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Depression and frailty in later life: a synthetic review

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Abstract

Background—Many of the symptoms, consequences, and risk factors for frailty are shared with late-life depression. However, thus far, few studies have addressed the conceptual and empirical interrelationships between these conditions. This review synthesizes existing studies that examined depression and frailty among older adults and provides suggestions for future research.

Methods—A search was conducted using PubMed for publications through 2010. Reviewers assessed the eligibility of each report and abstracted information on study design, sample characteristics, and key findings, including how depression and frailty were conceptualized and treated in the analysis.

Results—Of 133 abstracted articles, 39 full-text publications met inclusion criteria. Overall, both cross-sectional (n = 16) and cohort studies (n = 23) indicate that frailty, its components, and functional impairment are risk factors for depression. Although cross-sectional studies indicate a positive association between depression and frailty, findings from cohort studies are less consistent. The majority of studies included only women and non-Hispanic Whites. None used diagnostic measures of depression or considered antidepressant use in the design or analysis of the studies.

Conclusions—A number of empirical studies support for a bidirectional association between depression and frailty in later life. Extant studies have not adequately examined this relationship among men or racial/ethnic minorities, nor has the potential role of antidepressant medications been explored. An interdisciplinary approach to the study of geriatric syndromes such as late-life depression and frailty may promote cross-fertilization of ideas leading to novel conceptualization of intervention strategies to promote health and functioning in later life.

Keywords

depression; disability; aging; frailty; comorbidity

Introduction

In the past decade, a body of literature has developed on the characteristics of frailty, defined as a state or indication of being vulnerable to declining health in later life (Rockwood *et al.*, 1994; Fried *et al.*, 2001; Cigolle *et al.*, 2009). Currently, there are three distinct conceptual models of frailty (Cigolle *et al.*, 2009): the cumulative burden model (Rockwood *et al.*, 1994), in which frailty is modeled as the sum of diseases and health conditions, including psychiatric conditions, over the lifespan; the functional domains model (Strawbridge *et al.*, 1998), in which frailty is modeled as the accumulation in deficits in

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physical (i.e., balance), nutritive (i.e., weight loss), cognitive (i.e., memory impairments), and sensory (i.e., vision loss) domains; and the biological syndrome model (Fried *et al.*, 2001), in which frailty is modeled as syndrome characterized by weight loss, exhaustion, inactivity, slowness, and weakness (Fried *et al.*, 2001), akin to geriatric failure-to-thrive (Committee on a National Research Agenda on Aging, 1991). Frailty has also been linked to sacropenia (Frisoli *et al.*, 2011), vitamin D deficiency (Ensrud *et al.*, 2010), and related health conditions. Depending on the index used, the prevalence of frailty among adults 65 years and older is estimated to be 10.9%–20.3% (Cigolle *et al.*, 2009). Frailty is more common among women, thosewho are socially isolated (Rockwood *et al.*, 2004), and those who live in socioeconomically disadvantaged communities (Lang *et al.*, 2009). Support for the clinical and public health relevance of the frailty construct has been derived from its utility in predicting functional decline, disability, fracture, and mortality; it has been argued that frailty may be a pre-clinical, and potentially reversible, indicator of health status for older adults (Woods *et al.*, 2005; Ensrud *et al.*, 2007).

