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Combined cardiorespiratory and resistance training for people with stroke (Review)

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[Intervention Review]

Combined cardiorespiratory and resistance training for people with stroke

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ABSTRACT

Rationale

Levels of physical activity and physical fitness, including both cardiorespiratory fitness and muscle strength, are often low after stroke and are associated with post-stroke disability. Multicomponent exercise interventions that increase muscle strength and cardiorespiratory fitness could be effective for improving physical function and disability, and for secondary prevention.

Objectives

The primary objective of this review is to determine whether combined cardiorespiratory fitness and resistance training after stroke has any effects on death, disability, adverse events, risk factors, fitness, walking, and indices of physical function when compared to a non-exercise control.

Search methods

In January 2024, we searched nine databases (CENTRAL, MEDLINE, Embase, CINAHL, SPORTDiscus, PsycINFO, WoS, PEDro, and DORIS) and two trial registers (ClinicalTrials.gov and ICTRP). We also undertook reference checking, citation tracking, and contact with experts in the field, in order to identify eligible studies.

Eligibility criteria

We included randomised controlled trials (RCTs) that compared combined cardiorespiratory fitness and muscle strength training against usual care, no intervention, or a non-exercise intervention for people with stroke.

Outcomes

Our critical outcome domains were death, disability, adverse events, risk factors, fitness, walking, and indices of physical function. We assessed outcomes at the end of intervention and at the end of follow-up. Our other important outcome domains were indices of quality of life, mood, cognition, and fatigue.

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Risk of bias

We used the Cochrane tool RoB 1 to assess bias in the included studies.

Synthesis methods

Where possible, we synthesised results for each outcome at the end of intervention and end of follow-up using random-effects meta-analyses on arm-level data. For dichotomous outcomes, we calculated the risk difference (RD) and 95% confidence interval (CI). For continuous outcomes, we calculated a mean difference (MD) or standardised mean difference (SMD), and 95% CI. We used GRADE to assess certainty of evidence for critical outcomes.

Included studies

We included 30 studies with 1519 participants, who had an average age of 63.7 years. Most studies recruited ambulatory participants (28 of the 30 studies) during the early subacute (14 studies) and chronic (14 studies) stages of recovery. Most studies (26) took place in high-income countries. Most study interventions lacked a balanced dose of control exposure (23 studies). Eleven studies included a follow-up period (mean 7.3 months; range 3 to 12 months).

Most interventions combined cardiorespiratory training (usually walking or ergometer-based) and resistance training (weights, machines, bodyweight or elastic resistance) in a circuit-type format. Training occurred two to five days a week for between four weeks and one year.

Synthesis of results

Combined training does not increase or decrease **deaths** at the end of intervention (risk difference RD -0.00, 95% CI -0.02 to 0.01; 26 studies, 1352 participants; high certainty) or end of follow-up (RD -0.01, 95% CI -0.04 to 0.02; 8 studies, 531 participants; high certainty).

Combined training may improve indices of **disability** slightly at the end of intervention (standardised mean difference SMD 0.20, 95% CI 0.04 to 0.36; 13 studies, 789 participants; low certainty) but has little or no effect at the end of follow-up (SMD 0.10, 95% CI -0.07 to 0.28; 8 studies, 614 participants; low certainty).

Combined training does not increase or reduce the incidence of **secondary cardiovascular or cerebrovascular events** at the end of intervention (RD -0.00, 95% CI -0.02 to 0.01; 8 studies, 684 participants; high certainty) or end of follow-up (RD 0.01, 95% CI -0.06 to 0.09; 4 studies, 285 participants; high certainty).

Combined training may have little or no effect on **systolic blood pressure** (mmHg) at the end of intervention, but the evidence is very uncertain (mean difference MD -1.83, 95% CI -9.60 to 5.95; 5 studies, 140 participants; very low certainty); there were no follow-up data.

Combined training may improve indices of **cardiorespiratory fitness** and **musculoskeletal fitness** (lower limb strength), but the evidence is very uncertain. Few data were available at follow-up.

Combined training may improve comfortable **walking** speed (metres per second) at the end of intervention (MD 0.09, 95% CI 0.04 to 0.14; 13 studies, participants not available; very low certainty) but may have little or no effect at the end of follow-up (MD 0.03, 95% CI -0.07 to 0.13; 7 studies, 605 participants; very low certainty), although the evidence is very uncertain for both time points.

Combined training may improve **balance** slightly at the end of intervention (SMD 0.25, 95% CI 0.11 to 0.39; 16 studies, 839 participants; low certainty) and end of follow-up (SMD 0.24, 95% CI -0.00 to 0.49; 6 studies, 535 participants; low certainty).

In terms of **acceptability and tolerability**, interventions were closely adhered to, with no pattern of concerning adverse effects or participant losses attributable to combined training.

Overall, our **certainty** about the evidence is limited by imprecision (small number of studies and participants) and risks of bias (e.g. from imbalanced exposure doses).

Authors' conclusions

Combined training after stroke does not affect mortality or the incidence of secondary events at the end of intervention or end of follow-up. Since these events are infrequent, conclusions cannot be drawn about any protective effect on mortality or secondary events. Small beneficial effects on physical fitness and blood pressure at the end of intervention may represent a reduced risk of secondary events, but this is very uncertain.

Combined training may cause small improvements in fitness, disability, walking speed, and balance at the end of intervention. The small benefit observed for balance may be preserved after a follow-up period. The evidence for these effects is of low or very low certainty.

Combined training interventions were adhered to successfully without serious adverse events or adverse effects; the interventions were acceptable to and well tolerated by participants. Limited data at follow-up restricts the conclusions we can draw about the retention of any benefits observed. Larger, well-designed trials are needed to determine the optimal regimen for exercise prescription, the benefits, and long-term effects.

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Registration

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PLAIN LANGUAGE SUMMARY

What are the benefits and risks of combined training (exercise programmes that combine aerobic training and muscle strength training) for people with stroke?

Key messages

- People with stroke can complete programmes of exercise that target both aerobic fitness and muscle strength (this is called 'combined training').
- By engaging in combined training, people with stroke may experience small improvements in some aspects of fitness, balance, and walking speed.

What is stroke?

Stroke occurs when the blood supply to part of the brain is interrupted, and this leads to damage in some areas of the brain. The impact of stroke can be life-changing and vary depending on the severity of damage and where this occurs in the brain. The effects can be both physical and psychological, not only affecting the ability to move, but also the way someone thinks, behaves, and feels. These effects can persist throughout life after stroke. A physical impact of stroke is that aerobic fitness and muscle strength can be low; this makes physical movement more difficult, which may restrict a return to meaningful everyday activities.

What happens during rehabilitation after stroke?

After a stroke, many patients will receive rehabilitation, for example from a physiotherapist or other health professional, to help overcome physical problems with everyday activities. This therapy may involve different types of exercise, including aerobic training and strength training. Aerobic training (also called ‘cardiorespiratory training’) involves continuous exercise. It can increase aerobic fitness, which improves the endurance needed for repetitive activities like walking. Strength training (also called ‘resistance training’) can involve lifting weights or pulling against elastic resistance. It can improve fitness by strengthening muscles, which can help with activities like lifting objects, standing up, or walking. Patients may also be advised to do exercises at home. Therefore, the normal process of rehabilitation after a stroke may include elements of both aerobic training and muscle strength training.

What did we want to find out?

Since both aerobic fitness and muscle strength can be low after a stroke, combined exercise could improve both of these elements of fitness and the post-stroke physical problems arising from them.

We wanted to find out whether programmes of exercise that combine both an aerobic fitness training element and muscle strength training are beneficial at any time after stroke (whether in hospital, or later, after going home).

Specifically, we wanted to determine whether combined training after a stroke is safe, whether it improves physical fitness, improves movement (including walking and balance), changes the way people feel (including depression, quality of life) and whether it reduces the chance of having another stroke.

What did we do?

We searched for studies that tested exercise programmes in people after stroke. We only included studies where the exercise programme contained both an aerobic training element and a muscle strengthening element. We summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and number of people included.

What did we find?

We found 30 studies that involved 1519 people with stroke; most participants were able to walk. Some exercise programmes were delivered in the first few months after a stroke, and others were delivered later on, more than six months after the stroke. Most combined training programmes lasted less than 12 weeks, were safe, and combined several types of activities, including walking and lifting weights.

Main results

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Combined training does not affect the number of deaths or second strokes at the end of the training programme or after a period of follow-up. Since deaths and second strokes were uncommon, we cannot determine whether combined training reduces the chance of death or secondary events. Small beneficial effects on blood pressure at the end of the intervention may suggest there is a reduced risk of secondary events, but this is very uncertain.

Combined training may cause small improvements in fitness (aerobic fitness and muscle strength of the legs), disability, walking speed, and balance at the end of a combined training programme. These are important outcomes for people with stroke, but the evidence has many uncertainties. Twelve studies measured the effects again 3 to 12 months after the combined training had finished; there was some limited evidence that the positive effect on balance may be retained.

Combined training interventions were adhered to without serious adverse events or effects; the interventions were acceptable to participants and well tolerated. Larger trials are needed to determine the best approach to exercise prescription, and its benefits and long-term effects.

What are the limitations of the evidence?

Most studies involved people who could walk; little is known about the many people with stroke who have more limited mobility.

Most studies took place in high-income, industrialised countries; little is known about people with stroke in other countries.

There are lots of uncertainties and not enough evidence about the effects of combined aerobic training and strength training.

How up to date is this evidence?

This review updates evidence from a previous review (which was in a different format combining three separate programmes). The evidence is based on searches run up to January 2024.

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SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings table - Combined cardiorespiratory and resistance training compared to control for people with stroke at the end of intervention

Combined cardiorespiratory and resistance training compared to control for people with stroke at the end of intervention

Patient or population: people with stroke at end of intervention
Setting: home and hospital settings, mostly in Europe and North America
Intervention: combined cardiorespiratory and resistance training
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	Risk with combined cardiorespiratory and resistance training				
Death assessed with: numbers of deaths (all causes) follow-up: range 4 weeks to 6 months	9/653	**4/699**	**RD 0.00** (−0.02 to 0.01)	1352 (26 RCTs)	⊕⊕⊕⊕ High	Combined training does not increase or reduce deaths. Death during the intervention period is very uncommon in these participants, with only 13/1272 deaths overall and 4/13 deaths in the intervention group. Since deaths are already at a low level, any reduction in deaths due to combined training would be difficult to detect. Short intervention periods also decrease the likelihood of deaths.
Disability assessed with: any instruments assessing global disability (higher value more favourable) follow-up: range 4 weeks to 6 months	-	SMD **0.2 higher** (0.04 higher to 0.36 higher)	-	789 (13 RCTs)	⊕⊕⊖⊖ Low[a,b]	Combined training may improve indices of disability slightly (small effect > 0.2).
Secondary events assessed with: numbers of cerebrovascular or cardiovascular events	3/324	**4/360**	**RD 0.00** (−0.02 to 0.01)	684 (8 RCTs)	⊕⊕⊕⊕ High	Combined training does not increase or reduce the incidence of secondary cardiovascular or cerebrovascular events. However, since secondary events are already uncommon, any reduction in secondary events due

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follow-up: range 4 weeks to 6 months						to combined training would be difficult to detect. Adverse events are not systematically reported in these trials as preplanned outcomes.
Blood pressure (systolic) assessed with: systolic blood pressure (mmHg) follow-up: range 4 weeks to 6 months	The mean blood pressure was **130** mmHg.	MD **1.83 mmHg lower** (9.6 lower to 5.95 higher)	-	140 (5 RCTs)	⊕⊖⊖⊖ Very low[c,d,e]	Combined training may have little or no effect on systolic blood pressure, but the evidence is very uncertain. The MCID is +/-2 mmHg. Systolic blood pressure of 130 mmHg in the control group is already at the current treatment threshold for many people with stroke.[f]
Physical fitness assessed with: indices of cardiorespiratory fitness and musculoskeletal fitness follow-up: range 4 weeks to 12 months	See comment for summary of all outcomes relating to physical fitness components			508 (10 RCTs)	⊕⊖⊖⊖ Very low[f,g,h]	Combined training may improve different components of physical fitness, but the evidence is very uncertain. Combined training may improve cardiorespiratory fitness (peak oxygen uptake +2.29 ml/kg/min); the MCID is +3.5 ml/kg/min. Combined training may improve muscle strength of the least affected leg (moderate effect > 0.5), most affected leg (small effect > 0.2), and the least affected arm (small effect > 0.2), but has little or no effect on the most affected arm.
Walking speed (comfortable speed) assessed with: directly measured self-paced walking velocity follow-up: range 4 weeks to 6 months	The mean walking speed was **0.705** m/sec.	MD **0.09 m/sec higher** (0.04 higher to 0.14 higher)	-	(13 RCTs)	⊕⊖⊖⊖ Very low[c,i,j]	Combined training may improve comfortable walking speed, but the evidence is very uncertain. The MCID is +0.13 m/sec. Control group walking speed (< 0.8 m/sec) predicts 'limited community ambulation'.
Balance assessed with: any validated balance instrument (higher value more favourable) follow-up: range 4 weeks to 6 months	-	SMD **0.25 higher** (0.11 higher to 0.39 higher)	-	839 (16 RCTs)	⊕⊕⊖⊖ Low[k,l]	Combined training may improve balance slightly (small effect > 0.2).

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

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CI: confidence interval; **ES:** effect size; **MCID**: minimum clinically important difference; **MD:** mean difference; **SD:** standard deviation; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Serious risk of bias (downgraded once): performance bias introduced due to imbalanced intervention and control exposures in 11/13 included studies
[b]Serious imprecision (downgraded once): confidence interval includes the threshold of a trivial/small beneficial effect (ES > 0.2)
[c]Serious risk of bias (downgraded once): important risk of bias items including attrition and those connected to imbalanced exposure across trial arms
[d]Serious heterogeneity (downgraded once): all heterogeneity (I^2= 76%; 'substantial') is introduced by 1/5 studies, the exclusion of which changes the effect direction.
[e]Very serious imprecision (downgraded twice): confidence interval includes the MCID representing important harm (+2 mmHg) and important benefit (−2 mmHg)
[f]Serious risk of bias (downgraded once): important risk of bias items including attrition and those connected to imbalanced exposure across trial arms
[g]Serious heterogeneity (downgraded once): includes substantial heterogeneity (I^2 = 68 to 71%)
[h]Very serious imprecision (downgraded twice): confidence interval for cardiorespiratory fitness includes the MCID for VO_2 peak of 3.5 ml/kg/min. Confidence intervals for upper limb muscle strength of affected and unaffected sides, and lower limb muscle strength of the unaffected side, include thresholds for moderate harm (ES < −0.5), as well as moderate or large benefits (ES > 0.5 and > 0.8). The confidence interval for lower limb strength on the unaffected side includes the threshold for moderate benefit (ES > 0.5).
[i]Serious heterogeneity (downgraded once): unexplained heterogeneity I^2 = 68% 'substantial'
[j]Serious imprecision (downgraded once): confidence interval includes the threshold for MCID (+0.13 m/sec)
[k]Serious risk of bias (downgraded once): risk of performance, selection, and detection bias
[l]Serious imprecision (downgrade once): confidence interval includes the threshold of a trivial/small beneficial effect (ES > 0.2)

Summary of findings 2. Summary of findings table - Combined cardiorespiratory and resistance training compared to control for people with stroke after a post-intervention follow-up period

Combined cardiorespiratory and resistance training compared to control for people with stroke after a post-intervention follow-up period

Patient or population: people with stroke after a post-intervention follow-up period
Setting: home and hospital settings, mostly in Europe and North America
Intervention: combined cardiorespiratory and resistance training
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	Risk with combined cardiorespiratory and resistance training				

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Death assessed with: numbers of deaths (all causes) follow-up: range 3 weeks to 12 months	8/253	**4/278**	**RD −0.01** (−0.04 to 0.02)	531 (8 RCTs)	⊕⊕⊕⊕ High	Combined training does not increase or reduce deaths. Death is very uncommon in these participants, with 12/531 deaths occurring between baseline and end of follow-up, 4 of which were in the intervention group. However, since deaths are already at a low level, any reduction is difficult to detect. Short intervention and follow-up periods also decrease the likelihood of deaths.
Disability assessed with: any instruments assessing global disability (higher value more favourable) follow-up: range 3 months to 12 months	-	SMD **0.1 higher** (0.07 lower to 0.28 higher)	-	614 (8 RCTs)	⊕⊕⊖⊖ Low[a,b]	Combined training may result in little to no improvement in indices of disability.
Secondary events assessed with: numbers of cerebrovascular or cardiovascular events follow-up: range 4 months to 12 months	3/130	**7/155**	**RD 0.01** (−0.06 to 0.09)	285 (4 RCTs)	⊕⊕⊕⊕ High	Combined training does not increase or reduce secondary cardiovascular or cerebrovascular events. However, since secondary events are already uncommon, any reduction in secondary events due to combined training would be difficult to detect. Adverse events are not systematically reported in these trials as preplanned outcomes.
Blood pressure (systolic) assessed with: systolic blood pressure (mmHg)	Not pooled	Not pooled	Not pooled	(0 RCTs)	-	No study data available
Physical fitness assessed with: indices of cardiorespiratory fitness and musculoskeletal fitness follow-up: range 12 weeks to 4 months	See comment for summary of all outcomes relating to physical fitness components			108 (2 RCTs)	⊕⊕⊖⊖ Low[c]	Combined training may result in little to no effect (trivial effect < 0.2) on lower limb muscle strength on both the affected and unaffected sides after a follow-up period. There were no study data available for cardiorespiratory fitness or for indices of upper limb muscle strength after a follow-up period.
Walking speed (comfortable)	The mean walking speed (comfortable) was **0.812** m/sec.	MD **0.03 m/sec higher** (0.07 lower to 0.13 higher)	-	605 (7 RCTs)	⊕⊖⊖⊖ Very low[d,e]	Combined training may have little to no effect on comfortable walking speed, but the evidence is very uncertain. The control group walking speed of > 0.8 m/sec pre-

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assessed with: directly measured self-paced walking velocity follow-up: range 3 months to 12 months						dicts unlimited community ambulation. The MCID is +0.13 m/sec.
Balance assessed with: any validated balance instrument (higher values more favourable) follow-up: range 3 months to 10 months	-	SMD **0.24 higher** (0 to 0.49 higher)	-	535 (6 RCTs)	⊕⊕⊖⊖ Low[d,f]	Combined training may increase balance slightly (small effect > 0.2).

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ES:** effect size; **MCID**: minimum clinically important difference; **MD:** mean difference; **RD:** risk difference; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Serious risk of bias (downgraded once): 6/8 studies affected by performance and detection bias plus other bias domains
[b]Serious imprecision (downgraded once): confidence interval includes the threshold of a small beneficial effect (ES > 0.2)
[c]Serious imprecision (downgraded twice): confidence interval includes the threshold of a small harm (ES < −0.2) and thresholds of small and moderate benefits (ES > 0.2 and > 0.5)
[d]Serious risk of bias (downgraded once): some attrition and performance bias threats
[e]Serious inconsistency (downgraded one): substantial heterogeneity (I^2 = 69%)
[f]Serious imprecision (downgraded once): confidence interval includes the threshold of a small beneficial effect (ES > 0.2)

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BACKGROUND

Physical activity and exercise recommendations exist to promote and maintain health and well-being in healthy, older, and patient populations [1, 2, 3], including people with stroke [4, 5]. Multiple clinical guidelines incorporate exercise within stroke rehabilitation (e.g. Australia [6], Canada [7], UK [8]). A systematic review of stroke guidelines found that exercise is recommended as part of lifestyle modification for secondary prevention, and strongly recommended for rehabilitation [9]. Exercise refers to a subset of physical activity that is planned, structured, repetitive, and deliberately performed to train (improve) one or more components of physical fitness, physical performance, or health [10].

Physical fitness

Physical fitness is defined as "the ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and meet unforeseen emergencies" [10].

Key components of physical fitness are cardiorespiratory and musculosleletal.

- **Cardiorespiratory fitness** is the ability to transport and use oxygen and is usually expressed as maximal oxygen uptake ($\dot{V}O_2$ peak). Cardiorespiratory fitness confers 'endurance', that is, the ability to perform physical activity for an extended period.
- **Musculoskeletal fitness** is quantified in terms of muscle strength and power. Muscle strength is the ability of a specific muscle or muscle group to exert force (e.g. measured in newtons) and muscle power refers to the rate at which muscular work can be performed during a single explosive contraction (e.g. measured in watts). These attributes confer the ability to perform forceful movements such as pushing or lifting.

Determinants of fitness

There is a sex-dependent, age-related decline in cardiorespiratory fitness [11] and musculoskeletal fitness (strength) [12]. Cardiorespiratory fitness is around 27% lower in women than in men and both decline ~1% per year as a normal consequence of healthy ageing (20 to 80 years of age; [11]). Muscle strength is lower in women than men, and the age-related decline is non-linear, accelerating around the sixth decade of life [12]. Physical inactivity also causes rapid loss of fitness; just 10 days of bed rest causes rapid loss of muscle strength (−13.2%), muscle power (−14%), and cardiorespiratory fitness (−12%) [13]. Secondary consequences of chronic disease, such as inflammation, are also associated with loss of muscle strength and muscle mass [14, 15]. All fitness components can be improved by exercise [16].

Importance of fitness

When fitness is low (for any reason), important activities of daily living (ADL) may either become limited by fatigue or impossible to perform,as the following examples illustrate.

- Cardiorespiratory fitness, a $\dot{V}O_2$peak below 15 to 18 mL/kg/min is associated with loss of independence [17].
- Muscle strength of various lower limb muscles below threshold values prevent older people performing ADL [18].
- Muscle power impairment in older people is associated with reduced mobility and an increased risk of falls [19].

Therefore, an important hypothesis is whether exercise might improve activities of daily living and function?

Description of the condition

The classic definition of stroke is "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin" [20]. Stroke can result in death, or have disabling physical and psychological effects that change the way people move, think, feel, and behave. Globally, stroke is the second leading cause of death, and third leading cause of death and disability combined [21]. Stroke survivors have shorter life expectancy than age-matched populations (5.5 years shorter) and are at risk of secondary events; 19.8% have another stroke within 5 years and 26.8% within 10 years [22].

One neurological consequence of stroke is unilateral loss or limitation of motor control, leading to loss of muscle function, and loss or limitation of movement, mobility, and functional ability. These immediate, direct impacts of stroke are then compounded by indirect medical, physical, and psychological complications and impairments occurring over time post-stroke [23, 24].

Physical fitness is impaired after stroke. In community-dwelling stroke survivors (i.e. people not in residing in hospitals or care homes), cardiorespiratory fitness is around 53% of that of healthy people of the same age and sex [25]. Muscle strength [26] and muscle power [27] are around 48% of that of healthy people; these deficits are bilateral suggesting the influence of physical inactivity in addition to hemiparesis. Physical inactivity and low levels of fitness may already be present [28], as risk factors before stroke [29]. The neurological consequences of stroke and post-stroke inactivity may impair fitness further, increasing inactivity as an inpatient [30, 31], and as community-dwelling stroke survivors [32].

Low muscle strength [33, 34] and power [27] are related to reduced physical function. Limitation or loss of functional abilities after stroke (e.g. walking, stair climbing, rising from a chair) are associated with low levels of cardiorespiratory fitness, muscle strength, and muscle power [27, 35, 36].

Therefore, low levels of physical fitness (for whatever reason) may exacerbate or cause some common post-stroke physical limitations [37]. Restoring motor function to improve functional ability is a key focus within stroke rehabilitation, and a number of interventions have been investigated that involve exercise [38].

Description of the intervention and how it might work

Exercise interventions

Type, mode, and dose of exercise together define an exercise intervention and are guided by a common set of well-established principles [39].

Type

Exercise programmes are typically either:

- cardiorespiratory training (to improve cardiorespiratory fitness);
- resistance training (to improve musculoskeletal fitness); or

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- combined cardiorespiratory plus resistance training (to improve both cardiorespiratory and musculoskeletal fitness).

Mode

Cardiorespiratory training may involve continuous or intermittent bouts of activity, for example, walking and cycling. Resistance training modes involve making repeated resisted muscle contractions, for example, resisted by lifting weights or using body mass or elastic devices. Modes of exercise can mimic desired functional outcomes to allow task-related training or specific training.

Dose

Dose of exercise is controlled by manipulating the amount of training, for example, programme duration (number of weeks, or months), training frequency (number of days per week), training duration (number of minutes) of sessions, and training intensity (e.g. rate of work, resistance, or effort made). Resistance training exercises are usually prescribed in terms of numbers of sets and repetitions for each resisted exercise. A defining principle of exercise is that there should be a planned, progressive increase in dose throughout the duration of the training programme to maintain the stimulus.

How exercise might work

Secondary prevention

All types of exercise (particularly resistance training) can reduce blood pressure, the principal risk factor for stroke [40]. Cardiometabolic risk (glycaemic control and lipid levels) can also be improved by exercise, leading to significant reduction in coronary artery disease (CAD) risk and all-cause mortality [41, 42].

Exercise has potential to both reduce and increase incidence of secondary events; there is increased risk of stroke during and immediately after exercise, including resistance training where the haemodynamic effects are associated with subarachnoid haemorrhage (SAH) [43]. Sudden cardiac deaths due to the acute effects of exercise can occur, particularly when there are cardiac comorbidities [4]. Screening of participants using eligibility criteria may help mitigate the risk of cardiac death during exercise for people with stroke in clinical studies [4].

Physical benefits

Exercise can improve physical fitness [16], ADL [44], walking and balance [45], and reduce falls [46] in older people and clinical populations. Resistance training alone and cardiorespiratory training alone have each been shown to benefit balance after stroke [47], so either or both of these could be the active element within combined cardiorespiratory and resistance training.

Psychological benefits

Systematic review evidence indicates that physical activity, including exercise, can benefit anxiety and depression [48], quality of life [49], cognitive function [50], and fatigue [51] in a wide range of clinical and healthy populations. Exercise interventions may also have psychosocial benefits after stroke, via the mechanism of being delivered as group activity in a nonmedical setting [52].

In summary, exercise may not only increase fitness, but it may also provide risk reduction, physical benefits, and psychological benefits that align to known post-stroke problems [23, 24]. However, as well as benefits, there may also be a risk of training-induced adverse effects, such as soft tissue injuries, altered muscle tone, falls, and secondary vascular events.

Why it is important to do this review

Stroke has a high burden of death and disability globally, and this is predicted to increase [53]. Exercise interventions could reduce the risk of death and disability during life after stroke.

A systematic review of patient priority-setting exercises [54] showed that there are multiple outcomes important to people after stroke, which may be influenced by exercise. These relate to a) secondary prevention, b) physical outcomes (arm function, gait, mobility, balance, fitness), and c) psychological outcomes (quality of life, anxiety, depression, cognition, fatigue) [55, 56, 57].

Considering the high level of interest in exercise, and the clinical relevance of systematic reviews of exercise for improving patient care, it is important to update evidence from earlier versions (2004 to 2020) of the Cochrane review of fitness training after stroke [47]. That review showed exercise may reduce disability and improve post-stroke physical fitness and aspects of physical function. However, it also highlighted the lack of high quality studies, the need for a broader range of stroke participants and intervention doses.

To update the evidence we have divided the previous review into three new titles: a) cardiorespiratory training [58], b) resistance training [59], and c) combined cardiorespiratory plus resistance training (this review).

OBJECTIVES

The primary objective of this review is to determine whether combined cardiorespiratory fitness and resistance training after stroke has any effects on death, disability, adverse events, risk factors, fitness, walking, and indices of physical function when compared to a non-exercise control.

The secondary objective of this review is to determine whether combined cardiorespiratory fitness and resistance training after stroke has any effects on health status and quality of life, mood, cognitive function, and fatigue when compared to a non-exercise control.

METHODS

We followed the Methodological expectations for Cochrane intervention reviews (MECIR) guidance when conducting the review [60] and PRISMA 2020 for reporting [61].

We split the previous version of this review [47] into three new reviews on the basis of intervention type: cardiorespiratory training [58], resistance training [59], and combined cardiorespiratory and resistance training (this review). These were the three main comparisons present in all previous versions.

A full list of amendments to the previous review methods are documented in Supplementary material 9.

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Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs), including cluster-RCTs.

We included randomised cross-over studies if data from the first iteration were available because this is equivalent to an RCT design and is not influenced by carry-over effects.

We included studies examining effects of combined cardiorespiratory and resistance training interventions versus control in the following intervention groupings.

1. **End of intervention** - time point when a training programme finishes
2. **End of follow-up** - time point occurring after the end of the intervention. For studies with multiple follow-up phases, we analysed data from the longest follow-up period.

We included full-text reports of published and unpublished studies. Potentially relevant studies available only as conference proceedings or abstracts were retained as 'awaiting classification' pending further information or full publication.

We did not exclude studies on the basis of sample size.

We included studies published in languages other than English only when a suitable machine translation could be generated (Google Translate).

Where investigators published several reports based on data from a single study population, we adopted the most recent or most complete report as the primary publication, and listed other reports as additional publications of the included study.

Types of participants

We sought studies recruiting stroke survivors, 18 years of age or over, with any degree of stroke severity, at any stage of care, and any time since stroke. We included participants irrespective of their ability to walk independently, and irrespective of whether they had first or recurrent strokes.

In trials including both stroke and non-stroke participants, we determined whether the subset of data for stroke participants was accessible from the report or through contact with trial authors. If it was not, we excluded the study.

Types of interventions

Intervention

We included RCTs of combined cardiorespiratory and resistance training interventions and analysed these as a single intervention in Cochrane's Review Manager (RevMan) software [62].

Combined training is an exercise intervention including different activity components, intending to improve cardiorespiratory fitness and strength, power or muscular endurance; for example, a training programme comprising both cycling and weight training.

Cardiorespiratory training aims to improve cardiorespiratory fitness. It can include extended, continuous bouts of moderate intensity exercise or repeated, shorter, high intensity bouts of exercise (e.g. interval training or high intensity intermittent training (HIIT)). All forms of cardiorespiratory training can be performed using devices or ergometers (e.g. treadmill, cycling, rowing) or through modes of activity such as walking or climbing stairs.

