

Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bjsports-2014-094465>)

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Received 27 November 2014

Revised 6 March 2015

Accepted 15 May 2015

Published Online First

2 June 2015

ABSTRACT

Objectives To determine the effect of structured exercise on overall mobility in people after hip fracture. To explore associations between trial-level characteristics and overall mobility.

Design Systematic review, meta-analysis and meta-regression.

Data sources MEDLINE, EMBASE, CINAHL, the Cochrane Central Register of Controlled Trials, the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register and the Physiotherapy Evidence Database to May 2014.

Study eligibility criteria, participants and interventions

Randomised controlled trials of structured exercise, which aimed to improve mobility compared with a control intervention in adult participants after surgery for hip fracture were included.

Data extraction and synthesis Data were extracted by one investigator and checked by an independent investigator. Standardised mean differences (SMD) of overall mobility were meta-analysed using random effects models. Random effects meta-regression was used to explore associations between trial-level characteristics and overall mobility.

Results 13 trials included in the meta-analysis involved 1903 participants. The pooled Hedges' g SMD for overall mobility was 0.35 (95% CI 0.12 to 0.58, $p=0.002$) in favour of the intervention. Meta-regression showed greater treatment effects in trials that included progressive resistance exercise (change in SMD=0.58, 95% CI 0.17 to 0.98, $p=0.008$, adjusted $R^2=60\%$) and delivered interventions in settings other than hospital alone (change in SMD=0.50, 95% CI 0.08 to 0.93, $p=0.024$, adjusted $R^2=49\%$).

Conclusions and implications Structured exercise produced small improvements on overall mobility after hip fracture. Interventions that included progressive resistance training and were delivered in other settings were more effective, although the latter may have been confounded by duration of interventions.

INTRODUCTION

Hip fractures are one of the most common and severe forms of injury in older people.^{1 2} Most hip fractures are treated surgically and the post-operative recovery of physical function is poor. Only 30% of people regain prefracture physical function^{2 3} and many are left with impaired mobility, loss of physical independence and require long-term care.^{2 4}

Rehabilitation after hip fracture aims to improve mobility, maximise physical function and prevent or reverse physical deconditioning. Structured exercise⁵ improves fracture healing,⁶ enhances muscle

strength and coordination and consequently improves mobility, functional status and quality of life. Mobilisation as a form of structured exercise is a major component of rehabilitation after hip fracture. The UK National Institute for Health Care Excellence (NICE) 2011 clinical guidelines on the management of hip fracture in adults⁷ recommend early mobilisation with a physiotherapist to improve transfer ability,⁸ and mobilisation at least once a day to improve strength.^{9–11} Meta-analysis of outcomes on strength was not conducted due to concerns of heterogeneity between trials. The expert opinion of the Guideline Development Committee was that patients would benefit from more intensive rehabilitation therapy and ongoing structured exercise, but the Committee acknowledged there was a paucity of evidence to support this recommendation.

It is not known whether and to what extent exercise improves overall mobility after hip fracture in adults, nor is it clear what characteristics of interventions are associated with improved overall mobility. A Cochrane systematic review (initially reported in 2000¹² and most recently updated in 2011¹³) reported inconsistent effects of different exercise interventions on mobility after hip fracture. For example, single trials reported improved mobility after 2 weeks of weight-bearing exercise and quadriceps muscle strengthening, but no improvement after treadmill gait retraining, or 12 weeks of resistance training or 16 weeks of weight-bearing exercise. Meta-analysis was not conducted due to concerns of heterogeneity between trials. The limited use of meta-analysis in previous reviews of exercise after hip fracture precludes overall conclusions on the impact of structured exercise on mobility. However, if the aim of a study is to address a broader research question than the questions addressed by individual trials, meta-analysis with random effects models can be used to account for between-trial heterogeneity when combining trials with broadly similar interventions,^{14 15} and meta-regression can be used to examine whether trial-level characteristics explain heterogeneity of treatment effects between trials.¹⁶

This study aimed to provide broad conclusions about the impact of structured exercise on mobility after hip fracture in order to guide medical and physiotherapy clinical practice in rehabilitation. Specifically, this study aimed to determine (1) the effect of structured exercise on overall mobility (primary outcome) and particular aspects of mobility (secondary outcomes) in people after hip fracture, and (2) to explore the association between trial-level characteristics and effects of interventions on overall mobility.



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To cite: Diong J, Allen N, Sherrington C. *Br J Sports Med* 2016;**50**:346–355.

METHODS

Protocol

This systematic review and meta-analysis is reported according to the PRISMA statement¹⁷ and the protocol is available (see online supplementary appendix 1).

Eligibility criteria

All randomised controlled trials of structured exercise (such as mobilisation, physical training, resistance training, fitness training, etc) which aimed to improve mobility compared to a control intervention in adult participants after surgery for hip fracture were included. Trials in which interventions did not specifically aim to improve mobility, and trials investigating muscle stimulation or passive management strategies, and other multifactorial interventions were excluded. A multifactorial intervention was considered to be an intervention comprised of a number of components in which the treatment effect of structured exercise alone could not be isolated.

Information sources

This study assessed the trials identified in Handoll *et al*¹³ for eligibility and updated the search strategy used in that review. The following electronic databases were searched in May 2014: MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials. Since the review by Handoll *et al*, the database CINAHL changed platforms from OVID WEB to EBSCO, therefore search strategies for CINAHL were updated for searching on the EBSCO platform. In addition, the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register and the Physiotherapy Evidence Database (PEDro; <http://www.pedro.org.au/>) were searched.

Electronic search strategies

Search strategies for MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials databases are available (see online supplementary appendix 2). In general, searches included the following terms: (hip fracture) AND (gait OR movement OR locomotion OR mobilisation OR physiotherapy OR exercise OR rehabilitation OR early ambulation).

Trial selection

One investigator (JD) screened titles and abstracts of records retrieved by the searches. Relevant records were retrieved from database searches and duplicates removed (figure 1). For the updated search, titles and abstracts from 2010 onwards were screened for eligibility in May 2014. Full-text articles were retrieved if it was ambiguous from titles or abstracts whether or not the trial met the inclusion criteria. Trials included in the review by Handoll *et al*¹³ were screened for eligibility. All trials that fulfilled eligibility criteria were selected for inclusion in the systematic review. Trial selection was confirmed by consensus between investigators (JD, CS and NA).

Primary outcome

The primary outcome for this study was mobility, defined broadly as any measure of overall mobility (ie, the ability to walk, move around and change or maintain body position; International Classification of Functioning, Disability and Health codes d410–429 and d450–469). If a trial reported multiple measures of mobility, the most composite measure of mobility measured by a multidimensional instrument was chosen a priori as the primary outcome measure (eg, the

modified Physical Performance Test was chosen in preference to fast walking speed as the primary outcome measure of mobility).¹⁸

Secondary outcomes

Secondary outcomes for this study were categorised into specific and composite measures of mobility and associated outcomes were subcategorised. Separate analyses were conducted on each of the subcategories. The secondary outcomes were:

Specific measures

1. Mobility tasks
 - A. Sit-to-stand
 - B. Gait speed
 - C. Stair climb ability or step force generation
2. Balance tasks
 - A. Outcomes measuring a narrowing of base of support
 - B. Outcomes measuring the control of the body in space
 - C. Step tests
3. Self-reported measures of functioning
 - A. Activities of daily living
 - B. Quality of life
 - C. Self-reported mobility

Composite measures

1. General mobility
 - A. Timed up and go
 - B. Walking ability (eg, independent mobility on flat ground or up one step)
2. Mobility scales
 - A. Berg Balance Scale
 - B. Physical Performance Test

Data extraction

Where available, trial estimates of effect sizes for primary and secondary outcomes comparing treated and control participants at the first specified postintervention follow-up time point were extracted for meta-analysis. Data on effect sizes and trial-level characteristics from each included trial were extracted by one investigator (JD) and independently checked by another investigator (NA). Differences were resolved by consensus between investigators (JD, CS and NA).

Risk of bias within trials

The PEDro scale score^{19 20} was used as a combined measure of risk of bias and the methodological quality of individual trials. PEDro scores are reported in the Results (table 1).

