Are Aerobic Programs Similar in Design to Cardiac Rehabilitation Beneficial for Survivors of Stroke? A Systematic Review and Meta-Analysis

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***Background*—**Survivors of stroke face movement disability and increased cardiovascular disease and stroke risk. Treatment includes rehabilitation focused on functional movement with less emphasis on aerobic capacity. After rehabilitation, survivors of stroke must self-manage activity with limited appropriate community programs. Lack of structured activity contributes to sedentary behavior. The objective of this systematic review and meta-analysis is to review aerobic programs for stroke survivors similar in activity and dosage to cardiac rehabilitation programs to determine their efficacy for improving aerobic and walking capacity.

***Methods and Results*—**Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to review 5 databases. Group interventions for survivors of stroke with a primary aerobic component and dosage from 18 to 36 visits over 8 to 18 weeks (matching cardiac rehabilitation requirements in the United States) were included. The 6-minute walk test, maximal oxygen consumption (VO2) peak, and walking speed were included as measures of aerobic capacity. Summary effect sizes and outcome measure mean differences were calculated for preintervention to postintervention, and summary effect sizes were calculated for preintervention to follow-up. Activity type and initial 6-minute walk test moderator analyses were performed. Nineteen studies with 23 eligible groups were selected. Survivors of stroke improved their composite aerobic capacity with an effect size of 0.38 (95% CI, 0.27–0.49). Studies including 6-minute walk test demonstrated a pooled difference in means of 53.3 m (95% CI, 36.8–69.8 m). Follow-up data were inconclusive.

***Conclusions*—**Survivors of stroke benefit from aerobic programs with similar dosing to cardiac rehabilitation in the United States. The potential integration into existing programs could expand the community exercise options. **(*J Am Heart Assoc*. 2019;8:e012761. DOI: 10.1161/JAHA.119.012761.)**

Key Words: cardiac rehabilitation • exercise • stroke • stroke rehabilitation

Mobility impairments and accompanying sedentary behaviors are major health concerns for many of the 6.6 million survivors of stroke in the United States.[1] With a large number of survivors of stroke living with disability and facing a higher risk for stroke reoccurrence and other diseases, there is an increasing need for prevention and modification of risk factors.[2] Physical activity (PA) and exercise can positively impact a survivor's overall health by reducing risk factors and improving physical function and quality of life.[3,4] In addition, survivors of stroke engaging in PA can reduce risk for all-cause mortality and reduce 3-year risk for recurrent stroke, myocardial infarction, or vascular death.[5,6] The Centers for Disease Control and Prevention defines PA as "any bodily movement that is produced by the contraction of skeletal muscle and that substantially increases energy expenditure," whereas exercise is a subset of PA "that involves planned, structured and repetitive bodily movement done to maintain or improve one or more components of physical fitness."[7,8]

Many survivors of stroke receive rehabilitation care immediately after their stroke, which is focused primarily on recovery of function with limited or absent focus on aerobic fitness.[9,10] Patients are encouraged to continue with prescribed home exercise programs after discharge from rehabilitation, yet without support or guidance, most do not.[11] This drop-off of services contributes to failure of transition from rehabilitation patient to community PA participant.[12] Survivors of stroke take less than half the daily steps of healthy counterparts and spend >78% of their time in sedentary behaviors, regardless of time

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Accompanying Tables S1 and S2 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.012761

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Clinical Perspective

What Is New?

- Reviewing efficacy of aerobic programs for survivors of stroke similar in activity and dosing to cardiac rehabilitation in the United States provides a prerequisite knowledge base for considering application of cardiac rehabilitation after stroke.
- Results of the systematic review and meta-analysis indicate aerobic programs similar in activity and dosing to cardiac rehabilitation programs in the United States are effective at increasing aerobic capacity for survivors of stroke regardless of mode of exercise, functional mobility, or time since stroke.

What Are the Clinical Implications?

- Providing cardiac rehabilitation for survivors of stroke may positively impact health status and mobility without creating new programs; further research is warranted.

since stroke.[13,14] Structured community exercise programs, such as cardiac rehabilitation (CR), can potentially reduce the deconditioning remaining after rehabilitation and improve habitual PA and exercise for survivors of stroke. Since 1994, the American Heart Association has recommended multidisciplinary CR programs as an integral part of recovery after cardiac events and for the tertiary prevention of cardiovascular disease. CR programs improve participants' health through exercise and educational programs delivered by exercise physiologists and nurses, 2 to 3 times a week for 8 to 18 weeks with aerobic exercise for >30 minutes each visit.[15] Currently, CR programs are offered only to individuals with specific cardiac diagnoses in the United States.[16] Although survivors of stroke exhibit similar deficits in cardiovascular health, stroke is not among the covered diagnoses for CR services.[16,17] CR programs are generally widely available (in 2005, there were 2600 programs across the United States), with some variation across geographic areas.[18]

Several studies have tested the efficacy and feasibility of the multidisciplinary components of CR including aerobic exercise outside the United States, primarily in Canada.[19–27] However, international differences in frequency and duration make conclusions for US programs difficult. Although the American Heart Association and American Stroke Association support CR for survivors of stroke, there has not been support for widespread adoption or testing.

The objective of this systematic review and meta-analysis is to evaluate aerobic exercise interventions for survivors of stroke that are similar in dosing and activity to CR programs in the United States to determine their efficacy for improving aerobic and walking capacity. Secondary aims include the following: (1) evaluating whether gains are sustained in follow-up and (2) evaluating if type of exercise impacts the results.

Methods

All data and materials have been made publicly available at Open Science Framework.[28]

Search Strategy

The search approach included English-language clinical trials (randomized, quasi-experimental, and pilot study designs) that were published articles of interventions where aerobic exercise was the primary component of exercise for adult survivors of stroke. Published systematic review references were also screened for inclusion. PRISMA guidelines were used.[29] The following databases were searched: PubMed, Web of Science, Embase, Cochrane Trials, and CINAHL. The searches included articles up to November 1, 2018. The PubMed database search included the following syntax: (((cardiorespiratory[tiab] OR aerobic exercise[tiab] OR rehabilitation[tiab] OR physical activity[tiab]) OR ("cardiorespiratory fitness"[MeSH {Medical Subject Heading} Terms] OR "exercise"[MeSH Terms] OR "rehabilitation"[MeSH Terms])) AND ("stroke"[MeSH Terms] OR stroke [tiab] OR CVA[tiab] OR cerebrovascular accident[tiab])) AND (walking capacity[tiab] OR 6MWT[tiab] OR 6MWD[tiab] OR "six minute walk"[tiab] OR "six-minute walk test"[tiab] OR "walking test"[tiab] OR "walk test"[All Fields] OR "gait speed"[tiab] OR walking speed[tiab] OR walk speed[tiab] OR exercise test[tiab] OR endurance[tiab] OR exercise capacity[tiab] OR aerobic capacity[tiab] OR cardiorespiratory capacity[tiab]).

