Prescribing strength training for stroke recovery: a systematic review and meta-analysis of randomized controlled trials

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Data sharing statement: All data relevant to the study are included in the article or uploaded as supplementary information. All individual study data included in this review is available directly from the original manuscripts. Any other data used for this review are available upon reasonable request.

SUMMARY BOX

What is already known?

- Exercise-based rehabilitation is fundamental to stroke recovery, and has been shown to improve cardiovascular health, mobility, and health-related quality of life.
- Although strength training (ST) is recommended in clinical practice guidelines, there is limited available guidance on how to prescribe ST in people with stroke.
- ST has previously been shown to improve muscle strength, but it is less clear whether ST can improve other aspects of stroke recovery.

What are the new findings?

- This systematic review found that ST improves lower-body strength, walking capacity, balance, ADL/IADL disability, functional ability and mobility, habitual and fast-paced walking speeds in people with stroke.
- ST interventions that were more frequent (greater days per week), used high movement speeds (power-focused training), included more total ST sessions, and trained single muscle groups were superior to high intensity and functional ST for impacting stroke recovery outcomes.

ABSTRACT

Objective: To examine the effects of strength training on patient-important outcomes of stroke recovery and to quantify the influence of the exercise prescription on treatment effects.

Design: Systematic review and meta-analysis

Data Sources: Eight electronic databases (MEDLINE, EMBASE, EMCARE, AMED, PsychINFO, CINAHL, SPORTDiscus, and Web of Science) and 2 clinical trial registries (ClinicalTrials.gov, WHO International Clinical Trials Registry Platform) were searched from inception to 19 June 2024.

Eligibility criteria: Randomized controlled trials were eligible if they examined the effects of strength training compared to no exercise or usual care and reported at least one exercise prescription parameter. An advisory group of community members with lived experience of stroke helped inform outcomes most relevant to stroke recovery.

Results: Forty-two randomized trials (N=2,204) were included. Overall risk of bias was high across most outcomes. Strength training improved outcomes rated as 'critical for decision-making' by the advisory group, including: walking capacity (standardized mean difference [SMD]=1.07, [95% confidence interval: 0.47-1.66]), balance (SMD=1.32 [0.67-1.97]), functional ability and mobility (SMD=0.72 [0.15-1.29]), and habitual (mean difference [MD]=0.05 m/s [0.02-0.09]) and fast-paced walking speed (MD=0.09 m/s [0.01-0.17]), with very low to moderate certainty of evidence, mainly due to risk of bias and inconsistency. More frequent strength training, traditional strength training programs, and power-focused intensities (i.e., emphasis on movement velocity) were positively associated with walking capacity, health-related quality of life, and fast-paced walking speed.

Conclusion: Strength training alone or combined with usual care, improves stroke recovery outcomes that are important for decision making. More frequent strength training, power-focused intensities, and traditional program designs may best support stroke recovery.

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INTRODUCTION

Stroke is the third leading cause of death and disability in the world and occurs in over 12 million people each year.[1] The effects of stroke can be broad, but reductions in physical function such as weakness, motor coordination, and balance are common.[2-4] These effects can contribute to lower activity participation and subsequently an increased risk of stroke, termed the 'cycle of detraining post-stroke'.[5] Nearly a quarter of survivors will experience a recurrent stroke within 5 years of their index event,[6] making tertiary prevention strategies of utmost importance.

Exercise can improve physical function,[7] which may reduce the risk of recurrent stroke[5] and all-cause mortality,[8] and clinical practice guidelines have been developed to help clinicians prescribe exercise for their patients.[9 10] Studies focusing on aerobic exercise, such as cycling or walking, currently dominates the evidence on physical fitness training interventions for stroke recovery,[11] outnumbering the number of strength training (ST) trials twofold.[12] This has led to highly specific recommendations for aerobic exercise training in stroke,[9 10] while guidelines for ST are based on evidence extrapolated from other conditions, such as myocardial infarction.[9]

The lack of stroke-specific guidance is likely in part due to the ongoing uncertainty about the evidence on ST. Earlier reviews suggest that ST can improve strength but not necessarily other aspects of stroke recovery that may be clinically important from the perspectives of stroke survivors.[13-15] This is surprising, considering the known benefits of ST on mobility and neuroplasticity in older adults[16] and other neurological populations,[17] as well as the established associations between muscle strength and physical function after stroke.[18 19] However, it has been suggested that impairments such as motor coordination may confound the potential effectiveness of ST programs for stroke recovery.[13] Previous reviews also used strict eligibility restrictions based on the type,[14 20] intensity, and progression of the exercise programs.[13] Some reviews had analytical challenges for certain of the measured outcomes[7] or restricted analyses to select outcome measures.[13 20] Moreover, none considered the potential impact of population characteristics (e.g., time post-stroke) or program parameters (e.g., frequency, duration, intensity) on treatment effects to inform ST prescription for clinicians.

