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ACADEMIC LITERATURE REVIEW

Exercise and health in frail elderly people: a review of randomized controlled trials

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Abstract Frailty is a physiological syndrome that increases the risk of poor health. Although some research has been conducted to study the benefits of physical exercise in frail elderly populations, different operational definitions of frailty have been used, and this makes the studies difficult to compare. The present review was aimed at examining the influence of exercise on health in frail older adults. Studies using randomized controlled trials that administered an exercise program to a frail elderly population and that had an operational definition of frailty were selected from publications between January 2000 and October 2008. Information about the study population, frailty criteria, exercise program, principles of exercise training, randomization procedures, main and secondary outcome measures, study follow-up, and control group characteristics was taken from these studies, and the results from a final sample of 28 articles are discussed. Exercise training seems to be a safe and effective tool for promoting and maintaining optimal health levels in a wide variety of vulnerable older adults. However, the lack of studies on a well-defined frail older adult sample with selection procedures based on current knowledge in this field does not allow us, at the present time, to conclude that exercise influences health in this population. Further research is needed to confirm the benefits of exercise on health in frail older adults. The study population must be selected based on current knowledge in the area of frailty, and the design of the exercise program must be based on principles of training.

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Introduction

Frailty is a syndrome (sometimes with subclinical signs) that disturbs the function of several physiologic systems [1, 2]. This phenomenon has diverse etiological factors, possibly arising due to the interaction of biological (including genetics [3]), cognitive, social, clinical, psychological, and environmental aspects [4]. Researchers have been focusing their efforts in the study of the physical components of this syndrome, the so-called physical frailty. This review focuses on physical frailty. This health condition is directly associated with age [5] and enhances the risk of falls, hospitalization, morbidity, disability, and mortality [6, 7]. Its prevalence varies among researches, but in general, it is between 7% and 32% [8]. Despite its importance for a successful aging, there is a lack of consensus regarding operational definitions of frailty and "frail" older adults, which diminishes comparability among studies. Although there is a historical confusion in scientific publications concerning the usage of frailty, comorbidity, and disability [9], with the two latter often being utilized as a synonym for the former, current knowledge indicates that frailty is a singular entity different from disability and comorbidity [10, 11]. Frail older adults often present a comorbidity condition and functional limitations [6], which indicate a strong linkage among these conditions. Although the debate concerning operational definitions of frailty continues, the most utilized definition is the one proposed by Fried et al. [6]. These authors defined frailty as meeting at least three of the following five indicators: (1) low physical activity level; (2) weakness; (3) slowness; (4) shrinking; and (5) poor endurance and energy.

A physically inactive lifestyle decreases cardiorespiratory endurance, flexibility, strength, and mobility ability (balance and muscular coordination). In this sense, physical inactivity (or a low level of physical activity) is one of the most frequent indicators of frailty found in studies [12]. Growing scientific evidence has shown the influence of exercise on frailty [13]. However, the different exercise-related regimens (type, frequency, intensity, and duration) and some inconsistencies found in randomized controlled trials (RCT), such as differences in operational definitions of frailty or no definition at all of a supposed frail elderly population, make comparisons among researches difficult and add to further complications in the debate on this subject.

The aim of this review was to study the influence of exercise on health in elderly people (≥60 years old) defined as "frail." In this way, RCTs that administered an exercise program to a frail older adult population and that presented an operational definition of frailty were compiled, and results were discussed. Due to relatively recent advances in research on the frailty phenomenon, the present article selected RCTs published from January 2000 onwards.

Methods

Search strategy

Electronic searches were made in October 2008, utilizing three electronic databases: PubMed, Cochrane Library, and SciELO. Words for searches were entered in blocks of four, each block with a specific terminology (related to: exercise, elderly, frailty, and RCT). Similar to the recent systematic review on frailty made by Chin A Paw et al. [13], exercise-related terms (e.g., exercise, physical activity, and training) were exhaustively interchanged in AND combinations with age-related (e.g., older adult, elderly, oldest, very old, and elders), frailty-related (e.g., frailty, frail), and study design-related words (e.g., randomized, randomization, controlled trial, intervention, evaluation study, and treatment outcome). Some articles from the author's database and articles cited for another review [13] on exercise and frailty[1] were incorporated when they met inclusion criteria.

[1] The difference between the present review and the review written by Chin A Paw et al. [13] is that the former studied the impact of exercise programs on health (physiological, physical function, and psychological outcomes) in elderly population with a definition of frailty, whereas the latter studied physical performance as measured by performance-based tests of physical function in elderly people labeled as "frail" (a definition of frailty was not mandatory for inclusion in the study).

Inclusion criteria

The inclusion criteria were: (1) RCT study design; (2) presence of at least one exercise group and one control group (receiving no intervention, non-exercise activities, or light intensity exercise such as a flexibility exercise program); (3) exercise intervention was not overlapped for another intervention; and (4) to present an operational definition of frailty. All full-text articles written in English, French, Spanish, and Portuguese were searched. However, all articles found for this review had been written in English, except for one article written in Spanish that was excluded because it was not a RCT.