Inclusion and Exclusion Criteria

Inclusion of studies was further evaluated by the presence of the following characteristics to obtain similarity to US CR program requirements[16,17]:

1. A population of adult survivors of stroke.
2. A study design that included pretesting and posttesting for an intervention for at least one group.
3. An intervention type that was group based and included a primary aerobic exercise component with the optional addition of resistance exercise, stretching, or educational sessions.
4. An intervention dosage of 18 to 36 total visits over 8 to 18 weeks.
5. Outcome measures that included at least one measure of aerobic capacity: 6-minute walk test (6MWT), other time-limited walk tests, walking speed, or VO_2 peak.

Presence of the following excluded the study from the current review:

1. Studies that included physical therapy or other interventions in addition to aerobic exercise other than resistance exercise, stretching, or educational sessions.
2. Studies that provided physical assistance to the participant through mechanical, technological, or physical assistance other than assistive devices or equipment setup.
3. Studies that were individual (nongroup) based.
4. Studies that used aquatic-based activities.

Study Selection

After completion of the database searches, references and abstracts were uploaded to the covidence screening tool (http://www.covidence.org; Veritas Health Innovation, Australia) for review. Duplicates were removed. Initial title and abstract screening eliminated nonqualified studies based on inclusion and exclusion criteria by the primary author (E.R.). In addition, any relevant systematic review and meta-analysis reference lists were reviewed by the primary author during title and abstract screening. Studies that were not eliminated were reviewed further in full text against inclusion and exclusion criteria by 2 authors independently (E.R. and R.H.), with discrepancies resolved by discussion and consensus. Studies were included in the systematic review if they met all inclusion criteria, and studies were included in the meta-analysis if aerobic capacity data were available for preintervention and postintervention.

Quality Assessment

Quality assessment was completed by the lead author (E.R.) using the Physiotherapy Evidence Database quality (PEDro) scale for clinical trials.[30] PEDro is an accepted method for reviewing methodological rehabilitation studies independently and as part of systematic reviews,[31] and it has been recommended over other scales for evaluation of stroke rehabilitation literature.[32] PEDro assesses 11 criteria, awarding 1 point for each criterion that is clearly satisfied and 0 points when there is the possibility that the criterion is unsatisfied.

Data Extraction

Descriptive data extracted from studies included author, year of publication, study country, study setting, interventionalist, activities in intervention, total visits, frequency, duration, and participant demographic information. Outcome measure data were extracted from studies for comparison of pretest and posttest means and SDs. Follow-up data, where available, were also extracted. Data conversions were made for 2 studies to allow for use in the meta-analysis. The Severinsen et al (2014)[33] study was standardized from median to means and SDs using methods described by Hozo et al.[34] In the 2006 study by Olney et al,[35] 6MWT was presented in m/s and was converted to m. The authors of the study by Awad et al (2016)[36] were contacted to obtain 6MWT data that were not presented in the publication.

Data Analysis

Comprehensive Analysis Software (Version 3; Biostat) was used to perform all statistical calculations. A random-effects model was used for all comparisons as a conservative approach because of clinical heterogeneity of studies and multiple studies with small sample sizes.[37] The I^2 statistic was calculated to determine relative variance between studies.

Calculating Effect Sizes and Mean Differences

Summary effect sizes (Hedges g[38]) were calculated for all the studies preintervention to postintervention and preintervention to follow-up using a composite mean of aerobic capacity outcome measures: 6MWT, VO_2 peak, maximum walking speed (MWS), and self-selected walking speed (SSWS). In addition, pooled mean differences for each individual outcome measure were calculated. 6MWT, VO_2 peak, MWS, and SSWS are all accepted measures of aerobic capacity and often correlate with one another.[39]

Moderator Analysis

Evaluation of the summary effect sizes grouped by activity type (walking, cycling, or mixed aerobic activity) was a prespecified moderator analysis to determine if aerobic activity type impacted results. In addition, a post hoc moderator analysis of the 6MWT mean differences was performed by grouping those studies with a mean initial 6MWT value of $\geq$288 m (unlimited community ambulator) and $<$288 m (limited community ambulator) to examine differences in responses to aerobic activity between those with differing initial walking capacity.[40]

Sensitivity Analysis and Publication Bias

Sensitivity analysis was performed using a one study removed strategy by removing the study group with the largest and smallest effect size in preintervention to postintervention and preintervention to follow-up to determine impact on summary effect size.

Publication bias was evaluated using funnel plots of summary effect and classic fail-safe N statistic for summary effect size for preintervention to postintervention and for preintervention to follow-up.[41,42]

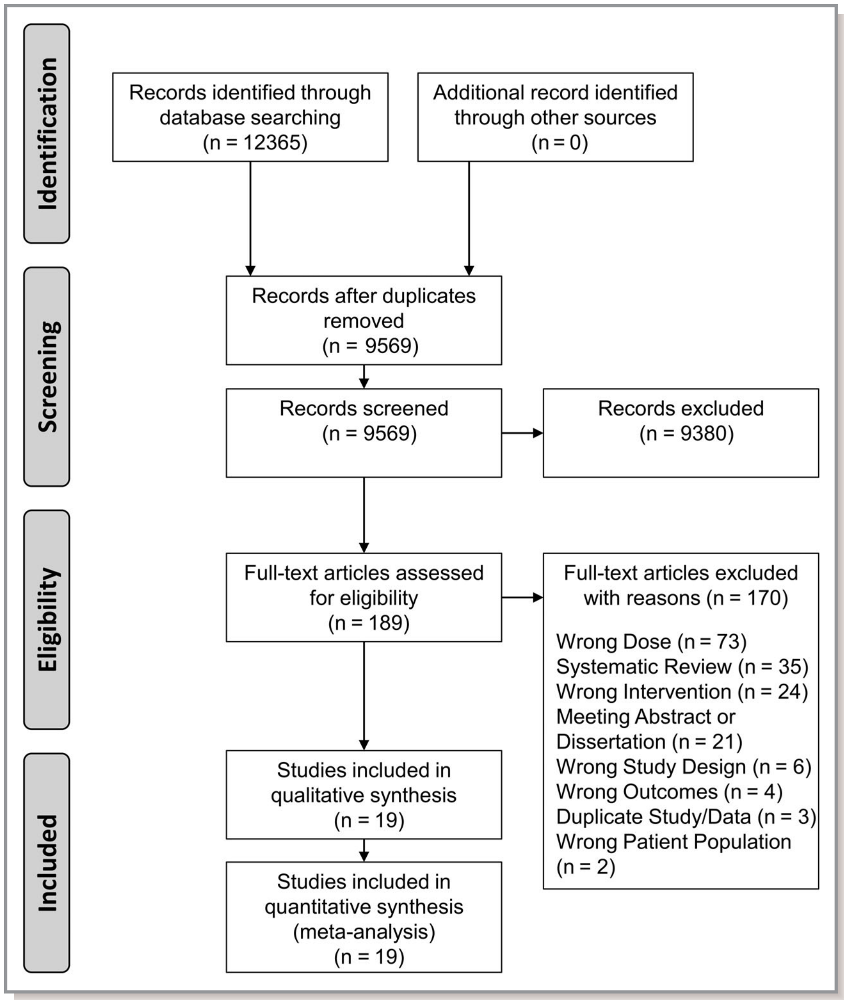

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) systematic review results.

