

## Delaying and reversing frailty:

### a systematic review of primary care interventions

#### Abstract

##### Background

Recommendations for routine frailty screening in general practice are increasing as frailty prevalence grows. In England, frailty identification became a contractual requirement in 2017. However, there is little guidance on 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

A systematic review of frailty interventions in primary care.

##### 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 or frailty indicators and ease of implementation in terms of human resources, marginal costs, and time requirements.

##### Results

A total of 925 studies satisfied search criteria and 46 were included. There were 15 690 participants (median study size was 160 participants). Studies reflected a broad heterogeneity. There were 17 different frailty screening methods. Of the frailty interventions, 23 involved physical activity and other interventions involved health education, nutrition supplementation, home visits, hormone supplementation, and counselling. A significant improvement of frailty status was demonstrated in 71% ( $n = 10$ ) of studies and of frailty indicators in 69% ( $n = 22$ ) of studies where measured. Interventions with both muscle strength training and protein supplementation were 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. A map of interventions was created that can be used to inform choices for managing frailty.

##### Keywords

feasibility; frailty; primary care; systematic review.

#### INTRODUCTION

Frailty has long been in the lexicon of everyday language. 'How easily the wind overturns a frail tree', Buddha reflected some 2500 years ago.<sup>1</sup> 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.<sup>2,3</sup> It increases the risks of illness, falls, dependency, disability, and death.<sup>2,3</sup>

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  $\geq 65$  years and increases to some 50% in those  $> 80$  years of age.<sup>4</sup> The United Nations estimates that the world population of individuals aged  $> 60$  years will more than double from 962 million in 2017 to 2.1 billion in 2050, whereas the population of individuals aged  $> 80$  years will triple from 137 million to 425 million in the same period.<sup>5</sup> In the UK, the number of individuals aged  $> 65$  years is estimated to grow from 10.4 million to 12.4 million by 2025 and life expectancy at 65 years is set to increase by 1.7 years.<sup>6</sup>

Frailty has been described as the most problematic expression of population ageing in the context of this considerable growth.<sup>3</sup> 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  $\geq 65$  years 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.<sup>7</sup>

A variety of tools has been proposed for frailty screening in primary care.<sup>8,9</sup> A commonly used method is Fried's frailty phenotype<sup>10</sup> (three or more criteria from: exhaustion, unexplained weight loss, slowness, weakness, and low physical activity, with one or two criteria present defining pre-frailty). The cumulative deficit model proposed by Rockwood and Mitnitski<sup>11</sup> provides a frailty index based on the presence of deficits as a proportion of total measured. There are several other indices, checklists, and indicators.<sup>12-14</sup> A general model of frailty that captures commonly involved domains is shown in Figure 1.

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### 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, and these findings may help the choice of appropriate primary care interventions.

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.<sup>9</sup> The ability of the frailty model to capture risk and biological age in this way has pushed the boundaries of care for a population's most vulnerable patients. This advance and the increase in prevalence have driven international consensus guidance to recommend identification of frailty in routine clinical encounters.<sup>15,16</sup>

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 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. The aim of the present study was to map their comparative effectiveness and ease of implementation, and help inform practitioners and patients on the most appropriate choices.

### METHOD

A search of PubMed, CINAHL, the Cochrane Library Register of Controlled Trials, and PEDro for English language articles using the terms 'primary care' or 'community'; 'screening' or 'intervention' or 'integrated-care'; and 'frailty' or 'pre-frail' was conducted. The search was conducted from inception to May 2017 by one researcher. A second researcher repeated the search in May 2018 to confirm the results and add any further findings. Any clarifications were resolved by two other researchers.

Studies were selected following an assessment of titles and abstracts. Studies chosen for inclusion were randomised controlled trials (RCTs) or cohort studies with control groups, which assessed interventions aimed at preventing or treating frailty in a primary care setting, and that 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 also excluded.

