Update of the Spanish Fisterra guideline "Frail elderly people: detection and management in Primary Health Care". What contributes and highlight

Iñaki Martín Lesende[1-3*], Ana Gorroñogoitia Iturbe[3,4], Pedro Abizanda Soler[5,6] and Soledad Justo Gil[7]

[1]Department of Medicine of the Basque Country University (UPV/EHU), Leioa, Bizkaia, Spain

[2]Indautxu Primary Health Centre, Bilbao-Basurto Integrated Health Organisation, Basque Health Service (Osakidetza), Spain

[3]Member of the Working Groups for the Care for Elderly People and Programme of Preventive Activities and Health Promotion (PAPPS) of the Spanish Society of Family and Community Medicine (semFYC)

[4]Bizkaia Unit for Multi-professional Training in Family and Community Care, Spain.

[5]Geriatrics Department, Albacete University Hospital, Spain

[6]Faculty of Medicine of the University of Castilla-La Mancha, Spain

[7]Subdirectorate General of Health Promotion, Prevention and Quality. Directorate General of Public Health. Spanish Ministry of Health.

Abstract

Objective: To highlight the additions and changes of the Fisterra guideline updated in 2020 "Frail elderly people: detection and management in primary care" (PC), as well as the points/ consolidated.

Content: The guideline answers main questions about concept, diagnosis and frailty treatment/management in PC, based on the evidence; bibliographic review, years 2013 to 2019, in Cochrane Library, MEDLINE-Pubmed, CINAH, EMBASE, IME data sources, and the information sources UpToDaTe and Dynamed and grey literature.

Conclusions: Frailty is a stage prior to disability, in which elderly people are more vulnerable to adverse health-related events, physical and functional decline, and death, because of decreased physiological reserves; with a prevalence in Europe which range from 4 to 27%, depending on the healthcare setting, sex, education or income level. Two important tables from the first guideline have been updated and must be highlighted: "Features of the main tools used to diagnose/detect frailty", and "Diagnostic validity of different tools used to detect frailty". Active systematic frailty diagnosis is recommended by means of a two-stage screening strategy, beginning with a screening process followed by a second stage involving more in-depth assessment (comprehensive geriatric assessment type) which determines the various interventions to be taken. The most effective interventions in frailty are physical exercise (multi-component exercise), nutrition (advice, weight maintenance, protein intake, and Mediterranean diet), and medication (review/adequacy). Integrated healthcare systems can benefit from a well-coordinated treatment approach from all the professionals involved, named the health system, the social services, and the community.

The **Spanish Fisterra guideline "Frail elderly people: detection and management in primary care"** was published in the European Geriatric Medicine journal as a form of diffusion in Europe in 2015 [1], followed by an update in 2020 [2]. It addresses some of the main questions about the diagnoses, management and treatment of this current and important geriatric condition in Primary Care (PC). For the update, starting from the first guideline and its bibliographic review, a new search was carried out, focusing on articles published during the years 2013 to 2019, for which the Cochrane Library, MEDLINE-Pubmed, CINAH, EMBASE, IME data sources, as well as the information sources UpToDaTe and Dynamed were used. The search was narrowed down by the following descriptors: frail, frailty, vulnerable, vulnerability, community-dwelling, functional decline, disability, primary care. In this article we highlight the additions and changes compared to the initial guide, as well as the points and aspects that have been consolidated. In line with the consensus document on detection and management of frailty of the Spanish National Health Service (NHS) [3]

https://www.mscbs.gob.es/profesionales/saludPublica/prevPromocion/Estrategia/docs/Fragilidad/Frailtyandfalls_Elderly.pdf, the

European ADVANTAGE Joint Action in frailty https://www.advantageja.eu/index.php/ [4], the recommendations of the Programme of Preventive Activities and Health Promotion of the Spanish Society of Family and Community Medicine (PAPPS-semFYC) [5]; it also considers some institutional global strategies such as that of the British [6] or Canadian [7] NHS ones. The ultimate goal of managing frailty is furthermore aligned with the World Health Organization (WHO) Guidelines on Integrated Care for Older People (ICOPE): improve musculoskeletal function, mobility and vitality, promote psychological well-being, prevent falls, maintain sensory capacity, support caregivers [8].