Results

Description of Studies

The review identified 19 qualified studies,[33,35,36,43–58] some with multiple eligible treatment groups, for a total of 23 qualified treatment groups, including 485 participants with treatment group mean ages between 54 (SD, 8.6) and 71 (SD, 7) years. PRISMA process results are presented in Figure 1. Details on the study and treatment group characteristics are provided in Table S1. Only 4 of the 19 qualified studies were performed in the United States; the remaining were performed in Australia (n=2), Canada (n=2), Europe (n=8), Israel (n=1), Jamaica (n=1), and Taiwan (n=1). Frequency, duration, and activity type varied. Frequency of sessions was either 2 or 3 times per week. Session duration varied from 30 to 90 minutes, with the longer sessions including activities in addition to the primary aerobic exercise. Walking (treadmill or over ground) was the most common aerobic exercise performed (47%), followed by stationary cycling (21%), mixed-mode aerobic exercise (21%), and recumbent stepping (11%). Aerobic activity was performed at various intensities and was either continuous (ie, 1 bout of 30 minutes) or interval (ie, 3 bouts of 10 minutes). Additional activity was included in some studies and was composed of resistance training (21%), flexibility interventions (5%), and education (5%). Participant time since stroke varied (treatment group means from 0.06 [SD, 0.06] to 9.15 [SD, 12.72] years), with 1 study[52] in the acute phase (≤30 days poststroke), 4 studies[45,48,53,55] in the subacute phase (>30 days to <6 months poststroke), 12 studies* in the chronic phase (≥6 months poststroke), and 2 studies[56,57] not reporting time since stroke. The functional level of participants at the start of the studies varied, with all except one study requiring some level of independent ambulation (with or without an assistive device); the exception

*References 33, 35, 36, 43, 44, 46, 47, 49–51, 54, 58.

was a cycling study, the study by Vanroy et al (2017),[55] which required pedaling at 50 revolutions per minute.

Quality Assessment

Results of the PEDro assessment are presented in Table S2. Study quality varied because of the different study designs, ranging from single-group convenience samples to randomized control trials with control groups and assessor blinding. PEDro scores ranged from 3 to 9, with a median of 7 of a possible 11. Existing stroke rehabilitation literature has a median score of 6.[59] Because concealment of therapists and participants is difficult in exercise intervention trials, these criteria are often unmet in rehabilitation studies.[31,59]

Preintervention to Postintervention Results

Changes in aerobic capacity for preintervention-postintervention are presented in Figure 2. The summary effect size of the 23 treatment groups for improving aerobic capacity preintervention-postintervention was 0.38 (95% CI, 0.27–0.49), indicating a small positive effect.[60] The I^2 statistic was 24.8%, indicating low variance in effect size between studies.

Individual outcome measure results also indicated small positive effects for each measure. The 6MWT results from 20 treatment groups had a summary effect size of 0.41 (95% CI, 0.25–0.58) and a pooled difference in means of 53.3 m (95% CI, 36.8–69.8 m). MWS (7 treatment groups) and SSWS (10 treatment groups) had similar improvements. MWS had a summary effect size of 0.28 (95% CI, 0.15–0.40) and a pooled difference in means of 0.12 m/s (95% CI, 0.07–0.18 m/s), whereas SSWS had a summary effect size of 0.29 (95% CI, 0.15–0.43) and a pooled difference in means of 0.12 m/s (95% CI, 0.06–0.17 m/s). VO_2 peak summary effect size was 0.38 (95% CI, 0.17–0.60), and the pooled difference in means was 2.08 mL/kg per minute (95% CI, 1.18–2.98 mL/kg per minute).

Preintervention to Follow-Up Results

When comparing the summary effect size for preintervention to follow-up, fewer data were available; 7 treatment groups within 6 studies resulted in a summary effect size of 0.22 (95% CI, −0.07 to 0.50), although this was not statistically significant. The forest plot is provided in Figure 3.

Moderator Results

Activity Type

Summary effects, moderated by activity type, resulted in a summary effect size 0.24 (95% CI, 0.10–0.57) for cycling or recumbent stepping (7 treatment groups), 0.37 (95% CI, 0.23–0.52) for walking (12 treatment groups), and 0.61 (95% CI,

