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Evidence on non-pharmacological interventions for preventing or reversing physical frailty in community-dwelling older adults aged over 50 years: overview of systematic reviews

Annemarie Money[1,2*], Aylish MacKenzie[1,2], Amelia Parchment[1,2], Gill Norman[4], Danielle Harris[1,2], Saima Ahmed[1,2], Lisa McGarrigle[2,5,6], Helen Hawley-Hague[1,2] and Chris Todd[1,2,3,5,6]

Abstract

Background A large proportion of older adults are pre-frail. Interventions aimed at this group provide opportunity to reduce progression of physical frailty. The aim of this overview of reviews is to evaluate evidence for non-pharmacological interventions for the prevention/reversal of physical frailty in community-dwelling adults aged ≥ 50 years.

Methods Medline, Embase, CINAHL, Cochrane Database of Systematic Reviews, Google Scholar and Social Science Citation Index were searched for non-pharmacological interventions that used a validated frailty measurement tool. Review quality was assessed using AMSTAR-2 and a Synthesis Without Meta-analysis (SWiM) approach was adopted.

Results Twenty-three reviews were included, six of which were of high quality. This included 18,768 unique participants from 98 unique primary studies. Physical activity containing an aspect of resistance training, for a minimum of twice per week, was evidenced as being beneficial for reversing frailty (28 primary studies and 3,246 unique participants). However, one randomised controlled trial (RCT) showed resistance training by pre-frail adults ($n = 66$) for eight weeks was not effective at reversing frailty status. Nutrition interventions combined with physical activity that include resistance training (9 studies, 1,812 participants) were effective at reversing/preventing frailty.

Conclusion The evidence synthesised in this overview of reviews suggests physical activity containing an aspect of resistance training is beneficial at reversing frailty status and preventing frailty progression. Nutrition interventions alone were inconclusive. It is recommended that future studies include a validated tool to assess frailty status, report samples by frailty status and make recommendations based on dose (frequency/duration of minutes per session) and adherence to dose.

Keywords Pre-frailty, Frailty, Older adults, Systematic reviews, Physical activity, Nutrition

*Correspondence:
Annemarie Money
annemarie.money@manchester.ac.uk

Full list of author information is available at the end of the article

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Introduction

Between 2015 and 2050 the proportion of adults over the age of 60 years worldwide is set to nearly double from 12 to 22% [1]. Frailty is a complex health state in which older adults are at risk of adverse outcomes such as disability, falls, hospitalisation, and the need for long-term care [2, 3]. Some 8.1% of adults aged 50 + in England are frail; prevalence increases with age, and for adults over the age of 90 years, prevalence rises to 40.8% [4]. England's Chief Medical Officer's 2023 annual report "Health in an Ageing Society" [5] highlighted the need for older adults to maintain their independence into later life, emphasising the importance of preventing, delaying or minimising frailty.

Healthcare costs are around 5–6 times higher in frail older people compared to older adults with zero frailty symptoms [6] and are equivalent to an additional cost of £5.8 billion per year across the NHS [7]. Frailty is also the strongest predictor of formal care costs. Social care costs are nearly 10 times higher amongst individuals with frailty living in their own homes compared to non-frail individuals [8]. The cost to health and social care is likely to increase as the number of people aged 75 + in the UK continues to grow.

The progression of frailty is not unidirectional and is modifiable, meaning it can be reversed [9]. Pre-frailty is a condition preceding frailty. It is an intermediate stage associated with minor immediate adverse health outcomes, the predominant risk being increased vulnerability to progress toward moderate or severe frailty, if no intervention is put in place. Some 41% of older adults are estimated to be pre-frail (~41%) [10], therefore interventions aimed at this group provide an opportunity to impact on progression of frailty and wider population health benefits [11]. Interventions to slow disability progression and improve recovery could significantly reduce the predicted increase in the cost for social care [12]. There has been much activity in frailty research since the early 2000s, and the evidence base for the impact of non-pharmacological interventions on frailty progression is considerable [13–16]. Encouragement of physical activity is a mainstay of public health approaches [5].

Despite the substantial research base there is still no agreement on an operational definition of frailty [17] although two operationalisations are widely accepted–the Rockwood Frailty Index [18] and the Fried Frailty Phenotype [19]. Within the published literature, frailty is diagnosed using multiple different tools and proxy measures (these are measures that indirectly point to frailty rather than a total measure of frailty status for example, muscle mass, muscle strength and physical function). A systematic review conducted in 2016 counted over 60 instruments used to measure frailty [20]. This inconsistency in frailty definitions and measurements makes it difficult to synthesise the available evidence [21].

In addition, in many systematic reviews, frail and pre-frail participants are often grouped together for analysis purposes which makes it difficult to determine whether changes in physical performance were clinically meaningful. This makes designing and testing interventions aimed at pre-frail older adults, based on such recommendations, problematic [22]. Combining the two populations could lead to true harm or benefit being diluted or masked for the specific populations of pre-frail rather than frail people.

Objective

The aim of this overview of reviews, therefore, is to synthesise the current evidence on non-pharmacological interventions in (a) preventing or (b) reversing physical frailty in community-dwelling adults aged ≥ 50 years in which a validated measure of frailty has been used. An additional objective is to report, where possible, on interventions aimed at different frailty status groups, e.g. pre-frail.

Method

The overview protocol was registered on PROSPERO (registration number CRD42021271391) [23]. This overview was carried out in accordance with guidance from the Cochrane Handbook for Systematic Reviews of Interventions [24], and reported following the Preferred Reporting Items for Overviews of Reviews (PRIOR) [25].

Box 1 PICO and exclusion criteria

Population	Community-dwelling adults ≥ 50 years categorised as frail, pre-frail or robust. As there is no consistent definition of frailty, authors included reviews that used a validated tool such as Fried Phenotype or the Rockwood Scale. Reviews were excluded if their participants were non-community-dwelling adults, institutionalised patients, hospital inpatients; prison populations; residents of nursing and residential care homes; participants with a terminal diagnosis of less than two years; or selected due to a specific illness or condition. Studies within reviews were also excluded on this basis so that only relevant primary studies are included within our analysis.
Intervention:	All non-pharmacological interventions. Interventions included exercise/physical activity interventions, nutrition interventions, combined exercise and nutrition interventions, telehealth interventions, and health education interventions. Pharmacological interventions within primary studies were excluded.
Comparison:	Usual care, no intervention or placebo in cases of nutritional supplementation.

Outcome:	Primary studies within reviews needed to measure frailty status before and after an intervention using a validated tool. Outcomes related to reversing or preventing frailty were measured. 'Preventing frailty' refers to participants that are pre-frail and robust. Reviews that only reported on proxy measures (i.e. not a validated tool) in relation to frailty were excluded.
Study design:	Systematic reviews of randomised controlled trials (RCTs), non-randomised trials (NRTs), controlled before-after studies (CBAs), with or without meta-analysis, were included. Systematic reviews with at least one relevant primary study measuring frailty status using a validated tool were included, but only the relevant primary studies were included in the analysis.

Search strategy and selection

The following online databases were searched up to April 2024 for systematic reviews with or without meta-analyses published from 2000 onwards: Medline, Embase (both OvidSP), CINAHL (EBSCO), Cochrane Database of Systematic Reviews, Google Scholar (results from first ten pages), Social Science Citation Index (Clarivate). Search terms included: frailty, pre-frail*, prefrail* and mild frailty (see supplementary Table 1 for example search strategy). Date limitation was used to reflect key peer-reviewed papers published from this date onwards that developed validated frailty tools (e.g. Fried Frailty Phenotype etc.). Search records were exported into Rayyan [26] and duplicates removed. Two reviewers independently screened title and abstract and full texts for relevance as per inclusion/exclusion criteria. Disagreement was resolved via a third reviewer.

