

# Topical Review

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## Physical Activity and Exercise After Stroke Review of Multiple Meaningful Benefits

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Although stroke is now the fourth, not the third, most common cause of death in the United States,<sup>1</sup> the burden of stroke has increased. Stroke is now the third (fifth in 1990) largest cause of disability-adjusted life years in the developed world.<sup>2</sup> Around half of those who do survive stroke are permanently disabled.<sup>3</sup>

There are a wide range of poststroke problems, including movement and function, mobility, balance, cognition, attention, memory, pain, sensation, perception, emotional problems, and psychological issues. The physical and psychosocial consequences of stroke are complex and long term.

Longer-term problems are reported by stroke survivors 1 to 5 years post stroke. The most common include mobility (58%), fatigue (52%), concentration (45%), and falls (44%). Around half of those surviving report that their needs relating to these problems are not being met and this is higher among those who are more disabled.<sup>4</sup>

Addressing the long-term needs of people during life after stroke is a priority from both a service provision and a research perspective—many uncertainties remain on how best to address long-term post stroke problems.

The aim of this review was to assess whether the multiple effects of exercise and physical activity correspond with the outcomes considered most important, by patients and carers, for life after stroke.

### Physical Activity, Exercise, and Fitness After Stroke

Physical activity is defined as all human movement produced by the action of skeletal muscle that substantially increases energy expenditure. Physical activity is essential for improving and maintaining physical fitness. Exercise is a subset of physical activity that is planned, structured, and repetitive and is performed deliberately with the intention of improving physical fitness.<sup>5</sup> Key indices of physical fitness include cardiorespiratory fitness and muscle strength and power; these determine our capacity to perform and tolerate physical activity.

Physical fitness is impaired after stroke. Cardiorespiratory fitness ( $\dot{V}O_2$  peak) is  $\approx 50\%$  of that in healthy people of the same age and sex.<sup>6</sup> Similarly, muscle strength<sup>7</sup> and muscle power<sup>8</sup> show substantial and variable impairment; bilateral limb weakness suggests that physical inactivity is at play.

Even in high functioning stroke survivors, the amount of physical activity is well below than that observed in healthy elderly people and patient populations.<sup>9</sup> Physical inactivity contributes to the low physical fitness observed after stroke.

### Potential Benefits of Fitness and Exercise After Stroke

Physical activity is recommended for health, fitness, and function in people of all ages within the general population. It reduces mortality and risk of noncommunicable diseases and improves physical fitness and the ability to engage in day to day physical activities.<sup>5</sup> These benefits in healthy people are also relevant to patient populations, including stroke.

Fitness impairments are associated with disability and common post stroke functional limitations, such as walking; these associations could be causal, ie, fitness impairments cause or exacerbate disability.<sup>10</sup> Therefore, increasing physical activity (including exercise) after stroke could improve fitness and improve common poststroke functional problems.

Physical activity also has the potential to provide psychosocial benefits, particularly through group activity. Furthermore, because physical inactivity and cardiorespiratory fitness are risk factors for first-ever stroke<sup>11,12</sup>; physical activity and exercise may also have a role reducing the chance of recurrent stroke and other comorbid conditions.

If participation in physical activity or exercise after stroke is possible, there are numerous plausible benefits; some may not be dependent on increasing physical fitness. Research into treatment effects tends to be on the basis of narrow, focussed questions, which then generate evidence outcome by outcome. Given the complexity of poststroke problems, and the wide range of plausible benefits from exercise, there is a value

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in taking stock of the multiple effects, including risks, which exercise could have during life after stroke as a whole.

A recently updated Cochrane review (45 trials, 2188 participants) takes this approach by examining the effects of exercise interventions after stroke on multiple outcomes measures, including mortality, disability, dependence, physical fitness, physical function, mobility, risk factors, mood, and quality of life.<sup>13</sup> Although the evidence is incomplete, this analysis suggests that exercise is safe and can improve fitness, walking speed, balance, and global indices of disability. The key findings are included among the next sections.

### Are Exercise Benefits Meaningful to Patients?

How well do the known or potential effects of exercise align with the needs of stroke survivors? The findings of a priority setting partnership help answer this.<sup>14</sup> A total of 226 unanswered treatment uncertainties relating to life after stroke were considered by a partnership of stroke survivors, caregivers, and health professionals; the partnership identified 24 shared research priorities. Taking into account overlapping questions, a consensus was reached on the Top-10 research priorities related to life after stroke (Table).

