

# Evidence on Physical Activity and the Prevention of Frailty and Sarcopenia Among Older People: A Systematic Review to Inform the World Health Organization Physical Activity Guidelines

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**Background:** Frailty and sarcopenia are common age-related conditions associated with adverse outcomes. Physical activity has been identified as a potential preventive strategy for both frailty and sarcopenia. The authors aimed to investigate the association between physical activity and prevention of frailty and sarcopenia in people aged 65 years and older. **Methods:** The authors searched for systematic reviews (January 2008 to November 2019) and individual studies (January 2010 to March 2020) in PubMed. Eligible studies were randomized controlled trials and longitudinal studies that investigated the effect of physical activity on frailty and/or sarcopenia in people aged 65 years and older. The Grading of Recommendations Assessment, Development and Evaluation approach was used to rate certainty of evidence. **Results:** Meta-analysis showed that physical activity probably prevents frailty (4 studies; frailty score pooled standardized mean difference, 0.24; 95% confidence interval, 0.04–0.43;  $P = .017$ ,  $I^2 = 57\%$ , moderate certainty evidence). Only one trial investigated physical activity for sarcopenia prevention and did not provide conclusive evidence (risk ratio 1.08; 95% confidence interval, 0.10–12.19). Five observational studies showed positive associations between physical activity and frailty or sarcopenia prevention. **Conclusions:** Physical activity probably prevents frailty among people aged 65 years and older. The impact of physical activity on the prevention of sarcopenia remains unknown, but observational studies indicate the preventive role of physical activity.

**Keywords:** exercise, aging, frail elderly

Frailty and sarcopenia are common age-related conditions associated with adverse outcomes, such as falls, mobility disorders, the need for long-term care, and death.<sup>1,2</sup> There is ongoing debate about how to best define frailty<sup>3</sup> and sarcopenia.<sup>4</sup>

Frailty is characterized by a decline in functioning across multiple physiological systems that increases susceptibility to stressors.<sup>2</sup> The concept of frailty generally involves a multidimensional condition that is part of the normal aging process.<sup>5</sup> Frailty is dynamic, which means that the severity of frailty can change in either direction over time.<sup>2,5</sup> Rockwood et al<sup>6</sup> define frailty as a “multidimensional syndrome of loss of reserves (energy, physical ability, cognition, health) that gives rise to vulnerability.” Fried et al<sup>7</sup> developed the phenotype model to classify frailty, which consists of 5 physical components: unintentional weight loss, low grip strength, self-reported exhaustion, slow walking speed, and low physical activity. Frailty can be lessened by exercise-based interventions.<sup>8</sup>

Sarcopenia is a musculoskeletal disorder affecting older people that involves accelerated loss of muscle mass and function.<sup>1</sup> Sarcopenia was defined by the European Working Group on Sarcopenia in Older People as (1) low muscle mass, (2) low muscle

strength, and/or (3) low physical performance.<sup>9</sup> The recent updated consensus statement from the European Working Group on Sarcopenia in Older People 2 defines sarcopenia as a “muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime,” notes that sarcopenia is common among adults of older age but can also occur earlier in life and focuses on “low muscle strength as a key characteristic of sarcopenia, uses detection of low muscle quantity and quality to confirm the sarcopenia diagnosis, and identifies poor physical performance as indicative of severe sarcopenia.”<sup>10</sup> Sarcopenia is a clinical biomarker to identify people at increased risk of mobility disability.<sup>4</sup> The Sarcopenia Definitions and Outcomes Consortium identified grip strength as an important discriminator of mobility disability and a predictor of health-related outcomes.<sup>4</sup> Given the importance of strength and function in predicting adverse outcomes in older adults and the role of factors outside the muscle in strength and function (particularly neurological input), others have questioned the focus on muscle structure that is implied by sarcopenia and suggest use of terms such as muscle strength and motor impairment.<sup>11</sup> It is well established that strength and function in older adults can be improved with exercise.<sup>2</sup>

Physical activity has also been identified as a potential preventive strategy to slow the development of both frailty and sarcopenia. We aimed to investigate evidence on the association between physical activity and prevention of frailty and sarcopenia in older people (aged 65 y and older). Questions were: (1) What is the association between physical activity and sarcopenia/frailty prevention? (2) Is there a dose–response association (volume, duration, frequency, and intensity) between physical activity and the prevention of frailty and sarcopenia? and (3) Does the association vary by type or domain of physical activity?

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## Methods

We conducted this review to inform the World Health Organization (WHO) Guideline Development Group in the update the WHO Global Recommendations on Physical Activity and Sedentary Behaviour (2020). The scope of the guideline, the Population, Intervention, Comparison, Outcome question, and the search strategy were decided by the Guideline Development Group. The Guideline Development Group initially requested an umbrella review (review of reviews). However, as we did not find any reviews, we extracted data from the individual studies that were reported in the reviews identified by the initial search strategy. We then conducted an updated and expanded search after submission of the report, to confirm that relevant studies were not missed. Therefore, this article includes the initial WHO report results as well as the updated search results.

### Search Strategy

An initial search for systematic reviews was conducted in the PubMed database from 2008 to November 2019 (see [Supplementary Material 1A](#) [available online]). In addition, we conducted an updated and expanded search in PubMed from January 2010 to March 2020 (see [Supplementary Material 1B](#) [available online]). We also screened reference lists of relevant reviews and trials for additional studies. The language of publication was restricted to English.

Articles were independently screened in 2 stages: screening of title and abstracts and screening of full-text articles by 2 reviewers (J.S.O. and W.K. or S.W. and T.C.F) using the eligibility criteria ([Supplementary Material 1C](#) [available online]). Disagreements regarding the eligibility of studies were resolved through discussion and, when necessary, with the help of a third reviewer (C.S. or J.S.O). We conducted this systematic review following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,<sup>12</sup> and the PRISMA study flow diagram documents the screening process.

### Selection Criteria

We initially conducted a search for systematic reviews and meta-analyses. As we did not find any eligible systematic reviews, we identified reviews that included potentially eligible studies and screened all included studies against our questions. As there were too few individual studies investigating the effect of physical activity on the prevention of frailty and sarcopenia, we updated the search strategy to target the relevant studies that we could have missed.