Data extraction and synthesis

Data were extracted independently by two researchers (AMK, AP) using a standardised data extraction form. Discrepancies were resolved by a third researcher (AMM). This overview reporting is guided by the Synthesis Without Meta-Analysis (SWiM) [27] methodology. The reported data from the reviews were separated into two groups based on the main aim: (a) prevention of frailty and/or pre-frailty and (b) reversal of frailty and/or pre-frailty. These are reported on for each major non-pharmacological intervention category. Since the use of validated tools to measure frailty status was a criterion for review inclusion, and most validated tools that measure pre-frailty focus on physical frailty, we extracted data related to physical frailty outcomes only.

The narrative synthesis structure is based on outcomes and comparisons present in the included reviews. Network Meta-Analyses (NMA) are reported on separately to ensure the level of detail from their analysis, such as sub-grouping, is reported sufficiently within this overview of reviews.

Risk of bias/quality appraisal for primary studies has been reported in the summary of findings, (Table 2) using the original review authors' risk of bias assessments, and GRADE assessments of certainty of evidence [28], where available, have been reported throughout. Statistical effect has been reported where available, although some reviews do not include a meta-analysis. To account for primary study overlap amongst reviews, we calculated the Corrected Covered Area (CCA) using GROOVE [29] (Graphical Representation of Overlap for Overviews). This software calculates the percentage of studies that appear in two reviews. This was to ensure primary studies weren't counted more than once which would potentially give false weighting to a result. A CCA score of > 15% indicates very high overlap.

To assess specific characteristics within the interventions, the TIDieR [30] (Template for Intervention Description and Replication) checklist was used to describe interventions, and if required, primary studies were consulted for additional relevant data not reported at review level. Methodological quality was assessed using AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews) [31]. Each review was assessed by two researchers (two of AMM, AMK, AP, DH) and discrepancies were discussed and resolved with a third researcher. For the full AMSTAR 2 results, refer to supplementary Table 2.

Results

Database searches identified 2,113 records. After title and abstract screening of 1,629 records and full-text screening of 410 potentially eligible records, 23 reviews met the full inclusion criteria for this overview (Fig. 1). This included 18,768 unique participants from 98 unique relevant primary studies (after considering study overlap). Seventeen of these primary studies included pre-frail participants, 28 included frail participants and 53 included mixed frail/pre-frail participants. Main review characteristics are presented in Table 1. Non-pharmacological intervention categories reported within reviews were physical activity, nutrition, telehealth, health education and physical activity plus nutrition. Interventions were between 6 weeks and 12 months in duration. Geographical locations were reported in 17 out of 23 reviews with most studies being carried out in European and Asian countries and some in North America, Mexico and Australia. Most interventions were compared to a control group described as 'no intervention' which includes usual care, health leaflet or booklet, nutrition placebo, usual activity, use of usual community services, and no more than one health promotion session. Validated tools used to measure frailty status were Fried criteria /

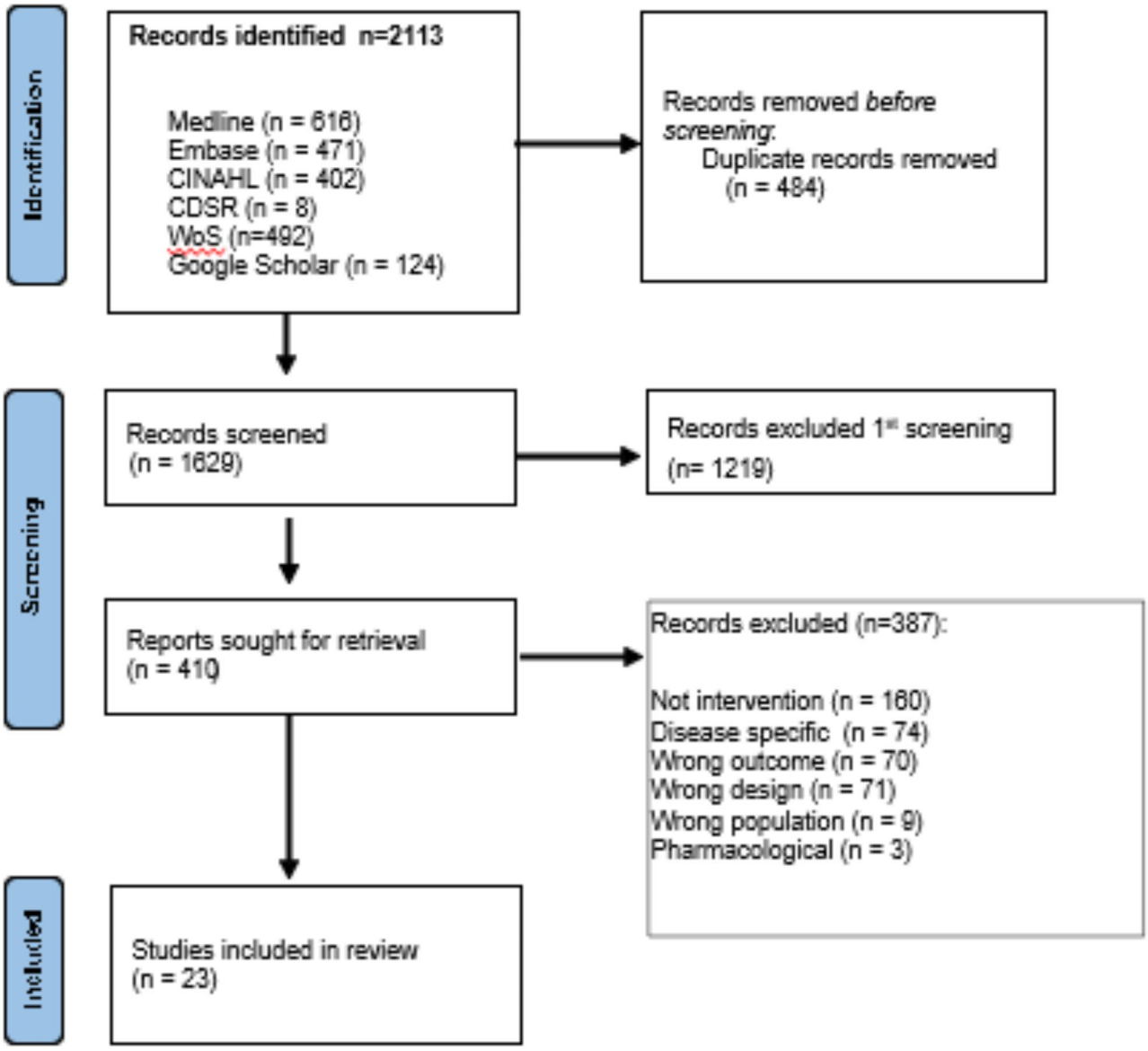

Fig. 1 PRISMA flowchart

frailty phenotype or modified Fried [19], Mob-T (Mobility Tiredness Scale) [32], Cardiovascular Health Study (CHS) [33], Rockwood Scale [34], Comprehensive Geriatric Assessment [35], Tilburg Frailty Indicator [36], SHARE-FI [37] (Survey of Health Ageing and Retirement in Europe Frailty Instrument), Checklist 15 [38], Edmonton Frailty Scale [39] Study of osteoporotic fractures frailty scale [40] and the Kihon Checklist for Frailty [41].

Included reviews addressed reversal of frailty [11, 14, 15, 42–57] or both prevention and reversal of frailty [58–61]. We have used these outcomes to structure the synthesis. Participants were often a mix of frail and pre-frail, unless stated otherwise, within the narrative synthesis (see Table 2).

There were six high quality reviews [42, 45, 49, 51, 53, 61] identified through AMSTAR 2 [31], with nine classed as moderate [11, 15, 43, 46, 47, 52, 57, 58, 60], five as low [14, 44, 50, 56, 59] and three as critically low [48, 54, 55] quality. The most common AMSTAR 2 items lowering the quality rating were those related to not reporting funding sources of the primary studies and not providing a discussion of heterogeneity observed in the results. As these common items relating to lower quality reviews did not directly relate to the quality of the search and data extraction in these reviews, we chose to include these lower quality reviews in the data synthesis (see supplementary Table 2).

