

# The use of aerobic exercise training in improving aerobic capacity in individuals with stroke: a meta-analysis

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**Objective:** To determine whether aerobic exercise improves aerobic capacity in individuals with stroke.

**Design:** A systematic review of randomized controlled trials.

**Databases searched:** MEDLINE, CINAHL, EMBASE, Cochrane Database of Systematic Reviews and Physiotherapy Evidence Database were searched.

**Inclusion criteria:** Design: randomized controlled trials (RCTs). Participants: individuals with stroke. Interventions: aerobic exercise training aimed at improving aerobic capacity.

**Outcomes:** Primary outcomes: aerobic capacity (peak oxygen consumption ( $V_{O_2}$ ), peak workload). Secondary outcomes: walking velocity, walking endurance.

**Data analysis:** The methodological quality was assessed by the PEDro scale. Meta-analyses were performed for all primary and secondary outcomes.

**Results:** Nine articles (seven RCTs) were identified. The exercise intensity ranged from 50% to 80% heart rate reserve. Exercise duration was 20–40 min for 3–5 days a week. The total number of subjects included in the studies was 480. All studies reported positive effects on aerobic capacity, regardless of the stage of stroke recovery. Meta-analysis revealed a significant homogeneous standardized effect size (SES) in favour of aerobic exercise to improve peak  $V_{O_2}$  (SES 0.42; 95% confidence interval (CI) 0.15–0.69;  $P = 0.001$ ) and peak workload (SES 0.50; 95% CI 0.26–0.73;  $P < 0.001$ ). There was also a significant homogeneous SES in favour of aerobic training to improve walking velocity (SES 0.26; 95% CI 0.05–0.48;  $P = 0.008$ ) and walking endurance (SES 0.30; 95% CI 0.06–0.55;  $P = 0.008$ ).

**Conclusions:** There is good evidence that aerobic exercise is beneficial for improving aerobic capacity in people with mild and moderate stroke. Aerobic exercise should be an important component of stroke rehabilitation.

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## Introduction

Stroke is a major cause of chronic disability.<sup>1</sup> Studies have indicated an increasing incidence of stroke, particularly in elderly people.<sup>2</sup> On the other hand, the stroke mortality rate has been declining,<sup>2</sup> which translates into a larger number of chronic stroke survivors. Many stroke survivors continue to live with residual physical impairments (i.e. reduced mobility, poor balance and muscle weakness), which may lead to physical inactivity and a sedentary lifestyle.<sup>3–5</sup>

Physical activity level is positively related to aerobic capacity,<sup>6–10</sup> which is the product of the capacity of the cardiorespiratory system to supply oxygen (i.e. cardiac output) and the capacity of the skeletal muscle to utilize oxygen (i.e. arterial–venous oxygen difference).<sup>11</sup> Therefore, it is not surprising that sustained physical inactivity (deconditioning) induces a reduction in aerobic capacity.<sup>12</sup> Peak oxygen consumption ( $\dot{V}O_2$ ), the criterion measure for aerobic capacity, is poor in the stroke population. Peak  $\dot{V}O_2$  in individuals with stroke has been found to be as low as 50–70% of the age- and sex-matched value in sedentary individuals.<sup>13,14</sup>

It is common that individuals with acute stroke have low peak  $\dot{V}O_2$ , indicating that these individuals are unfit before they have the stroke.<sup>14</sup> Indeed, poor aerobic fitness is an important risk factor for stroke.<sup>15</sup> Low aerobic fitness has also been related to an increased risk of various forms of cardiovascular disease in man.<sup>16–18</sup> Therefore, it is not surprising that a large proportion (up to 75%) of stroke patients have some form of cardiovascular disease.<sup>19</sup> Additional decline in aerobic fitness resulting from physical inactivity in stroke survivors may further increase the risk of cardiovascular disease in these individuals above that associated with stroke itself. Moreover, low aerobic fitness is a significant determinant of poor bone health (i.e. osteoporosis) in individuals with chronic stroke.<sup>20</sup> Therefore, improving aerobic capacity may be essential in prevention of secondary diseases due to lack of fitness in the stroke population. Prevention of secondary disabling conditions is a major component of health promotion for people with chronic disabilities and is an emerging practice in rehabilitation.<sup>21,22</sup>

Low aerobic capacity may also pose limitations on daily function of the individual. Peak  $\dot{V}O_2$  has been positively related to functional performance in elderly people.<sup>23</sup> Individuals with low peak  $\dot{V}O_2$  values work at a higher relative exercise intensity to complete the same daily functional activities, when compared with their more fit counterparts.<sup>24</sup> The reduction in fitness reserve can contribute to reduced activity endurance, which is the most striking area of difficulty for chronic stroke survivors in the community.<sup>5</sup> Previous studies have also indicated that a critical level of aerobic capacity must be met in order to function independently.<sup>25,26</sup> For example, Cress *et al.*<sup>25</sup> found that a peak  $\dot{V}O_2$  of 20 mL/kg/min was needed for independent living for adults aged 65–97 years. The low peak  $\dot{V}O_2$  values found in individuals with stroke suggest that many stroke survivors do not meet the minimum fitness level required for independent living.<sup>13,14,27</sup> Therefore, in addition to disease prevention, enhancing aerobic capacity in individuals with stroke may also have beneficial effects on promoting functional abilities and independent living.