Procedures

After electronic searches, articles with frailty-related words in the title were immediately accessed. Abstract and, if necessary, the methods topic of the text were read. This methodology allowed the author to immediately eliminate articles out of scope or that did not meet inclusion criteria. If inclusion criteria were met, with a frailty definition clearly indicated in the text, articles were selected (n=13 [14–26]). If complementary information were needed, the authors were contacted by e-mail (n=15; electronic address for one author was unavailable). Authors that did not answer the first e-mail were contacted once more 10 days after the first e-mail. Articles that met inclusion criteria were selected (n=8 [27–34]). Studies in which full text was not available but that were possible candidates to meet inclusion criteria were preselected, and their authors were contacted by e-mail to provide full text. From the nine authors contacted, seven sent their articles, but just two articles [35, 36] met inclusion criteria and were selected. Two articles [37, 38] cited in another review about exercise effectiveness in frail older adults [13] were selected for the present study. Finally, three studies [39–41] from the author's personal database took part in this review. Articles selected from other reviews and from the author's personal database did not necessarily have the terms "frail" or "frailty" in the title, but authors of these articles defined the study sample as frail in the text.

Information about study population, frailty criteria, exercise program, principles of exercise training, randomization, main and secondary outcome measures, study follow-up, and control group characteristics were extracted from each article. Some exercise regimen-related principles of training (progression, individualization, frequency, duration, intensity, and specificity—the latter was achieved when the exercise program was theoretically able to induce improvements on main outcome measures. For example, if strength is the main outcome measure of a study, and the exercise program consisted in resistance training in this case, exercise specificity was achieved) were evaluated herein on their "presence" or "absence" in the exercise program design (just when main outcome measures were physiological measures or physical performance-based measures). This evaluation, at least for frequency, duration, and intensity principles, was based on recommendations from the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) for older adults [42] (for strength training, the number of repetitions per set and the number of exercises per session were not evaluated). Continuity was not evaluated because exercise adherence is a very complex health behavior, and it is not the aim of this study. Balance/coordination and task-specific exercises do not have any precise prescription regarding frequency, duration, and intensity in elderly population [42]; that is why, they were considered as "present" herein if those exercises were met, at least twice a week during 20 min in a moderate to high intensity (as described by authors).

Results

The final sample was composed of 28 articles. Table 1 shows all studies arranged in alphabetical order, with information concerning the study sample, randomization, dropouts, and the operational criteria of frailty. Six studies [14, 19, 24, 37, 39, 41] based their criteria of frailty, at least in part, on functional limitation degree as measured by activities of daily living (ADL) and instrumental activities of daily living; disability in executing ADLs was the principal criteria for two of them [39, 41]. Performance in some functional fitness tests was the most utilized criteria to define frailty, being present in at least 19 articles [14, 15, 19–28, 31–34, 36, 37, 40], while physiological measures were found to characterize frailty in nine studies [14, 19, 20, 22, 25, 26, 34–36] and fall-related aspects in six studies [24, 28, 31–33, 38]. Nutritional status and metabolic aspects contributed to define a frail elderly population in six articles [16–18, 20, 29, 38], and a low physical activity level participated in ten definitions [16–18, 20, 22, 25, 26, 29, 34, 36].

Five articles [16–18, 20, 29] presented an operational definition of frailty that is different from disability and in accordance with current knowledge about this syndrome. They met two or more of the following aspects: physiological (for example, handgrip strength as measured by a dynamometer) and metabolic (for example, unintentional weight lost) aspects, poor endurance and energy, physical performance or mobility factors (for example, walking speed), and physical inactivity.

Sample size varied from 13 [23] to 311 [25, 26, 36] individuals among studies. In eight articles [16, 20, 22, 24–26, 34, 36], it was ≥200 persons, and in five others [19, 23, 27, 30, 35], it was ≤46. Mean age varied from 78.5 [17] to 86.8 [27] years of age.

Exercise program, study follow-up and intervention length, control group characteristics, and training principles can be seen in Table 2, arranged by type of exercise program. Most of the studies (n=25) utilized supervised exercise training, and the other three articles chose home-based exercise [21, 24, 40]. Multicomponent training was the choice for nine studies [14, 15, 19, 28, 29, 31–33, 37]. Tai chi exercise [22, 25, 26, 34, 36], resistance training [23, 24, 27, 35, 38], as well as skills and functional training [16–18, 39, 41] were found in five articles, and balance/gait/coordination in four other studies [20, 21, 30, 40]. Intervention length varied from a 48-week period with tai chi exercise [22, 25, 26, 36] to a 10-week intervention with resistance/balance program [24, 27, 35] or multicomponent training [31–33]. Control group characteristics also varied among studies, but most of them utilized group activities (either low-intensity exercise—commonly focused on flexibility or social groups) to prevent influence from "socializing and attention effects" on the results achieved. Regarding training principles, exercise specificity and frequency were the most prevalent principles being found in all studies followed by exercise individualization (except for one study [27]); exercise intensity was the least prevalent principle being "present" in 12 articles [14, 16, 19, 24, 28, 29, 31, 32, 35, 38, 39, 41].

