Delaying and reversing frailty: a systematic review of primary care interventions

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Abstract

Background: Recommendations for routine frailty screening in General Practice (GP) are increasing as frailty prevalence grows. In England, frailty identification became a contractual requirement in 2017. However, there is little guidance on which are the most effective and practical interventions once frailty has been identified.

Aim: To assess the comparative effectiveness and ease of implementation of frailty interventions in primary care.

Design and setting: Systematic review.

Method: Scientific databases were searched from inception to May 2017 for randomised controlled trials or cohort studies with control groups on primary care frailty interventions. Screening methods, interventions and outcomes were analysed in included studies. Effectiveness was scored in terms of change of frailty status and ease of implementation in terms of human resource, marginal cost and time requirements.

Results: 925 studies satisfied search criteria and 46 were included. There were 15,690 participants (median size was 160). Studies reflected a broad heterogeneity. There were 17 different frailty screening methods. 23 frailty interventions involved physical activity and other interventions involved health education, nutrition supplementation, home visits, hormone supplementation and counselling. 71% of studies measuring impact on frailty status demonstrated significant improvement. Interventions with both muscle strength training and protein supplementation consistently placed highest for effectiveness and ease of implementation.

Conclusion: A combination of muscle strength training and protein supplementation was the most effective intervention to delay or reverse frailty and the easiest to implement in primary care. We created a map of interventions that can inform choices for managing frailty.

Keywords: Primary care, frailty, intervention, effectiveness, feasibility, systematic review

INTRODUCTION

Frailty has long been in the lexicon of everyday language. “How easily the wind overturns a frail tree,” Buddha reflected some two and half thousand years ago[1]. From such historic prevalence has come an inherited instinct for recognising frailty. However, it is only in recent years that frailty has come into focus for more rigorous medical definition in a shift of emphasis from single-system conditions to unifying constructs for holistic patient care.

Frailty can be described as a state of physiological vulnerability with diminished capacity to manage external stressors[2, 3]. It increases the risks of illness, falls, dependency, disability and death[2, 3].

Frailty is becoming a more common challenge as populations age and life expectancy lengthens. The prevalence of frailty is estimated at 10.7% in adults aged 65 and over and increases to some 50% in over 80 year olds[4]. The United Nations estimates that the world population of over 60 year olds will more than double from 962m in 2017 to 2.1 billion in 2050, while the population of over 80 year olds will triple from 137m to 425m in the same period[5]. In the UK, the number of over 65 year olds is estimated to grow from 10.4m to 12.4m by 2025 and life expectancy at 65 is set to increase by 1.7 years[6].

Frailty has been described as the most problematic expression of population ageing in the context of this considerable growth[7]. It has forced fundamental changes in national health policies. For example, since 2017 the new General Medical Services (GMS) contract in England mandates that all primary care practices use an appropriate tool to identify patients aged 65 and over who are living with moderate or severe frailty. For patients living with severe frailty, the practice must undertake a clinical review, provide an annual medication review, discuss whether the patient has fallen in the last 12 months, activate an enriched Summary Care Record at the patient’s request (if not already in place) and provide any other clinically relevant interventions[8].

A variety of tools have been proposed for frailty screening in primary care[9, 10]. A commonly used method is Fried’s frailty phenotype[11] (3 or more criteria from: exhaustion, unexplained weight loss, slowness, weakness and low physical activity, with 1 or 2 criteria present defining pre-frailty). The cumulative deficit model proposed by Rockwood and Mitnitski[12] provides a frailty index based on the presence of deficits as a proportion of total measured. There are several other indices, checklists and indicators[13, 14, 15]. A general model of frailty which captures commonly involved domains is represented in Figure 1.

A common element in frailty tools is a consideration of *biological age* rather than *chronological age* alone. This fits the biopsychosocial model of primary care, and its use may help identify those who are at higher risk of adverse outcomes and promote equity of access to services[10]. The ability of the frailty model to capture risk and biological age in this way has pushed the boundaries for how we care for our most vulnerable patients. This advance and the increase in prevalence have driven international consensus guidance to recommend identification of frailty in routine clinical encounters[16, 17].

Identification of frailty was made a contractual requirement for GPs in England from April 2017. However, there appears to be a lack of clear guidance on which are the most effective and practical interventions for frailty once identified. There also appears to be no consistent approach to how frailty is dealt with in general practice at present. It seemed therefore both timely and necessary to conduct a systematic review of the evidence on primary care interventions. Our aim was to map their comparative effectiveness and ease of implementation and help inform practitioners and patients on the most appropriate choices.

HOW THIS FITS IN

Frailty screening is increasingly recommended in primary care and in some cases contractually required but there is a lack of guidance on interventions, once frailty has been identified. This study outlines both the relative effectiveness and ease of implementation of frailty interventions in primary care. Findings may help the choice of appropriate primary care interventions.

METHOD

We searched PubMed, CINAHL, the Cochrane Library register of Controlled Trials and PEDro for English language articles using the terms ("primary care" or "community") and (“screening” or "intervention" or "integrated-care") and ("frailty" or "pre-frail"). The search was conducted from inception to May 2017 by JT. A second reviewer (JB) repeated the search in May 2018 to confirm the results and add any further findings. Any clarifications were resolved by MTC and RRO.

Studies were selected following an assessment of titles and abstracts. Studies chosen for inclusion were randomised controlled trials (RCT) or cohort studies with control groups, which assessed interventions aimed at preventing or treating frailty in a primary care setting, and which quantified outcomes such as the measurement of a physical frailty phenotype, a frailty index or a similar established measurement. There was no restriction on age of participants in the search criteria. Studies that involved secondary or tertiary interventions were excluded. Letters, case studies, abstract only publications and editorials were excluded.

We recorded the type of study (e.g., RCT, cohort), frailty screening method (e.g., Fried), study size, length of study, intervention, outcome measure and outcome, for each study included.

We devised an analytical tool for comparing a set of heterogeneous interventions that was too diverse for meta-analysis. We applied a scoring system to map relative effectiveness and relative ease of implementation (summarised in figure 2). The tool was designed to map interventions in two dimensions, thereby providing a clear graphical differentiation and facilitating patients and practitioners in choosing the most appropriate interventions.

In analysing relative effectiveness, an outcome that demonstrated significant improvement of frailty status or prevalence was given three points. An outcome which improved frailty criteria but did not amount to a change in status or prevalence was given two points (i.e., improvement in Fried’s phenotype (e.g., 2 to 1, both pre-frail) or improvement in frailty index items not amounting to a significant change in status). An outcome which demonstrated neither of these but improved

relevant dimensions other than frailty (e.g., perceived quality of service, increased endurance) was given one point. An outcome showing no improvement scored zero. The relative placement of interventions along the effectiveness axis was further refined using the risk ratios for interventions that were directly comparable. For example, a discrete cluster of interventions that all involved strengthening exercises were differentiated in this way.

Relative ease of implementation was analysed by examining three key requirements of people, money and time. An intervention that required multidisciplinary team (MDT) involvement was given two points (e.g., physician, nurse and/or allied health professionals [AHPs] such as a physiotherapist, occupational therapist or dietician). An intervention that did not need an MDT but did require an AHP was given one point. An intervention that incurred additional marginal cost was given one further point (e.g., new personal equipment or consumable). The amount of time in minutes per week invested by the patient and the intensity of AHP involvement (e.g., one AHP leading group sessions versus one-on-one AHP-patient activity) was used to refine the relative placement of interventions along the ease of implementation axis.

RESULTS

925 studies from the database search were identified from our search criteria (figure 3). 47 full text articles were selected for eligibility assessment following review of titles and abstracts. 46 studies were included in the systematic review analysis, with 1 study excluded as its results were included in a subsequent updated study. The total number of participants in included studies was 15,690 and median study size was 160.

The recent focus on frailty as a medical concept was underlined by the fact that only 4 of the 46 studies pre-dated 2010. Japan was the leading country for number of studies conducted (10), followed by The US (8), The Netherlands (5), Sweden (5), Spain (3), Taiwan (3), Australia (2), China (2), South Korea (2), UK (2), Austria (1), Belgium (1), Finland (1) and Singapore (1).

13 (28%) of the 46 studies used the Fried criteria as a method for frailty screening, more than any other method, and 6 used modified Fried criteria. 4 used the Kihon checklist, 2 used a version of the Kaigo-Yobo checklist, 2 used the Tilburg frailty indicator, 2 used the Groningen frailty indicator, 1 used the cumulative deficit model, 11 used other approaches to screening frailty that were unique to their study and 5 appeared to have no formal frailty screening.

