REVIEW

Frailty and cognitive decline: how do they relate?

Marco Canevelli[a,b], Matteo Cesari[b,c,d], and Gabor Abellan van Kan[b,c]

Purpose of review
To provide a comprehensive review of the recent literature (published over the last 12 months) exploring the relationship between frailty and cognition.

Recent findings
Fourteen studies were retained for the present review. No randomized controlled trial was found. Overall, the main findings of the selected studies appeared to be mainly confirmatory of the previous evidence. In longitudinal studies, physical frailty was found to predict the incidence of cognitive impairment and dementia. Cross-sectional studies showed that frail individuals have lower cognitive performance compared with nonfrail persons. Interestingly, few studies examined the association between frailty and specific cognitive functions and domains, reporting a significant impairment of attention and executive functions Finally, we found several studies including cognitive measures in the operational definitions of frailty.

Summary
The present findings are suggestive of an almost complete lack of evidence on the addressed topic. In particular, randomized controlled trials are strongly needed in order to gain insights about the possibility of positively affecting the frailty syndrome by acting of cognition and improving cognitive impairment by targeting the physical components of frailty. Moreover, these studies may produce the first evidences about the novel concept of 'cognitive frailty' and its potential for reversibility.

Keywords
cognition, cognitive frailty, elderly, frailty, review

INTRODUCTION

Frailty is a multidimensional syndrome characterized by increased vulnerability to stressors, as a result of cumulative decline in different physiological systems occurring during the lifetime [1]. It is associated with increased risk of adverse health-related outcomes in older persons including falls, disability, hospitalization, and mortality [2,3]. This syndrome is triggering considerable attention not only in clinics and research, but also among public health authorities [4]. In fact, acting on frailty may positively influence the aging process of the older individual, resulting in improved quality of life and reduced costs of care [5].

Several operational definitions have been developed in order to translate into practice the theoretical concept of frailty. To date, most of the available definitions have privileged the physical dimension of the frailty syndrome, mostly relying on symptoms and signs like weight loss, muscle weakness, slow gait speed, and sedentary behavior [6]. Nevertheless, a growing body of evidence is suggesting that other factors (e.g., nutrition [7], mental health [8], and cognition [9▪]) may influence the frailty status of the older individual as well. In particular, cognition is increasingly recognized as a fundamental determinant of the individual's vulnerability and resiliency to stressors [10]. In fact, impaired cognitive functioning may affect the adoption of healthy lifestyle behaviors and the adherence to preventive and therapeutic interventions. Moreover, it is strongly related to socioeconomic disadvantage with possible limitations in access to healthcare services [10].

The relevant role that cognition may play in the determination of the elder's risk profile has led some authors at proposing the addition of a cognitive assessment within the operational definitions of frailty. Cognitive impairment has been

[a]Department of Neurology and Psychiatry, Memory Clinic, 'Sapienza' University, Rome, Italy, [b]Gérontopôle, Centre Hospitalier Universitaire de Toulouse, [c]Inserm UMR1027 and [d]Université de Toulouse III Paul Sabatier, Toulouse, France

Correspondence to Dr Marco Canevelli, Department of Neurology and Psychiatry, Memory Clinic, 'Sapienza' University, Viale dell'Università 30, 00185 Rome, Italy. Tel: +39 6 49914604; fax: +39 6 49914604; e-mail: marco.canevelli@gmail.com

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KEY POINTS

- The relationship between frailty and cognition is being increasingly investigated.
- Available evidence from the observational studies indicates that frail individuals have lower cognitive performance than nonfrail persons and increased risk of cognitive decline.
- Randomized controlled trials (RCTs) are needed in order to gain insights about the interactions between frailty and cognition.
- The implementation of the novel concept of 'cognitive frailty' may provide useful insights for better planning and designing preventive interventions and therapeutic actions against disability.

independently associated with several adverse outcomes (e.g., falls, hospitalization, and mortality), even when specific conditions (e.g., dementia and mild cognitive impairment [MCI]) were considered [11]. Cross-sectional studies have documented high rates of cognitive impairment in frail compared with robust older persons, being observed in nearly 20% of frail individuals living in the community [12]. Consistently, longitudinal studies have repeatedly reported that physical frailty predicts the onset of future cognitive decline and incident dementia [9▪]. The reciprocal association (i.e., cognitive impairment predicts future frailty) has also been observed [13]. In addition to these epidemiological evidences, various studies have suggested that several pathophysiological pathways (e.g., chronic inflammation, hormonal pathway, and vascular disease) and nutritional factors and deficiencies [14] (e.g., vitamin D, Mediterranean diet and olive oil, vitamin B12 and folate, and aerobic exercise) may be potentially shared by frailty and cognitive impairment. Nevertheless, there is still a lack of experimental evidence to support these observations [9▪].