Table 3 presents the main outcome measures and the secondary outcome measures, as well as respective results, arranged by type of main outcome measures. The results indicate significant differences that favored participants in the exercise group with relation to subjects in the control group. For some studies, results of secondary outcome measures were not reported because either there were no secondary outcome measures or authors did not clearly specify those measures in the articles. Most of the articles had physical function (self-reported and performance-based) and mobility ability measures as the main outcome of the study [14–16, 21, 27–32, 34, 36–41] followed by physiological measures [14, 16, 18, 19, 23, 29, 32, 34, 35, 38, 41]; psychological and mental aspects were found in seven articles [17, 22, 24, 25, 33, 34, 38] and fall risk in three studies [20, 24, 26]. Four articles [17, 24, 31, 38] did not present any difference between exercisers and control group participants regarding the results of the main outcome measures. Just in two studies, exercise training had a negative effect for frail elderly regarding main outcome measure (fall-risk [20] and cardiovascular endurance [34]). Results on secondary outcome measures were not achieved for six [17, 18, 21, 24, 28, 34] of the 14 studies concerned (i.e., those that clearly presented secondary outcome measures).

Table 1 Study sample, randomization, dropouts, and frailty criteria of all 28 articles

Study	Study sample	Randomization	Dropouts	Frailty criteria
Alexander et al. [39]	n=161 community-dwelling elderly (≥65 years, mean age 82 years)	Exercise group (EG) = 81 persons and Control group (CG) = 80	n=37, EG=21, and CG=16	Requiring assistance in performing ≥1 mobility-related ADL(transferring, walking, bathing, and going to the toilet)
Binder et al. [14]	n=119 (115 followed-up) community-dwelling older adults (≥78 years, mean age of 83±4 years)	3:2 ratio (EG and CG, respectively); EG=69 and CG=50	n=32, CG=9, and EG=23	Mild to moderate frailty—meeting ≥2 indicators: (1) score between 12 and 32 on the modified physical performance test (PPT); (2) difficulty or need ≥2 IADL or 1 ADL; and (3) VO2 peak between 10 and 18 ml/kg/min
Binder et al. [37]	n=90 (85 followed-up) community-dwelling older adults (≥65 years) with proximal femur fracture (within 16 weeks from screening evaluation)	Within strata based on surgical repair procedure; CG=44 and EG=46	n=22, CG=8, and EG=14	Modified PPT score between 12 and 28 and self-reported difficulty or requirement for assistance with ≥1 ADL
Brown et al. [15]	n=87 (men=37) community-dwelling independent-living (but with difficulty) older adults (≥78 years, mean age 83±4 years)	EG=48 and CG=39		PPT Score between 18 and 31 (extreme values included)
Chin A Paw et al. [16]	n=217 (70% women) community-dwelling elderly (≥70 years, mean age of 78.7)	Placebo-controlled intervention based on a 2×2 factorial design; EG (n=55); a group receiving enriched foods (EF, n=58); EG+EF (n=60); or CG (n=44)	n=56, 26–29% in intervention groups and 16% in CG	inactivity (weekly ≥30 min of brisk walking, cycling, and gymnastics) and involuntary weight loss or a body mass index (BMI) below average
Chin A Paw et al. [17]	n=139 community-dwelling independent-living elderly (≥70 years, mean age 78.5±5.7)	see Chin A Paw et al. [16]		see Chin A Paw et al. [16]
de Jong et al. [18]	n=143 community-dwelling independent-living elderly (≥70 years, mean age 78.6±5.6)	see Chin A Paw et al. [16]		see Chin A Paw et al. [16]
Dorner et al. [27]	n=42 long-term facility care residents(≥75 years, mean age 86.8±5.8)	Within strata based on sex, age, mini mental state exam score, and strength (EG=21 and CG=21)	n=12, EG=6, and CG=6	Impaired mobility (Tinetti score)
Ehsani et al. [19]	n=46 older adults extracted from Binder et al. 2002	EG=22 (83±3.6 years) who had increased their aerobic capacity due to training and CG=24 (84±4.2 years)		Binder et al. [14]
Faber et al. [20]	n=278 (79% women) residents of self-care and nursing care residences (63–98 years old, mean age 84.9±6 years)	Long-term care centers were randomized to one of the two exercise programs; participants of each center were randomized to EG and CG	n=40	Meeting ≥3 frailty indicators (≤2 for prefrailty): (1)unintentional weight loss, (2)weakness, (3)exhaustion, (4)slowness, and (5)low physical activity
Gill et al. [21]	n=188 elderly (≥75 years, mean age 83 years) who lived at home	Within strata based on the level of physical frailty; EG=94 and CG=94	n=43, EG=33, and CG=10	Meeting one (moderate) or two (severe) frailty indicators: (1) requiring more than 10 s to perform a gait test and (2) not being able to stand up from a seated position with their arms folded