Mode of delivery, where reported, included the use of qualified fitness instructors, nutritionists,

Table 1 Summary of included systematic reviews

Author	No of studies* (participants)	Intervention type	Comparator	Pre-frail or frail participants	Prevention or reversal of frailty	Frailty tool	AMSTAR2
Apostolo [58]	8 RCTs (1379)	Health education PA + nutrition PA	No intervention	Pre-frail and frail	Prevention Reversal	Fried Mob-t CHS Rockwood GCA	Moderate
Daryanti [42]	7 RCTs ($n=517$)	PA	No intervention	Frail	Reversal	Frailty phenotype Tilburg Frailty Indicator	High
De Labra [43]	1 RCT ($n=131$)	PA + nutrition PA	No intervention Home-based low level exercise program	Frail	Reversal	Fried	Moderate
Dedeyne [44]	5 RCTs ($n=674$)	PA PA + nutrition	Nutritional placebo Nutrition education No intervention	Pre-frail and frail	Reversal	Fried/modified Fried SHARE-FI	Low
Esfandiari [45]	3 RCTs ($n=419$)	Telehealth	No intervention	Not frail, pre-frail and frail	Reversal	Fried Rockwood	High
Frost [11]	1 RCT ($n=205$)	Telehealth	No intervention	Pre-frail	Reversal	Fried	Moderate
Han [46]	2 RCTs ($n=286$)	Telehealth	No intervention	Pre-frail and frail	Reversal	Fried	Moderate
Khor [47]	4 RCTs ($n=663$)	PA + Nutrition	No intervention, Intervention in cross over design.	Pre-frail and frail	Reversal	Fried, Checklist 15	Moderate
Kidd [14]	2 RCTs ($n=487$)	PA Nutrition PA + Nutrition Multicomponent	No intervention	Pre-frail and frail	Reversal	Fried	Low
Li [48]	7 RCTs ($n=1971$)	PA PA + nutrition	No intervention	Pre-frail and frail	Reversal	Cardiovascular Health Study criteria	Critically low
Liao [49]	1 RCT ($n=131$)	PA + nutrition	Protein supplement Physical activity & placebo	Frail	Reversal	Fried	High
Lim [59]	1 RCT ($n=80$)	PA + nutrition	Social support	Pre-frail and frail	Prevention Reversal	SHARE-FI	Low
Liu [15]	6 RCTs ($n=613$)	PA PA + nutrition	No intervention	Pre-frail	Reversal	Fried	Moderate
MacDonald [60]	12 RCTs ($n=2492$)	PA Nutrition PA + nutrition	No intervention; Health education; Social support; Resistance training only; 3-month delay; exercise & placebo/ placebo only/ nutrition supplementation only	Pre-frail and frail	Prevention Reversal	Fried	Moderate
Moraes [61]	3 RCTs ($n=432$)	Nutrition	Placebo Nutrition counselling	Pre-frail and frail	Prevention Reversal	Cardiovascular Health Study criteria	High
Morciano [50]	5 RCTs ($n=1128$)	PA PA + nutrition	Health education Control supplementation Routine exercises No intervention	Pre-frail and frail	Reversal	Cardiovascular Health Study Criteria Fried Frailty Criteria Edmonton Frailty Scale Frailty Index	Low
Negm [51]	16 RCTs ($n=5262$)	PA Nutrition PA + nutrition	Placebo Standard care Other interventions in network MA	Pre-frail and frail	Reversal	Fried Frailty Index	High
Racey [52]	6 RCTs, 1 NRT ($n=953$)	PA + nutrition Nutrition	No intervention routine care or minimal contact that did not include any intervention or treatment group components	Pre-frail and frail	Reversal	Fried CHS SHARE-FI	Moderate

Table 1 (continued)

Author	No of studies* (participants)	Intervention type	Comparator	Pre-frail or frail participants	Prevention or reversal of frailty	Frailty tool	AMSTAR2
Sun [53]	56 RCTs ($n=9530$)	PA Nutrition Telehealth Multicomponent	No intervention Wait list Health education Placebo Low-dose supplementation, Other training types	Pre-frail and frail	Reversal	Clinical Frailty Scale Edmonton Frailty Scale Frailty Index Frailty Phenotype Study of osteoporotic fractures frailty scale Tilburg Frailty Indicator	High
Travers [54]	14 RCTs ($n=2933$)	PA PA + nutrition Health education Nutrition	No intervention Placebo Nutrition only	Pre-frail and frail	Reversal	Fried SHARE-FI Cardiovascular Health Study criteria Kihon checklist for frailty	Critically low
Veninsek [55]	6 RCTs ($n=1677$)	PA PA + Nutrition Health education	Not reported in review	Pre-frail and frail	Reversal	Fried CHS	Critically low
Wan [56]	6 RCTs ($n=399$)	PA	No training Health education Resistance training Routine care	Pre-frail and frail	Reversal	Frailty Phenotype, Tilburg Frailty Indicator	Low
Yi [57]	2 RCTs ($n=153$)	PA	No intervention Health education	Pre-frail and frail	Reversal	Fried phenotype	Moderate

RCT = Randomised Controlled Trial; NRT = Non-Randomised Trial = Physical Activity;

*RCT and participant numbers are prior to overlap correction (CCA)

physiotherapists and medical professionals in the delivery of interventions. One primary study included the use of non-professional volunteers, but they had the support of health professionals. Eight reviews reported adherence rate [14, 52, 54–56, 59–61], six of which reported adherence rate of over 75% [52, 54, 55, 59–61] (often defined as proportion of completed exercise, nutrition counselling or health education sessions). One review reported a range between 25 and 49% adherence [14] while one review reported a 0–11% drop out rate [56]. Due to the nature of an overview, there were gaps in the robust reporting of interventions which have been highlighted in Table 1. Details on frequency, length and duration of an intervention in some cases were not reported in the systematic review and therefore were obtained directly from the primary studies. None of the included studies in this review reported any consideration of equity factors, as identified in the PROGRESS Plus framework [62].

Prevention and reversal

Physical activity and nutrition

Two moderate quality reviews [58, 60] and one low quality review [59] reported both reversal of frailty and prevention of frailty following a combined nutrition and physical activity intervention. After overlap was considered (Fig. 2), this result was based on nine primary studies and 1,812 unique participants. An improvement in frailty status was demonstrated in all reviews. All interventions included a resistance training component performed at least twice per week for a minimum of three months and up to twelve months. In some cases, resistance training was combined with balance or aerobic exercise. Interventions included a range of nutritional components including dietary advice, micronutrient supplements aimed at improving the participants' vitamin and mineral intake or macronutrient supplements aimed at increasing protein or overall caloric intake. One included RCT [60] studied pre-frail participants and found weak evidence favouring aerobic, strength and balance training in addition to nutritional education (Risk Ratio (RR) 0.32 [95% CI 0.09 to 1.10] $n=133$). This RCT was assessed by the original review authors as having a low risk of bias. The intervention showed a trend towards a reduction in the risk of frailty, but the wide confidence intervals reported indicate uncertainty.