In the updated/expanded review, we included randomized controlled trials (RCTs), prospective cohort studies, and retrospective cohort studies. We excluded cross-sectional, before-and-after studies, or non-RCTs.

### Type of Participants

Studies conducted with participants aged 65 years and older were included. No restriction was placed on the source of the participants, that is, patients from primary care as well as community settings were eligible. We did not include studies in which more than 15% of the total sample had frailty or sarcopenia at baseline.

### Type of Interventions

We included studies that involved physical activity of any type, mode, duration, frequency, or intensity. For the purpose of this review, physical activity encompasses any activity that requires energy expenditure such as walking, transport related, occupational, household chores, and structured exercises programs.<sup>13</sup> We excluded studies of multimodal interventions that did not present data on physical activity alone.

### Type of Outcome Measures

The outcome was measures of frailty or sarcopenia status. We included only studies that specified sarcopenia and/or frailty were the outcome of interest, and we accepted the authors' definition of sarcopenia and/or frailty.

We used the Prevention of Falls Network Europe (ProFANE) taxonomy to classify the physical activity and exercise programs in the included studies ([Supplementary Material 2](#) [available online]). The programs were classified as primarily involving the following exercise categories: (1) gait, balance, coordination, and functional task training (referred to as "balance and functional exercises" for simplicity); (2) strength/resistance training (including power training, using resistance so referred to as "resistance exercises"); (3) flexibility; (4) 3-dimensional (3D) exercise (with Tai Chi or dance subcategories); (4) general physical activity (walking programs); (5) endurance; (6) overall physical activity; and (7) other.

### Data Extraction

Two independent reviewers (J.S.O. and W.K. or S.W. and T.C.F) extracted the characteristics and intervention outcomes of each trial according to the PRISMA Statement.<sup>14</sup> The following data were extracted from each included trial: author, year of publication, country, sample characteristics (sample size, age and sex of participants, health status, and setting), intervention description (frequency, intensity, session duration, intervention duration, and who delivered the intervention), primary exercise according to ProFANE taxonomy,<sup>15</sup> and methodological quality assessment using the Physiotherapy Evidence Database (PEDro) scale. We extracted frailty and sarcopenia status outcomes.

### Methodological Quality Assessment and Quality of the Evidence

The PEDro scale was used to assess the internal validity of RCTs.<sup>16,17</sup> The PEDro scale evaluates 11 items: inclusion criteria and source, random allocation, concealed allocation, similarity at baseline, subject blinding, therapist blinding, assessor blinding, completeness of follow-up, intention-to-treat analysis, between-group statistical comparisons, and point measures and variability. Scores on the PEDro scale range from 0 (very low methodological quality) to 10 (high methodological quality) and were downloaded from the PEDro database (<https://www.pedro.org.au/>). Methodological quality was not an inclusion criterion for this review.

We used the Grading of Recommendations Assessment, Development and Evaluation system to assess the overall certainty of the evidence<sup>18</sup> for outcomes with results from 3 or more studies. We assigned a general rating of the certainty of the body of evidence as "High," "Moderate," "Low," or "Very low" based upon the presence or extent of 4 factors: risk of bias, inconsistency, imprecision, and publication bias. As we only included similar studies in terms of population, intervention, comparator, and outcome, we did not consider the indirectness criterion.

## Data Analysis

We performed meta-analyses with Comprehensive Meta-Analysis software (version 3; Biostat, Englewood, NJ) using the random effects model for frailty. We calculated treatment effects using standardized mean differences (Hedges  $g$ ) standardized by post-score SD (or its estimate) with 95% confidence intervals (CIs). The standardized mean difference was calculated using the premean and postmean and SD or, when this was unavailable, using the mean change score. If multiple follow-up data points were provided, the scores obtained as close to the completion of the intervention as possible were used for the primary analysis. If the trial had more than 2 arms, we examined the overall effects of both arms separately (mean and SD). Effect sizes were categorized as small (0.2), medium (0.5), or large (0.8 or greater). We assessed funnel plot asymmetry visually and by using Egger test, with  $P < .1$  considered as evidence of publication bias. For a study that only reported the number of sarcopenic participants in each group, we dichotomized the participants into 2 categories: nonsarcopenic and sarcopenic. We considered the occurrence of sarcopenia as the event, and we calculated risk ratio and 95% CI using RevMan's calculator.<sup>19</sup>

## Results

### Search

The initial search for systematic reviews and meta-analyses did not identify enough evidence to answer the review question. We screened the full text of 34 reviews and did not find any eligible reviews (Figure 1). The main reasons for exclusion were reviews including younger participants ( $n = 10$ ), not including frailty-/sarcopenia-related outcomes ( $n = 10$ ), participants with frailty/sarcopenia at baseline (management instead of prevention,  $n = 6$ ), and multimodal interventions (eg, combined physical activity and nutrition intervention,  $n = 5$ ). Among the 34 reviews which had their full text screened, 21 reviews included potentially eligible studies and their full texts were identified and assessed by 2 reviewers. We used the same eligibility criteria, but no restriction was applied for publication year of individual studies. We found 9 potential studies investigating the association between physical activity and the primary prevention of frailty/sarcopenia; however, frailty and sarcopenia status were an outcome in only 2 studies, which were included in the review.<sup>20,21</sup>

Our updated and expanded literature search identified a total of 1676 studies for the title and abstract screening, of which 172 were considered potentially eligible studies for full-text review. After the full-text screening, 8 eligible studies were identified and included in this review.<sup>20–29</sup>

We included a total of 10 studies in this review: 2 individual studies identified from the systematic reviews and 8 studies from the updated search. Figure 1 outlines the flow of studies through the review. We included 5 RCTs<sup>20,22–24,29</sup> and 5 longitudinal studies.<sup>21,25–28,30</sup> We pooled 4 included trials involving 1862 participants and 5 comparisons in the meta-analysis evaluating the effect of physical activity interventions on the prevention of frailty compared with control.<sup>20,22,29</sup> One trial assessed the impact of physical activity on sarcopenia status outcome and involved a sample of 40 participants.<sup>24</sup>

### Characteristics of Included Trials

Publication dates ranged from 2013 to 2019 (median, 2017) with 40% of studies published after 2018. Studies were conducted in

8 different countries: single trials were conducted in China,<sup>22</sup> Iceland,<sup>25</sup> Taiwan,<sup>23</sup> Spain,<sup>20</sup> and Hong Kong<sup>21</sup>; 2 in United States;<sup>28,29</sup> and 3 in Japan.<sup>24,26,27</sup> Details of all included studies are summarized in Tables 1 and 2.