Frailty is considered a condition that precedes disability or, for some experts, can identify it in its early stages [9]. Therefore, it is not comparable to disability, and this must be taken into consideration when developing strategies to face it, specially in situations such as the current COVID-19 pandemic [10]. It is defined, according to the WHO, as a clinically recognizable state that can be considered as a progressive age-related decline in physiological systems that results in decreased intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes [9,11] and the progression to disability [12], being a better predictor than multimorbidity for all of them [13]. In European communities, the prevalence values range from 4 to 27%, depending on the studies and criteria used. Figures of 12% have been described in PC, and up to 45% in nursing homes, with higher prevalence at an older age, in women, in lower educational levels, or in lower income groups [14].

PC is still considered the best healthcare setting to detect and manage frailty, including both prevention and treatment [3,4].

Table 1 shown in the Fisterra guideline [2], originally taken from the recommendations made in the PAPPS-semFYC [5] and completed with the content of subsequent publications [15-18] outlines the main and most common **tests and scales used to detect frailty**. Many of these are used in a first screening stage prior to a second, more extensive diagnosis stage which involves more thorough assessment. The most commonly used and recommended frailty detection tools in Primary Care nowadays are the Gait Speed test and Timed Up & Go tests, the Short Physical Performance Battery (SPPB) - being this the priority method in the Spanish NHS consensus document, [3,5,16] the Fried phenotype, and the Frailty Index (FI) [15]. The use of Information and Communication Technologies (ICT) facilitates the realization of these tools in clinical practice and the interaction-integration with electronic medical record, especially useful for the FI.

As there is no consensus in terms of which instrument is considered to be the "gold standard" when it comes to screening and diagnosis, it should be chosen based on the characteristics of the population being studied, the purpose of the assessment, and the context, Table 1 [16].

The **CGA** is probably the best method to confirm frailty and to assess the more appropriate interventions in a more individualized way; being the intervention the final objective to achieve maintenance or improvement in health. In consonance, a multidimensional clinical assessment type CGA is included in most of the frailty detection and management programmes and guidelines [5]. Nevertheless, there continues to be a dissociation between the recommendation and the current use in PC clinical practice, due to several reasons: completion time (generally more than 40 minutes), need for professional training, and poor evidence of effectiveness. Hence, the CGA application models and their effectiveness with frail older adults in PC should be a matter of future research [19,20].

Although it does not have a high support of evidence in the literature, routine monitoring of IADL may help in detecting newer or unreported functional decline, and frailty, using scales such as the VIDA questionnaire ***https://iakimar.wixsite.com/website*** [21] or the Lawton-Brody index.

Table 2, taken from the PAPPS-semFYC recommendations and used in the Fisterra guideline, provides the **diagnostic validity indices of the main tools** used in our healthcare setting [5]. This table is significant because it reflects the need to consider the diagnostic capacity of a certain tool and the magnitude and impact that the diagnostic error may have.

Active systematic frailty diagnosis is highly recommended in the literature by means of a **two-stage screening strategy**. It begins with the inclusion of candidates in the program for a screening test, followed by a second stage involving more in-depth corroboration and assessment (CGA type), which determines the **interventions and actions** to be implemented, as indicated in the Fisterra guideline [2,16,18]. Other guidelines and Health Services, such as the British and the Canadian NHS also establish this recommendation [6,7,22].

The British NHS included in the contract with general practitioners (2017-2019) the routine identification of potentially frail people over 65, using an electronic frailty index (eFI) or, if this should not be available, the PRISMA-7 questionnaire or gait speed test, as a first option, followed by the Clinical Frailty Scale (CFS) to confirm diagnoses and stratify risk. In addition, a CGA is recommended for moderate or severe cases of frailty [6].