The researchers recorded the type of study (for example, RCT or cohort), frailty screening method (for example, Fried), study size, length of study, intervention, outcome measure, and outcome for each study included.

An analytical tool for comparing a set of heterogeneous interventions that was too diverse for meta-analysis was devised by the authors and a scoring system to map relative effectiveness and relative ease of implementation (summarised in Figure 2) was applied. 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.

When analysing relative effectiveness, an outcome that demonstrated significant improvement of frailty status or prevalence was given 3 points. An outcome that improved frailty criteria but did not amount to a change in status or prevalence was given 2 points (improvement in Fried's phenotype [for example, 2 to 1, both pre-frail] or improvement

Figure 1. Domains commonly included in frailty definitions.

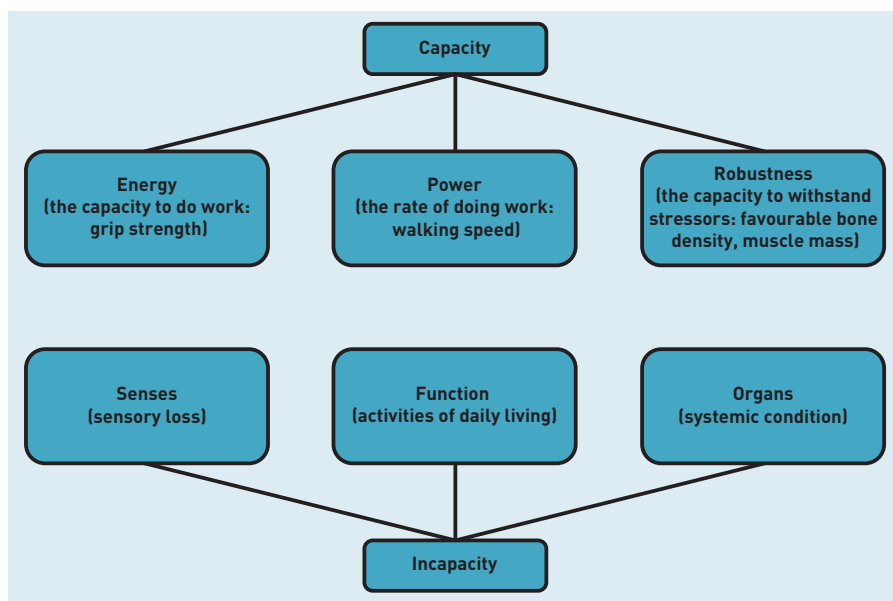
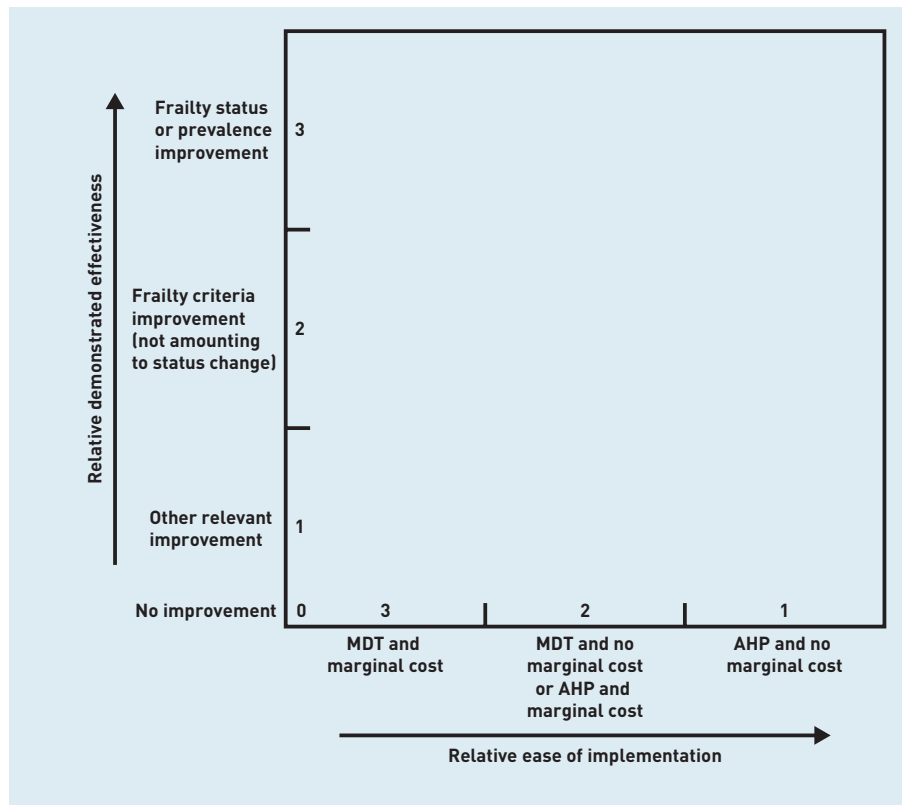