Physical activity

Two moderate quality reviews [58, 60] reported both reversal and prevention of frailty following physical activity interventions. After adjusting for overlap, this result was based on ten primary studies and 1,600 unique participants. Interventions were delivered both in-person or at home at least twice per week for durations of eight weeks to twelve months. An improvement in frailty status

Table 2 Summary of findings

Outcome: Prevention and Reversal		
Author/Review	**Comparison**	**Risk of Bias / quality**
Comparison: Physical activity + nutrition Vs. no intervention		
Apostolo [58]	5 RCTs: Exercise and nutrition interventions were amongst the most successful interventions to reduce frailty	All papers met a minimum quality when they obtained at least five "Yes" ratings on the JBI Critical Appraisal Checklist. GRADE: low
Lim [59]	Mean change in SHARE-Fi frailty score −0.71 (95% CI -1.07 to -0.35) in intervention group at 12 weeks. No significant difference in changes in scores between intervention and control groups.	Joanna Briggs Institute Score: 9/13.
MacDonald [60]	RR 0.69 (95% CI 0.58 to 0.82) I^2 =0%; 4 RCTs; n = 390 Pre-frailty RR 0.32 (95% CI 0.09 to 1.10) 1 RCT; n = 133	1: low risk 3: unclear risk
Comparison: Physical activity Vs. no intervention		
Apostolo [58]	5 RCTs: Interventions delivered in group sessions were more successful than exercise interventions delivered one-to-one.	All papers met a minimum quality when they obtained at least five "Yes" ratings on the JBI Critical Appraisal Checklist GRADE: low
MacDonald [60]	RR 0.63 (95% CI 0.47 to 0.84) I^2 =0%; 4 RCTs; n = 596 Pre-frailty RR 0.33 (0.01 to 7.90) 1 RCT; n = 66	2: unclear risk 2: high risk
Comparison: Nutrition Vs. no intervention		
MacDonald [60]	RR 0.91 (95% CI 0.63 to 1.33) I^2 =72%; 2 RCTs; n = 153	1: low risk 1: high risk
Moraes [61]	OR 2.30 (95% CI 0.72 to 7.01) I^2 =5.8%; 3 RCTs; n = 215.	1: low risk 1: unclear risk 1: high risk GRADE: very low
Outcome: Reversal		
Comparison: Telehealth Vs. no intervention		
Esfandiari [45]	2 RCTs; n = 338. Decreased frailty progression and lowered frailty status + Physical activity: 1 RCT; n = 81. Decreased frailty status	3: unclear risk
Frost [11]	1 RCT: No statistical comparison for pre-frail group; slightly higher transitions to non-frail and frail in usual care. During the first 6 months, the number of participants who transitioned to a worse or death state in telemonitoring and usual care groups was 19 (25%) and 17 (19%), respectively.	1: high risk
Han [46]	Study 1: In the intervention group, the proportion of frail was reduced by 18% over 6 months. Study 2: No significant increase in functional decline during the first six months (OR, 1.41; 95% CI, 0.65–3.06; p = 0.38) and the latter six months (OR, 5.94; 95% CI, 0.52–68.48; p = 0.15)	1: high risk 1: low risk
Comparison: Physical activity Vs. no intervention		
De Labra [43]	1 RCT: 3 months of exercise had a positive effect on reversing frailty status.	1: high quality PEDro scale
Kidd [14]	1 RCT; n = 246: Frailty scores were significantly reduced at 6 and 12 months in all groups (all p < 0.05), with physical therapy resulting in a mean change of 4.05).	1: high risk
Li [48]	MD = −0.73, (95% CI −1.05 to −0.41) I^2 =95%; 6 RCTs; n = 1887 The best dose-response for physical training was 60 min per session (MD = −0.93, 95% CI (−1.33, −0.53), Z = 4.60, p < 0.01), 3 times per week (MD = −1.30, 95% CI (−1.62, −0.99), Z = 8.16, p < 0.01, n = 324), for 3 months. (MD = −0.53, 95% CI (−0.83, −0.22), Z = 3.39, p < 0.01). Twice per week showed no effect.	1: low risk 3: unclear risk 1: high risk
Liu [15]	MD 0.32 (95% CI 0.13 to 0.76) I^2 =90%; 4 RCTs; n = 268	4: low risk
Morciano [50]	Significant improvements in frailty status p < 0.01, p = 0.01, p < 0.001. 3 RCTs; n = 765	3: good quality CONSORT 2010 checklist
Travers [54]	2 RCTs: Both studies were rated as easy to implement. One study including walking and strength training was rated more effective on frailty than mixed exercise in the second study.	ROB or quality not assessed.
Veninsek [55]	1 RCT: Regular physical activity effectively decreases the number of frailty criteria and the prevalence of frailty in community-dwelling sedentary older people.	Quality assessment tool not reported.
Wan [56]	One dimension of frailty: SMD −2.68 (95% CI −3.15 to −2.20) I^2 =0%; 2 RCTs; n = 133 Multi-dimensions of frailty: SMD −0.65 (95% CI −0.96 to −0.34) I^2 =0%; 3 RCTs; n = 175	4: Grade B 2: Grade A (as recorded by author) Cochrane risk of bias tool

Table 2 (continued)

Outcome: Prevention and Reversal		
Author/Review	**Comparison**	**Risk of Bias / quality**
Yi [57]	SMD −1.15 (95% CI −1.62 to −0.68); 1 RCT; *n* = 82 and SMD −0.57 (95% CI −1.04 to −0.09) 1 RCT; *n* = 71	1: low risk 1: unclear risk
Comparison: Physical activity (resistance) Vs. routine PA		
Daryanti [42]	12 weeks: SMD −0.13 (95% CI -0.30 to 0.04) I^2 = 0%; 5 RCTs; *n* = 378 24 weeks: SMD −0.29 (95% CI -0.55 to -0.03) I^2 =39.89%; 5 RCTs; *n* = 418	5: low risk
Comparison: Physical activity + nutrition Vs. no intervention		
Dedeyne [44]	4 RCTs: Significantly improved frailty status or score in the multi-domain intervention groups compared to mono-domain intervention groups or control group. One study found no significant difference on SHARE-FI score between a physical activity + nutrition advice and a social support intervention.	4: high quality MINORS criteria
De Labra [43]	1 RCT: 3-month exercise was combined with the nutrition supplementation program (Milk Fat Globule Membrane), the effect on frailty reversal was maximized.	1: high quality PEDro scale
Khor [47]	3 RCTs: Nutrition and physical activity with an additional component such as social support improved frailty status. One study of nutrition advice plus aerobic and strength training saw no positive effect on pre-frail participants.	Quality rating 3 = positive 1 = negative Academy Evidence Analysis Process
Kidd [14]	2 RCTs: one study found significant reductions in frailty status at 12 but not 3 month follow up. The second study reported Frailty scores significantly reduced frailty status at 6 and 12months.	1: low risk 1: high risk
Liao [49]	OR 2.79 (95% CI 1.24 to 6.31) I^2 = NA; 1 RCTs; *n* = 131	1: high quality PEDro scale
Li [48]	Positive effect of physical activity plus nutrition advice on frailty status. 2 RCTs; *n* = 1159	1: low risk 1: unclear risk
Liu [15]	MD 0.88 (95% CI 0.82 to 0.95) I^2 =0%; 2 RCTs; *n* = 306	1: low 1: unclear
Morciano [50]	Significant improvement in frailty status at 3 months ($p = 0.008$) and 12 months ($p < 0.01$); 2 RCTs; *n* = 363	2: good quality CONSORT 2010 checklist
Racey [52]	SMD −0.41 (95% CI −0.68 to −0.14) I^2 =0%; 2 RCTs; *n* = 213	2: not reported GRADE: moderate
Travers [54]	8 RCTs: All studies were reported effective at reversing frailty. There was variation reported for ease of implementation.	ROB or quality not assessed.
Veninsek [55]	4 RCTs: Multicomponent training interventions performed three times per week for 30–45 min per session over a period of more than 5 months are superior to other exercise programs. In a community-dwelling pre-frail or frail older people, nutrition, cognitive training, physical activity and combination treatment in duration of 6 months improve frailty score and frailty status	Quality assessment tool not reported.
Comparison: Health education Vs. no intervention		
Travers [54]	2 RCTs: Both studies were reported as easy to implement and less effective at preventing frailty.	ROB or quality not assessed.
Veninsek [55]	1 RCT: Health education group sessions followed by a home visit were inconclusive at showing an effect on frailty status.	Quality assessment tool not reported.
Comparison: Nutrition Vs. no intervention		
Kidd [14]	1 RCT; *n* = 246: Frailty scores were significantly reduced at 6 and 12 months in all groups (all $p < 0.05$), with nutrition resulting in a mean change of 2.98.	1: high risk
Racey [52]	SMD −0.22 (95% CI −0.44 to −0.01) I^2 =0%; 3 RCTs; *n* = 255	1: low risk 2: not reported GRADE: moderate
Travers [54]	1 RCT: high calorie supplement was not easy to implement nor effective at reversing frailty	ROB or quality not assessed.

