data points, the numbers in the very light/ light/ moderate/ vigorous categories respectively were: task-specific workstations (n=472) 3/ 100/ 350/ 19; ergometer workstations (n=204) 1/ 33/ 134/ 36; 6MWT (n=180) 2/ 19/ 144/ 15, cPXT (n=130) 3/ 53/56/18.

Data representing the average intensity maintained during the workstations and 6MWT are presented in Figure 6-2. For $VO_{2\text{mean}}$ (Figure 6-2 A) 81% (36/44) of task-specific workstations, 89% (16/18) of ergometer workstations and 92% (12/13) 6MWT were sustained at $\geq 10.5\text{mL/kg/min}$. $VO_{2\text{mean}}$ ranges were similar for the 6MWT, task-specific and ergometer workstations, with the highest values achieved on the treadmill. For $\%HR_{\text{max}}$ (Figure 6-2 B) 91% (40/44) of task-specific workstations, 89% (16/18) of ergometer workstations and 60% (6/10) 6MWT were sustained at $\geq 55\%HR_{\text{max}}$.

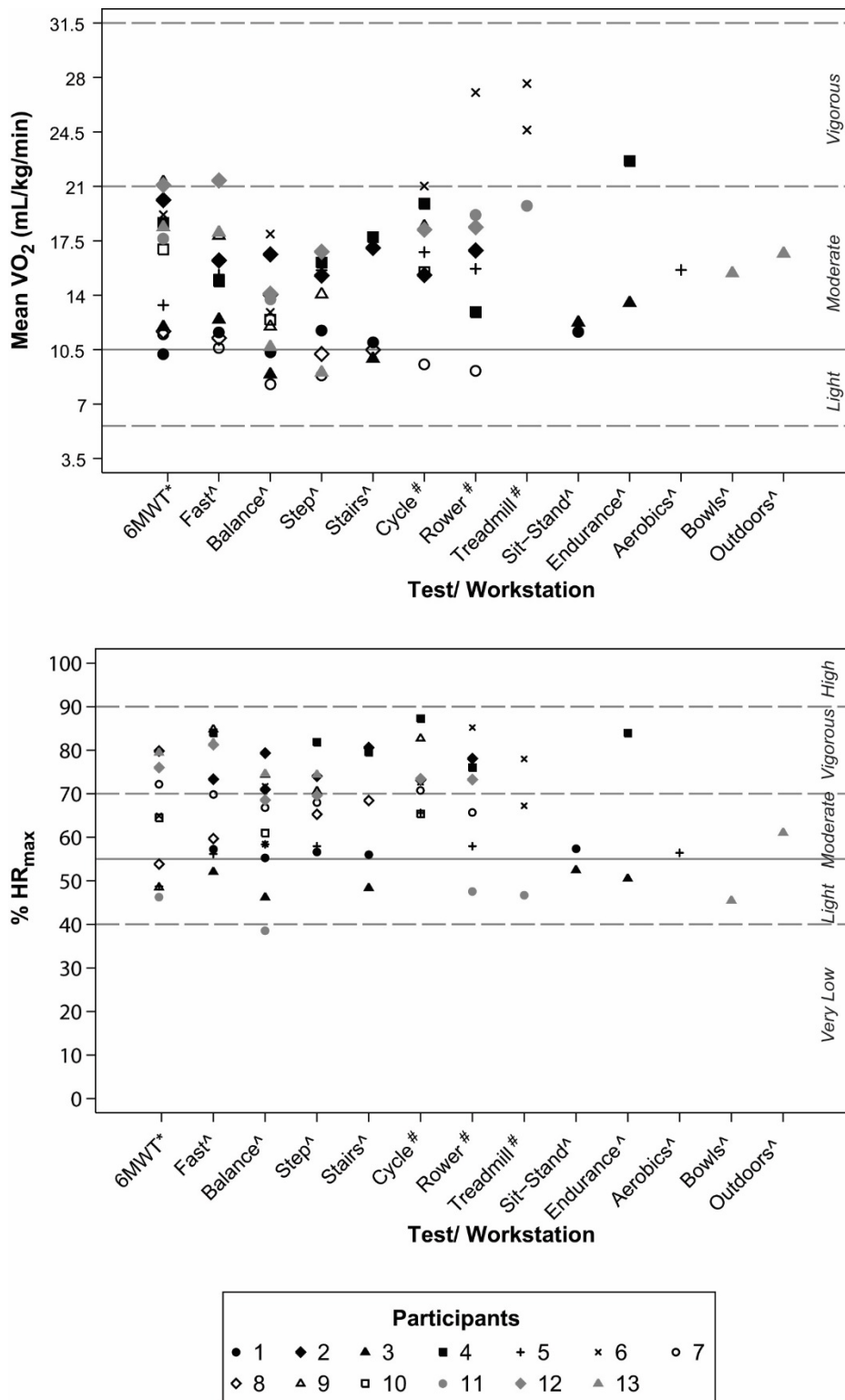
The duration and relative intensity ($\%HR_{\text{max}}$ category) achieved on each exercise test and the circuit are illustrated in Figure 6-3, which demonstrates the variation among individuals in the intensity and duration achieved. The circuit data indicate that all participants were able to exercise continuously for ≥ 10 minutes. Most spent a prolonged period of exercise in the moderate and vigorous categories.

Figure 6-1 Patterns of oxygen consumption (VO_2) over time (minutes) during workstations and exercise tests



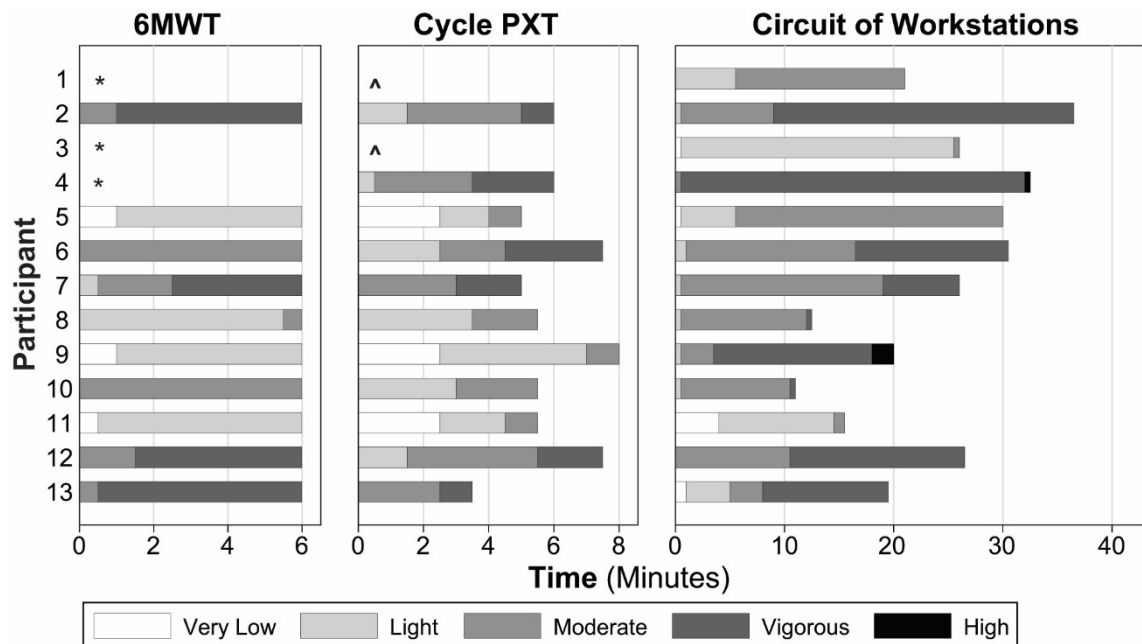
Legend: ^{*}= exercise test; [^]= task-specific workstation, [#]= ergometer workstation