Resistance training aims to improve musculoskeletal fitness (strength and muscular endurance or muscle power output, or both). It typically involves repeated muscle contractions resisted by body weight, elastic devices, masses, free weights or specialised machine weights, or isokinetic devices.

We defined 'training' as a systematic, progressive increase in intensity, resistance, frequency, or duration of exercise throughout a scheduled programme.

We excluded studies that combined fitness training with assistive or other technologies, such as robotic and electromechanical-assisted gait training devices during bodyweight-supported locomotor training. We also excluded studies investigating virtual reality approaches.

Control

We included studies in which controls were exposed to either usual care or no training.

1. **Usual care** - inpatient hospital care or other standard rehabilitation given to all stroke patients delivered as a normal part of stroke care in the region in which the study is performed.
2. **No training** - no intervention or a non-exercise intervention (e.g. cognitive tasks or sham training).

Comparisons

We included the following comparisons.

1. Combined training versus no intervention/waiting list control
2. Combined training versus attention control/sham intervention
3. Combined training versus usual care
4. Combined training plus % of usual care versus usual care
5. Combined training plus usual care versus usual care
6. Combined training plus usual care versus usual care plus attention control/sham intervention

Comparison 4 refers to combined training interventions that replace some, but not all, of usual care.

Outcome measures

We grouped all included outcomes at end of intervention and at end of follow-up.

For multiple measurement time points in a trial, we did the following.

- Only end of intervention time points were included; any interim time points were not included.
- Where multiple post-intervention time points were reported, we included the longest follow-up time point.

If multiple outcome measures within one outcome domain (e.g. disability scale scores; muscle strength measures) were reported within the same trial, one outcome was selected for meta analysis.

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Two review authors agreed the selected outcome based on the following hierarchy:

- stroke-specific measurement tool;
- outcome measure closest to category of outcome in the context of the specific exercise intervention;
- superior measurement properties (reliability, consistency, validity, ceiling effects etc).

Critical outcomes

The critical outcomes are those that represent physical measures and effects (see Table A below). As well as the confirmatory approach of recording adverse events (all causes), we also used an exploratory approach to record any reported adverse effects where the intervention was the probable cause [63]. As well as data selected for meta-analysis, we recorded other relevant outcomes within each outcome group and reported these naratively using a synthesis without meta-analysis approach (SWiM) [64].

Table A. Critical outcomes

Outcome group	Outcome domain	Outcomes for meta-analysis	**Outcomes for summary of findings tables**	
			End of intervention	**End of follow-up**
1. Death	Death	Numbers of deaths from all causes (N people)	Yes	Yes
2. Disability	Disability	Any relevant functional scales representing global indices of activity limitation (e.g. Functional Independence Measure [65]; Barthel Index [66]	Yes	Yes
3. Adverse events	Secondary events	Number of people experiencing secondary cardiovascular or cerebrovascular events (N people)	Yes	Yes
	Falls	Number of people experiencing falls (N people)	No	No
4. Risk factors	Blood pressure	Systolic blood pressure (mmHg)	Yes	Yes
		Diastolic blood pressure (mmHg)	No	No
5. Physical fitness	Cardiorespiratory fitness	$\dot{V}O_2$ peak (mL/kg/min)	Yes	Yes
	Musculoskeletal fitness	Strength, affected lower limb (e.g. kg, N)		
		Strength, unaffected lower limb (e.g. kg, N)		
		Strength, affected upper limb (e.g. kg, N)		
		Strength, unaffected upper limb (e.g. kg, N)		
6. Walking	Walking independence	Functional ambulation category score (0 to 5)	No	No
	Walking speed	Maximal (m/sec)	No	No
		Comfortable (m/sec)	Yes	Yes
	Walking endurance	Six-minute walk test (6-MWT) distance (metres)	No	No
7. Physical function	Balance	Any relevant scale or measure of balance (e.g. Berg Balance Scale [67])	Yes	Yes

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Functional mobility	3-metre timed up and go time (seconds)	No	No

Important outcomes

We recorded subjective measures of the following psychological concepts reported using any relevant scale or subscale.

- Health status and quality of life (overall, physical, mental, and social health)
- Mood (anxiety and depression)
- Cognitive function
- Fatigue severity (overall, physical, and mental fatigue)

Search methods for identification of studies

We searched for relevant studies in all languages and arranged translation of relevant articles where necessary.

Electronic searches

Search strategies used in this review were revised from the previous Cochrane review including this topic, in order to include new relevant terms and to improve sensitivity and specificity.

We searched the following electronic databases in January 2024. The search strategies are recorded in Supplementary material 1.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2024, Issue 1) in the Cochrane Library
- MEDLINE Ovid (from 1946 to January 2024)
- Embase Ovid (from 1947 to January 2024)
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; from 1937 to January 2024)
- SPORTDiscus EBSCO (from 1949 to January 2024)
- PsycINFO Ovid (from 1806 to January 2024)
- Conference Proceedings Citation Index - Science (Web of Science; from 1990 to January 2024)
- PEDro (Physiotherapy Evidence database (www.pedro.fhs.usyd.edu.au/index.html) January 2024)
- DORIS (Database of Research Into Stroke https://www.askdoris.org, 5 August 2022). DORIS was last updated on 5 August 2022.

The search strategy includes Cochrane filters for the identification of RCTs [68], and Cochrane Stroke's filters for the identification of 'stroke' studies in respective databases and other resources. These are supplemented with controlled vocabulary and plain text search terms to identify combined cardiorespiratory and resistance training interventions.

In order to identify other published, unpublished, and ongoing studies, we searched for ongoing studies using the following registries.

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov/)
- World Health Organisation International Clinical Trials Registry Platform (ICTRP; apps.who.int/trialsearch)

Searching other resources

We searched for grey literature and theses in January 2024 via the following sources (using the search terms in Supplementary material 1).

- ProQuest Dissertations and Theses Global (www.proquest.com/products-services/pqdtglobal.html)
- British Library EThOS (e-theses online service; (https://www.bl.uk/ EThOS currently offline due to a cyberattack)
- DART-Europe E-theses PortAL (www.dart-europe.eu/basic-search.php discontinued from 3 February 2025)
- Google Scholar

We used Citation Chaser software to identify the following [69].

- Backward citations from 50 relevant exercise-related systematic reviews identified during our searches.
- New forward citations from the studies included in the previous Cochrane review that included our topic.
- Forward and backward citations from the new studies included in this split review.

To identify potentially relevant studies, we also contacted researchers in the field via social media groups interested in stroke and exercise.

We contacted authors for clarification and further data if study reports were unclear.

Data collection and analysis

We used the Covidence [70] tool for study selection at the title and abstract stage and at the full-text stage, and we completed a PRISMA flow chart to depict the study selection process [61] (Figure 1).

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Figure 1. PRISMA flow diagram

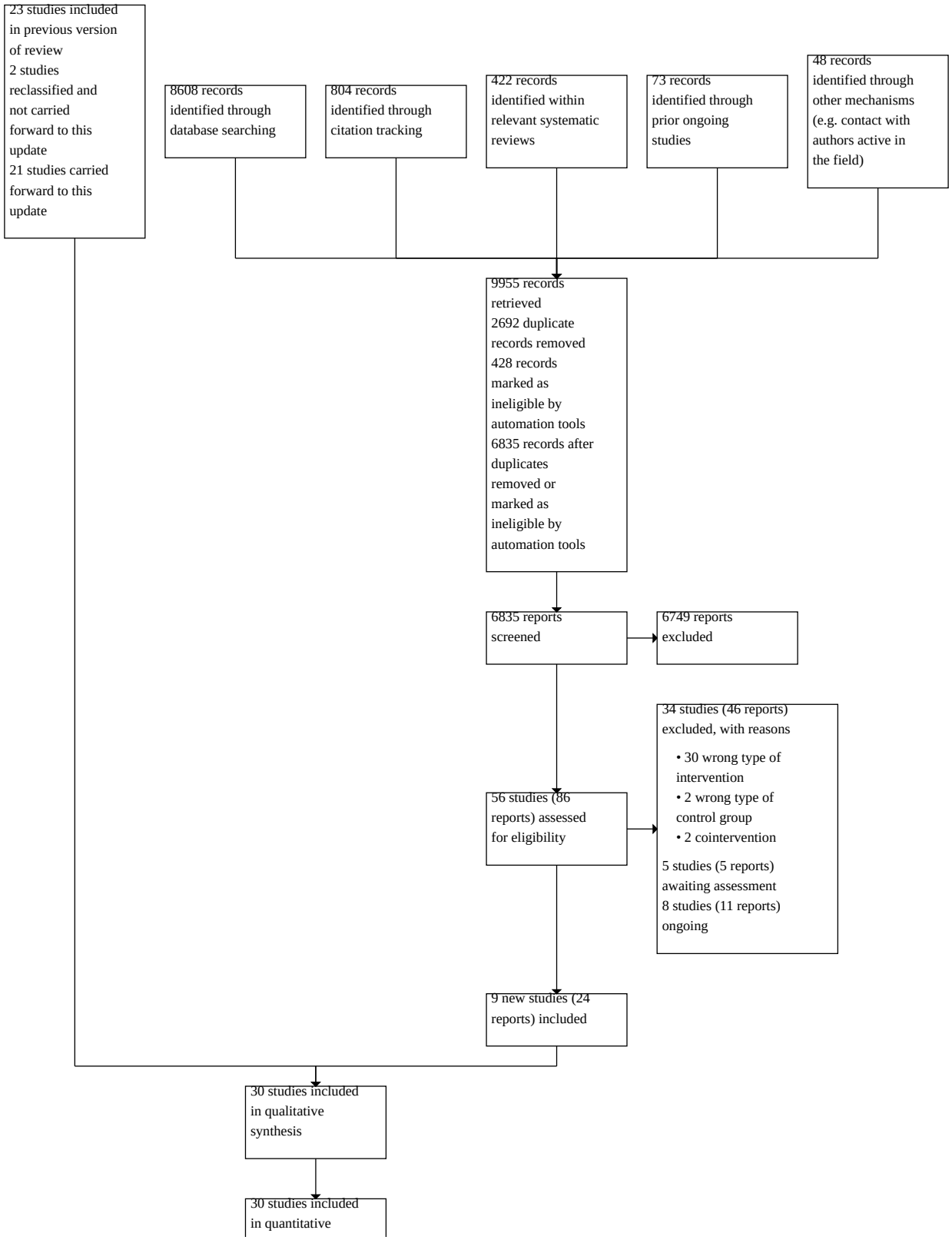

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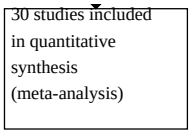
Figure 1. (Continued)



We used Covidence to automatically remove duplicates, and we used the Cochrane RCT classifier, integrated in Covidence, to automatically exclude studies that were not classified as an RCT design.

Selection of studies

Title and abstract screening

Two review authors (DS and either SC, MF, GM, JM, SM, or GW) independently screened titles and abstracts of unique references obtained from searches; we voted to either include or exclude. We excluded as irrelevant studies that two review authors classified as 'excluded'. We resolved any disagreements through discussion or, if required, we consulted a third review author. All studies with two 'included' votes entered full-text screening.

Full-text screening

Two review authors (DS and either SC, MF, JM, SM, or GW) independently screened full-text articles to identify studies for inclusion and record reasons for excluding ineligible studies. We resolved any disagreements through discussion or, if required, we consulted a third review author (GM). We collated multiple reports of the same study so each study, not each reference, was the unit of interest.

We included studies irrespective of publication status if available reports had sufficient detail to apply eligibility criteria and perform a risk of bias assessment.

We retained potentially relevant studies with insufficient information to either include or exclude in the Supplementary material 4 table.

Review authors with direct involvement in conduct, analysis, and publication of a study with potential for inclusion, did not make study eligibility decisions, extract data, carry out the risk of bias assessment, or perform GRADE assessments for those studies.

Post-publication-amendment screening

We used the Retraction Watch database to check whether any studies selected for inclusion (new or pre-existing) were known to have been retracted or have expressions of concern (https://retractionwatch.com/). We excluded studies known to be retracted. For studies with expressions of concern, we considered the nature of the concerns and the potential impacts on study validity and outcomes.

Data extraction and management

Study characteristics data

One review author (from DS, SC, MF, JM, SM, GW) extracted data from each included study and entered outcome data into Review Manager Web [62]. A second review author cross-checked all entered data. We contacted study authors to obtain any missing data if required.

The domains for data extraction included the following.

- **Publication details**: authors, year of publication, publication status (published, unpublished, or ongoing), citation of other relevant studies; publication concerns (e.g. predatory publishing indicated by listing in https://www.predatoryjournals.org/)
- **Study conduct**: study design, type of comparison (see Types of studies), geographical location of study; measurement time points and durations (e.g. end of 10-week intervention, end of 3-month follow-up)
- **Participants**: age, sex, stage of care, time since stroke onset, ambulatory status; inclusion and exclusion criteria; number of participants randomised, excluded, assessed, and lost to follow-up, and characteristics of losses
- **Intervention**: total number of intervention groups; exercise mode (e.g. walking, weight training); body segments trained (upper/lower limb, affected/unaffected side); dose parameters of intensity (e.g. 70% one-repetition maximum (1RM) or 70% maximum heart rate), frequency (days/week) and programme length (weeks/months), setting (e.g. hospital, community)
- **Outcome measures**: which critical outcomes (i.e. death, disability, adverse events, risk factors, physical fitness, walking, physical function measures) and important outcomes (health status and quality of life, mood, cognition, and fatigue) were reported.

Acceptability and tolerability data

We collated data relating to the acceptability and tolerability of interventions, including withdrawals before/during the intervention, adherence to intervention (i.e. attendance at and compliance with interventions), and adverse effects possibly/probably arising as a result of the intervention.

Study results data

We classified all outcome data as end of intervention or end of follow-up. We defined follow-up as any period of time after intervention completion.

- Data on deaths and cardiovascular or cerebrovascular events were included if data were available from the CONSORT flowcharts and/or study reports and there were no unexplained losses to follow-up.
- Data on falls were included where studies had a preplanned approach for recording adverse events, including falls, throughout the study period.
- We transformed median (interquartile range (IQR)) into mean (standard deviation (SD)) if necessary [71].

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- We transformed the mean (SD) of walking time data (sec/m) into mean (SD) walking velocity data (m/sec) using an approximation method involving reciprocal transforms (Taylor expansion).
- We collected arm-level data and/or contrast-level data where available.
- For data intended for mean difference meta-analysis, we collected change data (mean difference and SD_{diff}) where available.

One review author extracted outcome data and entered it into RevMan. A second person checked all the entered outcome data within RevMan. We used a checklist to ensure the following.

- All preplanned outcomes were included.
- Arm-level data and/or contrast-level data were included if available.
- Directions of beneficial effect in measurement instruments were correctly accounted for.
- All results data for each included outcome corresponded exactly to the report, and if not, that any calculations/transformations carried out were correct.
- All participant numbers (n) were correctly accounted for intention-to-treat or per-protocol analyses.

We resolved any disagreement by consensus or arbitration.

Risk of bias assessment in included studies

Two review authors (DS and either SC, MF, JM, SM, or GW) independently assessed each study using Cochrane's tool (RoB 1) for assessing risk of bias [72]. We resolved any disagreements by discussion or by involving another review author (GM). We assessed risk of bias for each standard domain in RoB 1, with the following exceptions and amendments.

Blinding of participants (performance bias and detection bias)

Participant blinding is often impossible to achieve in behavioural interventions. However, we considered studies to be at low risk of bias if authors described some attempt to disguise the true purpose of comparisons being made (e.g. describing a trial as a comparison of two different interventions or some kind of 'sham' intervention). We considered studies to be at high risk of bias if there was an imbalanced exposure time across trial arms; for example, if a control group had no exposure (as might occur with a waiting-list control).

Incomplete outcome data (attrition bias)

We assessed this domain at the end of intervention and at the end of follow-up. We considered studies to be at high risk of bias where we judged imbalanced losses to have occurred coupled with a per-protocol analysis. If overall participant attrition was 20% or greater of those randomised, we considered a study at high risk of bias [73], irrespective of distribution of losses, reasons given, or analytical approach (e.g. imputations, intention-to-treat).

Where missing supplementary information could not be obtained, we recorded an 'unclear' risk of bias. We recorded 'high', 'low', or 'unclear' risk of bias in risk of bias tables, along with a descriptive justification for our judgements.

Measures of treatment effect

Dichotomous data

For dichotomous outcome data (death, secondary events, falls), we calculated risk difference (RD) and 95% confidence intervals (CIs) [74].

Continuous data

Where possible, we presented intervention effects on all continuous outcome data as a mean difference (MD) and 95% CIs. Where studies used different scales to measure the same clinical outcome, we presented effects as standardised mean difference (SMD) and 95% CIs.

We calculated treatment effects using arm-level meta analysis at the end of intervention and end of follow-up as the primary analyses [75].

In addition, we calculated treatment effects by combining arm-level and contrast-level data (favouring contrast-level where both existed) where contrast-level data were available in addition to or in place of arm-level data. We tested the influence of this as a sensitivity analysis.

We categorised SMD effect sizes as small d > 0.2, moderate d > 0.5, and large d > 0.8 [76].

We considered MD effect sizes in relation to a minimal clinically important difference (MCID) where available.

- SBP and DBP −2mmHg [77]
- Cardiorespiratory fitness $\dot{V}O_2$peak (+3.5ml/kg/min) [78]
- Walking, comfortable speed +0.13m/sec; [79]
- Walking, 6-MWT +71m; [80]

Unit of analysis issues

Cross-over studies

We used data from the first-period of cross-over studies, and then treated these as if they were data from RCTs. We ignored subsequent periods of cross-over studies because of the influence of carry-over effects.

Lag-control or waiting-list studies

We dealt with these as for cross-over studies. We ignored delayed or waiting-list iterations of the study because of the influence of carry-over effects.

Multiple intervention arms

In studies with more than one relevant intervention group or more than one relevant control group, we included data from all trial arms within a meta-analysis; these were conflated by RevMan into a single overall group.

The time points for outcome measurement were the end of intervention and end of follow-up.

Dealing with missing data

Missing participants

We accounted for the nature and extent of missing participant data (e.g. losses to follow-up) and how the study authors dealt

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with this (e.g. intention-to-treat analysis) via one of the risk of bias assessments (Risk of bias assessment in included studies; incomplete outcome data). We did not perform imputations for missing data, but we did include data where study authors had performed imputations of missing outcome data.

Incomplete reporting

If RCTs had missing information, we contacted the study authors to request this. Where there was insufficient information to include or exclude a potentially relevant study, we retained the study in the Supplementary material 4 section in case the information emerges at a later date.

Reporting bias assessment

When meta-analyses included a minimum of 10 studies, we used a funnel plot to assess potential reporting bias [81].

Synthesis methods

Synthesis with meta-analysis

Where we considered studies to be sufficiently similar, we conducted meta-analysis by pooling appropriate data using RevMan [62].

We used random-effects meta-analysis models to calculate measures of effect and 95% CIs at end of intervention and end of follow-up for each outcome measure with sufficient suitable data to pool.

We used the Mantel-Haenszel method to calculate RD effect measures and the inverse variance method to calculate MD and SMD effect measures.

Different measurement scales were combined using SMD analyses. In some tools, a more favourable outcome is associated with a higher score, and in others, it is a lower score. To correct for this, we multiplied the mean values by −1 to change the effect direction in one set of studies.

We assessed heterogeneity using the I^2 statistic [82]. We investigated substantial heterogeneity (I^2 > 50%) by inspecting study effects and by using subgroup and sensitivity analysis.

We used only arm-level data as the primary analysis. We also performed sensitivity analysis comparing these with arm-level and/or contrast level data where these were available.

Synthesis without meta analysis

We synthesised outcomes not analysed using meta-analysis using the Synthesis Without Meta-analysis (SWiM) guidance to indicate the directions of effect [64].

Investigation of heterogeneity and subgroup analysis

When sufficient data were available, we planned to investigate heterogeneity between included studies (both clinical and statistical) by means of subgroup analysis. We attempted to compare effect estimates for all outcomes in the following main subgroups.

- Participant stage of recovery (acute (< 7 days)/early subacute (7 days to 3 months)/late subacute (3 to 6 months)/chronic (> 6 months)) [83]
- Intervention duration (< 12 weeks/≥ 12 weeks)
- Participant ambulatory status at baseline (ambulatory/non-ambulatory/mixed ambulatory and non-ambulatory/unclear)

Equity-related assessment

We did not investigate health inequities in this review; it was not planned at the protocol stage.

However, we recorded the geographical location (region and country) of each included study and considered this in our conclusions in terms of which were low- to middle-income countries [84].

Sensitivity analysis

We used sensitivity analysis to examine the effect of excluding studies with the following features.

- Imbalanced intervention exposures
- Outcome data imputed by review authors
- Predatory journal/publishers' concerns indicated by listing in https://www.predatoryjournals.org/

We used sensitivity analysis to examine the effect of including studies with contrast-level outcome data.

Certainty of the evidence assessment

We used GRADE [85] to assess the certainty of evidence for each of the following outcomes at a) the end of intervention, and b) the end of follow-up for the following outcomes (see Table A Critical outcomes).

1. Death
2. Disability
3. Secondary events
4. Blood pressure (systolic)
5. Physical fitness (cardiorespiratory and musculoskeletal fitness)
6. Walking speed (comfortable)
7. Balance

We held a consensus meeting (JM, GW SC) to grade outcomes. We downgraded the certainty of the evidence for outcomes if we identified serious or very serious concerns or limitations, as follows.

- **Indirectness**: all aspects of PICO (participants, interventions, comparisons, and outcomes) were considered for indirectness.
- **Imprecision**: we considered downgrading twice where the CI included an important threshold of interest (e.g. MCID harm or benefit) [86].
- **Risk of bias**: we downgraded where there were concerning and/or multiple high risk of bias items that could be influential for the outcome concerned.
- **Inconsistency**: we downgraded where we considered there to be high levels of unexplained heterogeneity (including I^2 > 50%).
- **Publication bias:** we downgraded where there was evidence of funnel plot asymmetry.

We used GRADEpro GDT software [85] to present the certainty of evidence assessments in two summary of findings tables, one for the end of intervention time point and one for the end of follow-up time point.

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Consumer involvement

There had been no consumer involvement specified in the previous protocols for the Cochrane review that included this topic [47]. Consumers were also not directly involved in this new version of the review. However, the review authors have ensured that the outcomes map onto those identified in current patient priority-setting partnerships relating to life after stroke. These are based on substantial consumer involvement in Norway (N = 589 [56]) and the UK (N = 28 [55], and N = 1400 [57]). These 'top 10' lists of patient priorities relate to multiple types of outcome known to be sensitive to exercise and important to patients; therefore, there is a good rationale to include these (see Table 1).

RESULTS

Description of studies

Results of the search

The previous version of this review included 23 studies investigating combined cardiorespiratory and resistance training interventions, involving 1207 participants [47]. Not all of the studies that were previously included (N = 21/23), awaiting classification (N = 11/35), or ongoing (N = 10/56) have been carried forward into this new review (see Supplementary material 8 for further details).

We conducted the literature searches in January 2024. We identified 50 new systematic reviews of exercise interventions, extracted all the backward citations and fed these into the screening process at title and abstract stage.

Search results are summarised in Figure 1.

The total number of records retrieved by the searches was 9955. These were identified from electronic databases (8608), citation tracking (804), screening systematic reviews (422), ongoing studies from the previous version that are now published (73), and studies found via other sources such as contact with researchers (48). After removal of duplicates and studies marked as ineligible by automation tools, we were left with 6835 titles and abstracts to screen. We rejected 6749 of the records, leaving 86 records (reporting on 56 studies) for full-text screening.

Of the 56 studies, we excluded 34 studies (30 tested an ineligible type of intervention, two had an ineligible control group, and two used a cointervention). The final number of new included studies was nine (Acheampong 2018 [87]; Aravind 2022 [88, 89]; Fotiadou 2019 [90]; Jarbandhan 2022 [91]; Kang 2022 [92, 93]; Klassen 2020 [94, 95, 96, 97, 98, 99, 100, 101]; Liu-Ambrose 2022 [102, 103, 104, 105]; Rizvi 2023 [106]; Vahlberg 2021 [107, 108, 109, 110]), which we added to the 21 carried forward from the previous version of the review. Thus, this review includes 30 studies.

There were five new studies awaiting classification, which we added to 11 carried forward from the previous review, giving 16 studies awaiting classification (Supplementary material 4).

There were eight new ongoing studies, which we added to 10 carried forward from the previous review, giving 18 ongoing studies (Supplementary material 5).

Included studies

Study characteristics

The characteristics of the 30 included studies are described in Supplementary material 2 (as mentioned above, nine were new and 21 were carried forward from a previous broader review).

The key characteristics of the study populations, interventions, comparators, and outcomes are summarised in the overview of synthesis and included studies (OSIS) table, see Table 2.

There were 1519 participants in the studies, with an average age of 63.7 years (study cohorts from 49.5 to 78.5 years). Most studies (28/30) recruited ambulatory participants who were in the early subacute (n = 14) and chronic (n = 14) phases of recovery. Most participants lived in high-income countries (12 studies from Europe, eight from North America, and six from Asia).

Study designs mostly had imbalanced exposures of the intervention that exceeded the control (23/30). Most interventions were of short duration (18 were less than 12 weeks; 12 were 12 weeks or more) and 12/30 studies included a post-intervention follow-up period (mean 7.3 months; range 3 to 12 months). Most studies were published in sources not implicated in predatory publishing (25/30); see key study covariates summarised in Table 3.

Modes and combinations of cardiorespiratory training and resistance training varied and were often delivered together in a circuit training format. In 19/30 studies, both upper and lower limbs were involved, with upper limbs being restricted to resistance training activity; 11/30 studies were lower limb only. All 30 studies employed bilateral training of the limbs. Cardiorespiratory training mode was most commonly walking (treadmill or overground), with or without additional stationary cycle training. Resistance training mode included weights, exercise machines, elastic resistance, and bodyweight exercises (see Table 2).

The dose of combined cardiorespiratory and resistance training interventions varied and could not always be aligned with the metrics used in current exercise recommendations for stroke [4]. Dose of intervention progressed in all studies based on intensity, duration, repetition number, speed, resistance/mass of objects, or ratings of perceived exertion. Cardiorespiratory training intensity was quantified in 17/30 studies using heart rate or rating of perceived exertion. Resistance training intensity was not often expressed in relation to one-repetition maximum (5/30 studies). Most studies (28/30) trained participants two to five days a week (range < 1 to 7 days/week). Training programmes lasted between four weeks and one year; most were of short duration (< 12 weeks 18/30, ≥ 12 weeks 12/30; Table 2).

We contacted the authors of eight included studies, either to request further information about the nature of the interventions (Aravind 2022; Duncan 1998 [111]; Jarbandhan 2022; Klassen 2020; Rizvi 2023) or to clarify outcome data (Fotiadou 2019; Furnari 2014 [112]; Moore 2015 [113, 114, 115]; Rizvi 2023). See notes in Supplementary material 2.

Acceptability and tolerability of interventions

We used withdrawals, adherence (attendance and compliance), and adverse effects to assess the acceptability and tolerability of combined training interventions (Table 4).

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Total losses during the combined training intervention period (63 participants) were very similar to those in the control groups' exposure (56 participants). Reasons for withdrawal included medical and practical issues. Only one participant who withdrew did so because of a preference for the alternative intervention. Four refused participation or were not interested, and eight did not have the time. These withdrawals could be connected directly or indirectly to the intervention demands. The control group also had losses connected to the control exposure (one participant wanted the training intervention, five were not interested or had no time, and two had no suitable transport).

Attendance at planned combined training sessions was reported in 16/30 studies; 13 studies had over 80% attendance, including seven that had over 90% attendance.

Compliance with prescribed training during combined training sessions was reported in 10/30 studies. There were no serious issues with tolerating the intensities.

Adverse effects (i.e. those possibly, probably, or definitely attributable to the intervention) were reported in 12/30 studies, including 5/30 studies where collecting these data was preplanned. In 9/12 studies, there were no reported adverse effects connected to the intervention. One of the 12 studies reported two serious adverse effects (fainting, transient ischaemic attack) and two reported 24 minor adverse effects (including fatigue, trips, and falls). Adverse effects attributable to combined training were very uncommon.

Excluded studies

We excluded 34 ineligible studies (see Supplementary material 3).

The most common reason for exclusion was that the intervention did not meet the criteria for fitness training ('ineligible intervention', 30 studies). Other studies were excluded as they were confounded by other intervention components ('co-intervention', 2 studies) or had inappropriate control groups, for example, an active physical intervention ('ineligible control', 2 studies).

We excluded two of 23 previously included studies because we considered one to be resistance training only and the other contained a problematic cointervention update (described in Supplementary material 8).

Risk of bias in included studies

We summarise our risk of bias assessments in Figure 2, Figure 3, and Supplementary material 2.

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Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. In studies with no follow-up measurement, we did not assess risk of bias for the item labelled 'incomplete outcome data (attrition bias): end of follow-up'; this results in some blank spaces.