Gill et al. [40]	see Gill et al. [21]	see Gill et al. [21]	see Gill et al. [21]	see Gill et al. [21]
Greenspan et al. [22]	n=267 transitionally frail older women (≥70 years); residents of independent-living facilities	EG=148 and CG=143	n=86, EG=45, and CG=41	Speechley and Tinetti (1991) criteria based on age, gait, and balance, walking activity for exercise, other physical activity for exercise, presence or absence of depression, use of sedatives, near–vision status, upper and lower extremity strength, and lower extremity disability
Greiwe et al. [23]	n=13 older adults (>75 years)	EG=8 and CG=5	n=0	Based on functional fitness tests
Jensen et al. [28]	n=187(75% women) elderly (65–98 years; median age 84) living in care facilities	Cluster randomization of the facility care residences with EG=89 and CG=98	n=35, EG=12, and CG=23	being most prone to falls (mobility interaction fall chart)
Latham et al. [24]	n=243 elderly (≥65 years; mean age 79.1±6.9 years)	2×2 stratified block randomization technique (6/block): EG=120 and CG=123; and Vitamin=121, and placebo=122	n=21, EG=8, and CG=13	Based on Winograd et al. (1991) criteria, i.e., meeting ≥1 indicators: (1) dependency in ADL; (2) prolonged bed rest; (3) impaired mobility; and (4) recent fall
Miller et al. [38]	n=100 older patients (≥70 years; mean age 84 years) from a medical center	Stratified (community or residential care), block randomization method (blocks of 12): EG=25, Nutritional Supplement (NS=25), EG+NS=24, and CG=26	n=7, EG=2, NS=2, EG+NS=2, and CG=1	Fall-related fracture of the lower limb and being proxy for low nutritional status (midarm circumference <25th percentile)
Rosendahl et al. [41]	n=191 older adults (≥65 years; mean age 84.7±6.5), residents of care facilities	stratified cluster-randomized, with a 2×2 model: CG=50, EG=45, EG+Protein (EG+P) =46, and CG+P=50	n=28, EG+P=5, EG=9, CG=5, and CG+P=9	being dependent in ≥1 ADL
Rydwik et al. [29]	n=96 community-dwelling elderly (>75 years)	Consecutive randomization in batches; started with the oldest individual: Nutrition (N, n=25), EG=23, EG+N=25, and CG=23	n=31, EG=4, EG+N=11, N=7, and CG=9	Unintentional weight loss ≥5% and/or BMI≤20 and low physical activity level
Sattin et al. [25]	n=311 (n=20 men) transitionally frail elderly (70–97 years; mean age 80.9 years), residents of independent-living facilities	EG=158 and CG=153	n=94, EG=49, and CG=44	see Greenspan et al. [22]
Seynnes et al. [35]	n=27 older adults (≥70 years); nursing home residents	Strata based on 1RM values: High intensity (EG-HI, n=8), Low intensity (EG-LI, n=6), or CG=8	n=5	being a nursing home resident with a knee extension <10 kg (1RM)
Shimada et al. [30]	n=34 older adults (67–91 years, mean age 80.8±6.6 years), attending a care facility	strata based on the ability to walk outdoors without help: EG-B(balance exercise=12), EG-G (gait training=12), and CG=10	n=2, CG=1, and EG-G=1	Living in/or utilizing a day-care program; subjects had a certification of long-term care need by the Japanese public nursing care insurance system for frailty
Timonen et al. [33]	n=68 older women (≥75 years; mean age 83±3.9 years) discharged from an acute hospital ward	EG (n=34) and CG (n=34)	n=16, EG=10, and CG=6	difficulties in mobility and balance and tendency to fall when walking unassisted during an acute disease
Timonen et al. [32]	see Timonen et al. [33]	see Timonen et al. [33]	see Timonen et al. [33]	see Timonen et al. [33]
Timonen et al. [31]	see Timonen et al. [33]	see Timonen et al. [33]	see Timonen et al. [33]	see Timonen et al. [33]

Table 1 (continued)

Study	Study sample	Randomization	Dropouts	Frailty criteria
Wolf et al. [26]	see Sattin et al. [25]	see Sattin et al. [25]	see Sattin et al. [25]	see Greenspan et al. [22]
Wolf et al. [34]	n=200 (19% of men) community-dwelling older adults (≥70 years)	2 EGs (tai chi, TC=72 and balance training, BT=64) and one CG (n=64). Randomization in cohorts of 32 (BT=10, CG=10, and TC=12) for each of the first four cohorts; the last two were randomized in cohorts of 36 (12 subjects to each group)	n=13, TC=6, BT=4, and CG=3	see Greenspan et al. [22]
Wolf et al. [36]	see Sattin et al. [25]	see Sattin et al. [25]	see Sattin et al. [25]	see Greenspan et al. [22]

Discussion

This review provides some evidence of exercise effectiveness on health in a population of older adults defined as frail. The results presented for the analyzed 28 articles show that physiological factors, as well as functional fitness (FF, especially performance-based measures) and mobility ability (balance and coordination) and psychological aspects may be improved by exercise intervention in several vulnerable elderly populations.

Frailty criteria varied very much among studies. It is not surprising that the operational definition of frailty was not the same among articles because frailty is a recent subject in this research area. Furthermore, a standardized criterion of frailty has not yet been achieved by experts in this field [43]. Although it is very early to propose a single definition of frailty and then to standardize its operational criteria, efforts must be done to clearly define a frail elderly sample based on current knowledge in this field, thus, dissociating this syndrome from "disability." Just five articles [16–18, 20, 29] presented an operational definition of frailty in accordance with current knowledge about this syndrome. In these studies, exercise was able to improve FF, mobility, lean body mass, and strength. One of them [20] presented contradictory results (FF and risk of falls were improved in prefrail older adults, but the opposite results were found among frail individuals). Although these results suggest a positive influence of exercise on health in frail older adults, it is too early to support this. More RCT studies are needed to confirm exercise benefits in a well-defined frail elderly population.