Parallel to this work on frailty, gerontologists and psychiatrists have characterized variation in the etiology and presentation of depression in later life. In 1994, Gallo and colleagues determined empirically that older adults are less likely to report symptoms of dysphoria but generally not other symptoms of depression (i.e., fatigue, guilt, appetite disturbances) relative to younger adults (Gallo *et al.*, 1994). They later described this phenomenon as “depression without sadness” (Gallo & Rabins, 1999) and argued that in the clinical context, “Older patients with depression may present with somatic complaints for which a medical etiology cannot be found or that are disproportionate to the extent of medical illness.” Other investigators have noted the difficulty in diagnosing depression in the context of comorbid medical conditions that are common in later life (Katon & Sullivan, 1990; Birrer & Vemuri, 2004), suggesting that one reason for the lower prevalence of depression among older adults is that this condition is often confused for or conflated with physical decline. One result of this work has been the development of psychiatric assessments designed specifically for older adults and for those with comorbid neurological conditions, including the Geriatric Depression Scale (GDS) (Yesavage *et al.*, 1983) and the Cornell Scale for Depression in Dementia (Alexopoulos *et al.*, 1988). Relative to traditional structured diagnostic depression measures (e.g., Schedules for Clinical Assessment in Neuropsychiatry (SCAN), Structured Clinical Interview for DSM (SCID), Diagnostic Interview Schedule (DIS), Composite International Diagnostic Inventory (CIDI)), these instruments emphasize vegetative and functional aspects of depression beyond the syndrome criteria set out in the Diagnostic and Statistical Manual of Mental Disorders (i.e., the GDS includes items Do you feel full of energy? Do you enjoy getting up in the morning?).

These conceptualizations of depression in later life share many characteristics with frailty. Depression in later life is predictive of many of the same kinds of out-comes as frailty, including cognitive impairment (Andersen *et al.*, 2005), disability (Bruce, 2001), fracture (Whooley *et al.*, 1999), and mortality (Rovner *et al.*, 1991; Laursen *et al.*, 2007). However, as yet, there has been relatively little attention paid in the literature as to how these two syndromes may be related. Because health conditions in later life are often predicted by a shared set of risk factors, Tinetti and colleagues have explicitly called for a unified approach to conceptualizing geriatric syndromes (Tinetti *et al.*, 1995). Similarly, in a recent editorial, Katz noted that “Depending on the definitions [of frailty] used, it is possible to make a case for each of these conditions [depression and frailty] as a cause, consequence, or comorbidity of the other. It is also possible to argue for their congruence.” (Katz, 2004). Despite these calls, few studies have rigorously examined the interrelationships between depression and frailty syndromes.

The motivations of this paper are to link these parallel bodies of literature by reviewing existing studies that address the interrelationships between depression and frailty, to suggest conceptual and methodological approaches to synthesize these constructs, and to identify pressing areas in need of additional research in this context.

Methods

Literature searches were conducted in PubMed with the assistance of a research librarian using combinations of the Medical Subject Heading (MeSH) terms “depression,” “depressive disorder,” “depressive disorder, major,” “aging,” and the word “frailty.” The term “frailty” is not currently indexed as a MeSH term, and therefore, searches were conducted using the related MeSH terms “frail elderly,” “fatigue,” “mobility limitation,” “lethargy,” “disability,” “atrophy,” “movement,” “postural balance,” and “muscle weakness.” The search was restricted to papers published in print or online prior to 1 October 2010 and in English. The reference lists of the citations identified in these searches, including review articles, were also examined. General population-based samples are the focus of this review because these study designs provide the best methodology for understanding the natural history of frailty and depression; clinic-based populations probably reflect a host of selection factors that make them inappropriate for exploring these epidemiologic questions (Schwartzbaum *et al.*, 2003).

Selection of studies

The searches returned 573 unique, empirical research articles, from which a group of four reviewers selected 133 for full-text abstraction (Supplemental Figure 1). To characterize the study population and main findings, the following information was extracted fromeach article: author, year of publication, geographic location, study design (i.e., cross-sectional, cohort), sample characteristics (i.e., age, sex, racial/ethnic composition), measure of frailty, the measure of depression or depressive symptoms, and a qualitative summary of the key findings. Studies were too varied in their analytic approach and reporting of results to extract a quantitative effect measure or to summarize the results in a formal (e.g., meta-analytic) manner. A handful of studies selected the entire population on thebasis of psychiatric (e.g.,Pijpers *et al.*, 2009) or frailty status (e.g., Smith Barusch *et al.*, 1999; Landi *et al.*, 2005). These reports were excluded because all study participants displayed some characteristics of frailty or disability, which precluded an examination of the differential relationship between depression and frailty. Several other reports were excluded because the study sample was selected from a clinic setting, including nursing homes (e.g., Parmelee *et al.*, 1998; Jongenelis *et al.*,2004; Onishi et al., 2004) or from a specific patient population (e.g., stroke or cancer patients). Two studies were excluded because they were randomized controlled trials rather than community-based cohorts (Fitzpatrick *et al.*, 2007; Gitlin *et al.*, 2007). Two independent reviewers examined the abstractions and identified 39 unique articles for inclusion in this review.