RCT = Randomised Controlled Trial, RR = Risk Ratio CI = Confidence Interval, SMD = Standardised Mean Difference, OR = Odds Ratio, RR = Risk Ratio

or prevention of progression was demonstrated in eight out of ten primary studies. This effect was not seen when the intervention was advice only, in which a professional discussed local activity options, community groups and exercise classes. One review [60] calculated the pooled Risk Ratio (RR) of physical activity on frailty status for four RCTs and found an effect in favour of physical activity compared to no intervention (RR 0.63 [95% CI 0.47 to 0.84] 4 RCTs *n* = 596). Two of these RCTs had high risk of bias. All interventions that contributed to an effect on frailty status included resistance training either exclusively or as part of a mixed exercise programme. One included RCT, (Chen [63] reported in [60]) studied pre-frail participants and found no significant effect of resistance exercise using a resistance band for eight weeks (RR 0.33 [0.01 to 7.90] *n* = 66). However, due to the small

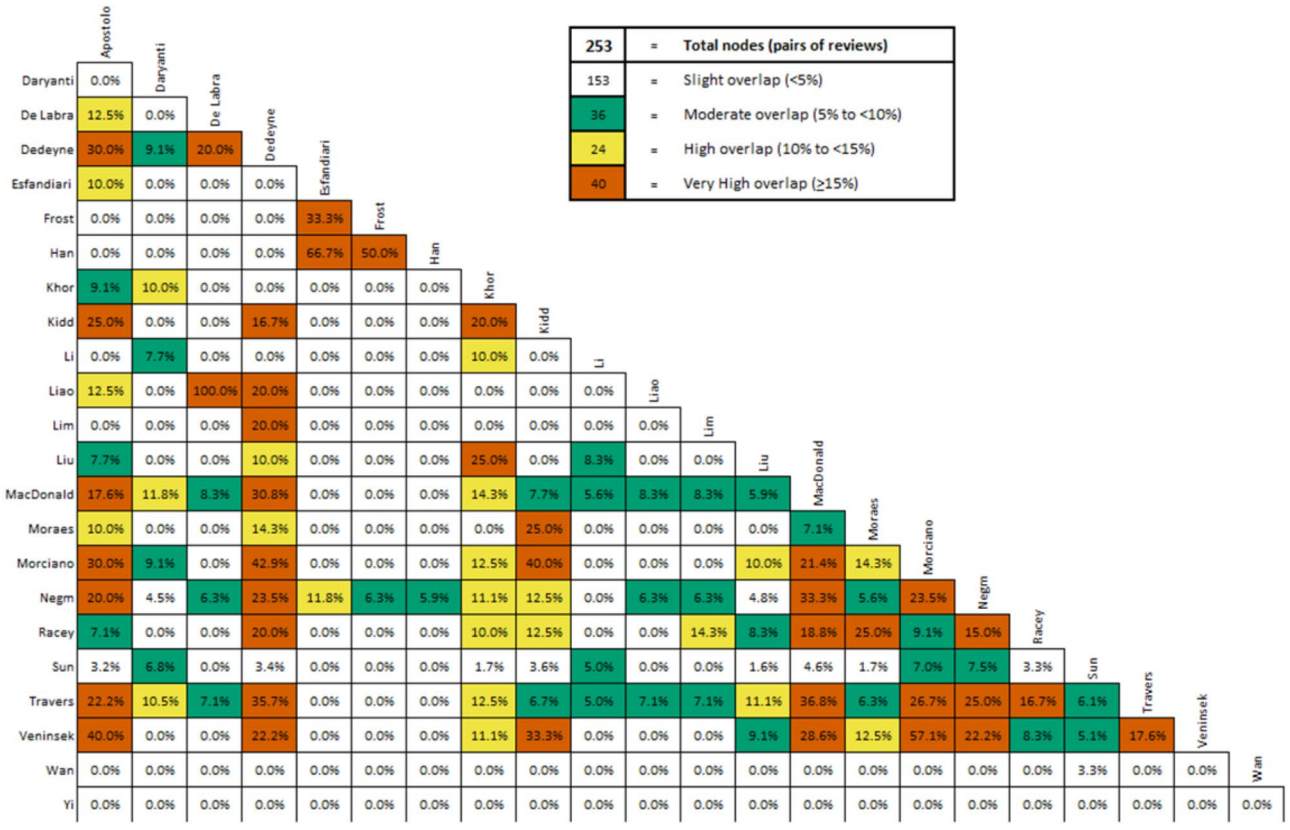

Fig. 2 Corrected covered area scores

sample size and wide confidence intervals, this is potentially an underpowered result that would benefit from a study with a larger pre-frail sample group. This RCT was rated by the original review authors as having a high risk of reporting bias.

Nutrition

One high quality review [61] and one moderate quality review [60] reported the effect of nutrition interventions for both prevention and reversal of frailty status. After considering primary study overlap, this result was based on four primary studies and 563 unique participants. Both reviews performed meta-analysis and reported no significant effect of nutrition interventions when compared to no intervention or placebo (RR 0.91 [95% CI 0.63 to 1.33]2 RCTs $n = 153$) [60], (OR 2.30 [95% CI 0.72 to 7.01] 3 RCTs $n = 315$) [61]. Both reviews reported one high risk of bias study contributing to the effect. All primary studies included nutrition supplementation from either micronutrients (e.g. vitamins, iron folate and calcium) or macronutrients (e.g. protein, fat and carbohydrates in various combinations), with the aim of increasing protein and caloric intake. These interventions lasted between three and six months with a high adherence rate as participants achieved the daily nutritional targets or consumed a daily nutritional supplement on at least 90% of the intervention days. Although two primary studies had a mixed sample, none focused solely on pre-frail participants.

Reversal

Telehealth

Telehealth interventions included a weekly phone call, an alert button or an Intel Health Guide (personalised care management from home, e.g. monitoring health measurements such as heart rate and blood pressure) [64]. Three reviews without meta-analysis, one high quality [45], and two moderate quality [11, 46], assessed whether telehealth interventions were effective at reversing frailty. After accounting for overlap, there were three primary studies [64–66], one of which had a high risk of bias, with 419 unique participants. Interventions lasted between six months and 54 weeks. Only one intervention included physical activity; this was tailored based on the participants' medical information. There was a positive effect when telehealth in the form of a pedometer and a weekly phone call was used in combination with high intensity physical activity for 24 weeks based on 81 participants [65]. However, results were inconclusive when assessing telehealth only, such as a weekly phone call or digital health monitor (see Table 2). Although two primary

studies had a mixed sample, none focused solely on pre-frail participants.

Physical activity

One high quality review [42], three moderate quality reviews [15, 43, 57], three low quality reviews [14, 50, 56] and three critically low-quality reviews [48, 54, 55] assessed the effectiveness of physical activity for reversing frailty status including 28 primary studies and 3,246 unique participants after accounting for overlap. All interventions were compared to no physical activity, apart from one review which compared a resistance band exercise programme to routine physical activity [42]. All but one review [56] included resistance or strength training for a range of 26–90 min per session, one to five times per week (one small primary study included physical activity seven days per week). One review [48] concluded there was a dose-response with no effect following activity twice per week, but a positive effect following activity three times per week based on three RCTs and 324 participants.