Principal summary measures

Estimates of effect sizes from each trial were entered into Comprehensive Meta-Analysis (CMA V.2, Biostat, Englewood, New Jersey, USA) and the data were used to compute Hedges' g standardised mean differences^{14 15} to standardise results of studies using different outcome measures to a uniform scale.

Synthesis of results

Data on primary and secondary mobility outcomes from comparable groups of trials were pooled using the *metan* command in Stata V.13 (Stata Corp., College Station, Texas, USA). Random and fixed effects models were used to compute pooled standardised mean differences and 95% CIs. Interpretations of effect sizes were based on suggestions by Cohen:^{21 22} an effect size of 0.2 is small, 0.5 is medium and 0.8 is large. Forest plots from random and fixed effects models were generated, visually inspected and compared for differences in magnitude and direction of effect estimates, especially if corresponding standardised

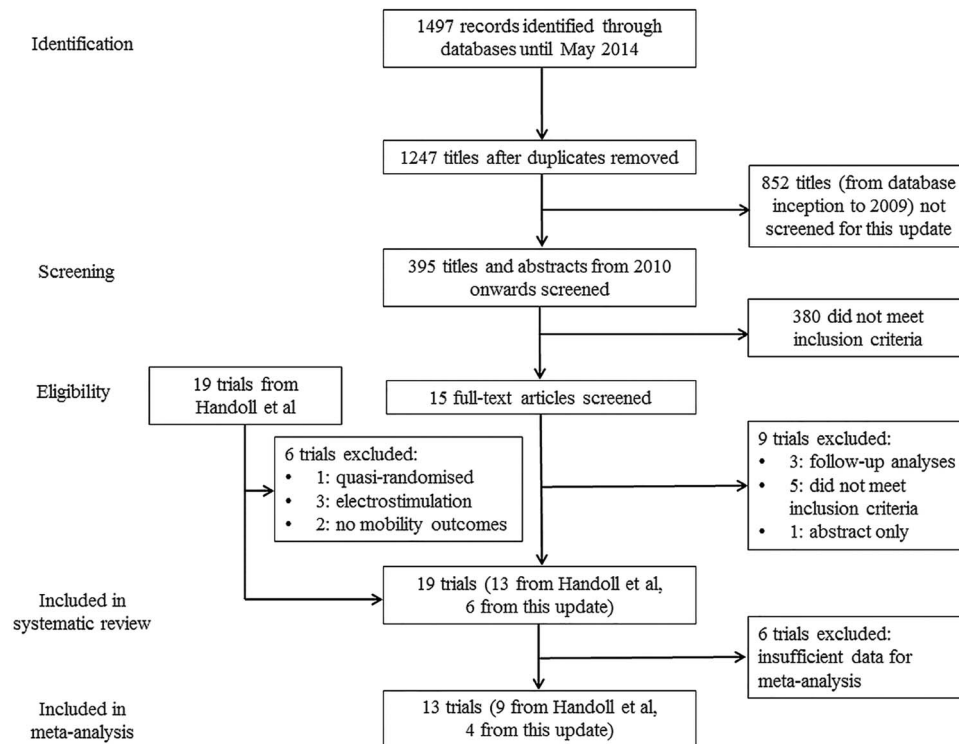


Figure 1 PRISMA statement¹⁷ flow diagram.

mean differences and 95% CI appeared different. Differences in appearance of forest plots and estimates of effects from random and fixed effects models were reported. Random effects estimates were reported for all outcomes. Fixed effects estimates were reported for the primary outcome, and for secondary outcomes where fixed and random effects estimates differed. Between-trial heterogeneity and consistency were assessed with the I^2 statistic, Q statistic, degrees of freedom and p value.^{14 23} A sensitivity analysis was conducted on meta-analysis of the primary outcome to determine the effect of excluding trials that used self-reported versus performance-based measures of mobility.

Where data on secondary mobility outcomes were measured using the same outcome measure, differences in means and 95% CI in units of the outcome measure were also calculated. The computation of differences in means and SEs from pre-intervention and post-intervention scores requires specification of the correlation between pre-intervention and post-intervention scores. This correlation ($r=0.65$) was calculated as the mean of correlations between pre-intervention and post-intervention data in treated and control participants, using data on the 6 min walk test from the trial by Sylliaas *et al*,²⁴ as recommended in the Cochrane Handbook.¹⁵ The correlation was applied in CMA to compute differences in means and 95% CI.

Small sample bias between trials

Funnel plots of SEs on standardised mean differences were visually inspected for indication of small sample bias, and the Egger test and 95% CI for funnel plot asymmetry were calculated using the *metabias* command in Stata. A high risk of small sample bias was considered to be present if distribution of points about the central value in the funnel plot (the fixed effect summary estimate) was asymmetrical and the Egger test was positive.

Additional analyses

Random effects meta-regression was used to examine whether trial-level covariates (ie, possible 'effect modifiers') explained heterogeneity of treatment effects between trials.¹⁶ Univariate meta-regressions were conducted using the *metareg* command in Stata. The effect of a 1 unit change of each trial-level characteristic on change in standardised mean difference, and the proportion of between-trial variability explained by the model containing each characteristic were reported.²⁵ The explained variability (ie, the adjusted R^2) for each model was calculated from the between-trial variance τ^2 and can take a negative value if the covariate explains less of the variability than expected by chance.²⁵ The *lincom* command was used to compute the effect of a 1 unit increase in each trial-level characteristic variable on improvement in standardised mean difference of the primary mobility outcome. It was not possible to explore the effects of some characteristics of the sample (eg, time since hip fracture, baseline functional ability) because these data were poorly reported or quantified using different outcomes. Trial-level characteristics and the methods used to analyse them were:

1. Trial quality

Methodological quality of trials was assessed using PEDro scale scores. The effect of trial quality on primary mobility outcomes was analysed as a continuous variable.

2. Characteristics of the intervention

A. Dose of intervention

Dose of intervention was analysed as a continuous variable and was measured by total number of hours of intervention from the product of duration (weeks), frequency (sessions per week) and session time (hours). If interventions were carried out on a daily basis, it was assumed that interventions were delivered 7 days per week unless otherwise stated. If a range of intervention times was reported, the mean of the session times was used.

Table 1 Characteristics of included trials

Study	Setting	Sample size	PEDro	Primary outcome*	Characteristics of intervention
Binder <i>et al</i> ^{18†}	H&C	90	7	Modified PPT	High-intensity progressive resistance
Bischoff-Ferrari <i>et al</i> ³⁴	H	173	6	Timed up and go	High-intensity physiotherapy
Hauer <i>et al</i> ^{9†}	H&C	28	6	Tinetti's POMA	High-intensity progressive resistance
Latham <i>et al</i> ^{35†}	H&C	232	6	SPPB	Home based exercise
Lauridsen <i>et al</i> ³⁶	H	88	6	Intervention time	High-intensity physiotherapy
Mangione <i>et al</i> ^{31†}	C	41	5	6 min walk distance	Resistance or aerobic exercise
Mangione <i>et al</i> ^{37†}	C	26	7	6 min walk distance	Home based resistance
Miller <i>et al</i> ³⁸	H	100	8	Gait speed	Resistance only or resistance and nutrition‡
Mitchell <i>et al</i> ³⁹	H	80	5	Elderly Mobility Scale	High-intensity progressive resistance
Moseley <i>et al</i> ^{10†}	H	160	8	PPME	High-intensity weight-bearing
Oldmeadow <i>et al</i> ⁸	H	60	6	Walking distance	Early weight-bearing (within 48 h)
Orwig <i>et al</i> ⁴⁰	H	180	6	6 min walk distance	Home-based exercise
Resnick <i>et al</i> ^{33†}	H	208	6	Self-efficacy WES	Exercise plus or Exercise only‡
Sherrington and Lord ^{41†}	C	42	5	Gait velocity	Weight-bearing
Sherrington <i>et al</i> ^{42†}	H	80	7	PPME	Weight-bearing
Sherrington <i>et al</i> ^{32†}	H	120	7	6 m walk time	Weight-bearing or non-weight-bearing
Sylliaas <i>et al</i> ^{24†}	C	150	8	6 min walk distance	Progressive resistance
Sylliaas <i>et al</i> ^{43†}	C	95	8	6 min walk distance	Prolonged resistance
Tsauo <i>et al</i> ^{44†}	C	54	4	Walking speed	Home-based physiotherapy