There is a critical gap in the evidence on ST after stroke needed to inform the next set of guidelines on exercise prescription parameters for this population. The objectives of this systematic review were to examine: (1) the effects of ST on patient-important stroke recovery outcomes informed by an advisory group of community members with lived experience; and (2) the association between ST prescription parameters (frequency, intensity, type, and duration) and stroke recovery.

METHODS

This systematic review was registered (PROSPERO CRD42023414077), and the protocol has been published.[21] There were no major deviations from the trial protocol, other than to the data extraction sheet and methods for handling multiple effects for a single outcome. These modifications are reported in the following sections. Reporting of the results and community partner involvement followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines.[22] Patient and public involvement was incorporated using the Authors and Consumers Together Impacting on eVidencE (ACTIVE) Framework.[23] We engaged a community advisory group of members with lived experience who were involved in planning the review methods (e.g., defining stroke recovery), selecting evidence (e.g., selecting clinically important outcomes), analysis (e.g., selecting data extraction items), interpretation of results, reviewing the manuscript, and knowledge translation activities.

Eligibility criteria

The full eligibility criteria are detailed elsewhere.[21] Briefly, eligible studies were randomized controlled trials examining ST compared to no exercise or usual care in people with stroke. We used the American College of Sports Medicine (ACSM) definition of ST to guide our eligibility criteria: “a form of exercise designed to improve muscular fitness by exercising a muscle or muscle group against external resistance.” Studies were excluded if they applied ST and a co-intervention, did not report ≥1 exercise prescription parameter (frequency, intensity, type, duration of intervention and/or sessions), were not in English, or if they compared ST to “conventional therapy” or “usual care” when participants were in the chronic phase of recovery (i.e., >6 months post-stroke) to account for contextually varying definitions of conventional or usual care.[24]

Information sources and search strategy

Eight electronic databases (MEDLINE, EMBASE, EMCARE, AMED, PsychINFO, CINAHL, SPORTDiscus, and Web of Science) and 2 clinical trial registries (ClinicalTrials.gov, and WHO International Clinical Trials Registry Platform) were searched from inception to June 19, 2024. Additional hand-searches were performed using included study reference lists and the Google Scholar ‘cited by’ function. An example of the search strategy is included in the review protocol,[21] as well as in the Appendix (Supplemental Appendix 1).

Study selection

Authors screened titles, abstracts, and full-text articles in duplicate (KSN and one of KM, EW, AM, or EH). Each screener pilot tested the selection process against the eligibility criteria with 100 titles and abstracts (25 per pair) and 20 full-text articles (5 per pair) using online systematic review management software (Covidence, Veritas Health Innovation Ltd, Melbourne, Victoria, Australia). Disagreements were resolved by consensus discussion.

Data items and extraction

Data from the included studies were extracted using a piloted template created on the online systematic review management software (Covidence, Veritas Health Innovation Ltd, Melbourne, Victoria, Australia). Two independent pairs of authors (KSN and one of: KM, EH, or EW) extracted the study information after piloting the extraction process with 10 articles (5 per pair). The extracted items are reported in the study protocol.[21] In brief, the items included publication information (e.g., trial registration, location, funding), participant demographic characteristics (e.g., sample size, age, time post-stroke), ST program details (e.g., frequency, type of exercise), and outcome measure data (e.g., type of outcome, means and standard deviations). The community advisory group provided feedback on the extracted study items. If data were only shown in figures, *WebPlotDigitizer* (Ankit Rohatgi, Version 4.6, Pacifica, USA) was used to capture the data. Interventions were also described as low, moderate, high, or power-focused intensities, and either functional or traditional ST, using contemporary definitions (Supplemental Appendix 2, and published elsewhere[21]). Briefly, power-focused intensities had no restrictions on external load, but movements were performed at high velocities. Traditional ST involved exercises with a goal to increase muscle strength, designed in blocks of sets and repetitions for a single muscle group per exercise. Functional ST were movements that simulate everyday activities over multiple planes of movement to develop multiple muscle groups.

The lead author, corresponding author, and community advisory group consulted to create a unified definition of stroke recovery: “Regaining function and adapting to one’s current capabilities, with a goal to participate in activities that are personally meaningful.” Then, the review team (n=6 people with stroke, n=2 researchers, n=3 clinician-researchers) evaluated the list of outcome measures extracted from each study that represented the new definition of stroke recovery and rated them using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) importance scale. This scale ranges from 1 (of least importance) to 9 (of most importance), and the scores were interpreted as: *of limited importance* (median score: 1 to 3), *important but not critical* (median score: 4 to 6), or *critical* (median score: 7 to 9).[25] Outcomes with a median score ≥4 were included in the review. Once the outcomes were approved, the results from individual studies were extracted by the same authors in duplicate.