The only intervention directly specified within the research priorities is exercise, clearly indicating its perceived value after stroke. The remaining 9 of 10 priorities do not specify interventions, instead they indicate the need to identify the best treatments or approaches; these can still include exercise. Because exercise is a complex intervention with complex effects, there is good reason to suspect that a single exercise intervention could benefit multiple poststroke problems identified within the top-10 research priorities.

### Mapping Exercise to the Top-10 Research Priorities

The remainder of this review examines the extent to which exercise interventions address each of the issues in the top-10 research priorities. Two of the priorities (2 and 8) describe unusual outcomes coming to terms and coping; these require further clarification and definition because they are not well supported by existing outcome frameworks. Therefore, research questions are currently difficult to form and there is little existing evidence. The remaining 8 research priorities mostly relate to impairments and secondary consequences and evidence is available, which allows the potential of exercise to be explored. We principally sought systematic review evidence but included other study types when evidence is still emerging. Although this review is narrative in nature, we searched the Cochrane Library, MEDLINE, and Embase by combining search terms for exercise or physical activity with terms derived from the outcomes in the top-10 research priorities.

#### Cognition (Priority 1)

Impairments in cognitive function are common (prevalence 64%) after stroke<sup>15</sup> and are associated with both arterial stiffness and physical fitness.<sup>16</sup> Exercise interventions improve cognitive function in older adults (>65 years) with cognitive impairment.<sup>17</sup> A recent systematic review examined

**Table. Top-10 Priorities for Research Relating to Life After Stroke**

1	What are the best ways to improve cognition after stroke?
2	What are the best ways to help people come to terms with the long-term consequences of stroke?
3	What are the best ways to help people recover from aphasia?
4	What are the best treatments for arm recovery and function?
5	What are the best ways to treat visual problems after stroke?
6	What are the best ways to manage or prevent fatigue?
7	What are the best treatments to improve balance, gait, and mobility?
8	How can stroke survivors and families be helped to cope with speech problems?
9	What are the best ways to improve confidence after stroke?
10	Are exercise and fitness programmes beneficial at (a) improving function, (b) improving quality of life, and (c) avoiding subsequent stroke?

These were identified from among 226 research uncertainties by a partnership of stroke survivors, caregivers, and health professionals. Adapted from Pollock et al<sup>14</sup> with permission of the publisher. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

whether physical activity (including exercise) interventions improved cognitive function after stroke; meta-analysis of 9 trials (n=716 participants) showed a significant improvement in cognitive function (standardized mean difference [SMD], 0.20; 95% confidence interval [CI], 0.04–0.36;  $P=0.015$ ).<sup>18</sup> Of the 9 studies included in the meta-analysis, 6 (n=455) examined specific exercise programmes involving cardiorespiratory exercise, such as treadmill walking and cycling. Therefore, there are both rationale and evidence that programmes of physical activity and cardiorespiratory exercise could improve cognitive function after stroke, but more trials are needed.

#### Aphasia (Priority 3) and Visual Problems (Priority 5)

Direct evidence connecting exercise interventions to improvements in aphasia or visual problems is lacking. However, in theory, exercise could elicit neurological improvements that indirectly benefit these (and other) poststroke impairments. For example, exercise has, in animal models, reduced the size of infarct.<sup>19</sup> In human beings, aerobic exercise stimulates secretion of brain-derived neurotrophic factor that facilitates neuroplasticity although this may mediate motor adaptations to rehabilitation. It also has a wider role in brain health and function.<sup>20</sup>

#### Arm Recovery and Function (Priority 4)

Upper limb motor impairments are common and persistent. Upper limb rehabilitation interventions may be delivered by combining a range of treatment modalities. These include active, repetitive interventions involving voluntary movement, which have been evaluated by systematic reviews as follows:

Resistance training to improve upper limb muscle strength increases in grip strength (6 trials; n=306 patients; SMD, 0.95; 95% CI, 0.05–1.85;  $P=0.04$ ) and upper limb function

(11 trials;  $n=465$  patients; SMD, 0.21; 95% CI, 0.03–0.39;  $P=0.03$ ) but not in performance of activities of daily living.<sup>21</sup>

Constraint-induced movement therapy<sup>22</sup> improves disability (6 trials;  $n=184$  patients; SMD, 0.36; 95% CI, 0.06–0.65) and arm motor function (11 trials;  $n=373$ ; SMD, 0.72; 95% CI, 0.32–1.12) at the end of intervention. The underlying effect here is likely to arise from an increase in physical activity of the habitually inactive affected arm.