Wan et al. [56] focused solely on traditional Chinese exercise, such as Baduanjin exercise (a form of traditional Chinese mind-body exercise) and Tai Chi and found an effect with three to five sessions per week. One included RCT compared Baduanjin exercise to resistance training and found a small effect in favour of Baduanjin exercise (SMD − 0.49 [95% CI − 0.96 to − 0.02] $n = 71$), risk of bias was not clearly reported by original review authors but there is risk of imprecision due to small participant numbers (see Table 2). Five reviews included other types of activity combined with resistance training such as balance, flexibility, walking and aerobic exercise. One review [42] assessed the effectiveness of exercise using resistance bands in comparison with routine physical activity at 12 and 24 weeks. 12-week interventions were between 90 min and 270 min of exercise per week with ranges of 2–3 times per week and 45–90 min per session. 24-week interventions were between 120 min and 325 min with ranges of 2–5 times per week and 45–65 min per session. An improvement in frailty was found after 24 weeks (SMD − 0.29 [95% CI -0.55 to -0.03] 5 RCTs $n = 418$) but not after 12 weeks (SMD − 0.13 [95% CI -0.30 to 0.04] 5 RCTs $n = 378$). Another review [57] looking solely at Otago exercises (strength and balance exercises aimed at falls prevention) found a reduction in frailty after 12 weeks based on two RCTs and 153 participants. One study from this review had low risk of bias and the other, unclear risk of bias.

Six primary studies from these ten reviews reported results for a pre-frail population based on 364 unique participants. A positive effect on frailty status was found following variations of Baduanjin exercise for two to twelve weeks. A positive effect was also reported following a combination of aerobic, resistance and balance training following 60-minute sessions for eight to twelve weeks. The frequency of sessions per week is inconclusive.

Physical activity and nutrition

One high quality review [49], four moderate quality reviews [15, 43, 47, 52], three low quality reviews [14, 44, 50] and three critically low-quality reviews [48, 54, 55] assessed the effectiveness of physical activity in combination with nutrition interventions for the reversal of frailty. After accounting for overlap, this included 13 primary studies and 3,629 unique participants. All 11 reviews showed a positive effect of physical activity interventions in combination with nutrition interventions however, not all effects were quantified due to lack of meta-analysis. Eight of these reviews included resistance or strength training either alone or combined with balance and/or aerobic training. All interventions were carried out for a minimum of 12 weeks. Nutrition interventions varied and were often combined within review analysis. These 11 reviews included: micronutrient supplementation [44, 50]; macronutrient supplementation often focussing on protein intake [14, 43, 44, 49, 54, 55]; Mediterranean diet advice and adherence monitoring [15, 47]; or more generalised nutrition education or counselling [14, 15, 44, 47, 48, 50, 52, 54, 55]. Three primary studies were carried out with solely pre-frail participants. Two included RCTs (345 participants) combined resistance, aerobic and balance training with diet advice or Mediterranean diet advice for 12 to 48 weeks and found a positive effect on frailty status. The third study [67] (89 participants) researched resistance training and diet counselling and saw an improvement in frailty markers after a three-month intervention, but this improvement was not sustained at the six-month follow up. See Table 2 for results and risk of bias.

Health education

Two critically low-quality reviews (narrative results only) [54, 55] assessed the effectiveness of health education for reversing frailty, including three primary studies and 634 unique participants and 0% overlap. One review compared this to no intervention and one review assessed frailty specific education versus generalised health education. The effect was inconclusive following four weekly education sessions, whereas six sessions over three months found a positive effect on frailty (narratively reported). This positive effect was found for both frailty specific and generalised health promotion education sessions. These education interventions were delivered as group sessions. One review [54] reported health education as easy to implement but ineffective at reversing frailty. However, risk of bias or quality assessment was

not carried out by the original review authors. Although two primary studies had a mixed sample, none focused solely on pre-frail participants.

Nutrition

One moderate quality review [52], one low quality [14] and one critically low-quality review [54] assessed the effectiveness of nutrition interventions for the reversal of frailty including four primary studies and 506 unique participants, after adjusting for overlap. One review [54] summarised a low-calorie supplement (142–191 kj/day) versus high calorie supplement (2108–2416 kj/day) plus testosterone intervention in which there was no effect at either six months or twelve months (the definition of high and low-calorie supplements were obtained from the original primary study). Another review [52] focused on macronutrient supplementation with a focus on protein intake in which there was a positive effect on frailty status when compared to no intervention (SMD − 0.22 [95% CI − 0.44 to − 0.01] 3 RCTs $n = 255$) with moderate certainty of evidence (as rated by original review authors). This moderate quality [52] review reported 0% heterogeneity across three RCTs potentially demonstrating consistency. Although three primary studies had a mixed sample, none focused solely on pre-frail participants.

Network meta-analysis (NMA)

Two of the included 23 reviews in this overview conducted a Network Meta-Analysis (NMA) [51, 53]. These reviews had an overlap of 5.9%. After adjusting for overlap, 68 unique primary studies were included, with 13,589 unique participants. Forty-eight of these primary studies only appeared in these NMAs and not in any of the other 21 reviews included in this overview. A further 31 unique primary studies were included in this present overview of reviews, which were not included in either NMA. Direct comparisons from the standard pairwise meta-analyses have been reported statistically in Table 3. Further results from indirect comparisons that also contributed towards Surface Under the Cumulative Ranking Curve (SUCRA) have been described narratively. This is a numerical way of ranking the likelihood of effect based on the surface area below the graphically displayed cumulative ranking curve. Sun et al. [53] broke down comparisons into types of physical activity and nutrition interventions as well as a sub-analysis on frailty status. Sun et al. [53] found that physical activity, nutrition and multicomponent interventions (defined as a combination of two or more of the mentioned intervention types [other than exercise training combination], including physical activity, nutrition, psychosocial or cognitive training, home telemonitoring, comprehensive geriatric assessment, case management and medication review) all improved frailty status, see Table 3 for comparisons and effect sizes [53]. However, all direct comparisons reported on in this review [53] were assessed as having either low or moderate certainty of evidence. Negm et al. [51] also found that physical activity and nutrition, separately, were the most effective interventions at reducing frailty. This review [51] also compared physical activity in combination with nutrition compared to nutrition only and found an effect, with moderate certainty of evidence, in favour of physical activity with nutrition. However, Negm et al. carried out a GRADE [28] assessment and reported low certainty of evidence for physical activity alone compared to no intervention.

Both reviews that presented Network Meta-Analysis [51, 53] further analysed interventions by using SUCRA to rank interventions effecting frailty status. Sun et al. [53] reported that physical activity was ranked the highest at being effective in reducing frailty. Resistance training (SUCRA = 90.0%) and mind-body exercises (SUCRA = 85.9%) had the highest probability to be the most effective interventions in reducing frailty. Negm et al. [51] reported physical activity (SUCRA 100%) and nutrition supplementation (71% SUCRA) as having the highest probability to be the most effective in reducing frailty. Sun et al. [53] carried out a sub-analysis on studies that included pre-frail participants only. From the direct comparisons they found a benefit following mixed training (SMD 0.47 [95% CI 0.13 to 0.82]), mind-body exercise (SMD 0.60 [95% CI 0.24 to 0.96]) and multicomponent exercise (SMD 0.44 [95% CI 0.16 to 0.73]) on frailty status. There was no clear effect following nutrition only interventions (SMD 0.23 [95% CI -0.33 to 0.79]).

Discussion

Summary of key findings

Reviews that assessed a change in frailty status in primary studies using a validated frailty tool were included in our synthesis. Twenty-three reviews in total were included, and these incorporated the findings of 98 unique primary studies. Seventeen of these primary studies enrolled a pre-frail participant population. Four reviews reported on both reversal and prevention of frailty, 19 reviews reported on reversal of frailty status. No reviews solely looked at the prevention of frailty.