Risk of bias and certainty assessment

Risk of bias assessments were performed for each study outcome using the Cochrane Collaboration risk of bias (RoB-2) tool by 2 independent authors (KSN, EW); disagreement was resolved by consensus discussion. The RoB-2 tool assesses trial biases in the randomization process, deviations from intended intervention, missing outcome data, measurement of the outcome, selection of the reported result. The GRADE approach was used to evaluate the certainty of evidence for all main and significant subgroup effects. The lead author, corresponding author, two clinician-researchers (KM, AM), a stroke researcher (EW), and the community advisory group provided their importance ranking again on the GRADE scale.[25] The results are also summarized using the GRADE summary of findings (SoF) tables.[26]

Statistical analysis

To examine the effectiveness of ST interventions on stroke recovery, we conducted random-effects meta-analyses comparing ST to no exercise or usual care. Pooled effect estimates were constructed with standardized mean differences (SMD) using Glass's delta (Δ), and mean differences (MD) were used for walking speed outcomes (meters per second, m/s). Missing data was handled according to our published protocol.[21] SMDs were considered small, moderate, or large if they were 0.00 to 0.49, 0.50 to 0.79, and ≥0.80, respectively.[27]

Multiple measures of the same outcome were observed within the same study (e.g., knee flexion and extension for lower-body strength), for which correlated-effects robust variance estimation (RVE) meta-analyses were applied to use all possible effect sizes and account for the dependence between effect estimates within a study.[28 29] The specified RVE models followed a correlated effects model, where a common within-study correlation was set to 0.8 by default.[28-30] Details about the model are shown in Equation 3 in Pustejovsky & Tipton (2022).[30] For all main effects, heterogeneity was explored across 3 covariates using univariable meta-regression analyses: time post-stroke (2 levels: sub-acute and chronic stroke), age (continuous variable), and sex/gender identity (3 levels, tertiles of low, moderate, and high proportion of women). The results were reported in-text, disaggregated into outcomes rated as "important, but not critical" and "critical for decision-making" based on the GRADE importance scale.

To determine the influence of ST parameters (frequency, intensity, type, and duration) on stroke recovery, univariable meta-regression analyses were used across 5 main variables: frequency, intensity, type, duration (length of sessions [minutes] and program [weeks]), and total number of sessions in the ST program. The response variables were the effect sizes (i.e., SMD or MD) and the explanatory variables were the prescription variables (e.g., frequency). Details regarding covariate selection (e.g., number of levels) were defined a priori.[21] Where studies had overlapping intensities, they were classified in the highest category (e.g., 60-90% 1-RM is high intensity). Where the explanatory variable was continuous (e.g., age, frequency, total number of sessions), we examined the linearity of the relationships by visual inspection of the bubble plots and including polynomial terms in the meta-regression models when the number of studies ≥10.

Visual examination of funnel plots and regression-based Eggar tests were used to examine the risk of publication biases for each outcome. Sensitivity analyses were conducted, removing studies with high risk of bias or small-study effects with high influence on funnel plots. Analyses were conducted using Stata SE (Version 17.0, StataCorp LLC, College Station, TX, USA), Microsoft Excel (Microsoft Corporation, Albuquerque, NM, USA), and R (The R Foundation for Statistical Computing, Vienna, Austria) using the *robumeta* and *clubSandwich* packages.

Equity, diversity, and inclusion

The review team consisted of fifteen people with diverse backgrounds in research and lived experience. The team included clinicians, people with lived experience, researchers, and trainees, as well as people who share multiple identities (e.g., clinician and researcher, person with lived experience and researcher). Seven women and eight men with varying ethnicities contributed to this work. In our review eligibility criteria, there was no restriction on sex, gender identity, race, ethnicity, or socioeconomic factors.

Patient and public involvement

We recruited a community advisory group to inform on several aspects related to this review. They have been detailed in the methods section, as well as in the published protocol.[21]

RESULTS

Study selection

The study flow diagram is in Figure 1. Forty-nine records met the eligibility criteria, of which 42 unique randomized controlled trials ($N_{randomized}$=2,204) examined the effects of ST compared to no exercise or usual care on stroke recovery.

Study characteristics

Trial characteristics and outcomes are presented in Table 1. The number of randomized participants ranged from 12[31] to 156.[32] Seventeen trials (40%, n=982) were in early subacute stroke (1 week to 3 months), 6 trials (14%, n=386) in late subacute stroke (3-6 months) and 19 (45%, n=836) in chronic stroke (>6 months). Mean age ranged from 49 to 78 years, and the median proportion of women was 39%. The tertiles for sex/gender identity were low (0-35% women), moderate (36-42% women), and high proportion of women (43-61% women). The severity of stroke or functional status was reported or could be inferred in 31 trials. Twenty-one trials (50%) compared ST to no exercise, while the remaining 21 trials compared ST to usual care physiotherapy (15 trials, 36%), education (2 trials, 5%), or a benign attention-control (3 trials, 7%), all of which limited the amount of ST exercises. Additional information is provided in Supplemental Appendix 3.