Given the potentially adverse health consequences of reduced aerobic capacity in individuals with stroke, there has been an increasing recognition of the importance of aerobic exercise training in this population. This increased awareness is reflected in the emergence of research studies on aerobic exercise in stroke over the past decade. However, this trend is not reflected in clinical practice as a recent study showed that the cardiovascular stress of a contemporary stroke rehabilitation programme is much too low to induce a positive aerobic training effect.<sup>28</sup>

Given the mounting research evidence on the effects of aerobic exercise training in stroke and the belief that clinical practice should follow research-based evidence, we feel that it is timely to perform a systematic review on aerobic training in individuals with stroke. A couple of systematic reviews on physical therapy trials in stroke have been published recently.<sup>29,30</sup> This systematic review, however, will provide specific information on aerobic training programmes and their efficacy in improving aerobic capacity in individuals with stroke. This review is intended to aid clinicians in translating the knowledge to their daily clinical practice.

## Methods

### Definition of review questions

We systematically reviewed the literature regarding aerobic exercise programmes in people with stroke to address the following questions: (1) Does aerobic exercise training improve aerobic capacity in individuals recovering from a stroke? (2) How much improvement in aerobic capacity can be obtained? and (3) What are the specific exercise protocols used to induce an aerobic training effect?

For the purpose of this systematic review, both peak  $\dot{V}O_2$  and peak workload obtained during a graded exercise test on a cycle ergometer or treadmill were used to indicate aerobic capacity. Peak  $\dot{V}O_2$  (mL/kg/min) measures the peak rate of oxygen consumption achieved and is a criterion measure for aerobic capacity.<sup>11</sup> Peak workload ( $W$ ) is also a useful indicator of aerobic capacity since it is directly related to peak  $\dot{V}O_2$ .<sup>11</sup>

### Definition of inclusion and exclusion criteria

The inclusion criteria were: (1) research studies on the effects of aerobic exercise training in individuals with stroke, (2) studies which used peak  $\dot{V}O_2$  or peak workload as outcome measures to indicate aerobic capacity, (3) randomized controlled trials (RCTs). Aerobic exercise training is defined as a structured exercise programme that involves the use of large muscle groups for extended periods of time in activities that are rhythmic in nature, including but not limited to walking, stepping, running, swimming, cycling and rowing.<sup>11</sup>

Exclusion criteria were: (1) doctoral dissertations, (2) reports published in books, and (3) reports published in conference proceedings. These exclusion criteria were used because books are considered secondary sources and reports in doctoral dissertations/conference proceedings are often not peer-reviewed. For the purpose of this systematic review, acute and subacute stages of stroke recovery were defined as 0–1 month, and 1–6 months after the onset of stroke, respectively. A poststroke duration of more than six months was considered chronic.

### Search strategy: location and selection of studies

The following electronic databases were searched online through the local university's library system:

MEDLINE (1966–July week 2, 2005), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1982–July week 3, 2005), and the Excerpta Medica database (EMBASE) (1980–week 29, 2005). The specific search strategy for the MEDLINE database is described in Appendix 1. An equivalent search strategy was used for the CINAHL and EMBASE databases, following the same logic as the MEDLINE search strategy, with a few modifications due to differences in indexing and syntax in different databases. In addition, the Cochrane Library Database of Systematic Reviews (2005, issue 2) and Physiotherapy Evidence Database<sup>31</sup> were also searched online. For these databases, the keyword 'stroke' was entered to search relevant articles. All of the databases were last searched in July 2005. For further iterations, manual searches were performed on the reference list of each selected paper.

### Qualitative assessment

All selected RCTs were evaluated by using the PEDro scale. The PEDro scale was originally developed to assess the methodological quality of physical therapy RCTs on the Physiotherapy Evidence Database.<sup>31</sup> It is an 11-item scale, in which the first item relates to external validity and the other 10 items assess the internal validity of a clinical trial. One point was given for each satisfied criterion (except for the first item, which was given a YES or NO), yielding a maximum score of 10. The higher the score, the better the quality of the study (9–10: excellent; 6–8: good; 4–5: fair; < 4: poor).<sup>32</sup> A point for a particular criterion was awarded only if the article explicitly reported that the criterion was met. The reliability of the PEDro scale has been demonstrated.<sup>33</sup> For those studies that had been listed on the Physiotherapy Evidence Database website at the time of the search, the PEDro score was independently determined by two individuals, who are physical therapists and have extensive experience in physical therapy research methods and are not involved in any of the studies reviewed. A third rater was consulted if consensus was not reached.