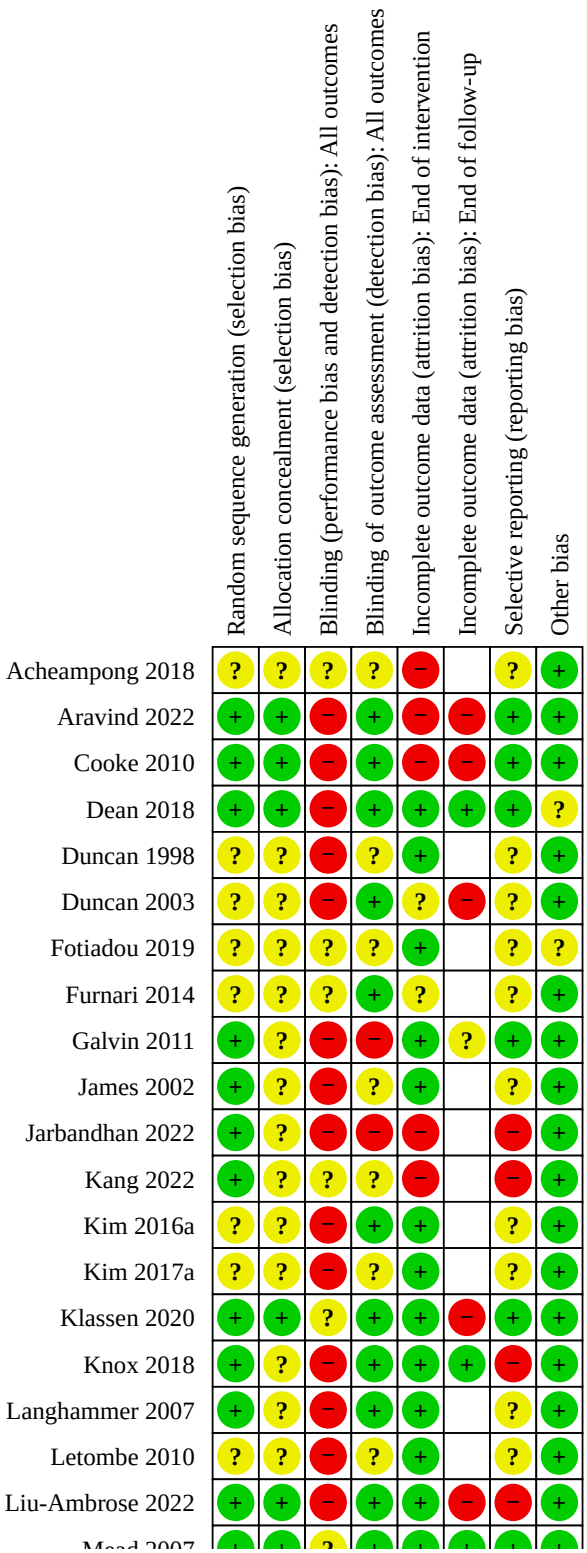

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Figure 2. (Continued)

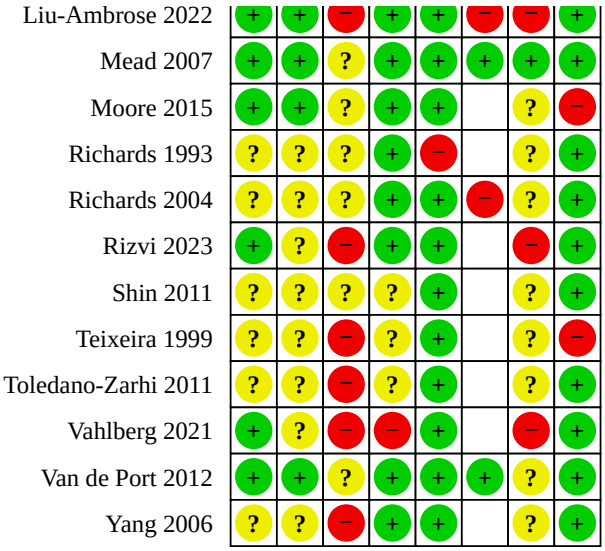
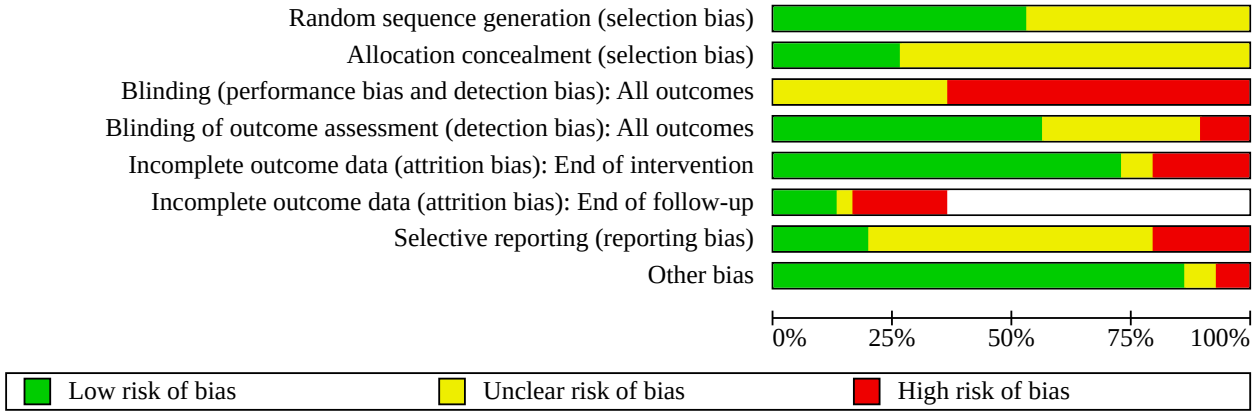


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies. In studies with no follow-up measurement, we did not assess risk of bias for the item labelled 'Incomplete outcome data (attrition bias): end of follow-up'; this results in some blank spaces



Participant blinding

Performance bias was the most prevalent issue that led to ratings of high risk of bias, affecting 19/30 (63%) studies. This issue arose when experimental and control group interventions were imbalanced with regard to the amount or dose of exposure. This systematic difference in dose of exposure means any kind of participant blinding is impossible. The lack of participant blinding has the potential to influence participant (and investigator) behaviour.

Attrition bias

High risk of bias due to participant losses occurred in 6/30 (20%) studies at the end of intervention. This increased in proportion to 6/11 (55%) studies with a follow-up time point (there is no judgement for Richards 1993 [116, 117], which was not included in any of our meta-analyses at follow-up.)

Synthesis of results

Critical outcomes

Synthesis with meta-analysis, including subgroup and sensitivity analysis, is described in detail for critical outcomes (Table 5) and important outcomes (Table 6). The definitive analysis emerging for each outcome is listed below.

There were few formally identified subgroup differences. Often there were too few data overall, or there was uneven covariate distribution across subgroups; the only caveats relate to disability and cardiorespiratory fitness (see below).

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Where there were multiple outcome measures within one outcome domain, we have recorded the justification for the outcome selected in Table 7.

Synthesis of outcomes without meta-analysis (SWiM) is described in Supplementary material 10.

The summary of findings tables for our selected critical outcomes at the end of intervention are reported in Summary of findings 1 and at the end of follow-up in Summary of findings 2.

Death

At the end of the intervention, combined training does not increase or reduce deaths (RD -0.00, 95% CI -0.02 to 0.01; I^2 = 0%; 26 studies, 1352 participants; high-certainty evidence; Figure 4). Deaths (n = 13) were confined to 3/26 studies commencing in the early subacute phase with interventions lasting 12 weeks or more. However, since deaths were so infrequent, any reduction in deaths would be difficult to detect. See Analysis 1.1.

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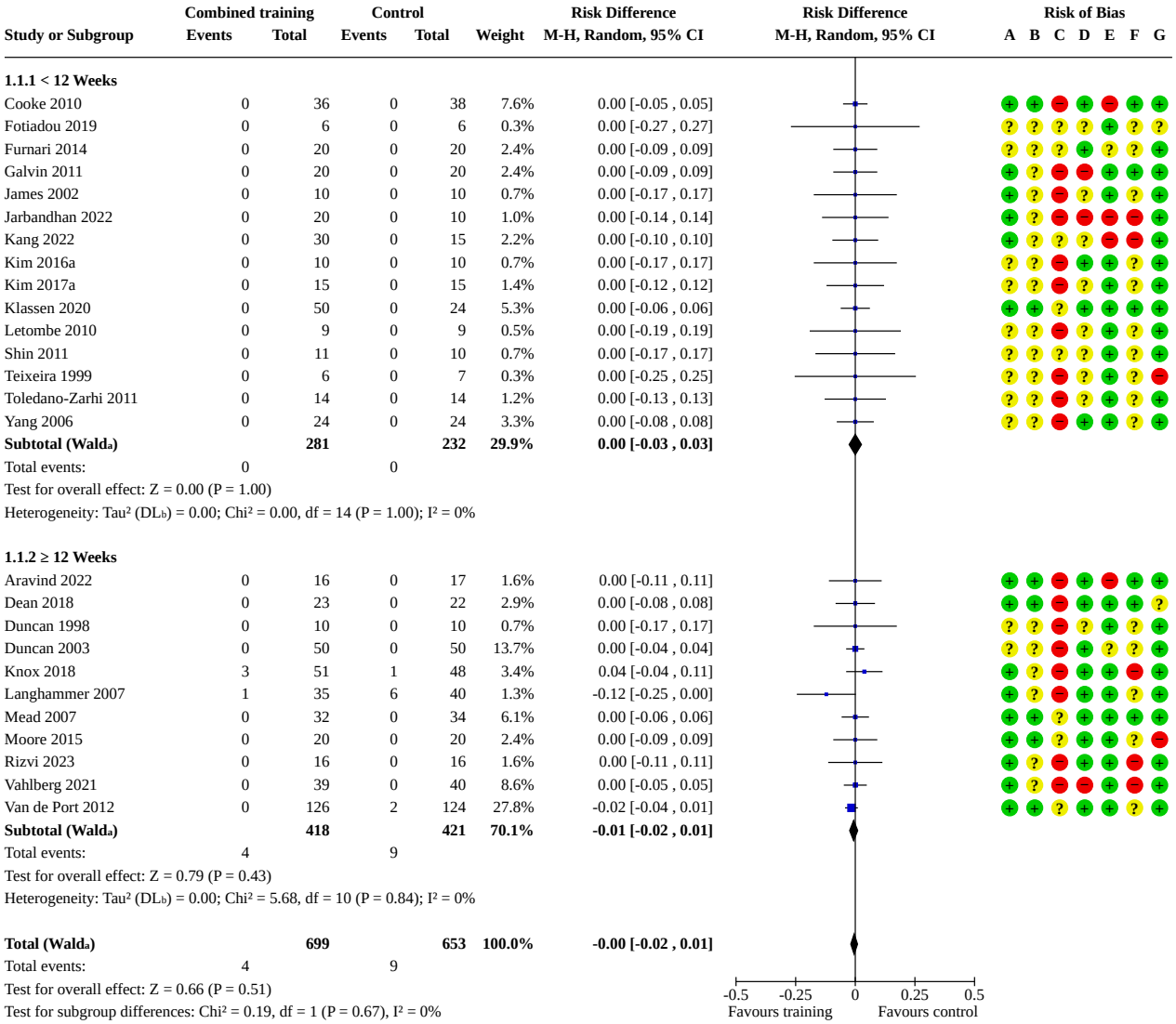
Figure 4. Forest plot of comparison 1.1: Effect of combined training versus control on deaths at end of intervention (<12 weeks or ≥ 12 weeks).



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of intervention
(F) Selective reporting (reporting bias)
(G) Other bias

At the end of follow-up (3 to 12 months), combined training does not increase or reduce deaths (RD -0.01, 95% CI -0.04 to 0.02; I^2 = 0%; 8 studies, 531 participants; high-certainty evidence; Figure 5). Deaths (n = 9) were confined to 3/7 studies in the early subacute phase, with 5/9 deaths after the end of intervention, during the follow-up period. However, since deaths were so infrequent, any reduction in deaths would be difficult to detect. See Analysis 2.1.

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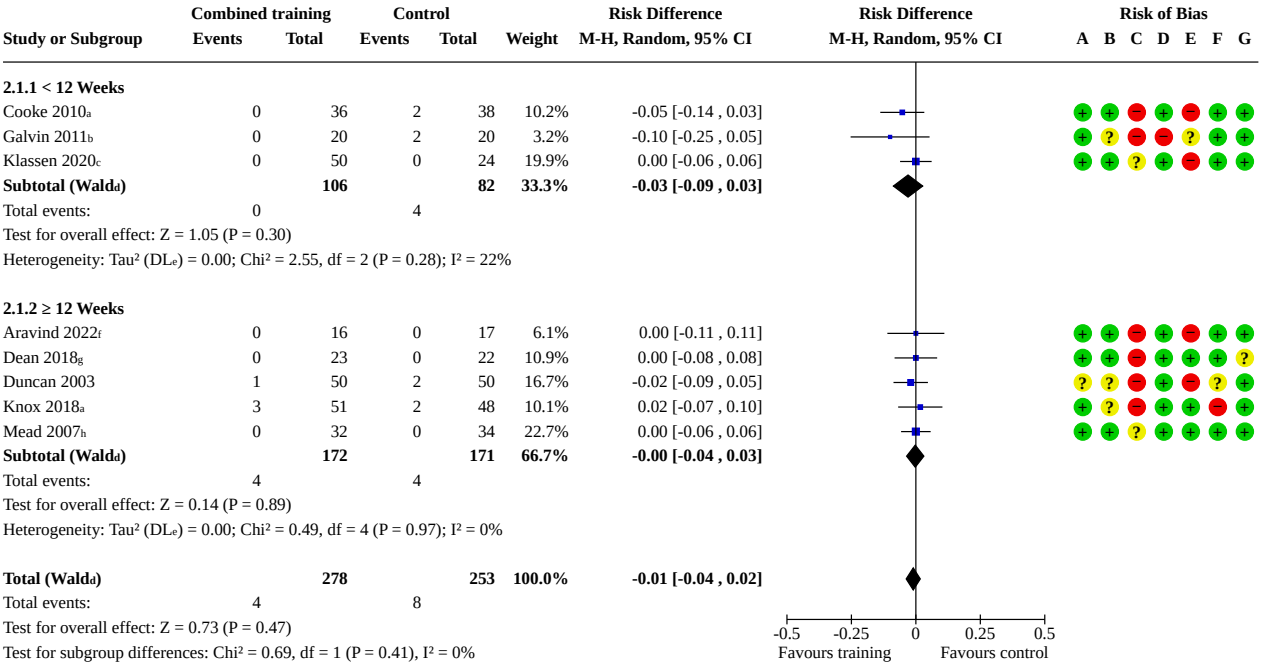
Figure 5. Forest plot of comparison 2.1: Effect of combined training versus control on death at end of follow-up (4 to 12 months).



Footnotes

a12 week follow-up period
b3 month follow-up period
c12 month post-stroke follow-up period
dCI calculated by Wald-type method.
eTau² calculated by DerSimonian and Laird method.
f10-month post-stroke follow-up
g9 month follow-up period
h4 month follow-up period

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of follow-up
(F) Selective reporting (reporting bias)
(G) Other bias

Disability

At the end of the intervention, combined training may improve indices of disability slightly (small effect size > 0.2) (SMD 0.20, 95% CI 0.04 to 0.36; I^2 = 11%; 13 studies, 789 participants; low-certainty evidence; Figure 6). In 11/13 studies, there was an imbalance in the exposure to the intervention or control condition. Although the overall subgroup analysis indicated no subgroup differences, the acute and late subacute subgroups only contained 1/13 studies. There was a subgroup difference between the early subacute and chronic subgroups (12/13 studies; P = 0.05; I^2 = 73.7%), which favoured the early subacute group. However, there is an uneven covariate distribution. See Analysis 1.2.

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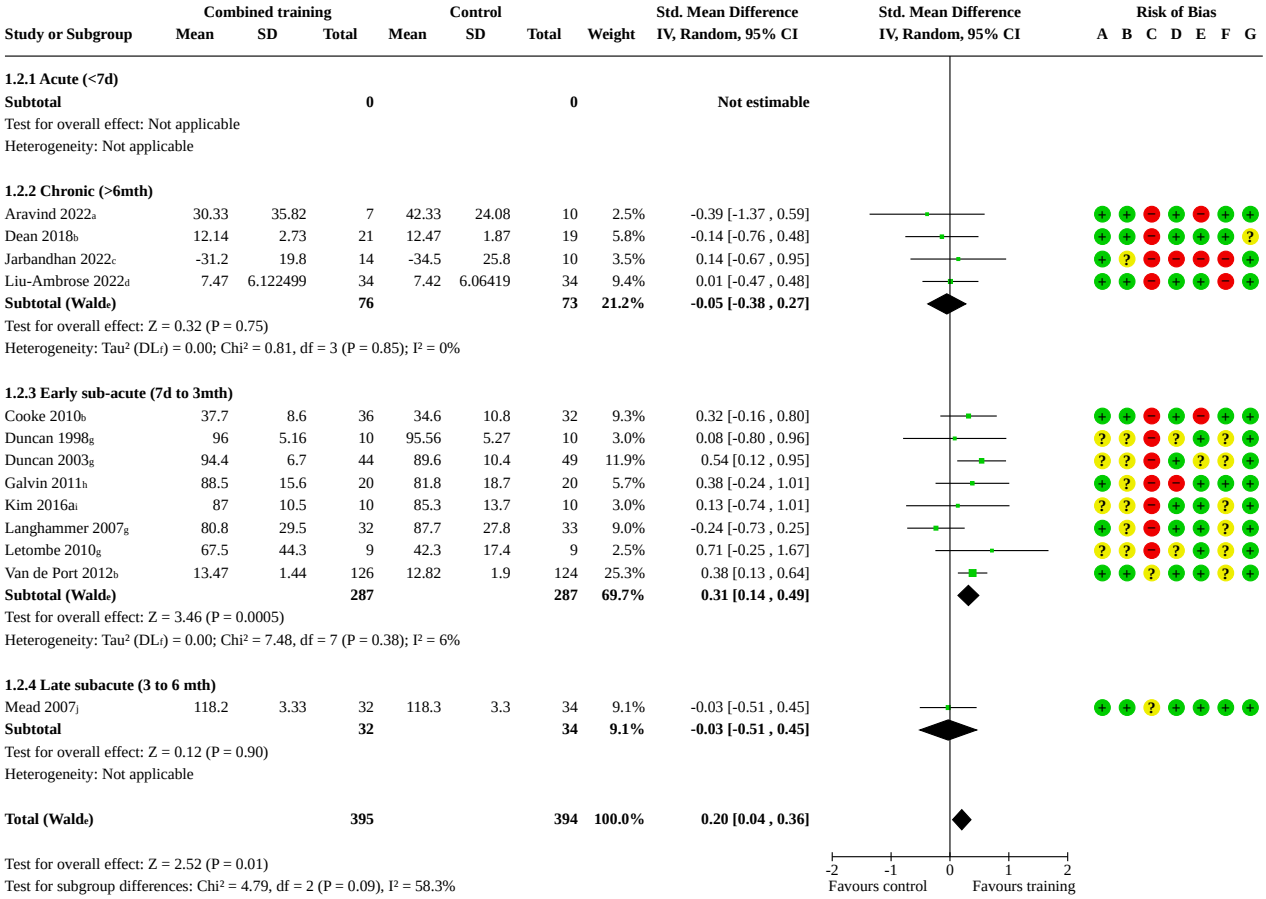
Figure 6. Forest plot of comparison 1.2: Effect of combined training versus control on indices of disability at end of intervention (<12 weeks or ≥ 12 weeks).



Footnotes

[a]NEADL (↑ score more favourable); Reviewer imputed data
[b]Rivermead Mobility Index (↑ score more favourable)
[c]DASH Score (↓ score more favourable)
[d]Lawton IADL (↑ score more favourable)
[e]CI calculated by Wald-type method.
[f]Tau² calculated by DerSimonian and Laird method.
[g]Barthel Index (↑ score more favourable)
[h]NEADL (↑ score more favourable)
[i]Modified BI (↑ score more favourable)
[j]Functional Independence Measure (↑ score more favourable)

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of intervention
(F) Selective reporting (reporting bias)
(G) Other bias

At the end of follow-up (3 to 12 months), combined training may result in little to no improvement in indices of disability (SMD 0.10, 95% CI -0.07 to 0.28; I^2 = 10%; 8 studies, 614 participants; low-certainty evidence; Figure 7). See Analysis 2.2.

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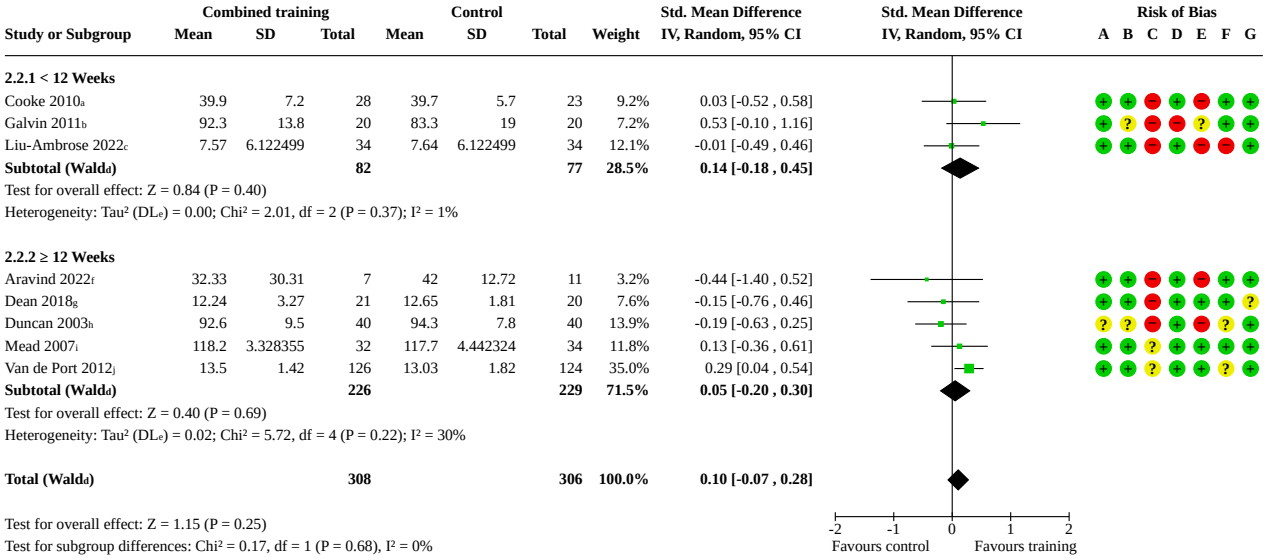
Figure 7. Forest plot of comparison 2.2: Effect of combined training versus control on indices of disability at end of follow-up (3 to 10 months).



Footnotes

[a]Rivermead Mobility Index (↑ score more favourable); 12 week follow-up period
[b]NEADL (↑ score more favourable); 3 month follow-up period
[c]Lawton IADL (↑ score more favourable); 12 month follow-up period
[d]CI calculated by Wald-type method.
[e]Tau² calculated by DerSimonian and Laird method.
[f]NEADL (↑ score more favourable); 10-month post-stroke follow-up; Reviewer imputed data
[g]Rivermead Mobility Index (↑ score more favourable); 9 month follow-up period
[h]Barthel Index (↑ score more favourable); 6 month follow-up period
[i]Functional Independence Measure (↑ score more favourable); 4 month follow-up period
[j]Rivermead Mobility Index (↑ score more favourable); 24 week follow-up period

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of follow-up
(F) Selective reporting (reporting bias)
(G) Other bias

Adverse events

Secondary events

At the end of the intervention, combined training does not increase or reduce the incidence of secondary cardiovascular or cerebrovascular events (RD -0.00, 95% CI -0.02 to 0.01; I^2 = 0%; 8 studies, 684 participants; high-certainty evidence; Figure 8). There were 7/684 people with secondary events (1 x transient ischaemic attack; 6 x recurrent strokes). Since secondary events are already uncommon, any reduction in secondary events due to combined training would be difficult to detect. See Analysis 1.3.

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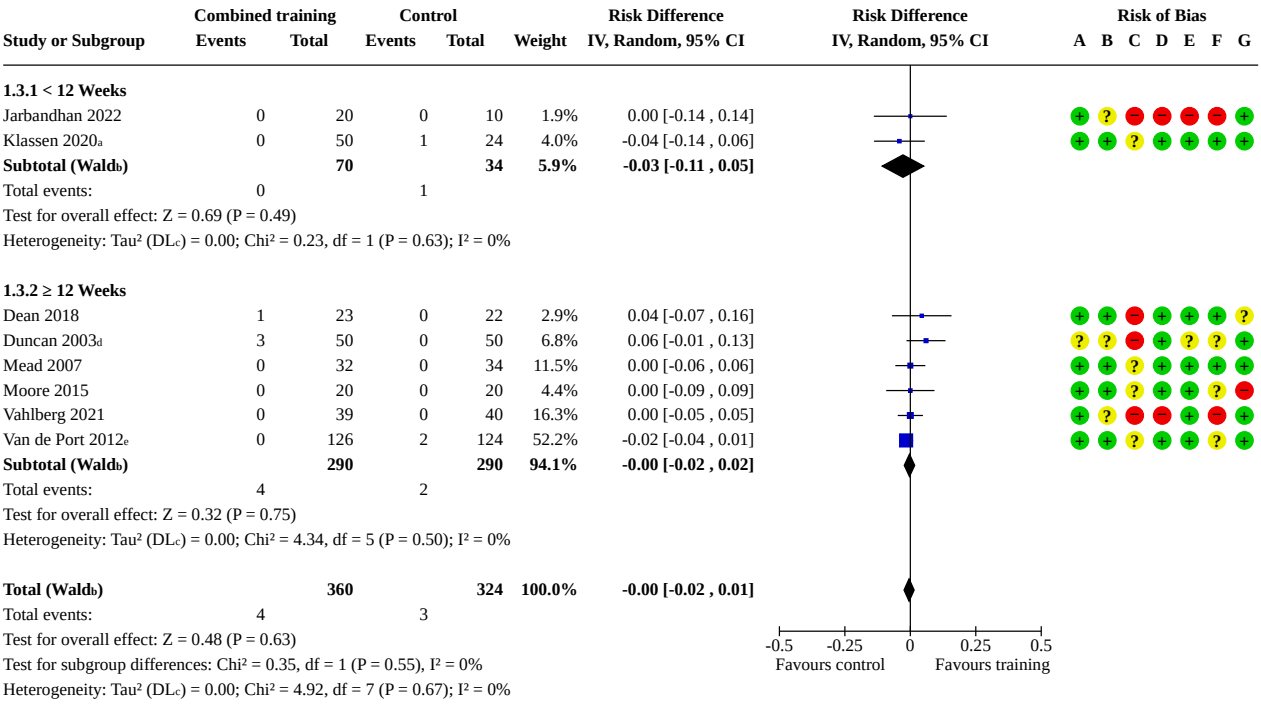
Figure 8. Forest plot of comparison 1.3: Effect of combined training versus control on incidence of secondary events (cardiovascular or cerebrovascular) at end of intervention (<12 weeks or ≥ 12 weeks).



Footnotes

[a]1 x transient ischaemic attack in control group
[b]CI calculated by Wald-type method.
[c]Tau² calculated by DerSimonian and Laird method.
[d]3 x recurrent strokes
[e]2 x recurrent strokes

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of intervention
(F) Selective reporting (reporting bias)
(G) Other bias

At the end of follow-up (4 to 9 months), combined training does not increase or reduce secondary cardiovascular or cerebrovascular events (RD 0.01, 95% CI -0.06 to 0.09; I^2 = 55%; 4 studies, 285 participants; high-certainty evidence; Figure 9). There were 10/285 people with secondary events (1 x transient ischaemic attack; 1 x myocardial infarction; 8 x recurrent strokes). Since secondary events are already uncommon, any reduction in secondary events due to combined training would be difficult to detect. See Analysis 2.3.

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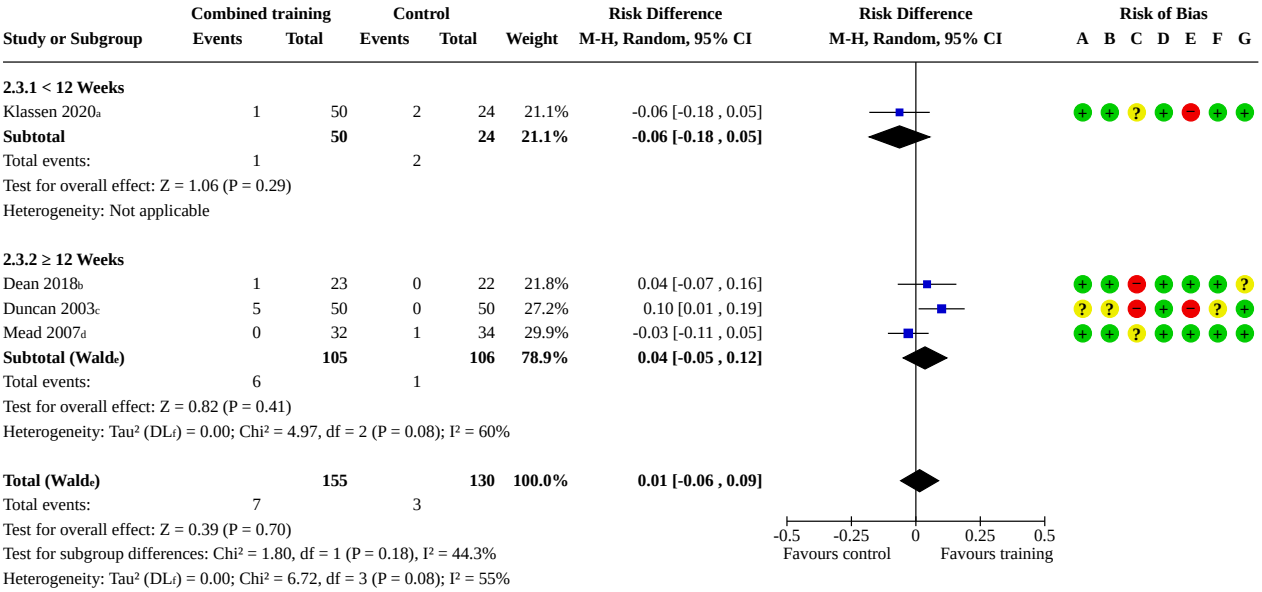
Figure 9. Forest plot of comparison 2.3: Effect of combined training versus control on the incidence of secondary events (cardiovascular or cerebrovascular) at end of follow-up (4 to 9 months).



Footnotes

[a]12 month post-stroke follow-up period; control group (1x recurrent stroke and 1 x myocardial infarction); intervention group (1 x transient ischaemic attack)
[b]9 month follow-up period
[c]6 month follow-up period; 5 x recurrent strokes
[d]4 month follow-up period
[e]CI calculated by Wald-type method.
[f]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of follow-up
(F) Selective reporting (reporting bias)
(G) Other bias

Falls

At the end of the intervention, combined training may lead to a small increase in the number of people having one or more falls at any time during the intervention period, but the 95% confidence interval includes no effect, so there is uncertainty (RD 0.07, 95% CI -0.00 to 0.15; I^2 = 0%; 3 studies, 174 participants). There were 18/174 people with one or more falls: 12 in the intervention groups and 5 in the control groups. See Analysis 1.4.