Interventions for frailty in the included studies:

The studies included in the review analysis reflected a broad heterogeneity of interventions. 30 (65%) of the 46 studies applied more than 1 intervention. 23 studies involved physical exercises, of which 10 involved mixed exercises (e.g., a combination of aerobic, strength, balance and coordination), 6 featured strength exercises as the central component, 2 featured walking as the central component, 2 focussed on basic mobilising exercises, 1 involved tai-chi, 1 involved robotic balance and 1 involved use of a 'Wii'. 10 studies involved health education such as classes on nutrition, medications, falls prevention and social supports. 8 studies involved intervention with nutritional supplements, of which 5 used both protein and calories with strength or mixed exercises,

1 used protein with strength exercises, 1 used protein and calorie supplementation alone and 1 used calories with testosterone. 8 studies involved medication management, 6 of these as part of a comprehensive geriatric assessment (CGA) and 2 as part of group education sessions. 7 studies involved home visits by nurses, AHPs or doctors, with activities including safety and falls risk assessment, giving information about support services and basic mobility exercises. 4 studies focussed on hormone supplementation, of which 2 involved testosterone, 1 involved DHEA and atamestane and 1 involved raloxifene and tibolone (discontinued). 4 studies involved counselling, of which 1 involved cognitive behavioural therapy alone, 1 involved psychotherapy along with mixed exercises, 1 involved behavioural change and 1 involved life-goal setting. 1 study focussed on acupressure. A summary of interventions is shown in figure 4.

Key findings on relative effectiveness and ease of implementation:

A map of relative effectiveness and ease of implementation of the interventions is shown in figure 5. Interventions with both strength training and protein supplementation consistently placed highest in terms of relative effectiveness and ease of implementation.

Interventions with mild intensity mixed exercises or singular exercises such as walking or tai-chi placed in the mid-zone for relative effectiveness and were easy to implement. Interventions targeting behavioural change placed low in relative effectiveness though were easy to implement. Educational or health promotion activities typically placed in the mid-zone for both relative effectiveness and ease of implementation. CGAs and home visits tended to place mid to low for both relative effectiveness and ease of implementation. Administration and management of hormone therapy placed mid to low for relative effectiveness and mid to low for ease of implementation.

14 (30%) of the 46 studies reported the outcome of an intervention on frailty status, 10 (71%) of which demonstrated significant improvement. 32 (70%) of the 46 studies reported the outcome of an intervention on singular frailty indicators or other criteria, 22 (69%) of which demonstrated significant improvement.

An overview of how clusters of key interventions compare is shown in figure 6. Interventions that feature in the top right quadrant are the most effective and easiest to implement. Strength training and nutritional supplementation (specifically protein) are most prominent in this quadrant, while mixed exercises and health education also feature.

All the analysed studies and interventions are summarised in supplementary table 1.

DISCUSSION

Summary

Our aim was to systematically review the evidence available on primary care interventions for frailty and compare their effectiveness and ease of implementation in the primary care setting. Our analysis suggests that a combination of strength exercises and protein supplementation is the most

effective and easiest to implement intervention to delay or reverse frailty. The map of interventions can be helpful to inform choices for managing frailty in our aging societies.

Strengths and limitations

We have provided an up to date systematic review of the range of interventions that have been studied to date and undertaken a novel mapping of both their relative effectiveness and ease of implementation in primary care. The resultant diagram may be helpful to practitioners and patients in discussing and agreeing on interventions to fit their specific circumstances. Our analysis seems a timely contribution as frailty screening becomes mandatory in the UK and more prevalent internationally.

There are several limitations: firstly, studies analysed were too heterogeneous to allow for a meta-analysis, though meta-analyses of sub sections (e.g., physical exercise) could be performed. Some interventions outlined changes to individual frailty criteria but did not calculate or demonstrably show impact on overall frailty status. It is possible that they might otherwise have scored higher in demonstrable effectiveness. A minority of studies did not provide details on the amount of time required to complete intervention activities. Although like-for-like comparisons could be made with other studies, this reduced the accuracy of refining positions along the ease of implementation axis. While the map is helpful in clearly differentiating relative effectiveness and ease of implementation, it does not provide absolute values and interventions are not positioned to linear scale.

Comparison with existing literature

Our findings for strength and protein are consistent with knowledge that interventions to improve frailty include exercise, nutrition and multi-component interventions[18, 19]. A 2017 scoping review of interventions to prevent or reduce frailty in community dwelling older adults included 14 studies and found that physical activity interventions reduced frailty indicators[19].

Our analysis included a wide variety of 46 intervention studies and we have mapped both effectiveness and feasibility specifically in the primary care setting, enabling a choice of complementary interventions. The importance of using an integrated and holistic approach is described in the British Geriatric Society and the Royal College of General Practitioners 'Fit for Frailty' guidance for GPs[20].

Implications for research and/ or practice

A typical exercise regime that may be proposed in general practice is: 20-25 minutes, 4 days per week at home, doing 15 exercises (3 for strengthening arms, 7 for strengthening legs, 5 for balance and coordination). Each exercise is repeated 10 times/minute (progressively reaching 15 times after 2-3 months) with rest of half a minute between each set[2].

Nutritional/protein supplementation regimes described in studies included appropriate dietary emphasis on daily milk, eggs, tuna or chicken; or where preferred, 2 x 200mL of formula per day (containing 25g protein, 400kcal energy, 9.4g essential amino acids, 400mL water).

Several studies found that participation rates in physical exercise activities remained as high as 90%[21, 22, 23], though some dipped to 50%[24]. A differentiator appears to have been the level of periodic encouragement to continue participation by practising medical professionals. Several studies highlighted that benefits were found 3-6 months after the intervention but to a lesser extent at 12 months[25, 26]. This underlines the need for patients to continue to participate and medical professionals to continue to encourage appropriate interventions. We suggest that increased use of technology, including group-chats and bespoke apps could contribute to higher participation rates and this may be a subject for further research.

Frailty remains a complex syndrome and no single intervention may suit all patients[27]. While some strength exercises can simply involve using water bottles or elastic bands, engaging in exercises may not be possible for patients with debilitating conditions. Activity prescription needs to be personalised in primary care to tailor for individual circumstances. Other options, such as health education, score in the mid zone for relative effectiveness and may be easy to implement. A toolkit for general practice that could be used for different patient needs would be a useful next step to this study.

This review identified several clusters of common interventions, namely: exercises, education, nutrition, home visits, hormone supplementation and counselling. Further quantitative analysis research of these clusters would outline benefits to a greater level of detail. For example, although strength exercises consistently feature strongly in terms of effectiveness and ease of implementation, there are some differences in effectiveness that may be due to different exercise regimes. Meta-analysis of such a cluster might identify an optimal regime.

The new NHS England GMS contractual practice interventions do not primarily include physical therapy and nutrition. The results of this review may be helpful in a future evaluation and revision of a new NHS contract.

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Ethical approval
Ethical approval was not required for this systematic review.

Competing interests
The authors have declared no competing interest.

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Figure 1: Domains commonly included in frailty definitions