Figure 6-2 Average intensity achieved during the 6MWT and circuit workstations



Legend: *= exercise test; ^= task-specific workstation, ^= ergometer workstation

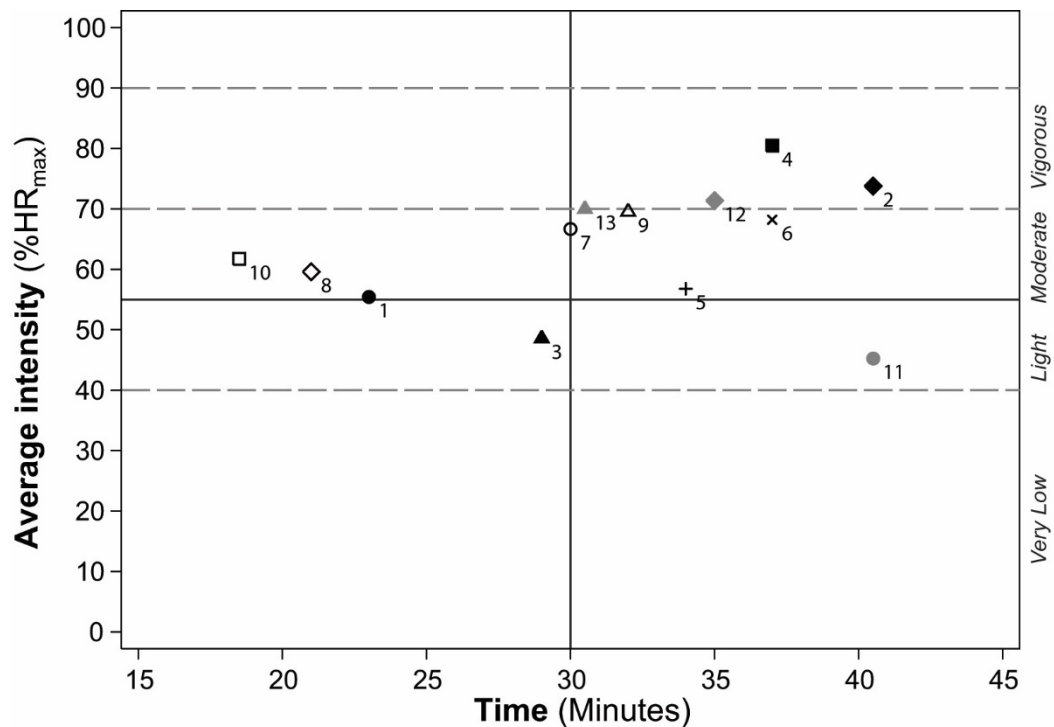
Figure 6-3 Time spent in HR-based exercise intensity categories during the 6MWT, cycle PXT and circuit



Legend: *= HR data missing for 3 participants during 6MWT; ^= Participants were unable to perform cPXT

The participants' ability to accumulate exercise for at least 30 minutes at an average of a moderate intensity is shown in Figure 6-4. Sixty-two percent (8/13: those in the upper right quadrant) met the exercise recommendations for both intensity ($\geq 55\%HR_{max}$) and duration (30 minutes). Of these, six achieved an average of at least vigorous intensity ($\geq 70\% HR_{max}$). Overall, 69% (9/13) of participants exercised for ≥ 30 minutes, although for Participant 3 the duration (29 minutes) was miscalculated by the researchers and was not limited by the participant. 86% (11/13) of participants maintained an average of moderate or higher intensity for at least 15 minutes. Eight exercise tests contributed data to six participants' results (6MWT: Participants 10, 11, 12, 13; cPXT: Participant 11; SWT: Participants 8, 9, 11).

Figure 6-4 Participants ability to accumulate at least 30 minutes of exercise at an average of $\geq 55\%$ age-predicted HR_{max}



Note: Participants who had exercise test data included: 8, 9, 10, 11, 12 and 13

6.6 Discussion

In this study we successfully applied interval training principles to a range of task-specific and ergometer workstations. By incorporating the workstations into a circuit session to accumulate activity, ambulant stroke survivors exercised at an intensity and duration recommended for improving CRF. The training approach was safe and feasible and is a promising approach to incorporating CRF training into management after stroke.

Our findings suggest that many activities currently used in therapy have the potential to provide both functional and CRF training simultaneously, if stroke survivors are encouraged to undertake them at sufficient intensity. These results were unexpected, given that previous studies have identified task-

specific therapy sessions are often low in exercise intensity [29,44,45]. In our study, by focusing on intensity as well as function, 78% of task-specific and 83% of ergometer workstations bouts were spent exercising at a moderate or higher intensity (Figure 6-1). Undertaking higher intensity exercise can result in greater improvement in $\text{VO}_{2\text{peak}}$ in people after stroke [46] and therefore may be the preferred option for people after stroke who are medically suitable and physically capable [14].

While moderate or even vigorous intensity exercise might be optimal for some stroke survivors it has been suggested low-intensity exercise can safely be prescribed for most people who have had a stroke [14]. In our study within the first 30 seconds all workstations and the 6MWT were being performed at a light or higher intensity (Figure 6-1). Light intensity may be a sufficient initial CRF training stimulus in deconditioned people [35], which includes many people after stroke [2]. $\text{VO}_{2\text{peak}}$ values for people after stroke often fall within the submaximal VO_2 range that healthy people use to undertake activities of daily living (ie 10.5 to 17.5 mL/kg/min) [3]. Generating even small improvements in $\text{VO}_{2\text{peak}}$ levels will reduce the effort associated with undertaking activities of daily living [3]. The potential for activities of daily living to provide a CRF training stimulus was identified by Rahman et al [47] who monitored HR while stroke survivors undertook the activities of the Modified Rivermead Mobility Index. In their study the 10m walk, ascending/descending flight of stairs, lying to sitting, sitting to standing, standing balance, transfer from bed to chair and chair to bed were all performed between 50% and 60% HR_{max} [47]. Our results build on these findings by demonstrating that task-specific activities can, not only be performed at a considerable intensity, but that such intensity can be sustained.

We have shown that participants were able to meet exercise recommendations for duration, as well as intensity [5,11]. Most participants (62%) were able to accumulate ≥ 30 minutes of exercise at a moderate or higher intensity. Three participants (23%) who ceased the circuit before reaching the accumulation target of 30 minutes were able to exercise at an average of moderate intensity for 11 to 21 minutes. This result is similar to Pang et al [28] who observed that stroke survivors were able to maintain target HR for 15 minutes during circuit training sessions. Accumulating exercise in bouts of 10 to 15 minutes has been recommended in guidelines as an alternative way to achieve a total of 30 minutes of physical activity over a day [5,11].

To date, interval training programs have been trialled with people after stroke on a single ergometer - cycle [21] or treadmill [19,20,23]. Our results suggest there is enormous potential to apply this training approach to task-specific, as well as ergometer, activities to achieve sufficient intensity and duration of physical activity with the potential to improve cardiorespiratory fitness.

The use of interval training may have been a reason some participants were able to reach a higher VO_{2peak} and HR_{peak} on the circuit of workstations than during the exercise tests. Participants knew they only had to push themselves for a short time during the high intensity interval before “resting” during a low intensity interval. In contrast the cPXT is unrelenting and increases workload with no recovery periods. During the 6MWT participants may, consciously or unconsciously, hold onto some reserve capacity to make sure they are able to complete the test. Participants may have been motivated by the positive feedback, enthusiasm and encouragement provided by the researchers during the workstations, which differed in nature to the standard instructions given

during the exercise tests. Individualising workstations allowed participants to undertake activities that used more muscle mass, such as jogging/running on a treadmill.

Utilising an array of workstation activities enabled tailoring to the individual capabilities of the stroke survivor. Workstations were individualised to each participant allowing them to practise activities that were relevant to them.

Participants commented that they enjoyed the circuit and expressed a sense of achievement. For a number of people it was their first opportunity to undertake activities they had not participated in since their stroke but were keen to resume. Many commented that they had not exercised for as hard or for as long since their stroke. Being monitored by trained staff assisted them to gain in confidence, and provided reassurance they could do it and it was safe.

Key requirements when we were selecting the exercise approach were that it could be undertaken readily in most clinical, community or home settings and was feasible, safe and relevant for each participant. We designed the workstations to be inexpensive so they could be used in a range of settings.

The task-specific activities required little or no equipment. The ergometers used are readily available in many inpatient settings, at community gyms and even in homes. The circuit of workstations was feasible and safe, with all participants able to complete two or more workstations with no serious adverse events.

Our results also highlight the benefits of incorporating exercise testing and monitoring of intensity during exercise sessions into post-stroke management. By assessing an individual's physical and physiological response to exercise, via an exercise test, exercise intensity can safely be prescribed according to

their actual capacity [5]. While exercise tests may not always elicit a stroke survivor's actual VO_{2peak} the use of a standardised testing procedure allows for repetition over time to measure for change. Quantifying the intensity achieved allows comparison to the amount prescribed but is often overlooked in clinical practice [48] and in post-stroke research [1,49]. Providing this information in the description of an intervention can inform replication in subsequent studies or allow comparisons between studies [50]. We have shown that it is feasible to track intensity throughout an exercise session and to quantify overall exercise intensity. HR monitors are a viable option for measuring intensity. They can be used in clinical [51] or community-based settings, are easy to apply and relatively inexpensive.