At the end of follow-up (4 to 10 months), combined training may lead to a small increase in the number of people having one or more falls at any time during the intervention plus follow-up periods period but the 95% confidence interval includes no effect, so there is uncertainty (RD 0.06, 95% CI -0.06 to 0.19; I^2 = 4%; 2 studies, 99 participants). There were 14/99 people with one or more falls at the end of follow-up: 9 in the intervention groups (1 fell during follow-up period) and 5 in the control groups (1 fell during follow-up period). See Analysis 2.4.

Risk factors

Blood pressure (systolic)

At the end of the intervention, combined training may have little or no effect on systolic blood pressure (in mmHg), but the evidence is very uncertain (MD -1.83, 95% CI -9.60 to 5.95; I^2 = 76%; 5 studies, 140 participants; very low-certainty evidence; Figure 10). The minimal clinically important difference (MCID) is −2 mmHg. See Analysis 1.5.

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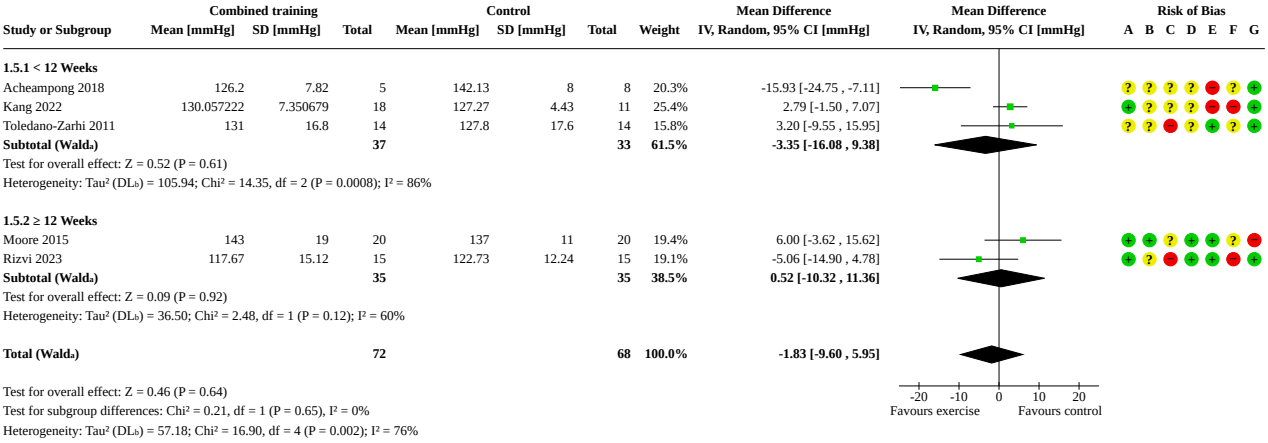
Figure 10. Forest plot of comparison 1.5: Effect of combined training versus control on systolic blood pressure (mmHg) at end of intervention (<12 weeks or ≥ 12 weeks).



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of intervention
(F) Selective reporting (reporting bias)
(G) Other bias

At the end of follow-up, no study data were available. See Analysis 2.5.

Blood pressure (diastolic)

At the end of the intervention, combined training may have little or no effect on diastolic blood pressure (in mmHg) (MD -1.03, 95% CI -2.73 to 0.67; I^2 = 0%; 5 studies, 140 participants). However, this is uncertain as the 95% confidence intervals include both no effect and the MCID of −2 mmHg. See Analysis 1.6.

At the end of follow-up, no study data were available. See Analysis 2.6.

Other measures

Four studies included 25 different cardiometabolic risk factors relating to body fatness, blood lipids, and glucose control; a beneficial direction of effect was shown for 20 of these outcomes (Supplementary material 10).

Physical fitness

For the purposes of GRADE, all the outcomes relating to cardiorespiratory fitness and musculoskeletal fitness were considered together as a single 'physical fitness' item to establish the certainty of evidence. Overall, combined training may improve cardiorespiratory fitness and some musculoskeletal components of physical fitness, but the evidence is very uncertain.

Cardiorespiratory fitness (peak VO_2)

At the end of the intervention, combined training may have a small beneficial effect on cardiorespiratory fitness, assessed as peak VO_2 in ml/kg/min (MD 2.29, 95% CI 0.64 to 3.93; I^2 = 71%; 5 studies, 215 participants; Figure 11). The MCID for VO_2 is +3.5 ml/kg/min, which is included within the 95% confidence interval. See Analysis 1.7.

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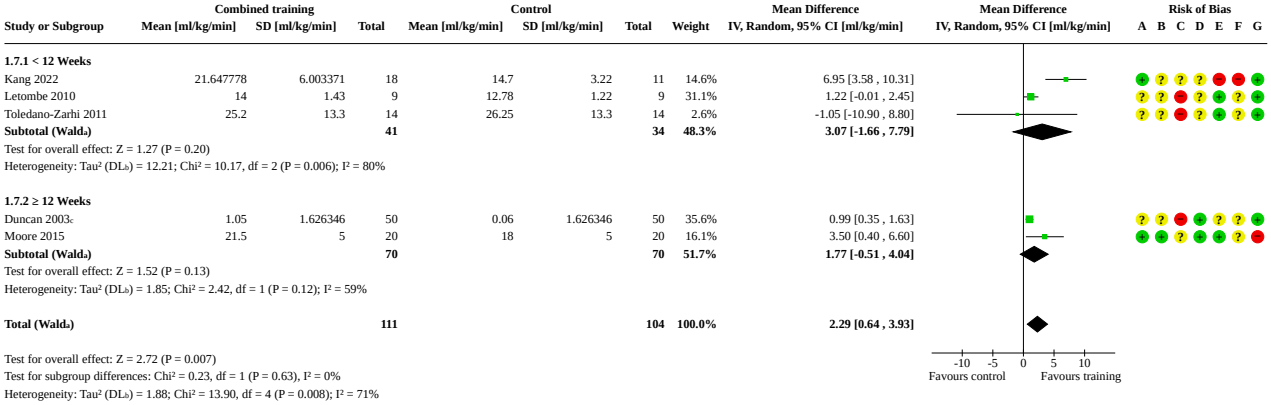
Figure 11. Forest plot of comparison 1.7: Effect of combined training versus control on cardiorespiratory fitness (peak VO_2 ml/kg/min) at end of intervention (<12 weeks or ≥ 12 weeks).



There is some evidence of a subgroup difference between early subacute versus chronic subgroups, which favours participants in the chronic stage of recovery (P = 0.02; I^2 = 82.1%). However, there are few studies, uneven covariate distribution, and unexplained heterogeneity.

At the end of follow-up, no study data were available. See Analysis 2.7.

Musculoskeletal fitness

Muscle strength, lower limb, affected side

At the end of the intervention, combined training may have a small beneficial effect (ES > 0.2) on leg and knee extensor strength, but the confidence intervals indicate uncertainty (SMD 0.30, 95% CI -0.05 to 0.65; I^2 = 36%; 4 studies, 217 participants). See Analysis 1.8.

At the end of follow-up (12 weeks to 4 months), combined training may have little or no effect (trivial effect < 0.2) on leg and knee extensor strength (SMD 0.10, 95% CI -0.28 to 0.47; I^2 = 0%; 2 studies, 108 participants). See Analysis 2.8.

Muscle strength, lower limb, unaffected side

At the end of the intervention, combined training may have a moderate beneficial effect (ES > 0.5) on leg and knee extensor strength, but the confidence intervals indicate uncertainty (SMD 0.59, 95% CI -0.53 to 1.70; I^2 = 82%; 2 studies, participants not available). See Analysis 1.9.

At the end of follow-up (4 months), combined training may have little or no effect (trivial effect < 0.2) on leg extensor power (SMD 0.14, 95% CI -0.35 to 0.62; I^2 not applicable; 1 study, 66 participants). There is only one small study and the confidence intervals indicate uncertainty. See Analysis 2.9.

Muscle strength, upper limb, affected side

At the end of the intervention, combined training may have little or no effect (trivial effect < 0.2) on handgrip strength (SMD 0.06, 95% CI -0.53 to 0.65; I^2 = 55%; 3 studies, participants not available), but the confidence intervals indicate uncertainty. See Analysis 1.10.

At the end of follow-up, no study data are available. See Analysis 2.10.

Muscle strength, upper limb, unaffected side

At the end of the intervention, combined training may have a small beneficial effect (ES = 0.2) on handgrip strength, but the confidence intervals indicate uncertainty (SMD 0.20, 95% CI -0.53 to 0.93; I^2 = 70%; 3 studies, 116 participants). See Analysis 1.11.

At the end of follow-up, no study data are available. See Analysis 2.11.

Walking

Walking independence (functional ambulation category)

At the end of the intervention, combined training may have a small beneficial effect on functional ambulation category scores (scored 0 to 5) in one large study (MD 0.13, 95% CI 0.01 to 0.25; I^2 not applicable; 1 study, 250 participants). See Analysis 1.12.

At the end of follow-up (24 weeks), combined training may have a small beneficial effect on functional ambulation category scores (scored 0 to 5) in one large study (MD 0.11, 95% CI 0.00 to 0.22; I^2 not applicable; 1 study, 250 participants). See Analysis 2.12.

Walking speed (comfortable)

At the end of the intervention, combined training may have a small beneficial effect on comfortable walking speed (m/sec), but

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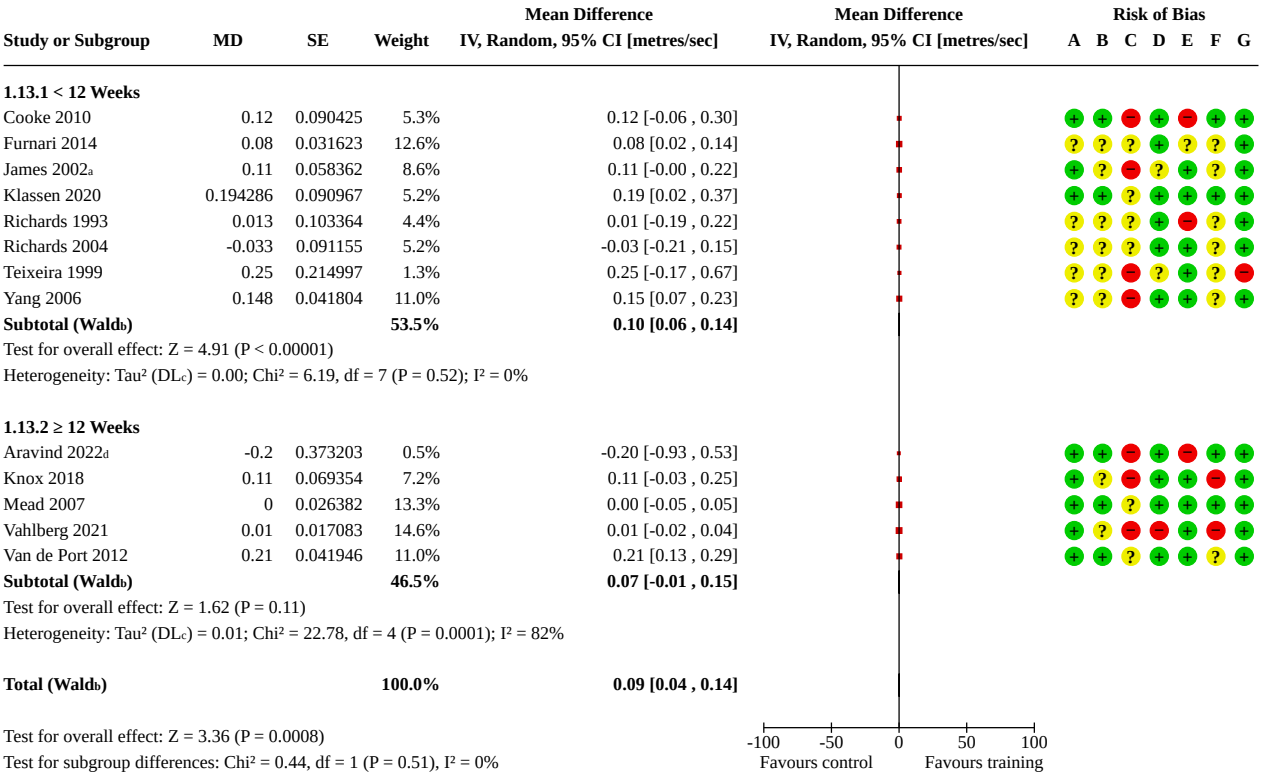
the evidence is very uncertain (MD 0.09, 95% CI 0.04 to 0.14; I^2 = 68%; 13 studies, participants not available; very low-certainty evidence; Figure 12). The 95% CI includes the MCID of +0.13 m/sec. Nine of 13 studies were confounded for exposure time; there is no effect without these. The comfortable walking speed of the control group is 0.812 m/sec, which exceeds the threshold of 'unlimited community ambulation' (> 0.8 m/sec). See Analysis 1.13.

Figure 12. Forest plot of comparison 1.13: Effect of combined training versus control on walking speed (comfortable speed m/sec) at end of intervention (<12 weeks or ≥ 12 weeks).



Footnotes

[a]Change from baseline data
[b]CI calculated by Wald-type method.
[c]Tau² calculated by DerSimonian and Laird method.
[d]Reviewer imputed data

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of intervention
(F) Selective reporting (reporting bias)
(G) Other bias

At the end of follow-up (3 to 12 months), combined training may have little or no effect on comfortable walking speed (m/sec), but the evidence is very uncertain (MD 0.03, 95% CI -0.07 to 0.13; I^2 = 69%; 7 studies, 605 participants; very low-certainty evidence; Figure 13). The MCID is +0.13 m/sec; the 95% CI includes no effect and the MCID. The control group walking speed of > 0.8 m/sec predicts 'unlimited community ambulation' (> 0.8 m/sec). See Analysis 2.13.

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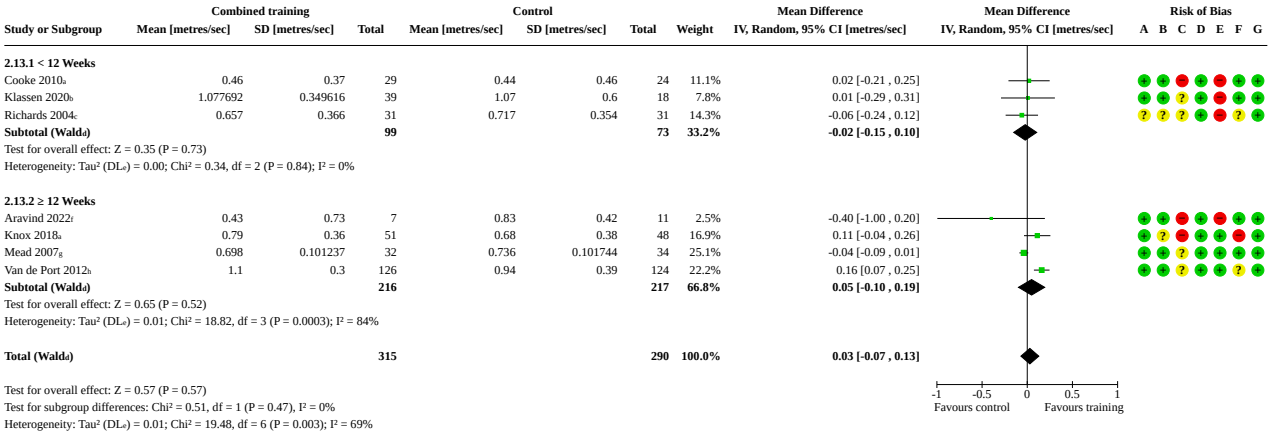
Figure 13. Forest plot of comparison 2.13: Effect of combined training versus control on ewalking speed (comfortable speed m/sec) at end of follow-up (3 to 10 months).



Footnotes

[a]12 week follow-up period
[b]12 month post-stroke follow-up period
[c]3 month follow-up period
[d]CI calculated by Wald-type method.
[e]Tau² calculated by DerSimonian and Laird method.
[f]10-month post-stroke follow-up; Reviewer imputed data
[g]4 month follow-up period
[h]24 week follow-up period

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of follow-up
(F) Selective reporting (reporting bias)
(G) Other bias

Walking speed (maximal)

At the end of the intervention, combined training may have a small beneficial effect on maximal walking speed (m/sec) (MD 0.09, 95% CI 0.02 to 0.16; I^2 = 59%; 5 studies, participants not available). Three of five studies are confounded for exposure time; there is no effect without these. See Analysis 1.14.

At the end of follow-up (12 weeks to 12 months), combined training may have little or no effect on maximal walking speed (m/sec) (MD 0.04, 95% CI -0.10 to 0.18; I^2 = 52%; 2 studies, 167 participants). See Analysis 2.14.

Walking endurance (6-MWT)

At the end of the intervention, combined training may improve walking endurance slightly (MD 33.99, 95% CI 21.53 to 46.45; I^2 = 33%; 15 studies, participants not available), but the 95% CI does not include the MCID for the 6-MWT of +71 m. Thirteen of 15 studies are confounded for exposure time; there was no effect without these. See Analysis 1.15.

At the end of follow-up (12 weeks to 12 months), combined training may improve walking endurance slightly (MD 32.73, 95% CI 4.61 to 60.85; I^2 = 36%; 6 studies, 530 participants), but the 95% CI does not include the MCID for the 6-MWT of +71 m. There is evidence of a difference between early subacute and chronic subgroups in favour of the early subacute subgroup (P = 0.02; I^2 = 81.2%). However, there are few studies and an uneven covariate distribution. See Analysis 2.15.

Physical function

Balance

At the end of the intervention, combined training may improve balance slightly (SMD 0.25, 95% CI 0.11 to 0.39; I^2 = 0%; 16 studies, 839 participants; low-certainty evidence; Figure 14). The effect size is small (effect size > 0.2). Most studies (11/16) were confounded by imbalanced exposure, with no significant increase when these were excluded. See Analysis 1.16.

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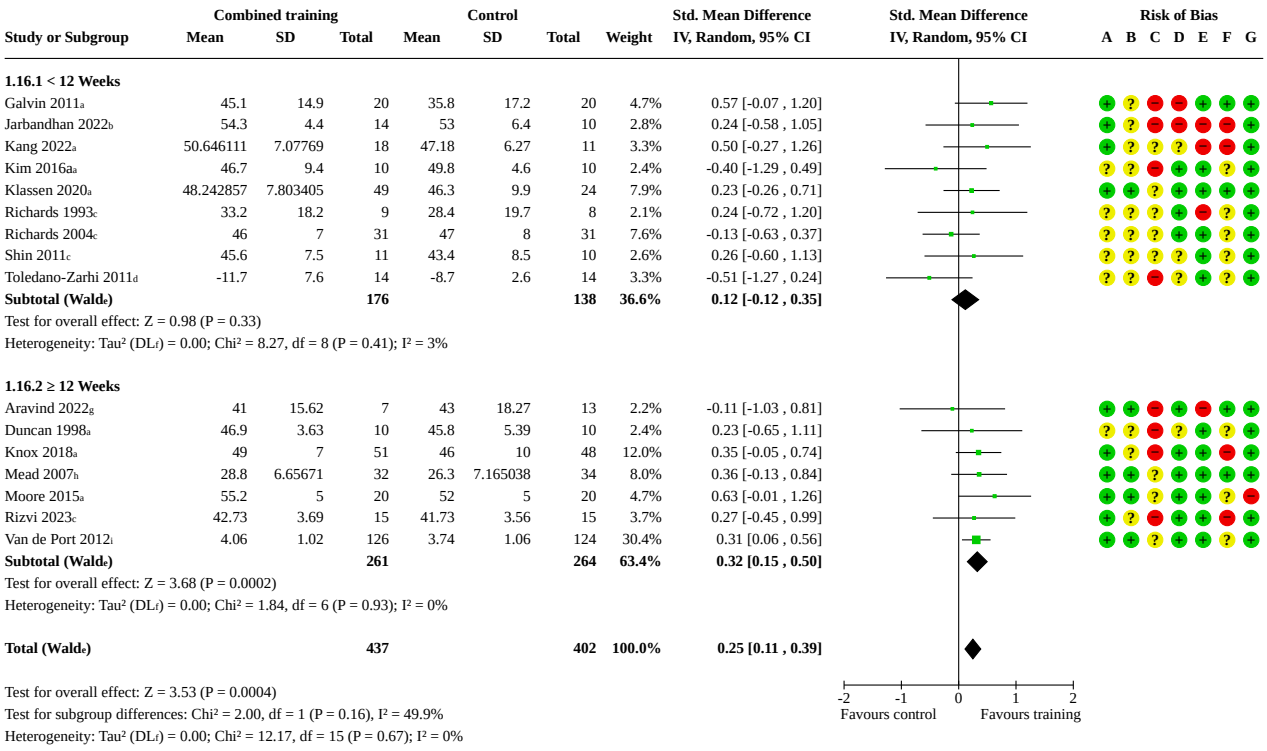
Figure 14. Forest plot of comparison 1.6: Effect of combined training versus control on indices of balance at end of intervention (<12 weeks or ≥ 12 weeks).



Footnotes

aBerg Balance Scale (↑ score more favourable)
bBerg Balance Scale (↑ score more favourable)
cBerg Balance Scale (↑ scores more favourable)
dFour Square Step Test (↓ scores more favourable)
eCI calculated by Wald-type method.
fTau² calculated by DerSimonian and Laird method.
gBerg Balance Scale (↑ score more favourable); Reviewer imputed data
hFunctional Reach(↑ score more favourable)
iTimed Balance Test (↑ scores more favourable)

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of intervention
(F) Selective reporting (reporting bias)
(G) Other bias

At the end of follow-up (12 to 24 weeks), combined training may improve balance slightly (SMD 0.24, 95% CI -0.00 to 0.49; I^2 = 39%; 6 studies, 535 participants; low-certainty evidence; Figure 15). The effect size is small (effect size > 0.2). Most (4/6) studies were confounded by imbalanced exposure, with no significant increase when these were excluded. See Analysis 2.16.

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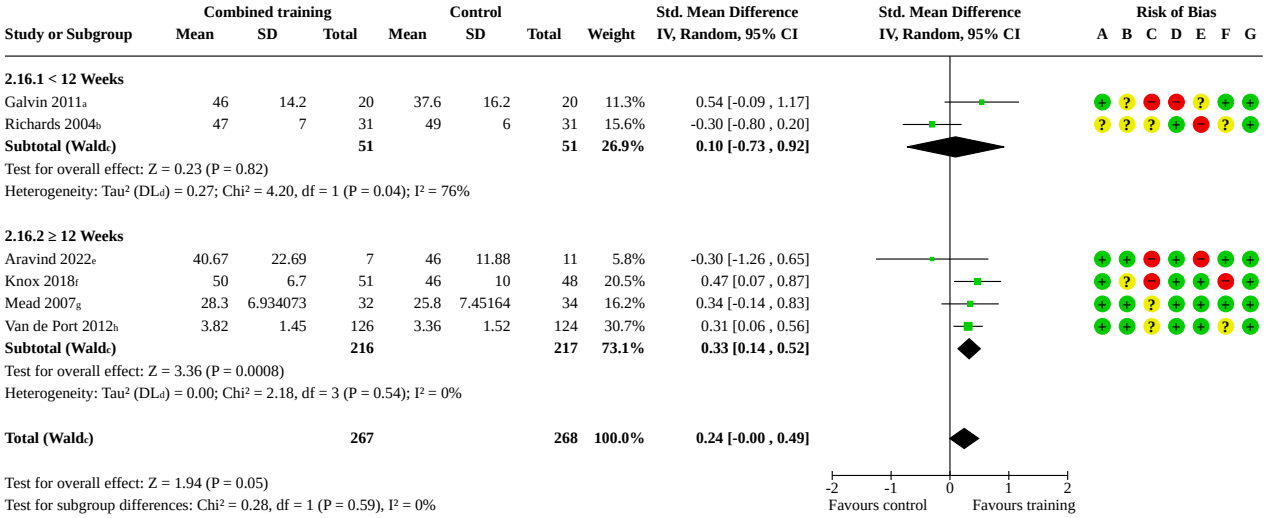
Figure 15. Forest plot of comparison 2.16: Effect of combined training versus control on indices of balance at end of follow-up (3 to 10 months).



Footnotes

[a]Berg Balance Scale (↑ score more favourable); 3 month follow-up period
[b]Berg Balance Scale (↑ scores more favourable); 3 month follow-up period
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.
[e]Berg Balance Scale; 10-month post-stroke follow-up; Reviewer imputed data
[f]Berg Balance Scale (↑ score more favourable); 12 week follow-up period
[g]Functional Reach (↑ score more favourable); 4 month follow-up period
[h]Timed Balance Test (↑ scores more favourable); 24 week follow-up period

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias): End of follow-up
(F) Selective reporting (reporting bias)
(G) Other bias

Functional mobility (timed up and go)

At the end of the intervention, combined training probably has a small beneficial effect on functional mobility assessed using the 3-metre timed up and go test (seconds) (MD -1.94, 95% CI -2.82 to -1.07; I^2 = 30%; 10 studies, participants not available). Analysis was sensitive to the inclusion of 1/10 studies with publication concerns, excluding this gave no significant effect (MD −1.79 sec, 95% CI −3.67 to 0.09; P = 0.06; I^2 = 42%; 9 studies, 663 participants). See Analysis 1.17.

At the end of follow-up (12 weeks to 9 months), combined training may have a small beneficial effect on functional mobility assessed using the 3-metre timed up and go test (seconds) (MD -1.43, 95% CI -3.77 to 0.92; I^2 = 48%; 5 studies, 518 participants). However, the confidence intervals indicate considerable uncertainty. See Analysis 2.17.

Other measures

Eleven studies included 20 physical function outcomes not pooled in meta-analysis, including stair climbing (n = 3), chair rising (n = 2), upper and lower limb functional tests (n = 13), and other scales (n = 2); 17/20 indicated a beneficial direction of effect (Supplementary material 10).

Important outcomes

The detailed synthesis of results for the effects of combined training on all important outcomes, including subgroup and any sensitivity analyses, is described in Table 6.

There were few studies available to pool. In summary, there were no observed beneficial effects (SMD effect size > 0.2) on mood (anxiety), mood (depression), cognitive function, and fatigue (overall), and no data at all for fatigue (physical) and fatigue (mental).

Amongst the health status and quality of life outcomes, there were some small and moderate-sized beneficial effects favouring combined training. These relate to overall, mental, and social domains of health status and quality of life, but they do not apply to the physical health domain.

Health status and quality of life

Health status and quality of life (overall)

At the end of the intervention, combined training may have a moderate-sized (> 0.50) beneficial effect on overall health status and quality of life at the end of intervention (SMD 0.67, 95% CI 0.17 to 1.17; I^2 = 68%; 5 studies, 267 participants). However, there is

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considerable heterogeneity and all the studies are confounded for exposure time. See Analysis 1.18.

At the end of follow-up (12 weeks to 12 months), combined training had little or no effect (< 0.2) at the end of follow-up (SMD 0.15, 95% CI -0.11 to 0.41; I^2 = 3%; 5 studies, 245 participants). There may be some evidence of a subgroup difference favouring the early subacute phase over the chronic phase, but there are few studies (P = 0.05; I^2 = 72.9%). See Analysis 2.18.

Health status and quality of life (physical)

At the end of the intervention, combined training may have little or no effect (< 0.2), but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.15, 95% CI -0.73 to 1.02; I^2 = 70%; 2 studies, 114 participants). See Analysis 1.19.

At the end of follow-up (6 to 10 months), combined training may have little or no effect (< 0.2), but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.10, 95% CI -0.24 to 0.44; I^2 = 0%; 3 studies, 135 participants). See Analysis 2.19.

Health status and quality of life (mental)

At the end of the intervention, combined training may have a small (> 0.2) beneficial effect, but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.25, 95% CI -0.11 to 0.62; I^2 = 0%; 2 studies, 118 participants). See Analysis 1.20.

At the end of follow-up (6 to 10 months), combined training may have a small (> 0.2) beneficial effect, but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.25, 95% CI -0.11 to 0.62; I^2 = 0%; 2 studies, 118 participants). See Analysis 2.20.

Health status and quality of life (social)

At the end of the intervention, combined training may have a small (> 0.2) beneficial effect, but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.31, 95% CI -0.09 to 0.71; I^2 = 4%; 2 studies, 111 participants). See Analysis 1.21.

At the end of follow-up (6 to 10 months), combined training may have a small (> 0.2) beneficial effect, but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.22, 95% CI -0.18 to 0.62; I^2 = 0%; 2 studies, 97 participants). See Analysis 2.21.

Mood (anxiety)

At the end of the intervention, combined training may have little or no effect (< 0.2), but there are few studies and the 95% confidence intervals indicate uncertainty (SMD -0.07, 95% CI -0.29 to 0.15; I^2 = 0%; 2 studies, 316 participants). See Analysis 1.22.

At the end of follow-up (4 months to 24 weeks), combined training may have little or no effect (< 0.2), but there are few studies and the 95% confidence intervals indicate uncertainty (SMD -0.02, 95% CI -0.24 to 0.20; I^2 = 0%; 2 studies, 316 participants). See Analysis 2.22.

Mood (depression)

At the end of the intervention, combined training may have little or no effect (< 0.2), but the 95% confidence intervals indicate uncertainty and 3/4 studies have imbalanced exposure (SMD -0.15, 95% CI -0.54 to 0.24; I^2 = 74%; 4 studies, 481 participants). See Analysis 1.23.

At the end of follow-up (4 months to 24 weeks), combined training may have little or no effect (< 0.2), but there are few studies and the 95% confidence intervals indicate uncertainty (SMD 0.06, 95% CI -0.16 to 0.28; I^2 = 0%; 2 studies, 316 participants). See Analysis 2.23.

Cognitive function

At the end of the intervention, combined training may have little or no effect (< 0.2), but the 95% confidence intervals indicate uncertainty (SMD -0.01, 95% CI -0.24 to 0.22; I^2 = 0%; 5 studies, 294 participants). See Analysis 1.24.

At the end of follow-up (6 to 12 months), combined training may have little or no effect (< 0.2), but the 95% confidence intervals indicate uncertainty (SMD 0.16, 95% CI -0.11 to 0.43; I^2 = 0%; 4 studies, 221 participants). See Analysis 2.24.