As proof of the increased interest toward the relationship between frailty and cognition, a novel concept of 'cognitive frailty' has recently been proposed by an international panel of experts [15▪]. The novel construct of 'cognitive frailty' was defined as a clinical condition characterized by the simultaneous presence of both physical frailty and cognitive impairment, occurring in the absence of overt dementia diagnosis or underlying neurological conditions. In other words, cognitive frailty was conceptualized as a non-neurodegenerative cognitive impairment sustained by (or associated with) physical frailty. The authors admitted that it may simply indicate an early sign of future dementia (i.e., anticipation of a still unknown diagnosis). At the same time, older persons with cognitive impairment unrelated to a neurodegenerative disease (but caused by a physical condition) may benefit from interventions against frailty and reduce their overall global risk profile (including possible amelioration of the cognitive status). Such differentiation between the cognitive impairment due to neurological vs. physical causes may indeed help at improving the design of personalized interventions in the heterogeneous elderly population.

In view of the growing interest on this topic, the aim of the present study is to provide a comprehensive, updated review of the recent literature (published over the last 12 months) exploring the relationship between frailty and cognition.

LITERATURE SEARCH

We performed a Medline literature search of studies published over the last 12 months (from 1 June 2013 to 31 May 2014) using the Medical Subject Heading (MeSH) terms 'Human' and 'English' combined with the following terms: ('frailty' OR 'frail') AND ('cognitive' OR 'cognition' OR 'dementia' OR 'Alzheimer' OR 'memory' OR 'brain'). Overall, 102 articles were retrieved. Based on titles and abstracts, a first set of articles ($n=65$) was excluded because it was clearly out of the specific aims of the present study. For the remaining studies, full articles were obtained and evaluated. Thus, 14 studies were finally selected [16–29].

RECENT EVIDENCE ON FRAILTY AND COGNITION

In this section, the studies retained for the present review will be presented as grouped into three categories: longitudinal studies, cross-sectional studies, and studies incorporating cognition in the operational definition of frailty. No RCT was instead found.

Longitudinal studies

Over the last year, three studies have explored the longitudinal relationship between frailty and cognitive functioning (Table 1). In a large study of 2619 community-dwelling older adults, physical frailty (operationalized according to a modified version of the frailty phenotype [6]) was associated with a 2.57-fold increased risk of developing non-Alzheimer's disease dementia (mean follow-up of 6.5 years) [18]. Conversely, frailty was not statistically associated with incident Alzheimer's disease. Interestingly, the association between frailty and dementia was found to vary according to the

Table 1. Studies exploring the relationship between frailty and cognition published over the last 12 months