### Quality

Supplementary Table 1 (available online) summarizes the methodological quality and reporting of eligible trials. The total PEDro score ranged from 4 to 7 (mean of 6). Three trials were of high methodological quality on the PEDro scale<sup>22,23,29</sup> (PEDro score  $\geq 6$ ) and 2 trials were of low quality (PEDro score  $< 6$ ).<sup>20,24</sup> All participants were randomly allocated and provided the calculation of point estimates and variability (PEDro items 2 and 11). Three trials out of 5 (60%) did not report an intention-to-treat analysis. As expected in this type of intervention, none of the trials included blinded participants or blinded intervention deliverers.

### Participants

In the studies reporting age, the mean age of participants ranged from 67 to 79 years. Nine studies recruited both men and women,<sup>20–25,27–29</sup> and a single recruited only women.<sup>26</sup> All participants from the included studies were recruited from the community. Four studies included prefrail participants at baseline, a single study involved a mix of frail and nonfrail, and 9 studies included a mix of presarcopenic and sarcopenic participants (see Tables 2 and 3).

### Outcome Measures

Frailty was an outcome for 6 of the included studies.<sup>20,22,23,26</sup> In 4 studies,<sup>20,22,23,26</sup> frailty was measured using the following 5 Fried criteria: (1) unintentional weight loss, (2) exhaustion, (3) low physical activity, (4) slow walking speed, and (5) poor grip strength. Participants were classified as prefrail if they fulfilled 1 and 2 criteria, and frail if they fulfilled 3 or more criteria. A single study<sup>29</sup> measured frailty according to the SOF frailty index that included (1) inability to rise from a chair 5 times without using the arms, (2) self-reported reduced energy level, and (3) weight loss  $\geq 4.55$  kg or  $\geq 5\%$  during the last 12 months, or  $\geq 2.275$  kg or  $\geq 2.5\%$  during the last 6 months. Subjects were considered “frail” if at least 2 of the 3 criteria were fulfilled. One study<sup>28</sup> measured frailty using gait speed and chair stand test. Frailty was indicated if (1) gait speed  $< 0.6$  m/s or (2) inability to rise from a chair without using one's arms.

Sarcopenia was an outcome in 4 studies.<sup>21,24,27,31</sup> Two studies were defined according to the European Working Group on Sarcopenia in Older People.<sup>21,25,30</sup> Participants who had (1) low muscle mass, (2) low muscle strength, and/or (3) low physical performance were classified as having sarcopenia. A single study<sup>27</sup> measured sarcopenia by the estimation of appendicular lean mass/height<sup>2</sup>. One study<sup>24</sup> assessed sarcopenia using Asia Working Group for Sarcopenia criteria.

### Exposure

The included studies investigated different modalities of physical activity and exercise. Following the ProFANE taxonomy, a single study primarily investigated resistance training and 4 studies investigated exercise including multiple ProFANE categories.