### Quantitative analysis

Since the purpose of this systematic review was to evaluate the effects of aerobic exercise on improving aerobic capacity in individuals with

stroke, the primary outcome variables of interest were peak  $\dot{V}O_2$  and peak workload. For each selected study, the mean change scores (postintervention scores – preintervention scores) in peak  $\dot{V}O_2$  and peak workload in experimental and control groups were extracted. The baseline standard deviations (SDs) in experimental and control groups were used to calculate the pooled population SD.<sup>34</sup> The baseline means and SDs were requested from the respective authors if they were not reported in the article.

The standardized effect size (SES) for each study was established by computing the difference between mean change scores of the experimental and control groups divided by the pooled population SD.<sup>34</sup> Since there was a tendency for the SES to overestimate the pooled effect size in studies with a small sample size, a correction was implemented to obtain the unbiased SES.<sup>34</sup> The 95% confidence interval (CI) for the SES was also computed. The SESs and 95% CIs were calculated using a custom spreadsheet (Microsoft Excel for Windows XP). Additionally, since many of the selected studies measured walking performance and ambulation is a key priority in stroke rehabilitation, the same quantitative analysis was also performed for walking velocity and walking endurance.

A meta-analysis was then performed for each set of SESs. Q statistic was used to determine whether there was significant heterogeneity. If significant heterogeneity was found, a random effects model was used.<sup>35</sup> Otherwise, a fixed effects model was applied.<sup>36</sup> The size of the pooled SES from meta-analysis was defined as small (0.2–0.5), medium (0.5–0.8) or large ( $\geq 0.8$ ).<sup>37</sup> The meta-analyses were performed using an online software program (Meta-analysis software, version 5.2). For all outcome variables of interest, the critical value for rejecting the null hypothesis (i.e. there is no evidence to support the use of aerobic exercise training in individuals with stroke) was set at 0.05.

## Results

Based on the information in the title and abstract, 29 papers were identified as being potentially relevant for this systematic review. A total of 20 articles did not meet the criteria and were excluded

from further analysis.<sup>38–57</sup> Of these, aerobic capacity was not measured in 18 articles.<sup>38–55</sup> One study did not use random allocation of subjects.<sup>56</sup> Carr and Jones<sup>57</sup> did not have a true control group which did not undergo aerobic exercise training. In their study, one group underwent aerobic exercise training whereas another group underwent aerobic and strength training, making it impossible to evaluate the effects of aerobic training.

A total of nine articles fulfilled all criteria and were selected for this review.<sup>58–66</sup> Of these, two reported duplicate results: da Cunha Filho *et al.*<sup>60</sup> used the same participants as da Cunha *et al.*<sup>61</sup> but used different outcome measures. Another article<sup>64</sup> was a six-month follow-up report of Katz-Leurer *et al.*<sup>63</sup> In summary, a total of nine articles (seven RCTs) were selected for this systematic review. The main characteristics of each selected study are described in Table 1.

## Subjects

The number of subjects included in each study ranged from 13 to 157. However, in Bateman *et al.*,<sup>59</sup> only 70 out of the 157 brain-injured subjects had a diagnosis of stroke. Subjects in acute,<sup>60,61,63</sup> subacute<sup>62</sup> and chronic<sup>58,65,66</sup> stages of recovery were used in two, one and three studies, respectively. Bateman *et al.*,<sup>59</sup> however, used subjects in all stages of recovery. In all selected studies, subjects had mild or moderate deficits in motor function and functional abilities. Examining the inclusion and exclusion criteria revealed that individuals in class C (moderate-to-high risk for cardiac complications during exercise; medical supervision required for all exercise sessions) and class D (unstable disease with activity restriction; no conditioning exercise recommended) according to the American Heart Association (AHA) Risk Stratification Criteria were excluded.<sup>11,67</sup>

## Exercise training protocol

Cycle ergometer was the most common method used for aerobic training (four studies).<sup>58,59,62,63</sup> Treadmill walking was employed in one study.<sup>60,61</sup> One study used a combination of stepping, brisk walking and repeated sit-to-stand.<sup>66</sup> In Chu *et al.*,<sup>65</sup> subjects performed aerobic exercises in the water. The exercise protocols described in the reviewed studies are similar to the guidelines recommended by American College of Sports