Table 1. Trial characteristics.

Variables	
Number of participants, *n (min-max)*	
Strength training group(s)	1,132 (6-76)
Control or usual care group	1,072 (6-85)
Age, *median (min-max)*	60.9 (49.5-78.4)
Geographical region, *n (%)*	
Africa	1 (2.4%)
Australia and New Zealand	6 (14.3%)
East/South/Southeast/West Asia	15 (35.7%)
Europe	11 (26.2%)
North America	8 (19.0%)
South America	1 (2.4%)
Sex/gender identity, *median (min-max)*	39% (0-61%)
Phase of stroke recovery, *trials (%)*	
Early subacute (1 wk – 3 mo)	17 (40.4%)
Late subacute (3 – 6 mo)	6 (14.3%)
Chronic (≥ 6 mo)	19 (45.2%)
Outcomes measured, *trials (%)*	
Lower-body strength	22 (52.3%)
Habitual walking speed	21 (50.0%)
Functional ability and mobility	20 (47.6%)
Balance	19 (45.2%)
Walking capacity	16 (38.1%)
Functional strength and power	13 (31.0%)
ADL/IADL disability	10 (23.8%)
Fast walking speed	10 (23.8%)
Health-related quality of life	10 (23.8%)
Upper-body strength	7 (16.7%)
Spasticity	6 (14.3%)
Quality of gait	5 (11.9%)
Falls efficacy	4 (9.5%)
Psychological wellbeing	4 (9.5%)
Physical activity	4 (9.5%)
Upper-extremity function	4 (9.5%)
Muscle power	3 (7.1%)
Aerobic fitness	3 (7.1%)
Muscle endurance	2 (4.8%)
Cardiometabolic health indicators	2 (4.8%)
Muscle mass/volume	1 (2.4%)

ADL = Activities of daily living, IADL=Instrumental activities of daily living, n=Number of participants, wk=Week, mo=Months

Intervention characteristics

The median frequency, duration and length of interventions were: 3 times per week (min-max: once every other week to 5 days/week), 50 minutes (min-max: 30-90 minutes), and 6 weeks (min-max: 1-52 weeks), respectively. A summary of the exercise prescriptions is in Supplemental Appendix 4. Intensity of ST was most often prescribed using percent repetition maximum or repetition ranges (e.g., 5 repetition maximum) (20 trials, 56%).[33-57] Other trials used self-report (e.g., rating of perceived exertion) (4 trials, 10%),[33-35 58-61] described as 'maximal effort' (3 trials, 9%),[62-64] maximal heart rate (1 trial, 2%),[65] or did not specify a method (2 trials, 6%).[32 64] Thirteen trials (31%)[31 50 66-76] did not report intensity. Of those that reported any intensities, most (19 trials, 70%)[37-40 42 43 45-53 56 59 60 62-64 77] used high intensities, while others used low to moderate (3 trials, 7%),[41 54 55 61] moderate (5 trials, 12%),[32-36 58 65] moderate to high (1 trial, 2%),[57] or power-focused intensities (2 trials, 5%).[78 79] Twenty-three trials (55%) used traditional ST, while 19 trials (45%) used functional ST. Most trials (32 trials, 76%) focused on lower-limb ST, while the remaining focused on upper-limb (4 trials, 10%) or full-body exercises (6 trials, 14%).

Risk of bias and publication bias

The risk of bias summary diagram is displayed in Figure 2, showing the risk of bias distribution for each outcome. The overall risk of bias was high across all outcomes, mainly from deviations from the intervention. Many studies used a per-protocol analysis that excluded trial participants with missing data and/or did not publish a trial protocol. Most outcomes had a low risk of bias for the randomization process, missing data, and the outcome measure. Traffic light plots displaying risk of bias for each individual study, by outcome, is shown in the Supplemental Appendix 5. Among outcomes with more than 10 studies meta-analyzed, publication bias was suspected due to either funnel plot asymmetry and/or regression-based Egger test for: lower-body strength, functional ability and mobility, balance, walking capacity, functional strength, and ADL/IADL disability (Supplemental Appendix 6).

Synthesis of results

The effects of the ST interventions on stroke recovery are summarized in Figure 3, in the summary of evidence table (Table 2), and are organized in order of importance from the GRADE importance scale. There was very low to moderate certainty of evidence across the outcomes.

Table 2. GRADE Certainty of Evidence Table.