Fatigue (overall)

At the end of the intervention, combined training may have little or no effect (< 0.2), but the 95% confidence intervals indicate uncertainty (SMD -0.01, 95% CI -0.21 to 0.19; I^2 = 0%; 5 studies, 387 participants). See Analysis 1.25.

At the end of follow-up (4 to 10 months), combined training may have little or no effect (< 0.2), but the 95% confidence intervals indicate uncertainty (SMD -0.07, 95% CI -0.27 to 0.14; I^2 = 0%; 4 studies, 365 participants). See Analysis 2.25.

Fatigue (physical)

No study data are available for this outcome. See Analysis 1.26.

Fatigue (mental)

No study data are available for this outcome. See Analysis 2.27.

Equity assessment

No equity assessment was undertaken, although we did record whether studies took place in high-income countries or low-to-middle-income countries (Table 3).

Reporting biases

We assessed funnel plot asymmetry in analyses involving 10 or more studies; these were restricted to the following end-of-intervention analyses.

- Death: no funnel plot asymmetry detectable, but the number of events is very small (Figure 16).
- Disability: funnel plot asymmetry suggests possible missing studies in the area favourable to the intervention, suggesting factors other than non-reporting bias. The small studies favouring the control exposure are also those carried out during the chronic phase (Figure 17). However, SMD effect estimates are known to produce spurious asymmetry [81].
- Walking speed (comfortable): most of the studies are a similar size, so the effects of small studies cannot be determined (Figure 18).
- Walking endurance (6-MWT): funnel plot asymmetry suggests missing studies in the area favourable to the intervention (Figure 19). This suggests factors other than non-reporting bias [81].
- Balance: funnel plot asymmetry suggests missing studies in the area favourable to the intervention (Figure 20). This suggests

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factors other than non-reporting bias, and SMD effect estimates are known to produce spurious asymmetry [81].

- Functional mobility (timed up and go): no funnel plot asymmetry detected (Figure 21).

Figure 16. Funnel plot of comparison 1.1: Effect of combined training versus control on deaths at end of intervention (<12 weeks or ≥ 12 weeks).

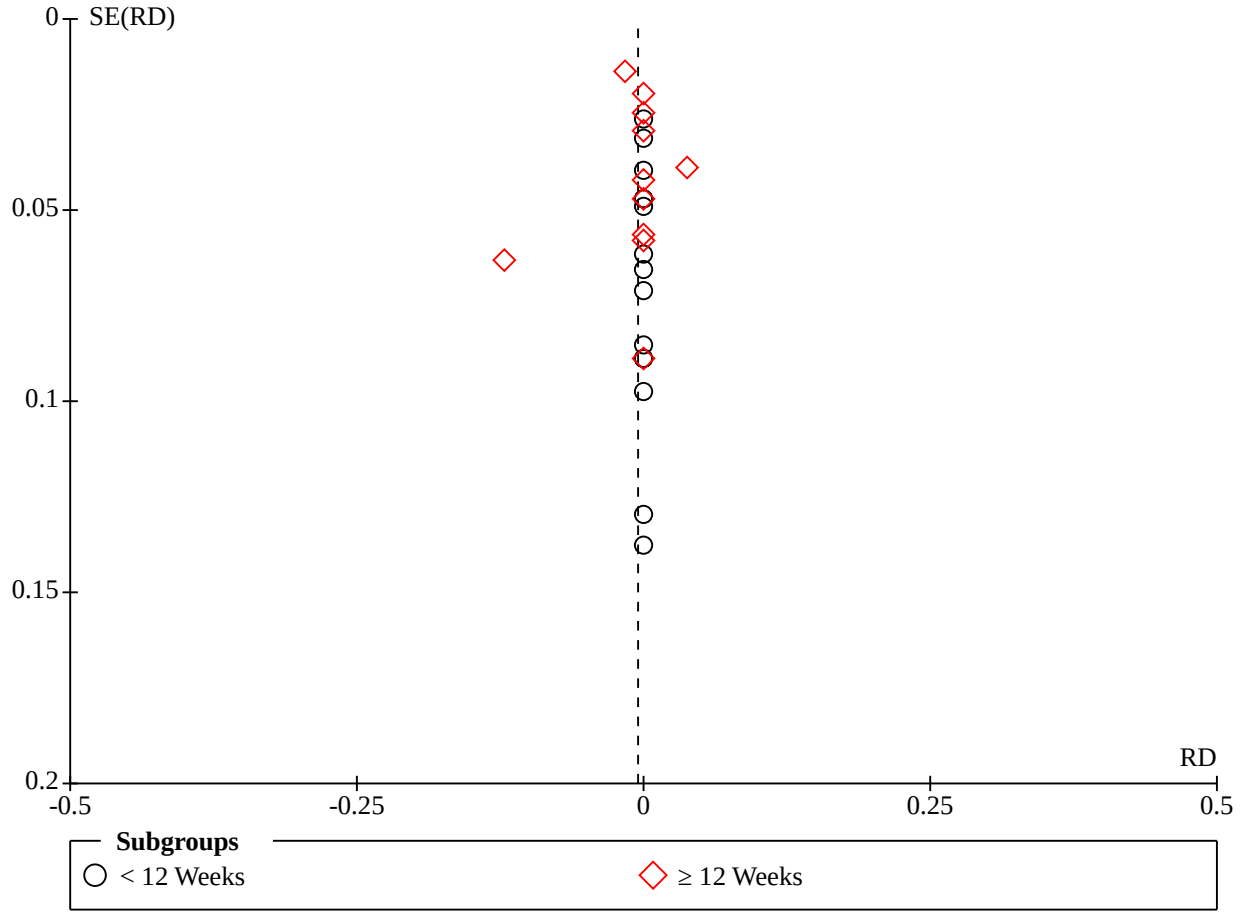

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Figure 17. Funnel plot of comparison 1.2: Effect of combined training versus control on indices of disability at end of intervention (<12 weeks or ≥ 12 weeks).

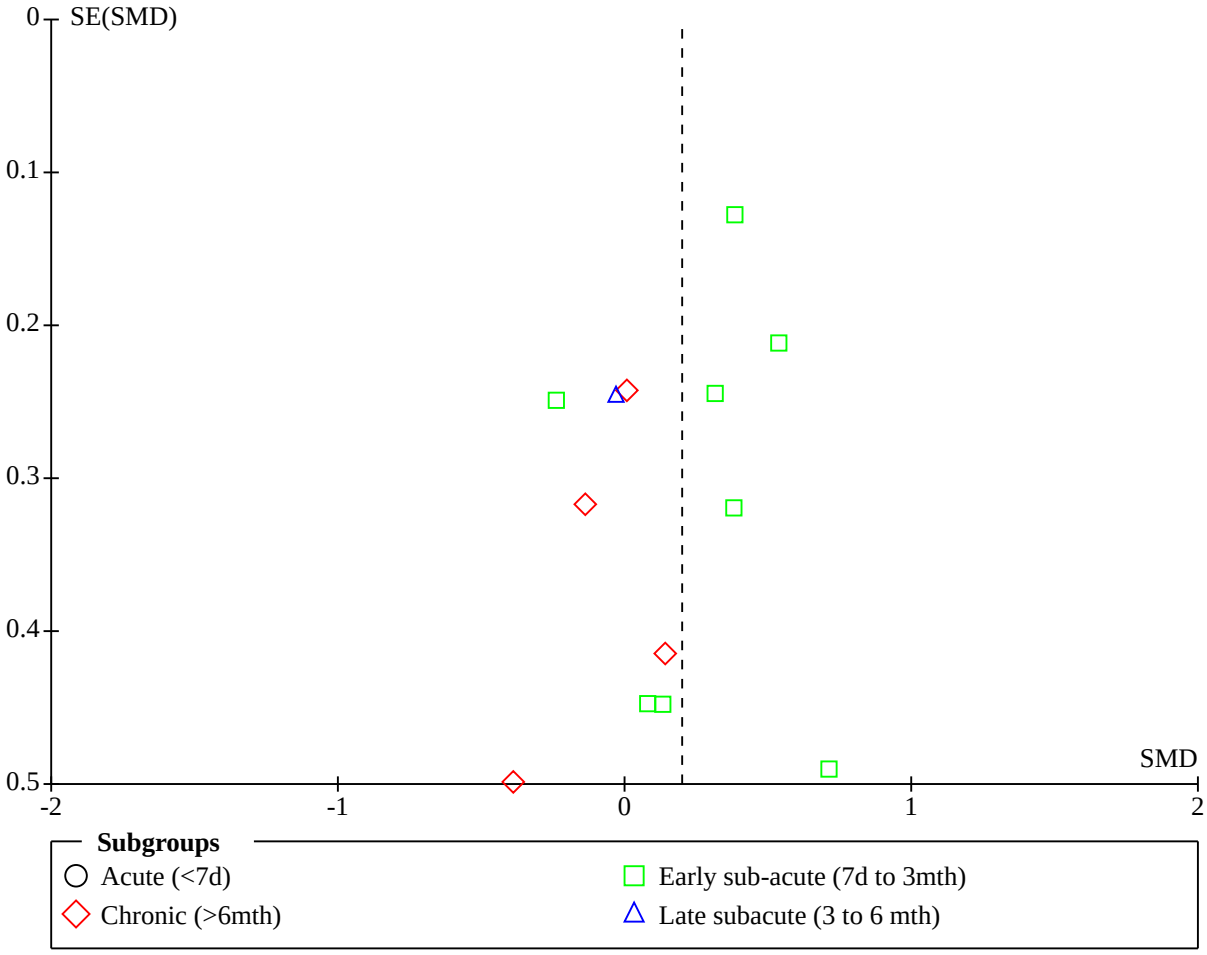

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Figure 18. Funnel plot of comparison 1.13: Effect of combined training versus control on walking speed (comfortable speed m/sec) at end of intervention (<12 weeks or ≥ 12 weeks).

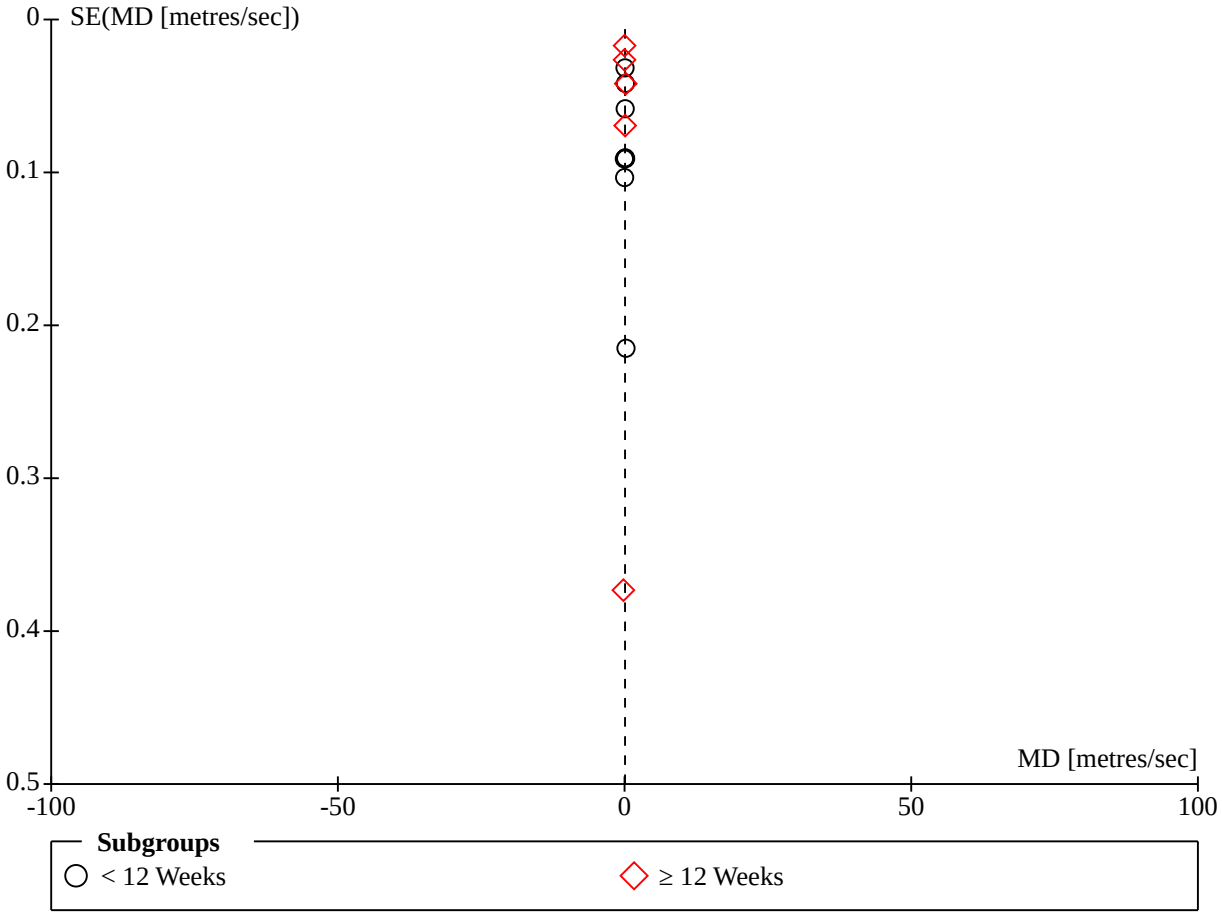

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Figure 19. Funnel plot of comparison 1.15: Effect of combined training versus control on walking endurance (6-minute walking test; metres/6 min) at end of intervention (<12 weeks or ≥ 12 weeks).

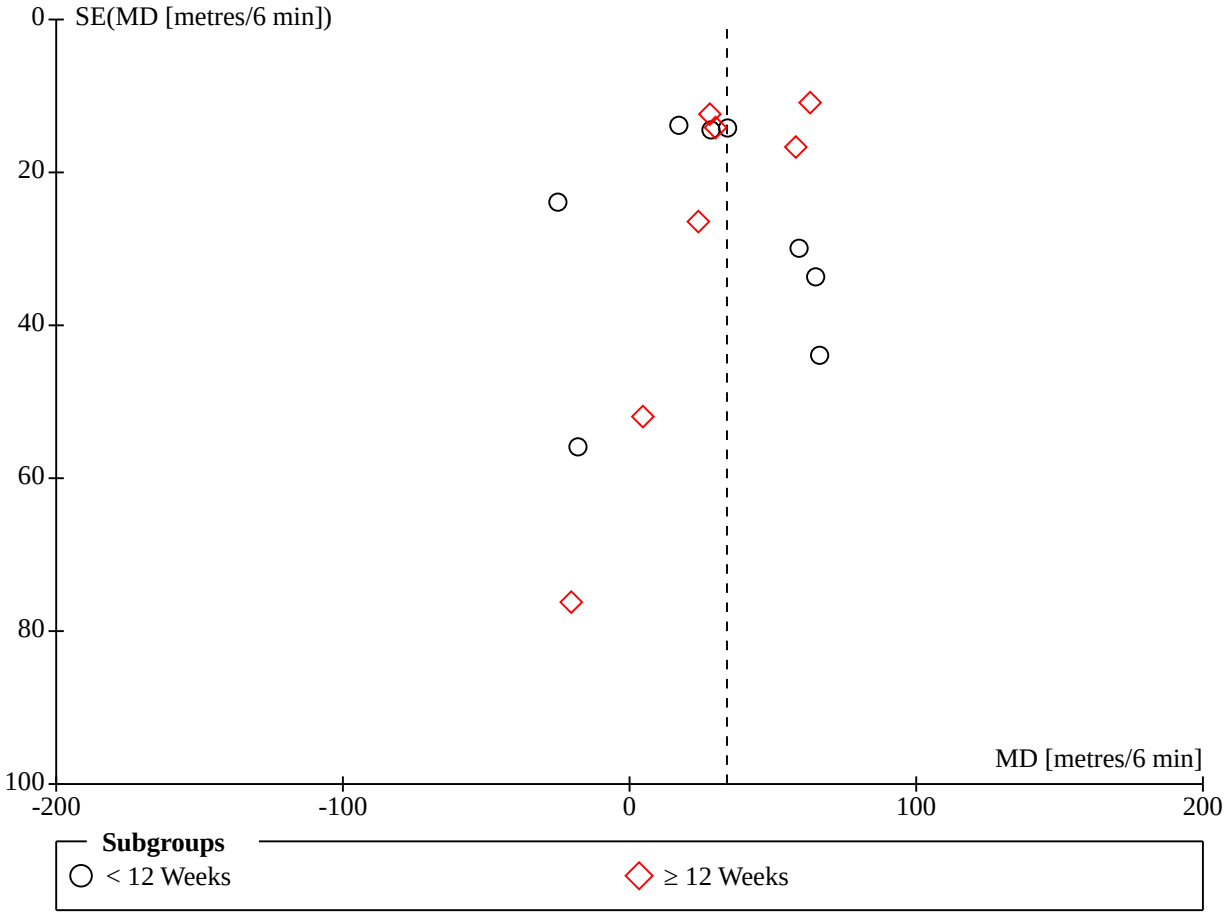

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Figure 20. Funnel plot of comparison 1.16: Effect of combined training versus control on indices of balance at end of intervention (<12 weeks or ≥ 12 weeks).

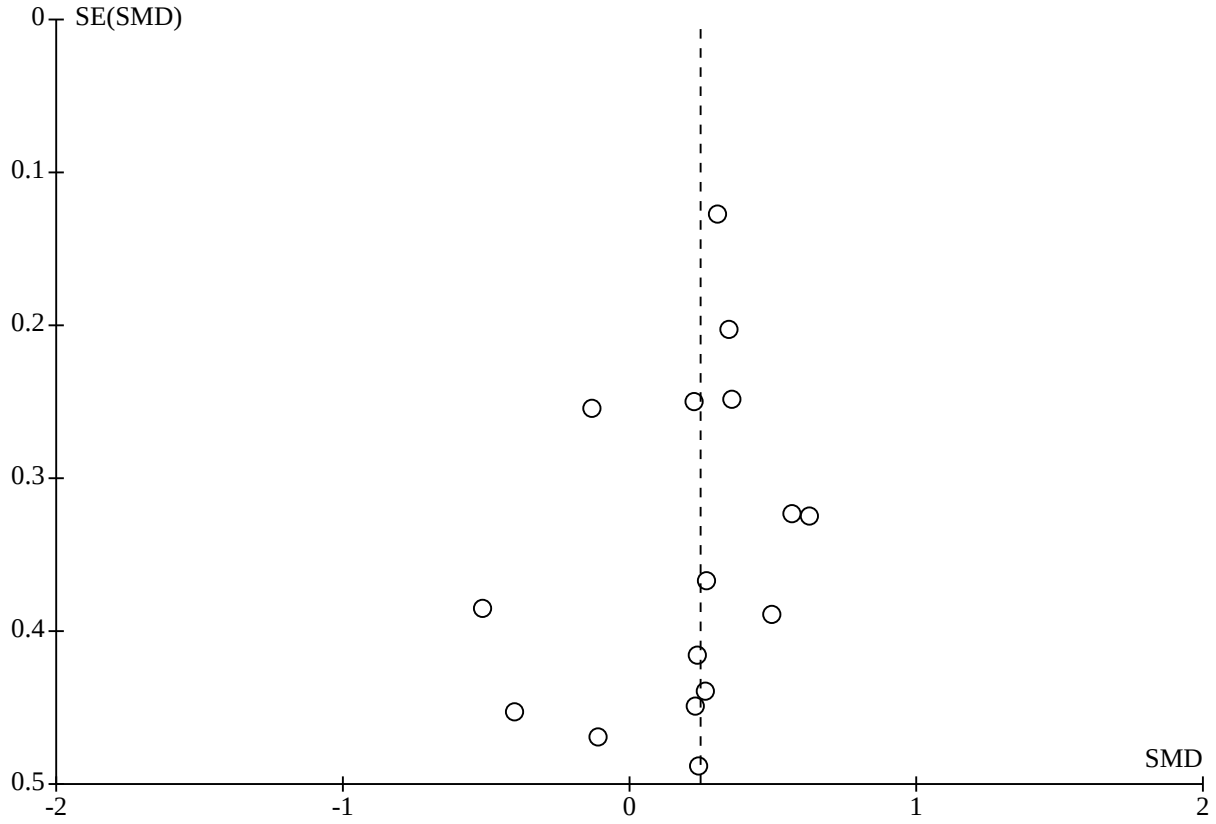

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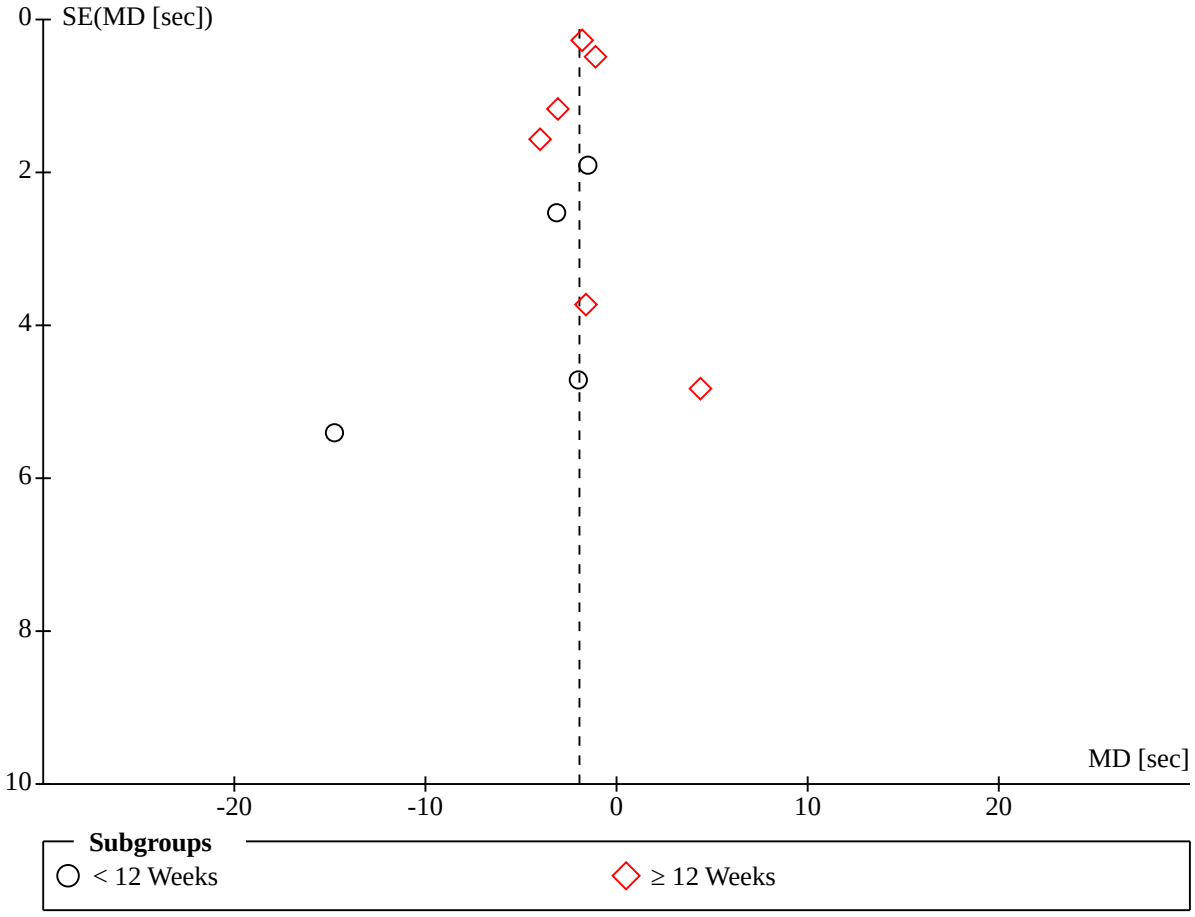
Figure 21. Forest plot of comparison 1.17: Effect of combined training versus control on functional mobility (3-metre timed up and go; sec) at end of intervention (<12 weeks or ≥ 12 weeks).



DISCUSSION

Summary of main results

1) Death

There was high-certainty evidence that combined training did not affect mortality at the end of intervention or end of follow-up. However, any reduction in mortality arising from a protective effect of combined training could not be determined since the number of deaths was already low amongst these participants.

2) Disability

There was low-certainty evidence of a small beneficial effect of combined training on indices of disability at the end of intervention. Ceiling effects in the instruments used to assess disability in these higher-functioning groups of people with stroke could have an influence; there is a tendency for smaller effects amongst studies started during the chronic phase when recovery of activities of daily living (ADL) and extended ADL functioning might be expected to have progressed. There was no overall retention of benefits at follow-up (low-certainty evidence).

3) Adverse events - secondary events

There was high-certainty evidence that combined training does not increase or reduce secondary cardiovascular or cerebrovascular events. However, any reduction in secondary events arising from a protective effect of combined training could not be determined since the number of events was already low amongst these participants. All-cause adverse events were rarely prespecified as an outcome; this makes it difficult to rule out unreported events.

4) Risk factors - systolic blood pressure

Combined training may have a small beneficial effect on systolic blood pressure at the end of intervention, but the evidence is very uncertain; there were no follow-up data. Control group data suggests blood pressure is already well controlled.

5) Fitness

Combined training may improve different components of physical fitness at the end of intervention, but the overall evidence is very uncertain. Combined training may lead to small improvements in cardiorespiratory fitness and muscle strength of the knee and hip extensors in both legs and grip strength of the least affected arm. At the end of follow-up, only leg strength data were available, which showed little or no effect (evidence very uncertain).

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6) Walking - comfortable speed

Combined training may have a small beneficial effect on comfortable walking speed at the end of intervention, but there was little or no effect at the end of follow-up; this evidence is very uncertain. These participants were already fairly mobile (walking speed > 0.8 m/sec).

7) Physical function - balance

There was low-certainty evidence that combined training led to a slight improvement in indices of balance at the end of intervention and at the end of follow-up, so there was some evidence of retention of the benefits for balance. Resistance training alone and cardiorespiratory training alone have each been shown to benefit balance after stroke, so either or both of these could be the active element within combined cardiorespiratory and resistance training.

Summary of other results

Some critical outcomes (i.e. those not included in the summary of findings tables), all important outcomes, and all outcomes synthesised without meta-analysis (SWiM) do not have the certainty of evidence established; therefore, we cannot infer too much from these data.

Critical outcomes

Falls

There are slightly higher numbers of people experiencing falls in the combined training interventions at the end of intervention and end of follow-up, but the number of events is low and there is uncertainty about the data.

Risk factors

Data for diastolic blood pressure reflect the systolic blood pressure data. Effect directions from SWiM suggest other indices relating to risk, including body fatness, blood lipids, and glucose control, may be sensitive to combined training interventions.

Walking

There were small improvements in maximum walking speed, walking endurance, and walking independence (functional ambulation category) at the end of intervention and end of follow-up. Maximum walking speed improved after intervention but not at the end of follow-up.

Physical function

Within physical function, there may be small improvements in functional mobility (timed up and go) at the end of intervention and end of follow-up. Effect directions from our synthesis without meta-analysis suggests that multiple areas of physical function of the lower limbs (stair climbing, chair rising) and upper limbs could be sensitive to combined training.

Important outcomes

Health status and quality of life, cognitive function, mood, and fatigue represent subjective measures and psychological concepts. These may not be the primary reason for using exercise interventions, but they do include patient-important outcomes, so it was important to assess these.

There may be some small and moderate-sized beneficial effects of combined training on the overall, mental, and social domains of health status and quality of life, but not on the physical health domain. There were too few data to draw conclusions about the effects of combined training on mood, cognitive function, and fatigue.

Tolerability and acceptability

Adverse effects were those that most likely occurred as a direct consequence of participating in resistance training (i.e. not all-cause events). Twelve of the 30 studies discussed adverse effects (Table 4); only a very small number of the adverse effects were categorised as serious events (two events in one study). Although there were some minor adverse effects, there was no evidence of people dropping out due to the content of the intervention; the interventions may have been acceptable to most people, although the time commitment may have put a small number of people off. Overall, the interventions could be considered safe and were tolerated by and seemed to be acceptable to most participants.

Limitations of the evidence included in the review

Predatory publication

There were 5/30 included studies with potential for publisher/journal concerns. Inclusion of these data did not influence conclusions.

Study designs

Only 12/30 studies included long-term follow-up data, ranging from 3 to 12 months after the end of intervention. It is important to examine the retention of any immediate gains associated with exercise, since any training-related gains mediated through increased physical fitness may be vulnerable to loss as a consequence of de-training/de-conditioning.

There are no cluster-randomised trials included; these designs could prevent between-group contamination of control and intervention, which could otherwise occur within a research location. Restricting intervention and control delivery to separate sites would mean that any local changes associated with delivery of an intervention and a control (e.g. staff behaviour) would not lead to contamination between groups [118].

Geographical location

Twenty-six of the 30 (87%) studies took place in high-income countries; there is a substantial knowledge gap for low-to-middle-income countries.

Participants

In studies where ambulatory status at recruitment could be determined, only 1/27 studies included non-ambulatory participants alongside those who could walk. The lack of non-ambulatory participants may be influenced by study eligibility criteria directly through the exclusion of non-ambulatory patients, and indirectly because impaired patients may be less likely to meet other eligibility criteria through greater burden of impairments and comorbidities. There can be substantial recovery of walking function in the first 12 weeks of rehabilitation [119], so the 15/30 studies recruiting later than three months after stroke may be less likely to recruit non-ambulatory participants.

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Overall, while the participants represent a more high-functioning subgroup amongst stroke as a whole, the restrictions of study eligibility criteria reflect commonly applied pre-exercise screening/contraindications to exercise used in the rehabilitation environment [4]. Therefore, the research findings are still broadly relevant to those who might receive these interventions in practice. However, participation/exclusion from trials is complex and caution is still needed when applying findings to the lower-functioning populations typically seen in rehabilitation.