**Table 1** Characteristics of randomized controlled trials on aerobic exercise training in individuals with stroke

Study	Subjects	Cardiovascular exclusion criteria	Exercise training protocol	Results <sup>a</sup>
Potempa <sup>58</sup>	42 subjects Chronic Age range: 43–72 Moderately impaired (mean FMA: 177/226)	Unstable cardiac disease Peripheral vascular disease Pulmonary disease Uncontrolled HTN Insulin-dependent diabetes.	Mode: 10 weeks of cycle ergometer exercise Intensity: 30–50% maximal workload, ↑ as tolerated (week 1–4), maintain the highest load achieved at end of 4 weeks (week 5–10) Duration: 30 min per session Frequency: 3 × /week  Control group: Passive range of motion	Peak $\dot{V}O_2$ : + (↑13.3%) Peak workload: + (↑44.3%) Peak minute ventilation: + Exercise time: +
Bateman <sup>59</sup>	157 subjects Brain injury of any cause in all stages of recovery (stroke: 44.6%) Mean age: 43.2 Moderately impaired (mean BI: 14/20)	Known cardiac disease or other comorbidities	Mode: 12 weeks of cycle ergometer exercise Intensity: 50 rpm, 60–80% APMHR Duration: 30 min per session Frequency: 3 × /week  Control group: Relaxation therapy.	At week 12: Peak workload ( $\log_e$ ): + (↑7.3%) RMI: 0 10-m walking speed: 0 BI: 0 FIM: 0 NEADL: 0 Fatigue questionnaire: 0
da Cunha <sup>60,61</sup>	13 subjects Acute Mean age: 58.4 Moderately impaired (National Institute of Health Stroke Scale: 4.3/15)	Recent myocardial infarction (< 4 weeks) Cardiac bypass surgery with complications Uncontrolled conditions (e.g. diabetes > 250 mg/dL, HTN > 190/110 mmHg)	Mode: 3 weeks of treadmill walking with body weight support Intensity: unknown Duration: 20 min/session Frequency: 5 × /week  Control group: Regular therapy (usual gait training without treadmill walking with body weight support)	At week 24: Peak workload significantly declined in the experimental group  Peak $\dot{V}O_2$ : + (↑34.8%) Peak workload: 0 Total cycling time: 0 FAC: 0 FIM (locomotion): 0 Gait speed: 0 Walking distance in 5 min: 0 Gait energy expenditure: 0 Gait energy cost: 0

Table 1 (Continued)

Study	Subjects	Cardiovascular exclusion criteria	Exercise training protocol	Results <sup>a</sup>
Duncan <sup>62</sup>	100 subjects Subacute Mean age: 70 Moderately impaired (mean FMA leg score: 24/34)	Uncontrolled HTN New York Heart Association III/IV heart failure Serious cardiac conditions Oxygen dependence	Mode: 36 sessions (12–14 weeks) of supervised home based therapy program including cycle ergometer exercise Intensity: up to 25–30 min at 40 rpm, ↑ resistance as tolerated Duration: 90 min per session (aerobic component up to 30 min) Frequency: 3 × /week	Peak $\dot{V}O_2$ : +(19.0%) Bike exercise duration: + 10-m gait speed: +(125.7%) 6MWT: +(125.9%)
Katz-Leure <sup>63,64</sup>	92 subjects Acute Mean age: 63.3 Moderately impaired (mean SSS: 31/58)	Abnormal ECG at rest or during the first stress test Significant blood pressure changes on exertion Arrhythmia Heart failure Rest blood pressure > 200/100 mmHg	Control group: Usual care (subjects had services as prescribed by their physicians). Mode: 8 weeks of cycle ergometer exercise Intensity: up to 60% of HRR Duration: up to 20 min (week 1–2), up to 30 min (week 3–8) Frequency: 5 × /week (week 1–2), 3 × /week (week 3–8)	Peak workload: +(176.9%) Number of stairs climbed until fatigued: + FIM: 0 10-m gait speed: 0 Walking distance until fatigued: 0 6-month follow-up: FAI: 0
Chu <sup>65</sup>	13 subjects Chronic Mean age: 62.5 Mildly impaired (CMSA lower extremity score: 9.4/14).	Unstable heart disease Unstable cardiovascular status Uncontrolled HTN Previous myocardial infarction	Control group: treatment not mentioned. Mode: 8 weeks of water-based endurance exercise Intensity: up to 80% HRR Duration: 1 h (30 min of aerobic activities) Frequency: 3 × /week	Peak $\dot{V}O_2$ : +(122.5%) Peak workload: +(19.2%) Self-selected gait speed: +(9.2%)
			Control group: a seated upper extremity exercise programme	



Pang <sup>66</sup>	63 subjects Chronic Mean age: 65.3 Mildly and moderately impaired (mean American Stroke Association Stroke Functional Classification: II)	History of serious cardiac disease (i.e. myocardial infarction) Uncontrolled blood pressure (systolic blood pressure > 140, diastolic blood pressure > 90)	Mode: 19 weeks of land-based exercise (stepping, walking, repeated sit-to-stand, functional strengthening, balance activities) Intensity: up to 80% HRR Duration: 1 h (up to 30 min of aerobic activities) Frequency: 3 x /week Control group: a seated upper extremity exercise programme with no aerobic exercise component	Peak $\dot{V}O_2$ : + (↑10.7%) 6MWT: + (↑19.7%) PASIPD: 0
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<sup>a</sup>Outcome measures not concerning aerobic capacity, activity endurance or mobility are omitted.

'+' refers to a significant difference in favour of the experimental group ( $P < 0.05$ ).