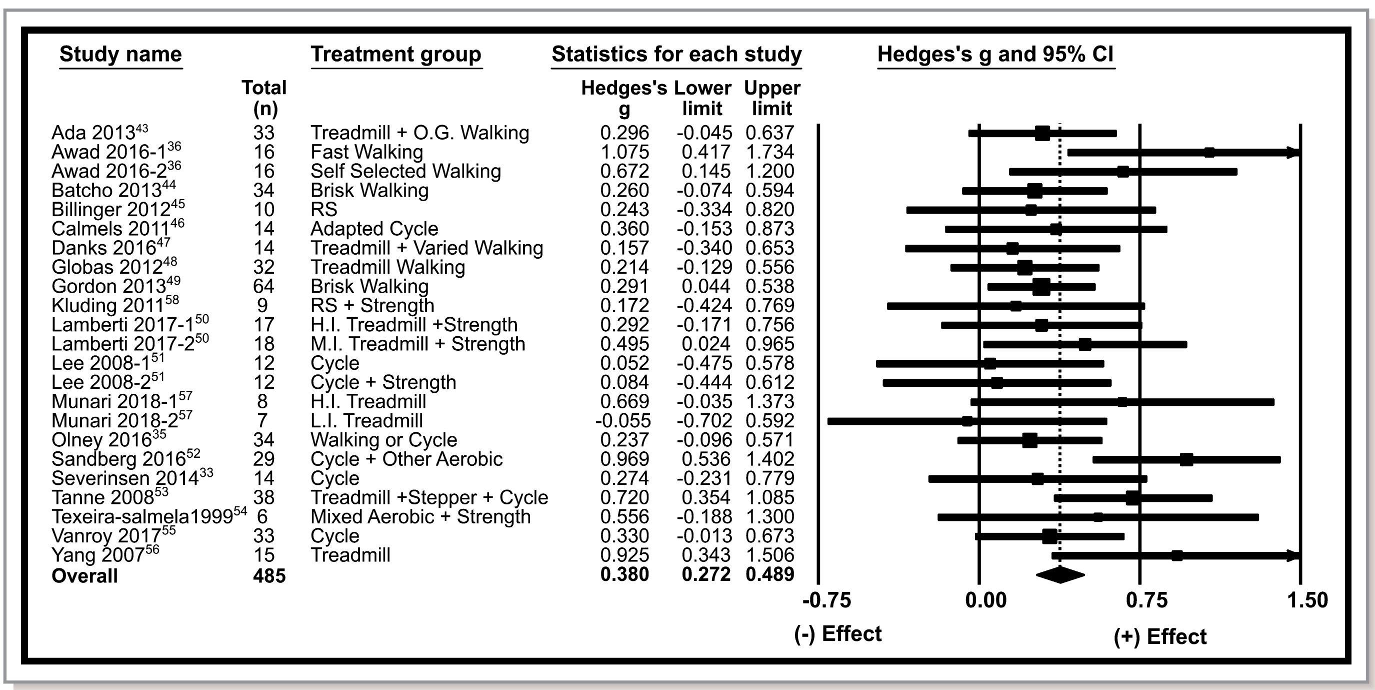

Figure 2. Forest plot results for summary aerobic capacity effects from preintervention to postintervention. H.I. indicates high intensity; L.I., low intensity; M.I., moderate intensity; O.G., over ground; RS, recumbent stepper.

Study name	Total (n)	Activity	Treatment group	Follow up	Hedges's g	Lower limit	Upper limit
Ada 2013[43]	33	Walk	Treadmill + O.G. Walking	6-month	0.194	-0.142	0.531
Awad 2016-1[36]	16	Walk	Fast Walking	3-month	0.998	0.360	1.635
Awad 2016-2[36]	16	Walk	Self Selected Walking	3-month	0.601	0.081	1.121
Batcho 2013[44]	34	Walk	Brisk Walking	3-month	0.119	-0.210	0.449
Billinger 2012[45]	8	Cycle/RS	RS	1-month	0.222	-0.404	0.847
Globas 2012[48]	32	Walk	Treadmill Walking	12-month	0.160	-0.180	0.500
Severinsen 2014[33]	14	Cycle/RS	Cycle	12-month	-0.600	-1.144	-0.056
Overall	**153**				**0.218**	**-0.066**	**0.501**

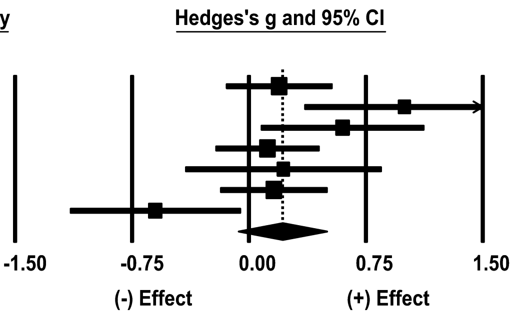

Figure 3. Pooled effects for aerobic capacity from preintervention to follow-up. O.G. indicates over ground; RS, recumbent stepper.

0.26–0.96) for mixed aerobic activity (4 treatment groups). The forest plot is displayed in Figure 4.

Initial Performance on the 6MWT

The 6MWT mean differences were divided into sets based on initial 6MWT of either <288 m (limited community ambulators) or ≥288 m (unlimited community ambulators).[40] Participants with an initial 6MWT of <288 m demonstrated a mean gain of 37.5 m (95% CI, 25.7–47.3 m), whereas participants with an initial 6MWT of ≥288 m demonstrated a mean gain of 81.4 m (95% CI, 58.2–104.6 m). Results are presented in the forest plot in Figure 5.

Sensitivity and Publication Bias Results

Preintervention to Postintervention

One study removed sensitivity analysis revealed the lowest overall resulting effect size of 0.35 (95% CI, 0.25–0.44) if the Sandberg et al (2016)[52] group was removed. Removing the Lee et al (2008-1)[51] treatment group (cycle only) resulted in the highest effect size of 0.39 (95% CI, 0.27–0.49). Neither of these changes significantly affected the results.

The funnel plot for review of publication bias for the preintervention-postintervention effects is slightly asymmetrical,

Activity	Study name	Treatment group	Hedges's g	Lower limit	Upper limit
Cycle/RS	Billinger 2012[45]	RS	0.243	-0.334	0.820
Cycle/RS	Calmels 2011[46]	Adapted Cycle	0.360	-0.153	0.873
Cycle/RS	Kluding 2011[58]	RS + Strength	0.172	-0.424	0.769
Cycle/RS	Lee 2008-1[51]	Cycle	0.052	-0.475	0.578
Cycle/RS	Lee 2008-2[51]	Cycle + Strength	0.084	-0.444	0.612
Cycle/RS	Severinsen 2014[33]	Cycle	0.274	-0.231	0.779
Cycle/RS	Vanroy 2017[55]	Cycle	0.330	-0.013	0.673
Cycle/RS			**0.238**	**0.053**	**0.423**
Mixed	Olney 2016[35]	Walking or Cycle	0.237	-0.096	0.571
Mixed	Sandberg 2016[52]	Cycle + Other Aerobic	0.969	0.536	1.402
Mixed	Tanne 2008[53]	Treadmill + OG Walking	0.720	0.354	1.085
Mixed	Texeira-salmela 1999[54]	Mixed + Strength	0.556	-0.188	1.300
Mixed			**0.612**	**0.263**	**0.961**
Walk	Ada 2013[43]	Treadmill + OG Walking	0.296	-0.045	0.637
Walk	Awad 2016-1[36]	Fast Walking	1.075	0.417	1.734
Walk	Awad 2016-2[36]	Walking	0.672	0.145	1.200
Walk	Batcho 2013[44]	Brisk Walking	0.260	-0.074	0.594
Walk	Danks 2016[47]	Treadmilll + Varied Walking	0.157	-0.340	0.653
Walk	Globas 2012[48]	Treadmill	0.214	-0.129	0.556
Walk	Gordon 2013[49]	Brisk Walking	0.291	0.044	0.538
Walk	Lamberti 2017-1[50]	H.I. Treadmill + Strength	0.292	-0.171	0.756
Walk	Lamberti 2017-2[50]	M.I. Treadmill	0.495	0.024	0.965
Walk	Munari 2018-1[57]	H.I. Treadmill	0.669	-0.035	1.373
Walk	Munari 2018-2[57]	L.I. Treadmill	-0.055	-0.702	0.592
Walk	Yang 2007[56]	Treadmill	0.925	0.343	1.506
Walk			**0.374**	**0.230**	**0.518**