The British Columbia recommends identifying possible medical, psychological, functional, medication or social frailty symptoms and, in the case that frailty is suspected, conducting a formal assessment to confirm it using appropriate PC tools (PRISMA-7 questionnaire, Gait Speed test or Timed Up & Go test and cognitive assessment tests, followed by more-in-depth assessment using CGA in the frail ones [22]. The Canadian C5-75 programme (Case-finding for Complex Chronic conditions in Seniors 75+) includes frailty screening by means of gait speed + grip strength test on an annual basis, as well as screening for other undiagnosed chronic comorbidities in people aged 75 and older, in a two-tiered screening process, followed by appropriate actions based on the results, all this process in a PC environment [7].

There is currently no direct evidence regarding the effectiveness of universal population frailty screening in PC. For this reason, **detecting cases by means of an active opportunistic search (opportunistic screening)** seems to be the most appropriate method, particularly for people older than 70 years of age [6,16,22-25]. This recommendation is based on the assumptions that frailty is a prevalent condition among people of this age or above, which may contribute to disability and dependence risk, and that potential treatments and relatively accurate methods exist for its detection and management [17].

Currently, the Spanish NHS consensus document recommends early diagnosis of frailty, in people over the age of 70, on an opportunistic basis when visiting a PC Centre, or actively for people who are in other programmes, when the patient shows no signs of any significant functional impairment (Barthel index ≥ 90 points). This is carried out using one of the three proposed performance tests, SPPB, Gait Speed or Timed Up & Go; which are ideally followed up with multidimensional assessment using CGA to confirm the diagnosis and, most importantly, to provide indications and help decide on the appropriate measures to be taken, mainly focusing on physical activity, multi-component physical exercise programmes, and comprehensive healthy lifestyle advice [3].

Although the diagnosis and screening of frailty in PC occupies a very important place, intervention is the key element to achieve changes or maintenance of health.

The main and most effective **interventions in frailty** are physical exercise, nutrition [26], and review and adequacy of medication [5].

Physical exercise and activity either on its own or combined with other treatments remains the intervention with the most evidence of effectiveness in the treatment of frailty [3,16,27-29] not only in terms of therapeutics but also as a primary prevention measure, mainly in the

Lesende IM (2021) Update of the Spanish Fisterra guideline "Frail elderly people: detection and management in Primary Health Care". What contributes and highlight