Results

Cross-sectional studies

As shown in Table 1, the majority of population-based cross-sectional studies reported a positive association between depressive symptomatology and frailty status. Six studies did not report the racial/ethnic composition of the sample, but the all those that did included primarily Whites, and three included only Asians. Most studies were primarily composed of or included only women, and only the study conducted by Blyth *et al.* (2008) included exclusively men. All but one (Cummings *et al.*, 2003) of the cross-sectional studies reported a statistically significant positive association between frailty and depressive

symptomatology that persisted after adjustment for covariates, whether depression was examined as the determinant or consequence of frailty. For example, Hybels *et al.* (2001) reported that persons with elevated depressive symptoms were over five times as likely to have activities of daily living (ADL) limitations as persons with-out depression (Hybels *et al.*, 2001). Several reports examined factors that influenced the depression–frailty relationship, including social support (Newsom and Schulz, 1996; Cummings *et al.*, 2003), sense of mastery (Jang *et al.*, 2002), religiosity (Cummings *et al.*, 2003), and perceived health (Jang *et al.*, 2006).

A wide range of metrics were used to index frailty, including traditional disability indices (e.g., ADL/instrumental activities of daily living scales) (Mirowsky and Ross, 1992; Davidson *et al.*, 1994; Newsom and Schulz, 1996; Prince *et al.*, 1997; Hybels *et al.*, 2001; Jang *et al.*, 2002; Cummings *et al.*, 2003; Stek *et al.*, 2004), history or fear of falling (Deshpande *et al.*, 2008; Wada *et al.*, 2008), number of medical conditions (Hybels *et al.*, 2001), cognitive functioning (Hajjar *et al.*, 2009), and specific frailty indices (Blyth *et al.*, 2008; Deshpande *et al.*, 2008; Chang *et al.*, 2010; Chen *et al.*, 2010). Three studies incorporated objective measures of physical performance (e.g., chair stands, grip strength) (Newsom and Schulz, 1996; Deshpande *et al.*, 2008; Hajjar *et al.*, 2009). Two-thirds (10 of 16) of studies used the Centers for Epidemiologic Studies–Depression (CES-D) scale to index depressive symptomatology (Mirowsky and Ross, 1992; Davidson *et al.*, 1994; Newsom and Schulz, 1996; Broe *et al.*, 1999; Hybels *et al.*, 2001; Cummings *et al.*, 2003; Jang *et al.*, 2006; Deshpande *et al.*, 2008; Hajjar *et al.*, 2009; Chen *et al.*, 2010). No studies that met the inclusion criteria used diagnostic instruments. One notable exception to the traditional regression approach used by these studies was a report by Hajjar and colleagues (2009) that examined the confluence of depressive symptoms, cognitive status, and slowness using latent variable modeling (Hajjar *et al.*, 2009); they reported that the clustering of these characteristics was consistent with the notion that they describe a common geriatric syndrome.