Figure 2. Comparison of interventions scoring system. AHP = allied health professionals. MDT = multidisciplinary team.



in frailty index items not amounting to a significant change in status). An outcome that demonstrated neither of these but improved relevant dimensions other than frailty, for example, perceived quality of service or increased endurance, was given 1 point. An outcome showing no improvement scored 0. 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 was differentiated in this way.

Relative ease of implementation was analysed by examining three key requirements: healthcare professionals, money, and time. An intervention that required multidisciplinary team (MDT) involvement, for example, physician, nurse, and/or allied health professionals (AHPs) such as a physiotherapist, occupational therapist, or dietician, was given 2 points. An intervention that did not need an MDT but did require an AHP was given 1 point. An intervention that incurred additional marginal cost, such as new personal equipment or consumable, was given 1 further point. The amount of time in minutes per week invested by the patient and the intensity of AHP involvement (for example, 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

From the database search, 925 studies were identified using the search criteria. Out of these, 47 full-text articles were selected for eligibility assessment following review of titles and abstracts. Of these, 46 studies were included in the systematic review analysis, with one study excluded as its results were included in a subsequent updated study.<sup>17-62</sup> The total number of participants in included studies was 15 690 and median study size was 160 participants.

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

The Fried criteria, as a method for frailty screening, was used by 13 (28%) of the 46 studies, more than any other method, and six used modified Fried criteria. Four used the Kihon checklist, two used a

version of the Kaigo-Yobo checklist, two used the Tilburg frailty indicator, two used the Groningen frailty indicator, one used the cumulative deficit model, and 11 used other approaches to screening frailty that were unique to their study giving a total of 17 different screening methods. Five 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. A summary is shown in Figure 3. Of the 46 studies, 65% ( $n=30$ ) applied more than one intervention. Of the interventions in the studies, 23 studies involved physical exercises: 10 involved mixed exercises, for example, a combination of aerobic, strength, balance, and coordination; six featured strength exercises as the central component; two featured walking as the central component; two focused on basic mobilising exercises; one involved tai-chi; one involved robotic balance; and one involved use of a Wii. Ten studies involved health education such as classes on nutrition, medications, falls prevention, and social supports. Eight studies involved intervention with nutritional supplements, of which five used both protein and calories with strength or mixed exercises, one used protein with strength exercises, one used protein and calorie supplementation alone, and one used calories with testosterone. Eight studies involved medication management, six of these as part of a comprehensive geriatric assessment (CGA) and two as part of group education sessions. Seven

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. Four studies focused on hormone supplementation, of which two involved testosterone, one involved dehydroepiandrosterone (DHEA) and atamestane, and one involved raloxifene and tibolone (discontinued). Four studies involved counselling, of which one involved cognitive behavioural therapy alone, one involved psychotherapy along with mixed exercises, one involved behavioural change, and one involved life-goal setting. One study focused on acupuncture.