Future RCT researches on physical frailty must pay attention to the selection process of the study sample. At least three studies [27, 28, 41] had a sample partially composed of cognitively impaired or demented individuals. As indicated by Ferrucci et al. [44], frailty as a result of reduced cognition is considered a distinct clinical entity, although, decline in cognition may be found in frail persons. Intervention length is also a very important aspect for achieving improvements by exercise intervention. Frail older adults constitute a more vulnerable population when compared to healthy elderly; then, to provide improvements in physiological factors (e.g., strength, cardiovascular endurance, and flexibility), as well as in FF, they may need much time to adapt to and to progress in exercise volume.

Multicomponent training was the most utilized type of exercise program followed by tai chi, and skills and functional training, and resistance exercises. However, some incoherencies in relation to exercise programs were found. First, some studies did not clearly expose the exercise regimen-related principles of training. Exercise frequency, intensity (and how it is monitored), specificity, progression, individualization, and session duration are

Table 2 Exercise program, study follow-up, control group characteristics, and training principles

Study	Exercise program	Study follow-up and intervention length	Control group characteristics	Training principles
Binder et al. [14]	Supervised multicomponent training (flexibility, balance, coordination, speed of reaction, strength, and endurance), three times per week during 9 months	9 months	Low-intensity home-based training (flexibility); 1 h/session, two to three times per week for 9 months	Frequency, duration, intensity, progression, individualization, and specificity
Ehsani et al. [19]	see Binder et al. [14]	see Binder et al. [14]	see Binder et al. [14]	progression, individualization, frequency, duration, intensity, and specificity
Brown et al. [15]	Supervised low-intensity multicomponent training, three times per week for 3 months (flexibility, balance, body handling skills, speed of reaction, coordination, and strength)	3 months	Low-intesity home-based exercise (flexibility); 1 h/session, three times per week for 3 months	Progression, frequency, individualization, and specificity
Jensen et al. [28]	11-week supervised multicomponent exercise program (balance, ambulation, strength, endurance, flexibility, and safe movement behavior) executed, in general, two to three times per week, 1–3 h/week	11-week intervention, 9-month follow-up	Usual care	Progression, individualization, intensity, duration, frequency, and specificity
Rydwik et al. [29]	Supervised multicomponent exercise program (endurance, strength, and balance), 1 h/session, two times per week for 12 weeks	3-month intervention, 9-month follow-up	General advice on physical training and diet	Progression, individualization, intensity, duration, frequecy, and specificity
Timonen et al. [33]	Supervised multicomponent exercise program (resistance training and functional exercises), two times per week, 90 min/session, for 10 weeks	10-month intervention, 9-month follow-up after intervention	Requested to perform a home-based functional exercise program, two to three times per week	
Timonen et al. [32]	see Timonen et al. [33]	see Timonen et al. [33]	see Timonen et al. [33]	Progression, individualization, intensity, duration, frequency, and specificity
Timonen et al. [31]	see Timonen et al. [33]	see Timonen et al. [33]	see Timonen et al. [33]	Progression, individualization, intensity, duration, frequency, and specificity
Binder et al. [37]	6 months of supervised multicomponent training (flexibility, balance, coordination, movement speed, strength, and endurance), 45–90 min/session (with possible breaks), three times per week	6 months	Low-intesity home-based exercise (flexibility); 1 h/session three times per week for 6 months	Progression, individualization frequency, specificity, and duration
Greenspan et al. [22]	Supervised tai chi exercise (trunk rotation, weight shifting, coordination, and gradual narrowing of the lower extremity stance), two times per week from 10 to 50 min for 48 weeks	48 weeks	wellness educational program (instructions on falls-prevention, exercise, balance diet, and nutrition) 1 h/week	
Sattin et al. [25]	see Greenspan et al. [22]	see Greenspan et al. [22]	see Greenspan et al. [22]	
Wolf et al. [26]	see Greenspan et al. [22]	see Greenspan et al. [22]	see Greenspan et al. [22]	Progression, individualization, duration, frequency, and specificity
Wolf et al. [36]	see Greenspan et al. [22]	see Greenspan et al. [22]	see Greenspan et al. [22]	Progression, individualization, frequency, duration, and specificity (for some measures)
Wolf et al. [34]	15 weeks of supervised tai chi (two times per week; subjects were requested to try two times per day for 15 min—not monitored) or balance training (once per week)	15-month intervention; 4-month after follow-up	Discussions with a nurse (e.g., sleep disorders), once a week, 1 h/session for 15 weeks	Progression, frequency individualization, and specificity
Greiwe et al. [23]	Supervised resistance training program, three times per week for 3 months, 50–90 min/session	3 months	Light stretching program for 3 months	
Latham et al. [24]	Home-based resistance quadriceps exercise (ankle cuff weights), three times per week during 10 weeks	10-month intervention, 6-month follow-up	Frequency-matched telephone calls and home visits	Individualization, specificity, intensity, and frequency
Dorner et al. [27]	three times per week, 50 min/session, of a supervised resistance exercise program focused on strength and balance	10 weeks		Frequency, duration, and specificity

Table 2 (continued)