Cohort studies

Table 2 illustrates prospective studies in which depression was studied as a risk factor for onset of frailty, and in which frailty was examined as a risk factor for onset or persistence of depressive symptoms. As shown by the top portion of Table 2, all studies reported a positive association between frailty with onset or worsening of depressive symptomatology at follow-up (Kennedy *et al.*, 1991; Ormel *et al.*, 2002; Taylor and Lynch, 2004; Yang & George, 2005; Han, 2006; Atkinson *et al.*, 2007; Schieman & Plickert, 2007; Gayman *et al.*, 2008; Chang *et al.*, 2009). For example, Yang and George (2005) reported that onset and persistence of frailty were stronger predictors of depressive symptoms than recovery from frailty over 6 years (Yang & George, 2005). As displayed in the lower portion of Table 2, most studies reported a significant positive association between depression and risk of frailty onset, at least in bivariate analyses (Buchner, 1996; Strawbridge *et al.*, 1998; Vaillant, 1998; Rantanen *et al.*, 2000; Sarkisian *et al.*, 2000; Mehta *et al.*, 2002; Avlund, 2006; Barry *et al.*, 2009). For example, Strawbridge *et al.* (1998) reported that persons with repeatedly elevated depressive symptoms were 3.2 times more likely to be frail at follow-up than those with no history of depression (Strawbridge *et al.*, 1998). However, studies were mixed as to whether depression was an independent risk factor for onset of frailty after accounting for overall health status (Hebert *et al.*, 1999; Ormel *et al.*, 2002; Avlund *et al.*, 2006; Gayman *et al.*, 2008; Xue *et al.*, 2008). For example, Avlund and colleagues reported that depressive symptoms were not significantly predictive of tiredness at 5-year follow-up after accounting for comorbidity, physical performance measures, and psychological factors, despite being significantly associated with tiredness at baseline (Avlund *et al.*, 2006). Hebert and colleagues did not find a significant association between depression and onset of frailty over

3 years in even bivariate analyses in their study of adults 75 years and older (Hebert *et al.*, 1999). Similarly, in 2007, Xue and colleagues reported that depression was not associated with onset of frailty but did predict frailty-free mortality over a 3-year period.

Three studies explicitly examined the bidirectional relationship between depression and frailty (Ormel *et al.*, 2002; Taylor and Lynch, 2004; Gayman *et al.*, 2008). In 2002, Ormel and colleagues reported that frailty was a stronger predictor of increasing depressive symptoms than baseline depression was of increasing frailty. Similarly, Gayman *et al.* (2008) found that although frailty was significantly associated with worsening of depression, depressive symptoms were only weakly predictive of functional decline over a 3-year period. In contrast, Chang *et al.* (2009) found that incident frailty was strongly associated with depressive symptoms at the time of frailty onset, but that frailty did not predict development of new depressive symptoms 6 months later.

As with the cross-sectional studies, a wide range of indices were used to measure frailty status, although four utilized specific syndrome criteria outlined by Fried *et al.* (2001) (Ostir *et al.*, 2004; Woods *et al.*, 2005; Xue *et al.*, 2008; Park-Lee *et al.*, 2009). Approximately 60% (14 of 23) of studies used the CES-D to index depressive symptomatology; no studies that met the inclusion criteria used diagnostic instruments. Six studies did not report the racial/ethnic composition of the sample; of the remainder, most did not include large samples of racial/ethnic minorities. No-table exceptions were the reports by Schieman and Plickert (2007), Yang and George (2005), Ostir *et al.*(2004), Gayman *et al.* (2008), Rantanen *et al.* (2000), and Taylor and Lynch (2004), which all used cohorts in which at least 40% of the sample was not White. There was some indication of heterogeneity in the association between depression and frailty across racial/ethnic groups; Schieman and Plickert (2007) reported that depressive symptoms were strongly associated with greater functional decline among Whites but not among Blacks.

Discussion

The primary findings from this review are as follows: (i) most studies report a positive, and potentially bidirectional, association between depressive symptoms and frailty status; (ii) few studies have examined the potential overlap between depression in late life and frailty, instead of treating them as independent geriatric syndromes; (iii) existing research is limited by the methods used to assess depression; (iv) no studies evaluated the role of medications to treat depression; and (v) few studies have included enough men or racial/ethnic minorities to examine variation in the depression–frailty relationship across these groups.