### 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 4. 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. Educational or health promotion activities typically placed in the mid-zone for both relative effectiveness and ease of implementation. Interventions targeting behavioural change placed low in relative effectiveness and the mid-zone for ease of implementation. Comprehensive geriatric assessments and home visits tended to place mid-low for both relative effectiveness and ease of implementation. Administration and management of

**Figure 3. Overview of types of interventions for frailty.**  
<sup>a</sup>30/46 studies (65%) had more than one intervention. CBT = cognitive behavioural therapy. DHEA = dehydroepiandrosterone.

Key interventions	Physical exercise	Health education	Nutritional supplements	Home visits	Hormone supplements	Counselling
Number of studies <sup>a</sup>	23	10	8	7	4	4
Types of activities	<ul style="list-style-type: none"> <li>Mixed exercises</li> <li>Strength</li> <li>Aerobic</li> <li>Balance</li> <li>Coordination</li> <li>Walking</li> <li>Tai-chi</li> <li>Mobility</li> </ul>	<ul style="list-style-type: none"> <li>Nutrition</li> <li>Medication</li> <li>Falls prevention</li> <li>Physical exercise</li> <li>Social and community supports</li> </ul>	<ul style="list-style-type: none"> <li>Protein</li> <li>Calories</li> <li>Milk fat globule membrane</li> </ul>	<ul style="list-style-type: none"> <li>Falls and safety assessment</li> <li>Information giving on municipal supports</li> <li>Basic mobility exercises</li> <li>Nurse-led, physio-led, or GP-led</li> </ul>	<ul style="list-style-type: none"> <li>Testosterone</li> <li>DHEA</li> <li>Atamestane</li> <li>Raloxifene</li> <li>Tibolone (discontinued)</li> </ul>	<ul style="list-style-type: none"> <li>CBT</li> <li>Psychotherapy</li> <li>Life-goal setting</li> <li>Behavioural change</li> </ul>

