Experimental Gerontology 163 (2022) 111767

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Review

Progressive machine-based resistance training for prevention and treatment of sarcopenia in the oldest old: A systematic review and meta-analysis

E. Mende [a,*], N. Moeinnia [a], N. Schaller [a], M. Weiß [a], B. Haller [b], M. Halle [a,c], M. Siegrist [a]

[a] Department of Prevention and Sports Medicine, School of Medicine, University Hospital rechts der Isar, Technical University of Munich, Munich, Germany
[b] Institute of AI and Informatics in Medicine, University Hospital rechts der Isar, Technical University of Munich, Munich, Germany
[c] DZHK (German Center for Cardiovascular Research), partner site Munich Heart Alliance, Munich, Germany

A R T I C L E I N F O

Section Editor: Christiaan Leeuwenburgh

Keywords:
Strength training
Weight machine
Older adult
Sarcopenia
Therapy
Physical performance

A B S T R A C T

The muscle disease sarcopenia, which is characterised by a loss of muscle strength, muscle quantity, and physical performance, restricts mobility and independence in an ageing society. The aim of this systematic review and meta-analysis is to analyse the effects that long-term progressive resistance training interventions performed on weight machines have on sarcopenia (European Working Group on Sarcopenia in Older People) and how the interventions are composed. In total, 779 articles published between 2000 and 2020 were scanned (PubMed, Web of Science, CINAHL) and 14 randomised controlled trials were included within the review. Populations, interventions, control groups and outcomes were analysed. Subsequent meta-analysis (10 studies, 902 participants) revealed that the time needed in a chair-stand-test, as an indicator for leg strength, was predominantly reduced, whereas grip strength remained unchanged after the interventions. Data concerning the effects of machine-based progressive resistance training on muscle quantity were insufficient for meta-analysis. Physical performance measured by undergoing the Timed-Up-and-Go-test, gait speed test, Short Physical Performance Battery and 6 min-walk-test improved significantly as well. The quality of evidence (GRADE) in the analysed studies was low or moderate. In summary, machine-based progressive resistance training has the potential to reverse sarcopenia in the oldest old, as reflected by enhanced muscle strength and physical performance. The systematic review revealed promising initial results for muscle quantity.

1. Introduction

Increasing inactivity and an ageing society are associated with a rising prevalence of sarcopenia among older adults (de Souto Barreto et al., 2016; Haskell et al., 2007). Sarcopenia is a key component of frailty (Fried et al., 2001) and it is defined by the decline of muscle strength, muscle quantity and muscle quality (Cruz-Jentoft et al., 2019). The resulting poor physical performance restricts the functionality and mobility of older adults in everyday life. Limited independence and an increased risk of falls often lead to institutionalisation and hospitalisation, reducing quality of late life and increasing health and social care costs in today's society.

In the new sarcopenia consensus from 2019 (Cruz-Jentoft et al., 2019), sarcopenia is determined by the European Working Group on Sarcopenia in Older People (EWGSOP) as a below-average chair-stand-test (CST) time or a sub-standard grip strength test (GS), in combination with sub-standard muscle mass. To assess the severity of sarcopenia, the following tests are recommended: gait speed test, Short Physical Performance Battery (SPPB), Timed-Up-and-Go-test (TUG), 6 min-walk-test (6MWT).

To counteract the muscle disease, exercise training over the entire life span is crucial and should become a daily routine in older adults' lives. A key component for preventing and treating sarcopenia is resistance training, as this stimulates the muscles effectively. Initial experiences with progressive machine-based resistance training go back to the beginning of the 1990s (Fiatarone et al., 1990). By that time, high-intensity progressive resistance training for very old people had become increasingly important. Small study samples had already confirmed strength gains, an onset of fat-free mass/muscle mass, enlarged mid-thigh muscle areas and reduced walking time for a predefined range (Fiatarone et al., 1990; Fiatarone et al., 1994; Fisher et al., 1991; Yarasheski et al., 1999). Further studies came to similar

* Corresponding author at: Department of Prevention and Sports Medicine, University Hospital rechts der Isar, Technical University of Munich, Georg-Brauchle-Ring 56, 80992 Munich, Germany.
E-mail address: Esther.Mende@mri.tum.de (E. Mende).

https://doi.org/10.1016/j.exger.2022.111767
Received 26 November 2021; Received in revised form 2 March 2022; Accepted 11 March 2022
Available online 19 March 2022

conclusions and additionally found improvements in leg strength, as reflected by a reduction in the time needed in a CST (Hauer et al., 2001) and in GS (Gudlaugsson et al., 2012).

The first reviews reporting progressive machine-based resistance training for older people were published in the late 2000s. Based on the results of several reviews conducted within the last ten years, resistance training of a suitable intensity (70–90% of one repetition maximum (1RM)) was established as the most promising treatment of sarcopenia (Martone et al., 2015). Most analysed younger people, aged 65–80 years, as they are easier to attain and to train compared to older people (Izquierdo and Cadore, 2014; Liu and Latham, 2009). Moreover, the exercise interventions were mostly performed at low intensity, e.g. sedentary gymnastics using small weights (poles, balls) or with insufficient adaptability (elastic bands, dumbbells, weight cuffs) (Liu and Latham, 2009; Lopez et al., 2018; Valenzuela, 2012). Additionally, home-based training usually comprised less intense training sessions due to the limited number of weight machines on offer (Giné-Garriga et al., 2014). Hence, there is a lack of studies that deal exclusively with the proven method of high-intensity training and the advantages of weight machines in combat against sarcopenia in the oldest old.

In comparison to other reviews addressing comparable scientific questions (Law et al., 2016), we approached the issue in a systematic format, summarising all of the relevant articles from the year 2000 until the end of 2020 that deal with progressive machine-based resistance training for the treatment of sarcopenia in the oldest old (80 years or older). A subsequent meta-analysis was furthermore conducted to provide additional information about the efficacy of the investigated interventions on sarcopenia-related parameters based on the EWGSOP (Cruz-Jentoft et al., 2019): CST, GS, dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), magnetic resonance imaging (MRI), computed tomography (CT), gait speed test, SPPB, TUG, 6MWT.

The aim of this review and the meta-analysis is to broaden knowledge of the composition and the effects of machine-based progressive resistance training in the prevention and therapy of sarcopenia in the oldest old.

2. Methods

A systematic review and meta-analysis were conducted based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (Moher et al., 2015). After finishing the review, the new PRISMA 2020 guidelines were additionally considered in form of PERSiST (Ardern et al., 2022), and important aspects were included subsequently.

2.1. Eligibility criteria

The average age of the study population of those studies included in the review was 80 years or older – designated as the oldest old in this review. Older people were included regardless of their health status. Study populations with hospitalised older people were excluded. The selected studies provided interventions for older people living in retirement homes as well as community-dwelling older adults.

To ensure high-intensity progressive strength training and a high comparability of the interventions, only studies which contained strength training interventions performed on weight machines for at least 3 months (12 weeks) were included in this review. Studies combining resistance training with other non-physical interventions, e.g. cognitive training or in conjunction with a multimodal training intervention (with additional endurance, coordination, and flexibility training) were included in the review, whereas interventions accompanied by any additional individual dietary supplementation were excluded.

In this review, only studies with a randomised controlled trial design were included, i.e. the study populations were randomly assigned to an intervention group or a control group.

To be included, articles needed to investigate the effect of the intervention on one of the parameters defining sarcopenia based on the EWGSOP: CST and GS as indicators for muscle strength, muscle mass (measured by DXA, BIA, MRI or CT), and physical performance (measured by gait speed test, SPPB, TUG, 6MWT).

2.2. Search strategy

To carry out the literature search, three different electronic databases were scanned on the fourth of November 2019 and new hits were added continuously until the end of 2020. The following electronic bibliographic databases were browsed: PubMed, Web of Science, CINAHL. The search strategy was developed based on a preliminary search and in accordance with a librarian. The search terms (Appendix A) described the study population (e.g. elderly, old), intervention (resistance training, strength training) and outcomes (muscle strength, muscle mass and physical function). To identify further relevant articles, authors were contacted, the reference lists of suitable manuscripts and reviews scanned and a hand search of unpublished (conference proceedings) or ongoing trials (study registries) was executed. Further hits were provided through a preliminary search.

2.3. Data extraction

The initial screening of titles and abstracts for eligibility and the subsequent assessment of retrieved full texts was performed independently (blinded) by two reviewers, in accordance with defined inclusion/exclusion criteria (Section 2.1). Where any discrepancies arose between the reviewers' individual assessments, its inclusion was discussed with a third person.

A standardised data extraction form was used to extract essential data from selected studies. Extracted data were appraised by a second person. Missing data were requested from study authors or consulted in the study protocol. The data extraction form included any useful information about the studies, such as the name, authors, year of publication, type of study, sample size (intervention and control group), residential status, characteristics of the participants and interventions, as well as the outcomes analysed. Extracted results were expressed as means and standard deviation (SD) or standard error (SE). Mean differences within the intervention and control groups in the result section (Section 3.2) were partly calculated using the existing data.

2.4. Outcome measures

Primary outcomes were muscle strength measured on the basis of CST and GS (Fig. 2) and muscle mass measured on the basis of DXA or BIA, CT or MRI methods. Outcomes were recommended measurement methods for diagnosing sarcopenia (Cruz-Jentoft et al., 2019).