The results of this review have implications for both the construct validity and measurement of geriatric syndromes. These results underscore the relevance of considering the consequences of a narrowing between psychological and physical aspects of health—the notion that “mental health becomes health” (Katz, 1996; Schnittker, 2005)—for clinical care. In line with the notion that frailty reflects psychological and social elements of health above and beyond the burden of chronic medical conditions, the correspondence between self-rated health and burden of chronic physical conditions declines with age, whereas the correlation between self-rated health and depressive symptoms increases with age (Schnittker, 2005). Similarly, geriatric failure-to-thrive, although primarily characterized by nutritive and functional decline, also reflects an integration of physical, functional, social, and psychological aspects of health (Rocchiccioli & Sanford, 2009). Despite the 20 years since the Institute of Medicine report stating that geriatric failure-to-thrive is “often accompanied by dehydration, *depressive symptoms*, impaired immune function, and low cholesterol” (emphasis added) (Committee on a National Research Agenda on Aging, 1991), empirical investigations of the potential overlap in depressive symptomatology and geriatric

frailty syndromes remain scant. Consistent with a developmental approach to examining the etiology and consequences of psychopathology, research efforts must reflect the protean nature of the relationship between mental and physical aspects of health, both within individuals over the life course and across population groups.

The next implication for research concerns efforts to measure frailty and related geriatric syndromes in later life. As this review illustrates, there is wide variation in the metrics used to operationalize frailty, and these measurement differences probably hamper efforts to develop prevention and intervention programs because of ambiguity about the clinical target. The conceptual development of frailty as a syndrome may be informed by the prior empirical work in psychiatry on alternate presentations of depression in later life (e.g., depression without sadness, vegetative depression). Latent variable approaches, which explicitly account for measurement error in ways that simple sum scores cannot, have been successfully employed to assess depression in later life and frailty (Gallo *et al.*, 1994; Bandeen-Roche *et al.*, 2006); this approach is well suited to investigating potential construct overlap between depression and frailty but has not yet been applied to this measurement problem. There is also a clear need to understand and explicitly assess how the behavioral signs of psychopathology (i.e., sleeping disturbances) interrelate with symptoms of frailty and related geriatric syndromes (i.e., fatigue), both from diagnostic and clinical care standpoints (Simon *et al.*, 1999; Dowrick *et al.*, 2005).

The limitations of the measurement of depression in these studies must be considered. None of the studies reviewed used diagnostic instruments to assess depression syndrome, instead assessing only recent depressive symptoms; as a result, there is probably substantial heterogeneity within cases of depression identified in these reports (Mezuk & Eaton, 2010). The most commonly used scale, the CES-D, has not been extensively validated against clinical diagnosis, particularly among older adults (Eaton *et al.*, 2007; Fiske & O'Riley, 2008), and there is evidence that the underlying factor structure of this scale differs across racial/ethnic groups (Guarnacia *et al.*, 1989). Because instruments such as the CES-D make no effort to separate symptoms attributable to medical illness or medication side effects from those due to psychopathology, they may be particularly inappropriate for examining the relationship between depression and geriatric syndromes that are characterized by non-specific physical complaints (e.g., fatigue, weakness). This measurement strategy hampers efforts to examine depression as a risk factor for frailty and associated geriatric conditions. Measurement error in depression may produce spurious findings as to the natural history, predictors, and consequences of thiscondition in later life and may have contributed to disparate findings across studies reviewed here.

