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Special Article

Frailty: An Emerging Public Health Priority

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The absolute and relative increases in the number of older persons are evident worldwide, from the most developed countries to the lowest-income regions. Multimorbidity and need for social support increase with age. Age-related conditions and, in particular, disabilities are a significant burden for the person, his or her family, and public health care systems. To guarantee the sustainability of public health systems and improve the quality of care provided, it is becoming urgent to act to prevent and delay the disabling cascade. Current evidence shows that too large a proportion of community-dwelling older people present risk factors for major health-related events and unmet clinical needs. In this scenario, the "frailty syndrome" is a condition of special interest. Frailty is a status of extreme vulnerability to endogenous and exogenous stressors exposing the individual to a higher risk of negative health-related outcomes. Frailty may represent a transition phase between successful aging and disability, and a condition to target for restoring robustness in the individual at risk. Given its syndromic nature, targeting frailty requires a comprehensive approach. The identification of frailty as a target for implementing preventive interventions against age-related conditions is pivotal. Every effort should be made by health care authorities to maximize efforts in this field, balancing priorities, needs, and resources. Raising awareness about frailty and age-related conditions in the population is important for effective prevention, and should lead to the promotion of lifelong healthy behaviors and lifestyle.

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Populations around the world are rapidly aging, and this trend is evident from the most developed countries to the lowest income regions.¹ This implies a realigning of health systems so as to better address the unmet needs of older people, independently of the socioeconomic background. The fast demographic transition

indeed demands a comprehensive public health response. Unfortunately, the debate on what such adaptations might be needed is still limited. In fact, evidence is rarely sufficient in many areas, and the evidence that is available comes mostly from developed countries.^{2,3}

Multimorbidity and need for social support increase with age. Age-related conditions and disabilities are burdening for the person, his or her family, and public health care systems. A close relationship between the percentage of older persons in the population and health care expenditure has been clearly described in high-income countries.⁴ Health care expenses for the older population have been increasing more rapidly than those for younger adults,⁵ mainly due to an inadequacy of systems at meeting the multiple and complex needs of frail and disabled elders.⁶ Such scenarios obviously endanger the sustainability of health and social care systems. For these reasons, in the past decade, there have been increasing calls for the implementation of preventive actions against age-related and disabling conditions in the elderly.⁷

In this context, the concept of the “frailty syndrome” is of special interest. Frailty is defined as a status of extreme vulnerability to endogenous and exogenous stressors exposing the individual to a higher risk of negative health-related outcomes.⁷ It is usually caused by the interaction of the progressive age-related decline in physiologic systems with chronic diseases and conditions, consequently leading to decreased functional reserve capacities. The condition has been described as a vicious cycle responsible for the onset of negative health-related outcomes,⁸ and a transition phase between successful aging and disability.⁹ Frailty may represent a novel approach to age-related conditions by replacing the obsolete concept of “chronological age” with the more accurate and person-tailored parameter of “biological age.”¹⁰

In 2014, the World Health Organization (WHO) was asked by its Executive Board to release a World Report on Aging and Health followed by a Global Strategy and Implementation Plan. Therefore, the WHO and the International Association of Gerontology and Geriatrics (IAGG) established a global network of experts (ie, the WHO-IAGG Frailty Network) to write a background article on “Frailty” as the key resource to inform the upcoming WHO World Report on Aging and Health. This article summarizes the main findings of the background document developed by the WHO-IAGG Frailty Network. In addition to literature searches, this article is based on consensus coming from a final expert meeting (held in Geneva, Switzerland, at the WHO Headquarters, on October 8–9, 2014). The following questions guided the present work:

- What is the worldwide prevalence of frailty?
- What are the preventive value and outcomes of frailty?
- What are the evidence-based public health interventions that can be implemented at primary care level to prevent and manage frailty so as to avoid negative health-related outcomes at old age?
- How should the health systems be reorganized to prevent and manage frailty?