Secondary outcomes included further parameters for assessing the severity of sarcopenia based on means of physical performance (Fig. 3, Appendix B). The parameters used were the gait speed test, SPPB, TUG and walk test (e.g. 400-m walk test or 6MWT) (Cruz-Jentoft et al., 2019).

Sarcopenia threshold values (EWGSOP) were applied to assess the sarcopenic status of intervention and control groups at baseline and after the interventions (group mean values) based on means of muscle strength and physical performance (Table 2).

The drop-out rate and adherence to training interventions were evaluated when available.

2.5. Quality assessment

The “Cochrane Risk of Bias (RoB) tool” (Higgins et al., 2011) for randomised trials was used to assess the quality of included studies. The following domains were analysed: random sequence generation and allocation concealment (selection bias), blinding of participants, personnel (performance bias) and outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other sources of bias.

In addition, quality of evidence for each outcome in the meta-analysis has been assessed using the "GRADE approach for systematic reviews" (The GRADE Working Group, 2013). The evidence was set at 'high quality' in the beginning and downgraded in each category by one level for serious (or by two for very serious) study limitations (RoB), inconsistency of results (heterogeneity), indirectness of evidence, imprecision of effect estimates or potential publication bias (Appendix C). A study quality assessment was conducted to support the classification of the findings of the meta-analysis. It was assessed by a third person where any disagreements emerged between the two independent reviewers.

2.6. Data synthesis

Meta-analysis was conducted using 'RevMan 5.3' (Review Manager, 2014) software. Heterogeneity was assessed by I^2 ('RevMan 5.3') using Cochrane Q test and considered in the GRADE approach. Mean values obtained immediately after the interventions plus SD were integrated into a fixed model for continuous outcome parameters (inverse variance weighting). If the necessary data were not available, the outcome was excluded from the meta-analysis. In one case, SD was calculated by SE and sample size. As for all outcomes different measures or units were used, treatment effects were quantified by standardised mean differences. A significance level of $\alpha = 0.05$ was used for all analyses. Subgroup analysis was calculated for two studies that performed GS in retirement homes. Further planned sub-group analyses considering different settings or time spans were not performed due to a small number of studies with institutionalised people exclusively (n = 3) or studies that applied 6-month intervention periods (n = 3).

3. Results

In total, 779 articles were identified, of which 662 remained after duplicates were removed. After screening the title and abstract according to the inclusion and exclusion criteria, 517 articles were excluded in a first run. Moreover, 129 articles were excluded after screening the manuscript. Once a definitive exclusion criterion was found, the screening was stopped. Ultimately, 14 studies remained for the systematic review, with ten of them useable for additional assessment in a subsequent meta-analysis (Fig. 1).

3.1. Study characteristics

Participants were included from examinations conducted in various countries, leading to a heterogeneous group in this review. The average age of the study populations was between 80 (Gudlaugsson et al., 2012) and 92 (Cadore et al., 2014) years old. Most of the study participants were female (Table 1). Some studies listed the distribution of frequent diseases among the participants. Within the non-communicable common diseases, hypertension was most widely distributed (>50%). Four studies described their population as frail, and two studies (Hassan et al., 2016; Kim et al., 2016) partly or entirely as sarcopenic. Five out of 14 studies were conducted with older people living in the community, three

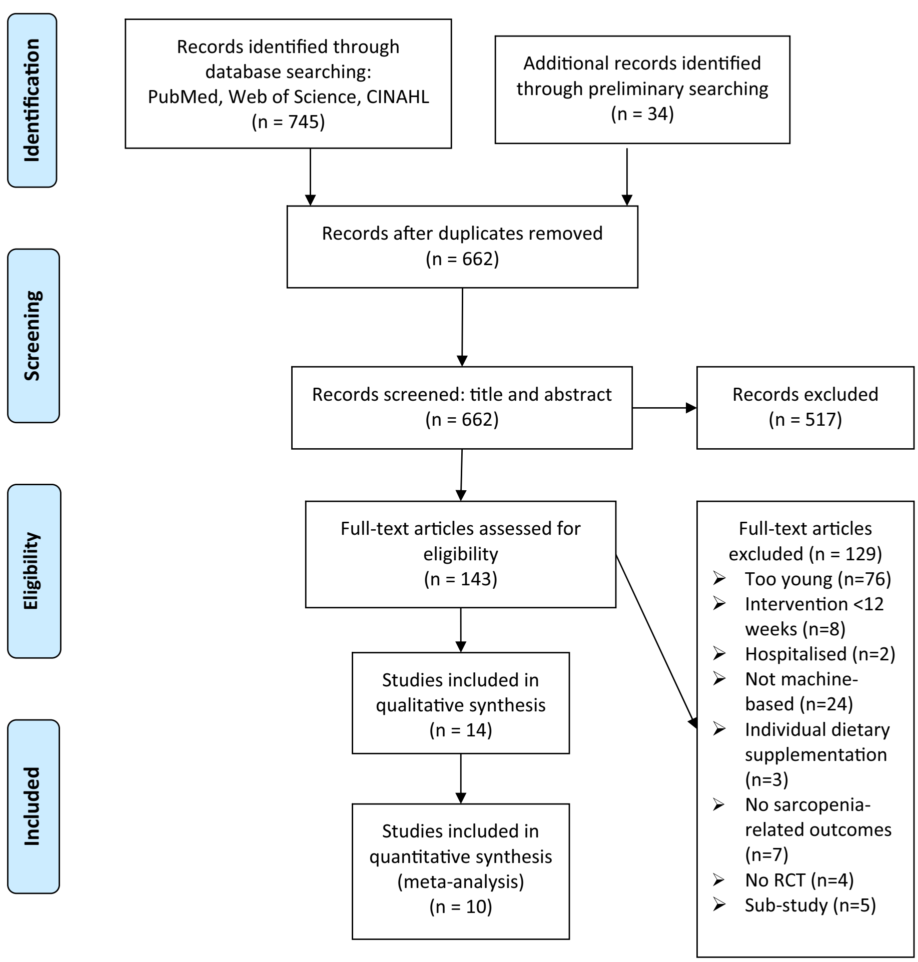


Fig. 1. PRISMA 2009 Flow Diagram.

Table 1
Study characteristics.

Study (Country)	N (IG/CG)	Sex F/M	Age MW ± SD [y]	Frailty; *Sarco-penia* Type (baseline propor-tion)	Residential status	Resistance training Components, equipment	Other treatments	Dose Time, frequency, duration	Outcomes related to sarcopenia
Ansai 2016 (Brazil)	69 (23/ 23) + *1 group (23)*	47/22	82.4 ± 2.4		Community-dwelling	6 adapted machines (Pró-physical): leg press, calf, rowing, chest press, abdominal, back extension	None	16 weeks, 3×/week, 1 h	CST (5 reps)
Cadore 2014 (Spain)	32[a] (16/ 16)	17/7 (n = 24)	91.9 ± 4.1 (n = 24)	Fried (all)	Institution-alised	3 resistance variable machines (Exercycle, S.L.): bilateral leg extension, bilateral knee extension, seated bench press	Balance exercises, gait retraining, functional exercises	12 weeks, 2×/week, 40 min	CST (30 s), GS (handheld), gait speed (5 m, habitual), TUG, CT (CSA m. quadriceps)
Caserotti 2008 (Denmark)	25 (12/ 13)	25/0	81.8 ± 2.7		Community-dwelling	5 exercises on iso-inertial resistance training equipment with variable velocities (Cybex): horizontal/inclined leg press, hamstring curls, bilateral knee extension, calf rise	Warm-up	12 weeks, 2×/week, duration N/A	BIA (lean mass)
Greiwe 2001 (USA)	13 (8/5)	7/6	81 ± 1	Reuben (all)	N/A	Weight machines; abdominal exercises and free weight squats	Supervised pre-training programme (light stretching), warm-up: stretching, light calisthenics, walking	12 weeks, 3×/week, 55–95 min	DXA (lean mass)
Gudlaugsson 2012 (Iceland)	117 (56/ 61)	63/54	IG: 80.8 ± 4.7 CG: 78.3 ± 4.1		Community-dwelling/ institution-alised	12 exercises on strength equipment (circuit series, Life Fitness): leg press, leg extension, calf raises, bench press, chest cross, shoulder press, pull down, biceps curl, triceps extension, abdominal, back	Stretching between circuits, endurance training (daily walking), seven lectures on nutrition, healthy ageing and physical training	25 weeks, 2×/week, duration N/A	CST (5 reps), GS (chair), gait speed (4 m, habitual), SPPB, TUG (8 ft), 6MWT
Hassan 2016 (Australia), sub-study of Hewitt	42 (21/ 21) *4 clusters*	29/16 (n = 45[a])	85.9 ± 7.5	*EWGSOP (35.7%)*	Institution-alised	5 pneumatic weight machines (HUR): hip abduction/ adduction, leg press, leg extension/curl, triceps dip, abdominal curl/back extension	Static and dynamic balance exercises, relevant stretches	25 weeks, 2×/week, 1 h	GS (handheld), gait speed (3 m, habitual), BIA (SMI, lean mass)
Hauer 2001 (Germany)	57 (31/ 26)	57/0	82 ± 4.8		Community-dwelling/ institution-alised	Leg press (Kaphingst): hip/ knee extensions in a sitting position; hip abduction/extension in a standing position (cable pulley), heel rises during erect standing	Aerobic exercise (stationary bicycle), stretching between sets, balance/functional exercises, physiotherapy (massaging, stretching, thermotherapy)	12 weeks, 3×/week, 1.5 h	CST (3 reps), gait speed (15 m, max.), TUG
Hauer 2012 (Germany)	122 (62/ 60)	IG: 74.2% F CG: 73.3% F	IG: 82.3 ± 6.6 CG: 82.9 ± 7.0		Community-dwelling/ institution-alised	Leg press (Kaphingst): hip/ knee extensions in a sitting position; hip abduction/extension in a standing position (cable pulley), heel rises during erect standing	Aerobic exercise (stationary bicycle), stretching between sets, balance/functional exercises	12 weeks, 2×/week, 2 h	CST (5 reps), gait speed (6 m, max.), TUG
Hewitt 2018 (Australia)	221 (113/ 108) *16 clusters*	65% F	86 ± 7.0		Institution-alised	5 pneumatic weight machines (HUR): hip abduction/ adduction, leg press, leg extension/curl, triceps dip, abdominal curl/back extension	Static and dynamic balance exercises, relevant stretches	25 weeks, 2×/week, 1 h (incl. balance)	SPPB
Kim 2016 (Japan)	139 (35/ 34) + *2 groups (34/36)*	139/0	IG: 81.4 ± 4.3 CG: 81.1 ± 5.1	*Sarcope-nic obesity (all)*	Community-dwelling	5 hydraulic exercise machines (Mizuno): abduction, leg press, leg extension, seated row, abdominal crunch; resistance band exercises	Aerobic exercise (stationary bicycle)	12 weeks, 2×/week, 1 h	GS (handheld), gait speed (5 m, habitual), BIA (SMI, ASM)
Kryger 2007 (Denmark)	30 (15/ 15)	23/7	Medi-an: 89.2 (85–97)	N/A (all)	Community-dwelling/ institution-alised	2 exercises on a quadriceps chair: knee extensors/flexors	Warm-up	12 weeks, 3×/week, 45 min	MRI (CSA m. quadriceps)
Mueller 2009 (Switzerland)	62 (23/ 16) + *1 group (23)*	36/26	80.6 ± 3.5		N/A	4 exercises: hip extension, leg press, knee extension, leg curl	Aerobic exercises, gymnastics, stretching	12 weeks, 2×/week, 45 min	TUG, DXA (thigh muscle mass)
Rydwik 2008 (Sweden)	96 (23/ 23) + *2*	58/38	83.2 ± 4	Fried (all)	Community-dwelling	3 exercises on stationary equipment (Scandinavian	Aerobic exercises (walking/ jogging on the spot, arm		