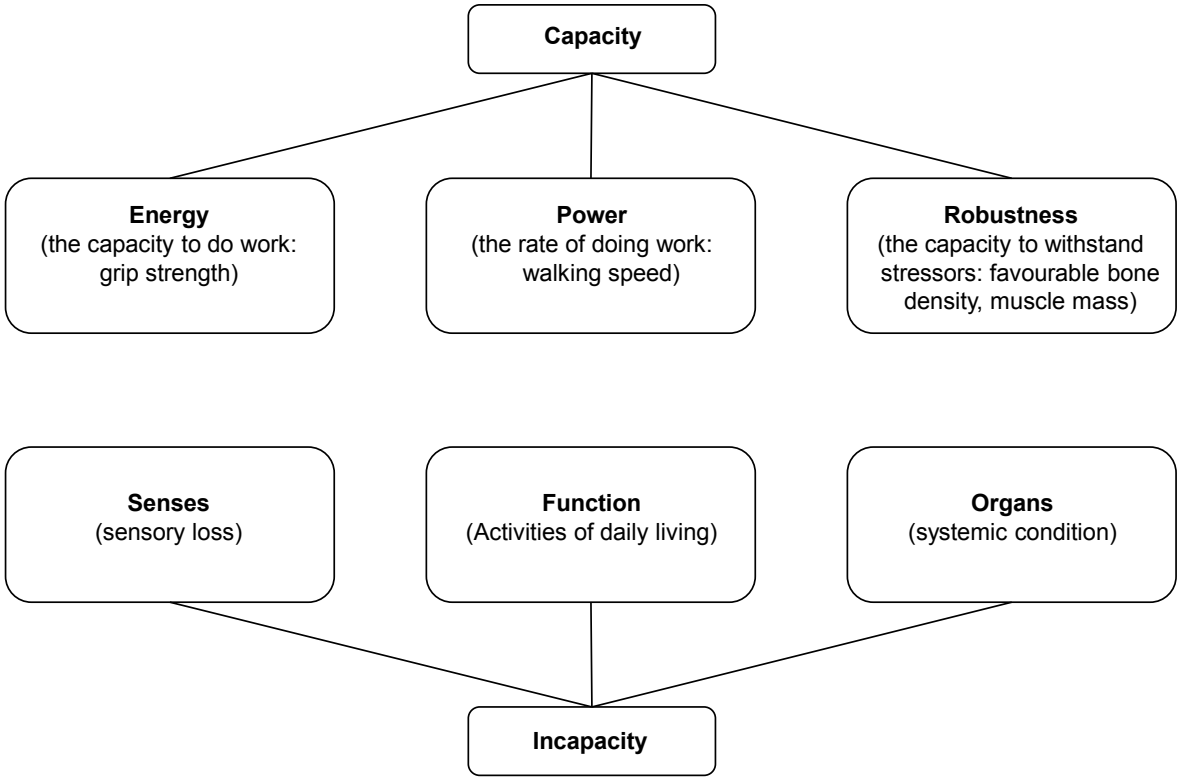


Figure 2: Comparison of interventions scoring system

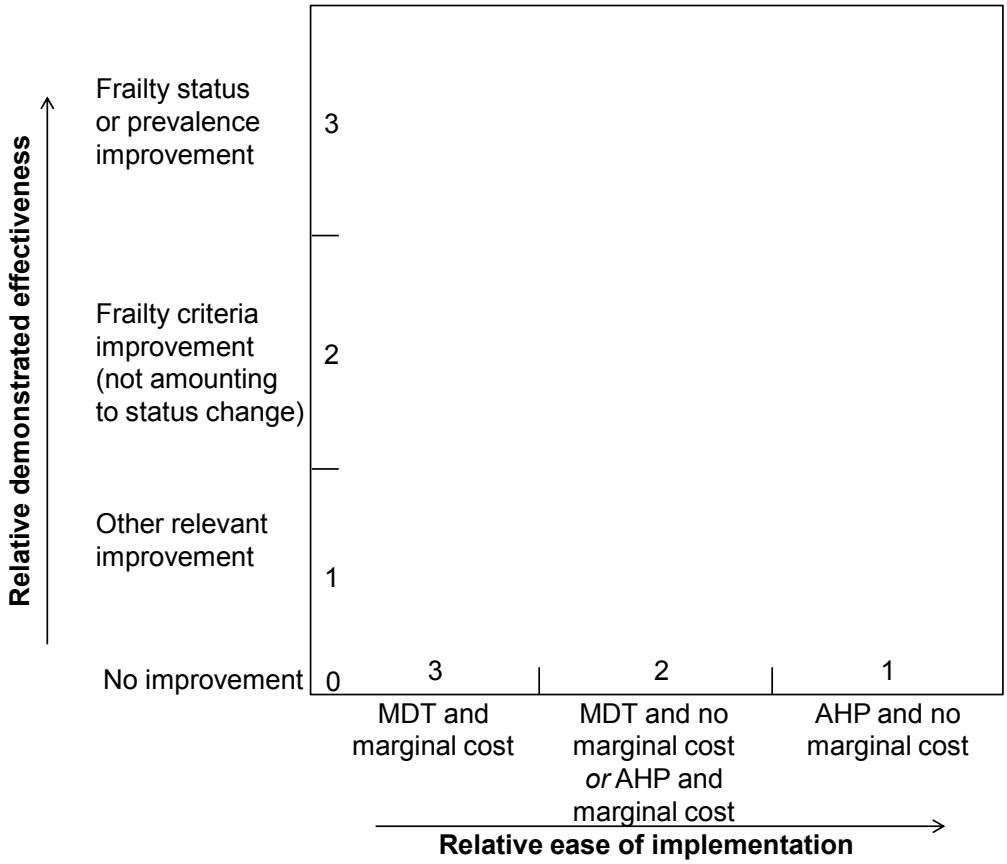


Figure 3: Literature search results

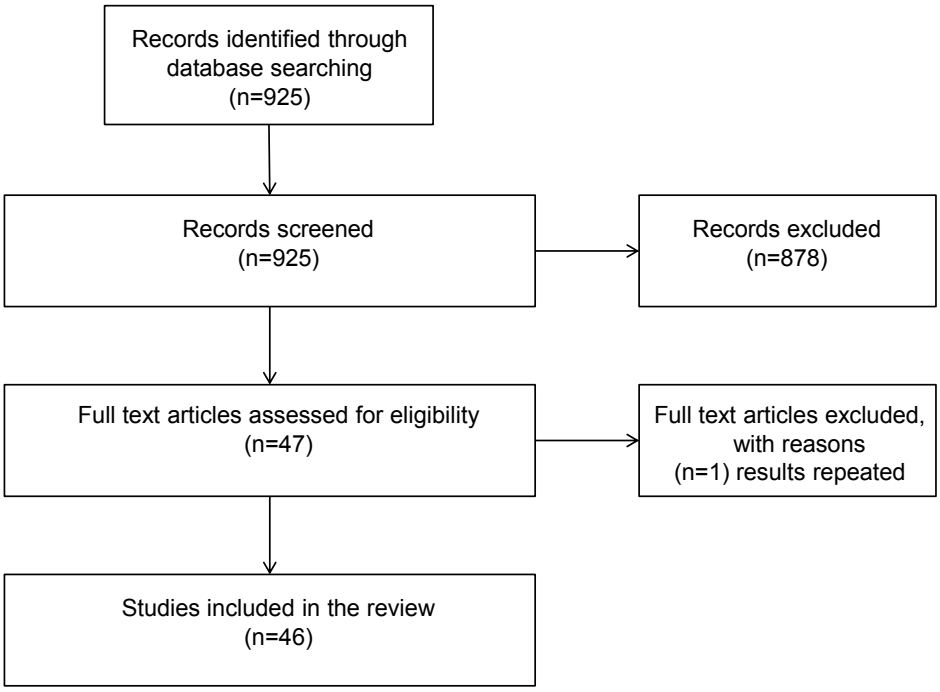


Figure 4: Overview of types of interventions for frailty

Key interventions	Physical exercise	Health education	Nutritional supplements	Home visits	Hormone supplements	Counseling	Other
Number of studies*	23	10	8	7	4	4	1
Types of activities	• Mixed exercises • Strength • Aerobic • Balance • Coord. • Walking • Tai-chi • Mobility	• Nutrition • Medication • Falls prevention • Physical exercise • Social and community supports	• Protein • Calories • Milk fat globule membrane	• Falls and safety assessment • Information giving on municipal supports • Basic mobility exercises • Nurse led, physio led or GP led	• Testosterone • DHEA • Atamestane • Ralixifene • Tibolone - discontinued	• CBT • Psychother. • Life-goal setting • Behavioural change	• Acupressure