Study	Comparator	Dose (hour)	Supervised	Group exercise	Balance	Progressive resistance	Follow-up (week)
Binder <i>et al</i> ^{18†}	Low-intensity non-progressive	81	Y	Y	Y	Y	24
Bischoff-Ferrari <i>et al</i> ³⁴	Standard physiotherapy		N	N	Y	N	24
Hauer <i>et al</i> ^{9†}	Placebo motor activity	36	Y	Y	Y	Y	12
Latham <i>et al</i> ^{35†}	Attention control	72	Y	N	Y	N	24
Lauridsen <i>et al</i> ³⁶	Standard physiotherapy		Y	N	Y	N	
Mangione <i>et al</i> ^{31†}	Education	12	Y	N	N	Y	12
Mangione <i>et al</i> ^{37†}	Attention control	12	Y	N	N	Y	10
Miller <i>et al</i> ³⁸	Education	15	Y	N	N	N	12
Mitchell <i>et al</i> ³⁹	Usual care	6	Y	N	N	N	6
Moseley <i>et al</i> ^{10†}	Usual care	112	Y	N	Y	N	16
Oldmeadow <i>et al</i> ⁸	Delayed weight-bearing		Y	N	N	N	1
Orwig <i>et al</i> ⁴⁰	Usual care	130	N	N	Y	N	8
Resnick <i>et al</i> ^{33†}	Usual care	9	Y	N	N	N	8
Sherrington <i>et al</i> ^{41†}	Usual care	14	N	N	Y	N	4
Sherrington <i>et al</i> ^{42†}	NWB	8	Y	N	Y	N	2
Sherrington <i>et al</i> ^{32†}	No intervention	60	N	N	Y	N	16
Sylliaas <i>et al</i> ^{24†}	No intervention	32	Y	Y	N	Y	12
Sylliaas <i>et al</i> ^{43†}	No intervention	53	Y	Y	N	Y	12
Tsauo <i>et al</i> ^{44†}	Bedside exercise	30	N	N	N	N	12

*Data on any measure of overall mobility in each trial were extracted as the primary outcome of mobility in this study.

†Denotes studies included in meta-analysis.

‡Only two of three comparison groups examined exercise interventions.

C, community only; H&C, hospital and community; H, hospital only; Modified PPT, modified Physical Performance Test; N, no; PPME, Physical Performance Mobility Examination; Self-efficacy WES, Self-efficacy for Walking Exercise Scale; SPPB, Short Physical Performance Battery; Tinetti's POMA, Tinetti's Performance Oriented Mobility Assessment; Y, yes.

B. Supervised exercise

Interventions that were supervised or unsupervised were analysed as a dichotomous variable. Interventions were regarded to be supervised if at least 50% of the intervention time was supervised.

C. Balance component

Interventions that did or did not include a component that challenged balance were analysed as a dichotomous variable. Components of interventions that challenged balance included exercises delivered in standing in which people aimed to decrease the base of support or minimise use of their hands to assist.

D. Progressive resistance component

Interventions that did or did not include strengthening exercises based on principles of progressive resistance training and muscle overloading were analysed as a dichotomous variable.

3. Characteristics of the sample

A. Mean age

Mean age of participants at recruitment in years was analysed as a continuous variable.

B. Setting of intervention

Setting of the intervention was analysed as a dichotomous variable comparing interventions delivered only in hospital with interventions delivered in other settings (mixed hospital and community, or only community).

RESULTS

Trial selection and characteristics

Database searches yielded 395 trials of which 15 were potentially appropriate for inclusion in the meta-analysis (figure 1).¹⁷ Of these, 9 trials were excluded (3 were follow-up analyses of previously published trial data, 5 failed to meet inclusion criteria, 1 was a published abstract) yielding 6 trials for inclusion in the systematic review. Of the 19 trials included in the review by Handoll *et al*,¹³ 6 were excluded (1 was quasi-randomised,²⁶ 3 investigated electrostimulation,^{27–29} 2 had no relevant mobility outcomes: outcomes were measures of mortality³⁰ or comparisons of walking ability between surgical interventions¹¹) yielding 13 trials for inclusion in the systematic review. The trials excluded by Handoll *et al* were also screened and none met the inclusion criteria for this review. Of the 19 trials included in this systematic review, 6 could not be included in the meta-analysis as data were insufficient for pooling, so 13 trials were included in the meta-analysis. Two trials had 2 intervention groups^{31 32} and 1 trial had 3 intervention groups of which only 2 groups examined exercise interventions,³³ consequently the 13 included trials yielded 16 comparisons and estimates of effects of structured exercise.

Characteristics of all 19 trials included in the systematic review are summarised (table 1). The 13 trials included in the meta-analysis involved a total of 1903 participants. Most trials demonstrated moderate to high study quality (table 1): the mean (SD) PEDro score was 6 (1). The mean (SD) dose of intervention across trials was 37 (31) hours, average follow-up time period was 12 (6) weeks, and average participant age was 80 (2) years. The trials examined overlapping combinations of structured exercise interventions (table 1): 5 trials examined high

intensity exercise (3 trials high intensity progressive resistance, 2 trials high intensity physiotherapy), 4 trials examined home based exercise (3 trials home based, 1 trial home based resistance), 5 trials examined weight-bearing exercise (3 trials weight-bearing, 1 trial early weight-bearing, 1 trial high intensity weight-bearing), 2 trials focused on resistance exercise (1 trial progressive resistance, 1 trial prolonged resistance), and 3 trials examined a combination of interventions (1 trial resistance or aerobic, 1 trial nutrition and resistance or resistance only, 1 trial exercise and motivation or exercise only). Interventions were supervised in 10 trials, contained a balance component in 7 trials, and contained a progressive resistance component in 6 trials. Interventions in 5 trials were delivered to participants only in hospital while interventions in 9 trials were delivered to participants in other settings (mixed hospital and community, or only community). One trial reported mobility outcomes using only self-reported measures³³ and the other trials used performance-based measures or a combination of both.

Meta-analysis of primary outcome

Structured exercise significantly improved mobility after hip fracture (random effects Hedges' g standardised mean difference=0.35, 95% CI 0.12 to 0.58, $p=0.002$, figure 2). There was a moderate to high level of heterogeneity in estimates of effects ($I^2=67\%$, $Q=45.0$, $df=15$, $p<0.001$). There was no conclusive evidence of small sample bias between trials (Egger's test=0.61, 95% CI -0.05 to 1.28, $p=0.066$, significance test of no small study effects: $p=0.45$, and the funnel plot of SE and Hedges' g appeared symmetrical). Fixed effects meta-analysis demonstrated a similar main effect in the same direction (fixed effects Hedges' g standardised mean difference=0.39, 95% CI