(*continued on next page*)

Table 1 (*continued*)

Study (Country)	N (IG/CG)	Sex F/M	Age MW ± SD [y]	Frailty; *Sarco-penia* Type (baseline propor-tion)	Residential status	Resistance training Components, equipment	Other treatments	Dose Time, frequency, duration	Outcomes related to sarcopenia
	groups (25/25)					Mobility): leg press, dips, pull-down; functional muscle strength training (chair stand, step-up, toe raise with or without a weight belt)	movements), balance exercises, stretching, Qigong, general diet advice	12 weeks, 2×/week, 1 h	CST (30 s), gait speed (10 m, max.), TUG
Sylliaas 2011 (Norway)	150 (100/50)	123/27	IG: 82.1 ± 6.5 CG: 82.9 ± 5.8		Community-dwelling	4 exercises: standing knee flexion (with weight belts), lunge (pass forward with weight belts), sitting knee extension (Technogym) and leg extension (Technogym)	Aerobic exercise (stationary bicycle or treadmill, daily walking), home training programme (knee flexion, lunge)	12 weeks, 2×/week, 45–60 min	CST (10 reps), gait speed (10 m, max.), TUG, 6MWT

Notes: CST, chair-stand-test; GS, grip strength test; SPPB, Short Physical Performance Battery; TUG, Timed-Up-and-Go-test; 6MWT, 6 min-walk-test; DXA, dual-energy X-ray absorptiometry; BIA, bioelectrical impedance analysis; MRI, magnetic resonance imaging; CT, computed tomography; IG, intervention group; CG, control group; CSA, cross-sectional area; N/A, not available; F, female; M, male; [a], randomised.

with institutionalised people, four with people both living in the community or in retirement homes, while two did not mention the residential status (Table 1).

The intervention time ranged between 12 (minimum for inclusion) and 25 weeks (Table 1). Training sessions were offered two (n = 10) or three times (n = 4) a week in groups (n = 8) of 2–17 participants. Six authors did not provide any detailed information about group size. Training was supervised by physiotherapists or other qualified instructors (coaches, health professionals). Weight-based or pneumatic weight machines were employed to perform progressive resistance training. Caserotti et al. (2008) used an isoinertial weight machine with variable velocities (Cybex) to emphasise explosive-type resistance training for the lower body. Up to six machines (Ansai et al., 2016) or more (Gudlaugsson et al., 2012) were used to carry out two (Hauer et al., 2001; Hauer et al., 2012; Kryger and Andersen, 2007; Sylliaas et al., 2011) to twelve (Gudlaugsson et al., 2012) exercises (Table 1). Six studies offered their intervention exclusively for the lower limbs. Resistance training was conducted as part of a multimodal training activity in all studies expect for Ansai et al. (2016). As a general rule, 2–3 sets were performed on each weight machine. Each set ranged between 8 and 15 repetitions (minimum 6–maximum 20) for most of the studies. Some studies started with a low number of repetitions and raised the training intensity additionally by increasing the number of repetitions (Ansai et al., 2016; Greiwe et al., 2001; Hassan et al., 2016; Hewitt et al., 2018), while some started at a high repetition rate (Caserotti et al., 2008; Gudlaugsson et al., 2012; Sylliaas et al., 2011) and raised the intensity primarily by increasing the weight in combination with a reduction of the repetition rate. The progressive resistance training was guided by the 1RM or multiple RM (n = 8) methods, BORG Scale (n = 4) or both (Rydwik et al., 2008). During the introduction period, or at high velocities (Cadore et al., 2014) resistance training was performed with 40–60% of 1RM. Subsequently, intensity was set to "somewhat hard" (12–14 according to the BORG Scale) or 70–80% of 1RM. In some cases, 90% (Hauer et al., 2001) to 100% of 1RM (Greiwe et al., 2001) were applied. The last set was predominantly performed until fatigue. Exercise order and resting/recovery periods were described only in two studies as 1 min between the sets or 3–4 min between the circuits. According to the authors, no adverse events related to the training interventions occurred during the interventions. However, seven studies made no reference to any adverse events (Cadore et al., 2014; Greiwe et al., 2001; Gudlaugsson et al., 2012; Kryger and Andersen, 2007; Mueller et al., 2009; Rydwik et al., 2008; Sylliaas et al., 2011).

The control groups experienced usual care, cognitive training, social interaction, general health education, mobility exercises, low-intensity training with body weight or hand-held weights (Hauer et al., 2001; Hauer et al., 2012) or physiotherapy (Hauer et al., 2001).

The measurement methods applied to CST, GS and gait speed test varied throughout the studies (Table 1), whereas those applied to SPPB, TUG and 6MWT were conducted relatively consistently. The CST (n = 7) was performed with 3–10 repetitions or in 30s, the GS (n = 4) with a handheld or fixed (chair) dynamometer and the gait speed test (n = 8) over 3–15 m with maximal or habitual velocity. The SPPB was applied (n = 2) according to Guralnik et al. (1994), TUG was applied (n = 7) according to Podsiadlo and Richardson (1991) and the walk test was conducted (n = 2) as a 6MWT. Most studies analysed muscle function using the gait speed test, followed by CST and TUG (Table 1).

3.2. Primary outcome measures (assessment and confirmation of sarcopenia)

3.2.1. Functional muscle strength tests (CST, GS)

In total, 513 participants were involved in the meta-analysis of the CST-results. Six out of seven studies improved in comparison to the control groups. The standardised mean difference was −0.92 (95% CI: −1.11, −0.73; $p < 0.01$), reflecting enhanced leg muscle strength after the interventions (Fig. 2). Meta-analysis of GS of 239 participants did not reveal any statistically relevant changes in the standardised mean difference (0.08; 95% CI: −0.18, 0.33; $p = 0.57$) (Fig. 2). Two out of 4 studies improved in comparison to the control groups.

Improvements in the CST of intervention groups involved in the seven studies ranged between 1.7 s and 21.7 s in a pre-set number of repetitions or 1 repetition and 3.6 repetitions in 30 s, respectively, and were significantly different from the control groups (Cadore et al., 2014; Gudlaugsson et al., 2012; Hauer et al., 2001; Hauer et al., 2012; Sylliaas et al., 2011) except for those of Ansai et al. (2016) and Rydwik et al. (2008). Most of the control groups (n = 5) demonstrated a decline in physical performance. The results of the GS measured in kilogrammes (kg) or Newton (N) were less consistent. The GS for the intervention groups in three out of four studies improved significantly in comparison to the control groups, by 2.2 kg, (Hassan et al., 2016) and 18 N (Cadore et al., 2014) or non-significantly, by 11.3 N (Gudlaugsson et al., 2012). Three studies stated a decline in GS within the control groups.