Reference	Study sample	Setting	Definition of frailty	Cognitive assessment[a]	Main results
Longitudinal studies					
Alencar *et al.* [16]	$n = 207$ older adults (aged ≥65 years) with or without cognitive impairment at baseline	Community follow-up: 12 months	Frailty phenotype[b]	BCSB CDR MMSE	Frailty at baseline was associated with cognitive decline as measured by MMSE score modifications at the end of the follow-up (RR 4.6; 95% CI 1.93–11.2)
Espinoza *et al.* [17]	$n = 749$ older adults (aged 65–80 years)	Community follow-up: 8.2 ± 2.9 years	Frailty phenotype	MMSE	Frailty was associated with increased risk of mortality (hazard ratio 2.13; 95% CI 1.45–3.14) When adjusting for cognitive impairment and depressive symptoms, this association was no longer present (hazard ratio 1.44; 95% CI 0.91–2.28)
Gray *et al.* [18]	$n = 2619$ nondemented older adults (aged ≥65 years)	Community follow-up: 6.5 ± 3.9 years	Modified frailty phenotype	CASI Comprehensive neuropsychological test battery	Frailty was associated with increased risk for non-Alzheimer's disease dementia (hazard ratio 2.57; 95% CI 1.08–6.11)
Cross-sectional studies					
Alencar *et al.* [16]	$n = 207$ older adults (aged ≥65 years) with or without cognitive impairment at baseline	Community	Frailty phenotype	BCSB CDR MMSE	Frail individuals exhibited a greater frequency of cognitive impairment and lower MMSE scores than prefrail and nonfrail participants ($P < 0.001$)
Alexandre Tda *et al.* [19]	$n = 1413$ older adults (aged ≥60 years)	Community	Frailty phenotype	MMSE	Cognitive decline (i.e., MMSE ≤18) was associated with weakness (OR 4.20; 95% CI 1.66–10.61) and slowness (OR 2.55; 95% CI 1.01–6.44) in male participants
McGough *et al.* [20]	$n = 201$ sedentary older adults (aged ≥70 years) diagnosed with aMCI	Residential facilities	Physical slowness (gait speed) Low physical activity (self-report) Muscle weakness (grip strength)	ADAS-Cog CDR MMSE TMT-A/B WMS-R LMI	Slower gait speed was associated with greater cognitive impairment as measured by ADAS-Cog score ($\beta = -0.19$; $P = 0.008$)

(*Continued*)

Table 1 (*Continued*)

Reference	Study sample	Setting	Definition of frailty	Cognitive assessment[a]	Main results
Moreira *et al.* [21]	$n=754$ nondemented older adults (aged ≥65 years)	Community	Frailty phenotype	MMSE	Frail was associated with lower cognitive performance as measured by MMSE score (OR 0.79; 95% CI, 0.76–0.83)
O'Halloran *et al.* [22]	$n=4317$ individuals aged ≥50 years	Community	Modified frailty phenotype	CRT CTT SART	Prefrailty and frailty were associated with reduced sustained attention performance and variability
Polidoro *et al.* [23]	$n=140$ consecutive individuals (aged 56–96 years) admitted to an Internal Medicine ward	Hospital ward	Frailty index (34 variables included)	MMSE	Frail patients had lower MMSE scores than nonfrail individuals ($P<0.01$) A negative correlation between MMSE scores and frailty index (rho = -0.517, $P<0.001$) was found
Shimada *et al.* [24]	$n=5104$ older adults (aged ≥65 years)	Community	Frailty phenotype	MMSE NCGG-FAT	The combined prevalence of frailty and MCI was 2.7% A significant association between frailty and MCI was observed (OR 2.0; 95% CI 1.5–2.5)

ADAS-Cog, Alzheimer's Disease Assessment Scale-Cognitive subscale; aMCI, amnestic mild cognitive impairment; BCSB, Brief Cognitive Screening Battery; CASI, Cognitive Abilities Screening Instrument; CDR, Clinical Dementia Rating; CI, confidence interval; CRT, choice reaction time; CTT, Color Trails Test; MMSE, Mini Mental State Examination; NCGG-FAT, National Center for Geriatrics and Gerontology-Functional Assessment Tool; RR, relative risk; SART, Sustained Attention to Response Task; TMT-A/B, Trail Making Test part A and B; WMS-R LMI, Wechsler Memory Scale-Revised Logical Memory I.

[a]Cognitive functions and domains assessed by the adopted cognitive tools and measures: ADAS-Cog: global cognitive performance; BCSB: global cognitive performance; CASI: global cognitive performance; CDR: dementia severity; CRT: concentration and cognitive processing speed; CTT: executive functions; MMSE: global cognitive performance; NCGG-FAT: global cognitive performance; SART: sustained attention; TMT-A/B: attention and executive functions; WMS-R LMI: immediate and delayed recall.