Table 1. Features of the main tools used to diagnose/detect frailty

Tool	Basis and composition	Characteristics
Physical frailty model		
Fried Phenotype	5 criteria: weight loss, muscle weakness, low endurance, slow gait speed, and low physical activity	It defines frailty. Good reliability and prognostic accuracy. A dynamometer is required, thereby limiting its use in Primary Care. It is considered by some as the "gold standard" because it first conceptualised frailty. <10 minutes. Use in diagnosis.
SHARE-FI scale	Modified Fried criteria. Online calculator: https://sites.google.com/a/tcd.ie/share-frailty-instrument-calculators/	Dynamometer required, as with the Fried phenotype.
Study of osteoporotic fractures (SOF) index	3 items: weight loss, low energy and unable to get out of the chair.	< 5 minutes. No equipment needed. Use in screening.
Multi-dimensional model		
Frailty Index (FI)	Cumulative score, 0 (no deficits) to 1 (all possible deficits); n deficits / total of ≥30 possible deficits in various aspects (physical, mental, social) or disabilities. Frailty cut-off of 0.25.	Frailty is defined by its multidimensional nature. Some authors advocate this as the "gold standard" as it provides a continuous measuring system and assesses the items in all three areas (physical, psychological and social). Approximately 20-30 minutes. No equipment needed. Use in diagnosis. Effective in distinguishing between different stages of frailty. Frailty progression can be assessed.
Electronic frailty index (eFI)	An electronic version of the FI, based on electronic clinical record (ECR).	This classifies the population's frailty risk, like the FI. Virtually no time (ECR data extraction). No equipment needed. Use in screening.
PRISMA-7	7 socio-demographic data items (gender, age >85 years-old, gender, social support), and performance (Activities of Daily Living, ADL). Self-administered.	Moderate prognosis possible. 5 minutes. No equipment needed. Use in screening.
Easycare- TOS	14 questions concerning functioning in somatic, psychosocial, and social factors	It has been proven to help predict fractures and functional decline
Inter-Frail	11 items: 1 concerning disability and 10 concerning frailty (yes/no answers)	10 minutes. No equipment needed. Use in screening.
Comprehensive Geriatric Assessment	Not useful in screening. Recommended for most frailty detection and management strategies, as a diagnosis confirmation and especially as a way of determining and customising response actions/intervention.	
Mixed scales (combining physical and multidimensional model)		
FRAIL scale	5 items: fatigue, resistance, ambulation, illnesses, loss of weight.	No equipment required. <10 minutes. Use in screening.
Tilburg Index	15 items in 3 areas (physical, psychological and social).	Excellent reliability and validity. Well researched. Can be self-administered.
Groningen Frailty Indicator	15 items that assess physical, cognitive, social and psychological factors.	Construct validity compared to the Tilburg index. No equipment or training required. Use in screening.
Performance tests		
Gait speed	Walk 4 to 6 metres at usual gait speed. Frailty cut-off in 1m/sec. or 0.8 m/s.	Predicts adverse conditions and functional decline. Excellent reliability and correlation with Fried criteria. Use in screening.
Timed Up and Go test	Time to get up from a chair, walk 3 metres, and sit down again. Frailty cut-off >20 sec. (some use 10).	Widely recommended to assess functions in primary care in our setting. Use in screening.
Short Physical Performance Battery, SPPB	It assesses 3 factors and 12 items: balance (feet together, semi-tandem and tandem), walking 4 metres, and getting up from and sitting down in a chair (weakness). Score scale from 0 to 12. Frailty cut-off <10.	Validated in Spain as having very good predictive and convergent validity with other physical and function measures, and also with the Fried criteria. <10 minutes. No equipment needed. Use in screening (recommended in the NHS strategy).
Professional criteria	Includes questions which involve reflections such as, "Would you consider this patient to be frail, understood as a loss of functional capacity (physical, psychological, social), with an increased risk of health conditions?	Low sensitivity and moderate specificity, although this improves when supported with objective measures.
Instrumental Activities of Daily Living scales, IADL		
VIDA Questionnaire	10 items-activities (taking medication, using a telephone, housework, financial matters, travel, risk control, shopping, opening doors, using transport, social interaction) and sum score from 10 to 38 points. Frailty cut-off <31 points.	Simple (3-4 minutes), valid and reliable, with a wide range and discrimination, created in our healthcare setting and with no gender bias.
Lawton-Brody Index	Assesses 8 IADL items: Using a telephone, shopping, using means of transport, taking responsibility for their medication, managing their finances, cooking, housework, laundry (for men, some versions only assess the first 4 items)	Seldom validated despite being widely used and not particularly discriminating. Likely to be gender biased.
Clinical Frailty Scale, CFS	A unique tool that assesses a person's condition based on the deterioration of their Activities of Daily Living (ADL), physical fitness and mobility, and the severity of their illness. The text includes bullet points which range from 1 which is very healthy to 9 which is terminally ill.	It measures frailty evolution based on ADL dependence. <5 minutes. No equipment needed. Use in screening/selection

Taken from Martín-Lesende I, Gorroñogoitia A, Abizanda P, Justo S. Persona mayor frágil: detección y manejo en atención primaria - Guía Fisterra (Spanish). 2020.

The tools and scales that are most used or recommended in primary care in Spain are underlined.