3.2.2. Muscle quantity tests (MRI, CT, DXA, BIA)

Different methods were used to analyse changes in muscle mass. The gold standard (MRI) was used only once by Kryger and Andersen (2007) to analyse the cross-sectional area (CSA) of the m. quadriceps femoris. Cadore et al. (2014) examined the same outcome through using the CT method. Both studies revealed a significant (from zero) improvement of 2.7 or 2.6 cm^2 in CSA in the intervention groups. The intervention group of Cadore et al. (2014) improved significantly in comparison to the control group, too. Other authors used BIA (Caserotti et al., 2008; Hassan et al., 2016; Kim et al., 2016) or DXA (Greiwe et al., 2001; Mueller et al., 2009) to measure the total body skeletal muscle mass index (SMI), appendicular skeletal muscle mass (ASM), lean body mass or relative thigh muscle mass (Table 1). Only Mueller et al. (2009) reported a significant improvement in relative thigh muscle mass for the intervention group (2%) in comparison to the control group. The data were too scarce and the methods too heterogenous for meta-analysis.

3.3. Secondary outcome measures (severity of sarcopenia)

In the meta-analysis, the standardised mean difference between intervention and control group for the gait speed test was 0.46 ($n = 582$; 95% CI: 0.29, 0.63; $p < 0.01$; $n = 8$); for the SPPB 0.63 ($n = 299$; 95% CI: 0.40, 0.86; $p < 0.01$; $n = 2$); for the TUG −0.62 ($n = 473$; 95% CI: −0.81, −0.44; $p < 0.01$; $n = 6$); and for the 6MWT 0.56 ($n = 256$; 95% CI: 0.30, 0.82; $p < 0.01$; $n = 2$), reflecting enhanced physical performance for all tests post-intervention as compared to the control groups (Fig. 3, Appendix B).

In all studies, physical performance improved after the exercise intervention in the intervention groups. For SPPB ($n = 2$), TUG ($n = 7$) and 6MWT ($n = 2$), the performances rose significantly in comparison to the control groups (Cadore et al., 2014; Gudlaugsson et al., 2012; Hauer et al., 2001; Hauer et al., 2012; Hewitt et al., 2018; Mueller et al., 2009; Sylliaas et al., 2011) except of the TUG in Rydwik et al. (2008). The times in the gait speed test ($n = 8$) only improved significantly in comparison to the control groups of Hauer et al. (2001, 2012) and Cadore et al. (2014).

The average baseline values of the participants for each study were classified as sarcopenic according to the EWGSOP for most of the included CSTs and gait speed tests. In contrast, baseline mean values for GS or TUG were classified less often as sarcopenic (Table 2). Baseline values for SPPB and 6MWT comprised both sarcopenic and normal mean values (1:1) in the analysed studies. After intervention, four intervention groups with sarcopenic mean values managed to improve to normal values, but only for CST (2 studies) and TUG (2 studies). Control groups only improved in TUG following the intervention phase (Sylliaas et al., 2011) and developed sarcopenic values in GS (2 studies) and TUG. In all other cases, the status of the intervention and control groups remained the same in terms of sarcopenia (Table 2).

3.4. Additional analysis

In the sub-group analysis, residents of retirement homes (Cadore et al., 2014; Hassan et al., 2016) ($n = 65$) showed improved GS following the interventions, with a standardised mean difference of 0.76 (95% CI: 0.25, 1.27; $p < 0.01$) (Appendix B). In comparison, Kim et al. (2016) (community-dwelling older adults, $n = 68$) and Gudlaugsson et al. (2012) (mixed population, $n = 106$) did not report significant differences in the GS between intervention and control groups at the end of the interventions.

The drop-out-rate, calculated from the baseline examination until the end of the intervention (retest) for both the intervention and control groups, was around 10% for most of the studies, reaching 25% (Cadore et al., 2014) at most. Adherence rates to the progressive resistance training were documented in half of the studies and ranged between 28.4% (Hassan et al., 2016) and 93.9% (Hauer et al., 2012).

3.5. Quality of evidence

The blinding of participants and personnel was exposed to high RoB for almost all studies except for Hauer (2001 & 2012). Random sequence generation demonstrated low or unclear RoB exclusively. The other categories were at low, unclear or high RoB for all studies (Table 3). The studies conducted by Hauer et al. (2012), Hewitt et al. (2018) and Sylliaas et al. (2011) were predominantly exposed to low RoB, while Greiwe et al. (2001) and Hassan et al. (2016) demonstrated three categories of high RoB (Table 3).

The total RoB score created for the GRADE approach weighted performance, detection and reporting bias less than the other categories. These categories were hard to accomplish and older studies were not rigorously structured by CONSORT guidelines (Schulz et al., 2010). Half of the studies were at high RoB (Table 3) and only one study was at low RoB (Hauer et al., 2012).

A quality assessment undertaken based on the GRADE approach (Appendix C) revealed that the quality of evidence for each outcome in the meta-analysis needed to be downgraded by one to three levels, from

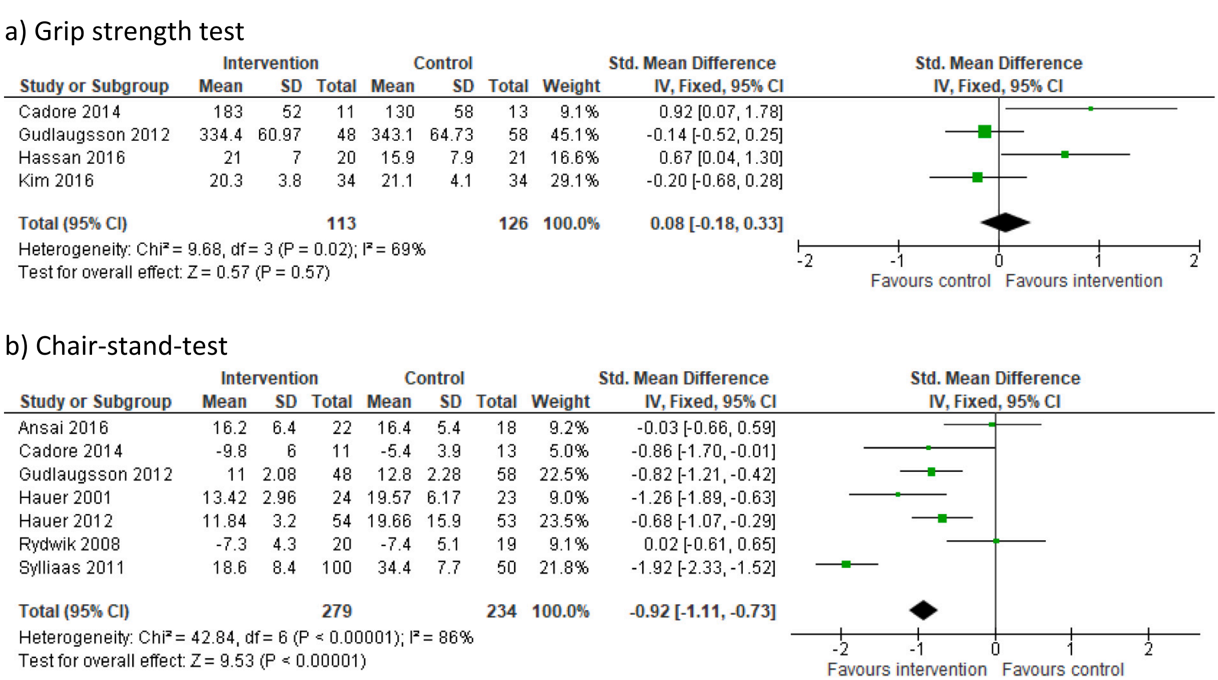


Fig. 2. Effects of machine-based progressive resistance training interventions on parameters of muscle strength.

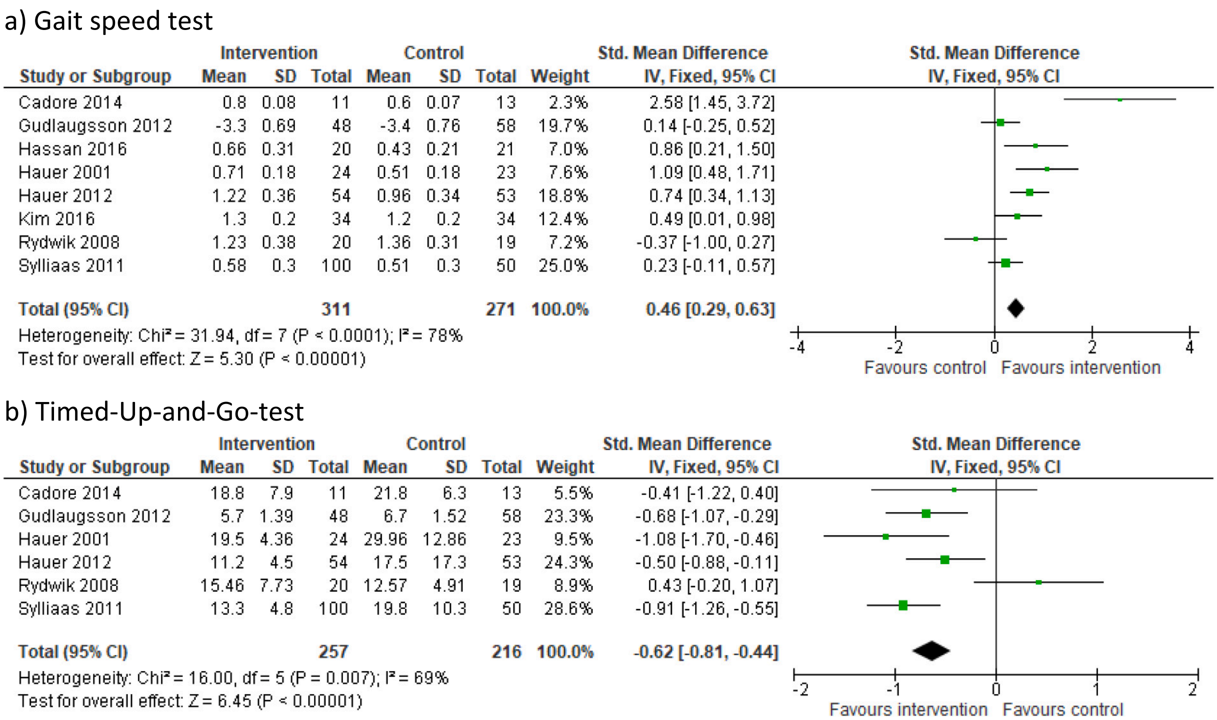


Fig. 3. Effects of machine-based progressive resistance training interventions on parameters of physical performance.