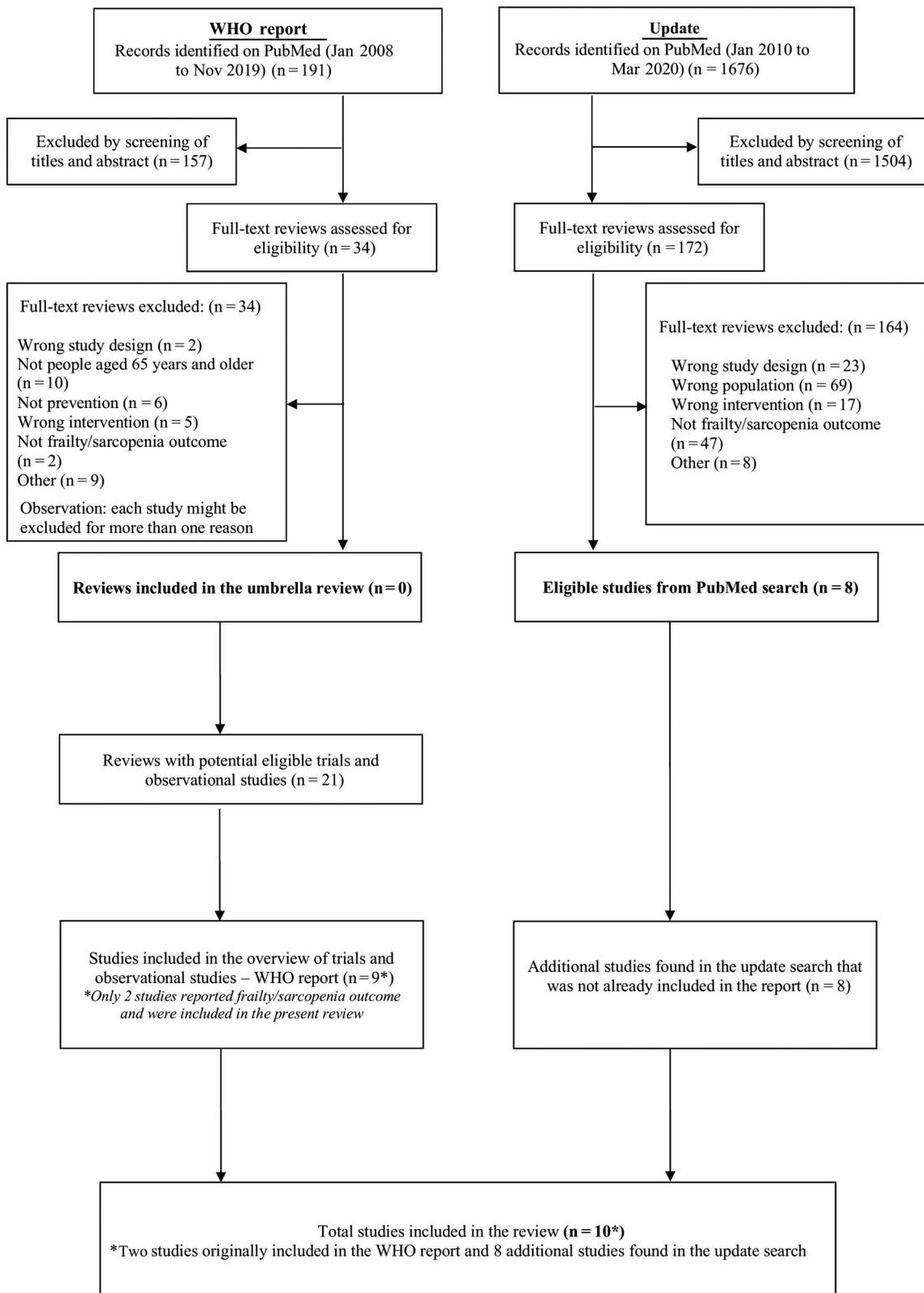


Figure 1 — Flow of studies through the review.

**Table 1 Description of Included Trials**

Reference	PE德罗 score	Study design	n, randomized/analyzed	Participants (setting; health status; n; age, mean [SD]; and % female by group)	Intervention/exposure Primary exercise type according to ProFANE	Control	Outcomes	Follow-up	Results
Frailty status outcome Chen et al <sup>22</sup>	7/10	RCT	70/66	Setting: Community, China Health status: Prefrail A. Intervention group n = 35 (randomized); 33 (analyzed) Age: 77 (5) Female: 64% B. Control group n = 35 (randomized); 33 (analyzed) Age: 75 (6) Female: 67%	A. Supervised group-based exercise program consisting of 6 elastic band movements and 2 body weight-based movement. Duration of the intervention (weeks): 8 Frequency: 3 sessions/wk Intensity: 2 sets of 10–15 repetitions with 1- to 2-min rest between each set using yellow elastic bands Session duration (min): 45–60 min Delivered by: Trained intervener (either a physiotherapist or a trained community center worker) Primary exercise type: Resistance A and C. Exercise program consisting of a combination of strength, flexibility, balance, and endurance training, and supplemented by a home-based training. Duration of the intervention (weeks): 24 (12-wk intervention and 12-wk self-maintenance periods) Frequency: 3–7 times/wk were recommended Intensity: NR Session duration (min): 5–60 (tailored to participants' capabilities) Delivered by: Physiotherapist and case managers Primary exercise type: Multiple: resistance, balance, function, and endurance	B. No intervention	Frailty status measured by the presenting Fried frailty phenotype that include: (1) unintentional weight loss ( $\geq 4.5$ kg in the last 12 mo); (2) self-reported exhaustion (more than 3 d in last 7 d); and (3) low physical activity, slow walking speed, and weak grip strength. One criterion represented a point. Higher the score, the more severe the frailty states. 1–2 points indicate prefrail; $\geq 3$ points indicate frailty.	8 wk	Effect size (95% CI): 0.84 (0.34 to 1.34)
Hsieh et al <sup>23</sup>	6/10	RCT	319/319	Setting: Community, Taiwan Health status: Mixed prefrail and frail (10%) A. Exercise group: n = 79 (randomized and analyzed) Age: 72.0 (6.0) Female: 41.8% B. Nutrition group: n = 83 (randomized and analyzed) Age: 70.4 (5.3) Female: 45.8% C. Combination group (exercise plus nutrition): n = 77 (randomized and analyzed) Age: 71.6 (6.0) Female: 35.1% D. Control group: n = 80 (randomized and analyzed) Age: 72.5 (5.5) Female: 36.3%	A. Supervised group-based exercise program consisting of 6 elastic band movements and 2 body weight-based movement. Duration of the intervention (weeks): 8 Frequency: 3 sessions/wk Intensity: 2 sets of 10–15 repetitions with 1- to 2-min rest between each set using yellow elastic bands Session duration (min): 45–60 min Delivered by: Trained intervener (either a physiotherapist or a trained community center worker) Primary exercise type: Resistance A and C. Exercise program consisting of a combination of strength, flexibility, balance, and endurance training, and supplemented by a home-based training. Duration of the intervention (weeks): 24 (12-wk intervention and 12-wk self-maintenance periods) Frequency: 3–7 times/wk were recommended Intensity: NR Session duration (min): 5–60 (tailored to participants' capabilities) Delivered by: Physiotherapist and case managers Primary exercise type: Multiple: resistance, balance, function, and endurance	B. Nutrition intervention D. No intervention	Frailty score measured using the Cardiovascular Health Study Criteria developed by Fried. The criteria comprise 5 components: (1) unintentional weight loss (involuntary loss $> 3$ kg in the preceding year), (2) exhaustion ( $> 3$ d in a week), (3) poor muscle strength, (4) slowness, and (5) low physical activity. One criterion represented a point. Higher the score, the more severe the frailty states: 0 point indicates robustness state; 1–2 points indicate prefrail; $\geq 3$ points indicate frailty.	26 wk	A vs D: Effect size (95% CI): 0.22 (–0.09 to 0.53) C vs B: Effect size (95% CI): 0.00 (–0.31 to 0.31)

(continued)

Table 1 (continued)

Reference	PE德罗 score	Study design	n, randomized/analyzed	Participants (setting; health status; n; age, mean [SD]; and % female by group)	Intervention/exposure Primary exercise type according to ProFANE	Control	Outcomes	Follow-up	Results
Seira-Prat et al <sup>20</sup>	5/10	RCT	172/133	Setting: Community, Spain Health status: Prefrail A. Intervention group: n = 80 (randomized); 61 (analyzed) Age: 77.9 (5.0) Female: 51.3% B. Control group: n = 92 (randomized); 72 (analyzed) Age: 78.8 (4.9) Female: 60.9%	A. Physical activity program including aerobic outdoor walking exercise and a combined home training that includes strengthening for arms and legs, balance, and coordination. Duration of the intervention (weeks): 52 Frequency: At least 4 times/week Intensity: Walking exercise: NR Mixed exercise: 10–15 times/min with a rest of 30 s between each set of the exercise and progressively increase up to 15 times/min after 2–3 mo Session duration (min): Walking: 30–45 min/d Mixed exercise: 20–25 min/d Delivered by: N/A Primary exercise type: Multiple: endurance, resistance, balance, and function Duration of the intervention (weeks): 52 Frequency: At least 4 times/wk Intensity: Walking exercise: NR Mixed exercise: 10–15 times/min with a rest of 30 s between each set of the exercise and progressively increase up to 15 times/min after 2–3 mo Session duration (min): Walking: 30–45 min/d Mixed exercise: 20–25 min/d Delivered by: N/A Primary exercise type: Multiple: endurance, resistance, balance, and function	B. Usual care	Prevalence of frailty: Presence of 3 or more Fried criteria. The 5 criteria are (1) unintentional weight loss, (2) exhaustion, (3) low physical activity, (4) slow walking speed, and (5) poor grip strength.	52 wk	Effect size (95% CI): 0.33 (–0.01 to 0.67)