The evidence highlights resistance training as a highly effective intervention component that can delay frailty progression in both early and late stages of its development [68]. All physical activity interventions, that were researched within the included reviews, that found an improvement in frailty status included a resistance training component. Two high-quality NMAs concluded that physical activity plus nutrition interventions were the most effective at reversing and preventing frailty with resistance training ranked as the most effective physical activity type. However, many direct comparisons included in these

Table 3 Summary of findings from network meta-analysis (NMA)

Review	Comparison	Result	Certainty of evidence (GRADE)
Negm [51]	Nutrition Vs. placebo/no intervention	SMD − 0.246 (95% CI − 0.372 to − 0.120) I^2 =8.8%; 6 RCTs; n = 1567	High
	Multicomponent Vs. placebo/no intervention	SMD − 0.086 (95% CI − 0.215 to 0.043) I^2 =14%; 5 RCTs; n = 2052	Moderate
	PA Vs. PA + nutrition	SMD 0.135 (955 CI − 0.400 to 0.670) 1 RCT; n = 66	Moderate
	PA Vs. nutrition	SMD − 0.187 (95% CI − 0.509 to 0.134) I^2 = 12%; 3 RCTs; n = 228	Moderate
	PA Vs. no intervention	SMD − 1.034 (95% CI − 2.454 to 0.386) I^2 =97%; 4 RCTs; n = 392	Low
	PA + nutrition Vs. nutrition	SMD − 0.686 (95% CI-1.256 to − 0.115) 1 RCT; n = 65	Moderate
	PA + nutrition Vs. placebo/no intervention	SMD − 0.335 (95% CI − 0.680 to 0.010) I^2 =28%; 2 RCTs; n = 237	Moderate
	CGA Vs. placebo/no intervention	SMD − 0.315 (95% CI − 0.718 to 0.089) 1 RCT; n = 133	High
	PA Vs. multicomponent	SMD − 0.113 (95% CI − 0.512 to 0.285) 1 RCT; n = 97	Moderate
	Nutrition Vs. multicomponent	SMD 0.000 (95% CI − 0.396 to 0.396) 1 RCT; n = 98	Moderate
Sun [53]	CGA Vs. no intervention (frail)	SMD 0.26 (95% CI − 0.08 to 0.60) I^2 =52%; 2 RCTs; n = 406	Moderate
	Mixed physical training Vs. usual care (frail)	SMD 0.65 (95% CI 0.39 to 0.91) I^2 =51%; 6 RCTs; n = 531	Low
	Mixed physical training Vs. active control (frail)	SMD 0.32 (95% CI 0.08 to 0.56) I^2 =29%; 4 RCTs; n = 586	Low
	Mixed physical training Vs. resistance training (frail)	SMD 0.01 (95% CI − 0.40 to 0.43) I^2 =0%; 2 RCTs; n = 89	Low
	Mixed physical training Vs. aerobic training (frail)	SMD 0.05 (95% CI − 0.42 to 0.52) I^2 =NA; 1 RCT; n = 70	Low
	Resistance training Vs. aerobic training (frail)	SMD 0.12 (95% CI -0.36 to 0.59) I^2 =NA; 1 RCT; n = 68	Low
	Resistance training Vs. active control (frail)	SMD 0.21 (95% CI − 0.26 to 0.68) I^2 =37%; 1 RCT; n = 69	Low
	Resistance training Vs. usual care (frail)	SMD 0.92 (95% CI − 0.01 to 1.86) I^2 =NA; 1 RCT; n = 20	Low
	Aerobic training Vs. active control (frail)	SMD 0.08 (95% CI − 0.39 to 0.55) I^2 =NA; 1 RCT; n = 70	Low
	Nutrition supplementation Vs. usual care (frail)	SMD 0.42 (95%CI 0.13 to 0.71) I^2 =0%; 2 RCTs; n = 184	Low
	Nutrition supplementation Vs. active control (frail)	SMD 0.29 (95% CI − 0.20 to 0.78) I^2 =NA; 1 RCT; n = 70	Low
	Multicomponent intervention Vs. usual care (frail)	SMD 0.44 (95% CI 0.21 to 0.67) I^2 =43%; 4 RCTs; n = 606	Low
	Multicomponent intervention Vs. resistance training (frail)	SMD − 0.20 (95% CI − 0.87 to 0.48) I^2 =NA; 1 RCT; n = 34	Moderate
	Mixed physical training Vs. no intervention (pre-frail)	SMD 0.47 (95% CI 0.13 to 0.82) I^2 =0%; 2 RCTs; n = 132	Low
	Mind-body exercise Vs. no intervention/usual care (pre-frail)	SMD 0.60 (95% CI 0.24 to 0.96) I^2 =0%; 2 RCTs; n = 125	Moderate
	Multicomponent intervention Vs. no intervention/usual care (pre-frail)	SMD 0.44 (95% CI 0.16 to 0.73) I^2 =0%; 2 RCTs; n = 193	Low
	Nutrition supplement Vs. no intervention/usual care (pre-frail)	SMD 0.23 (95% CI -0.33 to 0.79) I^2 =NA; 1 RCT; n = 50	Low
	CGA Vs. no intervention/usual care (mixed sample)	SMD 0.26 (95% CI − 0.08 to 0.60) I^2 =52%; 2 RCTs; n = 406	Moderate
	Mixed physical training Vs. nutrition supplementation (mixed sample)	SMD 0.23 (95% CI − 0.21 to 0.68) I^2 =0%; 2 RCTs; n = 78	Low
	Mixed physical training Vs. resistance training (mixed sample)	SMD 0.01 (95% CI − 0.41 to 0.43) I^2 =0%; 2 RCTs; n = 88	Low
	Mixed physical training Vs. active control (mixed sample)	SMD 0.28 (95% CI 0.11 to 0.46) I^2 =7%; 5 RCTs; n = 637	Low
	Mixed physical training Vs. aerobic training (mixed sample)	SMD 0.05 (95% CI -0.43 to 0.52) I^2 =NA; 1 RCT; n = 68	Low
	Mixed physical training Vs. usual care (mixed sample)	SMD 0.59 (95% CI 0.43 to 0.75) I^2 =35%; 12 RCTs; n = 1050	Low
	Aerobic training Vs. active control (mixed sample)	SMD 0.08 (95% CI − 0.39 to 0.55) I^2 =NA; 1 RCT; n = 70	Low
	Mind-body exercise Vs. no intervention/usual care (mixed sample)	SMD 0.60 (95% CI 0.24 to 0.96) I^2 =0%; 2 RCTs; n = 125	Moderate
	Resistance training Vs. active control (mixed sample)	SMD 0.47 (95% CI − 0.10 to 1.03) I^2 =53%; 2 RCTs; n = 111	Low
	Resistance training Vs. aerobic training (mixed sample)	SMD 0.12 (95% CI -0.36 to 0.59) I^2 =NA; 1 RCT; n = 68	Low
	Resistance training Vs. usual care (mixed sample)	SMD 0.92 (95% CI − 0.01 to 1.86) I^2 =NA; 1 RCT; n = 20	Low
	Nutrition supplementation Vs. active control (mixed sample)	SMD 0.07 (95% CI − 0.36 to 0.51) I^2 =33%; 2 RCTs; n = 123	Low
	Nutrition supplementation Vs. usual care (mixed sample)	SMD 0.30 (95% CI 0.11 to 0.49) I^2 =0%; 6 RCTs; n = 429	Low
	Multicomponent intervention Vs. usual care (mixed sample)	SMD 0.38 (95% CI 0.25 to 0.52) I^2 =40%; 10 RCTs; n = 1952	Low
	Multicomponent intervention Vs. mixed physical training (mixed sample)	SMD − 0.05 (95% -0.50 to 0.40) I^2 =0%; 2 RCTs; n = 76	Moderate

Table 3 (continued)