Repetitive task practice of functional movements does not benefit upper limb function,<sup>23</sup> and simultaneous bilateral arm training does not benefit performance of activities of daily living or functional movement of the arm or hand.<sup>24</sup>

Although these reviews explore different treatment approaches, they are all designed to cause an increase in physical activity of the upper limbs, which is repetitive, task-related, intended to increase fitness (muscle strength), or some combination of these. Despite gaps in knowledge, there is a rationale for upper limb exercise after stroke. This could be presented in a way that captures essence of several treatment modalities for the upper limb.

### Fatigue (Priority 6)

Fatigue is a damaging poststroke symptom with a high prevalence ranging from 38% to 77%.<sup>25</sup> The causes of fatigue are uncertain but are likely to include psychological and physiological mechanisms. Reduced physical fitness post stroke means the effort required to perform physical activity is greater and, therefore, more fatiguing. This may cause people to avoid or reduce physical activity, thus causing further deconditioning and increased susceptibility to fatigue. However, there are currently few data available to determine whether associations exist between fatigue and either physical fitness or physical activity.<sup>26</sup> A Cochrane review does exist that compares interventions for fatigue.<sup>27</sup> However, exercise interventions are not among the 3 included trials. A more recent trial of exercise<sup>28</sup> hints at benefits by showing that cognitive therapy and exercise reduced fatigue in more patients than cognitive therapy alone. In summary, fatigue after stroke is common, yet research into suitable interventions, particularly exercise, is uncommon.

### Balance, Gait, and Mobility (Priority 7)

Balance, gait, and mobility outcomes are addressed in the recent Cochrane review of exercise after stroke.<sup>13</sup>

With regard to balance, a meta-analysis of 6 trials ( $n=257$  participants) of cardiorespiratory training indicated a significant improvement in the Berg Balance Scale scores (MD, 3.14; 95% CI, 0.56–5.73;  $P=0.02$ ). There was no clear effect of mixed training on this outcome (5 trials;  $n=239$  participants; MD, 0.32; 95% CI, 0.00–0.65;  $P=0.05$ ). However, pooling mixed balance outcomes showed an overall beneficial improvement in balance at the end of intervention (8 trials;  $n=575$  participants; SMD, 0.26; 95% CI, 0.04–0.49;  $P=0.02$ ).

With regard to gait and mobility, cardiorespiratory training involving walking improved maximum walking speed (7.37 m/min; 95% CI, 3.70–11.03). Preferred gait speed was improved by cardiorespiratory training alone (4.63 m/min; 95% CI, 1.84–7.43) or combined with strength training (4.54

m/min; 95% CI, 0.95–8.14). Gait endurance capacity (distance covered in 6-minute walking) also improved after cardiorespiratory training alone (26.99 m; 95% CI, 9.13–44.84) or in combination with strength training (41.60 m; 95% CI, 25.25–57.95). Training that includes cardiorespiratory training using walking as the exercise mode improves the speed and tolerance of walking at the end of intervention. There is also some evidence of longer-term retention.

In summary, exercise involving walking, with or without resistance training, improves walking speed and also indices of balance.

### Improving Confidence (Priority 9)

Confidence is reduced after stroke.<sup>29</sup> Self-efficacy is a measure of confidence and is associated with better mobility, balance, and physical function after stroke.<sup>30</sup> Self-efficacy is often discussed in terms of barriers to the uptake and maintenance of exercise. However, it is plausible that this causality may exist in the opposite direction, whereby participating in exercise improves confidence and self-efficacy. Qualitative studies examining the community-based group exercise schemes suggest that stroke survivors gain social and physical confidence as a result of participation.<sup>31–33</sup>

### Exercise to Improve Function (Priority 10a)

Some of the specific functional benefits of exercise overlap with research priorities already discussed (exercise for gait, balance, and arm function). More general assessments of function using global disability scales have been examined by systematic reviews.<sup>13</sup> Cardiorespiratory training has a significant overall effect on pooled outcomes, including scales, such as the Functional Independence Measure (6 trials;  $n=289$ ; SMD, 0.37; 95% CI, 0.10–0.64;  $P=0.007$ ).