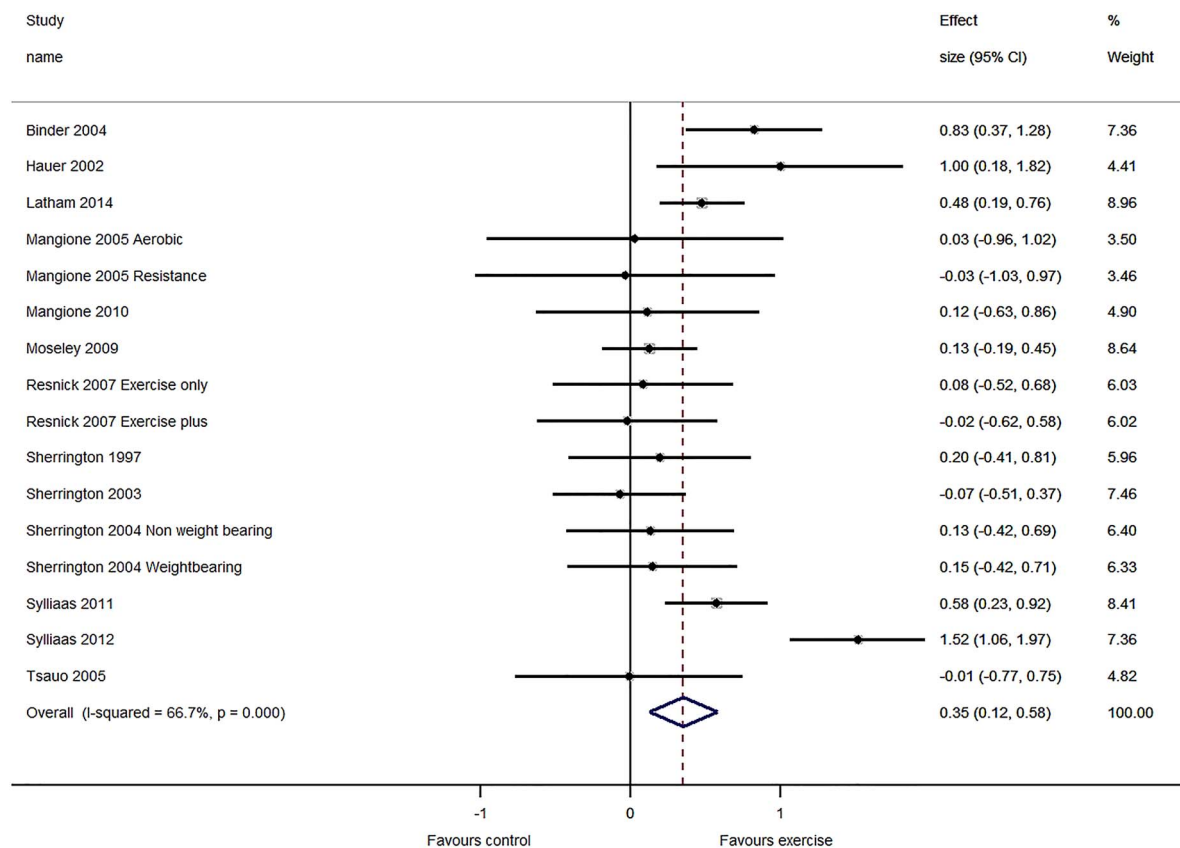


Figure 2 Forest plot of effect of structured exercise on the primary outcome of mobility after hip fracture determined by random effects meta-analysis. Effect sizes are indicated as Hedges' g standardised mean differences and 95% CI.

Review

Table 2 The impact of trial-level characteristics (involving 16 comparisons for each characteristic) on effects of structured exercise on mobility after hip fracture, determined by meta-regression

Characteristic	Change in standardised mean difference (95% CI)	p Value	Adjusted R ² (%)†
Study quality (PEDro score)	0.16 (−0.06 to 0.38)	0.14	11
Dose of intervention (hour)	0 (0 to 0.01)	0.28	−2
Supervision‡	0.30 (−0.30 to 0.89)	0.30	3
Balance component‡	−0.04 (−0.57 to 0.48)	0.87	−9
Progressive resistance‡	0.58 (0.17 to 0.98)	0.008*	60
Average participant age (year)	0.05 (−0.06 to 0.16)	0.32	−3
Setting of intervention§	0.50 (0.08 to 0.93)	0.024*	49

*p<0.05.

†The proportion of between-trial variability (ie, the adjusted R² calculated from the between-trial variance, τ^2)²⁵ explained by the univariate model containing this characteristic.

‡Whether interventions were supervised, or included a balance or progressive resistance component were analysed as dichotomous variables.

§Setting of intervention was analysed to compare interventions conducted only in hospital with interventions conducted in other settings (mixed hospital and community, or only community). These data show physical interventions conducted in other settings are more effective compared to interventions conducted only in hospital.

0.27 to 0.51, p<0.001). Sensitivity analysis also showed similar effects when the meta-analysis was conducted without the trial that used self-reported measures of mobility (standardised mean difference only of performance-based measures=0.39, 95% CI 0.15 to 0.64, 14 comparisons).

Meta-regression

The effect of a 1 unit change of each trial-level characteristic on change in standardised mean difference, and the proportion of between-trial variability explained by univariate models for each characteristic are summarised (table 2). Interventions that included a progressive resistance component, and interventions that were delivered in other settings were significantly associated with higher standardised mean differences in favour of the intervention, and these characteristics explained the greatest variability of changes in standardised mean differences (adjusted R²=60% and 49% respectively, table 2). The effect of including a progressive resistance component in the intervention, compared to interventions without a progressive resistance component, increased the standardised mean difference from 0.15 to 0.72 (change in standardised mean difference=0.58, 95% CI 0.17 to 0.98, p=0.008, adjusted R²=60%). The effect of delivering interventions in other settings, compared to delivering

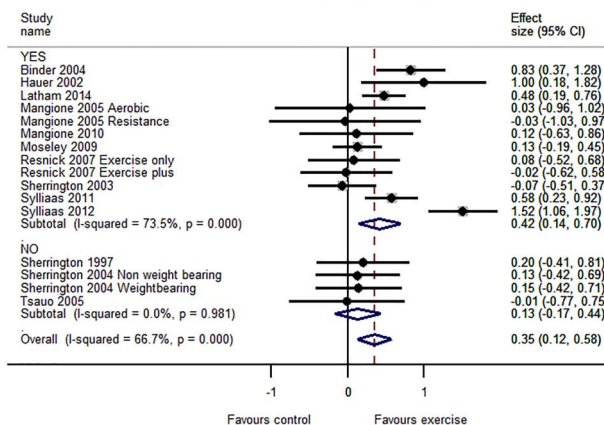
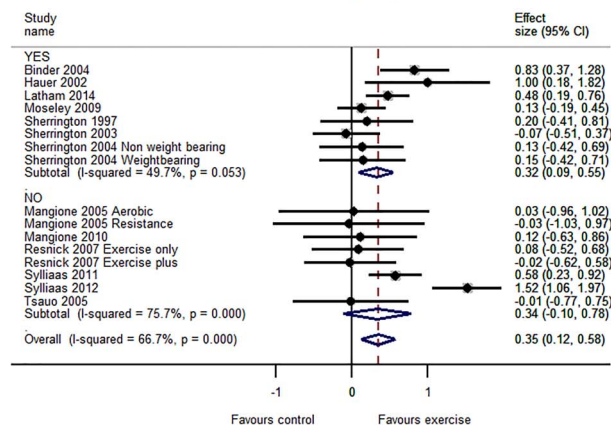
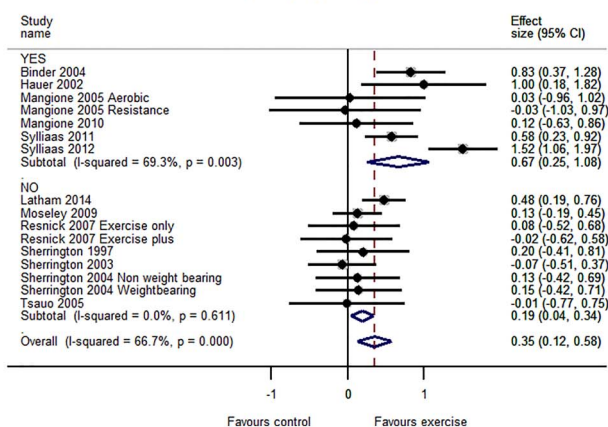
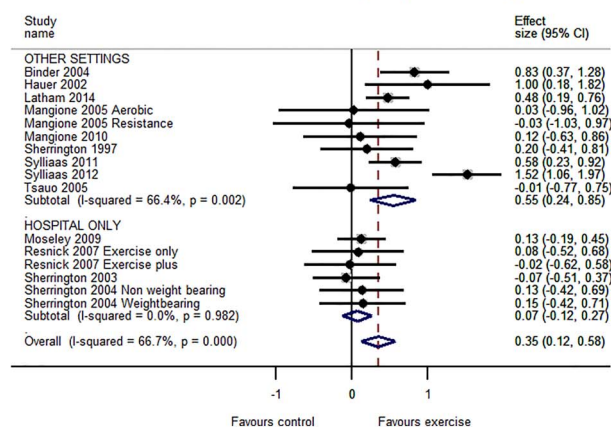
A Effect on mobility by supervision**B Effect on mobility by balance****C Effect on mobility by progressive resistance****D Effect on mobility by setting**