Table 2. Diagnostic validity of different tools used to detect frailty

Screening Test Reference standard: Phenotype	Sensitivity (95% CI)	Specificity (95% CI)	Positive probability ratio (95% CI)	Negative probability ratio (95% CI)
Gait speed Cut-off point <0.7 m/s Cut-off point <0.8 m/s	 93% (82-98) 99% (92-100)	 77% (71-78) 64% (58-70)	 4.19 (3.28-5.34) 2.80 (2.37-3.31)	 0.09 (0.03-0.26) 0.01 (0.00-0.38)
Gait speed + hand grip strength (C5-75 program) ≥ 6sec + percent 20%	87% (66-96)	99% (97-100)	103.5 (33.2-322.7)	-
TUG (Timed up and go test) cut-off point >10 s cut-off point ≥17.8 s	 93% (82-98) 93% (82-98)	 62% (56-68) 98% (95-99)	 2.46 (2.05-2.92) 46 (20-110)	 0.11 (0.04-0.33) 0.07 (0.02-0.21)
Short Physical Performance Battery (SPPB) cut-off point ≤6	88% (76-95)	88% (83-91)	7.3 (5.17-10)	0.14 (0.06-0.30)
PRISMA 7 cut-off ≥3 points	83% (60-91)	83% (78-87)	5 (3.69-6.78)	0.20 (0.10-0.39)
Self-perception of health cut-off point ≤6	83% (71-92)	72% (66-77)	3 (2.37-3.80)	0.23 (0.12-0.44)
General Practitioner criteria dichotomous	67% (52-77)	76% (71-81)	2.86 (2.12-3.87)	0.43 (0.28-0.66)
IADL-Lawton-Brody index cut-off point ≤3	86% (74-94)	93% (89-95)	12.3 (7.74-20)	0.15 (0.07-0.31)
IADL-VIDA questionnaire cut-off point <31 cut-off point <35	 75% (61-86) 78% (64-87)	 66% (60-71) 73.1% (67-78)	 2.21 (1.73-2.80) 2.9 (2.5-3.74)	 0.38 (0.23-0.63) 0.3 (0.17-0.52)

Taken from Martín-Lesende I, Gorroñogoitia A, Abizanda P, Justo S. Persona mayor frágil: detección y manejo en atención primaria - Guía Fisterra (Spanish). 2020.

form of multi-component exercises, which work on strength, balance, endurance, coordination, flexibility and aerobic performance. Good examples of this kind of exercise and how it can be carried out can be found at the VIVIFRAIL strategy https://vivifrail.com/ .

Nutrition is an important modifiable factor associated with frailty [16]. Considering nutritional advice, Body Mass Index (BMI) between 25 and 29.9 kg/m², a suitable protein intake of ≥ 1 g/kg of weight/day [30], nutritional supplements when needed, and favouring a Mediterranean diet [5,31]. PREDIMED (Prevention with the Mediterranean Diet, http://predimed-es.weebly.com/) is an interesting method by which to follow this diet. The use of oral vitamin D supplements has controversial aspects, screening is not recommended in asymptomatic patients, considering at risk those institutionalized, with low sun exposure, with osteoporosis, intestinal malabsorption, kidney disease or hyperparathyroidism [5]. The MNA-SF is a useful and widely used malnutrition risk assessment tool [5].

To review and adequate the usual medication [32] and **de-prescribe** [33], are other important interventions. Aanticholinergic burden [34] defined as the cumulative effect of taking medication which can decrease the body's cholinergic activity should be assessed. The STOPP/START and the Beers criteria are widely recommended to detect potentially inappropriate prescriptions (PIP) in older adults [3]. Medicines priorization and conciliation, adherence reinforcement, and monitoring of adverse reactions are also of interest in this vulnerable population. ICTs may play a role in polypharmacy management.

The importance of a correct **clinical treatment/management of prevalent pathologies/conditions** (cardiovascular, metabolic, neurologic, or osteoarticular diseases) **and geriatric syndromes** (delirium, incontinence, cognitive impairment, instability and falling, malnutrition) closely related to functional loss should be assessed and addressed early, referring patients to appropriate specialists when the complexity of the situation requires it. Geriatric Medicine may be an appropriate resource when available. Some evidence has been described of **occupational therapy** in frail older adults in the community [35]. And the correct approach to social situations as important in functional ability as loneliness or social deprivation should also be highlighted.

In addition, **multi-domain interventions**, which consist in combining a number of the aforementioned actions in a coherent and structured way, do appear to bear some benefits [28,36].

A recent review that compared evidence related to the main individual actions taken in a community environment regarding frailty (physical exercise, multi-component exercise, protein and nutritional supplements, treating separate medical conditions, health advice, social support, home environment condition adjustments) indicated that the evidence for all of them is still low [17]. Thus, there are already many inconclusive issues and we must keep working to clarify exactly which actions are most beneficial in general terms, given their inconsistencies [17,18].