(continued)

**Table 1 (continued)**

Reference	PEDro score	Study design	n, randomized/analyzed	Participants (setting; health status; n; age, mean [SD]; and % female by group)	Intervention/exposure Primary exercise type according to ProFANE	Control	Outcomes	Follow-up	Results
Trombetti et al <sup>29</sup>	7/10	RCT (secondary analysis)	1313/1304	Setting: Community, United States Health status: Mixed including participants that were frail Age: 78.9 (5.2) Female: 67.2% A. Physical activity intervention n = 656 (randomized); 653 (analyzed) B. Health education n = 657 (randomized); 651 (analyzed)	A. Comprised of center-based physical activity and home-based physical activity including walking, strength, balance, and flexibility exercises. The program divided into adoption phase (weeks 1–52) and maintenance phase (week 53 to end). Duration of the intervention (weeks): 104 Frequency: Adoption phase: Centre-based physical activity; 2 times/wk; home-based: 1 time/wk (week 1–4) up to 3–4 times/wk (week 8–52) Maintenance phase: Centre-based physical activity; 2 times/wk; home-based: to 3–4 times/wk Intensity: Walking: At intensity of 13 (“somewhat hard”) using the Borg scale; Strength training: 2 sets of 10 reps at an intensity of 15–16 using Borg’s scale Session duration (min): Centre-based: 60 min/session and weekly walking goal of up to 150 min/wk Delivered by: NR Primary exercise type: Multiple: endurance, resistance, balance, and function	B. Health education	Frailty status according to the SOF frailty index. Criteria include: (1) inability to rise from a chair 5 times without using the arms, (2) self-reported reduced energy level, and (3) weight loss $\geq 4.55$ kg or $\geq 5\%$ during the last, or $\geq 2.275$ kg or $\geq 2.5\%$ during the last 6 mo. Subjects were considered “frail” if at least 2 of the 3 criteria were fulfilled.	24 mo	Effect size (95% CI): 0.14 (0.03 to 0.25)
Sarcopenia status outcome									
Mariya et al <sup>24</sup>	4/10	RCT	52/40	Setting: Community, Japan Health status: Mixed presarcopenia and sarcopenia A. Intervention group: n = 34 (randomized); 26 (analyzed) Age: 69.2 (5.6) Female: 55.9% B. Control group: n = 18 (randomized); 14 (analyzed) Age: 68.5 (6.2) Female: 55.6%	A. Home-based exercise program with lower limb training (locomotion training). Resistance and balance exercises include squats, single-leg standing, and heel raises. The program combined with daily walking. Duration of the intervention (weeks): 24 Frequency: 7 d/wk Intensity: 3 sets of 1 repetition/set (1-min single-leg standing), 3 repetitions/set (squat), and 20 repetitions/set (heel raises) Session duration (min): Resistance and balance exercises: NR Walking: 20–30 min/d Delivered by: N/A (physical therapists provided a guidebook for participants) Primary exercise type: Multiple: resistance, balance, and function	B. Usual daily activities and exercise	Sarcopenia status measured using AWGS2 criteria. Participants were identified as presarcopenia if (1) SMI $< 7.0$ kg/m <sup>2</sup> for men and $< 5.7$ kg/m <sup>2</sup> for women. Participants were identified as sarcopenia if a handgrip strength $< 26$ kg for men and $< 18$ kg for women.	24 wk	Risk ratio (95% CI): 1.08 (0.095 to 12.193) <sup>a</sup>

Abbreviations: AWGS2, Asia Working Group for Sarcopenia; CI, confidence interval; N/A, not applicable; NR, not reported; PEDro, Physiotherapy Evidence Database; ProFANE, Prevention of Falls Network Europe; RCT, randomized controlled trial; SMI, skeletal muscle mass index; SOF, Study of Osteoporotic Fractures. We only included and extracted information for the groups and for the comparisons that were relevant to this study (ie, those where the effect of physical activity could be evaluated).

<sup>a</sup>Event of interest: Occurrence of sarcopenia.

**Table 2 Description of Longitudinal Studies Investigating the Association Between Physical Activity and Frailty/Sarcopenia Prevention**

Reference	PEDro score	Study design	n, recruited/analyzed	Participants (setting, health status, n, age mean (SD), and % female by group)	Exposure Primary exercise type according to ProFANE	Control	Outcomes	Follow-up	Results
<b>Frailty status outcome</b>									
Osuka et al <sup>26</sup>	N/A	Cohort study	1289/604	Setting: Community, Japan Health status: Healthy n = 1289 (included); 604 (analyzed) Age: median 78 (range 75–84) Female: 100% (only included female in this study)	Leisure physical activity assessed whether participants participated in 17 different exercise types by indicating yes or no. Classification: Planned physical activity (sports)	N/A	Frailty status measured by the Fried frailty criteria characterized by limitation in ≥3 of the following 5 conditions: slowness, weakness, exhaustion, low activity, and weight loss.	2 y	Adjusted OR (OR, 95% CI): 0.29 (0.07 to 1.23) *
Song et al <sup>28</sup>	N/A	Longitudinal	1333	Setting: Community, United States Health status: Healthy Female n = 730 Age: 67.2 (7.5) Male n = 603 Age: 66.1 (7.9)	Physical activity measured using uniaxial accelerometer placed on a belt at the natural waistline. Data were presented as daily sedentary time (<100 count/min) and time spent in moderate-intensity (>2020 counts/min) activity. Classification: Total physical activity	N/A	Frailty was measured using gait speed and chair stand test. Frailty indicated if (1) gait speed <0.6 m/s or (2) inability to rise from a chair without using one's arms.	2 y	Hazard ratio (95% CI): 0.18 (0.02 to 1.73)*
<b>Sarcopenia status outcome</b>									
Mijnarends et al <sup>25</sup>	N/A	Cohort study (secondary data analysis)	3316 /2309	Setting: Community, Iceland Health status: Mixed (reported 7.3% participants with sarcopenia at baseline) A. Baseline: n = 2309 (analyzed) Age: 74.7 (4.7) B. Follow-up: n = 2309 (analyzed) Age: 79.9 (4.7) Female: 57.8%	Physical activity measured by self-reported participation in moderate-vigorous physical activity in the past 12 mo. Classification: Total physical activity (moderate and vigorous).	N/A	Sarcopenia status measured by the algorithm of the EWGSOP that assessed muscle mass, muscle strength, muscle performance including maximum grip strength and walking speed.	5 y	Adjusted OR (OR, 95% CI): 0.64 (0.45 to 0.91) *