'0' refers to no significant difference between groups.

APMHR, age-predicted maximal heart rate; BI, Barthel Index; CMSA, Chedoke McMaster Stroke Assessment; DBP, diastolic blood pressure; ECG, electrocardiography; FAC, Functional Ambulation Category; FAI, Frenchay Activities Index; FIM, Functional Independence Measure; FMA, Fugl-Meyer Assessment; HRR, heart rate reserve; HTN, hypertension; min, minutes; NEADL, Nottingham Extended Activities of Daily Living; PASIPD, Physical Activities Scale for Individuals with Physical Impairments; RMI, Rivermead Mobility Index; 6MWT, Six Minute Walk Test; SBP, systolic blood pressure.

Medicine (ACSM) in terms of improving peak  $\dot{V}O_2$  (55–90% of maximal heart rate or 40–85% of heart rate reserve; 3–5 days, 20–30 min per session).<sup>11</sup> All reviewed studies used a protocol consisting of continuous exercise from 20 to 40 min. In earlier stages of training, however, periods of short exercise bouts were used in Katz-Leurer *et al.*<sup>63</sup>

### Stress test protocol

All reviewed studies used cycle ergometry to conduct the exercise test. The testing protocols and the criteria for termination of the exercise test differed slightly among the studies. In addition to volitional fatigue or exhaustion, many studies used other measures (e.g. respiratory exchange ratio, heart rate,  $\dot{V}O_2$ ) to indicate that effort had been maximal. Five studies reported reliability of the primary outcome measures for aerobic capacity (i.e. peak  $\dot{V}O_2$  or workload derived from the stress test) and the values were high (0.78–0.99).<sup>58,59,62,63,65</sup> da Cunha Filho *et al.*<sup>60</sup> provided a measure of reliability of the test. However, on closer examination, it was found that they simply quoted the reliability value derived from another study using a different testing protocol.<sup>58</sup>

### Adverse effects

Few adverse events were reported. Duncan *et al.*<sup>62</sup> reported that three of the 50 subjects (6%) in the intervention group had a recurrent stroke during the exercise trial. Two of the strokes occurred within two weeks after randomization and one occurred at seven weeks. The incidence rate of recurrent stroke reported was comparable to the recurrent stroke risk reported in the general stroke population (8% between one and six months after stroke).<sup>68</sup> Thus, the authors concluded that it is unlikely that the exercise training itself contributes to the recurrent strokes. Pang *et al.*<sup>66</sup> reported five falls from four individuals in the experimental group but none of the falls resulted in any injuries.

### Qualitative assessment

The methodological quality of all selected studies was assessed by the PEDro scale and the results are summarized in Table 2. Five of the seven studies were considered 'good' (score: 6–8)<sup>59,62–66</sup> and two studies were 'fair' (score: 4–5).<sup>58,60,61</sup>

**Table 2** Methodological quality (PEDro scale)

Criterion	Study							
	Potempa <sup>58</sup>	Bateman <sup>59</sup>	da Cunha <sup>60,61</sup>	Duncan <sup>62</sup>	Katz-Leurer <sup>63,64</sup>	Chu <sup>65</sup>	Pang <sup>66</sup>	
1) Eligibility criteria specified	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2) Random allocation to groups	1	1	1	1	1	1	1	1
3) Concealed allocation	0	1	0	1	0	0	0	1
4) Groups similar at baseline	1	1	1	1	1	1	1	1
5) Subject blinding	0	0	0	0	0	0	0	0
6) Therapist blinding	0	0	0	0	0	0	0	0
7) Assessor blinding	0	1	0	1	1	1	1	1
8) Less than 15% dropouts	0	0	0	1	1	1	1	1
9) Intent-to-treat analysis	0	1	0	1	0	0	0	1
10) Between groups statistics reported	1	1	1	1	1	1	1	1
11) Point estimates and variability data reported	1	1	1	1	1	1	1	1
Total score	4	7	4	8	6	6	8	8

**Meta-analysis: aerobic capacity**

Five RCTs used peak  $\dot{V}O_2$  as an outcome measure.<sup>58,60,62,65,66</sup> All of these studies reported statistically significant increase in peak  $\dot{V}O_2$  in the experimental group after aerobic exercise training, ranging from 9.0% to 34.8%.<sup>58,60,62,65,66</sup> Meta-analysis revealed a significant homogeneous SES (small size) (SES 0.42; 95% CI 0.15–0.69;  $Z = 3.06$ ;  $p = 0.001$ ) in favour of aerobic exercise training (Figure 1a).