Study	Exercise program	Study follow-up and intervention length	Control group characteristics	Training principles
Seynnes et al. [35]	Supervised 10-week resistance training (knee muscles), three times per week	10 weeks	Placebo exercise (empty cuff weights)	Progression, individualization, intensity, frequency, and specificity
Miller et al. [38]	Supervised resistance training (hip extensors and abductors, knee extensors, ankle dorsi, and plantar-flexors), three times per week, 20–30 min/session for 12 weeks	12 weeks	Usual care. matched visits ("attention effect"), three times per week (weeks 1–6); and once a week (weeks 7–12)	Progression, individualization, intensity, duration, frequency, and specificity
Chin A Paw et al. [16]	Supervised skills training program, two times per week for 17 weeks, 45 min/session (focused on strength, speed, endurance, flexibility, and coordination)	17 weeks	social program, once or twice a week, 90 min/session (adjustment for socializing and attention effects)	Progression, individualization, duration, frequency, intesity, and specificity
Chin A Paw et al. [17]	see Chin A Paw et al. [16]	see Chin A Paw et al. [16]	see Chin A Paw et al. [16]	
de Jong et al. [18]	see Chin A Paw et al. [16]	see Chin A Paw et al. [16]	see Chin A Paw et al. [16]	
Alexander et al. [39]	Supervised bed- and chair-rise task-specific training with emphasis on strength and range of motion (proximal upper and lower extremity, musculature, and trunk), performed for 12 weeks, three times per week, 1 h/session	12 weeks	12-week exercise program focused on flexibility, three times per week, 1 h/session	Progression, individualization, intensity, frequency, duration, and specificity
Rosendahl et al. [41]	Supervised functional exercise program (everyday tasks challenging leg strength, postural stability, and gait ability) with 45 min/session, five times every 2 weeks for 3 months	3-month intervention and 6-month follow-up	Social activities (watching films, reading, singing, and conversation)	Progression, individualization, frequency, duration, intensity, and specificity
Faber et al. [20]	Supervised fall-preventive exercise programs (focused on balance and functional strength, and/or tai chi principles), 60 min/session, once a week for 4 weeks, and two times per week for 16 weeks.	20-week intervention and 52-week follow-up		Progression, individualization, duration, frequency, and specificity
Gill et al. [21]	6-month home-based exercise program (balance once a day and leg and arm-conditioning and strengthening three times per week); participants received in average 14.9 visits of a physical therapist	6-month intervention and 12-month follow-up	educational program (attention and health education), 45–60 min/session for 6 months, with visits of a health educator	Individualization, specificity, and frequency
Gill et al. [40]	see Gill et al. [21]	see Gill et al. [21]	see Gill et al. [21]	Individualization, specificity, and frequency
Shimada et al. [30]	Two supervised exercise training (balance and gait training), two to three times per week during 40 min/session, for 12 weeks	12 weeks	Usual care	Individualization, duration, frequency, and specificity

basic data indispensable to analyze exercise effectiveness. Thus, they have to be clearly exposed in the text even when the training program has been detailed elsewhere. This does not mean that some of the researches evaluated herein did not base their exercise program on principles of training, but these data were not precise enough to be extracted from the text.

Second, some inadequacies were found in exercise program design, which led some authors to suggest that exercise was not effective. In a home-based quadriceps resistance exercise program, Latham et al. [24] concluded that this "form of resistance exercise was harmful to patients, as evidenced by the higher incidence of musculoskeletal injuries." However, the exercise program started with a high-intensity resistance training (60–80% of 1RM), which probably led to musculoskeletal injuries. This kind of problem can be prevented if exercise training is taken in a gradual or stepwise approach [42] (principle of load progression) in the beginning of the intervention, which Latham et al. [24] did after participants' complaints. Moreover, this inadequacy may have negatively influenced results achieved in relation to self-rated physical health, a main outcome measure of the study (there was no difference between exercisers and control individuals). In the same way, Faber et al. [20] indicated that the "absence of significant positive training effects (regarding frail individuals) might also be attributed to inadequacy of training intensity, frequency, duration, and/or specificity of the exercise mode." Brown et al. [15] did not find any difference on flexibility between exercisers and control

Table 3 Main outcome measures and secondary outcome measures with respective results