[b]Frailty phenotype [6]: presence of at least three of five signs/symptoms including poor muscle strength, slow gait speed, unintentional weight loss, exhaustion, and sedentary behavior.

baseline cognitive scores, being restricted only to participants with higher basal cognitive performance (upper three quartiles of global cognitive functioning). Among the individual components of frailty, only slowness (as measured by reduced walking speed) was significantly related to non-Alzheimer's disease dementia (hazard ratio 2.13; 95% confidence interval 1.09–4.16). In another study [16], physical frailty (always defined according to the criteria proposed by Fried *et al.* [6]) was found to predict subsequent cognitive decline (measured using the Mini Mental State Examination [MMSE]) after 12 months of follow-up. On the contrary, no association was found between frailty and dementia severity as measured by the Clinical Dementia Rating, and between frailty and incident cognitive decline (defined as testing positive at the end of follow-up on both the MMSE and the Brief Cognitive Screening Battery). Finally, in the last study [17], the relationship between frailty and mortality was investigated. In a sample of 749 older adults living in the community, frailty was significantly associated with mortality over a mean follow-up of 8.2 years. Nevertheless, this association was no longer significant after adjustment for cognitive impairment (assessed by the MMSE) and depressive symptoms. Thus, the authors concluded that both cognitive and mood factors may play a role in mediating the association between frailty and mortality.

Cross-sectional studies

Seven cross-sectional studies were identified (Table 1). Three studies described the association between physical frailty and global cognitive performance assessed by the MMSE [16,21,23]. Overall, frail individuals were found to exhibit lower MMSE scores compared with nonfrail individuals. Physical frailty was also associated with a higher prevalence of cognitive impairment (defined as a MMSE score $\leq$18) [16]. Moreover, a negative correlation between the MMSE score and frailty severity (measured by a Frailty Index) was observed [23]. Two out of these three studies enrolled community-dwelling older adults. In the other one [23], individuals admitted to an internal medicine hospital ward were consecutively recruited. In another study conducted on 201 sedentary elderly persons living in residential facilities, the association between individual frailty components and cognitive performance was specifically explored [20]. Slow gait speed was found to be associated with the severity of cognitive impairment (measured by the Alzheimer's Disease Assessment Scale-Cognitive subscale). Moreover, slow usual gait speed was associated with lower performance in the cognitive dimensions of attention, executive functions, and immediate recall. Higher levels of physical activity were associated with higher scoring on memory and executive functions tests, whereas grip strength was only associated with attention. Accordingly, in a large study involving 4317 individuals aged more than 50 years, both prefrailty and frailty were shown to be strongly associated with declining sustained attention [22]. Shimada *et al.* [24] estimated the prevalence of physical frailty and MCI in a sample of 5104 Japanese older adults living in the community. The combined prevalence of frailty (defined according to the frailty phenotype) and MCI was 2.7%. A significant association between frailty and MCI was observed. Finally, only one study explored the reciprocal association between cognition and physical frailty [19]. Cognitive decline (defined as a MMSE score $\leq$18) was found to be associated with the individual frailty components of weakness and slowness among male participants, whereas no significant association was found in women.

Studies incorporating cognition in the operational definition of frailty

In the last 12 months, five studies included cognition in the operational definitions and screening adopted for the identification of frail individuals (Table 2). In two studies [25,26], the cognitive assessment simply consisted of a single question referring to the presence of cognitive complaints or to a previous dementia diagnosis. Patel *et al.* [27] included impaired cognition in a Frailty Index composed of 19 clinical deficits. In another study, cognition was assessed by the use of a validated screening instrument evaluating global cognitive functioning (i.e., the Short Portable Mental Status Questionnaire) [28]. Finally, in the last study, a multistep cognitive assessment consisting of both open questions and structured cognitive testing was included in the screening of frailty [29]. Notably, the ability of 129 possible combinations of seven frailty markers (cognition, energy, mobility, mood, nutrition, physical activity, and strength) in predicting disability among 6657 older adults followed up for 6 years was also investigated [28]. The frailty 'model' with the best predictive fit was found to be composed of the five markers: cognition, mobility, nutrition, physical activity, and strength.