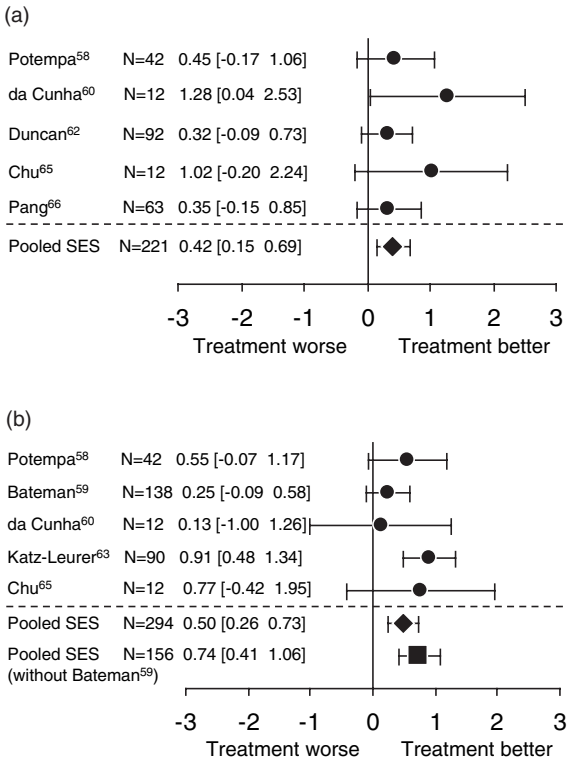
Five RCTs used peak workload as an outcome measure.<sup>58–60,63,65</sup> Four of these studies reported a statistically significant increase in peak workload in the experimental group following training, ranging from 7.3% to 176.9%.<sup>58,59,63,65</sup> da Cunha Filho *et al.*<sup>60</sup> reported a 50.0% increase in workload in the experimental group but it did not reach statistical significance ( $P = 0.226$ ), probably due to the small sample size. There was a significant homogeneous SES (medium size) (0.50; 95% CI 0.26–0.73;  $Z = 4.17$ ;  $P < 0.001$ ) in favour of aerobic exercise training (Figure 1b).

Since the sample used in Bateman *et al.*<sup>59</sup> did not all have a diagnosis of stroke, a sensitivity analysis was performed by excluding this study in the meta-analysis. A significant and greater homogeneous SES (medium size) in favour of aerobic exercise was found (SES 0.74; 95% CI 0.41–1.06;  $Z = 4.42$ ;  $P < 0.001$ ) when Bateman *et al.*<sup>59</sup> was excluded (Figure 1b).

**Meta-analysis: walking performance**

Five studies evaluated walking velocity.<sup>59,61–63,65</sup> The distance involved in the walking test varied slightly among different studies, ranging from 5 to 12 m. In Katz-Leurer *et al.*,<sup>63</sup> none of the patients were able to walk independently and the baseline walking velocity was considered zero. The other four studies all reported that after aerobic exercise training, walking velocity increased from baseline values, ranging from 9.2% to 63.8%.<sup>59,61,62,65</sup> However, statistical significance was obtained in two studies only.<sup>62,65</sup> The results were pooled in the meta-analysis. The calculation of SES for Katz-Leurer *et al.*<sup>63</sup> was based on the postintervention SDs because both experimental and control group had a pretest score of zero. A significant homogeneous SES (small size) in favour of aerobic exercise on walking velocity was found (0.26; 95% CI 0.05–0.48;  $Z = 2.43$ ;  $P = 0.008$ ) (Figure 2a).

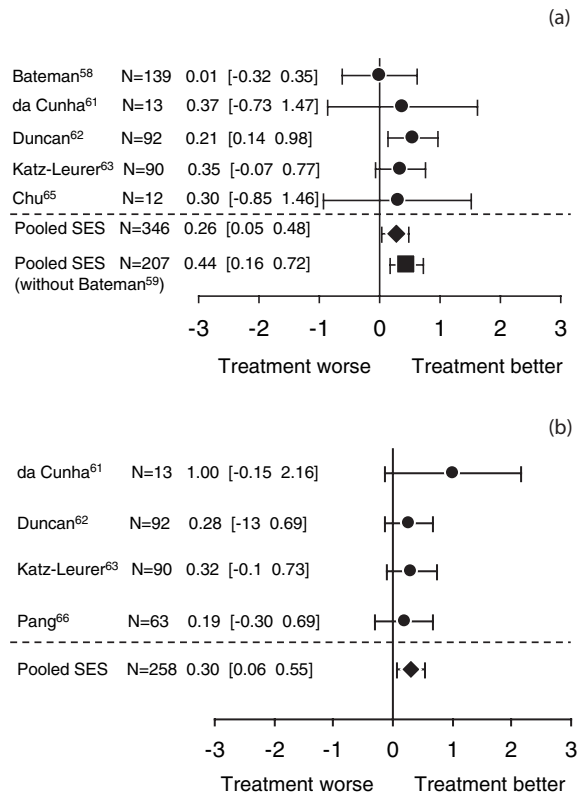




**Figure 1** Meta-analysis: aerobic capacity. (a) Peak  $\dot{V}O_2$ . (b) Peak workload. Each set of dot (●) and error bars represent the standardized effect size (SES) and its 95% confidence interval (CI), respectively, for each study. The first author, the number of subjects involved, the SES value and its 95% CI of each study were also indicated beside each respective set of dot and error bars. The pooled SES was indicated by ♦ (all studies) and ■ (without Bateman *et al.*<sup>59</sup>).