Prevalence of Frailty

Recently, a systematic review was conducted to estimate the prevalence of frailty in older persons.¹¹ Authors considered data from 21 studies and more than 61,500 community-dwelling older persons. The reported prevalence varied substantially across studies, ranging from 4.0% to 59.1% according to the adopted operational definition of frailty and the characteristics of the studied sample. Nevertheless, when analyses were restricted to studies using the phenotype model proposed by Fried and colleagues,¹² the weighted average prevalence was 9.9% (95% confidence interval [95% CI] 9.6–10.2) and 44.2% (95% CI 44.2–44.7) for frailty and prefrailty, respectively. These findings are

consistent with and extend a previous study conducted using data from the Survey of Health, Aging, and Retirement in Europe (SHARE; more than 18,000 community-dwelling individuals aged ≥ 50 years).¹³ Similar findings were here reported for the prevalence of frailty among participants aged 65 years and older (prefrailty: 42.3% [range by country 34.6%–50.9%], frailty: 17.0% [range by country 5.8%–27.3%]), together with variations across countries (tending to increase from northern to southern Europe). Similar estimates have also been documented in Asian countries, such as South Korea (prevalence of robust, prefrail, and frail elders: 48.4%, 42.3%, and 9.3%, respectively)¹⁴ or Japan (prevalence of frailty: 11.3%).¹⁵

There is consistent evidence across studies for an increasing prevalence of frailty with older age,^{13,16} for a higher prevalence in women compared with men,^{11,13} and for some variation across ethnic groups (eg, a higher prevalence in Hispanic and African Americans).^{12,17} Moreover, frailty has often been found to be associated with unfavorable socioeconomic circumstances including limited education and poverty.¹²

There have been few studies measuring the prevalence of frailty in low- and middle-income countries. The available data, largely coming from Central and South America, suggest a potentially higher prevalence among older people in those regions. For example, both Aguilar-Navarro and colleagues¹⁸ and Alvarado and colleagues¹⁹ showed a relatively high prevalence of prefrail and frail older persons among community-dwelling Mexicans. In a cohort of Cuban municipalities, the prevalence of frailty was 21.6% (95% CI 17.9%–23.8%).²⁰ In the Costa Rican Study on Longevity and Healthy Aging, the prevalence of frailty increases from 17.8% among 60- to 79-year-old participants to 57.0% among those 80 years and older.²¹ Recent studies conducted in Peru have reported frailty prevalence ranging from 12.2%²² to 27.8%.²³

In interpreting these data, it is important to note that although the reported findings are largely based on the frailty phenotype model proposed by Fried and colleagues,¹² the applied definition of frailty often deviates from the original version depending on the data and resources available in each study. Such modifications may not significantly affect results of some instruments (due to their inner constructs), but findings might still be biased or altered.²⁴ The validity of direct comparisons across studies is therefore debatable. At the same time, it is clear that a large proportion of community-dwelling older people currently present risk factors for major health-related events and unmet clinical needs.

The Course and Outcomes of Frailty

The predictive value of frailty for negative outcomes is consistently confirmed across assessment instruments, target populations, and settings. The increased risk of negative health-related events includes falls, hospitalizations, disability, institutionalization, and mortality.^{8,9} Nevertheless, the course of frailty varies from individual to individual and it is capable of change. In a study by Gill and colleagues,²⁵ nondisabled individuals aged 70 years or older were followed over time to explore changes in frailty status (measured using the frailty phenotype¹²). Among the 754 participants, 57.5% had at least 1 transition between any 2 of the 3 frailty states during the 54-month follow-up period. In the first 18 months of the study, 44.3% of robust participants at the baseline transitioned to a prefrailty (40.1%) or frailty (4.2%) state. Among participants with frailty at the baseline, 63.9% remained frail, 23.0% improved to a state of prefrailty, 13.1% died, and none reversed to robustness; 11.9% of prefrail participants at the baseline regained a robust state by the end of the follow-up. Similar findings were reported in the SHARE database,²⁶ where 31.7% of robust participants became prefrail and 2.6% became frail, whereas 32.4% of prefrail participants recovered to a robust state after 2 years of follow-up. As also described in the study by Gill and colleagues,²⁵ the number of frail elders having their robustness

restored at the end of the follow-up in SHARE was relatively small (approximately 7.0%). Thus, evidence suggests that the frailty condition (especially at its very earliest stages) might present characteristics of reversibility. Recently, a study by Lee and colleagues²⁷ reported specific characteristics significantly associated with negative (older age, history of cancer, hospitalization events, chronic obstructive pulmonary disease, cerebrovascular disease, osteoarthritis) and positive (higher cognitive function, absence of diabetes, higher socioeconomic status, and no history of cerebrovascular disease) change in frailty status.