* 30/46 studies (65%) had more than one intervention

Figure 5: Comparison of interventions for frailty

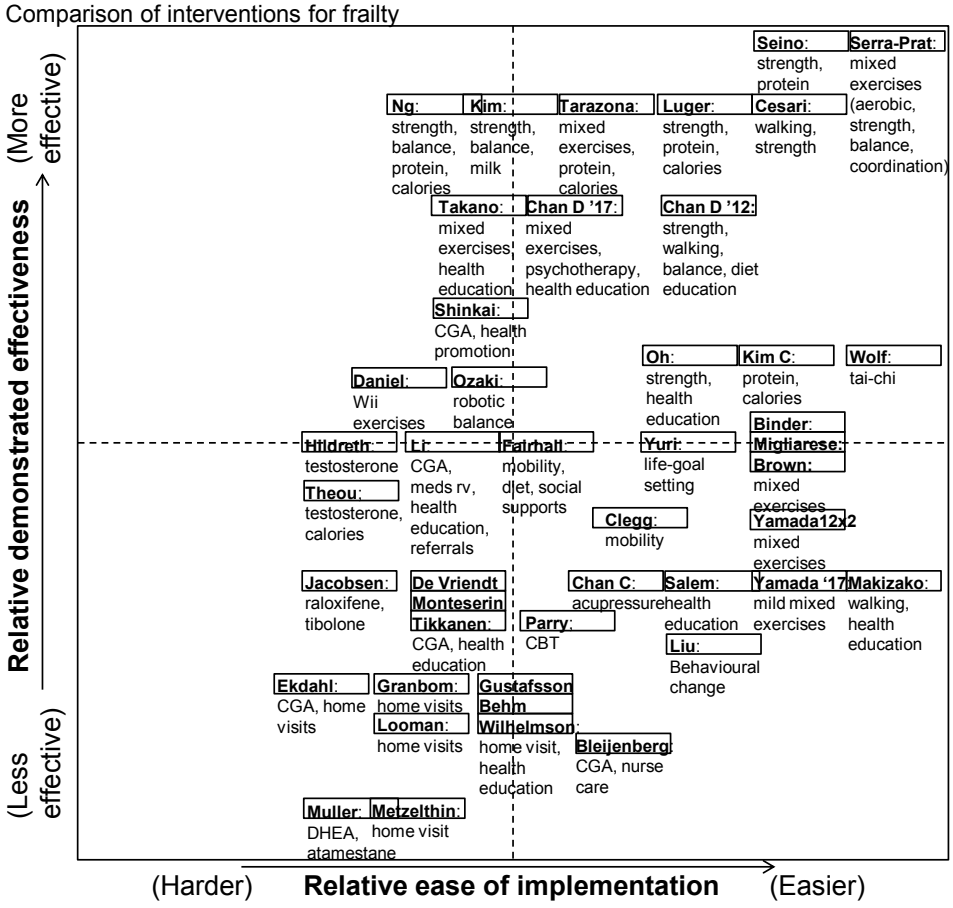
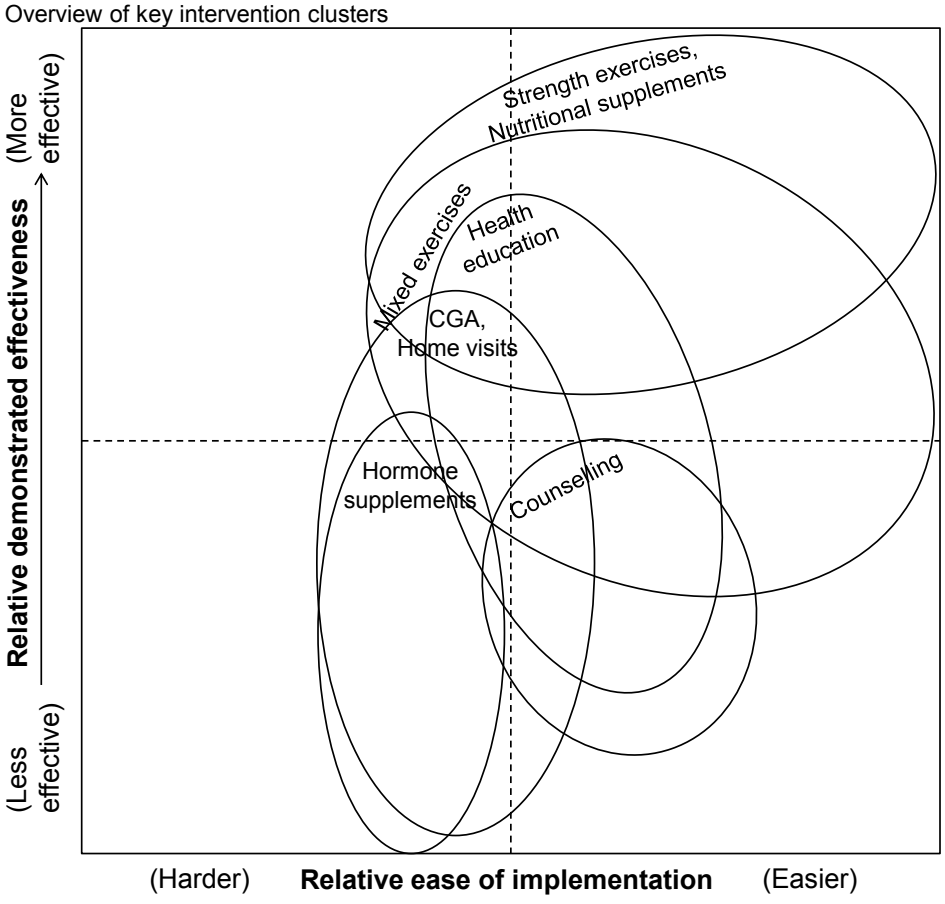


Figure 6: Overview of key intervention clusters



Supplementary table 1: Overview of studies included in analysis

Author. Study. Country. Year	Design	Frailty intervention	Study size	Length, follow up	Outcome measure	Outcome
Behm et al. Health Promotion Can Postpone Frailty: Results from the RCT Elderly Persons in the Risk Zone. Sweden. 2016	RCT	Intervention group 1: A weekly 2 hour meeting over four weeks ("senior meeting" giving information about the aging process, consequences, and providing tools and strategies for solving problems that arise in the home). Intervention group 2: A single preventive home visit (PHV) by one of OT, physio, social worker or nurse. Group 3: control	459 (n=171 meetings, n=174 home visit, n=114 control)	6-7 weeks, follow up at 3 months, 1 and 2 years	8 frailty indicators (as before) and Mob-T scale	Neither intervention group differed significantly from control wrt deterioration in the number of frailty indicators at 1 and 2 year follow ups. Frailty measured as tiredness in daily activities was significantly lower for intervention vs control at 1 year, OR 0.47 (95% CI: 0.27 to 0.81) for PHV and OR 0.55 (95% CI: 0.40 to 1.07) for senior meetings. No difference at 2 years.
Binder et al. Effects of exercise training on frailty in community-dwelling older adults: results of a randomized, controlled trial. USA. 2002	RCT	Exercise training 3 times weekly (3 months of flexibility, light resistance and balance), then 3 months added resistance (knee extension, knee flexion, seated bench press, seated row, leg press, biceps curl), then 3 months added endurance (treadmill, stationary bicycle, rowing machines) Vs. control group doing low intensity home exercise (flexibility) programme	115 (n=66 exercise training, n=49 home exercise)	9 months	Modified PPT score, VO2 peak, ADLs and functional status questionnaire	Statistically significant improvement for ET group in modified PPT (95% CI 1.0, 5.2), VO2 peak (95% CI 0.9, 3.6), FSQ (95% CI 1.6, 4.9); knee strength, balance
Bleijenberg et al. Effectiveness of a Proactive Primary Care Program on Preserving Daily Functioning of Older People: A Cluster Randomized Controlled Trial. Netherlands. 2016	RCT	Three arms: 1) frailty screening followed by routine GP care, 2) frailty screening followed by nurse led care (further screening with Groningen frailty indicator, self assessment, CGA, then personalized nursing care plans), 3) Control - GP care as usual	3,092 (n=790 screening, n=1,446 screening and nurse led care, n=856 usual care)	1 year	Primary: daily functioning using Katz-15 (6 ADLs, 8 IADLs,1 mobility item). Secondary: QOL, primary care consultations, hospital admissions, emergency department visits, NH admissions, mortality	Screening in primary care followed by personalised nurse led care had less decline in daily functioning but did not have a clear or convincing effect. Mean Katz-15: screening arm 1.87 (95% CI 1.77-1.97), screening and nurse led care arm 1.88 (95% CI 1.80-1.96), control group 2.03 (95% CI 1.92-2.13; P=0.03). No differences in QOL
Brown et al. Low-intensity exercise as a modifier of physical frailty in older adults. USA. 2000	RCT	22 supervised exercises for flexibility, balance, speed, coord, strength; 3 times per week; for 3 months Vs. home based flexibility	84 (n=48 exercises, n=36 home based flexibility)	3 months	Physical performance test, strength range of motion, balance, gait, coordination, sensation	Significant improvement was made by the exercise group on our primary indicator of frailty, a physical performance test (PPT) (29 +/- 4 vs 31 +/- 4 out of a possible 36 points), as well as many of the risk factors previously identified as contributors to frailty; eg, reductions in flexibility, strength, gait speed, and poor balance