Review	Comparison	Result	Certainty of evidence (GRADE)
	Multicomponent intervention Vs. nutrition supplementation (mixed sample)	SMD 0.18 (95% CI −0.27 to 0.62) I^2 =0%; 2 RCTs; n = 78	Low
	Multicomponent intervention Vs. resistance training (mixed sample)	SMD −0.20 (95% CI −0.87 to 0.48) I^2 =NA; 1 RCT; n = 34	Moderate
	Multicomponent intervention Vs. active control (mixed sample)	SMD 0.14 (95% CI -0.00 to 0.28) I^2 =NA; 1 RCT; n = 785	Moderate

*CGA (Comprehensive Geriatric Assessment)

*CGA, mixed physical training, mind-body exercise, aerobic training and resistance training are all included in "physical activity" comparisons within the narrative synthesis

NMAs were graded as having low or moderate certainty evidence, highlighting the need for better quality primary studies. This was consistent with findings for physical activity combined with nutrition interventions, suggesting that resistance training could be an important component for effective physical activity and multicomponent interventions. Due to the nature of an overview, the optimum session length (minutes per session) and programme duration are difficult to specify due to review level meta-analyses that combine primary study data. However, it was consistently found that physical activity with a resistance component needed to be carried out at least twice per week to see an effect on frailty status compared to no physical activity (session length ranged from 26 to 90 min). This same improvement in frailty status was not observed when the intervention was physical activity advice only (e.g. recommending local physical activity options and exercise classes), this has been shown in other studies looking at factors influencing engagement with physical activity [69–71].

Current evidence is largely focused on type of exercise; however, additional recommendations of type and dose-response in terms of frequency and minutes per session would be of value. As noted by Guo et al. [72], frailty research would benefit from more high-quality evidence on intensity and dose of physical activity to support the programming of exercise interventions.

Strengths and limitations

This overview of reviews has several strengths. First, it presents and synthesises the findings of a comprehensive and up-to-date search of the relevant systematic review literature. This includes findings of the only two NMAs that have so far been conducted to explore both the direct and indirect estimates of non-pharmacological intervention effects relating to frailty status. Forty-eight primary studies were unique to these NMAs, however, in carrying out an overview of reviews we have captured a further 31 unique primary studies that were not included in either NMA. Second, included reviews report on studies conducted in a wide range of geographical locations and therefore a strength of this overview of reviews is that these findings are representative for a large and diverse population of adults who are frail or at risk of frailty. Finally, high methodological and reporting rigour is demonstrated using the AMSTAR2 [31] quality appraisal tool, PRIOR [25] reporting checklist and TIDieR [30] checklist. We also present (where available) and consider the certainty of the evidence and report original authors' GRADE assessments [28]. One of the key limitations of this overview is that a large proportion of the included reviews were of moderate, low or critically low methodological quality (as assessed via AMSTAR-2). In addition, many of the included primary studies had very small sample sizes, wide confidence intervals and high reported risk of bias. There were also gaps in the reporting of interventions. Each of these issues may call into question the certainty of the evidence upon which this review is based.

Future recommendations

Eligible reviews for inclusion in this overview had to involve primary studies that used a validated tool to measure frailty status. This is due to the large number of tools and proxy measures [20] that relate to frailty, such as physical function and performance. This criterion improves the validity of our results as we compare measurements of frailty status. However, some potentially useful and relevant reviews are excluded due to the lack of validated tools. It is recommended that future studies include a validated tool to assess frailty status. Future research would also benefit from international agreement on an operational definition of frailty [21].

In addition, the reviews included in this overview report on populations that were often combined as frail and pre-frail, so it is difficult to separate and report on findings related to pre-frail participants only. To understand which interventions are most effective at preventing robust or pre-frail individuals from becoming frail, future reviews must have a clear working definition of frailty and report samples by frailty status, and both robust and pre-frail participants should be considered separately to frail participants in future intervention studies.

Evidence of nutrition interventions alone having a beneficial effect on frailty status is minimal. The main limitation of this evidence at review level is the combination of nutritional interventions. Grouping different interventions into one category makes it difficult to determine differences between supplements, dietary changes and dietary advice. It is therefore difficult to quantify whether specific nutrition recommendations are superior for preventing or reversing frailty. This is seen particularly in the combined physical activity and nutrition interventions, in which practitioners, professionals and patients would benefit from clear recommendations for the most effective combinations, but the evidence does not permit this level of recommendation. In future research studies of exercise interventions, it is recommended that diet, or at least protein intake, is collected and reported as a confounding factor.

As well as clarifying frailty status, future research should collect and report PROGRESS Plus [64] characteristics such as employment status, socioeconomic status, ethnicity and so on and preferably use such characteristics in the analysis of results. Physical inactivity is influenced by wider determinants of health [73–75] which therefore predispose some individuals to becoming frail. To ensure frailty interventions are applicable to those at risk of becoming frail, research must report on these influential factors.

More longitudinal studies are needed to show the preventative effect of pre-frailty interventions, as almost all primary study interventions included in this overview were no longer than 12 months. A small number of reviews were excluded due to their primary study design being ineligible for inclusion in this paper. These reviews often explored associations between nutrition and frailty status which, in the future, could be used to inform a longitudinal nutrition RCT. Research into prevention requires longitudinal studies otherwise we are often relying on proxy measures associated with the prevention of frailty. Studies also require more explicit reporting on dose and adherence to intended dose, in addition to follow up of the intervention, to provide clinically meaningful recommendations [72, 76].

Conclusion

The evidence synthesised in this overview of reviews suggests that physical activity containing an aspect of resistance training, for at least twice per week but preferably three times per week, is beneficial at reversing frailty status and preventing frailty progression. This dose-response is very similar to evidence within systematic reviews reporting on the effects of strength and balance training for falls prevention [77]. Nutrition interventions alone had inconclusive evidence for their effect on frailty. However, nutrition interventions, in combination with physical activity interventions that include resistance training, were effective at reversing and preventing frailty, suggesting that multicomponent interventions involving both may also be beneficial for improving frailty outcomes.

A limited number of reviews sub-analysed a pre-frail population. Such stratification is needed to inform the development of primary prevention interventions. It is also recommended that future studies use a validated tool to capture a change in frailty status so that interventions are valid and comparable and report on dose. Future research also needs to focus and report on disadvantaged populations that have an increased risk of developing frailty. The development and refinement of these primary interventions will allow earlier prevention, detection and intervention, ensuring longer lives spent independently and in good health. This will contribute to lowering the cost and burden that frailty places on health and social care.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Author contributions

Conceptualisation, AMM, CT; methodology, AMM, AMK, AP, GN; formal analysis, AMM, AMK, AP; data curation; AMK, AP; writing—original draft preparation, AMM, AMK, AP; writing— review and editing, AMM, AMK, AP, LMcG, SA, HHH, DH, GN, CT; funding acquisition, CT. All authors have read and agreed to the published version of the manuscript.

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Data availability

This overview of reviews includes only previously published data. Further information on aspects of the overview process not included (i.e., lists of excluded studies) are available on request from the authors; please email annemarie.money@manchester.ac.uk.

Declarations

Ethics approval and consent to participate

This study was performed according to the principles of the Declaration of Helsinki. The paper is an overview of reviews, using publicly available data published in systematic reviews, therefore it does not require ethical approval.

Consent for publication
The paper is an overview of reviews, using publicly available data published in systematic reviews, therefore it does not involve human participants and doesn't require ethical approval.

Competing interests
The authors declare no competing interests.

Author details
[1]National Institute for Health and Care Research, Applied Research Collaboration - Greater Manchester, School of Health Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester M13 9PL, UK
[2]School of Health Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester M13 9PL, UK
[3]Manchester University NHS Foundation Trust, Manchester M13 9WL, UK
[4]Innovation Observatory, National Institute for Health and Care Research, Newcastle University, Newcastle Upon Tyne NE4 5TG, UK
[5]National Institute for Health and Care Research (NIHR) Policy Research Unit in Healthy Ageing, School of Health Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester M13 9PL, UK
[6]Manchester Academic Health Science Centre, Manchester M13 9NQ, UK

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