Strengths and limitations

There are a number of strengths of this study. This has been one of the few studies to measure intensity (HR and VO_2) during task-specific activities or during a circuit of workstations. We applied interval training to task-specific activities and used workstations that were functionally relevant, low cost and individualised to each participant. While our participants covered a wide age range, a limitation was the small number of self-selected participants, all of whom were ambulant. Future research should investigate whether similar responses are achieved in less ambulant participants.

6.7 Conclusion

CRF has long been overlooked in people after stroke, with the focus predominantly being on functional retraining. Emerging evidence indicates that

improving CRF is likely to have a myriad of health and functional benefits. We have shown that task-specific and ergometer activities can be undertaken by people after stroke at intensities and durations sufficient to have CRF training effects. This is an important and clinically useful finding. Applying interval training principles to a circuit of workstation appears a safe and feasible approach. It can provide reassurance to people after stroke, their families and clinicians that exercising at the recommended intensity and duration is of low risk and is well tolerated. The exercise strategy is a promising way to combine CRF training with routine functional rehabilitation exercises post-stroke, and warrants further investigation.

6.8 Appendix

Workstations undertaken and interval approaches used (where applicable)

Station/ intensity	Set up	Lower intensity activity	Higher intensity activity
Fast/ Interval*	10m track	Slow or self-selected pace	Fast walk or jog
Balance/ Interval*	10m line set up on floor	Standing feet together, standing 1 leg, eyes open eyes closed, walking along a line (normal step length or heel-toe)	Side stepping +/- squats, side stepping crossing feet, backwards walking
Step/ Interval [†]	Using Reebok Aerobic Step, USA	Up and over forwards and sideways at self-selected pace	Increasing speed, adding arm activities
Stairs/ Interval [†]	Flight of 17 stairs with rail on either side	Walking on the spot	Up and down stairs
Cycle/ Interval [†]	Upright cycle, constant workload	Lower rpm	Higher rpm
Rower/ Interval [†]	Constant workload	Lower rpm	Higher rpm
Treadmill/ Interval [†]	No incline	Walking at self- selected pace	Jog or run
Sit-stand/ Interval [†]	Chair with arms, table	Side stepping around table self-selected pace	Sit to stand, aiming to increase speed
Endurance/ Self-paced [‡]	Instructions as per 6MWT	NA- Continuous walking; self-selected pace	
Aerobics/ Interval [†]	Aerobic moves- grapevine, stepping side-to-side, toe taps, 4 point squares, heel taps.	Self-selected pace	Increasing pace, adding arm activities
Bowls/ Interval [†]	Outdoor lawn bowls simulated by standing/ walking on a soft gym mat, bowling ball at skittles	Self-selected pace	Increasing pace during walking, bending to set up skittles
Outdoors/ Interval [†]	To reflect outdoor environment near home	Walking on flat concrete path	Walking on grass, ramps, steps, slopes

*= Alternating laps of lower and higher intensity activity; [†]= Alternating 30-60 second intervals of lower and higher intensity activity; [‡]= No intervals; rpm = revolutions per minute; NA = not applicable

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Declaration of interest

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CHAPTER 7: AN INDIVIDUALLY-TAILORED PROGRAM OF HOME- AND COMMUNITY-BASED PHYSICAL ACTIVITY CAN IMPROVE THE CARDIORESPIRATORY FITNESS AND WALKING ENDURANCE OF STROKE SURVIVORS: A PILOT STUDY

7.1Details

Authors and affiliations

Dianne Lesley Marsden ^{1 2 3}, Ashlee Dunn ^{1 3}, Robin Callister ^{1 3}, Patrick McElduff ¹, Christopher Royce Levi ^{1 2 3}, Neil James Spratt ^{1 2 3}

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

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7.2 Abstract

Purpose: To determine the feasibility of an individually-tailored home- and community-based exercise program to improve cardiorespiratory fitness (CRF) and walking endurance 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, and the intervention group undertook a 12-week, individually-tailored, home- and community-based exercise program, including once-weekly telephone/email support. Assessments were conducted at baseline and 12 weeks. Feasibility was determined by retention, program participation, and adverse events. Efficacy measures included change in CRF [peak oxygen consumption (VO_{2peak})] and distance walked during the Six-Minute Walk Test (6MWT).

Results: All participants completed the study with no adverse events. All intervention participants reported undertaking their prescribed program. VO_{2peak} improved by 16% more in the intervention group (baseline: 1.17 ± 0.29 L/min) than the control group (baseline: 1.24 ± 0.23 L/min) (between-group difference= 0.18, 95%CI 0.01 to 0.36). 6MWT distance improved by 66.5 ± 63.8 m (16%) in the intervention group compared to 14.5 ± 38.5 m (3%) in the control group (between-group difference= 45.2, 95%CI 0.3 to 90.2).

Conclusions: Our client-centred approach appears feasible in selected stroke survivors, requires few health resources, and is suited to most community settings. The 16% improvement in CRF is similar to that achieved in centre-based resource-intensive programs.

7.3 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 [2]. It has been estimated that over three-quarters of people after stroke have low levels of physical activity or are sedentary [3]. Stroke survivors spend a large proportion of their day (19.5 hours, 81%) in sedentary behaviours, often accumulated via prolonged bouts of inactivity (median= 1.7 hours) [4]. Stroke survivors spend four hours more per day in sedentary behaviour than age- sex- and BMI-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 to 15% [1]. Of the 28 studies included in a recent systematic review, 25 used multiple sessions of centre-based supervised training each week [1]; 2 studies used once-weekly centre-based supervised sessions in conjunction with a home-program; and one study used a one-on-one therapist-supervised home-program [1]. These studies demonstrated that cardiorespiratory fitness can be improved in people after stroke. However, in health services with limited, if any, community-based therapy services available, resource-efficient models of service provision are also required. The need for studies of home-based programs with intermittent supervision has been

recognised in a recent review, particularly to provide evidence for therapies that may help stroke survivors who live away from major centres [11].

Individualising 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 meaningful to them [12].

Aims

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

7.4 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: ACTRN12614000134628]. 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 12 weeks. 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 [13].

Participants

A convenience sample of 20 stroke survivors aged ≥ 18 years old, who were within one year of their most recent stroke and able to follow basic commands, were recruited via clinician referral. Key exclusion criteria were: unable to attend the centre for testing, pregnancy, and determined medically unfit to participate by a medical practitioner. Absolute and relative contraindications to exercise testing [14] were provided on the Medical Clearance form used in the study. Due to a logistical issue regarding access to the Human Performance Laboratory a block design was required, hence this was a controlled but not randomised trial; the first 10 participants recruited were assigned to the intervention group with the next 10 assigned to the control group. Data were collected in the Human Performance Laboratory at the University of Newcastle, Australia. All participants provided informed written consent.

Intervention

The intervention was designed so that it could be applied in most settings: metropolitan, regional or rural. An exercise program for each participant in the intervention arm was developed following completion of baseline assessments. Client-centred, individualised plans were devised by consultation between the participant and two experienced clinicians: a neurological physiotherapist (author DM) and exercise scientist (author AD). Carers who were present at the session were included in the discussion and planning.

The intervention aimed to increase daily physical activity and reduce sedentary time, using a whole-day approach to being more active [15]. The health benefits of regular ongoing physical activity, including at a level that has the potential to improve cardiorespiratory fitness, as part of a healthy lifestyle were discussed, including the potential benefits for preventing subsequent stroke. Strategies to overcome any perceived barriers to being active were also considered.

Programs were based on participant preferences for activities, including any pre-stroke activities they wished to resume or work towards resuming, their physical capacity, 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. It contained a core home-exercise program, based on task-specific exercises that participants could use as part of their intervention (see appendix). It contained information on how to progress these exercises over time. These activities were based on previously-reported programs [16-23]. Participants were strongly encouraged to exercise at a level with the potential to improve cardiorespiratory fitness by meeting the exercise recommendations [6,24] of accruing at least 30 minutes per 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 was discussed. Low intensity intervals were encouraged to be active rather than complete rest.

Pedometers and exercise diaries were provided to participants who were interested in using these strategies.

Following the development of the individually-tailored program, each participant practised their 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 provide participants with experience of applying interval training to the various activities practised.

Ongoing support during the 12 weeks was provided by one researcher (author AD) via weekly email or telephone calls. The support was tailored to each participant's specific requirements. It included some or all of: 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. 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

Both control and intervention group participants received usual care during the 12 weeks. Control participants were asked to continue their routine activities during this time. 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 level testing and a 12-week exercise program. It did not specify when the program would start. Any medical and therapy appointments were attended as usual. 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. The research team were independent of the usual-care therapists.