Table 2
Sarcopenia threshold values (EWGSOP) and classification of the study population.

Threshold EWGSOP	N	CST		Grip strength test[A]		Gait speed test		SPPB		TUG		6MWT	
		>15 s		♀ < 16 kg (♂ < 27 kg)		≤0.8 m/s		≤8 points		≥20 s		<400 m	
		Baseline	End	Baseline	End	Baseline	End	Baseline	End	Baseline	End	Baseline	End
Ansai, 2016	All	IG↑ CG↑	IG↑ CG↑										
Cadore, 2014	♀			IG ↑ CG ↑	IG ↑ **CG ↓**	IG ↓ CG ↓	IG ↓ CG ↓			IG ↓ CG ↓	IG ↓ **CG ↑**		
	♂			(IG ↓ (CG ↓	IG ↓) CG ↓)								
Gudlaugsson, 2012	♀	IG ↓ CG ↓	IG ↓ CG ↓	IG ↑ CG ↑	IG ↑ CG ↑	IG ↓ CG ↓	IG ↓ CG ↓	IG ↑ CG ↑	IG ↑ CG ↑	IG ↓ CG ↓	IG ↓ CG ↓	IG ↑ CG ↑	IG ↑ CG ↑
	♂			(IG ↑ (CG ↑	IG ↑) CG ↑)								
Hassan, 2016	♀			IG ↑ CG ↑	IG ↑ **CG ↓**	IG ↓ CG ↓	IG ↓ CG ↓						
	♂			(IG ↓ (CG ↓	IG ↓) CG ↓)								
Hauer, 2001	♀	IG ↑ CG ↑	**IG ↓** CG ↑			IG ↓ CG ↓	IG ↓ CG ↓			IG ↑ CG ↑	**IG ↓** CG ↑		
Hauer, 2012	All	IG ↑ CG ↑	**IG ↓** CG ↑			IG ↑ CG ↑	IG ↑ CG ↑			IG ↓ CG ↓	IG ↓ CG ↓		
Hewitt, 2018	All							IG ↓ CG ↓	IG ↓ CG ↓				
Kim, 2016	♀			IG↑ CG↑	IG↑ CG↑	IG ↑ CG ↑	IG ↑ CG ↑						
Rydwik, 2008	All					IG ↑ CG ↑	IG ↑ CG ↑			IG ↓ CG ↓	IG ↓ CG ↓		
Sylliaas, 2011	All	IG↑ CG↑	IG↑ CG↑			IG ↓ CG ↓	IG ↓ CG ↓			IG ↑ CG ↑	**IG ↓** **CG ↓**	IG ↓ CG ↓	IG ↓ CG ↓

Notes: CST, chair-stand-test; SPPB, Short Physical Performance Battery; TUG, Timed-Up-and-Go-test; 6MWT, 6 min-walk-test; IG, intervention group; CG, control group; ↑, test result higher than the threshold; ↓, test result lower than the threshold; [A], test results are for women and men combined; in bold, thresholds were exceeded after intervention.

high to moderate (SPPB, 6MWT), low (CST, gait speed test, TUG) or very low (GS). This assessment was due to limitations in study design or execution (GS, TUG). Evidence of GS and TUG contained predominantly studies with high RoB (Table 3). Furthermore, the evidence demonstrated a substantial (<0.01) inconsistency, i.e. heterogeneity (CST, gait speed test, TUG), and imprecision (GS, SPPB, 6MWT) due to small outcome sample sizes (Appendix C).

4. Discussion

Sarcopenia is a muscle failure which manifests itself in many forms and is becoming more widespread in today's ageing western community. To counteract the negative consequences of sarcopenia, progressive resistance training is an option that has been investigated in the past 30 years. This systematic review and meta-analysis summarised the body of evidence surrounding the potential of machine-based resistance training in preventing and treating sarcopenia in the fragile population of the oldest old.

The review and meta-analysis revealed remarkable improvements for the CST (−0.92; 95% CI: −1.11, −0.73) post-intervention, indicating that leg strength can be improved particularly effectively through progressive resistance training. Further literature suggests that these improvements may aid enhanced gait balance, reduced fear of falling (Toebes et al., 2015) and reduced risk of falling (Cho et al., 2012) as positive consequences.

In turn, the results of the meta-analysis for GS showed only slight, insignificant improvements (0.08; 95% CI: −0.18, 0.33; $p = 0.57$). Near-constant GS values post-intervention may reflect a difficulty in upper-limb strengthening among the oldest old in general. The high number ($n = 6$) of interventions included in the review that focus exclusively on lower limb training is an indication of the limited interest in and weighting of upper-body strength and GS (Tietjen-Smith et al., 2006) among the oldest old population, even though low GS is associated with death (Leong et al., 2015).

An analysis of muscle quantity tests revealed significant improvements in relative thigh muscle mass and CSA of m. quadriceps femoris due to progressive resistance training. These results indicated the existence of an association with the enhanced leg muscle strength in CST performance in this meta-analysis. Muscle quantity tests were examined less frequently than muscle strength tests and therefore these tests were not comparable in a meta-analysis. Moreover, inconsistent methodology and measuring devices complicated the comparability. The devices BIA

Table 3
Methodological quality assessment (risk of bias).

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	GRADE Total
Ansai 2016	Green	Green	Red	Red	Orange	Orange	Orange	Orange
Cadore 2014	Orange	Green	Red	Orange	Red	Orange	Orange	Red
Caserotti 2008	Orange	Orange	Red	Orange	Orange	Green	Orange	Orange
Greiwe 2001	Orange	Orange	Red	Orange	Orange	Red	Red	Red
Gudlaugsson 2012	Orange	Red	Red	Orange	Orange	Green	Orange	Red
Hassan 2016	Green	Orange	Red	Red	Red	Orange	Orange	Red
Hauer 2001	Orange	Red	Orange	Orange	Orange	Green	Green	Red
Hauer 2012	Green	Green	Orange	Green	Green	Green	Green	Green
Hewitt 2018	Green	Orange	Red	Green	Green	Green	Green	Orange/Green
Kim 2016	Green	Orange	Red	Orange	Orange	Orange	Orange	Orange
Kryger 2007	Orange	Orange	Red	Orange	Orange	Red	Orange	Orange
Mueller 2009	Orange	Red	Red	Orange	Orange	Orange	Orange	Red
Rydwik 2008	Orange	Red	Red	Orange	Green	Orange	Orange	Red
Sylliaas 2011	Green	Green	Red	Green	Orange	Orange	Green	Orange/Green

Notes: Green, low risk of bias; orange, some concerns; red, high risk of bias.

and DXA were predominantly employed as they are cheaper and portable (BIA) in comparison to MRI or emit less radiation (DXA) than a CT. Although muscle strength is the decisive factor for assessing sarcopenia (Cruz-Jentoft et al., 2019), further research should additionally address muscle quantity in order to draw valid conclusions about the state of sarcopenia in older populations and the efficacy of interventions. Further steps could include analysis of muscle quality.

Tests to determine the severity of sarcopenia were improved post-intervention in all of the reviewed studies, indicating better physical performance. Meta-analysis revealed significant improvements in the gait speed test, TUG, SPPB and 6MWT (Fig. 3, Appendix B), reflecting enhanced gait balance, leg strength, endurance (6MWT) and risk of falling (Welch et al., 2020). There were clear improvements in five out of six studies for the TUG post-intervention (−0.62; 95% CI: −0.81, −0.44). Without the outlier (Rydwik et al., 2008), the quality of evidence would be high. The gait speed test was less improved after intervention (0.46; 95% CI: 0.29, 0.63). It was performed with varying measurement methods in eight studies inducing a high inconsistency of the results, which may explain why less improvement was achieved than in the other examined lower-body functional tests (CST, TUG, SPPB, 6MWT). Although it is a very popular test for the ageing population, a standardised version should be compiled to achieve comparable results. It is already well accepted that the habitual gait speed test is more reliable than the maximal gait speed test (Rydwik et al., 2012). The included studies applied the maximal gait speed test until 2012 and, after this time, exclusively the habitual gait speed test. Both, SPPB and 6MWT were only conducted in two studies, with clear improvements following the intervention.

The prevalence of frailty or sarcopenia in the study population was rarely stated in the analysed articles. In addition, the applied methods for diagnosing sarcopenia were often not presented clearly (Table 1). Only Hassan et al. (2016) applied the approach of the EWGSOP to define their population as 35.7% sarcopenic. By comparison, Iannuzzi-Sucich et al. (2002) and Morley et al. (2014) defined sarcopenia by low muscle mass and identified 31 and 50% of the population over 80 years as sarcopenic, respectively.