Effect size (95% CI)	**N** (N studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Certainty of evidence**	**Importance**
Walking capacity (median [IQR] follow-up duration: 6.0 [6.0] weeks)								
SMD=0.95 (0.34 to 1.56)	**N=1,086** (16 studies)	Serious[b]	Serious[c]	Not serious	Not serious	None	⊕⊕◯◯ Low	Critical (9) [IQR=3, Q1-Q3: 6-9]
Habitual walking speed (median [IQR] follow-up duration: 6.0 [4.5] weeks)								
MD=0.05 m/s (0.02 to 0.09 m/s)	**N=1,109** (21 studies)	Serious[b]	Not serious	Serious[e]	Not serious	None	⊕⊕◯◯ Low	Critical (8) [IQR=1, Q1-Q3: 7-8]
Subacute phase **MD=0.09 m/s** (0.04 to 0.15 m/s)	**N=532** (9 studies)	Serious[b]	Not serious	Not serious	Not serious	None	⊕⊕⊕◯ Moderate	Critical (8) [IQR=1, Q1-Q3: 7-8]
Chronic phase **MD=0.02 m/s** (-0.02 to 0.07 m/s)	**N=577** (12 studies)	Serious[b]	Serious[c]	Not serious	Not serious	None	⊕◯◯◯ Very low	Critical (8) [IQR=1, Q1-Q3: 7-8]
Balance (median [IQR] follow-up duration: 6.0 [4.5] weeks)								
SMD=1.13 (0.51 to 1.75)	**N=1,162** (19 studies)	Serious[b]	Serious[c]	Not serious	Not serious	None	⊕⊕◯◯ Low	Critical (8) [IQR=1.5, Q1-Q3: 7.5-9]
Functional ability and mobility (median [IQR] follow-up duration: 6.0 [4.0] weeks)								
SMD=0.61 (0.09 to 1.14)	**N=1,246** (20 studies)	Serious[b]	Not serious	Serious[f]	Not serious	Publication bias[j]	⊕◯◯◯ Very low	Critical (8) [IQR=2, Q1-Q3: 7-9]
Health-related quality of life (median [IQR] follow-up duration: 6.0 [6.0] weeks)								
SMD=0.11 (-0.22 to 0.44)	**N=572** (10 studies)	Serious[b]	Not serious	Not serious	Serious[h]	None	⊕◯◯◯ Very low	Critical (8) [IQR=2.5, Q1-Q3: 6-8.5]
Functional strength and power (median [IQR] follow-up duration: 6.0 [6.0] weeks)								
SMD=0.48 (-0.20 to 1.16)	**N=775** (13 studies)	Serious[b]	Very serious[d]	Not serious	Serious[h]	None	⊕◯◯◯ Very low	Critical (7) [IQR=1.5, Q1-Q3: 6-7.5]
Fast walking speed (median [IQR] follow-up duration: 6.0 [4.5] weeks)								
MD=0.09 m/s (0.01 to 0.17 m/s)	**N=476** (10 studies)	Very serious[a]	Very serious[d]	Not serious	Serious[i]	None	⊕◯◯◯ Very low	Critical (7) [IQR=4.5, Q1-Q3: 4.5-9]
Falls efficacy (median [IQR] follow-up duration: 6.0 [4.0] weeks)								
SMD=4.55 (-14.2 to 23.3)	**N=315** (4 studies)	Serious[b]	Very serious[d]	Not serious	Very serious[g]	None	⊕◯◯◯ Very low	Critical (7) [IQR=3, Q1-Q3: 4-7]
Physical activity (median [IQR] follow-up duration: 6.0 [6.0] weeks)								