### Exercise to Improve Quality Of Life (Priority 10b)

Systematic reviews examining the effect of exercise interventions on quality of life outcomes after stroke are inconclusive.<sup>13,34</sup>

### Exercise to Avoid Subsequent Stroke (Priority 10c)

Recurrent cardiovascular events, including stroke ( $\approx 30\%$ ), are common among stroke survivors. No direct systematic review evidence shows that participating in exercise reduces the incidence of recurrent stroke<sup>13</sup>; however, there is some indirect rationale that it could. A recent network meta-analysis predicts that exercise after stroke is at least as effective as antiplatelet and anticoagulant drugs in reducing mortality.<sup>35</sup> Physical inactivity and low cardiorespiratory fitness positively predict risk of first stroke and both can be improved via exercise. For example, meta-analysis of 7 trials ( $n=247$  participants) showed that cardiorespiratory fitness (peak  $\dot{V}O_2$ ) increased significantly in people with stroke (MD, 2.46 mL/kg per minute; 95% CI, 1.12–3.80;  $P=0.0003$ ) after 1 to 6 months of cardiorespiratory training.<sup>13</sup> Exercise could reduce risk; some small trials of exercise after stroke indicate beneficial effects on known mechanistic factors, including improved glucose tolerance,<sup>36</sup> improved arterial function,<sup>37</sup> and reduced cholesterol and blood pressure (BP).<sup>38</sup>

BP is a key modifiable risk factor for recurrent stroke, and a reduction of 5 mmHg in systolic BP equates to a 10% reduction in the risk of major cardiovascular events, including stroke.<sup>39</sup> A recent systematic review of exercise in healthy adults<sup>40</sup> showed that cardiorespiratory training reduces BP, particularly among hypertensive participants (systolic BP, -8.3 mmHg; 95% CI, -10.7 to -6.0; diastolic BP, -5.2 mmHg; 95% CI, -6.8 to -3.4). Dynamic resistance training also has similar effects on BP but the most surprising finding is a greater effect of isometric (static) resistance training (systolic BP, -10.9 mmHg; 95% CI, -14.5 to -7.4; diastolic BP, -6.2 mmHg; 95% CI, -10.3 to -2.0).

Despite this, rationale BP is seldom reported as an outcome in trials of exercise after stroke.<sup>13</sup> Meta-analysis of 4 trials of cardiorespiratory training (n=267 participants) showed no significant effect on BP (systolic BP, 0.40 mmHg; 95% CI, -8.38 to 9.18; diastolic BP, -0.33 mmHg; 95% CI, -2.97 to 2.31). Trials of resistance training after stroke have overlooked BP outcome altogether. Isometric resistance training also has been overlooked as an intervention after stroke, perhaps, because of widespread feeling that task-related training, which is usually dynamic, might better promote functional benefit. Attention has, therefore, traditionally been focussed on resistance training to overcome low muscle strength and provide functional benefits rather than other physiological benefits, such as improvement of BP control.