Mean baseline muscle strength test results were predominantly sarcopenic for CST and age-appropriate for GS among the oldest old according to the sarcopenia threshold values of the EWGSOP (Table 2). Mean results of the CST improved in two studies – post-intervention – from sarcopenic to non-sarcopenic, while the mean results in GS changed from non-sarcopenic to sarcopenic in the control groups of two studies exclusively. These results indicated that upper-body strength among the oldest old, as measured by GS, was in a healthier condition than their leg strength, as measured by CST. Resistance training interventions had the potential to increase leg strength and regain healthy conditions.

The severity of the sarcopenia, based on the EWGSOP thresholds, was analysed in the reviewed articles. The mean results of the gait speed test in all of the studies were worse at baseline and remained sarcopenic post-intervention in contrast to those of the TUG (Table 2). It could be argued that the threshold for the gait speed test is probably too strict for the population of the oldest old as both tests measure similar capacities. Sarcopenic status in SPPB and 6MWT was difficult to evaluate, given the inclusion of just two studies.

Sub-group analysis of residential status revealed that the institutionalised population can be addressed particularly effectively in terms of GS (Appendix B). Inactivity and low upper-body strength pre-intervention may have contributed to the improvement in retirement home residents in comparison to older adults living in the community. Short in-house distances, coupled with the supporting staff, are two examples that might have enhanced adherence within retirement homes and therefore additionally improved the efficacy of the interventions. The definition of adherence, the intervention time span and the training frequency were different for each study. A direct comparison was therefore not possible. Further research should include populations from various retirement homes to demonstrate and confirm the cited advantages in terms of enhanced adherence and training efficacy for other sarcopenia-related parameters.

A high number of studies was excluded due to an intervention time of less than 12 weeks. Only four studies applied a longer intervention time (Table 1). Differences in efficacy due to the intervention time were not emphasised in this review. Follow-up tests revealed sustainable positive effects three (Hauer et al., 2012; Rydwik et al., 2008) or six months (Gudlaugsson et al., 2012) following the three and six-month intervention time spans, respectively.

No adverse events associated with machine-based progressive resistance training were found (or stated), an indication that the intervention was safe for the population of the oldest old. Similarly, no harm or injuries resulted during long, intensive training sessions lasting 1.5 h with up to 90% of 1RM, (Hauer et al., 2001). Moreover, adherence did not waive as a result of the intense training.

Some limitations must be considered in this review. A high average age of 80 years or older was chosen to address the oldest old. However, this proceeding also implies an inevitable small proportion of middle-aged people included in the review.

With regard to the study quality, the potential risk of bias was evaluated in all of the reviewed articles using the RoB tool as the common international standard in systematic reviews. Performance bias was difficult to avoid given the nature of the intervention (Table 3), i.e. that participants and study personnel in a training intervention can hardly be blinded for participation. Only one study managed to blind the participants as they had not been informed of the different degrees of effectiveness of the two training regimens, one of which was low-intensity resistance training that served as a control group (Hauer et al., 2012). The authors describe their procedure as "double-blinded", but it is uncertain whether, in addition to the participants and assessors, the study personnel were also blinded (which is unlikely). Attrition bias was hard to avoid due to the small study populations. Appraisals of very old people, especially during intervention studies involving physical activity, suffer from small sample sizes. In this review, more than half of the studies comprised less than 50 participants ($n = 8$ studies) indicating a low power of the original articles. Additionally, studies with participants belonging to different clusters were included (Hassan et al., 2016; Hewitt et al., 2018), i.e. retirement homes. Intention-to-treat analysis was not regularly applied, or was unclearly described. The definition of the primary endpoints (sample size calculation) was often neglected. Reporting bias was difficult to classify as study protocols were barely available and the outcomes of interest often poorly reported (e.g. missing concrete p-values). The latter is also due to the divergent requirements in former publications. Altogether, half of the studies were at high RoB (GRADE total), with limitations in study design or execution lowering the comparability and the impact of the results (Table 3).

The quality of evidence of the studies included in the meta-analysis was assessed using the GRADE approach (Appendix C). Quality of SPPB and 6MWT evidence was moderate, but with only two studies included (SPPB, 6MWT), it is important to acknowledge the large potential impact if the observed effect of one study differs in size or direction. It can be argued that enhanced heterogeneity (CST, gait speed test, TUG) is a result of outliers (Cadore et al., 2014; Rydwik et al., 2008; Sylliaas et al., 2011) in the first place. Without them, the evidence would be moderate or even high. The evidence of GS is of very low quality and must be contemplated with caution.

Strengths of the review and meta-analysis are rooted in the choice of

PICOs. They were chosen for the examination of sarcopenia based on the EWGSOP. To gain stimuli that are effective for muscle training, studies with progressive machine-based resistance training of at least 3 months (12 weeks) were included exclusively. To maintain a high level of quality, studies published before 2000 and those that did not meet the requirements of randomised controlled trials were excluded from the analysis. To generalise the results, studies that included hospitalised older adults were excluded from the review. In order to ensure greater comparability, interventions that were accompanied by any additional individual dietary supplementation were excluded. The resulting small number of included studies (14 out of 779) is also an indicator for a lack of adequate long-term progressive resistance training interventions for the oldest old in present society.

5. Conclusion

This systematic review indicated that progressive machine-based resistance training was an efficacious training method to enhance muscle strength, muscle quantity and physical performance in the oldest old. Although the data for muscle quantity were still insufficient for further meta-analysis.

The results of the meta-analysis revealed that the primary outcome measures which identify sarcopenia based on the EWGSOP improved significantly in terms of CST but not in terms of GS. As a secondary outcome of the meta-analysis, the physical performance tests TUG, gait speed test, SPPB and 6MWT also showed significant improvements. Thus, leg strength, gait balance, risk of falling and endurance may be specifically addressed through machine-based progressive resistance training in this age group.

Further analysis revealed that progressive resistance training interventions have the potential to shift sarcopenic into non-sarcopenic group mean values (threshold of the EWGSOP) especially for leg strength (CST) and physical performance (TUG).

The evidence comprised studies with high risk of bias, heterogeneity of measurement methods, and small sample sizes. More research is needed to address muscle quantity and upper-body strength in training and testing among the oldest old.

Registration and protocol

The systematic review and meta-analysis were registered in the International Prospective Register of Systematic Reviews (PROSPERO 2020 CRD42020163457).

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

EM and MS were responsible for the conception and design of the review. MS and NS validated the extracted data that were investigated by EM and NM. EM conducted meta-analysis that was coordinated by BH. EM wrote the initial draft. MS, NS, MH, MW and NM edited and revised the manuscript. MH supervised the research activity that was administrated by MS and EM.

Declaration of competing interest

None.

Acknowledgements

Many thanks to the authors of the included articles for their cooperation and supply of additional data for analyses.

Appendix A. Search strategy: progressive machine-based resistance training for prevention and treatment of sarcopenia in the oldest old.

PubMed (https://pubmed.ncbi.nlm.nih.gov/):

(((“Resistance Training” OR “strength training”) AND (“Sarcopenia”[Mesh] OR “Body Composition”[Mesh] OR “Hand Strength”[Mesh:NoExp] OR “chair stand test” OR “chair rise test” OR “sit to stand test” OR “short physical performance battery” OR “Walking”[Mesh] OR “timed up and go test” OR “exercise test”[Mesh])) AND (Randomized Controlled Trial[ptyp] AND (“2000/01/01”[PDat]: “2008/12/31”[PDat]) AND (German[lang] OR English[lang]) AND aged, 80 and over[Mesh)) OR (“Resistance Training”[Mesh] AND (“Sarcopenia”[Mesh] OR “Body Composition”[Mesh] OR “Hand Strength”[Mesh:NoExp] OR “chair stand test” OR “chair rise test” OR “sit to stand test” OR “short physical performance battery” OR “Walking”[Mesh] OR “timed up and go test” OR “exercise test”[Mesh]) AND (Randomized Controlled Trial[ptyp] AND (“2009/01/01”[PDat]: “2019/12/31”[PDat]) AND (German[lang] OR English[lang]) AND aged, 80 and over[Mesh]))

Filter: randomised controlled trial (RCT), 80+, language (English and German), time span (2000−2020).

Last update: 31.12.2020

Web of Science (www.webofknowledge.com):

((elderly OR old* OR age* OR resident*) AND (“resistance training” OR “strength training”) AND (sarcopenia OR “body composition” OR “grip strength” OR chair-stand-test OR chair-rise-test OR sit-to-stand-test OR “short physical performance battery” OR “walking speed” OR “gait speed” OR timed-up-and-go-test OR “walk test”) AND “randomi?ed controlled trial”)

Filter: language (English, German not available), time span (2000–2020), article*.

*Age and RCT not possible!

Last update: 31.12.2020

CINAHL (https://www.ebsco.com/de-de/produkte/datenbanken/cinahl-datenbank):

(((MH "Muscle Strengthening") OR (MH "Resistance Training")) AND (((MH "Sarcopenia") OR (MH "Body Composition") OR (MH "Grip Strength") OR (MH "Rising") OR (MH "Walking Speed") OR (MH "Exercise Test, Muscular") OR "short physical performance battery" OR timed-up-and-go-test))

Filter: language (English, German not available), time span (2000–2020), age (80+)*.