Assessments

Assessments were undertaken over one to three assessment sessions, depending on each participant's exercise capacity. Participant demographics (age, sex, country of birth, residence) and characteristics (stroke type, time since last stroke, number of strokes, side affected, thrombolysed with tPA, Body Mass Index, current modified Rankin Scale [25], Functional Ambulation Category [26]) were recorded. Assessors (authors DM and AD) were not blinded to group allocation. Standardised instructions were provided to participants for each test.

Three exercise tests were used to assess cardiorespiratory fitness. The associated performance measures were also recorded.

Six- Minute Walk Test (6MWT)

The 6MWT [27] was performed in accordance with the American Thoracic Society standards, with the exception of a 20m straight walkway used due to limited space. Standardised instructions and encouragement were provided according to the guidelines and no physical assistance or support was provided [28]. Distance walked was recorded.

Shuttle Walk Test (SWT)

For the SWT [29], participants were required to walk between markers spaced 9m apart (shuttles). Speeds were dictated by an audio CD (*Department of Respiratory Medicine, Glenfield Hospital NHS Trust, Leicester, UK*) and increased each minute. The test was terminated 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. The total number of shuttles walked was recorded.

Cycle progressive exercise test (cPXT)

The cPXT was performed on an upright cycle (818E Monark, Sweden). Each participant cycled for 2 to 3 minutes for familiarisation and to identify their preferred cadence (50 or 60 revolutions per minute) for the test. After a brief rest (2 to 3 minutes), the participant started pedalling 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. The final power output and duration of the test were recorded.

During each of these exercise 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. These were recorded using a portable metabolic system (Cosmed K4b2, Italy). Heart rate (HR) was recorded via a 12 lead wireless electrocardiogram (ECG) device (Cosmed Quark T12, Italy). Data were transmitted wirelessly to a laptop and exported as CSV files. Test end criteria were: participant's own volition; any concern with cardiac rhythm or participant wellbeing; and during the cPXT, inability to maintain cadence or reaching 85%

Heart Rate Reserve (HRR) calculated using the Karvonen Formula of 85%HRR = $\{[(220 - \text{age}) - \text{resting HR}] \times 0.85\} + \text{resting HR}$ [30]. Blood pressure was measured before and after each exercise test as a safety precaution. Reasons for stopping were recorded.

Other assessments included:

10m Walk Test

This test [31] was used to assess fast and self-selected walking speeds. The time taken to walk the middle 10m of a 14m walkway was recorded. Three trials were performed for each speed. The average of the three times was calculated then converted to velocity (m/s).

Step Test

The Step Test was used to assess dynamic standing balance using the protocol outlined by Hill et al [32]. It involved stepping one foot on, then off, a 7.5cm step as quickly as possible in a 15 second period. Both legs were tested.

Fatigue, depression and health-related quality of life

The Fatigue Assessment Scale [33], Patient Health Questionnaire (PHQ-9) [34], and the Stroke and Aphasia Quality of Life (SAQoL-39) [35] questionnaire were used to assess fatigue, depression and health-related quality of life, respectively. Higher scores represent worse levels of fatigue and depression whereas lower scores indicate worse health-related quality of life.

Outcome measures

Feasibility was assessed by retention (number returning for 12-week assessments) the occurrence of any adverse events during assessments

(documented) or the intervention period (self-report), and participation in the exercise program (intervention group; self-report) or other physical activities (both groups; self-report). At baseline, participants were interviewed about their usual physical activity. At the 12-week follow-up appointment participants were interviewed on their activity levels and the types of activities undertaken over the preceding 12 weeks. For intervention group participants this included their use of the prescribed program activities. Also, during their weekly phone calls/emails, participants in the intervention group reported 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.

The primary measure used to assess change in cardiorespiratory fitness was absolute VO_{2peak} (L/min) as relative VO_{2peak} (mL/kg/min) is affected by any change in weight over time. Changes in VO_{2peak} 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 VO_{2peak} , R-value and HR during the 6MWT, cPXT and SWT), performance measures [6MWT distance (m), cPXT maximum workload (W) and duration (seconds), number of shuttles completed during the SWT, fast and self-selected walking speed (time taken to walk 10m, m/s), number of steps during step test], and fatigue, depression and health-related quality of life scores were examined.

Statistical methods

Baseline characteristics are summarised as means and standard deviations (SD) 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 (ANCOVA) 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). Only those with data at both baseline and follow-up were included in analyses (ie complete case analysis not intention-to-treat) as this was a pilot study. 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 % change from baseline between the two 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, scatterplots illustrating data distribution and changes were used in addition to summary statistics [36]. Analyses were conducted in SAS 9.4 (SAS, USA) and Stata V13 (StataCorp LP, USA).

7.5 Results

Demographic and other characteristic data for the intervention and control groups at baseline were compared and are summarised in Table 7-1; there was no statistically significant difference between the groups. All participants had

suffered an ischaemic 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.

Feasibility

The target of 20 participants was reached, and all participants attended the 12-week assessments. 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 one intervention group participant had intermittent right bundle branch block on ECG and was referred to his general practitioner for investigation. Researcher (author DM) accompanied two intervention group participants to their first visit to a community exercise program and participated in the exercise session with them.

Table 7-1 Participant demographics and characteristics

Characteristic	Category or Mean(SD)	Intervention (n=10)	Control (n=10)	p-value
Sex	Male	3 (30%)	5 (50%)	0.65
Age (y)	Mean (SD)	54.4 (22.2)	62.0 (16.8)	0.42
Body Mass Index (kg/m ²)	Mean (SD)	27.5 (8.2)	28.5 (3.7)	0.72
Resides	Metropolitan	6 (60%)	5 (50%)	0.70
	Regional	1 (10%)	3 (30%)	
	Rural	3 (30%)	2 (20%)	
Country of birth	Australia	9 (90%)	9 (90%)	1.00
	Other	1 (10%)	1 (10%)	
Time since stroke (mths)	Mean (SD)	5.6 (5.3)	3.8 (1.2)	0.33
Number of strokes	One	9 (90%)	8 (80%)	1.00
	Two	1 (10%)	1 (10%)	
	Three		1 (10%)	
Modified Rankin Scale	0		1 (10%)	1.00
	1	8 (80%)	7 (70%)	
	2	1 (10%)	2 (20%)	
	3	1 (10%)		
Side affected	Left	4 (40%)	3 (30%)	0.73
	Right	4 (40%)	3 (30%)	
	Neither	2 (20%)	4 (40%)	
Thrombolysed with tPA	Yes	2 (20%)	2 (20%)	1.00
Functional Ambulation Category	Mean (SD)	4.9 (0.3)	4.9 (0.3)	1.00

Intervention efficacy

There was a 0.18 L/ min (95% CI: 0.01 to 0.36) greater improvement in VO_{2peak} on the 6MWT in intervention participants than in controls (Table 7-2). There were trends to improvement in the SWT [0.14 L/ min (95% CI: -0.04 to 0.32)] and cPXT [0.20 L/ min (95% CI: -0.04 to 0.43)]. Enhancing the plausibility of the 6MWT result, there was very strong concordance for the effect size estimate for VO_{2peak} and performance measures for each of the three exercise tests: all indicated 11-15% greater benefit in the intervention group compared to the control group (Table 7-2). Figure 7-1 shows the changes for individual participants for selected cardiorespiratory fitness and performance measures and for the questionnaires. There were some missing data from the exercise tests. Reasons for missing data were: two intervention and two control group participants were unable to undertake the cPXT due to pre-existing arthritic limitations (knee n=3, hip n=1); one control group participant was unable to do the 12-week cPXT as his resting HR was at 85% HRR, and one 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 one participant were excluded due to equipment problems resulting in physiologically impossible values. HR data were missing for three intervention group participants during the 6MWT due to data from the ECG unit not being recorded on the laptop. The intervention group improved 1.5 and 1.3 steps more ($p<0.05$) than the control group for the right and left leg, 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 7-2).