Excluding Bateman *et al.*<sup>59</sup> also resulted in a significant and greater homogeneous SES (small size) (SES 0.44; 95% CI 0.16–0.72;  $Z = 3.11$ ;  $P < 0.001$ ) in favour of aerobic training on walking velocity (Figure 2a).

Four studies measured walking endurance.<sup>61–63,66</sup> Two of the studies used the Six-Minute Walk Test as an indicator of walking endurance,<sup>62,66</sup> and one study measured the walking distance in 5 min.<sup>61</sup> All three studies reported an increase in walking distance in the experimental group by 19.7% to 109.4%, when compared with the baseline values.<sup>61,62,66</sup> Statistical significance was reached in two of the studies.<sup>62,66</sup> In Katz-Leurer *et al.*,<sup>63</sup> subjects were asked to cover as much distance as they could until



**Figure 2** Meta-analysis: walking performance. (a) Walking velocity. (b) Walking endurance. The same figure convention was used as in Figure 1.

volitional fatigue. The baseline walking endurance was zero for both groups of subjects as none of the subject could walk independently. Meta-analysis found a significant homogeneous SES (small size) (0.30; 95% CI 0.06–0.55;  $Z = 2.41$ ;  $P = 0.008$ ) in favour of aerobic training on walking endurance (Figure 2b).

## Discussion

### Mode of training

The mode of training varies in different studies, including cycle ergometer, treadmill or functional activities such as brisk stepping. Exercising on a cycle ergometer does not require as much postural control when compared to treadmill walking and thus may be a better alternative for those individuals with poor balance. A water-based

programme was implemented by Chu *et al.*<sup>65</sup> Water may serve as an excellent exercise medium because it offers resistance and the buoyancy of water reduces joint impact loading and provides partial weight support.<sup>69</sup> This may be relevant because individuals with stroke often have reduced ability to weight-bear on the paretic leg<sup>70,71</sup> and arthritis is also quite common in this population.<sup>62,66,72</sup> Higher impact activities (e.g. walking/running) tend to cause more injuries than non-impact activities (e.g. cycling/exercising in water) in the elderly.<sup>73–75</sup> This is also an important factor to consider when determining the mode of training for older individuals with stroke.

### Exercise protocol

Although the exercise protocols described in the reviewed studies are consistent with the guidelines recommended by ACSM for improving peak  $\dot{V}O_2$ , it is important to note that these guidelines are established for otherwise healthy individuals. It is not known whether lower exercise intensities would be sufficient to induce a positive outcome in individuals with stroke, many of whom have severe deconditioning.<sup>13,14,27</sup> The threshold for endurance training effects may be less for individuals with lower fitness levels. In fact, Swain and Franklin<sup>76</sup> found that aerobic training intensities as low as 30% oxygen uptake reserve were effective in improving cardiovascular fitness in less fit, but healthy individuals.

It has been established in healthy subjects that cumulative short periods of exercise bouts can achieve the same training effects as a long exercise session.<sup>77–79</sup> Whether this principle is true in individuals with stroke is not known. In a previous study by Macko *et al.*,<sup>80</sup> periods of short exercise bouts, consisting of 2–3 min of treadmill walking interspersed with rest periods of similar duration were used for chronic stroke patients who were more deconditioned and positive outcomes were reported. However, the study did not have a control group. Activity endurance is a major deficit in stroke survivors.<sup>5</sup> If short bouts of activity are equally effective, it may be an excellent way to train aerobic capacity for this population.

### Effect on aerobic capacity

Meta-analysis revealed a small effect size for improving peak  $\dot{V}O_2$  and medium effect size for

improving peak workload. Subjects in the acute stage of recovery tended to demonstrate a higher percentage increase in both peak  $\dot{V}O_2$ <sup>60</sup> and peak workload<sup>63</sup> than subacute<sup>62</sup> and chronic subjects,<sup>58,65,66</sup> probably due to the low aerobic capacity at baseline. Katz-Leurer *et al.*<sup>63</sup> showed that the control group had a 65.4% increase in maximal workload at the end of the training period, indicating that spontaneous recovery may play a role at the acute stage.

Two studies used a combination of aerobic exercise and strengthening exercise in the training regimen.<sup>62,66</sup> However, there is no evidence to suggest that aerobic plus resistive training is better than aerobic exercise alone to improve aerobic capacity. Water-based programme resulted in an impressively high percentage of improvement in peak  $\dot{V}O_2$  (22.5%)<sup>65</sup> compared with most land-based programmes with chronic subjects. It may also be due to the high intensity used in the exercise protocol (80% heart rate reserve).<sup>65</sup> It would be interesting to compare the efficacy of a land-based and a water-based programme in the future.