*RCT filter too strict!

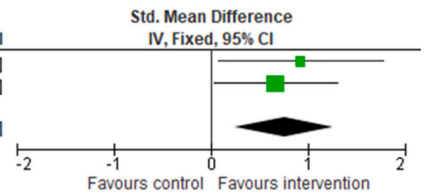
Last update: 27.04.2020

Appendix B. Effects of machine-based progressive resistance training interventions on parameters of muscle strength and physical performance.

a) Grip strength test institutionalised seniors

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Cadore 2014	183	52	11	130	58	13	35.4%	0.92 [0.07, 1.78]
Hassan 2016	21	7	20	15.9	7.9	21	64.6%	0.67 [0.04, 1.30]
Total (95% CI)			**31**			**34**	**100.0%**	**0.76 [0.25, 1.27]**

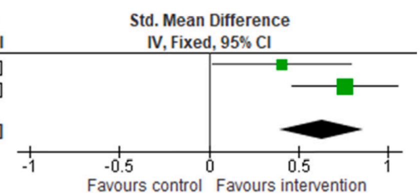
Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 2.94 (P = 0.003)



b) Short Physical Performance Battery

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Gudlaugsson 2012	10.7	1.39	48	10.1	1.52	58	36.4%	0.41 [0.02, 0.79]
Hewitt 2018	5.89	2.86	100	3.76	2.74	93	63.6%	0.76 [0.46, 1.05]
Total (95% CI)			**148**			**151**	**100.0%**	**0.63 [0.40, 0.86]**

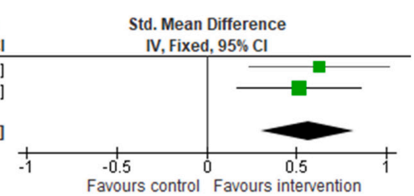
Heterogeneity: Chi² = 2.00, df = 1 (P = 0.16); I² = 50%
Test for overall effect: Z = 5.29 (P < 0.00001)



c) 6 min-walk-test

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Gudlaugsson 2012	491.1	67.9	48	447	71.59	58	43.6%	0.63 [0.23, 1.02]
Sylliaas 2011	297.2	120.8	100	240.7	80.7	50	56.4%	0.51 [0.17, 0.86]
Total (95% CI)			**148**			**108**	**100.0%**	**0.56 [0.30, 0.82]**

Heterogeneity: Chi² = 0.17, df = 1 (P = 0.68); I² = 0%
Test for overall effect: Z = 4.27 (P < 0.0001)



Appendix C. Quality of evidence (GRADE approach).

	CST	Grip strength test	Gait speed test	SPPB	TUG	6MWT
	Ansai 2016 Cadore 2014 Gudlaugsson 2012 Hauer 2001 Hauer 2012 Rydwik 2008 Sylliaas 2011	Cadore 2014 Gudlaugsson 2012 Hassan 2016 Kim 2016	Cadore 2014 Gudlaugsson 2012 Hassan 2016 Hauer 2001 Hauer 2012 Kim 2016 Rydwik 2008 Sylliaas 2011	Gudlaugsson 2012 Hewitt 2018	Cadore 2014 Gudlaugsson 2012 Hauer 2001 Hauer 2012 Rydwik 2008 Sylliaas 2011	Gudlaugsson 2012 Sylliaas 2011
Factors that can reduce the quality of the evidence (1 ⊖ or 2 ⊖⊖ levels)						
Limitations in study design or execution (Risk of Bias)	R/O/R/R/G/R/O-G	R/R/R/O ⊖	R/R/R/R/G/O/R/O-G	R/O-G	R/R/R/G/R/O-G ⊖	R/O-G
Inconsistency of results (unexplained heterogeneity)	I^2 = 86%, p < 0.001 substantial/ considerable ⊖⊖	I^2 = 69%, p = 0.02 substantial Sub-group analysis: I^2=0%, p = 0.64	I^2 = 78%, p < 0.001 substantial/ considerable ⊖⊖	I^2 = 50%, p = 0.16 moderate/ substantial	I^2 = 69%, p = 0.007 substantial ⊖	I^2 = 0%, p = 0.68 low
Indirectness of evidence						
Imprecision	n (outcome) = 513	n = 239 + benefit and harm balanced ⊖⊖	n = 582	n = 299 ⊖	n = 473	n = 256 ⊖
Publication bias						
Quality of evidence grades	⊖⊖	⊖⊖⊖	⊖⊖	⊖	⊖⊖	⊖
	Low	Very low	Low	Moderate	Low	Moderate

Notes:
Very low → We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
Low → Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Moderate → We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
High → We are very confident that the true effect lies close to that of the estimate of the effect.
R → Red, high risk of bias
O → Orange, some concerns
G → Green, low risk of bias
I^2 → Heterogeneity measure (%)
CST → Chair-stand-test
SPPB → Short Physical Performance Battery
TUG → Timed-Up-and-Go-test
6MWT → 6 min-walk-test

References

Ansai, J.H., Aurichio, T.R., Goncalves, R., Rebelatto, J.R., 2016. Effects of two physical exercise protocols on physical performance related to falls in the oldest old: a randomized controlled trial. Geriatr Gerontol Int 16, 492–499. https://doi.org/10.1111/ggi.12497.

Ardern, C.L., Büttner, F., Andrade, R., Weir, A., Ashe, M.C., Holden, S., Impellizzeri, F.M., Delahunt, E., Dijkstra, H.P., Mathieson, S., Rathleff, M.S., Reurink, G., Sherrington, C., Stamatakis, E., Vicenzino, B., Whittaker, J.L., Wright, A.A., Clarke, M., Moher, D., Page, M.J., Khan, K.M., Winters, M., 2022. Implementing the 27 PRISMA 2020 statement items for systematic reviews in the sport and exercise medicine, musculoskeletal rehabilitation and sports science fields: the PERSiST (implementing prisma in exercise, rehabilitation, sport medicine and SporTs science) guidance. Br. J. Sports Med. 56, 175–195. https://doi.org/10.1136/bjsports-2021-103987.

Cadore, E.L., Casas-Herrero, A., Zambom-Ferraresi, F., Idoate, F., Millor, N., Gomez, M., Rodriguez-Manas, L., Izquierdo, M., 2014. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. Age (Dordr.) 36, 773–785. https://doi.org/10.1007/s11357-013-9586-z.

Caserotti, P., Aagaard, P., Larsen, J.B., Puggaard, L., 2008. Explosive heavy-resistance training in old and very old adults: changes in rapid muscle force, strength and power. Scand. J. Med. Sci. Sports 18, 773–782.

Cho, K.H., Bok, S.K., Kim, Y.-J., Hwang, S.L., 2012. Effect of lower limb strength on falls and balance of the elderly. Ann. Rehabil. Med. 36, 386–393. https://doi.org/10.5535/arm.2012.36.3.386.

Cruz-Jentoft, A.J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A.A., 2019. Sarcopenia: revised european consensus on definition and diagnosis. Age Ageing 48, 16–31. https://doi.org/10.1093/ageing/afy169.

de Souto Barreto, P., Morley, J.E., Chodzko-Zajko, W., Pitkala, K.H., Weening-Djiksterhuis, E., Rodriguez-Manas, L., Barbagallo, M., Rosendahl, E., Sinclair, A., Landi, F., 2016. Recommendations on physical activity and exercise for older adults living in long-term care facilities: a taskforce report. J. Am. Med. Dir. Assoc. 17, 381–392. https://doi.org/10.1016/j.jamda.2016.01.021.

Fiatarone, M.A., Marks, E.C., Ryan, N.D., Meredith, C.N., Lipsitz, L.A., Evans, W.J., 1990. High-intensity strength training in nonagenarians: effects on skeletal muscle. JAMA 263, 3029–3034. https://doi.org/10.1001/jama.1990.03440220053029.

Fiatarone, M.A., O'Neill, E.F., Ryan, N.D., Clements, K.M., Solares, G.R., Nelson, M.E., Roberts, S.B., Kehayias, J.J., Lipsitz, L.A., Evans, W.J., 1994. Exercise training and nutritional supplementation for physical frailty in very elderly people. N. Engl. J. Med. 330, 1769–1775. https://doi.org/10.1056/NEJM199406233302501.

Fisher, N.M., Pendergast, D.R., Calkins, E., 1991. Muscle rehabilitation in impaired elderly nursing home residents. Arch. Phys. Med. Rehabil. 72, 181–185. https://doi.org/10.5555/uri:pii:000399939190150H.

Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W.J., Burke, G., McBurnie, M.A., 2001. Frailty in older adults: evidence for a phenotype. J. Gerontol. A Biol. Sci. Med. Sci. 56, M146–M156. https://doi.org/10.1093/gerona/56.3.M146.

Giné-Garriga, M., Roqué-Fíguls, M., Coll-Planas, L., Sitjà-Rabert, M., Salvà, A., 2014. Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: a systematic review and meta-analysis. Arch. Phys. Med. Rehabil. 95, 753–769. https://doi.org/10.1016/j.apmr.2013.11.007.

Greiwe, J.S., Cheng, B., Rubin, D.C., Yarasheski, K.E., Semenkovich, C.F., 2001. Resistance exercise decreases skeletal muscle tumor necrosis factor α in frail elderly humans. FASEB J. 15, 475–482. https://doi.org/10.1096/fj.00-0274com.