Study	Main outcome measures	Results (main outcome)	Secondary outcome measures	Results (secondary outcome)
Gill et al. [21]	Summary disability score (performance in ADLs)	Compared with CG subjects, EG ones improved: disability scores (moderately frail subgroup)	Admission to and number of days spent in a nursing home	No differences were achieved
Timonen et al. [31]	ADL and IADL levels (Joensuu classification)	No differences were achieved		
Binder et al. [37]	Modified PPT, functional status questionnaire (FSQ), and ADL instruments	Compared with CG subjects, EG ones improved: modified PPT score, and FSQ score	Strength knee extension (KET) and flexion torque (KFT); gait; balance (progressive Romerg Test, Berg balance Test (BBT), and single-limb stance); body composition; quality of life (SF-36), and a modified hip rating questionnaire (HRQ)	Compared with CG subjects, EG ones improved: KET (both limbs), 1RM (knee extension and flexion, seated bench press, seated row, leg press, and biceps curl), fast walking speed, Berg balance score, single-limb stance time (fractured leg), HRQ score, and the change in health and physical function subscale scores of the SF-36
Gill et al. [40]	Self-reported IADLs; mobility (modified performance oriented mobility assessment—POMA); timed rapid gait and chair stands; and modified PPT	Compared with CG subjects, EG ones improved: IADL, timed rapid gait, mobility, timed chair stands, and modified PPT		
Dorner et al. [27]	Muscle function, cognitive function (MMSE)	Compared with CG subjects, EG ones improved: muscle function	Lean body mass, ADLs, mobility (Tinetti score), and depression	Compared with CG subjects, EG ones improved: LBM
Alexander et al. [39]	Bed- and chair-rise task performance ability and time taken to rise	Compared with CG subjects, EG ones improved: bed- and chair-rise task performance ability and time taken to rise	strength, range of motion (ROM), and trunk lateral balance	Compared with CG subjects, EG ones improved: trunk lateral balance, ROM, and strength (mainly in trunk region)
Jensen et al. [28]	Ambulation (functional ambulations category scale), usual, and maximum gait speed, balance (BBT), and step height.	Compared with CG subjects, EG ones improved: step height and ambulation (not decreased), usual, and maximum gait speed	Risk of falling	No differences were achieved
Shimada et al. [30]	Balance (one leg standing, functional reach, manual perturbation test, functional balance scale, and POMA) and gait (timed up-and-go [TUG], and stair climbing/descending)	Compared with CG subjects, EG ones improved: balance		
Wolf et al. [36]	FF (e.g., gait speed, functional reach test, timed chair–stand, timed 360°–turn, and single limb stance)	Compared with CG subjects, EG ones improved: chair–stand (after 4 and 8-month training)	Height, weight, BMI, Systolic, diastolic blood pressure, and resting heart rate	Compared with CG subjects, EG ones improved: BMI, SBP, and resting heart rate
Binder et al. [14]	Modified PPT, VO2 peak, and ADL measures (FSQ)	Compared with CG subjects, EG ones improved: modified PPT score, VO2 peak, and FSQ score	KET and KFT; balance (leg stance time, and BBT); change health subscale of SF-36; and weight	Compared with CG subjects, EG ones improved: KET, KFT, balance (one leg stance time and BBT), and change in health subscale SF-36
Brown et al. [15]	PPT, balance, gait, strength, flexibility, speed of reaction, and coordination, peripheral sensation	Compared with CG subjects, EG ones improved: PPT score, stregth, balance, and gait		
Chin A Paw et al. [16]	FF tests (e.g., balance and gait speed), physical fitness (e.g., strength, flexibility, and reaction time), self-rated disabilities in ADLs	Compared with CG subjects, EG ones improved: FF score (mainly chair–stand, touching toes, and walking speed) and physical performance when adjusted for baseline scores		

Table 3 (continued)

Study	Main outcome measures	Results (main outcome)	Secondary outcome measures	Results (secondary outcome)
Rydwik et al. [29]	Muscle strength, FF (30-second chair–stand, balance tandem and one leg stance, TUG, and gait speed), ADLs (functional independence measure), and IADLs (instrumental activity measures)	Compared with CG subjects, EG ones improved: strength; no differences persisted achieved 9 months after randomization		
Timonen et al. [32]	Knee (KET) and hip abduction strength, balance (14-item BBT), and maximal walking speed	Compared with CG subjects, EG ones improved: hip abduction strength, KET, balance, and walking speed		
Wolf et al. [34]	Strength, flexibility, cardiovascular endurance, body composition, IADL score, depression, and fear of falling	Compared with CG subjects, EG ones improved: left handgrip strength and systolic blood pressure (TC group); however, TC exercisers reduced the distance ambulated (cardiovascular endurance)	Time-specific risk for falls	No differences were achieved
Miller et al. [38]	Weight, quadriceps strength, usual gait speed, and quality of life (SF-12)	No differences were achieved		
Rosendahl et al. [41]	Balance (BBT), gait, and lower limb strength (1RM or chair–stand)	Compared with CG subjects, EG ones improved: usual gait speed, balance, and lower-limb strength		
de Jong et al. [18]	Body composition (dual–energy X-ray absorptiometry)	Compared with CG subjects, EG ones improved: lean body mass;exercise had no effect on bone parameters	Weight, BMI, waist and hip, and waist-to-hip circumferences	No differences were achieved
Ehsani et al. [19]	Maximal cardiac output (heart rate, left ventricular [LV] function), arteriovenous O2 content difference	Compared with CG sujects, EG ones improved: cardiac output, LV stroke work (peak effort) and peak heart rate	Body composition LBM and weight	Compared with CG sujects, EG Ones improved: LBM
Greiwe et al. [23]	Cytokine tumor necrosis factor α (TNF-α) level, protein synthesis rate, and lipoprotein lipase (LPL)	EG had decreased skeletal muscle TNF-α and increased LPL expression and protein synthesis rate		
Seynnes et al. [35]	Knee extension strength (KET)	Compared with CG subjects and EG ones improved: KET	Functional limitations (6-min walking, chair-rising, and stair climbing) and self-reported disability (French version of health assessment questionnaire and disability index subscale)	Compared with CG subjects, EG ones improved: 6-min walking (just for EG-HI), chair-rising, and stair climbing
Chin A Paw et al. [17]	Subjective well being (subscales: health, self-respect, morale, optimism, and contacts)	No differences were achieved	Self-rated health	No differences were achieved
Greenspan et al.[22]	Perceived health status (sickness impact profile) and self-rated health	Compared with CG subjects and EG ones improved: perceived health status (physical dimension, mainly, ambulatory category)		
Sattin et al. [25]	Fear of falling (Activities-Specific Balance Confidence Scale [ABC], and fall efficacy scale)	Compared with CG subjects and EG ones improved: fear of falling (ABC)		
Timonen et al. [33]	mood (Zung self-rating depression scale)	Compared with CG subjects and EG ones improved: mood		