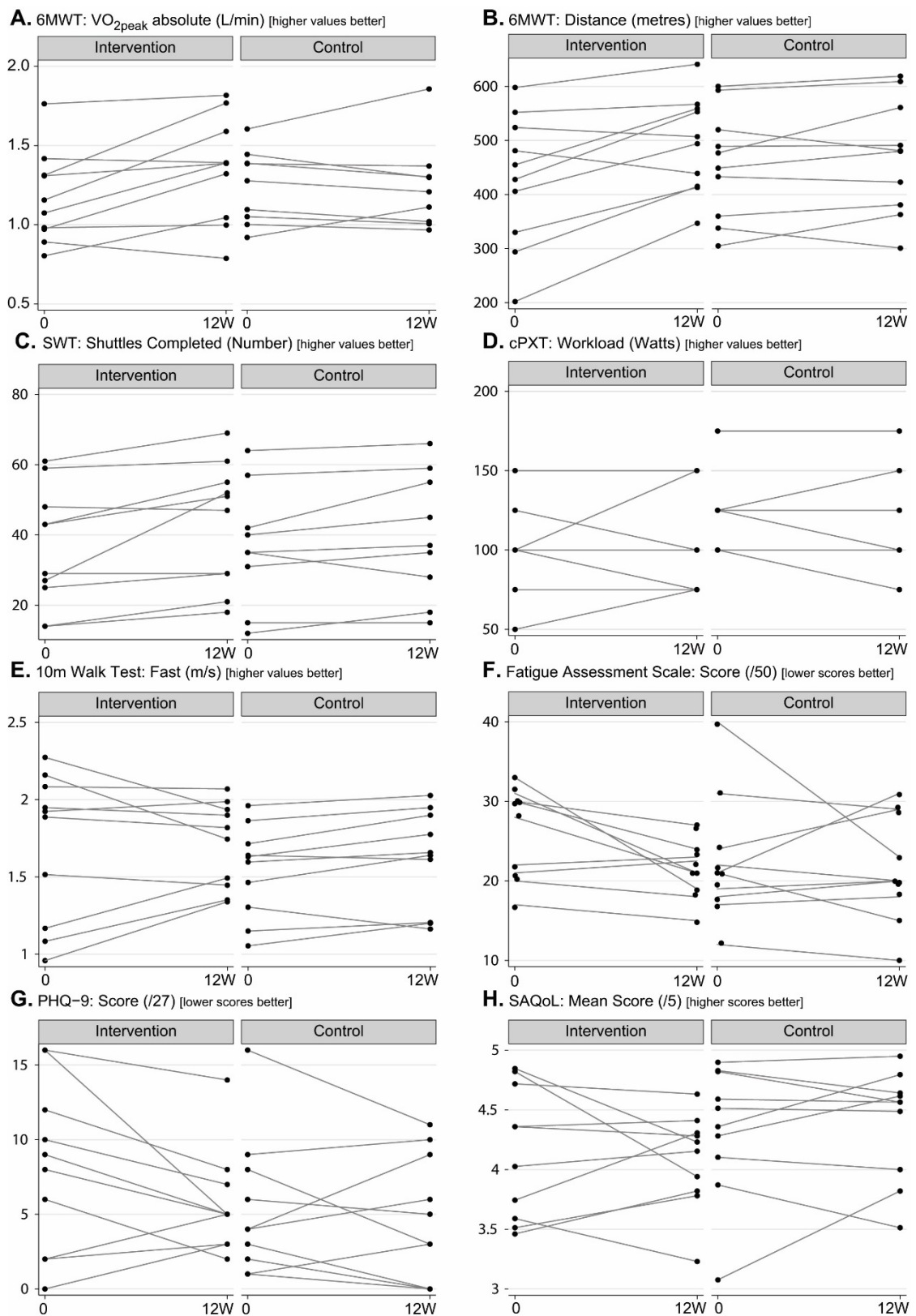
Table 7-2 Outcome measures: within and between group scores and differences

Test and outcome measure	Intervention			Control			Between-groups difference		
	Baseline	12 weeks	Change	Baseline	12 weeks	Change	Absolute difference (95% CI)	P-value	% difference
6MWT									
VO _{2peak} absolute (L/min)	1.17 (0.29)	1.35 (0.33)	0.18 (0.20)	1.24 (0.23)	1.24 (0.27)	-0.00 (0.13)*	0.18 (0.01 to 0.36)	0.044	15.6
VO _{2peak} relative (mL/kg/min)	16.0 (3.7)	18.6 (4.4)	2.6 (2.6)	15.2 (2.6)	15.2 (3.2)	0.1 (1.8)*	2.6 (0.3 to 4.9)	0.030	15.6
Heart rate (b/min)	109 (18)	113 (12)	4 (21)^	118 (21)	122 (25)	5 (12)	3 (-14 to 20)	0.731	0.1
R-value	0.99 (0.13)	1.01 (0.09)	0.02 (0.16)	0.99 (0.13)	1.09 (0.14)	0.10 (0.18)	0.08 (-0.03 to 0.19)	0.137	-8.1
Distance (m)	427.0 (123.0)	493.5 (89.6)	66.5 (63.8)	456.4 (100.9)	470.9 (105.7)	14.5 (38.5)	45.2 (0.3 to 90.2)	0.049	12.4
SWT									
VO _{2peak} absolute (L/min)	1.22 (0.30)	1.36 (0.40)	0.14 (0.21)	1.28 (0.36)	1.29 (0.33)	0.00 (0.11) ⁺	0.14 (-0.04 to 0.32)	0.117	11.3
VO _{2peak} relative (mL/kg/min)	16.9 (4.8)	18.7 (5.0)	1.8 (3.0)	16.2 (5.0)	16.3 (4.8)	0.1 (1.3) ⁺	1.8 (-0.7 to 4.2)	0.142	10.0
Heart rate (b/min)	114 (16)	116 (19)	1.60 (22)	134 (24)	134 (30)	0.3 (11)*	1 (-19 to 20)	0.919	1.2
R-value	1.02 (0.17)	0.92 (0.07)	-0.10 (0.20)	0.91 (0.10)	0.96 (0.11)	0.05 (0.13)*	0.04 (-0.05 to 0.14)	0.336	-15.3
Shuttles (count)	36.3 (17.0)	43.2 (17.7)	6.9 (7.5)	36.8 (17.0)	39.8 (17.9)	3.0 (5.3)*	3.9 (-2.7 to 10.5)	0.228	10.9
cPXT									
VO _{2peak} absolute (L/min)	1.26 (0.36)	1.35 (0.42)	0.10 (0.22) ⁺	1.31 (0.17)	1.21 (0.19)	-0.10 (0.12) [‡]	0.20 (-0.04 to 0.43)	0.091	15.6
VO _{2peak} relative (mL/kg/min)	17.3 (5.0)	18.9 (5.0)	1.6 (3.1) ⁺	16.6 (4.0)	15.4 (4.2)	-1.1 (1.4) [‡]	2.9 (-0.2 to 6.0)	0.067	15.9
Heart rate (b/min)	127 (25)	125 (24)	-2 (24) ⁺	136 (21)	131 (20)	-5. (10)^	0.1 (-20 to 20)	0.992	2.3
R-value	1.11 (0.17)	1.05 (0.20)	-0.06 (0.29) ⁺	1.04 (0.12)	1.06 (0.11)	0.03 (0.15) [^]	0.00 (-0.19 to 0.19)	0.997	-8.3
Duration (s)	303.8 (76.0)	318.8 (86.3)	15.0 (62.1) ⁺	334.3 (58.6)	317.1 (84.6)	-17.1 (29.3) [^]	32.6 (-27.4 to 92.6)	0.259	10.1
Workload (W)	100.0 (29.9)	109.4 (35.2)	9.4 (29.7) ⁺	121.4 (26.7)	117.9 (34.5)	-3.6 (17.3) [^]	10.2 (-20.8 to 41.2)	0.486	12.4
Step test (15 s)									
Steps right	14.7 (5.1)	17.2 (3.9)	2.5 (2.1)	16.4 (3.9)	17.0 (3.5)	0.6 (1.4)	1.5 (0.1 to 2.9)	0.036	13.3
Steps left	14.6 (5.4)	16.5 (4.6)	1.9 (1.6)	16.3 (3.9)	16.6 (3.4)	0.3 (1.4)	1.3 (0.1 to 2.5)	0.041	11.2

Test and outcome measure	Intervention			Control			Between-groups difference		
	Baseline	12 weeks	Change	Baseline	12 weeks	Change	Absolute difference (95% CI)	P-value	% difference
10 m walk test									
Fast speed m/s	1.7 (0.5)	1.7 (0.3)	0.01 (0.26)	1.5 (0.3)	1.6 (0.3)	0.08 (0.10)	0.01 (-0.13 to 0.16)	0.871	6.3
Self-selected speed m/s	1.2 (0.3)	1.3 (0.2)	0.1 (0.1)	1.2 (0.2)	1.3 (0.2)	0.1 (0.1)	0.0 (-0.1 to 0.1)	0.437	0.8
Fatigue Assessment Scale									
Score (possible range 10 to 50)	26.2 (5.6)	21.8 (3.8)	-4.5 (4.9)	22.5 (7.9)	21.5 (6.7)	-1.0 (7.1)	1.3 (-3.4 to 6.0)	0.567	-12.7
PHQ-9									
Score (/27)	8.1 (5.7)	5.7 (3.4)	-2.4 (4.1)	5.4 (4.6)	4.7 (4.2)	-0.7 (3.2)	0.4 (-2.4 to 3.2)	0.761	-16.7
SAQoL									
Mean score (/5)	4.1 (0.5)	4.1 (0.4)	-0.1 (0.5)	4.3 (0.6)	4.4 (0.5)	0.1 (0.3)	0.2 (-0.1 to 0.5)	0.160	-2.9