Figure 3 Forest plots of effects of trial-level characteristics of structured exercise analysed as dichotomous variables, on the primary outcome of mobility after hip fracture: (A) supervision of exercise, (B) inclusion of balance component, (C) inclusion of progressive resistance component and (D) setting of intervention (ie, whether interventions were conducted only in hospital or in other settings). Effect sizes are indicated as Hedges' g standardised mean differences and 95% CI. Changes in standardised mean differences by trial-level characteristics and 95% CI were estimated using meta-regression (table 2).

interventions only in hospital, increased the standardised mean difference from 0.07 to 0.57 (change in standardised mean difference=0.50, 95% CI 0.08 to 0.93, $p=0.024$, adjusted $R^2=49\%$). No other trial-level characteristics were significantly associated with changes in standardised mean differences. Sensitivity analyses conducted by excluding the strong, favourable effect in the trial by Sylliaas *et al*⁴³ did not substantially change the magnitudes or directions of estimates of effects (data not shown). Forest plots of effects of trial-level characteristics analysed as dichotomous variables (figure 3) and graphs of effects of trial-level characteristics analysed as continuous variables (figure 4) on the primary mobility outcome are shown.

Meta-analysis of secondary outcomes

Pooled standardised mean differences of effects of structured exercise on secondary outcomes of mobility after hip fractures are summarised (table 3). Structured exercise significantly improved gait speed, activities of daily living, self-reported mobility, Timed up and go and the Berg Balance Scale measures (table 3, figure 5). Fewer trials were included in meta-analysis of each secondary outcome (range 2–8 trials, figure 5) compared to the number of trials in meta-analysis of the primary outcome. Since data on gait speed, Timed up and go and the Berg Balance Scale were measured using the same outcome measure across trials, differences in means of the raw scores were also provided for these outcomes (table 3). Forest plots of effects of interventions on all secondary outcomes with effect sizes in standardised mean differences are available (see online supplementary figures 1–5). Standardised mean differences from random and fixed effects models were appeared different for the following outcomes: sit-to-stand (random 0.63, 95% CI –0.71 to 1.98, $p=0.35$; fixed 0.29, 95% CI –0.11 to 0.68, $p=0.16$; 2 comparisons), Timed up and go (random 2.50, 95% CI 0.04 to 4.95, $p=0.046$; fixed 1.62, 95% CI 1.32 to 1.93, $p<0.001$; 3 comparisons) and the Berg Balance Scale (random 1.01, 95% CI 0.23 to 1.80, $p=0.012$; fixed 0.74, 95% CI 0.56 to 0.93, $p<0.001$; 4 comparisons). Inspection of forest plots for these outcomes suggests the fixed effect sizes were more susceptible to influence by higher weights attributed to one or two large trials in the meta-analysis since only a few trials were included in meta-analyses of these outcomes (forest plots from random effects models for these outcomes shown in online supplementary figures 1, 4 and 5).

DISCUSSION

This systematic review and meta-analysis provides good evidence that structured exercise produces significant but relatively small improvements in overall mobility after hip fracture. In particular, univariate meta-regression showed the inclusion of progressive resistance training (compared to interventions that did not include progressive resistance training), and interventions delivered in other settings (compared to interventions delivered only in hospital) were associated with greater efficacy. Meta-analysis of secondary outcomes suggests structured exercise also improves aspects of mobility.

To the best of our knowledge this is the first meta-analysis of the overall impact of structured exercise on mobility after hip fracture. The improvements in overall mobility after hip fracture observed are broadly consistent with findings from other systematic reviews reporting favourable effects of physical fitness training on mobility and balance following stroke,⁴⁵ and effects of physical rehabilitation on mobility in older people in long-term care.⁴⁶

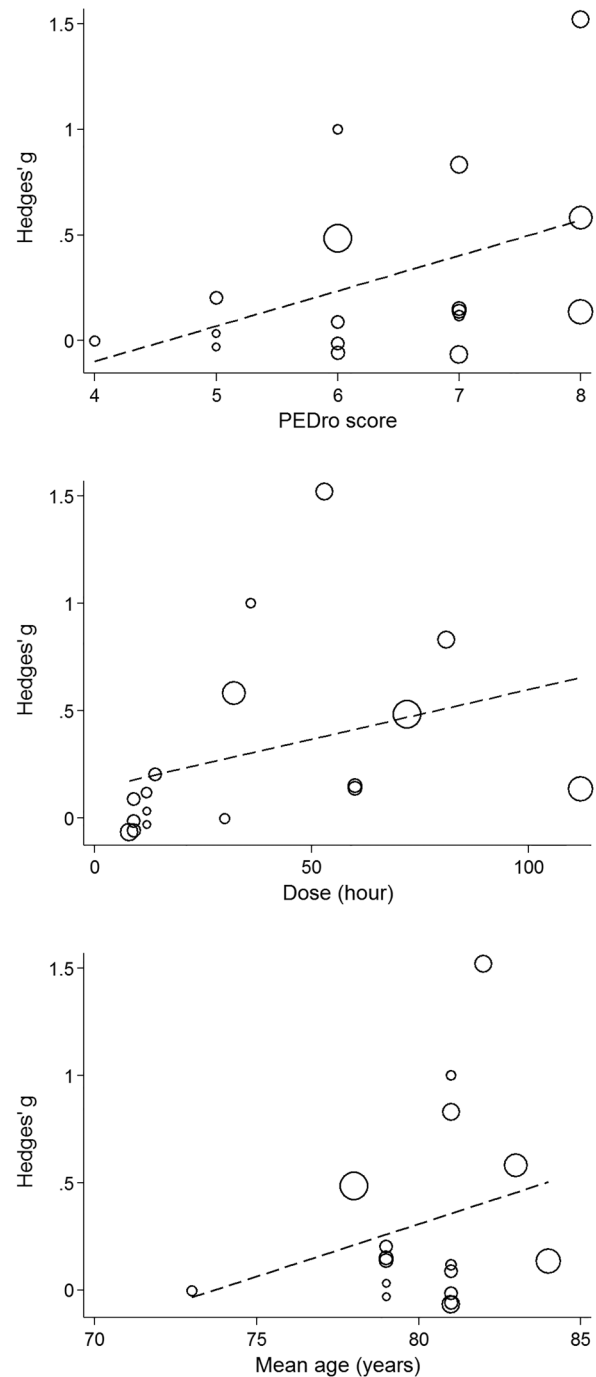


Figure 4 Graphs of effects of trial-level characteristics of structured exercise analysed as continuous variables, on the primary outcome of mobility after hip fracture: study quality measured using PEDro scale scores (panel 1), dose of intervention (panel 2), mean age of participants (panel 3). Effect sizes are indicated as Hedges' g standardised mean differences. The area of each circle is proportional to the inverse of the within-trial SE. Slopes of changes in standardised mean differences as trial-level characteristics changed and 95% CI were estimated using meta-regression (table 2).