As frailty is a multifactorial syndrome, treatment and action strategies should therefore also be multidimensional, ideally in the form of a **CGA** [3,5,25,27]; considering actions that have been proven to be effective in treating this condition, addressing reversible conditions, and even assessing referrals or the involvement of other relevant social or medical specialists. Adaptations and new implementation strategies in PC are required to increase both its effectiveness and application in this health care setting. **Integrated healthcare systems**, implying the importance of continuity and coordination of care, are effective structures to improve outcomes for patients with chronic diseases. Although in most cases they are not specifically designed to prevent and treat frailty, the fact that this is a complex and multidimensional condition suggests that it can benefit from a well-coordinated treatment approach from all the professionals involved, named the health system, the social services, and the community. However, the first entry point should always be PC. This setting must screen patients for frailty, make the first clinical approach and management, and coordinate the multidisciplinary team in both community and hospital settings. Electronic information and well-defined procedures must be shared by all the multidisciplinary team [16].

Acknowledgements and fundings

Competing interest

All the authors have filled out a competing interest form, in which they declare that there is no conflict of interest.

References

1. Martín-Lesende I, Gorroñogoitia A, Molina M, Abizanda P (2015) Frail elderly people: Detection and management in primary care. *Eur Geriatr Med* 6: 447-455. [Crossref].

2. https://www.fisterra.com/guias-clinicas/persona-mayor-fragil-deteccion-manejo-atencion-primaria/

3. https://www.mscbs.gob.es/profesionales/saludPublica/prevPromocion/Estrategia/docs/Fragilidad/Frailtyandfalls_Elderly.pdf

4. https://www.advantageja.eu/index.php/

5. Gorroñogoitia A, López-Torres J, Martín-Lesende I, Herreros Y, Acosta MA, et al. (2020) Actualización GdT Mayor 2020. *Aten Primaria* 52: 114-124. [Crossref]

6. Reeves D, Pye S, Ashcroft DM, Clegg A (2018) The challenge of ageing populations and patient frailty: can primary care adapt? *BMJ* 362: k3349.

7. Lee L, Patel T, Hillier LM, Locklin J, Milligan J, et al. (2018) Frailty Screening and Case-Finding for Complex Chronic Conditions in Older Adults in Primary Care. *Geriatrics (Basel)* 3: 39 [Crossref]

8. https://www.who.int/ageing/publications/guidelines-icope/en/#

9. Hoogendijk EO, Afilalo J, EnsrudKE, Kowal P, Onder G, et al. (2019) Frailty: implications for clinical practice and public health. *The Lancet* 394: 1365-1375. [Crossref]

10. https://www.mscbs.gob.es/en/profesionales/saludPublica/prevPromocion/Prevencion/EnvejecimientoSaludable_Fragilidad/Covid19_Fragilidad.htm

11. http://apps.who.int/iris/bitstream/10665/186466/1/9789240694873_spa.pdf

12. Junius-Walker U, Onder G, Soleymani D, Wiese B, Albaina O, et al (2018) on behalf of ADVANTAGE JA WP4 group). The essence of frailty: a systematic review and qualitative synthesis on frailty concepts and definitions. *Eur J Int Med* 56: 3-10. [Crossref]

13. http://advantageja.eu/images/SoAR-AdvantageJA_Fulltext.pdf

14. O'Caoimh R, Galluzzo L, Rodríguez-Laso A, der Heyden JV, Ranhoff AH, et al. (2018) Prevalence of frailty at population level in European ADVANTAGE Joint Action Member States: a systematic review and meta-analysis. *Ann Ist Super Sanita* 54: 226-238. [Crossref]

15. Dolenc E, Rotar-Pavlic D (2019) Frailty assessment scales for the elderly and their application in primary care: a systematic literature review. *Zdr Varst* 58: 91-100. [Crossref]

16. http://www.advantageja.eu/index.php/es/index.php?option=com_content&view=article&layout=edit&id=343%22

17. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD (2019) Management of frailty: opportunities, challenges, and future directions. *The Lancet* 394: 1376-1386 [Crossref]

18. Van der Elst M, Schoenmakers B, Duppen D, Lambotte D, Fret B, et al. (2018) Interventions for frail community-dwelling older adults have no significant effect on adverse outcomes: a systematic review and meta-analysis. *BMC Geriatr* 18: 249. [Crossref]