DISCUSSION

The present review was aimed at retrieving and discussing the recent evidence concerning the relationship between frailty and cognition. Overall, relatively few studies addressed this topic over the

Table 2. Studies including cognition in the operational definition and screening of frailty

Reference	Study sample	Frailty operationalization/screening	Cognitive assessment	Main results
Aaldriks *et al.* [25]	*n* = 143 older adults (aged ≥70 years) with colorectal cancer	GFI: frailty screening tool combining 15 physical, cognitive, emotional, and psychosocial items	Single question: 'Does the patient have any complaints about his/her memory or is the patient known to have a dementia syndrome?' No or sometimes = 0; yes = 1	Frailty was associated with an increased mortality risk in patients who underwent palliative chemotherapy (hazard ratio 2.72; 95% CI: 1.58–4.69)
Aaldriks *et al.* [26]	*n* = 55 older adults (aged ≥70 years) with advanced breast cancer	GFI: frailty screening tool combining 15 physical, cognitive, emotional, and psychosocial items	Single question: 'Does the patient have any complaints about his/her memory or is the patient known to have a dementia syndrome?' No or sometimes = 0; yes = 1	Frailty was associated with increased mortality risk (hazard ratio 3.40; 95% CI: 1.62–7.10)
Patel *et al.* [27]	*n* = 481 older adults (aged 60–105 years) with low-energy femoral neck fractures	Frailty Index (19 clinical deficits)	Absence/presence of impaired cognition (adjudicated diagnosis of dementia)	Higher modified frailty index scores were associated with increased 1-year (OR 4.97; 95% CI 3.06–8.09) and 2-year (OR 4.01; 95% CI 2.61–6.16) mortality risk
Sourial *et al.* [28]	*n* = 6657 older adults (aged ≥65 years) followed up for 6 years	Different combinations of seven frailty markers (cognition, energy, mobility, mood, nutrition, physical activity, strength)	Modified SPMSQ	The best frailty model in predicting disability included cognition, mobility, nutrition, physical activity and strength
Van Kempen *et al.* [29]	*n* = 587 older adults (aged 76.8 ± 4.8 years) Validation study	EASY-Care TOS: two-step frailty screening based on the individual functioning in different somatic, psychological, and social domains	First step (conducted by general practitioners): history of cognitive disturbances Second step (performed by a primary care nurse): 'Do you have any concerns about memory loss or forgetfulness?' 'Do you have problems with brain functions as memory, attention and thinking?' Memory test (6-CIT)	The EASY-Care TOS correlated better with the frailty index (0.63) than with the frailty phenotype (0.52)

6-CIT, 6-items Cognitive Impairment Test; CI, confidence interval; GFI, Groningen Frailty Indicator; OR, odds ratio; SPMSQ, Short Portable Mental Status Questionnaire; TOS, Two-step Older persons Screening.

last 12 months. The overwhelming majority of the selected studies assessed frailty using the criteria proposed by Fried *et al.* [6]. This is not surprising because these studies were primarily aimed at exploring the physical dimension of the frailty syndrome. Most of the works adopted the measure of global cognitive functioning (in particular, the MMSE) for assessing cognition, whereas only few use comprehensive neuropsychological test batteries. The sample populations mainly composed of community-dwelling older adults, whereas two studies enrolled institutionalized [20] and hospitalized [23] individuals.

It is noteworthy that no RCT was found, underlining the scarcity of available evidence in the field. In fact, RCTs could provide useful information concerning the possibility of positively affecting the frailty syndrome by acting of cognition and improving cognitive impairment by targeting the physical components of frailty. Also, these studies may produce the first evidences about the actual 'existence' of the recently proposed concept of 'cognitive frailty' and its potential for reversibility. As proof of the relevance of this topic (i.e., the possibility of simultaneously and reciprocally targeting the physical and cognitive trajectories of older adults), several RCTs have been recently conducted to investigate the efficacy of physical interventions in improving cognitive functioning among healthy elderly individuals [30▪,31]. These studies have mostly shown that physical exercise may result in enhanced cognitive performance. In parallel, some RCTs are currently ongoing aiming at evaluating the effectiveness of multidomain interventions (combining physical activity with nutritional advices, leisure activities, vascular care, and cognitive training) in preventing cognitive decline among older adults at risk of dementia [32]. Nevertheless, to date, no study has specifically targeted populations of frail elderly individuals.