Interventions

The interventions tended to be short (18/30 were < 12 weeks). Studies often lacked a clear description of exercise intensity and other characteristics. Therefore, evaluating the effects of different doses of exercise is difficult. Congruently, the results show limited effects on muscle strength, raising questions about the specificity of training for limb strength. The combined training approach may have focused more on functional strength training for gait than training of specific muscle groups, given that benefits for balance and gait were shown. Furthermore, cardiorespiratory and resistance training in combination may produce adaptation in cardiorespiratory fitness but not in muscle strength [16]. Impaired muscle strength gains after combined training compared with resistance training alone has been shown in clinical populations [120]. Cochrane review evidence about resistance training alone gives clear evidence of muscle strength improvement after stroke [59].

Comparisons

In 23/30 studies, the comparisons were imbalanced with regard to the relative amount of exposure in intervention and control groups. These comparisons were confounded by inflated exposure time/amount and are also at risk of performance bias because participant behaviours could be altered through clear knowledge of receiving 'something' rather than 'nothing'. Conclusions can still be drawn about the overall effect of participating in training, but it is more difficult to draw conclusions about the effects of exercise prescription content.

Outcomes

All-cause adverse events (secondary cardiovascular/cerebrovascular events and falls) and adverse effects were poorly reported in trials and rarely prespecified as an outcome.

The generalisability of some physical fitness results relating to muscle strength may be limited because a restricted number of muscle groups were assessed.

All types of exercise, particularly resistance training, may benefit blood pressure, so it is surprising that outcomes relating to principal risk factor reduction and secondary prevention (e.g. blood pressure) are often not included. This could be because many training studies are conducted in a rehabilitation environment where such metrics may be less of a focus compared with other clinical settings. Blood pressure is also typically well-controlled using antihypertensive medications, so it could be that other risk indicators should be considered.

Limitations of the review processes

Searches may have missed some relevant studies. However, we used a very comprehensive electronic search strategy.

One review author extracted outcome data, but every item of analysed data in RevMan was double-checked by a second review author.

We did not include adjunct cointerventions (such as virtual reality), which could modify the effectiveness of combined training.

We did not include active comparators, so some combined training interventions were excluded.

We examined multiple outcomes. One consequence was that small feasibility or pilot studies with high risk of bias and multiple outcomes may be more 'visible' in this review. Conversely, large studies focused on limited numbers of outcomes may be less 'visible'. Inclusion of multiple, diverse outcomes is justifiable because exercise has the potential for multiple benefits aligned to patient priorities [121].

Quality of life and cognitive function are complex and multidimensional, so the analysis of summary scores may not be the best way of examining these data.

Agreements and disagreements with other studies or reviews

Three recent systematic reviews specifically examined combined training interventions after stroke (see Table 8 for a summary).

There are agreements regarding improvements in physical function and cardiorespiratory fitness and no effect on mood; there are disagreements about effects on quality of life and muscle strength. It is clear there is substantial variation in the included data. The main issue is that the other reviews include studies that we excluded, and we included many studies not assessed in these recent publications; there is limited overlap.

The current data are very similar to the findings of our previous review version [47], including improvements in disability, muscle strength, walking, and physical function. However, current data now indicate that there could be small improvements in cardiorespiratory fitness, although this evidence is very uncertain.

AUTHORS' CONCLUSIONS

Implications for practice

Safety, acceptability, and tolerability

- Combined training does not increase mortality, and may have little or no effect on the incidence of secondary events.
- There were no concerning patterns of adverse effects, that is, those attributable to participating in combined training interventions.
- Combined training programmes are well attended and complied with; adherence is good.
- There was little evidence that participants dropped out because of the interventions; combined training interventions are acceptable and well tolerated, although the time commitment may discourage some people.
- Improved health status and quality of life outcomes could be important for patients when deciding whether to adhere to an intervention.

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Secondary prevention

- It is uncertain whether combined training can directly reduce mortality and the incidence of secondary events.
- It is uncertain whether combined training can benefit cardiometabolic risk factors. Blood pressure may already be well controlled by medications. The small increase in cardiorespiratory fitness may reflect some risk reduction.

Physical effects

- Combined training may result in small improvements in global indices of disability.
- Combined training may improve cardiorespiratory fitness; lower limb muscle strength may improve slightly, but the evidence is unclear.
- Combined training can improve walking (including speed, endurance, and independence); this may be retained after the intervention stops.
- Combined training improves aspects of lower limb physical function relating to balance and functional mobility; this could reduce the risk of falls, but there were too few data to demonstrate this directly.

Psychological effects

- Combined training had moderate or small beneficial effects on the overall, mental, and social aspects of health status and quality of life.
- The effects of combined training on anxiety, depression, cognitive function, and fatigue remain under-investigated even though they are important to people during life after stroke.

Equity-related implications for practice

Some interventions involved exercise equipment, whilst others involved walking and bodyweight exercises. This means that combined cardiorespiratory and resistance training interventions can be implemented without specialist equipment. This is relevant to low-resource countries and settings; in these instances, it is feasible to perform progressive exercise, but it may not always be possible to align this to exercise prescription frameworks (e.g. [4]).

Implications for research

Large, well-designed clinical studies are needed to assess the effects of combined exercise training after stroke and to determine the optimal regimen for improving cardiorespiratory fitness and musculoskeletal fitness. In the future, those who run trials in this area should do the following.

- Report studies more clearly, adhering to the CONSORT guidelines [122]
- Report exercise exposures more clearly; use of exercise-specific reporting guidelines (CERT Consensus Exercise Reporting Template; [123]). Dose parameters, particularly intensity, should be determined and aligned with those used in current exercise prescription guidelines where possible (e.g. [4]).
- Be aware of the recommendations of Cochrane reviews on cardiorespiratory training only [58] and resistance training only [59]
- Consider cluster-RCT designs
- Include a broader population of stroke survivors (particularly non-ambulatory stroke survivors) to allow stratification by sex, level of impairment, and functional ability
- Assess the effects of combined training on people with specific post-stroke problems, for example, people with depression or post-stroke fatigue
- All exercise interventions have the potential to influence a range of key outcomes. However, determining specific effects is challenging when a diverse range of measurement tools are used. There is therefore a strong case for developing a core outcome set for the evaluation of the effects of exercise in general; these should be guided by current priority-setting research alongside direct consumer input.
- Greater benefits could occur if combined intervention programmes partitioned cardiorespiratory training and resistance training into different sessions, different days, or separate, sequential periods of time (periodised training).
- Employ longer duration interventions (> 12 weeks) to optimise potential effectiveness, and longer follow-up periods (6 to > 12 months) to evaluate retention of effects
- Explore potential barriers and facilitators to resistance training. For example, there may be challenges in performing exercises correctly due to impairments, an increased need for supervision and guidance, and cognitive issues (e.g. poor memory and poor motor planning, lack of self-efficacy for exercise). If people were not active prior to stroke, there may be barriers to creating new behaviours in the longer term (e.g. cost of gym membership, transport, adequate carer support).
- Physical outcomes may be sensitive to confounding. Attention control exposures should be used to ensure control and intervention groups are balanced.

Equity-related implications for research

Current data are dominated by studies performed in high-income countries. It is essential that more research is carried out in low-to-middle income regions where the global burden of stroke is increasingly likely to have the most impact [53].

SUPPLEMENTARY MATERIALS

Supplementary materials are available with the online version of this article: 10.1002/14651858.CD016002.

Supplementary material 1 Search strategies

Supplementary material 2 Characteristics of included studies

Supplementary material 3 Characteristics of excluded studies

Supplementary material 4 Characteristics of studies awaiting classification

Supplementary material 5 Characteristics of ongoing studies

Supplementary material 6 Analyses

Supplementary material 7 Data package

Supplementary material 8 Studies in Previous Review

Supplementary material 9 Amendments to this review

Supplementary material 10 Synthesis without meta analysis

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ADDITIONAL INFORMATION

Acknowledgements

This review is one of a suite of three connected reviews split from the comparisons of a previous review title [47]. The methods, architecture, and some team members of the reviews are the same. As a consequence, there is substantive shared content and template text common to all three titles. Parts of the content are also similar to a review by some of the same author team investigating interventions to reduce sedentary behaviour after stroke [124]. The approach is permitted by the Cochrane Publication Policy.

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Editorial and peer-reviewer contributions

The following people conducted the editorial process for this article.

- Sign-off Editor (final editorial decision): Jordi Pardo Pardo, Campbell and Cochrane Equity Thematic Group, University of Ottawa, Canada
- Managing Editor (selected peer reviewers, provided editorial guidance to authors, edited the article): Sam Hinsley, Cochrane Central Editorial Service
- Editorial Assistant (conducted editorial policy checks, collated peer-reviewer comments, and supported editorial team): Addie Smyth and Leticia Rodrigues, Cochrane Central Editorial Service
- Copy Editor (copy editing and production): Laura MacDonald, Cochrane Central Production Service
- Peer reviewers (provided comments and recommended an editorial decision: Jennifer Hilgart, Cochrane (methods), Jo Platt, Central Editorial Information Specialist (search); Larissa Tavares Aguiar, Faculdade Ciências Médicas de Minas Gerais, Brazil (clinical); Christina DCM Faria, Department of Physiotherapy, Universidade Federal de Minas Gerais (clinical); Luis Rafael Moscote-Salazar, International Center for Advanced Clinical Studies, CIECA (consumer)

Contributions of authors

Original review

DH Saunders, CA Greig, GE Mead, and A Young contributed to writing the review protocol.
DH Saunders developed and ran searches, selected studies, extracted and interpreted data, performed the analyses, and co-wrote the review.
CA Greig and GE Mead selected studies, extracted and interpreted data, performed the analyses, and co-wrote the review.
A Young provided comments on interim drafts of the review.

Previous update

DH Saunders developed and ran searches, selected studies, extracted and interpreted data, performed the analyses, and wrote the review.
MF Sanderson, S Hayes, L Johnson, S Kramer, D Carter, and H Jarvis selected studies, extracted and interpreted data, and contributed to writing the review.
M Brazzelli advised on the methodology, interpreted data, and contributed to writing the review.
GE Mead helped select studies and provided comments on a draft version of the review.

This update

DH Saunders developed and ran searches, selected studies, extracted and interpreted data, performed the analyses, and wrote the review.
JD Cheyne developed and ran searches and contributed to writing the review.
SA Carstairs, M Fileman, J Morris, S Morton, G Wylie selected studies, extracted and interpreted data, and contributed to writing the review.
GE Mead helped select studies and provided comments on a draft version of the review.

Some authors involved in previous published versions of this review between 2004 and 2020 are no longer included on the author byline: CA Greig, A Young, MF Sanderson, S Hayes, L Johnson, S Kramer, D Carter, H Jarvis, and M Brazzelli. Some of the content retained in this review reflects their contributions.

Declarations of interest

DH Saunders received royalties in 2024 (about £857.78) for contribution to education events up until 11 July 2024, involving delivery of four one-hour tutorials for Edinburgh Clinical Research Facility (CRF). DHS was a co-author of one included study (Mead 2007 [125, 126, 127]), which was a randomised trial of exercise based at University of Edinburgh hospitals and funded by the Chief Scientist Office.

SA Carstairs has no declarations of interest.

JD Cheyne has no declarations of interest.

M Fileman has no declarations of interest.

J Morris has no declarations of interest.

S Morton has no declarations of interest.

G Wylie has no declarations of interest.

GE Mead receives royalties (about GBP 100 a year) for a book about fitness training after stroke [128]. These royalties are used to support further research. GEM has led a study included in the review (Mead 2007), which was a randomised trial of exercise based at University of Edinburgh Hospitals and funded by the Chief Scientist Office. GEM was editor of Cochrane Stroke from 2010 to 2023 and received about an hour's worth of funding per week; from 2015 to 2023, she received one hour's salary. Since 2023, she has co-led the Cochrane thematic group in Heart Stroke and Circulation, but she is not remunerated for this role. She played no role in editing

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this review. GEM performs occasional consultancy for LaterLife Training.

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Update (2020) DOI/10.1002/14651858.CD003316.pub7

Data, code and other materials

As part of the published Cochrane review, the following are made available for download for users of the Cochrane Library: search strategies (Supplementary material 1); characteristics of included studies (Supplementary material 2); characteristics of excluded studies (Supplementary material 3); characteristics of studies awaiting classification (Supplementary material 4); characteristics of ongoing studies (Supplementary material 5); analyses (Supplementary material 6); data package (Supplementary material 7); studies in previous review (Supplementary material 8); amendments to this review (Supplementary material 9).

Appropriate permissions have been obtained for such use. Analyses and data management were conducted within Cochrane's authoring tool, RevMan, using the inbuilt computation methods. Template data extraction forms are available from the review authors on reasonable request.

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ADDITIONAL TABLES

Table 1. Stroke patient priorities and exercise intervention targets

Top 10 priority	Pollock et al 2014 [55] **N = 28**	Rudberg et al 2021 [56] **N = 589**	Stroke Association 2021 [57] **N = 1400**
1	What are the best ways to improve understanding (**cognition**) after stroke?	**Balance** and **walking** problems	**Mental and emotional** (psychological) problems can be caused by stroke/TIA (transient ischaemic attack).
2	What are the best ways of helping people come to terms with the long-term consequences of stroke?	Post-stroke **fatigue**	Thinking and memory (**cognitive**) problems
3	What are the best ways to help people recover from aphasia?	**Upper and lower limb** problems	Interventions for the range of communication difficulties
4	What are the best treatments for **arm recovery and function**?	Impact of **exercise on rehabilitation**	What are the best ways to recognise, reduce, treat and self-manage **fatigue**?
5	What are the best ways to treat visual problems after stroke?	Lifestyle to avoid a **new stroke**	How can community stroke services best be resourced and organised in all regions to provide effective **home/community-based rehabilitation**
6	What are the best ways to manage and/or prevent **fatigue**?	**Cognition** and memory	What and how common are the long-term impacts of stroke on **abilities necessary for everyday life**; what, and how can, interventions be made available to facilitate these abilities?
7	What are the best treatments to improve **balance**, **gait**, and **mobility**?	Aphasia	What is the best time, place, and amount of therapy (e.g. speech and language therapy, **physiotherapy**, occupational therapy) to get the best outcomes for stroke survivors?
8	How can stroke survivors and families be helped to cope with speech problems?	Visual problems	How can people supporting stroke survivors work best with the stroke care team?
9	What is the best way to improve **confidence** after stroke?	**Depression**/**anxiety**	What are the best interventions including exercise to improve **strength** and **fitness**, promote recovery, and prevent **further stroke** in stroke survivors?

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Table 1. Stroke patient priorities and exercise intervention targets *(Continued)*

10	Are exercise and fitness programs beneficial at improving **function** and **quality of life** and avoiding **subsequent stroke**?	Other	What do stroke survivors think and feel works well, or needs improvement as they move through the stroke pathway, including **the intensity of rehabilitation**; what can be done to improve the stroke survivor and carer experiences?

Text in **bold** represents domains where there is a rationale for exercise benefits

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Table 2. Overview of synthesis and included studies (OSIS)

Summary

- Modes and combinations of cardiorespiratory training and resistance training varied and were often delivered in a circuit training format.
- 19/30 studies involved both upper and lower limbs, with upper limbs being restricted to resistance training activity; 11/30 studies involved lower limbs only.
- All 30 studies employed bilateral training of the limbs.
- Progression: interventions progressed based on intensity, duration, repetition number, speed, resistance/mass of objects or perceived exertion.
- Cardiorespiratory training mode was most commonly walking (treadmill or overground), with or without additional stationary cycle training.
- Cardiorespiratory intensity was prescribed in 17/30 studies using heart rate or RPE.
- Resistance training mode included weights, exercise machines, elastic resistance, and bodyweight exercises.
- Resistance training intensity was not often measured in relation to one-repetition maximum (5/30 studies).
- Most studies (28/30) trained 2 to 5 days/week (range from < 1 to 7 days/week).
- Programmes lasted 4 weeks to 1 year; shortest duration(< 12 weeks 18/30 studies; ≥ 12 weeks 12/30 studies).

Study ID (country)	**Participants: sample size (intervention:control), ambulatory status, and recovery stage**	**Intervention exposure**		**Comparator exposure**	**Outcome group with data**	**Outcome**	**Synthesis method**	
		Intervention mode (limbs recruited)	**Intervention dose (intensity, duration, frequency, programme length) Bold = AHA 2014 recommendations**				**End of intervention (time point)**	**End of follow-up (time point)**
Acheampong 2018 Ghana	M = 21 (10:11) Ambulatory Chronic	Cardiorespiratory walking, cycling, stepping Resistance training using free weights Bilateral UL + LL	40% to **70% of HRM** **45 to 60 min/d** **3 d/wk** 10 weeks	No intervention	Vascular risk factors	Blood pressure (SBP & DBP)	MA (10 wk)	-
						Blood lipids and cholesterol	SWiM (10 wk)	-
Aravind 2022 Canada	N = 33 (16:17) Ambulatory Chronic	Group circuit training involving walking and bodyweight exercises Bilateral UL + LL	Intensity unclear **60 min/d** 2 d/wk 12 weeks	Waitlist control	Death	Death	MA (12 wk)	MA (10 mth)
					Disability	NEADL	MA (12 wk)	MA (10 mth)
					Adverse effects	Falls, secondary events	MA	

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

					Walking	Endurance (6-MWT)	MA (12 wk)	MA (10 mth)
						CWS	MA (12 wk)	MA (10 mth)
					Physical function	Balance (BBS)	MA (12 wk)	MA (10 mth)
						Sit to stand	SWiM (12 wk)	SWiM (10 mth)
					Health status & quality of life	Overall (EQ-5D-5L)	MA (12 wk)	MA (10 mth)
						Physical (SIPSO)	MA (12 wk)	MA (10 mth)
						Social (SIPSO)	MA (12 wk)	MA (10 mth)
					Mood	Depression (GDS)	MA (12 wk)	MA (10 mth)
					Cognition	Trail making test B	MA (12 wk)	MA (10 mth)
					Fatigue	Overall (SF-36 Vitality)	MA (12 wk)	MA (10 mth)
Cooke 2010 [129, 130, 131, 132, 133, 134, 135] UK	N = 109 (36:38) Mixed ambulatory status Early subacute (7 d to 3 mth)	Resistance training + treadmill training Bilateral LL Plus conventional physiotherapy	Intensity unclear 60 min/d 4 d/wk 6 weeks	Conventional physiotherapy	Death	Death	MA (6 wk)	MA (12 wk)
					Disability	RMI	MA (6 wk)	MA (12 wk)
					Fitness	Musculoskeletal (strength)	MA (6 wk)	MA (12 wk)
					Walking	Speed (comfortable)	MA (6 wk)	MA (12 wk)
					Health status & quality of life	Overall (Euroqol)	MA (6 wk)	MA (12 wk)
Dean 2018 [136, 137, 138, 139, 140] UK	N = 45 (23:22) Ambulatory Chronic (> 6 mth)	Group circuit training (0 to 3 months) + home training (0 to 6 months) Bilateral UL + LL	Intensity unclear Unclear min/d 2 d/wk (+ home exercise) 6 months (0 to 3 months group exercise; 0 to 6 months home exercise)	Usual care	Death	Death	MA (6 mth)	MA (9 mth)
					Disability	RMI	MA (6 mth)	MA (9 mth)
					Physical Function	Functional mobility (TUG)	MA (6 mth)	MA (9 mth)

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

		Plus usual care			Health status & quality of life	Overall (SSQOL)	MA (6 mth)	MA (9 mth)
						Mental (SF-12)	MA (6 mth)	MA (9 mth)
					Fatigue	Overall (Fatigue Assessment Scale)	MA (6 mth)	MA (9 mth)
Duncan 1998 USA	N = 20 (10:10) Ambulatory Subacute (7 d to 6 mth)	Walking or cycle ergometry; elastic-resisted contractions Bilateral UL+LL	Intensity unclear 90 min/d **3 d/wk** 12 weeks	Usual care 44 min/d, 3.25 d/wk for 12 weeks	Death	Death	MA (12 wk)	-
					Disability	BI	MA (12 wk)	-
					Walking	Endurance (6-MWT)	MA (12 wk)	-
						Speed (comfortable)	NEE	-
					Physical Function	Balance (BBS)	MA (12 wk)	-
						Jebsen Hand Test	SWiM (12 wk)	-
						Fugl-Meyer (UL & LL)	SWiM (12 wk)	-
					Health status & quality of life	SF-36	NEE	-
Duncan 2003 [141, 142, 143, 144, 145] USA	N = 100 (50:50) Ambulatory Early subacute (7 d to 3 mth)	Cycle ergometer interval training, elastic resisted strength training, balance, and upper limb functional exercises Bilateral LL	Intensity **50% to 60% heart rate reserve** 90 to 120 min/d **3 d/wk** 12 to 14 weeks	Usual outpatient care plus home visit 30 min/d 1 d/2wks	Death	Death	MA (12 to 14 wk)	MA (6 mth)
					Disability	BI	MA (12 to 14 wk)	MA (6 mth)
					Adverse effects	Secondary events	MA (12 to 14 wk)	MA (6 mth)
					Fitness	Musculoskeletal (strength) Cardiorespiratory (VO_2 peak)	MA (12 to 14 wk)	MA (6 mth)

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

					Walking	CWS Endurance (6-MWT)	MA (12 to 14 wk)	MA (6 mth)
					Physical function	Balance (BBS)	MA (12 to 14 wk)	MA (6 mth)
						Fugl-Meyer (UL & LL)	SWiM (12 to 14 wk)	SWiM (6 mth)
					Health status & quality of life	Physical (SF-36) Mental (SF-36) Social (SF-36) Overall (SIS)	MA (12 to 14 wk)	MA (6 mth)
					Mood	Depression (GDS)	MA (12 to 14 wk)	MA (6 mth)
					Cognition	FIM Cognitive	MA (12 to 14 wk)	MA (6 mth)
Fotiadou 2019 Greece	N = 12 (6:6) Ambulatory Chronic (> 6 mth)	Combined training based on American Heart Association Guidelines Bilateral UL + LL	Intensity; **RPE: 11 to 14** 60 min/d **3 d/wk** 8 weeks	No intervention	Death	Death	MA (8 wk)	-
Furnari 2014 Italy	N = 40 (20:20 Ambulatory Chronic (> 6 mth)	Aquatic exercise Bilateral UL or LL Plus % of usual care	Intensity unclear (difficulty progressed weekly) 60 min/d **3 d/wk** 8 weeks Plus Usual care 1 h/d	Usual care 1 h/d 6 d/wk 8 weeks	Death	Death	MA (8 wk)	-
					Walking	CWS	MA (8 wk)	-
					Physical function	Balance (postural stability)	MA (8 wk)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

			3 d/wk 8 weeks					
Galvin 2011 [146, 147] Ireland	N = 37 (19:18) Ambulatory Early subacute (7 d to 3 mth)	Family-mediated gait and strength training Bilateral LL Plus conventional physiotherapy	Intensity unclear **35 min/d** 7 d/wk 8 weeks	Conventional physiotherapy	Death	Death	MA (8 wk)	MA (3 mth)
					Disability	BI	MA (8 wk)	MA (3 mth)
					Walking	Endurance (6-MWT)	MA (8 wk)	MA (3 mth)
						Community ambulation	SWiM (8 wk)	SWiM (3 mth)
					Physical function	Balance (BBS)	MA (8 wk)	MA (3 mth)
						Fugl-Meyer (LL)	SWiM (8 wk)	SWiM (3 mth)
James 2002 [148] Ireland	N = 20 (10:10) Ambulatory Chronic (> 6 mth)	Circuit training Bilateral UL + LL	Cardiorespiratory intensity **50% to 60% HRR** Resistance intensity UC 90 min/d **3 d/wk** 4 weeks	No intervention	Death	Death	MA (4 wk)	-
					Walking	CWS	MA (4 wk)	-
						Functional walking	SWiM (4 wk)	-
					Fatigue	Overall (SF-36 vitality)	MA (4 wk)	-
Jarbandhan 2022 Suriname	N = 30 (20:10) Ambulatory Chronic (> 6 mth)	Home-based exercise programme (mobility exercises including upper limb; stair climbing; sit-to-stand and walking) Bilateral UL + LL	Stair climbing (RPE 4 to 5 out of 10), sit-to-stand (**2 sets** of 5 progressing to **3 sets** of **10**), walking (progressing step count target and RPE 4 to 5 out of 10) 70 min/d **3 d/wk** 8 weeks	No intervention No usual care	Death	Death	MA (8 wk)	-
					Disability	DASH score	MA (8 wk)	-
					Adverse effects	Secondary events	MA (8 wk)	-
					Fitness	Musculoskeletal (strength)	MA (8 wk)	-
					Walking	Endurance (6-MWT)	MA (8 wk)	-
					Physical Function	Balance (BBS)	MA (8 wk)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

Kang 2022 South Korea	N = 45 (11:7:11) Ambulatory Chronic (> 6 mth)	Circuit training (cardiorespiratory training and high-speed resistance training) Bilateral UL + LL	Intensity: **15RM** and **50% to 70% HRM** 60 min/d **3 d/wk** 8 weeks	Static stretching 60 min/d 3 d/wk 8 weeks	Death	Death	MA (8 wk)	-
		Circuit training (cardiorespiratory training and low-speed resistance training) Bilateral UL + LL	Intensity: **10RM** and **50% to 70% HRM** 60 min/d **3 d/wk** 8 weeks		Vascular risk factors	Blood pressure (SBP & DBP)	MA (8 wk)	-
						Body fat %	SWiM (8 wk)	-
					Fitness	Cardiorespiratory (VO_2 peak) Musculoskeletal (strength)	MA (8 wk)	-
					Walking	Endurance (6-MWT)	MA (8 wk)	-
					Physical Function	Balance (BBS) Functional mobility (TUG)	MA (8 wk)	-
Kim 2016a [149] South Korea	N = 20 (10:10) Ambulatory Early subacute (7 d to 3 mth)	Circuit training Bilateral UL + LL	Treadmill increasing speed/gradient TheraBand increasing repetitions/load 90 min/d 5 d/wk 4 weeks	Usual care	Death	Death	MA (4 wk)	-
					Disability	BI	MA (4 wk)	-
					Walking	Endurance (6-MWT)	MA (4 wk)	-
					Physical Function	Balance (BBS)	MA (4 wk)	-
						Fugl-Meyer (LL)	SWiM(4 wk)	-
Kim 2017a [150] (South Korea)	N = 30 (15:15) Ambulatory Chronic (> 6 mth)	Handgrip resistance training + treadmill walking with some added load to unaffected leg Bilateral	Resistance increase Treadmill speed increase 30 min/d **3 d/wk** 6 weeks	Conventional physiotherapy alone	Death	Deaths	MA (6 wk)	-
					Fitness	Musculoskeletal (strength)	MA (6 wk)	-
					Walking	Speed (maximum)	MA (6 wk)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

		UL + LL Plus conventional physiotherapy			Physical Function	Functional mobility (TUG)	MA (6 wk)	-
					Cognition	Trail making test B	NEE	-
Klassen 2020 Canada	N = 74 (25:25:24) Ambulatory Early subacute (7 d to 3 mth)	Gait-related training (steps); strengthening, functional, and balance training Bilateral LL Plus % of regular inpatient physiotherapy	DOSE1: gait = **≥ 40% HRR** progressing to **> 60% HRR**; SFB = **2 to 3 sets;** intensity 8 to 10RM **60 min/d** 5 d/wk 4 weeks DOSE2: gait = **≥ 40% HRR** progressing to **> 60% HRR**; SFB = 2 to 3 sets; intensity 8 to 10RM 120 min/d 5 d/wk 4 weeks	Regular inpatient physiotherapy	Death	Death	MA (4-5 wk)	MA (12 mth post stroke)
					Adverse effects	Secondary events	MA (4-5 wk)	MA (12 mth post stroke)
					Fitness	Musculoskeletal (strength)	MA (4-5 wk)	-
					Walking	Speed (comfortable) Endurance (6-MWT)	MA (4-5 wk)	MA (12 mth post stroke)
					Physical Function	Balance (BBS)	MA (4-5 wk)	-
					QoL	Overall (EQ-5D-5L)	MA (4-5 wk)	MA (12 mth post stroke)
					Mood	Depression (PHQ-9)	MA (4-5 wk)	-
					Cognition	Trail making test B	MA (4-5 wk)	MA (12 mth post stroke)
Knox 2018 [151] South Africa	N = 99 (51:48) Ambulatory Early subacute (7 d to 3 mth)	Task-oriented strength balance and walking circuit training (+ home-based walking) Bilateral UL(?) + LL	Reduced support and increased complexity and increasingly demanding tasks and home-based walking **60 min/d** 0.5 d/wk (average of 6 sessions) 12 weeks	Attention control – single session	Death	Death	MA (12 wk)	MA (12 wk)
					Walking	Speed (comfortable) Speed (maximum) Endurance (6-MWT)	MA (12 wk)	MA (12 wk)
					Physical Function	Balance (BBS) Functional mobility (TUG)	MA (12 wk)	MA (12 wk)
	N = 75 (35:40)	Walking, stationary bicycling, stair walking,	**70% to 80% HRM** (cardiorespiratory compo-	Usual care	Death	Death	MA (12 mth)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

Langhammer 2007 [152, 153] Norway	Ambulatory Early subacute (7 d to 3 mth)	treadmill, and resistance training Bilateral UL + LL	nent); **50% to 60% 1RM** (resistance component) Minimum 20 hours every third month in the first year after stroke 45 min/d 2 to **3 d/wk** 1 year		Disability	BI	MA (12 mth)	-
					Adverse effects	Falls	MA (12 mth)	-
					Fitness	Musculoskeletal (strength)	MA (12 mth)	-
Letombe 2010 [154] France	N = 18 (9:9) Ambulatory status UC Early subacute (7 d to 6 mth)	Cycle ergometry, treadmill walking, and isokinetic resistance training Bilateral UL + LL Plus usual care	Cardiorespiratory training: **70% to 80% maximal cycling power** Strength training; 6 sets of **10 repetitions** at **50% to 60% maximum** **40 to 60 min/d** 4 d/wk 4 weeks	Usual care	Death	Death	MA (4 wk)	-
					Disability	BI	MA (4 wk)	-
					Fitness	Cardiorespiratory (VO_2 peak)	MA (4 wk)	-
Liu-Ambrose 2022 Canada	N = 68 (34:34) Ambulatory Chronic (> 6 mth)	Warm-up, strength training, aerobic and balance exercises Bilateral UL + LL	1 RPE/month with a final target of RPE = 16 at month 6 min/d 2 d/wk 26 weeks	Attention control	Disability	Lawton IADL	MA (6 mth)	MA (12 mth)
					Walking	Endurance (6-MWT) Speed (maximum)	MA (6 mth)	MA (12 mth)
					Mood	Depression (CES-D)	MA (6 mth)	MA (12 mth)
					Physical function	SPPB	SWiM (6 mth)	SWiM (12 mth)
					Cognition	ADAS-Cog-Plus	MA (6 mth)	MA (12 mth)
Mead 2007 UK	N = 66 (32:34) Ambulatory Late subacute (3 to 6 mth)	Circuit including walking, stepping, cycle ergometry; resistance training body mass, weights, and elastic Bilateral UL + LL	**RPE: 13 to 16** progression in duration, repetition number, speed, mass of objects, and resistance of TheraBand **40** to 75 min/d **3 d/wk** 12 to 14 weeks (total of 36 sessions)	Attention control	Death	Death	MA (12 to 14 wk)	MA (4 mth)
					Disability	FIM	MA (12 to 14 wk)	MA (4 mth)
					Adverse effects	Secondary events Falls	MA (12 to 14 wk)	MA (4 mth)