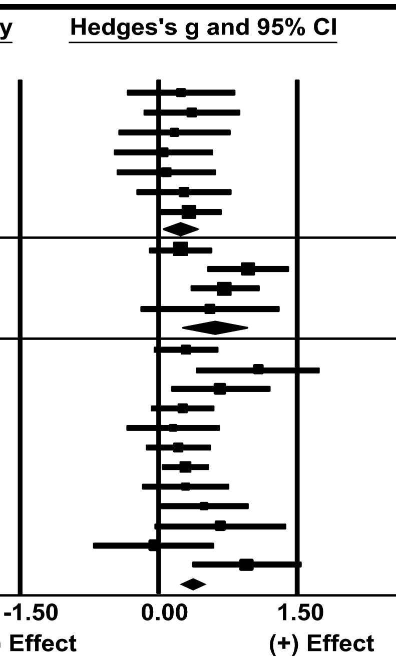

Figure 4. Pooled effects for aerobic capacity preintervention to postintervention by activity type. H.I. indicates high intensity; L.I., low intensity; M.I., moderate intensity; OG, over ground; RS, recumbent stepper.

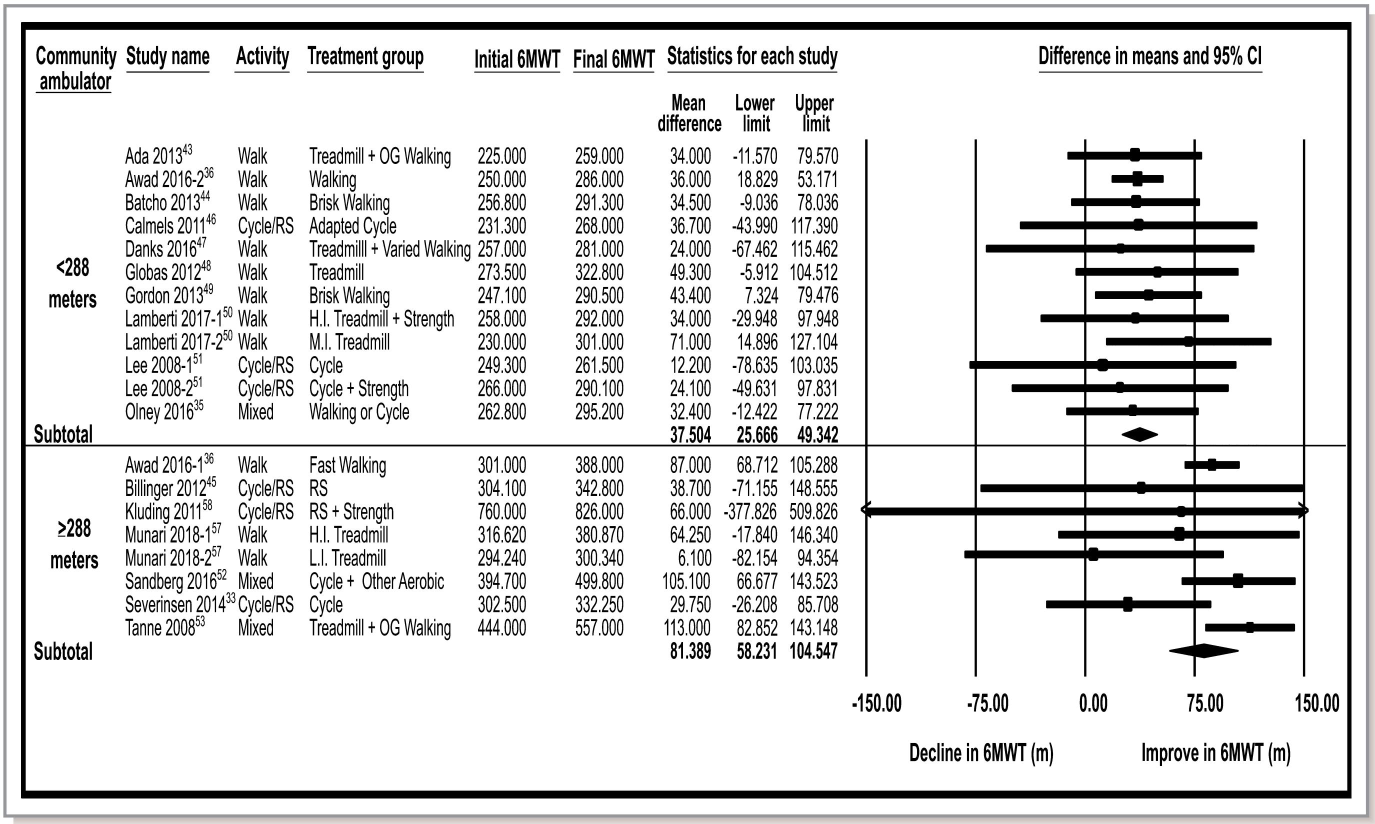

Figure 5. Pooled mean differences in 6-minute walk test (6MWT) distance (in meters) grouped by initial 6MWT mean <288 and ≥288 m. H.I. indicates high intensity; L.I., low intensity; M.I., moderate intensity; OG, over ground; RS, recumbent stepper.

suggesting some bias toward smaller effect sizes. The funnel plot is presented in Figure 6. The classic fail-safe N is 364, which can be interpreted as needing 364 more studies to change the direction of the effect size.[42] The funnel plot combined with the classic fail safe N statistic suggest no impact of publication bias.

Preintervention to Follow-Up

The preintervention to follow-up results were not statistically significant. However, when removing the Severinsen et al (2014)[33] treatment group (cycle), which had the only negative effect size, the summary effect size of 0.30 (95% CI, 0.08–0.53) became statistically significant. The reverse is also true: if the largest positive effect size treatment group, Awad et al (2016-1)[36] (fast walking), is removed, the pooled effect became smaller and remains not statistically significant at 0.13 (95% CI, −0.12 to 0.38). Classic fail-safe N suggested only 5 more studies would be required to change the direction of effect. This result indicated publication bias and sensitivity to one study; therefore, preintervention to follow-up results are cautiously interpreted.