Progressive resistance training

The inclusion of progressive resistance training in structured exercise programmes for people after hip fracture appears to be important. Structured exercise interventions that included components of progressive resistance training were significantly associated with greater improvements in mobility (compared to

Table 3 Estimates of Hedges' g standardised mean differences and 95% CI of effects of structured exercise on secondary outcomes, categorised into specific and composite measures

Theme	Subtheme	Study	Standardised mean difference (95% CI)	p Value	I ² (%)	Q statistic, df, p Value
Specific measures						
Mobility tasks	Sit-to-stand	Hauer <i>et al</i> ⁹ Sherrington <i>et al</i> ⁴²	0.63 (−0.71 to 1.98)	0.35	87	7.7, 1, 0.006
	Gait speed	Binder <i>et al</i> ¹⁸ Hauer <i>et al</i> ⁹ Mangione <i>et al</i> ³¹ Aerobic Mangione <i>et al</i> ³¹ Resistance Mangione <i>et al</i> ³⁷ Moseley <i>et al</i> ¹⁰ Sherrington <i>et al</i> ⁴² Sylliaas <i>et al</i> ²⁴ Sylliaas <i>et al</i> ⁴³	0.24 (0.06 to 0.42) Difference in means: 0.07 (0.01 to 0.14) metres per second	0.010* 0.018*	17 49	9.6, 8, 0.30 15.8, 8, 0.05
Balance tasks	Stair climb or step force generation	Hauer <i>et al</i> ⁹ Sherrington <i>et al</i> ⁴²	0.10 (−0.91 to 1.12)	0.85	78	4.6, 1, 0.032
	Narrowing base of support Controlling body in space	Hauer <i>et al</i> ⁹ Sherrington <i>et al</i> ³² NWB Sherrington <i>et al</i> ³² WB	1.03 (0.21 to 1.86) 0.31 (−0.09 to 0.71)	0.014 0.13	NA 0	NA 0.7, 1, 0.40
Self-reported measures of functioning	Step tests	Sherrington and Lord ⁴¹	0.46 (−0.24 to 1.16)	0.20	NA	NA
	Activities of daily living	Binder <i>et al</i> ¹⁸ Hauer <i>et al</i> ⁹ Latham <i>et al</i> ²⁵ Moseley <i>et al</i> ¹⁰ Sylliaas <i>et al</i> ²⁴ Sylliaas <i>et al</i> ⁴³	0.24 (0.08 to 0.41)	0.005*	16	5.9, 5, 0.31
	SF36 quality of life	Mangione <i>et al</i> ³¹ Aerobic Mangione <i>et al</i> ³¹ Resistance Mangione <i>et al</i> ³⁷	0.02 (−0.49 to 0.54)	0.93	0	0.9, 2, 0.65
	Self-reported mobility as good	Latham <i>et al</i> ²⁵ Moseley <i>et al</i> ¹⁰	0.31 (0.10 to 0.52)	0.004*	0	0.4, 1, 0.52
Composite measures						
General mobility	Timed up and go	Hauer <i>et al</i> ⁹ Sylliaas <i>et al</i> ²⁴ Sylliaas <i>et al</i> ⁴³	2.50 (0.04 to 4.95) Difference in means: 7 (4 to 10) seconds	0.046* <0.001*	98 69	80.3, 2, <0.001 6.4, 2, 0.041
	Walking ability	Moseley <i>et al</i> ¹⁰ Oldmeadow <i>et al</i> ⁸ Sherrington <i>et al</i> ³² NWB Sherrington <i>et al</i> ³² WB	−0.15 (−0.57 to 0.27)	0.49	65	8.6, 3, 0.035
Mobility scales	Berg Balance Scale	Binder <i>et al</i> ¹⁸ Latham <i>et al</i> ²⁵ Sylliaas <i>et al</i> ²⁴ Sylliaas <i>et al</i> ⁴³	1.01 (0.23 to 1.80) Difference in means: 3 (2 to 4) of 56 points	0.012* <0.001*	94 23	50.3, 3, <0.001 3.9, 3, 0.27
	Physical Performance Test	Mangione <i>et al</i> ³⁷	0.53 (−0.23 to 1.29)	0.17	NA	NA

Differences in means and 95% CI were calculated for gait speed, Timed up and go, and the Berg Balance Scale as these outcomes were measured using the same outcome measure across studies. Heterogeneity is indicated by the I² statistic, Q statistic, degrees of freedom (df) and p value.

*p<0.05 for pooled effect sizes.

NA, not applicable; NWB, non-weight-bearing; WB, weight-bearing.

interventions without progressive resistance training) and explained 60% of variability in effect sizes. Given the heterogeneity across trials, it is possible that some people benefit more from resistance training than others. In the general older population, leg strength is more strongly associated with walking speed in those who are weaker compared to those who are stronger.⁴⁷ There is perhaps a threshold of muscle strength below which strength training is especially useful at enhancing gait speed. There may well be additional benefits of strength training for people who have muscle strength above this threshold, perhaps in building reserve capacity or in the performance of more demanding daily tasks such as stair climbing. The benefits of progressive resistance training after hip fracture are consistent with benefits observed in other groups. Resistance training improved mobility and muscle strength in older nursing home residents who had impaired mobility after 8 weeks of intervention,⁴⁸ and improved physical impairments and

functioning at 3 months in people after hip arthroplasty.^{49 50} Consequently, our findings support the inclusion of progressive resistance training in structured exercise to improve mobility after hip fracture.

Intervention location, duration, timing and dose

It appears that interventions delivered in other settings are associated with greater efficacy compared to interventions delivered only in hospital. However, it is likely this finding was confounded by duration of interventions. It is also possible that people after hip fracture have a greater capacity to improve with delayed exercise interventions after surgery when some recovery has occurred.

None of the other trial-level characteristics significantly influenced effects of interventions. Overall, the trials demonstrated moderate study quality and applied interventions with moderate to high dose of intervention (greater than 30 h on average) in

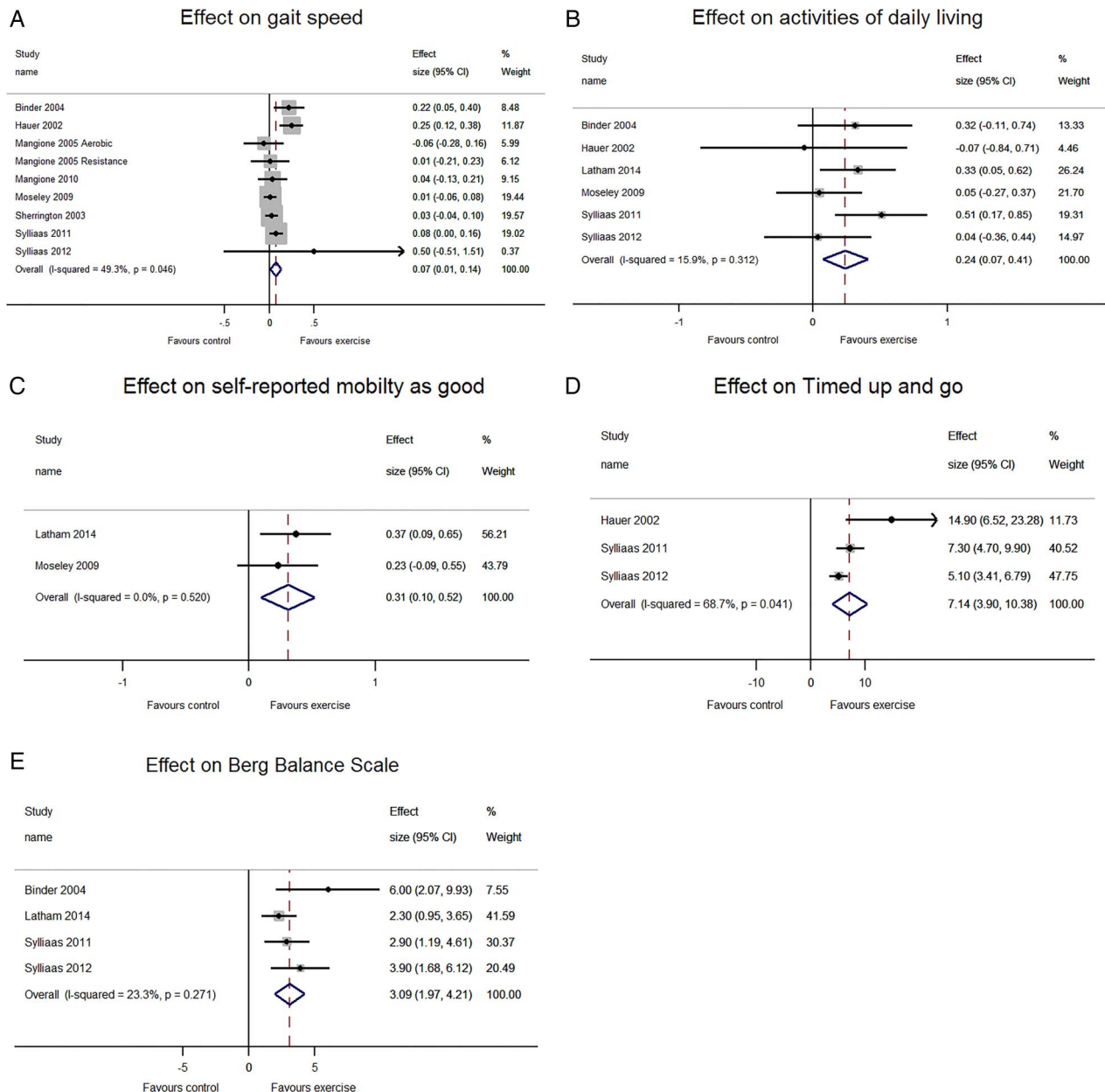


Figure 5 Forest plots of effects of structured exercise on secondary outcomes that improved: (A) gait speed, indicated as difference in means measured in metres per second, (B) activities of daily living, indicated as Hedges' g standardised mean differences, (C) self-reported mobility as good, indicated as Hedges' g standardised mean differences, (D) Timed up and go, indicated as difference in means measured in seconds and (E) Berg Balance Scale, indicated as differences in means measured on a scale of 0 to 56 points.