SMD=0.43 (-0.17 to 1.02)	**N=432** (4 studies)	Serious[b]	Serious[c]	Serious[f]	Serious[h]	None	⊕○○○ Very low	Critical (7) [IQR=1.5, Q1-Q3: 5.5-7]
Psychological wellbeing (median [IQR] follow-up duration: 6.0 [6.0] weeks)								
SMD=0.21 (-0.47 to 0.89)	**N=175** (4 studies)	Serious[b]	Not serious	Not serious	Serious[h]	None	⊕⊕○○ Low	Critical (7) [IQR=2, Q1-Q3: 5.5-7.5]
Lower-body strength (median [IQR] follow-up duration: 6.0 [5.5] weeks)								
SMD=1.25 (0.64 to 1.85)	**N=1,170** (22 studies)	Serious[b]	Serious[c]	Serious[e]	Not serious	None	⊕○○○ Very low	Important (6) [IQR=2, Q1-Q3: 6.5-8.5]
Upper-body strength (median [IQR] follow-up duration: 6.0 [5.5] weeks)								
SMD=3.17 (-0.48 to 6.81)	**N=297** (7 studies)	Serious[b]	Very serious[d]	Not serious	Serious[h]	None	⊕○○○ Very low	Important (6) [IQR=2, Q1-Q3: 4.5-6.5]
ADL/IADL disability (median [IQR] follow-up duration: 6.0 [6.0] weeks)								
SMD=0.50 (0.05 to 0.94)	**N=722** (10 studies)	Serious[b]	Not serious	Not serious	Serious[h]	None	⊕⊕○○ Low	Important (6) [IQR=2, Q1-Q3: 6-8]
Upper-extremity function (median [IQR] follow-up duration: 6.0 [4.0] weeks)								
SMD=0.26 (-0.07 to 0.58)	**N=130** (4 studies)	Very serious[a]	Not serious	Serious[f]	Very serious[g]	None	⊕○○○ Very low	Important (6) [IQR=1.5, Q1-Q3: 5-6.5]
Muscle power (median [IQR] follow-up duration: 6.0 [3.8] weeks)								
SMD=2.52 (-3.81 to 8.84)	**N=87** (3 studies)	Very serious[a]	Very serious[d]	Not serious	Very serious[g]	None	⊕○○○ Very low	Important (6) [IQR=1.5, Q1-Q3: 4.5-6]
Spasticity (median [IQR] follow-up duration: 6.0 [3.8] weeks)								
SMD=0.11 (-0.34 to 0.55)	**N=183** (6 studies)	Serious[b]	Not serious	Not serious	Serious[h]	None	⊕○○○ Very low	Important (5) [IQR=3, Q1-Q3: 4-7]

Risk of bias: [a]Downgraded 2 levels where most evidence is from studies with a high risk of bias in more than 1 domain; [b]Downgraded 1 level where most evidence is from studies with high risk of bias in 1 domain or some concerns in more than 1 domain.
Inconsistency: [c]Downgraded 1 level for considerable statistical heterogeneity (I^2=75-100%), but some overlap in 95% CIs; [d]Downgraded 2 levels for considerable statistical heterogeneity (I^2=75-100%) and no/very minimal overlap in 95% CIs.
Indirectness: [e]Subgroup differences present based on time post-stroke; [f]Types of outcomes included in meta-analysis varied substantially (e.g., subjective and objective measures)
Imprecision: [g]Downgraded 2 levels for small sample size (n<400) and 95% CI includes large positive and negative effect; [h]Downgraded 1 level for small sample size (n<400) and very wide 95% CI which includes no effect; [i]Downgraded 1 level for very wide 95% CI that does not include no effect, but large sample size (n>400).
Other: [j]Downgraded 1 level for evidence of publication bias from Egger test/visual inspection of funnel plot and result was significantly different in sensitivity analyses.
N=number of participants, SMD=standardized mean difference, IQR=interquartile range, RoB-2=Revised Cochrane Risk of Bias Assessment Tool.

Critical for decision-making (GRADE scale: 7-9)

There was a large effect of ST on walking capacity (16 trials; n=1,086; SMD=0.95; 95% CI: 0.34, 1.56, p=0.002, I^2=94.3%) and balance (19 trials; n=1,162; SMD=1.13; 95% CI: 0.51, 1.75, p=0.001, I^2=75.8%). There was an increase in habitual (21 trials; n=1,109; MD=0.05 m/s, 95% CI: 0.02, 0.09 m/s, p=0.002, I^2=88.4%) and fast walking speed (10 trials; n=476; MD=0.09 m/s, 95% CI: 0.03, 0.14 m/s, p=0.002, I^2=77.4%) following ST compared to usual care or no exercise. There was a moderate effect of ST on functional ability and mobility (20 trials; n=1,246; SMD=0.61; 95% CI: 0.09, 1.14, p=0.02, I^2=75.6%). There were small to very large, albeit not statistically significant point estimates favouring ST on functional strength and power (13 trials; n=775; SMD=0.48, 95% CI: -0.20, 1.16, p=0.15, I^2=70.7%), health-related quality of life (10 trials; n=572; SMD=0.11; 95% CI: -0.22, 0.44, p=0.46, I^2=39.9%), falls efficacy (4 trials; n=315; SMD=4.55, 95% CI: -14.2, 23.3, p=0.50, I^2=98.4%), psychological wellbeing (4 trials; n=175; SMD=0.21; 95% CI: -0.47, 0.89, p=0.39, I^2=0.0%), or physical activity levels (4 trials; n=432; SMD=0.43, 95% CI: -0.17, 1.02, p=0.10, I^2=1.5%).