19. Gilardi F, Capanna A, Ferraro M, Scarcella P, Marazzi MC, et al. (2018) Frailty screening and assessment tools: a review of characteristics and use in Public Health. *Ann Ig* 30: 128-139. [Crossref]

20. Briggs R, McDonough A, Ellis G, Bennett K, O'Neill D, et al. (2017) Comprehensive Geriatric Assessment for community-dwelling, high-risk, frail, older people. *Cochrane Database Syst Rev* 2017: CD012705. [Crossref]

21. Martin-Lesende I, Vrotsou K, Vergara I, Bueno A, Diez AI, et al. (2015) Design and Validation of the VIDA Questionnaire, for Assessing Instrumental Activities of Daily Living In Elderly People. *J Gerontol Geriatr Res* 4: 2.

22. https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/frailty-full_guideline.pdf

23. Ambagtsheera RC, Beilbya JJ, Visvanathana R, Dent E, Yu S, et al. (2019) Should we screen for frailty in primary care settings? A fresh perspective on the frailty evidence base: A narrative review. *Prev Med* 19: 63-69. [Crossref]

24. Rodríguez-Laso A, O'Caoimh R, Galluzzo L, Carcaillon-Bentata L, Beltzer N, et al. (2018) Population screening, monitoring and surveillance for frailty: three systematic reviews and a grey literature review. Ann Ist Super Sanità 54: 253-262. [Crossref]

25. https://www.bgs.org.uk/sites/default/files/content/resources/files/2018-05-23/fff_full.pdf

26. Travers J, Romero-Ortuno R, Bailey J, Cooney MT (2019) Delaying and reversing frailty: a systematic review of primary care interventions. *Br J Gen Pract* 69: e61-e69. [Crossref]

27. https://www.uptodate.com/contents/frailty

28. Dedeyne L, Deschodt M, Verschueren S, Tournoy J, Gielenet E (2017) Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: a systematic review. *Clin Interv Aging* 12: 873-896. [Crossref]

29. De Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millán-Calenti JC (2015) Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. BMC Geriatrics 15: 154. [Crossref]

30. Liao CD, Chen HC, Huang SW, Liou TH (2019) The Role of Muscle Mass Gain Following Protein Supplementation Plus Exercise Therapy in Older Adults with Sarcopenia and Frailty Risks: A Systematic Review and Meta-Regression Analysis of Randomized Trials. *Nutrients* 11: 1713. [Crossref]

31. Kojima G, Avgerinou C, Iliffe S, Walters K (2018) Adherence to Mediterranean Diet Reduces Incident Frailty Risk: Systematic Review and Meta-Analysis. *JAGS* 66: 783-788.

32. Martinot P, Landré B, Zins M, Goldberg M, Ankri J, et al. (2018) Association Between Potentially Inappropriate Medications and Frailty in the Early Old Age: A Longitudinal Study in the GAZEL Cohort. *J Am Med Dir Assoc* 19: 967-973. [Crossref]

33. Gutiérrez-Valencia M, Izquierdo M, Cesari M, Casas-Herrero Á, Inzitari M, et al. (2018) The relationship between frailty and polypharmacy in older people: A systematic review. *Br J Clin Pharmacol* 84: 1432-1444. [Crossref]

34. Brombo G, Bianchi L, Maietti E, Malacarne F, Corsonello A, et al. (2018) Association of anticholinergic drug burden with cognitive and functional decline over time in older inpatients: results for the CRIME Project. *Drugs Aging* 35: 917-924. [Crossref]

35. De Coninck, L, Bekkering GE, Bouckaert L, Declercq A, Graff MJL, et al. (2017) Home- and Community-Based Occupational Therapy Improves Functioning in Frail Older People: A Systematic Review. *J Am Geriatr Soc* 65: 1863-1869. [Crossref]

36. Inzitari M, Pérez LM, Enfedaque MB, Soto L, Díaz F, et al. (2018) Integrated primary and geriatric care for frail older adults in the community: Implementation of a complex intervention into real life. *Eur J Int Med* 56: 57-63. [Crossref]