Discussion

Aerobic exercise programs that match the dosage of US CR programs improve aerobic capacity for survivors of stroke, regardless of the type of aerobic activity performed. Additional analysis by activity type suggests that walking (effect size (ES)=0.37) or mixed aerobic activity (ES=0.61) may be more beneficial to aerobic capacity than cycling alone (ES=0.24). Individual treatment groups with large overall aerobic capacity effect sizes, Hedges g >0.8[38] (Awad et al [2016-1],[36] Sandberg et al [2016],[52] and Yang et al [2007][56]), were either mixed activity or treadmill walking; and all included participants with high levels of function (participants with minor stroke or the study had sizeable walking requirements). These results are clinically important because they indicate that applying walking or mixed aerobic exercise for those with mild impairments may maximize gains in aerobic capacity.

The 6MWT is a reliable measure of walking capacity and community ambulation for survivors of stroke.[61] Survivors of stroke obtain clinically meaningful improvements in 6MWT distance after participation in aerobic exercise programs regardless of mode of exercise, functional level, or time since

SYSTEMATIC REVIEW AND META-ANALYSIS

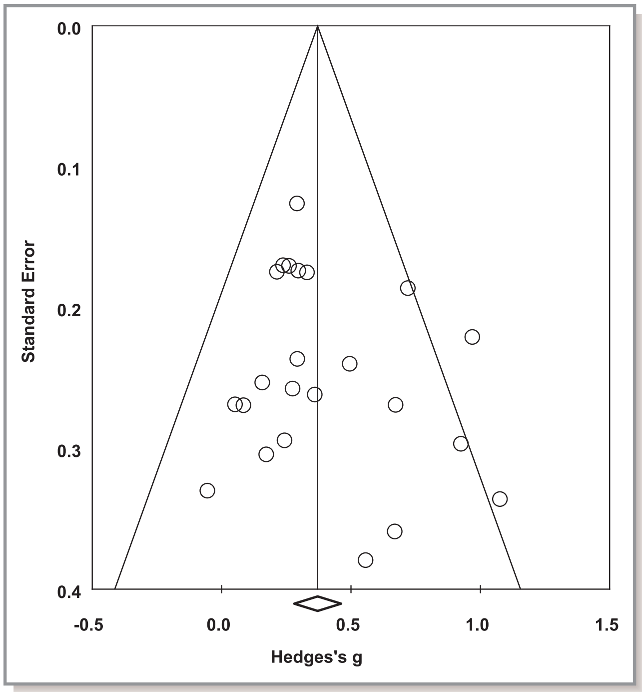

Figure 6. Funnel plot for pooled aerobic effects from preintervention to postintervention.

stroke. Despite different baseline 6MWT distances (capacities), all groups experienced improvements in aerobic capacity postintervention, as evident by the pooled difference in means of 37.5 m for those with an initial 6MWT <288 m and 81.4 m for those with an initial 6MWT ≥288 m. Although the quantity of improvement in the 6MWT was greater in treatment groups with higher initial performance, all exceeded the minimal clinically important difference of 34.4 m for survivors of stroke.[62] The substantially higher result (81.4 m) for those with a higher initial 6MWT indicates that those with the mildest impairments may make the most overall gains. However, impact on community ambulation may be more pronounced for participants with a lower initial 6MWT. A study by Fulk et al demonstrated that the 6MWT has strong predictive value for determining whether survivors of stroke are home ambulators (<205 m), limited community ambulators (>205 and <288 m), or unlimited community ambulators (≥288 m).[40] Limited community ambulation consists of walking outside the house to at least the mailbox or car, and as far as down the block.[63] Unlimited community ambulation includes the ability to navigate uneven terrain, shopping, and public venues.[63] Each treatment group with baseline 6MWT distances of <288 m demonstrated an overall mean of 250.6 m in initial 6MWT distance, with a range of 225 to 273.5 m, corresponding to the limited community ambulator category; many (58%) transitioned to the unlimited community ambulator category after the intervention. For survivors of stroke, additional capacity may lead to improved community participation and independence. This noteworthy finding supports the benefits of aerobic exercise interventions for survivors of stroke regardless of initial performance on the 6MWT.

Walking speed mirrored 6MWT results, with all studies reporting initial MWS in the limited (0.4–0.8 m/s) or unlimited (>0.8 m/s) community ambulation category.[64] In addition, initial SSWS were primarily at community ambulation speeds, except for one study, Vanroy et al (2017),[55] which had an initial SSWS of 0.35 m/s, indicating household ambulation status. Although walking speed improved from preintervention to postintervention, the pooled mean differences of 0.12 m/s in both MWS and SSWS failed to meet the minimal detectable change in survivors of stroke (0.18 m/s for SSWS and 0.13 m/s for MWS).[64] The treatment group in the study by Vanroy et al (2017)[55] improved SSWS to 0.53 m/s and, therefore, all SSWS postintervention treatment group values had community ambulation status. In addition, all postintervention MWS treatment group values were in the unlimited community ambulation status.

VO_2 peak values reflect peak oxygen consumption levels achieved during exercise as a reflection of aerobic capacity.[65] Activities of daily living expend energy in the range of 10.5 to 17.5 mL/kg per minute.[65] To function in higher-level activity above activities of daily living, more capacity is required.[65] Treatment groups in this meta-analysis had initial VO_2 peak values ranging from 11.24 to 20.88 mL/kg per minute. Although a pooled change of 2.08 mL/kg per minute is not large, the gains in VO_2 peak could have a significant impact in activity tolerance and community engagement for survivors of stroke.

The results of follow-up data were inconclusive. Except for one study group (Severinsen et al [2014][33]) with clear reversal of improvements at the 12-month follow up, the remaining studies all maintained gains in the follow-up period. Although the pooled results, including the study by Severinsen et al, were not statistically significant, removing the study by Severinsen et al from the analysis resulted in a statistically significant summary effect size of 0.30 (95% CI, 0.08–0.53) with a maintenance of aerobic capacity gains. With few studies presenting follow-up data, and follow-up periods varying from 1 to 12 months, the true capacity in postintervention follow-up is unknown but results suggest gains can be maintained after intervention completion. Further studies including follow-up periods are required to determine if program gains are maintained over time and if program participation leads to independently managed exercise.

Existing CR programs are one programmatic opportunity for filling the gap in available aerobic activity programs for survivors of stroke. Our meta-analysis demonstrates that dosing and activity similar to CR programs benefits survivors of stroke across the recovery continuum (acute, subacute, and chronic) by improving aerobic capacity. Using CR programs could provide a safe environment for survivors of stroke to exercise within existing healthcare infrastructure after formal rehabilitation ends. Survivors of stroke with mild impairments are potentially the simplest group to integrate into existing CR programs because of their similarities with traditional CR participants (few mobility impairments), and our results suggest that those with mild impairments can achieve the most gains in aerobic capacity. CR programs have been adopted in Canada with positive health results for those without mobility impairments in traditional CR and separately in CR-based programs specifically for survivors of stroke with mobility impairments.[19] Additional research into the feasibility of US CR programs and other existing community-based aerobic programs for survivors of stroke could make a significant impact on their lives and health status without creation of entirely new programs.