Among the 14 retained studies, only five [16,18,20,22,24] were specifically focused on the interactions between physical frailty and cognitive functioning. The remaining articles were primarily centered on the identification and characterization of the frailty syndrome among elderly individuals, and included measures of cognitive performance only as part of the comprehensive, multidimensional assessment of participants. The main findings of the selected studies appeared to be mainly confirmatory of the previous evidence [9▪,11]. In longitudinal studies, physical frailty was found to predict the incidence of cognitive impairment and dementia in older individuals. Cross-sectional studies showed that frail individuals have lower cognitive performance compared with nonfrail persons. The relatively most novel evidence comes from the few studies examining the association between frailty and specific cognitive functions and domains, showing a significant impairment of attention and executive functions [20,22]. Previous studies conducted on this topic had produced conflicting results, showing that frailty (and its individual components) was associated with the additional involvement of other cognitive functions such as processing speed, orientation, and verbal fluency [9▪]. Finally, we found several studies including measures of cognitive performance in the adopted operational definitions of frailty.

Interestingly, one study has indirectly increased the knowledge regarding the recently proposed construct of 'cognitive frailty' that has been conceptualized as the simultaneous occurrence of both physical frailty and cognitive impairment in the absence of an overt dementia condition [15▪]. In fact, though not directly mentioning this novel concept, Shimada *et al.* [24] observed a combined prevalence of frailty and MCI of 2.7% in a large sample population. To our knowledge, this represents one of the first estimates of the prevalence of cognitive frailty and should represent a reference for future research on this topic.

CONCLUSION

During the last 12 months, a limited number of studies investigated the relationship between frailty and cognition. The findings of these studies were mainly confirmatory of the previous evidence. Moreover, no RCT was found, indicating an almost complete lack of evidence on this topic. These studies are strongly advocated because they may provide important insights for better planning and designing preventive interventions and therapeutic actions against disability. Moreover, they could consent to explore the recently proposed concept of 'cognitive frailty'. In parallel, investigating the interactions between the physical components of frailty and the specific cognitive functions and domains may represent a useful approach to achieve a better comprehension of the frailty syndrome.

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Conflicts of interest

Matteo Cesari has received a grant for a research project (unrelated to the present study) from Pfizer. He has also served as consultant for the preparation of education material for Novartis, France, and conducted oral *presentations at scientific meetings for Nestlé (all unrelated to the present study). The other authors have no conflicts of interest to disclose.*

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
▪ of special interest
▪▪ of outstanding interest

1. Clegg A, Young J, Iliffe S, *et al.* Frailty in elderly people. Lancet 2013; 381:752–762.
2. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. J Am Geriatr Soc 2010; 58:681–687.
3. Ensrud KE, Ewing SK, Taylor BC, *et al.* Frailty and risk of falls, fracture, and mortality in older women: the study of osteoporotic fractures. J Gerontol A Biol Sci Med Sci 2007; 62:744–751.
4. Morley JE, Vellas B, van Kan GA, *et al.* Frailty consensus: a call to action. J Am Med Dir Assoc 2013; 14:392–397.
5. Cesari M, Vellas B, Gambassi G. The stress of aging. Exp Gerontol 2013; 48:451–456.
6. 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.
7. Kelaiditi E, van Kan GA, Cesari M. Frailty: role of nutrition and exercise. Curr Opin Clin Nutr Metab Care 2014; 17:32–39.
8. Brown PJ, Roose SP, Fieo R, *et al.* Frailty and depression in older adults: a high-risk clinical population. Am J Geriatr Psychiatry 2013; 22:1083–1095.
9. ▪ Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment – a review of the evidence and causal mechanisms. Ageing Res Rev 2013; 12:840–851.

This review summarizes the available evidence concerning the relationship between frailty and cognition. Moreover, possible mechanisms sustaining their interaction are discussed.

10. Canevelli M, Troili F, Bruno G. Reasoning about frailty in neurology: neurobiological correlates and clinical perspectives. J Frailty Aging 2014; 3:18–20.
11. Houles M, Canevelli M, Abellan van Kan G, *et al.* Frailty and cognition. J Frailty Aging 2012; 1:56–63.
12. Avila-Funes JA, Amieva H, Barberger-Gateau P, *et al.* Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the three-city study. J Am Geriatr Soc 2009; 57:453–461.
13. Raji MA, Al Snih S, Ostir GV, *et al.* Cognitive status and future risk of frailty in older Mexican Americans. J Gerontol A Biol Sci Med Sci 2010; 65:1228–1234.
14. Shah R. The role of nutrition and diet in Alzheimer disease: a systematic review. J Am Med Dir Assoc 2013; 14:398–402.
15. ▪ Kelaiditi E, Cesari M, Canevelli M, *et al.* Cognitive frailty: rational and definition from an (I.A.N.A./I.A.G.G.) International Consensus Group. J Nutr Health Aging 2013; 17:726–734.