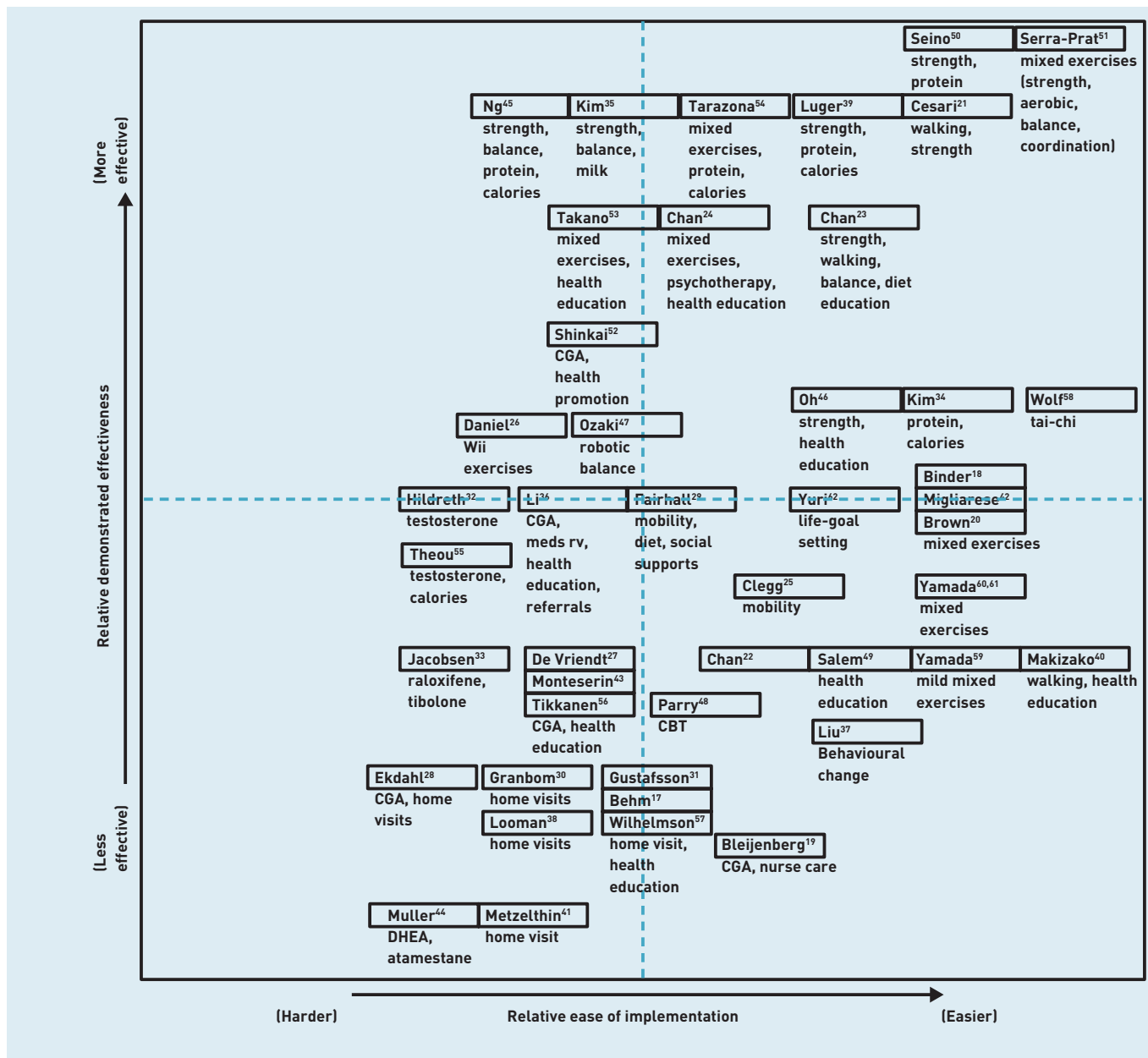


Figure 4. Comparison of interventions for frailty. CBT = cognitive behavioural therapy. CGA = comprehensive geriatric assessment. DHEA = dehydroepiandrosterone. meds rv = medication review.

hormone therapy placed mid-low for both relative effectiveness and ease of implementation.

An overview of how clusters of key interventions compare is shown in Figure 5. 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, whereas mixed exercises and health education also feature.

Of the 46 studies, 30% ( $n = 14$ ) reported the outcome of an intervention on frailty status, 71% ( $n = 10$ ) of which demonstrated significant improvement. Of the 46 studies,

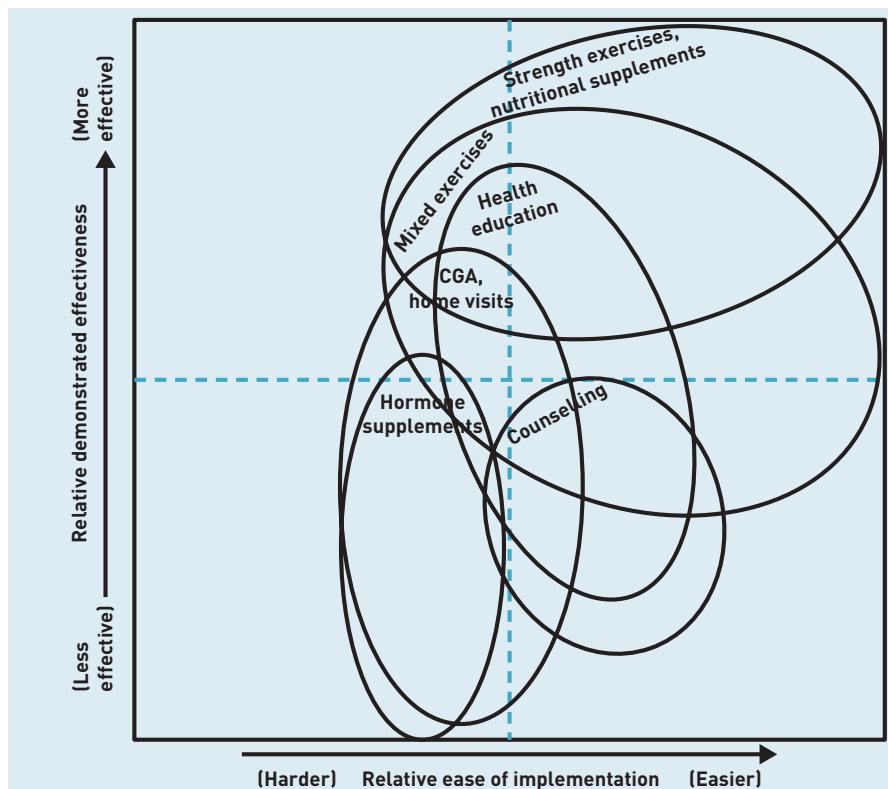
(70% [ $n = 32$ ]) reported the outcome of an intervention on singular frailty indicators or other criteria, 22 (69%) of which demonstrated significant improvement. Summaries of all the studies analysed are available from the authors.