Group scores are means(SD). Legend: 6MWT= Six-Minute Walk Test, SWT= shuttle walk test, cPXT= cycle progressive exercise test, PHQ-9= Patient Health Questionnaire, SAQoL= Stroke and Aphasia Quality of Life-39, for Change scores: the number of participants included in the analysis= 10 except where * n=9, + n=8, ^n= 7, ‡ n= 6

Figure 7-1 Changes for individual participants for selected cardiorespiratory fitness, performance and questionnaire measures



Legend: 6MWT= 6 Minute Walk Test, SWT= shuttle walk test, cPXT= cycle progressive exercise test, PHQ-9= Patient Health Questionnaire, SAQoL= Stroke and Aphasia Quality of Life- 39

Physical activity levels

Based on the self-reports the intervention participants were more physically active than control group participants over the 12-week period. All of the intervention group participants reported that they undertook their program. Eight of the 10 (80%) reported being active for 20 minutes or more on most days of the week; the other two 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); the individualised home-exercise program in their manual (n=5). Two participants continued with outpatient physiotherapy 1 to 2 times per week. One person commenced Masterstroke; a 9-week secondary prevention group program run by health professionals that included one hour of exercise in each twice-a-week session [37]. Three people returned to leisure activities they participated in prior to their stroke including lawn bowls, horse riding and dancing.

The control group participants reported more varied levels of physical activity during the 12 weeks. One person self-reported increasing community-based activities including walking; one self-reported increasing, by a small amount, their 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 received physiotherapy at some stage during the 12 weeks: two attended outpatient therapy and one was admitted for two weeks to a rehabilitation unit for inpatient therapy.

7.6 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]. The program was feasible for the self-selected, independently-ambulant stroke survivor participants, with no serious adverse events and no withdrawals. The intervention design enabled stroke survivors from regional and rural, as well as metropolitan communities, to participate.

The intervention was feasible, with all participants completing the program and no adverse events during the 12-week intervention period. Tolerance of physical activity is variable, and initially there may be some merit to getting those least active to be less sedentary rather than more physically active when changing activity behaviour [15]. All our 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 [6,24]. Our intervention was designed to overcome the barriers of travel [38] and program cost [38] while enhancing self-efficacy [39]; to provide ongoing professional support [39] while minimising the requirements on health resources; and to be sustainable beyond the end of the 12-week program.

The 11 to 16% increases in absolute VO_{2peak} achieved via our individually-tailored program, with once-weekly telephone or email clinician support, is comparable to more resource-intensive programs, which resulted in 10-15% improvements in VO_{2peak} [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, they required participants to attend a centre 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 are exciting as they 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. This session provided participants with evidence that they could exercise for a reasonable period of time (all performed for at least 10 minutes) using activities that they had identified they were interested in (client-centred). The session gave them an experience of interval training and how to vary the intensity, and how to use a variety of activities. The circuit training approach appeared to minimise muscle fatigue. Most participants reported that they were more confident to exercise after undertaking this supervised session.

The VO_{2peak} results during baseline testing were similar to those identified in systematic reviews of cardiorespiratory fitness after stroke [1,2] and highlight the low levels of fitness of people after stroke. The mean value for VO_{2peak} of our participants at baseline fell in the 15-18 mL/kg/min range that has been suggested as being a minimum requirement for independent living [40]. These values are well below published values for healthy people aged 60-69 years (men 33 ± 7.3 and women 27 ± 4.7 mL/kg/min) [41]. Improving

cardiorespiratory fitness reduces the percentage of VO_{2peak} required to undertake activities of daily living, thus increasing submaximal exercise tolerance and endurance [6].

The ability to “get out and about” in the community is considered very important by stroke survivors [42]. It can reduce isolation and dependence while increasing social participation and physical activity [43]. Walking endurance and speed are key components of community ambulation [44]. In our study the intervention group increased the distance walked during the 6MWT by 66m, to 493m. This distance is similar to the longest distances recorded by studies included in a recent systematic review [28] and is approaching the distance of healthy people aged 60-69 years (men 560m, women 505m) [45]. An improvement of >50m is considered clinically significant [46]. These results highlight the potential for interventions to assist community-dwelling stroke survivors to continue to improve walking endurance, even months after stroke. The change observed was similar to those reported in a number of meta-analyses investigating the impact on walking distance of: gait-orientated training (41m) [47], cardiorespiratory fitness training involving walking (47m) [9] and mixed training involving walking (31m) [9] but only half that of more intensive cardiovascular conditioning (111m) [10]. In our study, 7/10 (70%) of the intervention group used walking as an activity compared to 2/10 (20%) of 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.

Our results of improved walking distance but not self-selected walking speed are consistent with the meta-analysis of Mehta et al [10] who examined

cardiovascular conditioning. At baseline, our cohort would already be considered community ambulators, with self-selected walking speed >0.8 m/s [48]. The values were similar to healthy people aged 60-69 years (men 1.3 m/s, women 1.2 m/s) [49,50]. Interestingly participants were able to maintain their fast walking speed, measured over 10m, to complete a one-minute stage during the SWT. The ability to sustain speed is important for community activities such as safely crossing the road [51].

The distribution in data and the change in scores for individual participants (figure 1) illustrate a number of interesting patterns in the data. Eighty percent of participants in the intervention group improved their 6MWT VO_{2peak} and 78% of control group participants had lower levels of cardiorespiratory fitness (figure 1a). 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 (figure 1b, e-g). This suggests that such a program may particularly benefit those with the most to gain.

Strengths and limitations

A major strength of this 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 centre-based interventions in metropolitan settings. Our VO_2 results (peak and change) were consistent across the three exercise tests we used. The lack of statistically significant change for the SWT and cPXT may be due to 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 [20]. We used the TIDieR checklist and guide [52] to report the intervention. The study was limited by the small number of self-selected participants and that it was not a randomised controlled trial. For this pilot study there was no blinding of assessors to group allocation. However, standardised 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 challenge of measuring exercise dose accurately in the real-world has been recognised, as has the potential for emerging, low-cost wearable technology in measuring activity over time at home [11]. The use of this technology would need to be considered for a larger trial.

7.7 Conclusion

The results of this 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 innumerable health benefits to stroke survivors. This study demonstrates a promising, resource-efficient intervention to improve the physical activity levels of community-dwelling stroke survivors and warrants further investigation in a large multicentre, randomised trial using wearable technology to examine dose-response relationships.

7.8 Appendix 1

Summary of activities included in the home-exercise manual

Activity	Equipment	Description	Progressions
Sit to stand	Chair with/ without arm rests	Sit to stand, aiming to increase speed reduce upper limb	↑ speed, number of repetitions ↓ use of arm rests, seat height
Fast/ self-selected paced walking	Track eg hallway, length of drive way, between telegraph poles	Self-selected pace	↑ walking speed or jog
Balance	Line on floor	Standing feet together, standing 1 leg, eyes open eyes closed, walking along line (normal step length or heel-toe)	Side stepping +/- squats, side stepping crossing feet, backwards walking
Step	Block between 5 and 25cm high	Up and over forwards Up and over sideways Stepping up forward and down backwards Use table/ bench for balance if required	↓ use of table/ bench ↑ speed, Add in arm activities Start at a lower height and gradually build up
Squat	Chair or bench	Perform squat Start with small range of movement Use bench or chair for balance if required	↑ increase depth of squat Hold arms out in front ↑ speed, number of repetitions
Side stepping around a table	Table or bench	Side-step around the table- to both left and right sides Hold onto table/ bench for balance if required	Take wider steps Add in a squat ↑ speed, number of repetitions
High knee walking	Track eg hallway	March on the spot March up and down a walkway Start with small range of movement Hold onto table/ bench for balance if required	Bring knees up higher Add in simultaneous arm activities ↑ speed, number of repetitions
Leg side raises	Chair or bench	Hip abduction- left and right Hold onto chair/ bench for balance if required	↑ range of motion Add weight around ankle ↑ speed, number of repetitions