(continued)

**Table 2 (continued)**

Reference	PEDro score	Study design	n, recruited/analyzed and % female by group	Participants (setting, health status, n, age mean (SD), and % female by group)	Exposure type according to ProFANE	Control	Outcomes	Follow-up	Results
Shephard et al <sup>b,27</sup>	N/A	Longitudinal	468	Setting: Community, Japan Health status: Ambulatory, with initial bioimpedance scores above the sarcopenia threshold Male: n = 200 Age: 73.5 (4.3) Female: n = 268 Age: 73.8 (4.6)	Physical activity was measured using electronic pedometer/accelerometer that was attached to a waist belt. The parameters presented were the number of steps per day. Classification: Total physical activity	N/A	Sarcopenia (class I and II) was indicated if the estimate of appendicular lean mass/height <sup>2</sup> fell more than 1 SD below the corresponding mean value for a young, healthy reference population. The cutoff values were 9.37 kg/m <sup>2</sup> in men and 7.01 kg/m <sup>2</sup> in women.	5 y	Step count relative risk (95% CI)* Men: P = .04 Q1: 2.33 (1.43 to 4.51) Q2: 1.97 (1.00 to 2.86) Q3: 0.95 (0.43 to 2.01) Women: P = .03 Q1: 2.99 (1.91 to 3.42) Q2: 2.01 (1.01 to 3.03) Q3: 1.03 (0.58 to 2.25)
Yu et al <sup>c,21</sup>	N/A	Observational	4000	Setting: Community, Hong Kong Health status: Mixed (9% of participants had sarcopenia) n = 4000 (included and analyzed) Age: 72.5 (5.2) Female: 50%	Daily physical activity level assessed using the PASE. Classification: Total physical activity	N/A	Sarcopenia defined using according to the EWGSOP algorithm that include (1) low muscle mass (ASM/mass index (ASM/height <sup>2</sup> ) <6.52 kg/m <sup>2</sup> for males and <5.44 kg/m <sup>2</sup> for females), (2) low muscle strength (grip strength ≤28 kg for males and ≤18 kg for females), and/or (3) low physical performance (gait speed ≤0.8 m/s for both males and females).	48 mo	Physical activity associated with incident sarcopenia after adjustment (OR, 95% CI): adjusted 0.995 (0.991 to 0.999)*

Abbreviations: ASM, appendicular skeletal muscle mass; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Older People; N/A, not applicable; NR, not reported; OR, odds ratio; PASE, Physical Activity Scale of the Elderly; PEDro, Physiotherapy Evidence Database; ProFANE, Prevention of Falls Network Europe.  
<sup>a,b,c</sup>Indicates studies which detected a statistically significant difference between-group difference.  
<sup>\*</sup>Event of interest: Occurrence of frailty or sarcopenia.

### Overview of Included Studies

A total of 4 RCTs<sup>20,22–24,29</sup> investigated physical activity interventions compared with a control group. Overall, the sample size for the trials was reasonably large (median: 100, mean: 373, range: 40–1304) and the median follow-up length was 26 weeks. We identified 4 studies involving frailty outcomes and one study including sarcopenia outcome (Table 2).

The duration of the interventions investigating the effect of physical activity compared with control on frailty ranged from short (ie, 8 wk) to as long as 104 weeks, and the median duration was 38 weeks (mean = 47 wk). The intervention dose ranged from 3 to 7 sessions per week with the sessions ranging from 30 to 60 minutes. Only one trial investigated the effect of physical activity compared with control on sarcopenia.<sup>24</sup> The duration of the intervention was 24 weeks and the frequency of the intervention was 7 times per week, including 20 to 30 minutes of supplemented walking exercise.

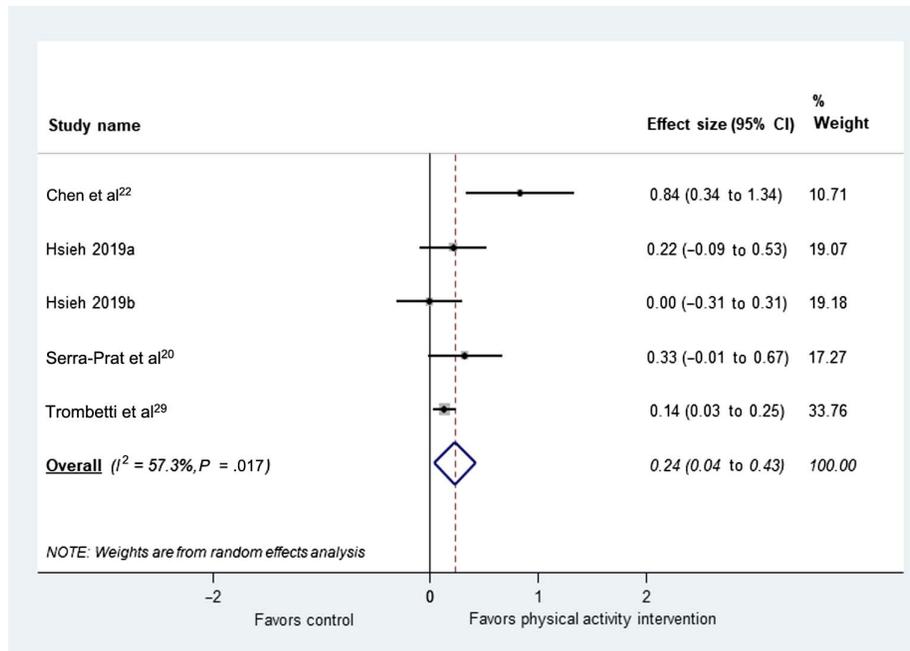
### Physical Activity and the Prevention of Frailty and Sarcopenia