Table 3 (continued)

Study	Main outcome measures	Results (main outcome)	Secondary outcome measures	Results (secondary outcome)
Latham et al. [24]	Self-rated physical health (physical component of the SF-36) and risk of falls	No differences were achieved	ADL, physical performance (strength, balance, mobility, and gait speed), FF, fear of falling, social activities, and mental health	No differences were achieved
Faber et al. [20]	Fall risk	Fall risk in prefrail subjects (EGs) decreased but it increased in frail elderly (EGs)	mobility (POMA) and FF and self-reported disability (ADL, and IADL)	Compared with CG subjects and EG ones improved: mobility (POMA score) and FF (prefrail subgroup); FF decreased in frail subgroup (EG)
Wolf et al. [26]	Fall risk	EG presented lower fall risk from months4 to 12		

subjects, though the control group met an exercise program focused on range of motion, 1 h per session, three times a week (more than the minimum prescribed for older adults by ACSM and AHA) during the intervention period. Furthermore, both groups presented improvements when compared to baseline assessments, which suggests that the exercise program was able to improve flexibility. In the study of Wolf et al. [34], tai chi exercisers reduced their cardiovascular endurance (distance ambulated in a 12-min walking test) after a 15-week period intervention. In a review study, Kuramoto et al. [45] indicated that "Tai Chi may be an additional form of aerobic exercise." However, two meta-analyses concerning the effects of tai chi on aerobic capacity [46, 47] concluded that the average effect size was small and nonsignificant for subjects enrolled in the experimental studies. Further studies are needed to know the real influence of tai chi on cardiovascular endurance.

Third, several of these studies were, apparently, part of the same trial (same sample and exercise training) with different main outcome measures. Thus, the exercise program may have been more adequate for some of the outcome measures in one study than it was for other measures in another study. This may have influenced some of the results. In those cases, the absence of positive results of exercise training on outcome measures does not necessarily mean an absence of the effect (see comments about Brown et al. [15] just above).

Furthermore, general guidelines for balance exercise, such as ACSM and AHA, are not precise enough to guide the design of RCT studies. As indicated by Nelson et al. [42], "the preferred types, frequency, and duration of balance training are unclear," which makes it difficult to design a study based on current recommendations to improve balance in a frail older adult population. It may partially explain the ineffectiveness of intervention in some trials (in main outcome measures [20], as well as in secondary ones [24]).

The present study has some limitations. First, in order to be selected through electronic searches, articles had to contain the terms "frail" or "frailty" in the title, which may have limited the final sample. Second, articles had to present an operational definition of frailty to meet the inclusion criteria, which may also have reduced the final sample. Finally, the several operational definitions of frailty found among studies characterized a large range of vulnerable populations. It is possible that other studies, with similar samples, have not been found by electronic searches and, therefore, were not included because authors did not label their population as "frail."

However, to the author's knowledge, it is the first review that compiles RCTs that studied exercise effects on health in frail elderly populations with a defined criterion of frailty. The study methodology, with direct contacts with authors of the original RCTs to clarify some points of the trials, was a strong aspect of the present review. This permitted the compilation of articles that had not presented a clear definition of frailty in the text.

Conclusion

Frailty is a physiological syndrome that increases the risk of poor health. Researches that studied exercise benefits in frail elderly populations utilized different operational definitions of frailty, which renders comparisons among them difficult to make. However, an increasing amount of evidence supports the affirmation that exercise training is an important tool to improve health in various at-risk populations. This review suggests that exercise is able to improve physiological factors (e.g., strength, cardiovascular endurance, and flexibility), as well as FF (especially performance-based measures) and mobility ability (balance and gait), and psychological (e.g., perceived health status, fear of falling, and mood) aspects in diverse vulnerable elderly populations. However, some efforts must be done to strengthen result consistencies from RCTs that study frail older adults. A frail elderly population must be defined based on current knowledge in this field before further conclusions can be drawn. Furthermore, the exercise program must be designed in accordance with current guidelines regarding exercise frequency, duration, and intensity, and it must take into account population heterogeneity (individualization) and other training principles, such as progression and specificity. Experimental researches that focus on long-term exercise adherence in frail older adults are also needed. In sum, exercise training seems to be a safe and effective tool to promote and maintain optimal health levels in a large variety of vulnerable older adults. However, lack of RCTs that utilize a well-defined frail older population based on current knowledge in this field does not permit us to establish that exercise influences health in the elderly. To confirm exercise benefits on health in frail older adults further researches are needed.

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