## DISCUSSION

### Summary

This analysis of the evidence available on primary care intervention for frailty 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 subsequently

Figure 5. Overview of key intervention clusters. CGA = comprehensive geriatric assessments.



produced can be helpful to inform choices for managing frailty in ageing societies.

### Strengths and limitations

A key strength of this study is that it has provided an evidence-based map of interventions to delay and reverse frailty in primary care. The resultant model may be helpful to practitioners and patients in discussing and agreeing interventions to fit their specific circumstances. The researchers' analysis seems a timely contribution as frailty screening becomes mandatory in the UK and more prevalent internationally.

There are several limitations to this study: studies analysed were too heterogeneous to allow for a meta-analysis, although meta-analyses of subsections, for example, physical exercise, could be performed. Some interventions outlined changes to individual frailty criteria but did not calculate or demonstrably show an 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. Although the map is helpful in clearly

differentiating relative effectiveness and ease of implementation, it does not provide absolute values.

### Comparison with existing literature

Findings from the present study on strength exercises and protein supplements are consistent with knowledge that interventions to improve frailty include exercise, nutrition, and multicomponent interventions.<sup>63,64</sup> 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.<sup>64</sup>

The current analysis included a wide variety of 46 intervention studies and, having mapped both effectiveness and feasibility, specifically in the primary care setting, enabled a choice of complementary interventions. The importance of using an integrated and holistic approach is described in the British Geriatrics Society and the Royal College of General Practitioners *Fit for Frailty* guidance for GPs.<sup>65</sup>

### Implications for research and practice

A typical exercise regime that may be proposed in general practice is: 20–25 minutes of activity, 4 days per week at home, comprising 15 exercises: three for strengthening arms, seven for strengthening legs, and five for balance

and coordination. Each exercise is repeated 10 times per minute, progressively reaching 15 times after 2–3 months, with a rest of half a minute between each set.<sup>2</sup>

Nutrition or protein supplementation regimes described in studies included appropriate dietary emphasis on daily milk, eggs, tuna, chicken, plant-based protein, or, where preferred, 2 × 200 mL of formula per day (containing 25 g protein, 400 kcal energy, 9.4 g essential amino acids, and 400 mL water).<sup>34</sup>

Several studies found that participation rates in physical exercise activities remained as high as 90%,<sup>66–68</sup> though some dipped to 50%.<sup>54</sup> 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.<sup>69,70</sup> This underlines the need for patients to continue to participate and medical professionals to continue to encourage appropriate interventions. The authors 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.<sup>71</sup> Although 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 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 regimen.

The new NHS England GMS contractual practice interventions do not primarily include physical therapy and nutrition.<sup>7</sup> 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.

### Provenance

Freely submitted; externally peer reviewed.

### Competing interests

The authors have declared no competing interests.

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