Cesari et al. A physical activity intervention to treat the frailty syndrome in older persons-results from the LIFE-P study. USA. 2015	Analysis of RCT	1) physical activity (40-60mins three times weekly, 50mins walking and 10mins strengthening eg ankle weights, intensity increased on Borg scale) Vs. 2) aging education group	424 (n=213 physical activity, n=211 education)	12 months	Frailty prevalence	Significant difference in frailty prevalence between groups (10.0% in PA vs 19.1% in education). OR was 2.12 (95% CI 1.17 to 3.84). Sedentary behaviour/ low physical activity was Fried criterion most affected. Change in frailty status RR: 0.51 (95% CI 0.31, 0.83) 21/213 vs 41/211
Chan et al. A pilot randomized controlled trial to improve geriatric frailty. Taiwan. 2012	RCT	All received an educational booklet on frailty, diet, exercise, self-coping. 1) Exercise and nutrition (EN) 1 hour session three times weekly for three months (15 min warm up, 10 min brisk walk, 20-30 min resistance training with bands and water bottles for major muscle groups UL and LL 15 repetitions, 10 mins postural and balance, 5 min warm down), 2) problem solving therapy (PST) 6 sessions over 3 months	117 (n=55 EN, n=57 PST, n=62 non-EN, n=60 non PST)	3 months. follow up 3, 6 12 months	Primary: improvement on CHS-PCF by one category (e.g., frail to pre-frail or robust, pre-frail to robust)	EN frailty improvement rate higher than non EN (45% vs 27%, P=0.008) at 3 months but not 6 or 12. Higher vit D (4.9 vs 1.2, p=0.006) and lower % osteopenia (74% vs 89%, p=0.042) at 12 months. PST better improvement (2.7 vs. 0.2, p=0.035, 6 month) and less deterioration (-3.5 vs. -7.1, p=0.036, 12 month) of dominant leg extension than non-PST. Change in frailty status RR: 0.87 (95% CI 0.66, 1.14) 33/55 vs 43/62
Chan et al. Acupressure for frail older people in community dwellings-a randomised controlled trial. China. 2017	RCT	15mins acupuncture 4 times a week for 12 weeks. Control group received same treatment after 12 weeks.	106 (n=54 treatment, n=52 control)	12 weeks	QOL (measured by WHOQOL-BREF); psycho-social wellbeing (15 item geriatric depression scale); Sleep quality (Pittsburg sleep quality index); pain (0-10)	Significant differences between treatment and control groups in WHOQOL-BREF P=0.001; Sleep quality P<0.001; pain intensity P=0.006; depression P=0.002
Chan et al. Integrated care for geriatric frailty and sarcopenia: a randomized control trial. Taiwan. 2017	RCT	Low level care (LLC) group received 2hour education course on frailty, sarcopaenia, coping, nutrition and exercise. High level care (HLC) group also received 6 psychotherapy sessions and 48 exercise sessions (15min warm-up, 10min walk, 20-30min resistance - water bottle and rubber band, 10min balance) in 6 months.	289 (n=143 HLC, n=146 LLC)	6 months	Fried's criteria	35% of entire group had improvement in frailty status at 3 months, 40% at 6m and 39% at 12m. Cohort improved walking speed (28-31%) with little diff between LLC and HLC; HLC greater improvement in grip strength (14% vs. 24%), energy of walking, walking speed, timed up and go, one leg stand time at 6 and 12 month assessments
Clegg et al. The Home-based Older People's Exercise (HOPE) trial: a pilot randomised controlled trial of a home-based exercise intervention for older people with frailty. UK. 2014	RCT	12 weeks x exercise repititions 3 times a day, 5 days a week (strengthening for basic mobility, e.g., getting out of bed, standing from a chair, walking a short distance), facilitated by a physio in 5 home visits (1:1) and 7 phone calls	84 (n=45 intervention, n=39 control)	12 weeks	Primary: mobility - timed up and go test. Secondary: ADLs, health related QOL, depression	Non-significant improvement in intervention for TUGT (28.6s, 95% CI -8.5, 65.9s). No differences in secondary outcomes

Daniel K. Wii-hab for pre-frail older adults. USA. 2012	RCT	15 weeks of: 1) wii-fit, 2) seated exercise, 3) control	23	15 weeks	Senior fitness test, body weight, balance efficiency scale, CHAMPS, late-life function, disability index, MOS SF-36.	Improvements in senior fitness test (incl chair stands, arm curls, step 2, six minute walk, sit and reach, timed up and go) for both wii-fit and seated exercise groups compared to control
De Vriendt et al. Improving Health Related Quality of Life and Independence in Community Dwelling Frail Older Adults through a Client-Centred and Activity-Oriented Program. A Pragmatic Randomized Controlled Trial. Belgium. 2016	RCT	CGA, therapy plan (function training - cognitive and sensi-motor; education of primary care giver; advice on assistive devices), delivered by OT, reported to GP, over 8-10 weeks	168 (n=86 intervention group, n=82 control group	10 weeks	Primary: b-ADL evaluated with WHO questionnaire; Secondary: QOL; physical function; physical role functioning; bodily pain; mental health; vitality	Improvement in b-ADL index (p=0.013), pain (p=0.049). Improvement in all other measures, except mental health
Ekdahl et al. Long-Term Evaluation of the Ambulatory Geriatric Assessment: A Frailty Intervention Trial (AGe-FIT): Clinical Outcomes and Total Costs After 36 Months. Sweden. 2016	RCT	CGA based care for 25 to 31 months with follow up home visits, patient attendance at geriatric ambulatory unit and telephone calls Vs. care as usual	382 (n=208 intervention group IG, n=174 care as usual group CG)	36 months	Mortality, transfer to NH, days in hospital, total costs after 36 months	IG group lived 69 days longer; 27.9% of IG and 38.5% of CG died; inpatient days in IG 15.1, CG 21; costs did not differ significantly ($71,905 IG vs. $65,626 CG)
Fairhall et al. Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: randomised controlled trial. Australia. 2012	RCT	Tailored intervention depending on frailty phenotype. Delivery by 2 physios/ dietician/ geriatrician/ rehab physician/ nurse primarily in patient's home but also outpatient clinic. Included 45-60 min physio sessions x 5 in first three months and x5 in next nine months.	241 (n=120 intervention, n=121 control)	12 months	Disability (using International Classification of Functioning, Disability and Health framework). Participation in life situations (using Life Space Assessment and Goal Attainment score). Activity in mobility tasks (using 4-metre walk and self reporting measures)	Intervention group scored higher on Goal Attainment (OR 2.1, 95% CI 1.3, 3.3, P-0.004) and Life space assessment (4.68 points, 95% CI 1.4, 9.9, P=0.005), and walked 0.05 m/s faster over 4 metres (95% CI 0.0004, 0.1, P=0.048)
Granbom et al. Effects on leisure activities and social participation of a case management intervention for frail older people living at home: a randomised controlled trial. Sweden 2017	RCT	Monthly hour-long home visits by nurses (case management, info giving, safety)	153 (n=80 intervention, n=73 control)	12 months	Social participation; leisure activities	No difference in social participation. Intervention group performed more leisure activities (incl physical) P=0.034