Study Limitations

Because of the inclusion of multiple study designs, no control group comparisons were included as part of our review. Determining if intervention groups improve more than control groups could provide additional information on efficacy. Lack of available studies with follow-up data prevented full conclusions on the persistence of gains after intervention cessation. The narrow duration and frequency criteria limit the ability to determine if shorter duration or less frequent interventions could provide similar gains. Available studies are primarily in survivors of stroke with mild mobility impairments, preventing conclusions of aerobic capacity benefits for survivors of stroke with more severe limitations.

Conclusions

After formal rehabilitation, many survivors of stroke exhibit deficits in aerobic capacity, which impacts their health status and community participation. Group-based aerobic exercise can be an alternative to continued one-on-one care or discontinuing services completely. Survivors of stroke of varying time since stroke, age, sex, and initial aerobic capacity can benefit from structured group aerobic exercise. Those with fewer mobility impairments and better initial capacity achieve the largest gains in aerobic capacity. Integrating survivors of stroke into existing CR programs could address the deficit of available community programs appropriate for survivors of stroke and requires further research in the United States. More studies with follow-up periods after primary group intervention and evaluation of cost and healthcare use could provide insight on the importance of continued services and their economic impact.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Included Studies Descriptions.

First Author & year of publication - Group	Country	Time Exercising	Duration	Total Sessions	Activity	Intensity	Setting	Delivering Intervention	Stroke Stage Requirement	Ambulatory Status	Sample	Mean Age (SD)	Mean Time since stroke (SD)	Sex (% female)
Ada 2013[1]	Australia	30 min	3 x week x 8 weeks	24	Treadmill and Overground Walking with progressive difficulty	Unknown	Community	therapist	<5 years post stroke; completed rehab	Slow walkers (10m walk test > 9 sec)	33	64(12)	20 (15) months	29%
Awad 2016[2] - Fast Walking	United States	36 min	3 x week x 12 weeks	36	Treadmill and Overground Walking	Fast Walking Speed	Research center	Unknown	Not Specified	Independent walking for 6 min with observable gait deficit and no bracing or assistive device; passive hip and ankle ROM requirements	16	55.3(5.8)	1.73 (2.47) Years	44%
Awad 2016[2] -Self Selected Walking	United States	36 min	3 x week x 12 weeks	36	Treadmill and Overground Walking	Self Selected Walking Speed	Research center	Unknown	Not Specified	Independent walking for 6 min with observable gait deficit and no bracing or assistive device; passive hip and ankle ROM requirements	16	61.44(5.9)	1.52 (1.08) Years	43%
Batcho 2013[3]	Belgium and Benin (Africa)	Unknown	3 x week x 12 weeks	36	Brisk walking	Faster than normal walking	Sports center facilities	PTs	> 6 months post stroke	minimal ambulatory capacity (able to complete 10m walk test)	34	57.97(11.02)	37.7 (31.7) months	29%
Billinger 2012[4]	United States	30-50 min	3 x week x 8 weeks	24	recumbent exercise	4 weeks 50-59% Heart Rate Reserve (HRR), 4 weeks 60-69% HRR	Research Center	Unknown	< 6 months post stroke	ambulatory (w or w/o AD, standby assist)	10	61.2(4.7)	66.7 (41.5) days	40%
Calmels 2011[5]	France	30 min	3 x week x 8 weeks	24	adapted cycloergometer	Intervals 40-80% (4:1)	Outpatient rehab clinic	Unknown	> 3 months and < 2 years post stroke	walk independently w or w/o orthosis or AD	14	53.7(8.6)	12.1(7.52) months	17%
Danks 2016[6]	United States	40 min	3x week x 12 weeks	36	Treadmill walking + 10 minutes real world stepping activity	walking @ 80% target MHR	research lab	PT	> 6 months post stroke	walk w or w/o AD / orthosis	14	58.2(12.4)	50.8(44.1) months	43%

First Author & year of publication - Group	Country	Time Exercising	Duration	Total Sessions	Activity	Intensity	Setting	Delivering Intervention	Stroke Stage Requirement	Ambulatory Status	Sample	Mean Age (SD)	Mean Time since stroke (SD)	Sex (% female)
Globas 2012[7]	Germany	10-20 min progressing to 30-50 min	3x week 12 weeks	36	treadmill walking	40-50% MHR progressing to60-80% MHR	outpatient rehab	physician and/or PT	>6 months post stroke	Gait impairments and ability to treadmill ambulate at >=0.3 km/h for 3 min w/handrail	32	68.7(6.3)	65.1(57.3) months	19%
Gordon 2013[8]	Jamaica	30 min, (may progress from 15 min)	3 x week 12 weeks	36	Brisk Walking	60-85% MHR progressive	Unknown	trained instructors	6-24 months post stroke	able to walk w/ or w/o AD	64	63.4(9.4)	11.8(3.6) months	55%
Kluding 2011[9]	United States	60 min (30 min aerobic, 30 min strength)	3 x week 12 weeks	36	Recumbent Stepper + strengthening	50% VO^2 peak	Unknown	Unknown	> 6 months post stroke	Able to walk 30 ft without help from another person	9	63 (9.1)	50.4 (37.9) months	44%
Lamberti 2017[10] - Mod Intensity	Italy	60 min	3 x week x 8 weeks	24	Interval treadmill walking (20min) + stretching (4 weeks), Interval treadmill walking (10 min) + 40-50% 1RM max strengthening (4 weeks)	Fixed progression interval	adapted physical therapy center	Exercise Physiologist	> 6 months post stroke	able to ambulate 10m on stable ground	18	69(9)	34(46) months	12%
Lamberti 2017[10] - High Intensity	Italy	60 min	3 x week x 8 weeks	24	Continuous treadmill walking (30-35 min) + stretching (4 weeks); Continuous treadmill walking (10 min) + 70% 1RM max strengthening (4 weeks)	60-70% MHR	adapted physical therapy center	Exercise Physiologist	> 6 months	able to ambulate 10m on stable ground	17	67(10)	40(51) months	14%
Lee 2008[11] – Cycle	Australia	30 min	3 x week x 10-12 weeks	30	Cycling	50-70% VO^2 peak	Research Lab	Trained Personnel	> 3 months post stroke	LE hemiparesis, walking 0.15 - 1.4 m/s	12	67.2(10.6)	52.4(2.2) months	42%