Recently, the concept of “resilience” (the individual’s ability to adapt in the face of stresses and adversities) has become increasingly used in the field of frailty.²⁸ A frail individual with low resilience is more likely to fall into a disabling cascade and quickly develop negative outcomes, whereas high resilience may be protective and facilitate maintenance of health status. As with frailty, resilience is a complex construct depending on a network or interaction of biological, clinical, social, and environmental factors that characterize each individual. Attempting to define resilience offers us an opportunity to explore the stage (or “threshold”) at which an individual’s ability to limit injury or damage due to stressors declines. After this hypothetical point, recovery of health status may be less certain.

Evidence-based Interventions for Targeting Frail Older People

Functional health at old age is the result of the cumulative effects of disease and physiologic changes occurring with ageing.²⁹ The age-related accumulation of deficits is also influenced by the individual’s behaviors as well as social and economic factors (eg, access to health care) to which the person is exposed during his or her life. It follows that the health status of an older person should not only be “cross-sectionally” assessed, but also assessed “longitudinally” through a careful evaluation of his or her background and history. Consequently, preventive interventions targeting age-related conditions need not be restricted to older age. Young age and adulthood might offer opportunities for prevention and modification of risk factors. Attention to structural determinants including poor socioeconomic conditions and limited access to health care play a pivotal role as well.³⁰

Frailty is not considered a disease, but rather a syndrome requiring a multidomain and multidisciplinary approach. This is because it is unlikely that a single cause underlies the presence of frailty, and this latter state may instead represent the manifestation or consequence of multiple concurrent factors. Thus, after frailty is detected, a comprehensive assessment should follow to identify and treat the underlying causes of the identified extreme vulnerability.

An extensive literature attests to the importance of conducting and acting on a comprehensive geriatric assessment (CGA) approach. Multiple systematic reviews and meta-analyses have clearly shown significant improvements in the management and outcomes of frail older persons when CGA-driven models of care are implemented.^{31–33} Such benefits have been demonstrated across different settings (eg, community,³⁴ home care,³⁵ acute care,³⁶ nursing home³⁷).

A relevant meta-analysis was conducted in 1993 by Stuck and colleagues³² comprising 28 randomized controlled trials (>9000 participants) testing the effects of CGA-based interventions versus controls. Findings clearly demonstrate that CGA-based programs linking geriatric evaluation with long-term management are effective for improving survival and function in older people. Interestingly, another meta-analysis³⁸ showed that earlier studies (started before 2000) testing complex interventions against functional decline showed more evident benefits than those more recently conducted. Such a finding suggests the possibility that the CGA principles and approach might have already been implemented in many health systems.

In this context, the increasing implementation of close liaisons between several medical specialties with geriatric medicine with the

aim of improving the assessment and management of frail older persons in the clinical setting is noteworthy. Such multidisciplinary collaborations are easily explained by the rising prevalence of frail older people (with all their complexities and peculiarities) in almost every clinical ward and service. Such patients require adaptations of care, personalization of interventions, and modifications of standard protocols that can be achieved only through the implementation of CGA and the techniques and model of care usually conducted under the geriatrics approach.³⁹ The positive results obtained in specific clinical settings have fostered research into the possible extension of the multidimensional and multidisciplinary approach even into primary care, and as part of preventive strategies targeting community-dwelling older people.^{40,41}

Realigning Health Systems for Frailty Care Programs

As any other preventive strategy, the intervention for frailty should be evaluated after an adequate time period, in particular for appreciating its possible cost-effectiveness.⁴² It is likely that during the scaling-up phase such activity may lead to an increase in health care costs, for example, due to staff training, screening and assessment procedures, and additional investigations and interventions once a clinical problem is detected. Benefits may be considerable, but would be accrued some time later. Cost savings may be indirect (reduced disability and needs for informal care) and fall outside of the health sector (delayed institutionalization) and therefore not considered in the cost-effectiveness equation. Policy makers and legislators may find themselves balancing the costs of prevention with those necessary for ensuring the sustainability of traditional clinical care services. Such allocation decisions, which may be particularly vexed in low-resource settings, should foster ethical discussions.⁴² However, it cannot be ignored that the only way to compress the burden of disabilities is by preventive actions when these are still amenable to being reversed.⁷

The critical time window for interventions that target frailty has not yet been clearly established. On a spectrum from prefrailty, to frailty, to disability, it is often assumed that early intervention to prevent the onset of disability is crucial and optimal; however, that is not to say that established disability cannot be reduced, or its progression slowed, or its impact on the older person and his or her caregivers mitigated. This continues to be an active area for research, exploring the role of community-based models of care, individual-tailored multicomponent interventions, and various approaches to integrated case management. Frailty provides an attractive theoretical framework within which the primary care clinician can devise holistic assessment and treatment of the older patient with complex multimorbidity in a simple and structured way.⁴³ The introduction of this approach may be particularly advantageous in low-resource settings, in which older people often have limited access to health care, and where current systems do not meet their needs for continuing person-centered care.⁴⁴