Gustafsson et al. Health-promoting interventions for persons aged 80 and older are successful in the short term--results from the randomized and three-armed Elderly Persons in the Risk Zone study. Sweden. 2012	RCT	3 arms: 1) preventive home visit (single 1.5-2 hour visit) by OT, physio, nurse or SW providing info on municipal support services, assessing falls risks), 2) Multiprofessional senior group meetings with one follow-up home visit (four weekly 2 hour session with OT, physio, nurse, SW led group discussions on aging, activity, food, medicines, coping, technology, other. Home visit 2-3 weeks after meetings). 3) control	459 (n=114 control, n=174 preventive visit, n=171 senior meetings). Not double counted with Behm	3 months	Change in frailty, self rated health, ADLs between baseline and 3 month follow up	Both interventions delayed deterioration of self rate health (OR = 1.99, 95% CI 1.12,3.54). Senior meetings most beneficial intervention for postponing dependence in ADLs (OR = 1.95, 95% CI 1.14,3.33). No effect on frailty demonstrated (although 71% control showed no progression to frailty, 70% preventive visit, 64% senior meetings group)
Hildreth et al. Effects of testosterone and progressive resistance exercise in healthy, highly functioning older men with low-normal testosterone levels. USA. 2013	RCT	Placebo or transdermal T gel (either low dose 400-550 ng/dL or high dose 600 - 1000 ng/dL) and either progressive resistance training (prt) or no exercise	167 (n=28 placebo+prt, n=56 Tgel+prt, n=28 placebo +no prt, n=55 Tgel+no prt)	12 months	Primary: functional performance. Secondary: strength, body composition	In PRT group, T made no difference in function or strength but body composition (fat mass, P=0.04 and fat free mass P=0.01) was improved compared with placebo. In non PRT group, T did not improve function but did improve body composition (fat mass P=0.005 and fat free mass P=0.03) and upper body strength P=0.03 (average upper body strength 12.4% vs 7.3%, grip strength 15.3% vs 7.8%) compared with placebo.
Jacobsen et al. Raloxifene and Tibolone in Elderly Women: A Randomized, Double-Blind, Double-Dummy, Placebo-Controlled Trial. Netherlands. 2012	RCT	1) 60mg Raloxifene (selective oestrogen receptor modulator, for treating osteoporosis), 2) Tibolone 1.25mg (synthetic steroid with oestrogenic, progestational and androgenic properties, for preventing osteoporosis)- stopped mid study due to risk of CVA. 3) control placebo	318 (n=97 placebo, n=101 raloxifene, n=92 tibolone)	3, 6, 12, 24 months	Primary: body mass and handgrip strength. Secondary: muscle power and strength, mobility, body composition, verbal memory, mental processing speed, anxiety, mood, QOL.	Raloxifene and tibolone improved body mass density but had no effect on handgrip strength. Bone mineral density significantly increased by ral and tib at 24 months. Raloxifene improved verbal memory and health status Euro Qol
Kim C, Lee K. Preventive effect of protein-energy supplementation on the functional decline of frail older adults with low socioeconomic status: a community-based randomized controlled study. S Korea. 2013	RCT	Intervention group: 2 x 200mL cans of commercial formula (additional 400kcal energy, 25g protein, 9.4g essential amino acids, 400mL water) per day for 12 weeks, Vs. Control: no supplement	87 (n=43 intervention, n=44 control)	12 weeks	Primary: Change in physical functioning and short performance battery (SPPB). Secondary: gait speed, timed up and go test, hand grip strength, one legged stance	Physical functioning increased by 5.9% in intervention group, no change in control group (p=0.52). SPPB stable in IG, decreased 12.5% in control (p=0.39). Gait speed decreased 1% IG vs. 11.3% control (p=0.039). TUG improved 7.2% IG, decreased 3.4% control (p=0.038). No difference in grip strength or one-legged stance

Kim et al. Effects of exercise and milk fat globule membrane (MFGM) supplementation on body composition, physical function, and hematological parameters in community-dwelling frail Japanese women: a randomized double blind, placebo-controlled, follow-up trial. Japan. 2015	RCT	1) exercise (60 min training twice weekly x three months: 5mins warm up, 30min strength with resistance bands, 20min gait and balance, 5min warm down) and MFGM (pills of milk derived protein and lipids) supplementation, 2) exercise and placebo, 3) MFGM, 4) placebo	131 (n=33 ex+MFGM, n=33 ex+placebo, n=32 MFGM, n=32 placebo)	3 months, followed for 4 months	Primary: Change in frailty status (Fried). Secondary: body composition, physical function, haematological parameters, lifestyle factors	Significant groupxtime interactions for walking speed (p=0.005), TUG (P<0.001). Weight loss, exhaustion, low physical activity, slow walking speed all reversed but low muscle strength did not change. Reversal rate ex+MFGM (57.6%), MFGM (28.1%), placebo (30.3%) at intervention end; ex+MFGM (45.5%), ex+placebo (39.4%) at 4 month follow up. Change in frailty status 1 RR: 0.71 (95% CI 0.52, 0.97) 20/33 vs 28/33. Change in frailty status 2 RR: 0.64 (95% CI 0.46, 0.91) 18/33 vs 28/33
Li et al. The effectiveness of a comprehensive geriatric assessment intervention program for frailty in community-dwelling older people: a randomized, controlled trial. Taiwan. 2010	RCT	CGA assessment followed by appropriate intervention, including meds adjustment (52.6%), exercise instruction (37.9%), exercise prescriptions (25.3%) nutrition support (23.6%), physical rehab (27.4%), sw consultation (5.3%), specialty referral (e.g., 12.6% to neurology).	310 (n=152 CGA intervention, n=158 control)	6 month follow up	Re-evaluation of frailty and barthel index 6 months later	No significant outcomes, but intervention group more likely to improve frailty status and Barthel (OR = 1.19 95% CI 0.48, -3.04, p=0.71 and OR = 3.29 95% CI 0.65, 16.64) and also less likely to deteriorate
Liu et al. An individualized exercise programme with and without behavioural change enhancement strategies for managing fatigue among frail older people: a quasi-experimental pilot study. China. 2017	Three armed, single blinded, quasi exper-imental study	16 weeks of 1) combined exercise training and behavioural enhancement programme, 2) exercise training and health talks, 3) health talks (control group)	79 (n=34 combined group, n=30 exercise and health talks, n=21 health talks control)	16 weeks	Feasibility, fatigue, physical endurance, self-efficacy, self-perceived compliance	No significant differences among all outcomes. Some improvement in physical endurance in the combined group
Looman et al. The effects of a pro-active integrated care intervention for frail community-dwelling older people: a quasi-experimental study with the GP-practice as single entry point. Netherlands. 2016	Quasi exper-imental control trial	Walcheren Integrated care model. Nurse visit and assessment of care needs using EASYcare model, agreed by GP, delivered by GP nurse practitioner	377 (n=184 integrated care, n=193 care as usual)	12 months	Health experience, mental health, social functioning (RAND-36 questionnaire). Functional ability (Katz-15 instrument for ADLs). QOL (RAND-36, EQ-5D, ICECAP)	Positive effect on love and friendship, moderately positive on qol. No significant differences found on health outcomes (experienced health, mental health, social functioning and functional abilities)

Luger et al. Effects of a Home-Based and Volunteer-Administered Physical Training, Nutritional, and Social Support Program on Malnutrition and Frailty in Older Persons: A Randomized Controlled Trial. Austria. 2016	Cluster RCT	Physical training at home (6 strengthening exercises and circuit training for 1 hour twice weekly for 12 weeks) and nutritional (discussion) intervention group (PTN) Vs. social support group (social contact and cognitive training) (SoSu)	80 (n=39 phys training and nutrit, n=41 soc support)	12 weeks	SHARE-FI, Mini nutritional assessment long form (MNA-LF)	Significant improvement in MNA-LF (1.54 points (95% CI 0.51-2.56, P=0.004)) and SHARE-FI score (-0.71 95% CI -1.07 to -.35, P<0.001) in PTN group. Prevalence of nutritional impairment decreased by 25% in PTN and 23% in SoSu groups. Prevalence of frailty decreased by 17% in PTN and 16% in SoSu groups.
Makizako et al. Effects of a community disability prevention program for frail older adults at 48-month follow up. Japan. 2017	Cohort study	90 min walking exercise ('usual' or 'robotic') bi-weekly for 12 weeks and then weekly for 24 weeks. Increasing intensity, to 60% of max heart rate at 5 weeks. Total of 9 months. 3 x 90 min health education classes over period.	514 (n=74 usual walking class, n=73 robotic walking, n=110 health education, n=257 non-participants	9 months (48 months follow up)	Disability (incidence of certification of need for care according to Japanese long term care insurance (LTCI)). Co-variates: cognitive function; grip strength, walking speed; serum albumin, brain derived neurotrophic factor	Disability incidence of participants (11.3%); non-participants (19.8%) P=0.007. No difference for grip strength or walking speed
Metzelthin et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: cluster randomised controlled trial. Netherlands. 2013	RCT	Intervention group: Prevention of Care approach: frailty screening -> assessment by practice nurse during home visit-> treatment plan agreed with GP and other mdt if needed -> toolbox for meaningful, social or physical activities -> evaluation. Vs. Control group: care as usual	346 (n=193 intervention, n=153 control)	Follow up 6,12,24 months	Primary: disabilty as per Groningen Activity Restriction Scale. Secondary: depressive symptoms, social support interactions, fear of falling, social participation	No significant differences between groups in primary or secondary outcomes
Migliarese et al. Fighting Frailty in Underserved Communities. USA. 2017	RCT	6-week mixed exercise programme vs. control group	62 (n=34 exercise, n=28 control)	6 weeks	Functional Assessment of Chronic Illness Therapy Fatigue Scale, grip strength, Short Physical Performance Battery	Significant increases in Functional Assessment of Chronic Illness Therapy Fatigue Scale (P = .042), grip strength (P < .001), and Short Physical Performance Battery (P < .001)
Monteserin et al. Effectiveness of a geriatric intervention in primary care: a randomized clinical trial. Spain. 2010	RCT	CGA followed by interventions for those with 'non-risk of frailty' (45 min info on healthy habits and adherence to treatment) and with 'risk of frailty' (30 min visit by geriatrician) Vs. Control group care as usual	620 (n=308 intervention, n=312 control)	18 month follow up	Risk of frailty, other variables/ endpoints such as death, admissions to an institution, need for home care	Risk of frailty (as per definition) HR 1.33 95% CI 0.71, 2.51; 33.8% of CG switched from not at risk of frailty to at risk, while 20.4% of IG did; 27.9% of IG and 13.5% of CG reversed their initial risk of frailty status, p=0.027