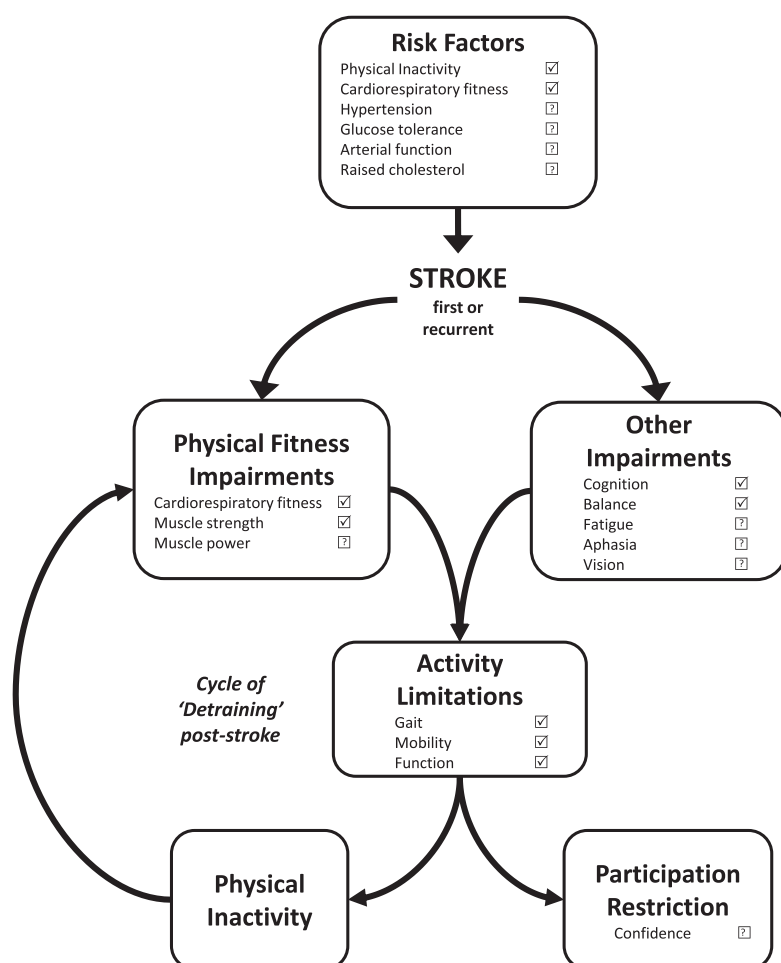
In summary, there is a rationale for all types of exercise to contribute to BP control after stroke but limited evidence. The least researched intervention, isometric exercise, could be the one from which patients stand to gain the most benefit. It is plausible that interventions combining both cardiorespiratory training and strength training may offer the most scope for reducing risk of subsequent stroke.

## Summary

There is evidence that exercise interventions have a beneficial role in addressing 4 of the top-10 shared research priorities; cognition (priority 1), arm function (4), balance and gait (7), and exercise programmes (10). In addition, there is an emerging evidence supporting a rationale for potential benefit with respect to further 2 priorities, fatigue (6) and confidence (9).

Poststroke disability is complex; low fitness and other impairments interact to drive poststroke activity limitations and participation restriction. Exercise and activity influence, or have the potential to influence, the process of poststroke disablement at various points (Figure).

The current evidence supports a role for exercise which combines cardiorespiratory training (including walking as an exercise mode) and strength training (particularly involving the upper body) presented in a group setting with other stroke survivors. Although central benefits, such as improved fitness and cognition, might arise from nontask-specific exercise



**Figure.** The interaction of physical inactivity and impairment on the process of poststroke disablement exercise and activity are known to influence ☒ or have the potential to influence ☐ this process at various points. Adapted from Saunders and Greig<sup>10</sup> with permission of the publisher. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.



program, task-related training would seem more efficient because it would enable retention of these benefits as well as offer functional advantage.

Exercise is a complex intervention covering many separately defined components, for example, the type (cardiorespiratory or resistance training), mode of exercise (eg, walking, circuits training) setting, and various dose parameters (duration, frequency, intensity, and progression). This does mean that there are many opportunities to tailor the content in a way that could produce different patterns of responses and benefits. For example, the optimal exercise program for improving gait and mobility after stroke may not be beneficial for other areas of need (eg, upper limb function).

Broad, less-focussed questions are discouraged in science, but such an approach could be beneficial in this instance. There is a need to take stock of the global effects of exercise interventions rather than restricting questions to more limited outcomes of interest. There is a clear rationale that future trials of exercise should gather data on a wider range of relevant outcome measures; this is not data dredging.

Physical activity and exercise after stroke continue to be recommended.<sup>41</sup> Even though the evidence is incomplete, exercise after stroke programmes are being developed and implemented, eg, in the United Kingdom and Australia.<sup>42</sup> The diverse benefits of exercise may have broad appeal but participating in exercise may not; it is important that we do more research to establish the best ways to encourage stroke survivors to be more active in the long term by understanding the barriers and motivators that influence participation.<sup>43</sup>

## Disclosures

Dr Mead has received research funding for exercise after stroke, honoraria from Later Life Training to develop an educational course for exercise after stroke professionals and honoraria and expenses to present work on exercise after stroke at conferences.

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