The first step is to raise awareness about frailty among policy-makers, public health authorities, practitioners, and the general population.⁴⁵ Older people (with possible support of their family members) need to be alert to warning signs of frailty, empowered with knowledge and skills to take increased responsibility of their own health status, and motivated both to seek help as well as modify their unhealthy behaviors. Health professionals need to be trained to confirm signs of frailty and implement evidence-based packages of care. Public health authorities must become familiar with the increasing burdens that age-related conditions (in particular, frailty) will impose on their health care systems, and become proactive in planning and implementing counteractive strategies.

Primary care is the first point of contact for health services in many countries. It is probably the ideal place for delivering prevention and care for frail older people. A major objective is to enhance access to

care and achieve a universal coverage of health needs. To achieve this goal, processes need to be simplified as much as possible, with an emphasis on efficiency. This aim might be more easily accomplished with a single point of entry into the system for frail individuals, and a case manager to assess needs using standardized assessment instruments and coordinate the evidence-based and personalized care for the frail old. To promote the adoption of care pathways, screening tools should be inexpensive, require little if any special training or equipment, and be sufficiently robust in accuracy.

Given the pace of global population aging, all countries need to give more priority to the reshaping of health and social care systems taking into account the special needs of frail older people. A widespread and systematic case finding of frail elders is not feasible, at least at this time, especially in low- and middle-income countries. This approach has even been discouraged in some high-income countries.^{46,47} The detection of frailty might instead follow a more opportunistic pattern, by using any formal and informal contact that the older individual may have with health care (eg, general practitioners, outpatient clinics, emergency departments, immunization campaigns) and social services (eg, senior centers, programs of social support). Although resource-poor settings in low- and middle-income countries pose particular challenges, there are also opportunities arising from the widespread availability of generic community health workers who provide outreach into homes in the community. Their focus tends to be on maternal and child health, but this could be extended to include appraisal of the status of older residents, simple home-based interventions, and referral pathways to primary and secondary care.

Measurements for Frailty

Multiple instruments have been developed to detect frailty and render it objectively measurable. Overall, the available instruments to measure frailty present a strong predictive value for negative outcomes.⁴⁸ Unfortunately, the agreement between them is quite modest.⁴⁸ Analyses conducted by van Iersel and colleagues⁴⁹ compared the prevalence of frailty using 4 different tools (the frailty phenotype, the Frailty Index, usual gait speed, and handgrip strength). The prevalence of frailty varied depending on the criterion used. Moreover, each tool identified a specific population with only partial overlap with other definitions. In other words, each assessment tool captures a different risk profile, and none of them is comprehensive in itself. Preferring one instrument to another implies the possible exclusion from interventions of individuals who may otherwise benefit from them. Therefore, at this time, the choice of the most appropriate frailty instrument should rely on the purpose of the evaluation, the outcome for which the definition was originally validated, the validity of the tool, the studied population, and the setting in which the assessment will be conducted. In this context, the use of objective tests (eg, physical performance measures⁵⁰) might be preferable to those relying on subjective evaluations because they are potentially less influenced by the sociocultural background and more focused on the actual functioning of the individual.

Conclusions

Frailty represents a public health priority for multiple reasons. It is a highly and increasingly prevalent condition in the aging populations. Moreover, frailty is a strong predictor of major negative health-related outcomes in older persons (in particular, disability, hospitalization, institutionalization, death). Besides affecting the quality of life of the individual, frailty also severely threatens the long-term sustainability of health care systems, at least as they are traditionally designed. It is necessary to redesign models of care for rendering them more responsive to the unmet clinical needs of the growing frail population worldwide. Models of care relying on the CGA approach seem

particularly promising and are supported by relevant literature. In this context, the identification of frailty (even relying on opportunistic patterns taking advantage of any formal and informal resource) is pivotal for implementing multidimensional preventive interventions against age-related and disabling conditions.