Gudlaugsson, J., Gudnason, V., Aspelund, T., Siggeirsdottir, K., Olafsdottir, A.S., Jonsson, P.V., Arngrimsson, S.A., Harris, T.B., Johannsson, E., 2012. Effects of a 6-month multimodal training intervention on retention of functional fitness in older adults: a randomized-controlled cross-over design. Int. J. Behav. Nutr. Phys. Act. 9, 107. https://doi.org/10.1186/1479-5868-9-107.

Guralnik, J.M., Simonsick, E.M., Ferrucci, L., Glynn, R.J., Berkman, L.F., Blazer, D.G., Scherr, P.A., Wallace, R.B., 1994. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J. Gerontol. 49, M85–M94. https://doi.org/10.1093/geronj/49.2.m85.

Haskell, W.L., Lee, I.-M., Pate, R.R., Powell, K.E., Blair, S.N., Franklin, B.A., Macera, C.A., Heath, G.W., Thompson, P.D., Bauman, A., 2007. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med. Sci. Sports Exerc. 39, 1423–1434. https://doi.org/10.1249/mss.0b013e3180616b27.

Hassan, B.H., Hewitt, J., Keogh, J.W., Bermeo, S., Duque, G., Henwood, T.R., 2016. Impact of resistance training on sarcopenia in nursing care facilities: a pilot study. Geriatr. Nurs. 37, 116–121. https://doi.org/10.1016/j.gerinurse.2015.11.001.

Hauer, K., Rost, B., Rutschle, K., Opitz, H., Specht, N., Bartsch, P., Oster, P., Schlierf, G., 2001. Exercise training for rehabilitation and secondary prevention of falls in geriatric patients with a history of injurious falls. J. Am. Geriatr. Soc. 49, 10–20. https://doi.org/10.1046/j.1532-5415.2001.49004.x.

Hauer, K., Schwenk, M., Zieschang, T., Essig, M., Becker, C., Oster, P., 2012. Physical training improves motor performance in people with dementia: a randomized controlled trial. J. Am. Geriatr. Soc. 60, 8–15. https://doi.org/10.1111/j.1532-5415.2011.03778.x.

Hewitt, J., Goodall, S., Clemson, L., Henwood, T., Refshauge, K., 2018. Progressive resistance and balance training for falls prevention in long-term residential aged care: a cluster randomized trial of the sunbeam program. J. Am. Med. Dir. Assoc. 19, 361–369. https://doi.org/10.1016/j.jamda.2017.12.014.

Higgins, J.P., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savović, J., Schulz, K.F., Weeks, L., Sterne, J.A., 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 343, d5928. https://doi.org/10.1136/bmj.d5928.

Iannuzzi-Sucich, M., Prestwood, K.M., Kenny, A.M., 2002. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. J. Gerontol. A Biol. Sci. Med. Sci. 57 https://doi.org/10.1093/gerona/57.12.M772. M772-M777.

Izquierdo, M., Cadore, E.L., 2014. Muscle power training in the institutionalized frail: a new approach to counteracting functional declines and very late-life disability. Curr. Med. Res. Opin. 30, 1385–1390. https://doi.org/10.1185/03007995.2014.908175.

Kim, H., Kim, M., Kojima, N., Fujino, K., Hosoi, E., Kobayashi, H., Somekawa, S., Niki, Y., Yamashiro, Y., Yoshida, H., 2016. Exercise and nutritional supplementation on community-dwelling elderly japanese women with sarcopenic obesity: a randomized controlled trial. J. Am. Med. Dir. Assoc. 17, 1011–1019. https://doi.org/10.1016/j.jamda.2016.06.016.

Kryger, A.I., Andersen, J.L., 2007. Resistance training in the oldest old: consequences for muscle strength, fiber types, fiber size, and MHC isoforms. Scand. J. Med. Sci. Sports 17, 422–430.

Law, T.D., Clark, L.A., Clark, B.C., 2016. Resistance exercise to prevent and manage sarcopenia and dynapenia. Annu. Rev. Gerontol. Geriatr. 36, 205–228. https://doi.org/10.1891/0198-8794.36.205.

Leong, D.P., Teo, K.K., Rangarajan, S., Lopez-Jaramillo, P., Avezum, A., Orlandini, A., Seron, P., Ahmed, S.H., Rosengren, A., Kelishadi, R., Rahman, O., Swaminathan, S., Iqbal, R., Gupta, R., Lear, S.A., Oguz, A., Yusoff, K., Zatonska, K., Chifamba, J., Igumbor, E., Mohan, V., Anjana, R.M., Gu, H., Li, W., Yusuf, S., 2015. Prognostic value of grip strength: findings from the prospective urban rural epidemiology (PURE) study. Lancet 386, 266–273. https://doi.org/10.1016/S0140-6736(14)62000-6.

Liu, C.J., Latham, N.K., 2009. Progressive resistance strength training for improving physical function in older adults. Cochrane Database Syst. Rev. 2009, CD002759 https://doi.org/10.1002/14651858.CD002759.pub2.

Lopez, P., Pinto, R.S., Radaelli, R., Rech, A., Grazioli, R., Izquierdo, M., Cadore, E.L., 2018. Benefits of resistance training in physically frail elderly: a systematic review. Aging Clin. Exp. Res. 30, 889–899. https://doi.org/10.1007/s40520-017-0863-z.

Martone, A.M., Lattanzio, F., Abbatecola, A.M., La Carpia, D., Tosato, M., Marzetti, E., Calvani, R., Onder, G., Landi, F., 2015. Treating sarcopenia in older and oldest old. Curr. Pharm. Des. 21, 1715–1722. https://doi.org/10.2174/1381612821666150130122032.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L.A., Group, P.-P., 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst. Rev. 4, 1. https://doi.org/10.1186/2046-4053-4-1.

Morley, J.E., Anker, S.D., von Haehling, S., 2014. Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology-update 2014. J. Cachexia. Sarcopenia Muscle 5, 253–259. https://doi.org/10.1007/s13539-014-0161-y.

Mueller, M., Breil, F.A., Vogt, M., Steiner, R., Lippuner, K., Popp, A., Klossner, S., Hoppeler, H., Dapp, C., 2009. Different response to eccentric and concentric training in older men and women. Eur. J. Appl. Physiol. 107, 145–153. https://doi.org/10.1007/s00421-009-1108-4.

Podsiadlo, D., Richardson, S., 1991. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J. Am. Geriatr. Soc. 39, 142–148. https://doi.org/10.1111/j.1532-5415.1991.tb01616.x.

Review Manager, 2014. (RevMan) [Computer program]. Version 5.3. The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen.

Rydwik, E., Lammes, E., Frändin, K., Akner, G., 2008. Effects of a physical and nutritional intervention program for frail elderly people over age 75. A randomized controlled pilot treatment trial. Aging Clin. Exp. Res. 20, 159–170. https://doi.org/10.1007/BF03324763.

Rydwik, E., Bergland, A., Forsen, L., Frändin, K., 2012. Investigation into the reliability and validity of the measurement of elderly people's clinical walking speed: a systematic review. Physiother. Theory Pract. 28, 238–256. https://doi.org/10.3109/09593985.2011.601804.

Schulz, K.F., Altman, D.G., Moher, D., 2010. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Ann. Intern. Med. 152, 726–732. https://doi.org/10.7326/0003-4819-152-11-201006010-00232.

Sylliaas, H., Brovold, T., Wyller, T.B., Bergland, A., 2011. Progressive strength training in older patients after hip fracture: a randomised controlled trial. Age Ageing 40, 221–227. https://doi.org/10.1093/ageing/afq167.

The GRADE Working Group, 2013. In: Schünemann, H., Brożek, J., Guyatt, G., Oxman, A. (Eds.), GRADE Handbook for Grading Quality of Evidence and Strength of Recommendations.

Tietjen-Smith, T., Smith, S.W., Martin, M., Henry, R., Weeks, S., Bryant, A., 2006. Grip strength in relation to overall strength and functional capacity in very old and oldest old females. Phys. Occup. Ther. Geriatr. 24, 63–78. https://doi.org/10.1080/J148v24n04_05.

Toebes, M.J.P., Hoozemans, M.J.M., Furrer, R., Dekker, J., van Dieën, J.H., 2015. Associations between measures of gait stability, leg strength and fear of falling. Gait Posture 41, 76–80. https://doi.org/10.1016/j.gaitpost.2014.08.015.

Valenzuela, T., 2012. Efficacy of progressive resistance training interventions in older adults in nursing homes: a systematic review. J. Am. Med. Dir. Assoc. 13, 418–428. https://doi.org/10.1016/j.jamda.2011.11.001.

Welch, S.A., Ward, R.E., Beauchamp, M.K., Leveille, S.G., Travison, T., Bean, J.F., 2020. The Short Physical Performance Battery (SPPB): a quick and useful tool for fall risk stratification among older primary care patients. J. Am. Med. Dir. Assoc. https://doi.org/10.1016/j.jamda.2020.09.038. S1525-8610(20)30838-0.

Yarasheski, K.E., Pak-Loduca, J., Hasten, D.L., Obert, K.A., Brown, M.B., Sinacore, D.R., 1999. Resistance exercise training increases mixed muscle protein synthesis rate in frail women and men $\geq$ 76 yr old. Am. J. Physiol. Endocrinol. Metab. 277, E118–E125. https://doi.org/10.1152/ajpendo.1999.277.1.E118.