Legend: ↑= increase, ↓= decrease

Appendix 2 Data for Individual participants for the 6MWT and cPXT (absolute VO₂peak and performance measures)

	6 Minute Walk Test						Cycle Progressive Exercise test					
	Absolute VO ₂ peak (mL)			Distance walked (m)			AbsoluteVO ₂ peak (mL)			Workload (W)		
	Baseline	12 weeks	Change	Baseline	12 weeks	Change	Baseline	12 weeks	Change	Baseline	12 weeks	Change
Intervention Group												
1	1074	1390	315.67	294	415	121	Unable to do test					
2	804	1045	241.12	202	347	145	Unable to do test					
3	1309	1387	77.63	406	494	88	1458	1148	-310.1	125	100	-25
4	972	1322	349.51	455	559	104	876	1086	210.46	75	75	0
5	1313	1768	455.73	598	641	43	1659	1777	117.84	150	150	0
6	981	998	16.27	330	413	83	976	984	7.91	100	100	0
7	1763	1817	54.1	428	553	125	1665	1878	213.58	100	150	50
8	1418	1392	-25.52	524	507	-17	1332	1308	-24.25	100	75	-25
9	1156	1590	433.21	552	567	15	1379	1835	456.48	100	150	50
10	891	788	-103.6	481	439	-42	698	802	103.26	50	75	25
Control Group												
1	1002	967	-34.37	338	301	-37	Unable to do test					
2	1278	1208	-69.54	489	491	2	1267	1068	-199.3	100	100	0
3	1445	1299	-146.1	360	381	21	1475	1185	-290.4	100	100	0
4	919	1112	192.2	433	423	-10	Unable to do test					
5	1051	1006	-45.34	600	619	19	1375	1315	-59.83	125	125	0
6	1385	1371	-14.24	520	481	-39	1264	1229	-35.13	125	100	-25
7	Equip	1229	-	593	609	16	Equip	1446	-	175	175	0
8	1388	1303	-85.03	449	480	31	485	Unable to do	-	75	Unable to do	-
9	1605	1858	253.05	477	561	84	1467	1501	33.65	125	150	25
10	1096	1021	-75.16	305	363	58	1009	958	-51.91	100	75	-25

Equip= no data due to equipment issues

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CHAPTER 8: DISCUSSION AND CONCLUSION

8.1 Summary of key findings

This project has contributed important findings to the field of assessing and training cardiorespiratory fitness after stroke. Our findings have implications for clinical practice and for further research. We have identified:

- via systematic review and meta-analysis that even modest doses of interventions that include an aerobic component can improve cardiorespiratory fitness by 10-15%. The type of activity seems less important than that it has an aerobic component (Chapter 4)
- independently ambulant stroke survivors achieve similar peak oxygen consumption (VO_{2peak}) values during the Six-Minute Walk Test (6MWT) and Shuttle Walk Test (SWT) as the cycle progressive exercise test (cPXT). VO_{2peak} for each test is highly correlated with its associated performance measure. All three tests are feasible in this population (Chapter 5)
- task-specific and ergometer activities can be performed by stroke survivors at an intensity and for a duration that can improve cardiorespiratory fitness. Interval training on a circuit of task-specific and ergometer workstations is a safe and feasible approach for stroke survivors to accumulate a dose of exercise sufficient to produce cardiovascular benefits (Chapter 6)
- an individually-tailored, home- and community-based intervention with minimal face-to-face support is a safe and feasible way for ambulant stroke survivors to increase their levels of physical activity. It can result in similar levels of improvement in cardiorespiratory fitness as more

resource-intensive programs and can improve distance walked in the 6MWT. The program may particularly benefit those with the most to gain in improving walking distance, fast walking speed, fatigue, depression, and health-related quality of life (Chapter 7).

8.2 Findings from the systematic review with meta-analysis

The potential benefits for incorporating cardiorespiratory fitness into post-stroke management were highlighted in the systematic review with meta-analysis [1] (Chapter 4). People after stroke are very unfit compared to non-stroke people of a similar age and sex. The meta-analysis indicated cardiorespiratory fitness improved with the interventions trialled despite none of the studies meeting exercise guideline recommendations of 30 minutes of moderate intensity activity on most days of the week. There appears to be great scope to improve cardiorespiratory fitness for people after stroke. Improved fitness could result in improved physical function and health-related quality of life, decreased levels of depression and fatigue, and reduced chance of a subsequent stroke.

The effects of “time since stroke” on cardiorespiratory fitness were unable to be determined as study level data did not allow for the planned meta-analysis. If individual participant data were available for all 1090 people enrolled in the 28 included studies it may have been possible to explore the relationship. Two potential ways to overcome this are pooling patient-level data for meta-analyses [2] or establishing an international register for research groups to share data on cardiorespiratory fitness assessment and training after stroke.

Studies with small sample sizes can have limitations in the findings [3]. Studies included in the systematic review used sample sizes, ranging from 10 [4] to 113 [5] with 61% of the studies enrolling less than 50 participants. A large data set that includes people after stroke with a range of participant and stroke characteristics and outcomes could be used to answer questions that smaller studies cannot.

In my review the presence or absence of adverse events was not always reported. If the adverse events were included as a data item for each participant on an international register the risks of testing and interventions could be examined in more detail.

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Since the publication of my systematic review a number of reviews have been published regarding cardiorespiratory fitness after stroke. In one review it was identified five types of ergometers have been used to date for testing cardiopulmonary fitness in people after stroke [6]. The authors reported that although included studies referred to established exercise testing guidelines, these were not or were incorrectly adhered to. The review outlines suggestions to guide the conducting and reporting of maximal cardiopulmonary testing in stroke survivors. Outermans et al [7] identified VO_{2peak} and distance walked had moderate correlations, however the included studies had low methodological quality. Ammann et al [8] identified that to improve the utility and reproducibility of exercise programs after stroke, studies should better report prescribed

exercise interventions, based on the FITT (frequency, intensity, time, type) components and patients' adherence to this prescription. A review by Billinger et al [9] outlines how exercise prescription using the FITT principles for people after stroke can be applied across the continuum of care. Morris et al found that tailored home exercise was the only predominantly exercise-based intervention to demonstrate higher physical activity participation at 12 months for stroke survivors [10]. This finding highlights the potential benefit of the HowFITSS? intervention. The growing body of knowledge can inform how to improve cardiorespiratory fitness assessment and training in clinical practice and research.

8.3 Findings from the studies using the How Fit Is The Stroke Survivor (HowFITSS?) cohort of participants

The findings from the HowFITSS? studies (Chapters 5-7) demonstrate that it may be feasible to incorporate cardiorespiratory fitness assessment and training into existing post-stroke management. In Australia it appears that therapy time is often limited and tends to focus on functional recovery. Stroke survivors are often discharged home with little if any access to ongoing therapy [11]. Effective and resource-efficient models of service provision for improving the recovery of stroke survivors are required. My findings have the potential to contribute to these models.

I have shown that the performance measures of the 6MWT, SWT and cPXT can be used as proxies for cardiorespiratory fitness. All three tests are feasible and safe to undertake with independently-ambulant stroke survivors. The tests have the potential to be used in most clinical settings, even where resources

(clinicians, equipment and time) are scarce. Unfortunately HR_{peak} did not correlate well with VO_{2peak} , so this may not be a useful measure. However, the VO_{2peak} and performance measures for each of the three tests were highly correlated for the independently-ambulant cohort. This correlation is clinically important and useful; change in performance is likely to reflect a change in cardiorespiratory fitness and can indicate the effectiveness of a training program. While the performance measures correlated highly with VO_{2peak} there may be a cut-point of performance where the relationship does not hold true. By examining a larger pool of individual data, as discussed above, relationships between cardiorespiratory fitness and performance measures could be further investigated.

The results from the circuit of workstations exercise session demonstrated that if clinicians extend their focus to include exercise intensity during therapy sessions a cardiorespiratory fitness stimulus may be provided. A key component of the circuit session was the use of an interval training approach. Interval training is an emerging approach for exercise training after stroke. To date exercise regimes using a single ergometer and high and low intensity intervals of set duration and exercise intensity have been tested [12-16]. I have provided evidence that an alternative option of individualising the training session in terms of length and intensity of intervals and using activities that are typically used in therapy enables stroke survivors to sustain activities at a moderate or higher intensity. The choice of task-specific and ergometer activities included in the circuit session was to simulate what could be done at home, in a community facility or in a therapist-led rehabilitation program.