In this consensus study from an international panel of experts, the first definition of 'cognitive frailty' is provided.

16. Alencar MA, Dias JMD, Figueiredo LC, Dias RC. Frailty and cognitive impairment among community-dwelling elderly. Arq Neuropsiquiatr 2013; 71:362–367.
17. Espinoza SE, Jung I, Hazuda H. The Hispanic paradox and predictors of mortality in an aging biethnic cohort of Mexican Americans and European Americans: the San Antonio Longitudinal Study of Aging. J Am Geriatr Soc 2013; 61:1522–1529.
18. Gray SL, Anderson ML, Hubbard RA, *et al.* Frailty and incident dementia. J Gerontol A Biol Sci Med Sci 2013; 68:1083–1090.
19. Alexandre Tda S, Corona LP, Nunes DP, *et al.* Similarities among factors associated with components of frailty in elderly: SABE Study. J Aging Health 2014; 26:441–457.
20. McGough EL, Cochrane BB, Pike KC, *et al.* Dimensions of physical frailty and cognitive function in older adults with amnestic mild cognitive impairment. Ann Phys Rehabil Med 2013; 56:329–341.
21. Moreira VG, Lourenço RA. Prevalence and factors associated with frailty in an older population from the city of Rio de Janeiro, Brazil: the FIBRA-RJ Study. Clinics (São Paulo) 2013; 68:979–985.
22. O'Halloran AM, Finucane C, Savva GM, *et al.* Sustained attention and frailty in the older adult population. J Gerontol B Psychol Sci Soc Sci 2014; 69:147–156.
23. Polidoro A, Stefanelli F, Ciacciarelli M, *et al.* Frailty in patients affected by atrial fibrillation. Arch Gerontol Geriatr 2013; 57:325–327.
24. 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.
25. Aaldriks AA, van der Geest LGM, Giltay EJ, *et al.* Frailty and malnutrition predictive of mortality risk in older patients with advanced colorectal cancer receiving chemotherapy. J Geriatr Oncol 2013; 4:218–226.
26. Aaldriks AA, Giltay EJ, le Cessie S, *et al.* Prognostic value of geriatric assessment in older patients with advanced breast cancer receiving chemotherapy. Breast 2013; 22:753–760.
27. Patel KV, Brennan KL, Brennan ML, *et al.* Association of a modified frailty index with mortality after femoral neck fracture in patients aged 60 years and older. Clin Orthop 2014; 472:1010–1017.
28. Sourial N, Bergman H, Karunananthan S, *et al.* Implementing frailty into clinical practice: a cautionary tale. J Gerontol A Biol Sci Med Sci 2013; 68:1505–1511.
29. Van Kempen JAL, Schers HJ, Melis RJF, Olde Rikkert MGM. Construct validity and reliability of a two-step tool for the identification of frail older people in primary care. J Clin Epidemiol 2014; 67:176–183.
30. ▪ Kamegaya T, Araki Y, Kigure H, Yamaguchi H; Long-Term-Care Prevention Team of Maebashi City. Twelve-week physical and leisure activity programme improved cognitive function in community-dwelling elderly subjects: a randomized controlled trial. Psychogeriatrics 2014; 14:47–54.

In this randomized controlled trial enrolling healthy elderly individuals, a 12-week intervention consisting of physical and leisure activities resulted in an improved cognitive functioning and quality of life.

31. Maki Y, Ura C, Yamaguchi T, *et al.* Effects of intervention using a community-based walking program for prevention of mental decline: a randomized controlled trial. J Am Geriatr Soc 2012; 60:505–510.
32. Kivipelto M, Solomon A, Ahtiluoto S, *et al.* The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER): study design and progress. Alzheimers Dement 2013; 9:657–665.