The pooled effect of physical activity intervention on frailty showed that physical activity significantly prevented frailty in

intervention participants versus control participants (4 studies and 5 comparisons; frailty score standardized mean difference = 0.24; 95% CI, 0.04 to 0.43;  $P = .017$ ,  $I^2 = 57%$ ; Figure 2). The overall quality of evidence for the effect of physical activity on frailty was rated as “moderate quality”. Details on the criteria used to apply the Grading of Recommendations Assessment, Development and Evaluation rating are provided in Table 3 and Supplementary Figure 1 (available online).

Only one trial reported the effect of physical activity intervention on sarcopenia outcome. This trial did not provide evidence of an association between physical activity and sarcopenia prevention (risk ratio 1.08; 95% CI, 0.10 to 12.19).

We included 5 observational studies, 2 studies investigated the association of physical activity with frailty prevention and 3 studies investigated the association with sarcopenia prevention. We were unable to perform meta-analysis due to the wide variation of design, statistical approach, and measures of physical activity across the studies. Each of these studies suggested a positive association between physical activity and prevention of frailty and sarcopenia (Table 3). The results in the 2 studies with frailty outcomes did not reach statistical significance, but there was statistically significant association between physical activity and the prevention of sarcopenia in each of the 3 studies with sarcopenia outcomes.



**Figure 2** — Effect size (95% CI) of physical activity interventions on frailty outcome by pooling data from 4 studies comparing physical activity versus control using random effects meta-analysis (n = 1862). CI indicates confidence interval.

**Table 3 Summary of the Quality of Evidence and Strength of Recommendation**

Outcome	Summary of findings		Quality of evidence assessment (GRADE)				Overall
	Effect size <sup>a</sup> (95% CI)	n (trials)	Study limitations <sup>b</sup>	Imprecision <sup>c</sup>	Inconsistency <sup>d</sup>	Publication bias <sup>e</sup>	
Frailty outcome	0.24 (0.04 to 0.43)	1862 (4)	None	None	↓	None	Moderate

Abbreviations: ↓ downgraded; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PEDro, Physiotherapy Evidence Database.

<sup>a</sup>Pooled standardized effect size and 95% confidence intervals (positive value favors physical activity interventions). <sup>b</sup>Greater than 50% of studies in the meta-analysis had a PEDro score <6/10. <sup>c</sup>Total number of participants >400 across all studies. <sup>d</sup>Heterogeneity >50%. <sup>e</sup>Serious small study effects suggested by visual inspection of funnel plot.

## Dose–Response Associations, Type of Physical Activity

We were unable to make clear statements about the optimal type of exercise or dose–response associations. Studies that detected impacts on relevant outcomes involved resistance training, combinations of resistance, balance and endurance exercise, as well as overall physical activity.

## Discussion

We systematically reviewed the association between physical activity and the prevention of frailty and sarcopenia. Overall, we found that physical activity interventions may be effective in preventing frailty among people aged 65 years and older. The observational evidence also points toward beneficial associations between physical activity and frailty prevention. However, there was limited evidence evaluating preventive effects of physical activity on sarcopenia. As we only identified one trial evaluating the impact of physical activity on sarcopenia, no conclusion can be reached. This review was unable to draw firm conclusions on the modality of physical activity or the dose necessary to produce preventive benefits on frailty and sarcopenia. The results suggest that interventions involving resistance training and the combination of resistance, endurance, balance, and function probably have positive impact on frailty and sarcopenia; however, further investigation is warranted.

To the best of our knowledge, this is the first systematic review to evaluate the effectiveness of physical activity targeting the prevention of frailty and sarcopenia among people aged 65 years and older. Nonetheless, our study had several limitations. The initial aim of this review was to summarize the evidence of physical activity on prevention of frailty and sarcopenia in older people by conducting an umbrella review; however, we did not find any systematic reviews. We included the relevant studies that were in the reviews we found, and we conducted further searches to ensure that important studies were not missed. Furthermore, as the literature search was limited to PubMed and the English language, we may have missed relevant studies. Finally, another potential limitation is that we only included outcome data from the immediate postintervention time point, limiting our results to the short-term or immediate effect of physical activity on frailty and sarcopenia without consideration of the long-term effects.

We identified evidence of the effect of physical activity on frailty among people aged 65 years and older, but limited evidence on sarcopenia was found. There is a need for future research that evaluates the preventive impact of physical activity on sarcopenia. In addition, the optimal dose and type of physical activity for maximizing the preventive effect of physical activity on frailty sarcopenia is not clear, warranting further research. Furthermore, the longer of effect of physical activity on frailty and sarcopenia remains unknown, as our results were limited to the short-term effects. Studies that evaluate the long-term sustainability of physical activity behavior on frailty and sarcopenia are needed.

## Conclusion

This review provides moderate certainty evidence that physical activity is an effective intervention for preventing frailty among people aged 65 years and older. We found limited evidence of any effect of physical activity on sarcopenia but promising results from observational studies. Further research is warranted to determine

the impact, ideal dose, and modality of physical activity on frailty and sarcopenia. Future studies are also needed to explore the long-term sustainability of physical activity interventions.