Muller et al. Effects of dehydroepiandrosterone and atamestane supplementation on frailty in elderly men. Netherlands. 2006	RCT	Four arms: 1) atamestane (100mg/d) and placebo, 2) DHEA (50mg/d) and placebo, 3) atamestane (100mg/d) and DHEA (50mg/d), 3) two placebo tablets	100 (random assignment to 4 arms)	36 weeks	Physical frailty	"The results do not support the hypothesis that hormone replacement with DHEA and/or atamestane might improve the course of frailty"
Ng et al. Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal Among Older Adults: A Randomized Controlled Trial. Singapore. 2015	RCT	1) Physical intervention: 90 mins exercise class (strength/ resistance and balance) twice a week for 12 weeks, followed by exercises for 12 weeks at home. 2) Nutritional intervention: 24 weeks of daily Fortisip multi fibre formula and iron, folate, vitamin B6, B12, D supplements. 3) Cognitive intervention: 12 weeks of weekly 2 hour session (short term memory, attention and info processing, reasoning, problem solving), followed by 12 weeks of fortnightly 2 hour booster sessions. 4) Combination intervention: all 3 of aforementioned. 5) Control group: care as usual and placebo supplement	246 (n=49 nutritional supplememtation, n=50 cognitive training, n= 48 physical training, n=49 combination treatment, n=50 usual care control)	24 weeks. Assess at 0,3,6,12 months	Primary: frailty score, BMI, knee extension strength, gait speed, energy/ vitality, physical activity levels. Secondary: ADLs, hospitalisation, falls	Frailty score over 12 months was reduced in all groups, including control (15%), but significantly higher in intervention groups (35.6% to 47.8%): nutritional (OR 2.98), cognition (OR 2.89), physical (OR 4.05), combination (OR 5.0). Improvement in physical frailty domains: knee strength (physical, cognitive, combination), physical activity (nutrition), gait speed (physical), energy (combination). No major differences in in secondary outcomes. Change in frailty status RR: 0.71 (95% CI 0.54, 0.93) 27/45 vs 29/46; Change in frailty status RR: 0.62 (95% CI 0.45, 0.83) 24/46 vs 39/46
Oh et al. Effects of an integrated health education and elastic band resistance training program on physical function and muscle strength in community-dwelling elderly women: Healthy Aging and Happy Aging II study. S Korea. 2017	RCT	Intervention group: health education, individualised counselling, twice weekly 60 min elastic band exercises for 18 weeks (8 supervised, 10 at home)	38 (n=19 intervention, n=19 control)	18 weeks	Body composition (skeletal muscle index, fat free mass, total lean mass and total fat mass), muscle strength and quality, physical functioning	No significant changes in skeletal muscle index, body composition for intervention and control. Interaction effect was significantly different in SPPB score ($P < 0.05$), isokinetic strength (60 deg/s, $P < 0.001$; 120 deg/s; $P < 0.05$) and muscle quality ($P < 0.05$) after 18 weeks of intervention relative to baselines of control and intervention groups. Supervised elastic band training for 8 weeks did not improve SPPB score and isokinetic strength, but significant increase of those outcomes (10.6% improvement, 9.8-23.5% improvement) after 10 weeks of self-directed exercise

Ozaki et al. Training with a balance exercise assist robot is more effective than conventional training for frail older adult. Japan. 2017	RCT	1) Robotic exercise moving centre of gravity by a balance exercise assist robot or 2) conventional balance training combining muscle strengthening exercise, postural training and applied motion exercises. 6 weeks, twice a week.	27 (random assignment)	6 weeks	Preferred and maximum gait speeds, tandem gait speeds, timed up and go test, functional reach test, functional base of support, centre of pressure and muscle strength of the lower extremities	Robotic exercise achieved significant improvements for tandem gait speed (P = 0.012), functional reach (P = 0.002), timed up-and-go (P = 0.023) and muscle strength of lower extremities (P = 0.001-0.030) compared with conventional exercise. In frail or prefrail older adults, robotic exercise was more effective for improving dynamic balance and lower extremity muscle strength than conventional exercise
Parry et al. Cognitive-behavioural therapy-based intervention to reduce fear of falling in older people: therapy development and RCT-Strategies for Increasing Independence, Confidence and Energy (STRIDE). UK. 2016	RCT	Cognitive behavioural therapy delivered by health care assistant for 8 weeks with a 6 month booster session vs. usual care	415 (n=210 CBT, n=205 usual care)	8 weeks, 6 month booster and 12 month follow up	Primary: fear of falling (FES-I) at 12 months; Secondary: falls, injuries, anxiety/ depression, qol, social participation, loneliness, physical function.	Significant reduction in FES-I score by 4.02 (95% CI 2.1 to 5.95); depression score (HADS) fell by -1 (95% CI -1.6 to -0.3); no differences in other secondary outcome measures
Salem et al. Impact of a Community-Based Frailty Intervention Among Middle-Aged and Older Prefrail and Frail Homeless Women: A Pilot Randomized Controlled Trial. USA. 2017	Pilot RCT	Frailty Intervention (FI) vs. Health promotion (HP): FI consisted of 6 x 60min health education classes focussing on physical, psychological and social frailty topics and 20min nurse case management. HP consisted of 6x60min group education sessions led by a community health worker, focussing on community resources, safety, htn, DM, arthritis, cholesterol.	32 (n=15 FI, n=17 HP)	3 months	15 items from Tilburg frailty index	No significant difference between FI and HP groups. HP has 'medium to large effect sizes'
Seino et al. Effects of a multifactorial intervention comprising resistance exercise, nutritional and psychosocial programs on frailty and functional health in community-dwelling older adults: A randomized, controlled, cross-over trial. Japan. 2017	RC cross over trial with Hatoyama cohort study	100min twice weekly resistance exercise (60min, increasing intensity), rest (10min), nutritional (dietary variety and protein) or psychosocial teaching (30min biweekly)	77 (n=38 immediate intervention, n=39 delayed intervention)	3 months	Check list-15 and Fried's criteria; physical, psychosocial and nutritional intake	Significant reduction in check list-15 score (-0.36 points, 95% CI -0.74 to -0.03), frailty prevalence (-23.5% , 95% CI -40.4 to -6.7), timed get up and go (-0.25s), ger dep score (-0.92 points), dietary variety (0.65), protein intake (1.9%). Change in frailty status RR: 0.47 (95% CI 0.18, 0.22) 5/38 vs 11/39