First Author & year of publication - Group	Country	Time Exercising	Duration	Total Sessions	Activity	Intensity	Setting	Delivering Intervention	Stroke Stage Requirement	Ambulatory Status	Sample	Mean Age (SD)	Mean Time since stroke (SD)	Sex (% female)
Lee 2008[11] - Cycle + Strength	Australia	60 min	3 x week x 10-12 weeks	30	Cycling (30 min) + progressive lower extremity strengthening (30 min)	50-70% VO^2 peak	Research Lab	Trained Personnel	> 3 months post stroke	LE hemiparesis, walking 0.15 - 1.4 m/s	12	60.5(10.6)	63.2(40.5) months	33%
Munari 2018[12] - High Intensity Treadmill	Italy	50-60 min	3 x week for 12 weeks	36	Treadmill walking 10 min warm up, 5x5 minute intervals with 3 minute active breaks, 5 min cool down	85-95% VO^2 peak	Unknown	Unknown	> 6 months post stroke	Able to walk on treadmill with handrail >= 0.3km/h for 3 minutes	8	61(5.77)	Unknown	13%
Munari 2018[12] – Low Intensity Treadmill	Italy	50-60 min	3 x week for 12 weeks	36	Treadmill Walking, self-selected speed / 1% incline, 10 min warm up, 40 min exercise period, 5 min cool down	40% VO^2 peak	Unknown	Unknown	> 6 months post stroke	Able to walk on treadmill with handrail >= 0.3km/h for 3 minutes	7	62(11.27)	Unknown	0%
Olney 2006[13]	Canada	90 min	3 x week x 10 weeks	30	Physical Conditioning = warm up, aerobic (walking or cycling), strength, cool down	50-70% MHR	Unknown	Unknown	Mixed, no requirement	walk 15 min with rests w/ or w/o AD except 4pt walker	34	63.5(12)	4.1(4.4) years	38%
Sandberg 2016[14]	Sweden	60 min	2 x week x 12 weeks	24	Cycle and other mixed cardiovascular exercise	> 50% MHR for parts 1-3, and >80% MHR for 2-8 min cycle	Hospital	PT	acute stroke, post hospital discharge	Mild Stroke	29	71.3(7)	22.2(10.1) days	52%
Severinsen 2014[15]	Denmark	60 min	3 x week x 12 weeks	36	group aerobic intensity training including 15 min of high intensity cycling	50-70% first 4 weeks, then 75% HRR	Unknown	PT	6-26 months post stroke	Independent fast walking at less than 1.4 m/sec w/ or w/o AD	14	69(Median), Range 50-80	14(Median), Range 11-29, months	31%
Tanne 2008[16]	Israel	60 min	2 x week x 12 weeks	24	Treadmill, stairstepper or cycling	60-70% MHR after 15 min warm up	Cardiac Rehab site	PT / cardiac rehab staff	< 6 months post stroke	minor stroke (modified Rankin Scale <=2)	38	61(10)	65(37) days	7%
Texeira-salmela 1999[17]	Canada	60-90 min	3 x week x 10 weeks	30	Graded Walking + stepping + strengthening	50-70% MHR, (5 weeks), 70% (5 weeks)	Unknown	PT and Exercise Physiologist	>9 months post stroke	Walking Independently w/ or w/o AD for 15 min	6	65.87 (10.16)	9.15(12.72) years	83%

First Author & year of publication - Group	Country	Time Exercising	Duration	Total Sessions	Activity	Intensity	Setting	Delivering Intervention	Stroke Stage Requirement	Ambulatory Status	Sample	Mean Age (SD)	Mean Time since stroke (SD)	Sex (% female)
Vanroy 2017[18]	Belgium	30 min	3x week x 12 weeks	36	Cycling (interval (first 8 weeks), continuous (final 4 weeks) + 4 1 hour ed sessions	60-75% HRR	rehab hospital	Unknown	3-10 weeks post stroke	able to pedal at 50 revolutions/min	33	66.7(8.8)	50.5(19.8) days	39%
Yang 2007[19]	Taiwan	50 min	3 x week x 12 weeks	36	Treadmill	40-50% progressing to 50-60% HRR as tolerated	Unknown	Unknown	< 1 year post stroke	walking disability with asymmetry	15	64.13 (7.58)	Unknown	40%

Table S2. Physiotherapy Evidence Database quality scale (PEDro scale) for clinical trials.

Author	Study Design	Eligibility criteria specified	Subjects randomly allocated to groups	allocation was concealed	the groups were similar at baseline	there was blinding of all subjects	there was blinding of all therapists who administered therapy	there was blinding of assessors	measures of at least 1 key outcome obtained from >85% of subjects	all subjects received allocated treatment or control, or "intent to treat" analysis	the results of between group statistical comparisons are reported	the study provides both point measures and measure of variability	Total
Ada 2013[1]	Randomized Control Trial	1	1	0	0	0	0	0	1	1	1	1	6
Awad 2016[2]	Randomized Control Trial	1	1	0	1	0	0	1	1	1	0	1	7
Batcho 2013[3]	Single Group Cohort	1	0	0	0	0	0	0	1	1	0	1	4
Billinger 2012[4]	Single Group Pre-Post	1	0	0	0	0	0	0	1	1	0	1	4
Calmels 2011[5]	Single Group Pre-Post	1	0	0	0	0	0	0	1	0	0	1	3
Danks 2016[6]	Randomized Control Trial	1	1	0	1	0	0	1	1	1	1	1	8
Globas 2012[7]	Randomized Control Trial	1	1	1	1	0	0	0	1	0	1	1	7
Gordon 2013[8]	Randomized Control Trial	1	1	0	1	0	0	1	1	1	1	1	8
Kluding 2011[9]	Single Group Pre-Post	1	0	0	0	0	0	0	1	1	0	1	4
Lamberti 2017[10]	Randomized Control Trial	1	1	1	1	0	0	0	1	1	1	1	8
Lee 2008[11]	Randomized Control Trial	1	1	1	1	0	0	1	1	1	1	1	9
Munari 2018[12]	Multi-Group Pre-Post	1	0	1	1	0	0	1	1	1	0	1	7
Olney 2016[13]	Randomized Control Trial	1	1	1	0	0	0	0	1	1	1	1	7
Sandberg 2016[14]	Randomized Control Trial	1	1	1	1	0	0	0	1	1	1	1	8
Severinsen 2014[15]	Randomized Control Trial	1	1	1	1	0	0	0	1	1	1	1	8
Tanne 2008[16]	Single Group Pre-Post	1	0	0	1	0	0	0	1	0	1	1	5
Texeira-salmela 1999[17]	Randomized Wait-List Design with combined results	1	0	0	0	0	0	1	1	0	0	1	4
Vanroy 2017[18]	Randomized Control Trial	1	1	1	1	0	0	1	1	1	1	1	9
Yang 2007[19]	Single Group Pre-Post	1	0	0	0	0	0	0	1	1	0	1	4

Supplemental References:

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