Aerobic fitness, muscle endurance, and cognition were not pooled for meta-analysis. Three trials (n=63) measured aerobic fitness;[41 45 46 65] only 1 study (33%) found an improvement.[41] Two trials (n=63) measured muscle endurance of the knee extensors and flexors,[45 46] plantarflexors,[45 46] and on a leg press machine.[41 45 46] Both (100%) found improvements in muscular endurance. One trial (n=32) found mixed results on cognitive function.[78]

Important, but not critical (GRADE scale: 4-6)

There was a large effect of ST on lower-body strength (22 trials; n=1,170; SMD=1.25, 95% CI: 0.64, 1.85, p<0.001, I^2=78.1%) and a moderate effect on ADL/IADL disability (10 trials; n=722; SMD=0.50, 95% CI: 0.05, 0.94, p=0.03, I^2=48.7%). There were small to very large, but not statistically significant point estimates favouring ST on upper-body strength (7 trials; n=297; SMD=3.17; 95% CI: -0.48, 6.82, p=0.08, I^2=93.6%), upper-extremity function (4 trials; n=130; SMD=0.26; 95% CI: -0.06, 0.58, p=0.08, I^2=0.0%), muscle power (3 trials; n=87; SMD=2.52; 95% CI: -3.81, 8.84, p=0.23, I^2=90.1%) or spasticity (6 trials; n=183; SMD=0.11, 95% CI: -0.34, 0.55, p=0.56, I^2=0.0%).

Quality of gait, cardiometabolic health markers, and muscle size were not pooled in meta-analyses. Five trials (n=237)[37 48 49 69 77] measured the quality of gait using outcomes such as step length and stride length. Four trials (80%) found improvements in at least 1 quality of gait outcome. Two trials (n=123) measured cardiometabolic health markers and found between-group differences in body fat percentage,[54 55] fasting insulin,[56] 2-hour glucose levels,[56] insulin resistance,[56] and serum insulin-like growth factor-1; mixed results for total cholesterol, high- and low-density lipoprotein cholesterol favouring ST;[54-56] and no differences in albumin,[54 55] c-reactive protein,[54 55] fat-free mass,[54 55] fasting glucose,[56] glycated hemoglobin concentrations,[56] and body mass index.[54-56] One trial (n=32) found between-group differences for quadriceps muscle volume and cross-sectional area favouring ST.[78]

Effect modification of covariates

There was a subgroup effect of time post-stroke for habitual walking speed (p=0.03). The subgroup effect estimates are presented in Table 3. Older age was negatively associated with improvements in quality of life (β=-0.04, 95% CI: -0.08, -0.01, p=0.03). There was no influence of biological sex/gender identity in any of the meta-analyses.

Influence of ST prescription parameters

The association between prescription parameters and stroke recovery outcomes are displayed in Figure 4. The frequency of ST was positively associated with improvements in walking capacity (β=0.48, 95% CI: 0.03, 0.92, p=0.04). Power-focused ST intensities showed the largest improvements in fast walking speed (MD=0.29 m/s, 95% CI: 0.16, 0.42 m/s), compared to moderate (MD=0.09 m/s, 95% CI: 0.07, 0.12 m/s) and high-intensity programs (MD =-0.01 m/s, 95% CI: -0.08, 0.06 m/s) (p<0.001). Traditional ST showed larger effects compared to functional ST for health-related quality of life (estimated β=0.66, 95% CI: 0.17, 1.14, p=0.02). There was a small positive association between the total number of sessions and changes in lower-body strength (estimated β=0.05, 95% CI: 0.005, 0.10, p=0.03). There was no association between ST duration (minutes per session), length (weeks) on any outcome measure.

Sensitivity analyses

In sensitivity analyses for publication bias, there was no change in the interpretation of any of the results except for functional ability and mobility, where the effects were no longer significant. After removing studies with a high overall risk of bias, results for lower-body strength, functional ability and mobility, fast walking speed, and ADL/IADL disability were not statistically significant, but the remaining results were unchanged.

DISCUSSION

This systematic review and meta-analysis of 42 randomized trials (49 records) found that ST may improve stroke recovery, demonstrated by changes in outcomes rated as important by people with stroke, clinicians, and stroke rehabilitation researchers. These outcomes included: lower-body strength, habitual and fast walking speed, functional ability and mobility, balance, walking capacity, and ADL/IADL disability.

Improving strength is fundamental to completing functional tasks in everyday life.[80-82]

This synthesis demonstrates that ST after stroke can elicit the necessary adaptations to muscle strength, but in contrast to the findings of previous reviews,[13 15] also demonstrates the benefits of ST for other aspects of stroke recovery identified as important to people with stroke. To demonstrate the clinical significance of these results, the standardized mean differences may be re-expressed to reflect core outcome measures in neurological rehabilitation. For instance, the observed changes in walking capacity and balance approximates a 118-metre difference in the 6-minute walk test and a 5.6-point difference in the Berg Balance Scale, both of which are clinically meaningful.[83 84] The disparities between the present and previous systematic reviews are likely due to differences in definitions of ST.[13 14] We defined ST as per the ACSM[85] as "a form of exercise designed to improve muscular fitness by exercising a muscle or muscle group against external resistance". In contrast, previous reviews either defined ST as "pure resistance training",[14] or as "exercising against an external load that corresponds to 8 to 12 RM, at least twice per week, with resistance increased as strength increases".[13] Thus, earlier reviews may have excluded ST programs that were beyond the scope of those definitions, but met the scope of our review.