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## References

1. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. 2019;393(10191):2636–2646. PubMed ID: [31171417](#) doi:[10.1016/S0140-6736\(19\)31138-9](#)
2. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. *Lancet*. 2019;394(10206):1376–1386. PubMed ID: [31609229](#) doi:[10.1016/S0140-6736\(19\)31785-4](#)
3. Rockwood K, Howlett SE. Fifteen years of progress in understanding frailty and health in aging. *BMC Med*. 2018;16(1):220. doi:[10.1186/s12916-018-1223-3](#)
4. Cawthon PM, Trivison TG, Manini TM, et al. Establishing the link between lean mass and grip strength cut-points with mobility disability and other health outcomes: proceedings of the sarcopenia definition and outcomes consortium conference. *J Gerontol A Biol Sci Med Sci*. 2019;75(7):1317–1323. PubMed ID: [30869772](#) doi:[10.1093/gerona/glz081](#)
5. Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med*. 2011;27:1–15.
6. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *Can Med Assoc J*. 2005;173:489–495.
7. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146–M156. PubMed ID: [11253156](#) doi:[10.1093/gerona/56.3.M146](#)
8. Cameron ID, Fairhall N, Langron C, et al. A multifactorial interdisciplinary intervention reduces frailty in older people: randomized trial. *BMC Med*. 2013;11(1):65. PubMed ID: [23497404](#) doi:[10.1186/1741-7015-11-65](#)
9. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on sarcopenia in older people. *Age Ageing*. 2010;39(4):412–423. PubMed ID: [20392703](#) doi:[10.1093/ageing/afq034](#)
10. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16–31. PubMed ID: [30312372](#) doi:[10.1093/ageing/afy169](#)
11. Menant JC, Weber F, Lo J, et al. Strength measures are better than muscle mass measures in predicting health-related outcomes in older people: time to abandon the term sarcopenia? *Osteoporos Int*. 2017;28(1):59–70. PubMed ID: [27394415](#) doi:[10.1007/s00198-016-3691-7](#)
12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535. PubMed ID: [19622551](#) doi:[10.1136/bmj.b2535](#)
13. World Health Organization. *Global recommendations on physical activity for health*. World Health Organization; 2010.
14. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that

- evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339:b2700. doi:10.1136/bmj.b2700
15. Lamb SE, Becker C, Gillespie LD, et al. Reporting of complex interventions in clinical trials: development of a taxonomy to classify and describe fall-prevention interventions. *Trials*. 2011;12(1):125. PubMed ID: 21586143 doi:10.1186/1745-6215-12-125
  16. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther*. 2003;83(8):713–721. PubMed ID: 12882612 doi:10.1093/ptj/83.8.713
  17. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. *Aust J Physiother*. 2009;55(2):129–133. PubMed ID: 19463084 doi:10.1016/S0004-9514(09)70043-1
  18. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines 6. Rating the quality of evidence—imprecision. *J Clin Epidemiol*. 2011;64(12):1283–1293. PubMed ID: 21839614 doi:10.1016/j.jclinepi.2011.01.012
  19. *Review Manager (RevMan)*. [computer program]. Version 5.3. Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014.
  20. Serra-Prat M, Sist X, Domenich R, et al. Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial. *Age Ageing*. 2017;46(3):401–407. PubMed ID: 28064172 doi:10.1093/ageing/afw242
  21. Yu R, Wong M, Leung J, Lee J, Auyeung TW, Woo J. Incidence, reversibility, risk factors and the protective effect of high body mass index against sarcopenia in community-dwelling older Chinese adults. *Geriatr Gerontol Int*. 2014;14(suppl 1):15–28. PubMed ID: 24450557 doi:10.1111/ggi.12220
  22. Chen R, Wu Q, Wang D, et al. Effects of elastic band exercise on the frailty states in pre-frail elderly people [published online ahead of print February 11, 2019]. *Physiother Theory Pract*. PubMed ID: 30741081 doi:10.1080/09593985.2018.1548673
  23. Hsieh TJ, Su SC, Chen CW, et al. Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial. *Int J Behav Nutr Phys Act*. 2019;16(1):119. PubMed ID: 31791364 doi:10.1186/s12966-019-0855-9
  24. Maruya K, Asakawa Y, Ishibashi H, Fujita H, Arai T, Yamaguchi H. Effect of a simple and adherent home exercise program on the physical function of community dwelling adults sixty years of age and older with pre-sarcopenia or sarcopenia. *J Phys Ther Sci*. 2016; 28(11):3183–3188. PubMed ID: 27942146 doi:10.1589/jpts.28.3183
  25. Mijnders DM, Koster A, Schols JM, et al. Physical activity and incidence of sarcopenia: the population-based AGES-Reykjavik Study. *Age Ageing*. 2016;45(5):614–620. PubMed ID: 27189729 doi:10.1093/ageing/afw090
  26. Osuka Y, Kojima N, Yoshida Y, et al. Exercise and/or dietary varieties and incidence of frailty in community-dwelling older women: a 2-year cohort study. *J Nutr Health Aging*. 2019;23(5):425–430. PubMed ID: 31021359 doi:10.1007/s12603-019-1166-1
  27. Shephard RJ, Park H, Park S, Aoyagi Y. Objectively measured physical activity and progressive loss of lean tissue in older Japanese adults: longitudinal data from the Nakanajo study. *J Am Geriatr Soc*. 2013;61(11):1887–1893. PubMed ID: 24219190 doi:10.1111/jgs.12505
  28. Song J, Lindquist LA, Chang RW, et al. Sedentary behavior as a risk factor for physical frailty independent of moderate activity: results from the osteoarthritis initiative. *Am J Public Health*. 2015;105(7): 1439–1445. PubMed ID: 25973826 doi:10.2105/AJPH.2014.302540
  29. Trombetti A, Hars M, Hsu FC, et al. Effect of physical activity on frailty: secondary analysis of a randomized controlled trial. *Ann Intern Med*. 2018;168(5):309–316. PubMed ID: 29310138 doi:10.7326/M16-2011
  30. Antoniak AE, Greig CA. The effect of combined resistance exercise training and vitamin D3 supplementation on musculoskeletal health and function in older adults: a systematic review and meta-analysis. *BMJ Open*. 2017;7(7):e014619. PubMed ID: 28729308 doi:10.1136/bmjopen-2016-014619
  31. Milder DA, Pillinger NL, Kam PCA. The role of prehabilitation in frail surgical patients: a systematic review. *Acta Anaesthesiol Scand*. 2018; 62(10):1356–1366. PubMed ID: 30094821 doi:10.1111/aas.13239