Raising awareness about the risk of the disabling cascade, providing the necessary knowledge to actively prevent, and improving access to care to favor optimal aging represent crucial steps to undertake. Every effort should be made by health care authorities to maximize efforts in the prevention of age-related and disabling conditions, balancing priorities, needs, and resources. It is noteworthy that prevention of frailty should not be considered a task exclusively delegated to older persons. Effective prevention of age-related and disabling conditions should indeed start at younger ages and adulthood.

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References

1. United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects: The 2015 Revision. Available from: <http://esa.un.org/unpd/wpp/index.htm>. Accessed January 7, 2016.
2. Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: The challenges ahead. *Lancet* 2009;374:1196–1208.
3. Beard JR, Bloom DE. Towards a comprehensive public health response to population ageing. *Lancet* 2015;385:658–661.
4. Yang Z, Norton EC, Stearns SC. Longevity and health care expenditures: The real reasons older people spend more. *J Gerontol B Psychol Sci Soc Sci* 2003;58:S2–S10.
5. Rice DP, Fineman N. Economic implications of increased longevity in the United States. *Annu Rev Public Health* 2004;25:457–473.
6. Congressional Budget Office. Rising demand for long-term services and supports for elderly people. Washington, DC: Congressional Budget Office; 2013.
7. Morley JE, Vellas B, Abellan van Kan G, et al. Frailty consensus: A call to action. *J Am Med Dir Assoc* 2013;14:392–397.
8. Fried LP, Walston JD, Ferrucci L. Frailty. In: Halter JB, Ouslander JG, Tinetti ME, et al., editors. *Hazzard's Geriatric Medicine and Gerontology*. New York, NY: McGraw-Hill Medical; 2009. p. 631–645.
9. Clegg A, Young J, Iliffe S, et al. Frailty in elderly people. *Lancet* 2013;381:752–762.
10. Cesari M, Gambassi G, Abellan van Kan G, Vellas B. The frailty phenotype and the frailty index: Different instruments for different purposes. *Age Ageing* 2014;43:10–12.
11. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: A systematic review. *J Am Geriatr Soc* 2012;60:1487–1492.
12. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146–M156.
13. Santos-Eggimann B, Cuénoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009;64:675–681.
14. Han ES, Lee Y, Kim J. Association of cognitive impairment with frailty in community-dwelling older adults. *Int Psychogeriatr* 2014;26:155–163.
15. Shimada H, Makizako H, Doi T, et al. Combined prevalence of frailty and mild cognitive impairment in a population of elderly Japanese people. *J Am Med Dir Assoc* 2013;14:518–524.
16. Rockwood K, Song X, Mitnitski A. Changes in relative fitness and frailty across the adult lifespan: Evidence from the Canadian National Population Health Survey. *CMAJ* 2011;183:E487–E494.
17. Espinoza SE, Hazuda HP. Frailty in older Mexican-American and European American adults: Is there an ethnic disparity? *J Am Geriatr Soc* 2008;56:1744–1749.
18. Aguilar-Navarro S, Gutierrez-Robledo LM, Garcia-Lara JM, et al. The phenotype of frailty predicts disability and mortality among Mexican community-dwelling elderly. *J Frailty Aging* 2012;1:111–117.
19. Alvarado BE, Zunzunegui MV, Beland F, Bamvita JM. Life course social and health conditions linked to frailty in Latin American older men and women. *J Gerontol A Biol Sci Med Sci* 2008;63:1399–1406.
20. Libre Jde J, Lopez AM, Valhuerdi A, et al. Frailty, dependency and mortality predictors in a cohort of Cuban older adults, 2003–2011. *MEDICC Rev* 2014;16:24–30.