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

					Fitness	Musculoskeletal (power)	MA (12 to 14 wk)	MA (4 mth)
						Cardiorespiratory (economy)	SWiM (12 to 14 wk)	SWiM (4 mth)
					Walking	Speed (comfortable)	MA (12 to 14 wk)	MA (4 mth)
					Physical Function	Balance (functional reach) Functional mobility (TUG)	MA (12 to 14 wk)	MA (4 mth)
						Sit to stand	SWiM (12 to 14 wk)	SWiM (4 mth)
					Mood	Anxiety (HADS) Depression (HADS)	MA (12 to 14 wk)	MA (4 mth)
					Fatigue	Overall (SF-36 vitality score)	MA (12 to 14 wk)	MA (4 mth)
Moore 2015 UK	N = 40 (20:20) Ambulatory Chronic (> 6 mth)	Community-based group classes including warm-up, stretching, functional strengthening, balance, agility, and cardiorespiratory training Bilateral UL + LL	Increasing load and repetitions 40% to 50% HRM increasing to **70% to 80% HRM** **40 to 60 min/d** **3 d/wk** 19 weeks	Attention control (stretching)	Death	Death	MA (19 wk)	-
					Vascular risk factors	Blood pressure (SBP & DBP)	MA (19 wk)	-
						Cholesterol, body composition, blood glucose control	SWiM (19 wk)	-
					Fitness	Cardiorespiratory (VO_2 peak)	MA (19 wk)	-
					Walking	Endurance (6-MWT) Speed (maximum)	MA (19 wk)	-
					Physical Function	Balance (BBS)	MA (19 wk)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

						Functional mobility (TUG)		
					Health status & quality of life	Overall (SIS)	MA (19 wk)	-
					Cognition	ACE-R	MA (19 wk)	-
Richards 1993 Canada	N = 18 (10:8) Ambulatory Subacute (7 d to 6 mth)	Treadmill walking, resisted exercises using Kinetron and a tilt table Bilateral LL Plus usual care	Intensity unclear Treadmill velocity and Kinetron resistance increments were progressed. 1.74 h/dd 5 d/wk 5 weeks	Usual care 0.73 h/d 5 d/wk 5 weeks	Walking	Speed (comfortable)	MA (5 wk)	NEE
					Physical function	Balance (BBS)	MA (5 wk)	NEE
						Fugl-Meyer (UL & LL)	SWiM (5 wk)	NEE
Richards 2004 [155] Canada	N = 63 (32:31) Ambulatory Early subacute (7 d to 6 mth)	Treadmill walking, resisted exercises using Kinetron and limb load monitor Bilateral LL Plus % of usual care	Intensity unclear Treadmill velocity and Kinetron resistance increments were progressed. **60 min/d** 5 d/wk 8 weeks	Usual care PT sessions 60 min/d 5 d/wk 8 weeks	Physical function	Balance (BBS) Functional mobility (TUG)	MA (8 wk) MA (8 wk)	MA (3 mth) MA (3 mth)
						Fugl-Meyer (UL)	SWiM (8 wk)	Unclear
						Fugl-Meyer (LL)	Unclear	Unclear
Rizvi 2023 India	N = 32 (15:15) Ambulatory Early subacute (7 d to 3 mth)	Treadmill walking, cycle ergometry; continuous or intervals resistance training Bilateral UL + LL Plus usual care	Cardiorespiratory training **60% to 80% HRR** and below **RPE 12 to 14** **3 to unclear d/wk** Resistance initial load **60% 1-RM**, 11 to 14%, **10 to 15 repetitions** **2 d/wk** **60** to 75 min/d Unclear overall d/wk 12 weeks	Usual care	Death	Death	MA (12 wk)	-
					Vascular risk factors	Blood pressure (SBP & DBP)	MA (12 wk)	-
					Physical function	Balance (BBS) Functional mobility (TUG)	MA (12 wk)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

Shin 2011 [156] South Korea	N = 21 (11:10) Ambulatory status UC Chronic (> 6 mth)	Functional strength training (bridging and stepping) plus treadmill and cycle ergometry Bilateral LL	Cardiorespiratory training progressive but < 40% HRR Resistance training described as 'medium intensity' of 5 to **15** repetitions **60 min/d** 5 d/wk 4 weeks	Usual care; conservative physical therapy 60 to 90 min/d 3 d/wk 10 weeks	Death	Death	MA (4 wk)	-
					Physical function	Balance (BBS)	MA (4 wk)	-
Teixeira 1999 [157, 158, 159] Canada	N = 13 (6:7) Ambulatory Chronic (> 6 mth)	Walking and stepping or cycle ergometry; resistance training 7 exercises using body mass, weights and elastic resistance Bilateral LL	Cardiorespiratory training progressing **50% to 70% maximum work rate** Resistance training progressing **50% to 80% 1RM** **3 sets** of **10** repetitions **60 to** 90 min/d **3 d/wk** 10 weeks	No intervention	Death	Death	MA (10 wk)	-
					Physical function	Balance (BBS)	MA (10 wk)	-
Toledano-Zarhi 2011 [160] Israel	N = 28 (14:14) Ambulatory Early subacute (7 d to 3 mth)	Treadmill, hand bike, cycle ergometer + group exercise for strength, balance and co-ordination exercise Bilateral UL + LL	Cardiorespiratory 50% to **70% HRM** **35 to 55 min/d** **3 d/wk** 6 weeks	Non-exercise attention control	Death	Death	MA (6 wk)	-
					Vascular risk factors	Blood pressure (SBP & DBP)	MA (6 wk)	-
					Fitness	Cardiorespiratory (VO_2 peak)	MA (6 wk)	-
					Walking	Endurance (6-MWT)	MA (6 wk)	-
					Physical function	Balance (four-square step test)	MA (6 wk)	-
						Stair ascent & descent	SWiM (6 wk)	-
Vahlberg 2021 Sweden	N = 79 (40:39)	Regular walking and functional leg exercises	Walking intensity **RPE 12 to 13** increasing perceived exertion to **15** by the 3rd month.	Usual care	Death	Death	MA (3 mth)	-
					Adverse effects	Secondary events	MA (3 mth)	-

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

	Ambulatory Acute (< 7 d)	Bilateral LL Plus usual care	Functional exercises: repetitions increased from **10 to 15** unclear min/d (but **> 30 min/d**) 6 d/wk 3 months			Falls	NEE
					Vascular risk factors	Body composition, lipids, and glucose control	SWiM (3 mth)
					Walking	Endurance (6-MWT)	MA (3 mth)
						Speed (comfortable)	MA (3 mth)
Van de Port 2012 [161, 162, 163] Netherlands	N = 250 (124:126) Ambulatory Subacute (7 d to 6 mth)	Task-orientated circuit training. 8 workstations targeting balance, stair walking, turning, transfers, and speed walking Bilateral LL	Intensity unclear 90 min/d **2 d/wk** 12 weeks	Usual outpatient care	Death	Death	MA (12 wk)
					Disability	RMI	MA (12 wk)
					Adverse effects	Secondary events	MA (12 wk)
						Falls	NEE
					Walking	Independence (FAC)	MA (12 wk)
						Endurance (6-MWT)	MA (12 wk)
						Speed (comfortable)	MA (12 wk)
					Physical function	Balance (timed balance test)	MA (12 wk)
						Modified stair text	SWiM (12 wk)
						Motricity Index (UL & LL)	SWiM (12 wk)
					Health status & quality of life	Overall (SIS)	MA (12 wk)
					Mood	Anxiety (HADS)	MA (12 wk)
						Depression (HADS)	
					Fatigue	Overall (SIS fatigue severity)	MA (12 wk)

		MA (24 wk)
		MA (24 wk)
		MA (24 wk) NEE
		MA (24 wk) MA (24 wk) MA (24 wk)
		MA (24 wk)
		SWiM (24 wk)
		SWiM (24 wk)
		MA (24 wk)
		MA (24 wk)
		MA (24 wk)

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Table 2. Overview of synthesis and included studies (OSIS) *(Continued)*

Yang 2006 [164] Taiwan	N = 48 (24:24) Ambulatory Chronic (> 6 mth)	Functional stepping and chair rising. Circuit of 6 exercises each of 5-min duration Bilateral LL	Intensity unclear Repetitions, stair height, and chair height were changed to introduce progression. 30 min/d **3 d/wk** 4 weeks	No intervention	Death	Death	MA (4 wk)	-
					Fitness	Musculoskeletal (strength)	MA (4 wk)	-
					Walking	Endurance (6-MWT)	MA (4 wk)	-
						Speed (comfortable)	MA (4 wk)	-
					Physical function	Functional mobility (TUG)	MA (4 wk)	-

AHA 2014 [4] recommendations for exercise after stroke are cardiorespiratory training: intensity 40% to 70% VO_2 reserve, or HR reserve; 55% to 80% HR max; RPE 11 to 14 (6 to 20 scale) for 3 to 5 d/wk for 20 to 60 min/session (or multiple 10-min sessions), and resistance training: 50% to 80% of 1RM 1 to 3 sets; 10 to 15 repetitions; 8 to 10 exercises involving the major muscle groups for 2 to 3 d/wk.

ACE-R: Addenbrooke's Cognitive Examination Revised; **ADAS-Cog-Plus:** Alzheimer's Disease Assessment Scale-Cognitive-Plus; **AHA:** Amercian Heart Association; **BBS:** Berg Balance Scale; **BDI:** Beck Depression Inventory; **BI:** Barthel Index; **CES-D:** Center for Epidemiologic Studies Depression Scale; **CWS:** comfortable walking speed; **d:** day(s); **DASH:** disabilities of the arm, shoulder and hand; **DBP:** diastolic blood pressure; **FTHUE:** functional test of the hemiparetic upper extremity; **FAC:** functional ambulation category; **GDS:** Geriatric Depression Scale-short version; **HADS:** Hospital Anxiety and Depression Scale; **HR:** heart rate; **LL:** lower limb; **MA:** meta-analysis; **max:** maximum; **min:** minute(s); **mth:** month(s); **MWS:** maximum walking speed; **NEE:** no effect estimate; **RM:** repetition maximum; **RMI:** Rivermead Mobility Index; **RPE:** rating of perceived exertion; **SAI:** State Anxiety Inventory; **SBP:** systolic blood pressure; **SPPB** Short Performance Physical battery; **SIPSO:** Subjective Index of Physical and Social Outcome; **SIS:** Stroke Impact Scale; **SSQoL:** stroke-specific quality of life; **SWiM:** synthesis without meta-analysis; **TUG:** timed up and go; **UL:** upper limb; **VO_2:** maximal oxygen update; **wk:** week(s); **6-MWT:** 6-minute walk test

Table 3. Overview of combined training study covariates

Summary
• **Participants:** N = 1519 participants
• **Age**: average age 63.7 years (study cohorts from 49.5 to 78.5 years)
• **Ambulatory status**: most studies recruited ambulatory participants (ambulatory N = 26, mixed ambulatory/non-ambulatory N = 1, non-ambulatory N = 0, unclear N = 3).
• **Stage of recovery**: most studies commenced during the early subacute and chronic phases (acute (< 7 d) N = 1, early subacute (7 d to 3 mth) N = 14, late subacute (3 to 6 mth) N = 1, chronic (> 6 mth) N = 14).
• **Balanced exposure**: most study designs had an imbalanced exposure of intervention that exceeded the control (balanced N = 7, imbalanced, N = 23).
• **Duration**: most interventions were of short duration (< 12 weeks N = 18, ≥ 12 weeks N = 12).
• **Follow-up period:** N = 12 studies (mean 7.3 months; range 3 to 12 months)
• **Region**: Europe N = 12, North America N = 8, Asia N = 6, Africa N = 2, Middle East N = 1, South America N = 1, Central America N = 0, Pacific N = 0.
• **Economy**: most studies took place in high-income countries (N = 26; low-/middle-income countries N = 4).
• **Predatory publication concerns**: most studies were published in sources not implicated in predatory publishing (concerns N = 5, no concerns N = 25).
• **Publication retractions:** there were no known retracted publications or expressions of concern.

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Table 3. Overview of combined training study covariates *(Continued)*

Study	Participants (N)	Age (years	Ambulatory Status	Intervention duration	Exposure	Predatory publishing concerns	Publication retractions	Stage of recovery	Follow-up period	Region	Country	Income
Acheampong 2018	21	58.9	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	Africa	Ghana	Low/ Middle
Aravind 2022	33	68.9	Ambulatory	≥ 12 wk	Imbalanced	Concerns	No	Chronic (> 6 mth)	10 mth	North America	Canada	High
Cooke 2010	109	68.7	Mixed ambulatory/non-ambulatory	< 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	3 mth (12 w)	Europe	UK	High
Dean 2018	45	70.5	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	9 mth	Europe	UK	High
Duncan 1998	20	65.8	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	-	North America	USA	High
Duncan 2003	100	69.4	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	6 mth	North America	USA	High
Fotiadou 2019	12	64.4	Ambulatory	≥ 12 wk	Imbalanced	Concerns	No	Chronic (> 6 mth)	-	Europe	Greece	High
Furnari 2014	40	70	Ambulatory	< 12 wk	Balanced	No concerns	No	Chronic (> 6 mth)	-	Europe	Italy	High
Galvin 2011	37	66.6	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	3 mth	Europe	Ireland	High
James 2002	20	78.5	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	Europe	Ireland	High
Jarbandhan 2022	30	61.8	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	South America	Suriname	Low/ Middle

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Table 3. Overview of combined training study covariates *(Continued)*

Kang 2022	45	55	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	Asia	South Korea	High
Kim 2016a	20	65.6	Ambulatory	< 12 wk	Imbalanced	Concerns	No	Early subacute (7 d to 3 mth)	-	Asia	South Korea	High
Kim 2017a	30	51.3	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	Asia	South Korea	High
Klassen 2020	74	57.4	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	12 mth post-stroke	North America	Canada	High
Knox 2018	99	49.5	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	3 mth (12 wk)	Africa	South Africa	Low/ Middle
Langhammer 2007	75	73.9	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	-	Europe	Norway	High
Letombe 2010	18	59.9	Unclear	< 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	-	Europe	France	High
Liu-Ambrose 2022	68	69.4	Ambulatory	< 12 wk	Balanced	No concerns	No	Chronic (> 6 mth)	12 mth	North America	Canada	High
Mead 2007	66	71.8	Ambulatory	≥ 12 wk	Balanced	No concerns	No	Late subacute (3 to 6 mth)	4 mth	Europe	UK	High
Moore 2015	40	69	Ambulatory	≥ 12 wk	Balanced	No concerns	No	Chronic (> 6 mth)	-	Europe	UK	High
Richards 1993	18	68.6	Unclear	< 12 wk	Balanced	No concerns	No	Early subacute (7 d to 3 mth)	3 mth	North America	Canada	High
Richards 2004	63	61.8	Ambulatory	< 12 wk	Balanced	No concerns	No	Early subacute (7 d to 3 mth)	3 mth	North America	Canada	High
Rizvi 2023	32	60	Ambulatory	≥ 12 wk	Imbalanced	Concerns	No	Early subacute (7 d to 3 mth)	-	Asia	India	Low/ Middle
Shin 2011	21	57.7	Unclear	< 12 wk	Balanced	Concerns	No	Chronic (> 6 mth)	-	Asia	South Korea	High

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Table 3. Overview of combined training study covariates *(Continued)*

Teixeira 1999	13	67.8	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	North America	Canada	High
Toledano-Zarhi 2011	28	65	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	-	Middle East	Israel	High
Vahlberg 2021	79	63.9	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Acute (< 7 d)	-	Europe	Sweden	High
Van de Port 2012	250	57	Ambulatory	≥ 12 wk	Imbalanced	No concerns	No	Early subacute (7 d to 3 mth)	6 mth (24 wk)	Europe	Netherlands	High
Yang 2006	48	58.4	Ambulatory	< 12 wk	Imbalanced	No concerns	No	Chronic (> 6 mth)	-	Asia	Taiwan	High

d: day(s); **mth:** month(s); **N:** number; **wk:** weeks(s)

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Table 4. Intervention acceptability and tolerability

SUMMARY

- 63 total losses before/during intervention exposure
- 56 total losses before/during control exposure
- Attendance at planned training sessions was reported in 16/30 studies; 7 with > 90% attendance and 13 > 80% attendance.
- Compliance with prescribed training during training sessions was reported in 10/30 studies. There were no serious issues tolerating the intensity or progression of the training.
- Adverse effect monitoring of interventions was reported in 12/30 studies, including 5/30 studies where this was preplanned. Nine of 12 studies reported no AE or SAE connected to the intervention; 1/12 studies reported 2 SAE; and 2/12 studies reported 24 minor AE. Adverse effects attributed to the intervention were very uncommon.

Study ID	Mode of intervention	WITHDRAWALS		ADHERENCE		ADVERSE EFFECTS
		Intervention n/N (%) and reasons	Control n/N (%) and reasons	ATTENDANCE (at intervention sessions)	COMPLIANCE (during intervention sessions)	(related to intervention)
Acheampong 2018	Cardiorespiratory walking, cycling, stepping Resistance training using free weights	5/10 (50%) (5 UC reason)	3/11 (27%) (3 UC reason)	62.5% participants fully participated	Unclear	Unclear
Aravind 2022	Group circuit training involving walking and bodyweight exercises	1/16 (6%) (1 back injury)	2/17 (12%) (2 unwilling to wait)	For 5/16, 45% attendance For 10/16, 92% attendance	Unclear	**Preplanned monitoring** No injuries or incidents related to the intervention reported
Cooke 2010	Resistance training + treadmill training	0/36 (0%)	7/38 (18%) (3 unwell; 3 withdrew; 1 abroad)	Unclear	Unclear	Unclear
Dean 2018	Group circuit training (0 to 3 months) + home training (0 tp 6 months)	2/23 (9%) (1 unwell, 1 family crisis)	2/22 (9%) (1 unwell, 1 wanted to be in the experimental group)	Reported only as 'good' attendance at classes	Reported as 'good' adherence to home training	**Preplanned monitoring** 19/22 AE (2 fatigue, 10 falls, 1 trips, 9 other) 2/6 SAE (1 fainted; 1 TIA)

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Table 4. Intervention acceptability and tolerability *(Continued)*

Duncan 1998	Walking or cycle ergometry; elastic-resisted contractions	0	0	Unclear	Reported as 'excellent'; intervention tolerated and able to progress	Unclear
Duncan 2003	Cycle ergometer interval training, elastic resisted strength training, balance and upper limb functional exercises	6/50 (12%) (1 renal insufficiency, 1 subclavian steal syndrome, 1 chose withdrawal, 3 recurrent stroke)	2/50 (4%) (1 withdrew, 1 non-return)	Mean 33.4/36 (93%) of sessions attended.	100% people progressed in strengthening 95% of people progressed in endurance	**Preplanned monitoring** No major SAE during exercise
Fotiadou 2019	Combined training based on American Heart Association Guidelines	0	0	Unclear	Unclear	Unclear
Furnari 2014	Aquatic exercise	0	0	Unclear	Unclear	Unclear
Galvin 2011	Family-mediated gait and strength training	2/19 (11%) (1 myocardial infarction; stroke)	1/18 (6%) (1 unwell)	227/245 (93%) of planned hours of intervention achieved.	Exercise diaries and caregiver involvement resulted in 'good compliance'	Unclear
James 2002	Circuit training	0	2/10 (20%) (2 neurological problems)	Unclear	Unclear	Unclear
Jarbandhan 2022	Home-based exercise programme (mobility exercises including upper limb; stair climbing; sit-to-stand and walking)	6/20 (30%) (2 rainy season; 1 glaucoma; 2 diabetes and hospitalisation for respiratory problems; 1 preference for supervised physiotherapy)	0/20 (0%)	Preplanned 70% participants completed full intervention	Unclear	No AE related to the activity
Kang 2022	Intervention 1 Circuit training (aerobic and resistance + game-based recreational) High speed	4/15 (27%) (1 refused participation; 3 lack of time)	4/15 (27%) (2 refused participation; 2 lack of time)	Unclear	Unclear	Unclear

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Table 4. Intervention acceptability and tolerability *(Continued)*

	Intervention 2 Circuit training (aerobic and resistance + game-based recreational) Low speed	8/15 (53%) (2 refused participation; 5 lack of time; 1 illness)				
Kim 2016a	Circuit training	0	0	100%	Training reported as well tolerated	Reported there were no SAE
Kim 2017a	Handgrip resistance training + treadmill walking with some added load to unaffected leg	0 (discharged home)	0	Unclear	Unclear	Unclear
Klassen 2020	Intervention 1 (DOSE1) Gait-related training (steps); strengthening, functional and balance training	0/25 (0%)	0/24 (0%)	99% of sessions	Mean 27 min > 40% HRR	**Pre-planned monitoring**: AE recorded but no effects during intervention mentioned
	Intervention 2 (DOSE2) Gait-related training (steps); strengthening, functional and balance training	1/25 (4%) (1 cardiology concerns)		94% of sessions	Mean 52 min > 40% HRR	
Knox 2018	Task-oriented circuit training (+ home-based walking)	6/51 (11%) (3 deceased, 2 moved away, 1 return to work)	5/48 (10%) (1 deceased, 2 no transport, 1 return to work, 1 private healthcare)	Unclear	Unclear	Unclear
Langhammer 2007	Walking, stationary bicycling, stair walking, treadmill, and resistance training	3/35 (9%) (1 dead and 2 withdrawals)	9/40 (23%) (6 dead; 3 withdrawals)	Unclear	Reported as 'high' in 28/35 (80%) participants	Unclear
Letombe 2010	Cycle ergometry, treadmill walking, and isokinetic resistance training	0	0	Unclear	Unclear	Unclear
Liu-Ambrose 2022	Warm-up, strength training, aerobic and balance exercises	6/34 (18%) (1 no longer interested; 3 health reasons; 1 did not have time; 1 could not contact)	5/34 (15%) (1 no longer interested; 3 health reasons; 1 could not contact)	80% (41.6 of 52 sessions) for the intervention group	Unclear	**Pre-planned monitoring** 4/19 minor AE were identified as connected to the study

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Table 4. Intervention acceptability and tolerability *(Continued)*

Mead 2007	Circuit including walking, stepping, cycle ergometry; resistance training body mass, weights, and elastic	0 /32 (0%)	1/34 (3%) (1 withdrew before intervention)	100% attendance in 19/32 (59%) participants	94 to 99% for individual exercises	No falls during intervention
Moore 2015	Community-based group classes including warm-up, stretching, functional strengthening, balance, agility and cardiorespiratory training	0	0	90% of sessions 53 hours out of a possible 57 hours of exercise completed	Unclear	No AE No SAE
Richards 1993	Treadmill + Kinetron + tilt table	0/10	0/8	84.4%	Unclear	Unclear
Richards 2004	Treadmill + Kinetron + limb load monitor	2/32 (6%) (1 hip fracture, 1 cardiac problem)	1/31 (3%) (1 withdrew)	33.63/40 (84%) sessions	Unclear	Unclear
Rizvi 2023	Treadmill walking: cycle ergometry +resistance training	1/16 (6%) (1 UC reason)	1/16 (6%) (1 UC reason)	Unclear	Unclear	Unclear
Shin 2011	Functional strength training (bridging and stepping) + treadmill and cycle ergometry	0	0	Unclear	Unclear	Unclear
Teixeira 1999	Walking and stepping or cycle ergometry; resistance training body mass, weights and elastic	0	0	Unclear	Unclear	Unclear
Toledano-Zarhi 2011	Treadmill, hand bike, cycle ergometer + group exercise for strength, balance and co-ordination exercise	1 /14 (7%) (n = 1 discontinued intervention)	0	84%	5/14 achieved highest level of progression	No AE reported during study
Vahlberg 2021	Regular walking and functional leg exercises	4/40 (10%) (3 comorbidity; 1 UC)	4/39 (10%) (2 comorbidity; 1 UC reason; 1 transportation)	Unclear	60 to 100% (median 86%) compliance with recommended intervention content	No AE reported during intervention period
Van de Port 2012	Task-orientated circuit training. 8 workstations targeting balance, stair walking, turning, transfers and speed walking	5/124 (4%) (4 participants did not start intervention,	7/126 (6%) (1 participant at the end of in-	83% of sessions	Unclear	1 AE (1 person with arrhythmia

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Table 4. Intervention acceptability and tolerability *(Continued)*

		1 participant withdrew without reason)	tervention missing assessment, 2 participants died from cancer, 2 participants had recurrent stroke, 2 participants withdrew without reason)			during session)
Yang 2006	Functional stepping and chair rising	0	0	100% of sessions	100% of planned exercises	Unclear

AE adverse effect(s); **HRR:** heart rate reserve; **n:** number of events; **N:** number of participants; **SAE** serious adverse event(s); **TIA** transient ischaemic attack

Table 5. Synthesis with meta-analysis - critical outcomes

DEATH		End of intervention Analysis 1.1	End of follow-up Analysis 2.1
Analysis level	Arm	RD -0.00, 95% CI -0.02 to 0.01; I^2 = 0%; 26 studies, 1352 participants; high-certainty evidence; Figure 4	RD -0.01, 95% CI -0.04 to 0.02; I^2 = 0%; 8 studies, 531 participants; high-certainty evidence; Figure 5
	Arm + contrast	NA	NA
Subgroup analysis	Stage	No evidence of subgroup differences (early subacute vs chronic) Uneven covariate distribution	No evidence of subgroup differences Uneven covariate distribution
	Duration	No evidence of subgroup differences	No evidence of subgroup differences Uneven covariate distribution
	Ambulatory	No evidence of subgroup differences Uneven covariate distribution	No evidence of subgroup differences Uneven covariate distribution
Sensitivity analysis exclusions	Imbalanced exposure	22/26 studies RD −0.01, 95% CI −0.04 to 0.04; P = 1.0; I^2 = 0%; 4 studies, 1272 particpants	7/8 studies
	Imputed data	None	None

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

	Predatory publishing	5/26 studies RD −0.01, 95% CI −0.04 to 0.04; P = 1.0; I^2 = 0%; 21 studies, 1272 particpants	1/7 studies RD −0.01, 95% CI −0.04 to 0.02; P = 0.78; I^2 = 0%; 7 studies, 498 particpants
Funnel plot		No funnel plot asymmetry detectable (Figure 16) Number of events is very small.	NA
Other exclusions		In Langhammer 2007, three of the six deaths in the control group and the one death in the training group occurred before discharge and before the intervention began; after excluding these data, the effect of training was still not statistically significant.	None
DISABILITY		End of intervention Analysis 1.2	End of follow-up Analysis 2.2
Analysis level	Arm analysis	SMD 0.20, 95% CI 0.04 to 0.36; I^2 = 11%; 13 studies, 789 participants; low-certainty evidence; Figure 6	SMD 0.10, 95% CI -0.07 to 0.28; I^2 = 10%; 8 studies, 614 participants; low-certainty evidence; Figure 7
	Arm + contrast	No data	No data
Subgroup analysis	Stage	No evidence of overall subgroup differences Uneven covariate distribution Borderline subgroup difference between early subacute and chronic subgroups (P = 0.05; I^2 = 73.7%), which favoured early subacute. Uneven covariate distribution	No evidence of subgroup differences Uneven covariate distribution
	Duration	No evidence of subgroup differences	No evidence of subgroup differences Uneven covariate distribution
	Ambulatory	No evidence of subgroup differences Uneven covariate distribution	Uneven covariate distribution
Sensitivity analysis exclusions	Imbalanced exposure	11/13 studies SMD −0.01, 95% CI −0.35 to 0.33; P = 0.95; I^2 = 0%; 2 studies, 134 participants	6/8 studies SMD 0.06, 95% CI −0.28 to 0.39; P = 0.75; I^2 = 0%; 2 studies, 134 participants
	Imputed data	1/13 studies; trivial influence SMD 0.22, 95% CI 0.07 to 0.37; P = 0.005; I^2 = 8%; 12 studies, 772 participants	1/8 studies SMD 0.12, 95% CI -0.05 to 0.30; P = 0.15; I^2 = 7%; 2 studies, 596 participants
	Predatory publishing	2/13 studies; trivial influence	1/8 studies

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

		SMD 0.21, 95% CI 0.05 to 0.38; P = 0.01; I^2 = 0%; 11 studies, 752 participants	SMD 0.12, 95% CI −0.05 to 0.30; P = 0.15; I^2 = 7%; 2 studies, 596 participants
Funnel plot		Funnel plot asymmetry suggests possible missing studies in area favourable to the intervention suggesting factors other than non-reporting bias (Figure 17). The small studies favouring the control exposure are also those carried out during the chronic phase. However, SMD effect estimates are known to produce spurious asymmetry [81].	NA
Oher exclusions		None	None
SECONDARY EVENTS		End of intervention Analysis 1.3	End of follow-up Analysis 2.3
Analysis level	Arm	RD -0.00, 95% CI -0.02 to 0.01; I^2 = 0%; 8 studies, 684 participants; high-certainty evidence; Figure 8	RD 0.01, 95% CI -0.06 to 0.09; I^2 = 55%; 4 studies, 285 participants; high-certainty evidence; Figure 9
	Arm + contrast	No data	No data
Subgroup analysis	Stage	No evidence of subgroup differences Uneven covariate distribution	Too few studies Uneven covariate distribution
	Duration	No evidence of subgroup differences Uneven covariate distribution	Too few studies Uneven covariate distribution
	Ambulatory	No evidence of subgroup differences Uneven covariate distribution	Too few studies Uneven covariate distribution
Sensitivity analysis exclusions	Imbalanced exposure	6/8	Only 1/5 studies with balanced exposure
	Imputed data	None	None
	Predatory publishing	None	None
Funnel plot		NA	NA
Oher exclusions		None	None
FALLS		End of intervention Analysis 1.4	End of follow-up Analysis 2.4
Analysis level	Arm	RD 0.07, 95% CI -0.00 to 0.15; I^2 = 0%; 3 studies, 174 participants	RD 0.06, 95% CI -0.06 to 0.19; I^2 = 4%; 2 studies, 99 participants