older people after hip fracture. In meta-regression analyses on falls prevention interventions, trial-level characteristics such as dose of intervention and interventions that challenged balance were associated with more favourable effects of interventions on prevention of falls in older people.^{51 52} The number of studies included in this meta-analysis was relatively small, and so the meta-regression may have lacked power to detect differences in effects of trial-level characteristics on effects of interventions.²⁵ The extent to which trial-level characteristics influence outcomes requires ongoing investigation.

Limitations

This study extends the work by others in the field^{13 53} and provides an overview of the literature to guide clinical practice. However, there are some limitations to this analysis. Meta-

regression analysis describes observational associations across trials because comparisons of trial-level characteristics lack the benefit of randomisation to support causal interpretation of findings. Consequently, associations between trial-level characteristics and effects of interventions are subject to the same limitations as findings from observational studies, such as bias by unmeasured confounding.¹⁶ In addition, the relationship between effect sizes and average participant characteristics across trials may not be the same as the relationship between treatment effects and participant characteristics within trials. For example, a significant association between effect sizes and participant averages may be demonstrated across trials but not within trials, or vice versa—a phenomenon known as 'aggregation bias' or the 'ecological fallacy'.^{16 54} Without individual participant data, aggregation bias cannot be investigated in meta-

Review

regression of trial-level data and so findings from meta-regression analyses need to be interpreted with some caution. Finally, meta-analyses of secondary outcomes suggest structured exercise to improve some aspects of mobility (gait speed, activities of daily living, self-reported mobility, Timed up and go and Berg Balance Scale). However, these findings were obtained from multiple subgroup comparisons based on analyses with much fewer trials and are subject to a higher type I error; so these estimates of effects need to be interpreted with caution.

In summary, this systematic review provides good evidence that structured exercise improves overall mobility after hip fracture. Specifically, clinicians can be confident that greater improvements are possible with progressive resistance training. Such interventions need to be implemented carefully as resistance training in older people could increase the risk of musculoskeletal injury and has been associated with greater reports of pain that interferes with daily tasks.³⁵ Future research would benefit from meta-analysis of combined individual participant data to determine how effects of interventions may change in participants with different characteristics.

What are the new findings?

- ▶ Meta-analyses of randomised controlled trials showed structured exercise produced significant but relatively small improvements in overall mobility after hip fracture.
- ▶ Meta-regression analyses of trial-level characteristics found greater improvements in overall mobility from structured exercise interventions that included progressive resistance training or were delivered in settings other than only in hospital.

How might it impact on clinical practice in the near future?

Clinicians can be confident that greater improvements in overall mobility are possible with progressive resistance training.

Contributors JD and CS created and designed the study. JD conducted the literature search, trial selection and data extraction. NA independently checked the data. Trial selection was achieved by consensus between JD, CS and NA. JD conducted data analysis. JD and CS interpreted the data. JD drafted the manuscript. All authors critically revised the manuscript for intellectual content, discussion of findings and overall conclusions. JD is the guarantor.

Competing interests All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: CS is supported by the National Health and Medical Research Council of Australia.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression

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Br J Sports Med 2016 50: 346-355 originally published online June 2, 2015

doi: 10.1136/bjsports-2014-094465

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Correction: Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression

Diong J, Allen N, Sherrington C. Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression. *Br J Sports Med* 2016;50:346–55. The data reported in table 1, figures 3(D) and 4 were incorrect due to a minor error in the original calculation. The authors apologise for this error. The conclusions of the study remain the same. Corrected figures and table are as shown:

Table 1 Characteristics of included trials

Study	Setting†	Sample size	PEDro	Primary outcome‡	Characteristics of intervention
*Binder 2004 ¹⁸	H&C	90	7	Modified PPT§	High-intensity progressive resistance
Bischoff-Ferrari 2010 ³⁴	H	173	6	Timed up and go	High-intensity physiotherapy
*Hauer 2002 ⁹	H&C	28	6	Tinetti's POMA	High-intensity progressive resistance
*Latham 2014 ³⁵	H&C	232	6	SPPB¶	Home based exercise
Lauridsen 2002 ³⁶	H	88	6	Intervention time	High-intensity physiotherapy
*Mangione 2005 ³¹	C	41	5	6 minute walk distance	Resistance or aerobic exercise
*Mangione 2010 ³⁷	C	26	7	6 minute walk distance	Home based resistance
Miller 2006 ³⁸	H	100	8	Gait speed	Resistance only or resistance and nutrition**
Mitchell 2001 ³⁹	H	80	5	Elderly Mobility Scale	High-intensity progressive resistance
*Moseley 2009 ¹⁰	H	160	8	PPME‡	High-intensity weight-bearing
Oldmeadow 2006 ⁸	H	60	6	Walking distance	Early weight-bearing (within 48 hrs)
Orwig 2011 ⁴⁰	H	180	6	6 minute walk distance	Home based exercise
*Resnick 2007 ³³	H	208	6	Self-efficacy WES#	Exercise plus or Exercise only**
*Sherrington 1997 ⁴¹	C	42	5	Gait velocity	Weight-bearing
*Sherrington 2003 ⁴²	H	80	7	PPME‡	Weight-bearing
*Sherrington 2004 ³²	C	120	7	6 metre walk time	Weight-bearing or non-weight-bearing
*Sylliaas 2011 ²⁴	C	150	8	6 minute walk distance	Progressive resistance
*Sylliaas 2012 ⁴³	C	95	8	6 minute walk distance	Prolonged resistance
*Tsaou 2005 ⁴⁴	C	54	4	Walking speed	Home-based physiotherapy

Study	Comparator	Dose (hour)	Supervised	Group exercise	Balance	Progressive resistance	Follow-up (week)
*Binder 2004 ¹⁸	Low-intensity non-progressive	81	Y	Y	Y	Y	24
Bischoff-Ferrari 2010 ³⁴	Standard physiotherapy	.	N	N	Y	N	24
*Hauer 2002 ⁹	Placebo motor activity	81	Y	Y	Y	Y	12
*Latham 2014 ³⁵	Attention control	72	Y	N	Y	N	24
Lauridsen 2002 ³⁶	Standard physiotherapy	.	Y	N	Y	N	.
*Mangione 2005 ³¹	Education	12	Y	N	N	Y	12
*Mangione 2010 ³⁷	Attention control	12	Y	N	N	Y	10
Miller 2006 ³⁸	Education	15	Y	N	N	N	12
Mitchell 2001 ³⁹	Usual care	6	Y	N	N	N	6
*Moseley 2009 ¹⁰	Usual care	112	Y	N	Y	N	16
Oldmeadow 2006 ⁸	Delayed weight-bearing	.	Y	N	N	N	1
Orwig 2011 ⁴⁰	Usual care	130	N	N	Y	N	8
*Resnick 2007 ³³	Usual care	9	Y	N	N	N	8
*Sherrington 1997 ⁴¹	Usual care	14	N	N	Y	N	4
*Sherrington 2003 ⁴²	Non weight-bearing	8	Y	N	Y	N	2
*Sherrington 2004 ³²	No intervention	60	N	N	Y	N	16
*Sylliaas 2011 ²⁴	No intervention	32	Y	Y	N	Y	12
*Sylliaas 2012 ⁴³	No intervention	53	Y	Y	N	Y	12
*Tsaou 2005 ⁴⁴	Bedside exercise	30	N	N	N	N	12

*Denotes studies included in meta-analysis

†H: Hospital only; H&C: Hospital and community; C: Community only

‡Data on any measure of overall mobility in each trial were extracted as the primary outcome of mobility in this study.