By using the ACSM definition of ST, we were able to include a broad range of exercise prescriptions, enabling analyses of different program variables on recovery outcomes that are important to the stroke community. Namely, we found that more frequent ST was beneficial for walking capacity – similar to previous work reporting associations between higher frequency of stroke rehabilitation and lower risk of recurrent stroke and mortality,[86] reduced length of stay and more favourable motor function gains.[87] We also found that power-focused intensities (exercises performed at high speeds) were superior to moderate and high intensities for fast walking speed – differences that may also be clinically meaningful.[88] Power-focused ST may elicit increased neural output to high-threshold motor units,[89] creating adaptations to type 2 muscle fibers that are often affected post-stroke.[90] We posit that the stimulus provided through power-focused ST improved the rate of force development needed for fast walking. Interestingly, there was no difference between traditional and functional ST for improving outcomes of physical function (e.g., balance, functional ability and mobility). It may be that functional ST (i.e., ST involving everyday tasks) may have provided greater training specificity for functional movements. Conversely, functional ST often used lower or unspecified training intensities whereas traditional ST (i.e., using free-weights or machines) may have offered a more intense stimulus to enhance skeletal muscle adaptations. It is therefore possible that traditional and functional ST provide unique mechanisms to elicit changes in outcomes related to stroke recovery.

Based on the available evidence, any ST is likely effective for promoting stroke recovery versus none, but to maximize recovery, more frequent and traditional ST programs, as well as programs that emphasize the development of muscle power may have the most beneficial effects, particularly for physical function and health-related quality of life. Future research should explicitly test these types of prescriptions to confirm our hypotheses and associations.

Our review also reveals gaps in the existing evidence for ST after stroke. There were few trials examining some outcomes such as falls efficacy, psychological well-being, and upper-extremity function, all areas rated as important by our advisory group of people with lived experience, researchers, and clinicians. This may, in part, be explained by limited interventions focusing on upper-extremity strength and function, but mainly highlights the importance of partnership, particularly involving people with lived experience, in the research process to ensure that research is relevant and addresses the needs of those affected. Additionally, we note that nearly 70% of studies excluded participants with cognitive impairment or aphasia, known to impact 22-44% of people living with stroke.[91 92] Most studies included middle-aged to older participants with mild to moderate stroke severity and functional status, also limiting the generalizability of our findings for younger or more severely impacted groups. We urge trialists to remain inclusive of measured outcomes and population groups to enhance the strength of the evidence.

We acknowledge the limitations of this review. Most studies had a high risk of bias in several domains or showed evidence of publication bias, resulting in very low to moderate certainty of evidence for our outcome measures. Most of the risk of bias was due to deviations from the intended intervention and/or selection of the reported result, since many studies did not follow an intention to treat analysis or did not publish trial protocols and statistical analysis plans. Although it is difficult to blind participants or those delivering interventions to the allocation in exercise-based rehabilitation trials, we recommend that investigators publish their trial protocols when reporting the results of their studies to limit these biases.

There was also a relatively small number of studies for certain outcomes (e.g., falls efficacy, N=4), which resulted in large confidence intervals that included no effect of ST. This small number of studies also prevented us from exploring interactions between program variables (e.g., intensity and frequency together) on stroke recovery. As the evidence continues to grow for ST after stroke, it will be possible to conduct multi-arm trials and network meta-analyses to explore these interactions. We also acknowledge that the language restriction of our articles to only English may have introduced selection bias in our screening. Relevant articles in other languages may have been missed. Moreover, some studies included in the meta-analyses had small sample sizes, which may lead to small sample biases.[93] Finally, we acknowledge the large number of meta-regression analyses, however this was a necessary approach to address the research question.

CONCLUSIONS

The results of this review demonstrate that ST, compared to no exercise or in addition to usual care, may support outcomes of stroke recovery that were deemed important by an advisory group of people with lived experience of stroke, clinicians, and stroke rehabilitation researchers. ST may not only improve lower-body strength, but also physical function and health-related quality of life. Moreover, different ST prescription parameters may result in an improved recovery for some outcomes: more frequent ST may be optimal for improving walking capacity; power-focused ST may be optimal for improving fast walking speed; and traditional ST may be optimal for health-related quality of life. On the basis of this systematic review of the evidence, clinicians should encourage regular ST participation to promote stroke recovery.

COMPETING INTERESTS

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