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

	Arm + contrast	No data	No data
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis Exclusions	Imbalanced exposure	2/3 studies	1/2 studies
	Imputed data	None	None
	Predatory publishing	1/3 studies	1/2 studies
Funnel plot		NA	NA
Other exclusions		None	None
Blood pressure SBP		End of intervention Analysis 1.5	End of follow-up Analysis 2.5
Analysis level	Arm	MD -1.83, 95% CI -9.60 to 5.95; I^2 = 76%; 5 studies, 140 participants; very low-certainty evidence; Figure 10	No study data
	Arm + contrast	Does not add additional studies MD −3.50 mmHg, 95% CI −11.79 to 4.78; P = 0.23, I^2 = 74%; 5 studies, 140 participants	NA
Subgroup analysis	Stage	No evidence of subgroup differences Uneven covariate distribution Unexplained heterogeneity	NA
	Duration	No evidence of subgroup differences Unexplained heterogeneity	NA
	Ambulatory	Uneven covariate distribution	NA
Sensitivity analysis Exclusions	Imbalanced exposure	Only 1/5 studies with balanced exposure	NA
	Imputed data	None	NA
	Predatory publishing	1/5 studies; not sensitive MD −1.07 mmHg, 95% CI −10.62 to 8.48; P = 0.42; I^2 = 0%; 4 studies, 110 participants	NA
Funnel plot		NA	NA
Other exclusions		All heterogeneity (I^2 = 76%; 'substantial') is introduced by 1/5 studies (Acheampong 2018); exclusion changes the effect direction.	NA

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

Blood pressure DBP		End of intervention Analysis 1.6	End of follow-up Analysis 2.6
Analysis level	Arm	MD -1.03, 95% CI -2.73 to 0.67; I^2 = 0%; 5 studies, 140 participants	No study data
	Arm + Contrast	Introduced heterogeneity and does not add new studies MD −2.38 mmHg, 95% CI −7.10 to 2.35; P = 0.32, I^2 = 93 %; 5 studies, 140 participants	NA
Subgroup analysis	Stage	No evidence of subgroup differences Unexplained heterogeneity	NA
	Duration	No evidence of subgroup differences Unexplained heterogeneity	NA
	Ambulatory	Uneven covariate distribution	NA
Sensitivity analysis exclusions	Imbalanced exposure	4/5 imbalanced exposure	NA
	Imputed data	None	NA
	Predatory publishing	1/5 studies; not sensitive MD −1.52 mmHg, 95% CI −3.84 to 0.79; P = 0.20; I^2 = 17%; 4 studies, 110 participants	NA
Funnel plot		NA	NA
Other exclusions		None	NA
Cardiorespiratory fitness		End of intervention Analysis 1.7	End of follow-up Analysis 2.7
Analysis level	Arm	MD 2.29, 95% CI 0.64 to 3.93; I^2 = 71%; 5 studies, 215 participants; Figure 11	No study data
	Arm + contrast	No change MD 2.13 ml/kg/min, 95% CI 0.50 to 3.75; P = 0.01, I^2 = 76%; 5 studies, 215 participants	NA
Subgroup analysis	Stage	Evidence of subgroup differences (Early subacute vs chronic) favouring chronic (P = 0.02; I^2 = 82.1%) Uneven covariate distribution Unexplained heterogeneity	NA
	Duration	No evidence of subgroup differences Uneven covariate distribution Unexplained heterogeneity	NA
	Ambulatory	Uneven covariate distribution	NA

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

		(4/5 ambulatory)	
Sensitivity analysis exclusions	Imbalanced exposure	4/5 studies	NA
	Imputed data	0/5 studies	NA
	Predatory publishing	0/5 studies	NA
Funnel plot		NA	NA
Other exclusions		Heterogeneity source Kang 2022 MD 1.11 ml/kg/min, 95% CI 0.56 to 1.67; P < 0.001, I^2 = 0%; 4 studies, 186 participants	NA
Strength affected lower limb		End of intervention Analysis 1.8	End of follow-up Analysis 2.8
Analysis level	Arm	SMD 0.30, 95% CI -0.05 to 0.65; I^2 = 36%; 4 studies, 217 participants	SMD 0.10, 95% CI -0.28 to 0.47; I^2 = 0%; 2 studies, 108 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies Uneven covariate distribution	NA
	Duration	Too few studies Uneven covariate distribution	NA
	Ambulatory	Too few studies Uneven covariate distribution	NA
Sensitivity analysis exclusions	Imbalanced exposure	3/4 studies	NA
	Imputed data	None	NA
	Predatory publishing	None	NA
Funnel plot		NA	NA
Other exclusions		NA	NA
Strength unaffected lower limb		End of intervention Analysis 1.9	End of follow-up Analysis 2.9
Analysis level	Arm	SMD 0.59, 95% CI -0.53 to 1.70; I^2 = 82%; 2 studies, participants not available	SMD 0.14, 95% CI -0.35 to 0.62; I^2 not applicable; 1 study, 66 participants

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	1/2 studies	1/1 studies
	Imputed data	None	NA
	Predatory publishing	None	None
Funnel plot		NA	NA
Other exclusions		NA	NA
Strength affected upper limb		End of intervention Analysis 1.10	End of follow-up Analysis 2.10
Analysis level	Arm	SMD 0.06, 95% CI -0.53 to 0.65; I^2 = 55%; 3 studies, participants not available	No study data
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	NA
	Duration	Too few studies	NA
	Ambulatory	Too few studies	NA
Sensitivity analysis exclusions	Imbalanced exposure	None	NA
	Imputed data	None	NA
	Predatory publishing	None	NA
Funnel plot		NA	NA
Other exclusions		NA	NA
Strength unaffected upper limb		End of intervention Analysis 1.11	End of follow-up Analysis 2.11
Analysis level	Arm	SMD 0.20, 95% CI -0.53 to 0.93; I^2 = 70%; 3 studies, 116 participants	No study data
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	NA

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

	Duration	Too few studies	NA
	Ambulatory	Too few studies	NA
Sensitivity analysis exclusions	Imbalanced exposure	3/3 imbalanced	NA
	Imputed data	None	NA
	Predatory publishing	None	NA
Funnel plot		NA	NA
Other exclusions		NA	NA
FUNCTIONAL AMBULATION CATEGORY		End of intervention Analysis 1.12	End of follow-up Analysis 2.12
Analysis level	Arm	MD 0.13, 95% CI 0.01 to 0.25; I^2 not applicable; 1 study, 250 participants	MD 0.11, 95% CI 0.00 to 0.22; I^2 not applicable; 1 study, 250 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	1/1 studies	1/1 studies
	Imputed data	None	NA
	Predatory publishing	None	NA
Funnel plot		NA	NA
Other exclusions		NA	NA
WALKING SPEED COMFORTABLE		End of intervention Analysis 1.13	End of follow-up Analysis 2.13
Analysis level	Arm	MD 0.09 m/sec, 95% CI 0.04 to 0.14; P < 0.001; I^2 = 59%; 12 studies, 776 participants	MD 0.03, 95% CI -0.07 to 0.13; I^2 = 69%; 7 studies, 605 participants; very low-certainty evidence; Figure 13
	Arm + contrast	MD 0.09, 95% CI 0.04 to 0.14; I^2 = 68%; 13 studies, 855 participants; very low-certainty evidence	NA

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

		MD 0.09, 95% CI 0.04 to 0.14; I^2 = 68%; 13 studies, participants not available; very low-certainty evidence; Figure 12	
Subgroup analysis	Stage	Evidence of overall subgroup differences (P < 0.001); I^2 = 83.0%) However, this is an artefact of uneven covariate distribution 2/4 groups have only 1 study. No evidence of subgroup difference between early subacute and chronic subgroups, which contain most (11/13) studies.	Uneven covariate distribution
	Duration	No evidence of subgroup differences Uneven covariate distribution Unexplained heterogeneity	No evidence of subgroup differences Unexplained heterogeneity
	Ambulatory	Uneven covariate distribution 11/13 ambulatory	Uneven covariate distribution
Sensitivity analysis exclusions	Imbalanced exposure	9/13 studies MD 0.03 m/sec, 95% CI −0.02 to 0.08; P = 0.28; I^2 = 30%; 4 studies	5/7 studies MD 0.03 m/sec, 95% CI −0.02 to 0.08; P = 0.10; I^2 = 0%; 2 studies, 128 participants
	Imputed data	1/13 studies; trivial influence MD 0.08 m/sec, 95% CI 0.04 to 0.13; P < 0.001; I^2 = 70%; 12 studies	1/7 studies MD 0.04 m/sec, 95% CI −0.06 to 0.14; P = 0.42; I^2 = 72%; 4 studies, 587 participants
	Predatory publishing	1/13 studies; trivial influence MD 0.08 m/sec, 95% CI 0.04 to 0.13; P < 0.001; I^2 = 70%; 12 studies	1/7 studies MD 0.04 m/sec, 95% CI −0.06 to 0.14; P = 0.42; I^2 = 72%; 4 studies, 587 participants
Funnel plot		Effects of missing data explored using a funnel plot (Figure 18); most of the studies are a similar size, so effects of small studies cannot be determined.	NA
Other exclusions		Much of the substantial heterogeneity is explained from the largest study of Van de Port 2012, but this has no risk of bias concerns so not excluded.	NA
WALKING SPEED MAXIMUM		End of intervention Analysis 1.14	End of follow-up Analysis 2.14

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

Analysis level	Arm	MD 0.06 m/sec, 95% CI −0.00 to 0.13; P = 0.07; I^2 = 31%; 4 studies, 307 participants	MD 0.04, 95% CI -0.10 to 0.18; I^2 = 52%; 2 studies, 167 participants
	Arm + contrast	Introduces additional study MD 0.09, 95% CI 0.02 to 0.16; I^2 = 59%; 5 studies, participants not available	NA
Subgroup analysis	Stage	No evidence of subgroup differences (early subacute vs chronic) Uneven covariate distribution Unexplained heterogeneity	Too few studies
	Duration	No evidence of subgroup differences Unexplained heterogeneity	Too few studies
	Ambulatory	Uneven covariate distribution 5/5 ambulatory	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	3/5 studies MD 0.10 m/sec, 95% CI −0.10 to 0.29; P = 0.33; I^2 = 89%; 2 studies	1/2 studies
	Imputed data	None	None
		None	None
Funnel plot		NA	NA
Other exclusions		None	None
WALKING 6-MINUTE WALKING TEST		End of intervention Analysis 1.15	End of follow-up Analysis 2.15
Analysis level	Arm	MD 30.71 m/6min, 95% CI 15.75 to 45.67; P < 0.001; I^2 = 15 %; 14 studies, 847 participants	MD 32.73, 95% CI 4.61 to 60.85; I^2 = 36%; 6 studies, 530 participants
	Arm + Contrast	Introduces additional study MD 33.99, 95% CI 21.53 to 46.45; I^2 = 33%; 15 studies, participants not available	NA
Subgroup analysis	Stage	No evidence of subgroup differences Uneven covariate distribution (14/15 studies in early subacute and chronic subgroups) Unexplained heterogeneity	Evidence of subgroup difference (early subacute vs chronic subgroups) favouring early subacute (P = 0.02; I^2 = 81.2%) Uneven covariate distribution

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

	Duration	No evidence of subgroup differences	No subgroup differences Unexplained heterogeneity
	Ambulatory	Uneven covariate distribution 15/15 ambulatory	Uneven covariate distribution 6/6 ambulatory
Sensitivity analysis exclusions	Imbalanced exposure	13/15 studies MD 40.90 metres/6 min, 95% CI −3.97 to 85.76; P = 0.07; I^2 = 85%; 2 studies	5/6 studies
	Imputed data	1/15 studies; trivial influence MD 34.31 m/6 min, 95% CI 21.63 to 46.99; P < 0.001; I^2 = 37%; 14 studies	1/6 studies; trivial influence MD 34.82 metres/6min, 95% CI 5.12 to 64.52, P = 0.02; I^2 = 45%; 5 studies, 514 participants
	Predatory publishing	2/15 studies; trivial influence MD 38.05 m/6 min, 95% CI 27.57 to 48.53; P < 0.001; I^2 = 13%; 13 studies	1/6 studies; trivial influence MD 34.82 metres/6min, 95% CI 5.12 to 64.52, P = 0.02; I^2 = 45%; 5 studies, 514 participants
Funnel plot		Funnel plot asymmetry suggests missing studies in the area favourable to the intervention suggesting factors other than non-reporting bias (Figure 19) [81].	NA
Other exclusions		None	None
BALANCE		End of intervention Analysis 1.16	End of follow-up Analysis 2.16
Analysis level	Arm	SMD 0.25, 95% CI 0.11 to 0.39; I^2 = 0%; 16 studies, 839 participants; low-certainty evidence; Figure 14	SMD 0.24, 95% CI -0.00 to 0.49; I^2 = 39%; 6 studies, 535 participants; low-certainty evidence; Figure 15
	Arm + Contrast	NA	NA
Subgroup analysis	Stage	No evidence of subgroup differences Uneven covariate distribution (15/16 studies in 2 of the 4 subgroups)	Too few studies. Uneven covariate distribution.
	Duration	No evidence of subgroup differences	No evidence of subgroup differences. Uneven covariate distribution.

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

			Unexplained heterogeneity.
	Ambulatory	Uneven covariate distribution (14/16 ambulatory; 2/16 unclear)	Uneven covariate distribution (6/6 ambulatory)
Sensitivity analysis **exclusions**	Imbalanced exposure	11/16 studies SMD 0.24, 95% CI −0.04 to 0.51, P = 0.09; I^2 = 0%; 5 studies	4/6 studies SMD 0.02, 95% CI −0.61 to 0.66, P = 0.94; I^2 = 0%; 2 studies; 128 participants
	Imputed data	1/16 studies SMD 0.26, 95% CI −0.12 to 0.40, P < 0.001; I^2 = 0%; 15 studies	1/6 studies SMD 0.28, 95% CI 0.03 to 0.52, P = 0.03; I^2 = 41%; 5 studies; 517 participants
	Predatory publishing	4/16 studies SMD 0.27, 95% CI 0.13 to 0.42, P < 0.001; I^2 = 0%; 12 studies	1/6 studies SMD 0.28, 95% CI 0.03 to 0.52, P = 0.03; I^2 = 41%; 5 studies; 517 participants
Funnel plot		Funnel plot asymmetry suggests missing studies in the area favourable to the intervention suggesting factors other than non-reporting bias (Figure 20) [81].	NA
Other exclusions		In 13/16 studies, the Berg Balance Scale was recorded. Calculating MD of these gave a similar effect: MD 1.65, 95% CI 0.43 to 2.87, P = 0.008; I^2 = 0%; 13 studies, 495 participants	NA
TIMED UP AND GO		End of intervention Analysis 1.17	End of follow-up Analysis 2.17
Analysis level	Arm	MD −2.01 sec, 95% CI −3.59 to −0.42, P = 0.01; I^2 = 43%; 10 studies, 693 participants	MD -1.43, 95% CI -3.77 to 0.92; I^2 = 48%; 5 studies, 518 participants
	Arm + Contrast	Adds no new studies but less heterogeneity MD -1.94, 95% CI -2.82 to -1.07; I^2 = 30%; 10 studies, participants not available	NA
Subgroup analysis	Stage	No evidence of subgroup differences Uneven covariate distribution Unexplained heterogeneity	Uneven covariate distribution
	Duration	No evidence of subgroup differences Unexplained heterogeneity	Uneven covariate distribution
	Ambulatory	Uneven covariate distribution (10/10 ambulatory)	Uneven covariate distribution

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Table 5. Synthesis with meta-analysis - critical outcomes *(Continued)*

			(5/5 ambulatory)
Sensitivity analysis **exclusions**	Imbalanced exposure	7/10 studies MD −0.97 sec, 95% CI −1.90 to −0.04; I^2 = 0%). Heavily influenced by a single study (Mead 2007; weight 94.7%)	3/5 MD −0.30 sec, 95% CI −1.14 to 0.55, P = 0.49; I^2 = 0%; 2 studies, 128 participants
	Imputed data	None	None
	Predatory publishing	1/10 studies; analysis is sensitive MD −1.79 sec, 95% CI -3.67 to 0.09; P = 0.06; I^2 = 42%; 9 studies, 663 participants	None
Funnel plot		No funnel plot asymmetry detected (Figure 21).	NA
Other exclusions		All the heterogeneity could be explained by a single study (Kim 2017a; weight 0.7%), which reported change data. Excluding this study increased precision (MD −1.73 sec, 95% CI −2.18 to −1.29; P < 0.001; I^2 = 0%; 9 studies, 664 participants).	None

CI: confidence interval; **M:** metre(s); **MD:** mean difference**; NA:** not applicable; **P:** probability; **RD:** risk difference; **sec:** second(s); **SBP:** systolic blood pressure; **SMD:** standardised mean difference; **vs:** versus

Table 6. Synthesis with meta-analysis - important outcomes

HEALTH STATUS, OVERALL		End of intervention (Analysis 1.18)	End of follow-up (Analysis 2.18)
Analysis level	Arm	SMD 0.67, 95% CI 0.17 to 1.17; I^2 = 68%; 5 studies, 267 participants	SMD 0.15, 95% CI -0.11 to 0.41; I^2 = 3%; 5 studies, 245 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies No evidence of subgroup differences Unexplained heterogeneity	Evidence of subgroup differences Early subacute vs chronic (P = 0.05; I^2 = 72.9%)
	Duration	Too few studies No evidence of subgroup differences Unexplained heterogeneity	No evidence of subgroup differences
	Ambulatory	Too few studies Uneven covariate distribution Unexplained heterogeneity	Uneven covariate distribution (4/5 ambulatory)
Sensitivity analysis exclusions	Imbalanced exposure	5/5 studies	5/5 studies
	Imputed data	1/5 studies; not sensitive	1/5 studies; not sensitive

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Table 6. Synthesis with meta-analysis - important outcomes *(Continued)*

	Predatory publishing	1/5 studies; not sensitive	1/5 studies; not sensitive
Funnel plot		NA	NA
Other exclusions		None	None
HEALTH STATUS, PHYSICAL HEALTH		End of intervention (Analysis 1.19)	End of follow-up (Analysis 2.19)
Analysis level	Arm	SMD 0.15, 95% CI -0.73 to 1.02; I^2 = 70%; 2 studies, 114 participants	SMD 0.10, 95% CI -0.24 to 0.44; I^2 = 0%; 3 studies, 135 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	3/2 studies	3/3 studies
	Imputed data	0/2 studies	0/3 studies
	Predatory publishing	1/2 studies	1/3 studies
Funnel plot		NA	NA
Other exclusions		None	None
HEALTH STATUS, MENTAL HEALTH		End of intervention (Analysis 1.20)	End of follow-up (Analysis 2.20)
Analysis level	Arm	SMD 0.38, 95% CI -0.03 to 0.79; I^2 not applicable; 1 study, 93 participants	SMD 0.25, 95% CI -0.11 to 0.62; I^2 = 0%; 2 studies, 118 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	1/1 studies	2/2 studies
	Imputed data	0/1 studies	0/1 studies
	Predatory publishing	0/1 studies	0/2 studies
Funnel plot		NA	NA
Other exclusions		None	None

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Table 6. Synthesis with meta-analysis - important outcomes *(Continued)*

HEALTH STATUS, SOCIAL HEALTH		End of intervention (Analysis 1.21)	End of follow-up (Analysis 2.21)
Analysis level	Arm	SMD 0.31, 95% CI -0.09 to 0.71; I^2 = 4%; 2 studies, 111 participants	SMD 0.22, 95% CI -0.18 to 0.62; I^2 = 0%; 2 studies, 97 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	2/2 studies	2/2 studies
	Imputed data	1/2 studies	1/2 studies
	Predatory publishing	1/2 studies	1/2 studies
Funnel plot		NA	NA
Other exclusions		None	None
ANXIETY		End of intervention (Analysis 1.22)	End of follow-up (Analysis 2.22)
Analysis level	Arm	SMD -0.07, 95% CI -0.29 to 0.15; I^2 = 0%; 2 studies, 316 participants	SMD -0.02, 95% CI -0.24 to 0.20; I^2 = 0%; 2 studies, 316 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	1/2	1/2
	Imputed data	0/2	0/2
	Predatory publishing	0/2	0/2
Funnel plot		NA	NA
Other exclusions		None	None
DEPRESSION		End of intervention (Analysis 1.23)	End of follow-up (Analysis 2.23)
Analysis level	Arm	SMD -0.15, 95% CI -0.54 to 0.24; I^2 = 74%; 4 studies, 481 participants	SMD 0.06, 95% CI -0.16 to 0.28; I^2 = 0%; 2 studies, 316 participants
	Arm + contrast	NA	NA

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Table 6. Synthesis with meta-analysis - important outcomes *(Continued)*

Subgroup analysis	Stage	Too few studies	Too few studies
	Duration	Too few studies	Too few studies
	Ambulatory	Too few studies	Too few studies
Sensitivity analysis exclusions	Imbalanced exposure	3/4	3/4
	Imputed data	0/4	0/4
	Predatory publishing	0/4	0/4
Funnel plot		NA	NA
Other exclusions		None	None
COGNITIVE FUNCTION		End of intervention (Analysis 1.24)	End of follow-up (Analysis 2.24)
Analysis Level	Arm	SMD -0.01, 95% CI -0.24 to 0.22; I^2 = 0%; 5 studies, 294 participants	SMD 0.16, 95% CI -0.11 to 0.43; I^2 = 0%; 4 studies, 221 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	No evidence of subgroup differences (early subacute vs chronic) Uneven covariate distribution	No evidence of subgroup differences (early subacute vs chronic) Uneven covariate distribution
	Duration	No evidence of subgroup differences	Too few studies No evidence of subgroup differences
	Ambulatory	Uneven covariate distribution (5/5 ambulatory)	Uneven covariate distribution (4/4 ambulatory)
Sensitivity analysis exclusions	Imbalanced exposure	3/5 studies; trivial influence	3/4 studies
	Imputed data	1/5 studies; trivial influence	1/4 studies; trivial influence
	Predatory publishing	1/5 studies; trivial influence	1/4 studies; trivial influence
Funnel plot		NA	NA
Other exclusions		None	None
FATIGUE SEVERITY, OVERALL		End of intervention (Analysis 1.25)	End of follow-up (Analysis 2.25)
Analysis level	Arm	SMD -0.01, 95% CI -0.21 to 0.19; I^2 = 0%; 5 studies, 387 participants	SMD -0.07, 95% CI -0.27 to 0.14; I^2 = 0%; 4 studies, 365 participants
	Arm + contrast	NA	NA

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Table 6. Synthesis with meta-analysis - important outcomes *(Continued)*

Subgroup analysis	Stage	Uneven covariate distribution	Too few studies Uneven covariate distribution
	Duration	No evidence of subgroup differences Uneven covariate distribution	Too few studies Uneven covariate distribution
	Ambulatory	Uneven covariate distribution (5/5 ambulatory)	Too few studies Uneven covariate distribution (5/5 ambulatory)
Sensitivity analysis exclusions	Imbalanced exposure	4/5 studies	3/4 studies; not sensitive
	Imputed data	1/5 studies; not sensitive	1/4 studies; not sensitive
	Predatory publishing	1/5 studies; not sensitive	1/4 studies; not sensitive
Funnel plot		NA	NA
Other exclusions		None	None
FATIGUE SEVERITY, PHYSICAL		End of intervention (Analysis 1.26)	End of follow-up (Analysis 2.26)
Analysis level	Arm	Not estimable; 0 studies, 0 participants	Not estimable; 0 studies, 0 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	NA	NA
	Duration	NA	NA
	Ambulatory	NA	NA
Sensitivity analysis exclusions	Imbalanced exposure	NA	NA
	Imputed data	NA	NA
	Predatory publishing	NA	NA
Funnel plot		NA	NA
Other exclusions		NA	NA
FATIGUE SEVERITY, MENTAL		End of intervention (Analysis 1.27)	End of follow-up (Analysis 2.27)
Analysis Level	Arm	Not estimable; 0 studies, 0 participants	Not estimable; 0 studies, 0 participants
	Arm + contrast	NA	NA
Subgroup analysis	Stage	NA	NA

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Table 6. Synthesis with meta-analysis - important outcomes *(Continued)*

	Duration	NA	NA
	Ambulatory	NA	NA
Sensitivity analysis exclusions	Imbalanced exposure	NA	NA
	Imputed data	NA	NA
	Predatory publishing	NA	NA
Funnel plot		NA	NA
Other exclusions		NA	NA

CI: confidence interval; **MD:** mean difference**; NA:** not applicable; **P:** probability; **RD:** risk difference; **SMD:** standardised mean difference; **vs:** versus

Table 7. Multiple outcome measures within one domain - review author decisions

Study	Outcome domain	Outcomes reported	Outcome analysed	Rationale
Aravind 2022	Disability	NEADL BI	NEADL	Avoids the ceiling effect of BI
	Physical function	BBS; ABC scale	BBS	ABC measure of confidence not balance
	Health status & quality of life	Euroqol-5D-5L (EQ-5D-5L) Visual analogue scale (EQ-VAS)	Euroqol-5D-5L	Five domains rather than one in the VAS
	Cognitive function	Trail making test A Trail making test B	Trail making test B	Part B is more complex and sensitive to change and predictive of functional outcomes.
Cooke 2010	Physical fitness	Knee extension strength Knee flexion strength	Knee extension strength	Knee extension more functionally relevant
	Health status & quality of life	Euroqol health state Euroqol thermometer	Euroqol health state	Five domains rather than one in what is presumed to be the VAS
Dean 2018	Disability	RMI Modified Patient-Specific Functional Scale	RMI	Patient-Specific Functional Scale lacks standardised outcome domains
	Health status & quality of life	Stroke-Specific QoL scale	Stroke-Specific QoL scale	Stroke -specific tool

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Table 7. Multiple outcome measures within one domain - review author decisions *(Continued)*

		EQ-5D-5L, EQ5 (QoL)		
Duncan 1998	Disability	BI Lawton ADL	BI	BI based on more items than Lawton, more relevant to global disability
Duncan 2003	Disability	BI Lawton ADL	BI	BI based on more items than Lawton, more relevant to global disability
	Physical fitness	Ankle strength Knee strength	Knee strength	Knee extension more functionally relevant
	Physical function	BBS Functional reach	BBS	Greater range of domains relevant to overall balance
	Health status & quality of life	SF-36 SIS	SIS	Stroke-specific tool
Kang 2022	Physical fitness	Leg extension strength Leg flexion strength	Leg extension	Knee extension more functionally relevant
Galvin 2011	Disability	BI NEADL	BI	NEADL avoids the ceiling effect of BI, but is only available at follow-up, not at the end of intervention. BI was adopted for both time points.
Kim 2017a	Cognitive function	MOCA (Korean version) Trail making test A Trail making test B Stroop test	Trail making test B	MOCA low sensitivity Part B is more complex and sensitive to change and predictive of functional outcomes.
Klassen 2020	Cognitive function	MOCA Trail making test A Trail making test B Digit Symbol Substitution Test	Trail making test B	MOCA low sensitivity Part B is more complex and sensitive to change and predictive of functional outcomes.
Letombe 2010	Disability	BI Katz ADL	BI	BI based on more items than Katz, more relevant to global disability
Liu-Ambrose 2022	Cognitive function	ADAS-Cog-Plus Stroop task	ADAS-Cog-Plus	ADAS-Cog-Plus is more relevant to global cognitive function.
Mead 2007	Disability	FIM NEADL RMI	FIM	FIM covers a greater range of domains relevant to global disability.

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Table 7. Multiple outcome measures within one domain - review author decisions *(Continued)*

Richards 1993	Balance	BBS Fugl-Meyer balance	BBS	Fugl-Meyer balance domains have been criticised as being less well suited and with better tools available.
Van de Port 2012	Disability	RMI NEADL	RMI	NEADL summary score not available

ABC: Activities-Specific Balance Confidence Scale; **ADL:** activities of daily living; **ADAS-Cog-Plus:** Alzheimer's Disease Assessment Scale-Cognitive-Plus; **BBS:** Berg Balance Scale; **BI:** Barthel Index; **D:** dimension; **EQ:** Euroqol; **FIM:** Functional Independence Measure; **L:** level; **MOCA:** Montreal Cognitive Assessment; **NEADL:** Nottingham Extended Activities of Daily Living; **QoL:** quality of life; **RMI**: Rivermead Mobility Index; **SF-36:** Short Form 36 Health Survey; **SIS:** Stroke Impact Scale

Table 8. Other systematic reviews

Systematic review	Studies included in this review	Findings
Lee 2020 [165]	2/18	Indicates improvement in cardiorespiratory fitness, muscle strength, and walking
Pogrednoy 2020 [166]	4/8	Indicates that AHA-compliant interventions [4] improve 6-MWT and TUG
Song 2023 [167]	6/9	Indicates benefit to quality of life but not anxiety or depression

AHA: American Heart Association; **6-MWT:** six-minute walk test; **TUG: t**imed up and go

INDEX TERMS

Medical Subject Headings (MeSH)

Bias; *Cardiorespiratory Fitness; Muscle Strength; Quality of Life; Randomized Controlled Trials as Topic; *Resistance Training [methods]; *Stroke [mortality]; *Stroke Rehabilitation [methods]; Walking

MeSH check words

Aged; Humans; Male; Middle Aged

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