### Effect on walking performance

To rehabilitation practitioners, whether aerobic exercise actually improves functional abilities is also a topic of clinical importance. A small effect size was found in favour of aerobic exercise for improving walking velocity and walking endurance. Two studies used walking as part of the training protocol.<sup>60,61,66</sup> It is thus possible that the improvement in walking performance reported might be partly attributable to repeated gait practice. The effects of aerobic training on other daily functions in individuals with stroke will require further investigations.

### Limitations of studies reviewed

Several weaknesses in the studies reviewed can be identified. First, certain medications (i.e. beta-blockers) can alter the cardiovascular response to exercise.<sup>81–83</sup> Only one study reported whether the subjects changed medications during the course of the study.<sup>58</sup> Failure to report information on medications may have lowered the quality of some of the studies. Second, the scarcity of adverse events may be because the selected studies did not track or report adverse events. Third, four of the

### Clinical messages

- There is good evidence to support the use of aerobic exercise to improve aerobic capacity in individuals with stroke.
- The results can be generalized to those who are mildly or moderately impaired by stroke and who have relatively low risk of cardiac complications with exercise.

selected studies used the same task to assess and train aerobic capacity.<sup>58,59,62,63</sup> Therefore, the possibility that the improvement of performance in the exercise test posttraining was due to a practice effect rather than a true aerobic adaptation could not be ruled out. Fourth, there was a lack of long-term follow-up. Only Bateman *et al.*<sup>59</sup> performed follow-up assessment of aerobic capacity 12 weeks after the termination of training and found no significant group by time interaction in peak workload. Finally, most studies used individuals with a single ischaemic or haemorrhagic stroke who were mildly or moderately impaired and did not have any unstable or serious cardiovascular conditions. Therefore, the effects of aerobic exercise training in other subpopulations (i.e. individuals with severe impairments, higher cardiac risks) will require further investigations.

### Limitations of the systematic review

The major limitation of this systematic review is related to the difficulty in defining what studies have investigated aerobic exercise. For example, a number of studies investigated treadmill walking for the purpose of gait training in individuals with stroke.<sup>38–47</sup> In addition to improving gait, this training method may potentially have an aerobic training effect. However, these studies did not include any outcome measure on aerobic capacity. Since the focus of this systematic review was to investigate the effect on aerobic capacity, these studies were eventually excluded from analysis. Although walking endurance was used in some of these studies,<sup>39–41,47</sup> it was not necessarily a good indicator of aerobic fitness in individuals with stroke because other impairments such as balance and muscle strength also impact on walking endurance.<sup>84</sup> Moreover, it is very difficult

to determine whether the improvement in walking performance reported in these studies is due to repeated gait practice or increase in aerobic capacity. Nevertheless, our methodology might have eliminated some studies that have investigated an exercise programme with a potential aerobic training effect.

### Conclusion

From the systematic review of the current literature, we have good evidence to suggest that aerobic exercise training (50–80% heart rate reserve, 3–5 days a week for 20–40 min) is beneficial in improving aerobic capacity in stroke survivors. The results could be generalized to those who are mildly or moderately impaired by stroke and who have relatively low risk of cardiac complications with exercise. Further research is needed to determine the optimal protocol to train individuals with different levels of physical impairment and cardiac risk, the long-term effects of aerobic exercise training as well as the relationship between improvement in aerobic capacity and daily function.

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### Contributors

MYCP: data collection, designing the methodology, writing the paper.

JJE (the guarantor): initiating the study, designing the methodology, monitoring progress, revising the paper.

ASD: monitoring progress, revising the paper.

SG: data collection, writing the paper.

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## Appendix 1 – Search strategy (MEDLINE)

- 
- 1) exp Cerebrovascular accident/
  - 2) (stroke or cva\$ or cerebrovascular or cerebral vascular).tw.
  - 3) exp Brain Injuries/
  - 4) exp Hemiplegia/
  - 5) (hemipleg\$ or hemipar\$ or brain injur\$).tw.
  - 6) or/1–5
  - 7) exp Exercise Therapy/ or exp Exercise/
  - 8) exp Physical Fitness/
  - 9) exp Physical Endurance/
  - 10) treadmill.tw.
  - 11) ((aerobic or endurance or cardio\$ or fitness) adj5 (train\$ or program\$ or protocol\$ or intervention\$)).tw.
  - 12) or/7–11
  - 13) exp Randomized Controlled Trials/
  - 14) Clinical trial.pt.
  - 15) exp Random Allocation/
  - 16) Randon\$.tw.
  - 17) exp Cross-Over Studies/
  - 18) Control\$.tw.
  - 19) experimental\$.tw.
  - 20) exp Follow-Up Studies/
  - 21) or/13–20
  - 22) 6 and 12 and 21
- 

Free text terms (.tw.); MESH controlled vocabulary (/); truncation (\$)

adj5: adjacency operator, retrieves records that contain the search term within five words of each other in either direction;  
exp: explode.