Serra-Prat et al. Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial. Spain. 2017	RCT	Nutritional assessment; physical activity programme (aerobic: 30-45 mins outdoor walking x4/week, mixed strengthening, balance and coordination: 20-25 min exercises x4/week)	172 (n=80 intervention, n=92 control)	12 months	Fried's criteria; secondary: functional capacity (Barthel index and timed up and go), falls, nutritional status (short form mini nutritional assessment), self reported QOL	4.9% of intervention group (IG) and 15.3% of control had evolved to frailty, OR 0.29, adjusted OR 0.19; IG higher outdoors walking per day (0.97 vs. 0.73 P = 0.019) but no difference in muscle strength, gait speed or other functional indicators. Change in frailty status RR: 0.32 (95% CI 0.09, 1.10) 3/61 vs 11/72
Shinkai. Public health approach to preventing frailty in the community and its effect on healthy aging in Japan. Japan. 2016	Cohort study	1) Community forum; 2) promotion of physical activity, nutrition and social participation; 3) annual health check up with CGA if secondary prevention; 4) long term care prevention programmes (physical, nutritional, social) for those identified as frail	686	10 years	Mobility, instrumental ADLs, intellectual activity, social role, healthy life expectancy, nutritional markers (serum albumin and Hb), walking speed, grip strength, GDS, MMSE	Functional health increased for men and women (e.g., walking speed, grip strength, one leg stance, GDS, MMSE all improved with significance in women P<0.001, walking speed, one-leg stance, grip strength improved sig in men, GDS, MMSE not sig. Life space mobility increased 80.8% to 86.9% in men and 63.7% to 74.3% in women), healthy life expectancy increase 0.5 years for men and 1.2 years for women
Takano et al. Differences in the effect of exercise interventions between prefrail older adults and older adults without frailty: A pilot study. Japan. 2016	Cohort	90 min education classes with physical therapist, OT, 2 nurses and a doctor twice a month x 4months (on 'training methods, falls, healthcare'). Exercises were daily 'locomotion' including one leg stands, squats, calf raises, front lunges x 4months	41 (n=17 pre-frail, n=24 robust)	4 months	Timed get up and go; grip strength; one leg balance; knee extension strength, fall risk index	Significant differences (P<0.01) for timed get up and go; one leg balance; knee extension strength. 4 pre-frail patients returned to robust after intervention
Tarzona-Santabalbina et al. A Multicomponent Exercise Intervention that Reverses Frailty and Improves Cognition, Emotion, and Social Networking in the Community-Dwelling Frail Elderly: A Randomized Clinical Trial. Spain. 2017	RCT	Trained group: proprioception (10-15min), aerobic (40->65% max HR), strength (elastic bands), stretching exercises for 65 mins, 5 days per week, 24 weeks (4 physios and 4 nurses) Vs. Control group. Protein-calorie and vit D supplementation in both groups.	100 (n=51 intervention, n=49 control)	24 weeks	Frailty (Fried), Barthel, Lawton and Brody, Tinetti, SPPB, physical perf test, MMSE, GDS, QOL, Duke soc support, visits to primary care	Frailty (Fried) number needed to treat to recover robustness is 3.2, OR 4.4, 31.4% retruned to robustness. Barthel (trained group 91.6 vs. 82 control), Lawton and Brody (6.9 vs. 5.7), Tinetti (24.5 vs. 21.7), SPPB (9.5 vs. 7.1), physical perf test (23.5 vs. 16.5), MMSE (28.9 vs. 25.9), GDS (2.3 vs. 3.2), EuroQOL (8.2 vs. 7.6), Duke soc support (48.5 vs. 41.2), visits to primary care (1.3 vs. 2.4). Change in frailty status RR: 0.69 (95% CI 0.57, 0.83) 35/51 vs 49/49

Theou et al. Can an Intervention with Testosterone and Nutritional Supplement Improve the Frailty Level of Under-Nourished Older People? Australia. 2016	RCT	Oral testosterone undecanoate and high calorie supplement (2108-2416 kJ/day) in intervention group vs. placebo and low calorie supplement (142-191 kJ/day) in non-intervention group	53 (random assignment)	6 and 12 month follow ups	Frailty as per: FI-lab, FI-self-report, FI-combined	No significant differences in changes in frailty scores at either 6 or 12 months between two treatment groups. However, intervention group 4.8 times more likely to improve FI-combined score and 6 and 12 months
Tikkanen et al. Effects of comprehensive geriatric assessment-based individually targeted interventions on mobility of pre-frail and frail community-dwelling older people. Finland. 2015	Sub group analysis of a compar-ative study	CGA with 2 nurses and 2 doctors, followed by nutritional support, oral hygiene, physical activity counselling from physio.	605 (n-314 intervention, n=291 control)	Over a two year period	Mobility: ability to walk 400m	Intervention prevented loss of ability to walk 400m (OR 0.74, 95% CI 0.59, 0.93, P=0.01)
Wilhelmson K, Eklund K. Positive Effects on Life Satisfaction Following Health-Promoting Interventions for Frail Older Adults: A Randomized Controlled Study. Sweden. 2013	RCT	1) four, weekly, multi professional senior group meetings (discussing aging and consequences, encouraging an active lifestyle) and a follow up home visit (by nurse, physio, OT or SW describing available municipal supports and assessing falls risks), 2) one preventive home visit, 3) control	459 (n=171 meetings, n=174 home visit, n=114 control). Not double counted with Behm	4+ weeks. Follow up at 3,12, 24 months	Life satisfaction as per LiSat-11 (8 questions)	Life satisfaction decreased in all groups but at a lesser rate in the intervention groups. Odds of still being satisfied doubled in the intervention groups vs control at 1 and 2 years follow up. No significant difference between intervention groups.
Wolf et al. Reducing frailty and falls in older persons: an investigation of Tai Chi and computerized balance training. Atlanta FICSIT Group. Frailty and Injuries: Cooperative Studies of Intervention Techniques. USA. 1996	RCT	1) Tai-chi (TC, 15 mins twice a day of 108 forms condensed into 10 forms for body and trunk rotation, reciprocal arm movements, progression in gradual reduction of base of standing support to single limb stance), 2) computerised balance training (BT, moveable standing base), 3) education (ED, instructed not to change their exercise regime. Weekly discussions on meds, sleep, cognitive deficits, coping)	200 (n=72 TC, n=64 BT, n=64 ED)	15 weeks, 4 month follow up	Primary: biomedical (strength, flexibility, CV endurance (HR and BP before and after 12 min walk), body composition), functional and psychological (depression) indicators of frailty. Secondary: occurrences of falls	Lowered blood pressure before and after 12 minute walk following TC participation. Grip strength declined in all groups but least in TC group. Lower extremity range of motion limited but stat significant changes. Fear of falling and intrusiveness responses reduced after TC compared with ED (FoF actually increased in BT group). TC reduced the risk of multiple falls by 47.5%. No other stat sig findings on other measures
Yamada et al. Community-based exercise program is cost-effective by preventing care and disability in Japanese frail older adults. Japan. 2012	Prospect-ive study using propens-ity score matching	Once weekly, 90 mins x 16 weeks physical exercise (20 mins aerobic, 30 mins progressive strength, 20 mins flexibility and balance, 20 mins cool-down) supervised by physiotherapist Vs. Control	610 (n=305 exercise, n=305 control)	16 weeks	Primary: Long term care insurance requirement 1 year post intervention. Secondary: change in frailty checklist, care and medical cost.	25 subjects (8.1%) in IG were newly certified for long-term care insurance after 1 year Vs. 55 (18%) in control group (RR=2.16, 95% CI 1.46, 3.20). IG frailty checklist score over 1 year: 7.41 to 7.11 vs. Control: 7.34 to 8.02

Yamada et al. Nutritional Supplementation during Resistance Training Improved Skeletal Muscle Mass in Community-Dwelling Frail Older Adults. Japan. 2012	RCT	3-month mixed physical exercise with multinutrient supplement (S/ex) vs exercise alone (ex)	77 (n=38 S/ex, n=39 ex)	3 months	Skeletal muscle mass index (SMI) and several physical performance tests	Participants in S/Ex group had significant improvements for the outcome measures, including SMI and maximum walking time (P<0.05), compared to those in Ex group. The prevalence of sarcopenia decreased from 65.7% to 42.9% in S/Ex group, while that in Ex group remained unchanged (68.6% to 68.6%) (relative risk = 1.60, 95% CI: 1.03-2.49).
Yamada M, Arai H. Self-Management Group Exercise Extends Healthy Life Expectancy in Frail Community-Dwelling Older Adults. Japan. 2017	Analysis of cohort data from a prospect-ive study	60 min group exercise sessions once or twice every two weeks from Dec 2012 to Dec 2016. Standard format: 10min light aerobic, 20mild strength, 20min flexibility and balance, 10min cool down	3,240 (n=1620 intervention, n=1620 control)	4 years	Disability (incidence of certification of need for care according to Japanese long term care insurance (LTCI))	No difference at 2 years (9.6% of both participant and control groups were newly certified for LTCI, HR 1.01 95% CI = 0.81-1.26). At 4 years difference was 15.2% vs. 20.6%, HR 0.73 (95% CI = 0.62-0.86)
Yuri et al. The effects of a life goal-setting technique in a preventive care program for frail community-dwelling older people: a cluster nonrandomized controlled trial. Japan. 2016	Cluster non-RCT	All received 120 min preventive care exercise classes each week for 3 months as well as oral care and nutrition education. Intervention group received OT and PHN life goal setting support	143 (n=80 intervention, n=63 control group)	3 months with follow up at 3, 6 and 9 months	Primary: Kihon checklist for frailty, QOL. Secondary: physical function and assessment of life goals.	Significant difference in Kihon checklist between groups at 3 months (P=0.043) and 6 months (p=0.015) but not at 9 months (p=0.098). QOL improved at 3 months for intervention group and at no time for control group