21. [Rosero-Bixby L, Dow WH. Surprising SES gradients in mortality, health, and biomarkers in a Latin American population of adults. J Gerontol B Psychol Sci Soc Sci 2009;64:105–117.](#)
22. [Curcio CL, Henao GM, Gomez F. Frailty among rural elderly adults. BMC Geriatr 2014;14:2.](#)
23. [Runzer-Colmenares FM, Samper-Ternent R, Al Snih S, et al. Prevalence and factors associated with frailty among Peruvian older adults. Arch Gerontol Geriatr 2014;58:69–73.](#)
24. [Theou O, Cann L, Blodgett J, et al. Modifications to the frailty phenotype criteria: Systematic review of the current literature and investigation of 262 frailty phenotypes in the Survey of Health, Ageing, and Retirement in Europe. Ageing Res Rev 2015;21:78–94.](#)
25. [Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. Arch Intern Med 2006;166:418–423.](#)
26. [Borrat-Besson C, Ryser VA, Wernli B. Transitions between frailty states: A European comparison. In: Börsch-Supan A, Brandt M, Litwin H, Weber G, editors. Active Ageing and Solidarity Between Generations in Europe. First Results From SHARE After the Economic Crisis. Berlin: De Gruyter; 2013. p. 175–185.](#)
27. [Lee JS, Auyeung TW, Leung J, et al. Transitions in frailty states among community-living older adults and their associated factors. J Am Med Dir Assoc 2014;15:281–286.](#)
28. [Ferrucci L, Giallauria F, Schlessinger D. Mapping the road to resilience: Novel math for the study of frailty. Mech Ageing Dev 2008;129:677–679.](#)
29. [Cesari M, Vellas B, Gambassi G. The stress of aging. Exp Gerontol 2013;48:451–456.](#)
30. [Elwood P, Galante J, Pickering J, et al. Healthy lifestyles reduce the incidence of chronic diseases and dementia: Evidence from the Caerphilly cohort study. PLoS One 2013;8:e81877.](#)
31. [Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of geriatric evaluation and management programs on defined outcomes: Overview of the evidence. J Am Geriatr Soc 1991;39:8S–16S. discussion 17S.](#)
32. [Stuck AE, Siu AL, Wieland GD, et al. Comprehensive geriatric assessment: A meta-analysis of controlled trials. Lancet 1993;342:1032–1036.](#)
33. [Van Craen K, Braes T, Wellens N, et al. The effectiveness of inpatient geriatric evaluation and management units: A systematic review and meta-analysis. J Am Geriatr Soc 2010;58:83–92.](#)
34. [Stuck AE, Minder CE, Peter-Wüest I, et al. A randomized trial of in-home visits for disability prevention in community-dwelling older people at low and high risk for nursing home admission. Arch Intern Med 2000;160:977–986.](#)
35. [De Almeida Mello J, Hermans K, Van Audenhove C, et al. Evaluations of home care interventions for frail older persons using the interRAI Home care instrument: A systematic review of the literature. J Am Med Dir Assoc 2015;16:173.e1–173.e10.](#)
36. [Ellis G, Whitehead MA, Robinson D, et al. Comprehensive geriatric assessment for older adults admitted to hospital: Meta-analysis of randomised controlled trials. BMJ 2011;343:d6553.](#)
37. [Fiatarone MA, O'Neill EF, Ryan ND, et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med 1994;330:1769–1775.](#)
38. [Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: A systematic review and meta-analysis. Lancet 2008;371:725–735.](#)
39. [Royal College of Physicians. Hospital workforce: Fit for the future? London \(UK\): Royal College of Physicians; 2013.](#)
40. [Subra J, Gillette-Guyonnet S, Cesari M, et al. The integration of frailty into clinical practice: Preliminary results from the Gérontopôle. J Nutr Health Aging 2012;16:714–720.](#)
41. [Maggio M, Ceda GP, Lauretani F. The multidomain mobility lab in older persons: From bench to bedside. Curr Pharm Des 2014;20:3093–3094.](#)
42. [Cesari M, Vellas B. Frailty in Clinical Practice. Nestle Nutr Inst Workshop Ser 2015;83:93–98.](#)
43. [De Lepeleire J, Iliffe S, Mann E, Degryse JM. Frailty: An emerging concept for general practice. Br J Gen Pract 2009;59:e177–e182.](#)
44. [Prince MJ, Wu F, Guo Y, et al. The burden of disease in older people and implications for health policy and practice. Lancet 2015;385:549–562.](#)
45. [Rodriguez-Artalejo F, Rodriguez-Manas L. The frailty syndrome in the public health agenda. J Epidemiol Community Health 2014;68:703–704.](#)
46. [Sub-directorate of Health Promotion and Epidemiology Prevention among the Elderly. Prevention and Health Promotion Strategy of the Spanish NHS. Madrid, Spain: Ministry of Health, Social Services, and Equality; 2014.](#)
47. [Fit for Frailty: Consensus best practice guidance for the care of older people living in community and outpatient settings: A report from the British Geriatrics Society. London \(UK\): British Geriatrics Society; 2014.](#)
48. [Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. J Am Geriatr Soc 2013;61:1537–1551.](#)
49. [van Iersel MB, Rikkert MG. Frailty criteria give heterogeneous results when applied in clinical practice. J Am Geriatr Soc 2006;54:728–729.](#)
50. [Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. J Am Geriatr Soc 2003;51:314–322.](#)