§Modified Physical Performance Test

||Tinetti's Performance Oriented Mobility Assessment

¶Physical Performance Mobility Examination

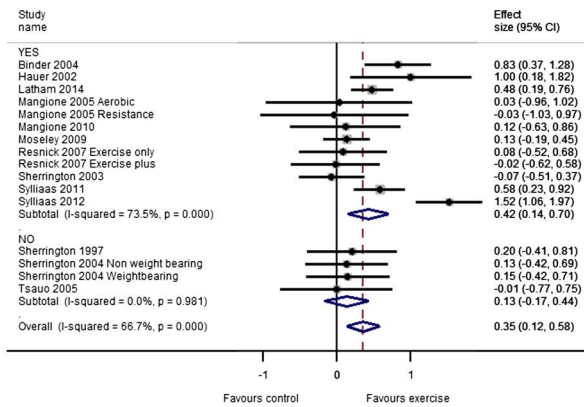
#Self-efficacy for Walking Exercise Scale

¶¶Short Physical Performance Battery

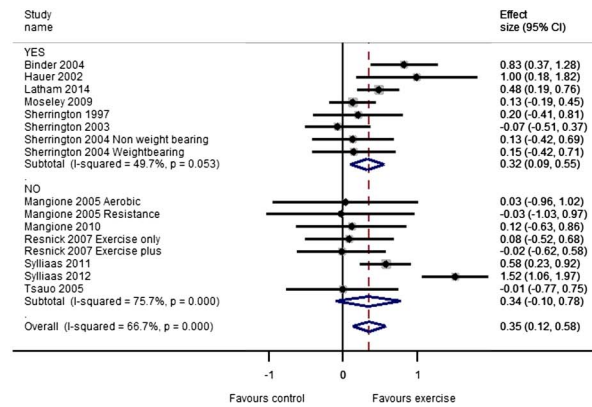
**Only 2 out of 3 comparison groups examined exercise interventions

Y: Yes; N: No

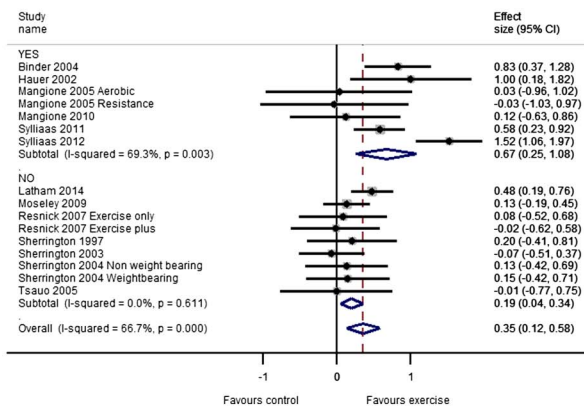
A Effect on mobility by supervision



B Effect on mobility by balance



C Effect on mobility by progressive resistance



D Effect on mobility by setting

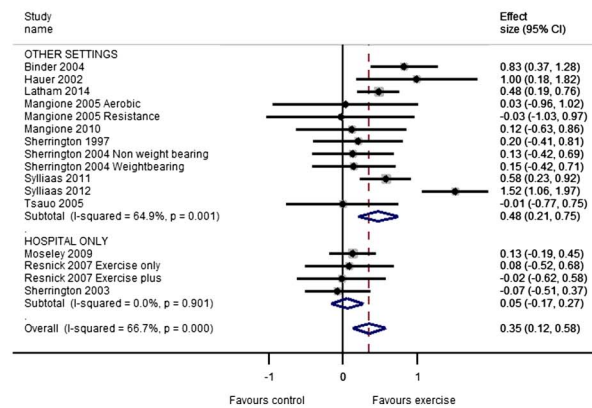


Figure 3 Forest plots of effects of trial-level characteristics of structured exercise analysed as dichotomous variables, on the primary outcome of mobility after hip fracture: (A) supervision of exercise, (B) inclusion of balance component, (C) inclusion of progressive resistance component, (D) setting of intervention (that is, whether interventions were conducted only in hospital or in other settings). Effect sizes are indicated as Hedges' g standardised mean differences and 95% CI. Changes in standardised mean differences by trial-level characteristics and 95% CI were estimated using meta-regression (table 2).

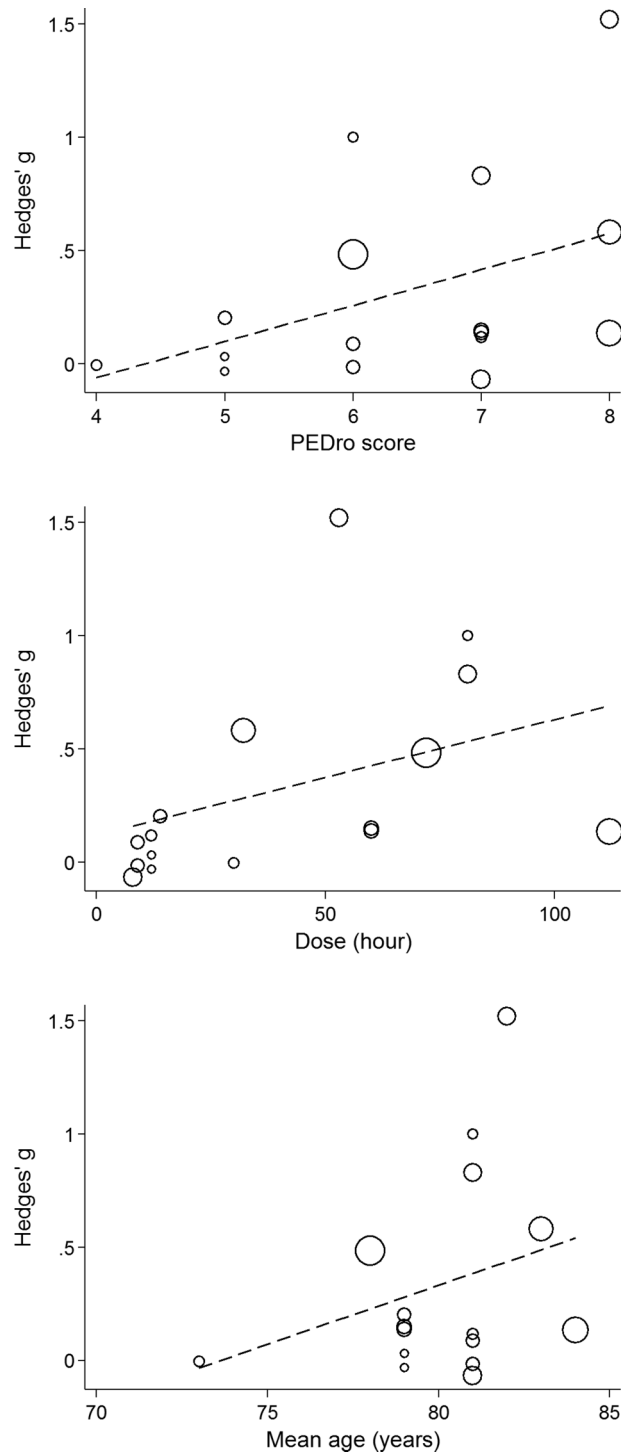


Figure 4 Graphs of effects of trial-level characteristics of structured exercise analysed as continuous variables, on the primary outcome of mobility after hip fracture: study quality measured using PEDro scale scores (panel 1), dose of intervention (panel 2), mean age of participants (panel 3). Effect sizes are indicated as Hedges' g standardised mean differences. The area of each circle is proportional to the inverse of the within-trial standard error. Slopes of changes in standardised mean differences as trial-level characteristics changed and 95% CI were estimated using meta-regression (table 2).

Br J Sports Med 2016;**50**:e3. doi:10.1136/bjsports-2014-094465corr1