The individually-tailored, home- and community-based program trialled provides a model that can incorporate exercise into the everyday life of stroke survivors while limiting demands on the health system. The program was structured to incorporate activities that each participant wished to pursue and to overcome the need to travel to a centre. The program did not use regular face-to-face contact. Instead it used an initial practice exercise session on a circuit of workstations (Chapter 6) with subsequent support provided via weekly email/ phone calls. It builds on the growing home- and community-based exercise options available to engage stroke survivors in regular physical activity. Other models include partnering with community-based exercise providers [17]; linking with stroke recovery groups [18]; and supervised, once-a-week programs with a concurrent home-based exercise program such as the FAME program [19,20].

My 12-week exercise program may not be appropriate for all stroke survivors but it appears there is at least a subgroup that this program is suitable and effective for. This group may include people who were already active before their stroke and wish to re-engage in physical activity or those who were inactive but are now motivated to change their behaviour. If these people can be readily identified my model could be offered as an exercise strategy. A self-selected cohort were recruited for HowFITSS?. In future studies it would be beneficial to determine the characteristics of those who declined and why they chose not to participate. This may help us to target the program or make changes to make it more appealing to a larger number of stroke survivors.

Providing support and feedback without face-to-face contact with the participants was a key component of the 12-week home- and community-based program. A simple system of emails/ phone calls was used. Tele-rehabilitation

is emerging as a potential model of care for providing support for participants, whether they live in metropolitan, regional, rural or even remote settings [21,22]. The wearable technology that is emerging may also assist in providing feedback and motivate stroke survivors to be more physically active.

8.4 Fatigue as an issue after stroke

Post-stroke fatigue (PSF) and exertion fatigue were issues for our HowFITSS? participants. Tseng et al have identified that PSF and exertion fatigue are two different constructs after stroke [23].

All of the HowFITSS? participants reported that PSF was a problem limiting their recovery. This was despite the cohort having minimal mobility deficits; they were community-dwelling stroke survivors who were independent in activities of daily living including walking and most had resumed many of their pre-stroke activities including returning to work or university study. For many decades it was considered that fatigue was a symptom of depression, and while a third of stroke survivors who have depression have PSF, fatigue has been observed in 14 to 50% of non-depressed people after stroke [24]. PSF and depression after stroke have been shown to be associated in 45 of 48 studies included in a recent review, however the relationship between the two is not well understood [24]. There is also potential for confounding in the tests for the two. This is highlighted in the fatigue and depression measures we used in HowFITSS?. Half of the Fatigue Assessment Scale questions (questions 6 to 10) may be indicative of depression as well as fatigue [25]. Questions 4 and 7 of the Patient

Health Questionnaire ask about fatigue-related symptoms of poor concentration and low energy levels.

Participants with the worst levels of fatigue and depression in the intervention group of the home- and community-based study had reduced levels of both after the program. These results suggest that it is plausible that exercise programs can have a positive influence on PSF [26], and that reductions in depressive symptoms are evident immediately after exercise programs end [27], at least for the participants with higher levels of depression. Physical activity levels may influence PSF and depression, and vice versa. Inclusion of measures of PSF and depression are warranted in research investigating cardiorespiratory fitness after stroke to help to improve our understanding of the relationships.

Overcoming exertion fatigue is a possible reason three-quarters of our participants were able to exercise for ≥ 29 minutes when undertaking the circuit of workstations. Exertion fatigue has an acute and rapid onset, lasts for a brief period and has a short recovery period [23]. For stroke survivors it can limit their ability to continue activity, which was evident during the baseline cPXT. Exertion fatigue contributed to 8 of 20 participants (40%) ceasing the test (Chapter 5). In contrast only 2 of the 13 participants (15%) stopped their circuit exercise session due to exertion fatigue (Chapter 6). Periods of recovery (active or rest) during exercise is a key component of interval training [9,28,29]. To enable participants to sustain activity the exercise intensity and duration of the high and low intensity intervals were adjusted to suit each individual's exercise response during every workstation.

The short duration and quick recovery typical of exertion fatigue was observed during our assessment sessions. A rest of approximately 15 minutes between the exercise tests appeared sufficient for participants to recover and move onto the next test. This observation highlights that bouts of exercise may help overcome exertion fatigue.

The use of interval training and exercising in bouts with rest periods between bouts is relevant for clinicians. Structuring therapy sessions and home-programs to include interval training and bouts of exercise may be effective in enabling stroke survivors to accumulate exercise throughout the day to reach the recommended 30 minutes of exercise a day.

8.5 The challenges of measuring exercise dose

In my systematic review I identified that while the prescribed dose is often stated for interventions, the dose received is often poorly reported, particularly in terms of exercise intensity [1]. These findings have since been supported by those of Ammann et al [8]. While the changes in cardiorespiratory fitness of HowFITSS? participants could be determined the dose of exercise they undertook was not able to objectively measure, but relied on self-report. Most of the participants in the community-based study could recall the duration, frequency and type of exercise they had undertaken but exercise intensity was almost impossible to ascertain. To gain a better understanding of the change in cardiorespiratory fitness produced by different doses of exercise after stroke the dose received needs to be measured. The emerging wearable device technology that is relatively low-cost (less than AU\$400 per unit) has great

potential for assessing dose. Wearable devices can capture physical activity related data including duration, frequency, intensity, energy expenditure, patterns of activity and rest/ sleep, as well as step and activity counts [30]. They can provide an insight into whole-of-day, whole-of-week or even whole-of-month activity. The dose-response relationship between physical activity and cardiorespiratory fitness could be investigated further using wearable technology.

8.6 Implications

My HowFITTs? study has Implications for future research and clinical practice.

I have shown in a controlled trial with a small, self-selected sample of stroke survivors with minimal mobility issues that testing and training in community settings is feasible and can improve fitness and function. These findings provide support to the growing evidence base that cardiorespiratory training should be incorporated into post-stroke management. While my small sample size and study designs may limit the generalisability of the findings, the studies were designed to provide preliminary data for a more definitive trial. Future studies in a similar population need to be conducted with a more rigorous methodology, such as a randomised controlled trial or a cluster randomised trial that is sufficiently powered.

Strategies to increase the cardiorespiratory fitness of more disabled stroke survivors, many of who are admitted for rehabilitation, are also required.

Environmental enrichment strategies do not appear to improve physical activity levels [31]. Studies investigating strategies to incorporate cardiorespiratory

fitness training are required. My findings that ergometer and task-specific activities can be performed at level sufficient to improve cardiorespiratory fitness may help to guide therapy and research study designs. Testing oxygen consumption during inpatient therapy activities, such as walking, side-lying to sitting, sit to stand, balanced standing with reaching, with an emphasis placed on exercise intensity may show if more disabled stroke survivors can exercise at a level sufficient to train cardiorespiratory fitness.

While no serious adverse events occurred during our study there were some safety issues. These included poor balance on turning that precluded the SWT being performed by one participant, lower limb musculoskeletal issues that could have been aggravated on the cycle ergometer and a minor cardiac abnormality during a cPXT. To minimise the risks to stroke survivors participating in exercise a number of strategies can be used. Medical clearance can be gained before enrolling in testing or exercise programs. A thorough medical history could help prevent aggravation of pre-existing conditions, such as musculoskeletal pain and to prevent falls and identify risk for cardiac events.

We were able to monitor cardiac rhythm throughout testing and exercise on the circuit of workstations, however this is not always feasible or necessary.

Exercise testing can be a difficult issue. High false positive rate leads to risk of needlessly stopping exercise and leading to a string of potentially unnecessary (and occasionally dangerous) additional tests. If indicated by the person's history or presentation a PXT should be performed [32]. If a PXT is not indicated or is not available exercise training within the stroke survivor's capabilities should still be undertaken [32].

8.7 Conclusions

My thesis studies have contributed significantly to the evidence base by investigating clinically-applicable ways to assess and train cardiorespiratory fitness after stroke. I have shown that: interventions with an aerobic component, including the individually-tailored, home- and community-based program, can improve cardiorespiratory fitness after stroke by 10-15%; the SWT, 6MWT and cPXT are feasible with independently ambulant stroke survivors; the associated performance measures of each test have the potential to be proxy measures of cardiorespiratory fitness; activities typically used in therapy have the potential to be undertaken at an intensity and duration that can improve cardiorespiratory fitness; interval training and exercising in short bouts may overcome exertion fatigue and enable stroke survivors to accumulate exercise; and that the 12-week exercise intervention trialled is a feasible approach for stroke survivors. My studies have provided preliminary data to inform the design for a future large, multicentre randomised controlled trial to further test my innovative intervention. The individually-tailored, home- and community-based program has shown potential to enhance post-stroke recovery by improving cardiorespiratory fitness, walking ability and psychosocial function for stroke survivors living in metropolitan, regional and rural settings.

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