The apparent link between depression and frailty begs the question of the role that psychotropic medications may play in this relationship. No studies included in this review considered the impact of medications used to treat depression (e.g., antidepressants) in the study design or the analytic strategy. Antidepressants have been associated with many of same outcomes as frailty, including osteoporosis (Mezuk *et al.*, 2008), falls (Ensrud *et al.*, 2002), and fracture (Takkouche *et al.*, 2007), and studies are needed to determine whether these agents potentially mediate the observed associations between depression and frailty. This research also has clear implications for efforts to treat depression in later life; although selective serotonin reuptake inhibitors are considered a first-line therapy for treating depression among older adults, there is a paucity of effectiveness data on these medications in this age group (Mottram *et al.*, 2006). Most trials are of short duration, and therefore, it is difficult to identify the potential complications from prolonged use or the role of polypharmacy (Fialova & Onder, 2009). Antidepressant classes may also confer differential fracture risk (Gagne *et al.*, 2011). Frailty may contribute to withdrawal from pharmacotherapy (Katz *et al.*, 1994), which emphasizes the need to explore multimodal,

non-pharmacological interventions for depressed, frail adults (Schulz & Williamson, 1993; Fairhall *et al.*, 2008), or at least more focused targeting of antidepressant medications that reflects the patient's needs in a holistic manner (Mezuk & Golden, 2009).

Variation in study design may have contributed to differences in findings across studies. Few studies had meaningful numbers of men or racial/ethnic minorities to permit evaluation of whether the associations between depression and frailty vary across these groups; there is reason to believe that these relationships may differ because the burden of depression is lower among men and racial/ethnic minorities relative to women and non-Hispanic Whites, respectively (Breslau *et al.*, 2006; Needham & Hill, 2010). Also, most studies focused on adults 65 years and older, precluding an investigation of how depressive episodes earlier in the life course may have contributed to frailty risk; studies that included younger adults would address this issue. Finally, some studies examined worsening or persistence of depressive symptoms, rather than onset of new symptoms, as an outcome, and thus, it is unclear whether frailty should be thought of as a potential prognostic, rather than etiologic, factor for late-life depression.

Conclusions

This review provides support for the bidirectional relationship between depression and frailty. Understanding the extent to which depression and frailty reflect plieotropic effects of common risk factors, or are simply variants in expression of the same underlying pathology, is paramount. If depression and frailty are overlapping syndromes, as opposed to etiologically distinct aspects of health, this has implications for the development of tools to appropriately measure and track changes in symptomatology over time. Shifting the paradigm for conceptualizing and measuring depression and frailty is also likely to significantly impact approaches to prevention and intervention. The plieotropic risk model acknowledges that interventions targeted at specific pre-clinical signs or symptoms will be inefficient and calls for comprehensive efforts to reduce morbidity and mortality in later life. Furthering understanding of these relationships may have important implications for the development of public health and clinical care interventions to reduce disability in later life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Supporting information may be found in the online version of this article.

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Key points

- Existing research demonstrates a link between depression and frailty in later life.
- There is limited research on the depression-frailty relationship among men or racial/ethnic minorities.
- (Mis)measurement of depression and frailty may have contributed to conflicting findings.
- Future research should explicitly examine how the signs and symptoms of depression and frailty interrelate, and whether antidepressant medications contribute to the depression-frailty relationship.

Table 1

Community-based cross-sectional studies of the relationship between frailty and depression

First author	Year	Sample characteristics	Measure of frailty	Measure of depression	Main findings
Frailty as determinant, depression as outcome					
Mirowsky	1992	USA *n* = 2840 Age range: 18–90 years Gender & racial composition unknown	IADL index	CES-D	Physical dysfunction was significantly associated with depressive symptoms.
Davidson	1994	USA *n* = 303 Age range: 65–102 years 85% women 47% White	ADL index	CES-D	Functional limitations were significantly associated with the somatic, but not negative affect, positive affect, or interpersonal subscales of the CESD.
Newsom	1996	USA *n* = 4734 Mean age: 72.8 years 57% women 95% White; 5% Black	IADL index Exercise tolerance Upper extremity strength Timed walk	CES-D	Functional impairment was associated with depressive symptoms. This relationship was partially mediated by social support.
Broe	1999	Australia *n* = 434 Mean age: 80.6 years (SD: 4.0) 46% women Racial composition unknown	Life Satisfaction Index-A Medical/neurological assessment	CES-D	Gait slowing was positively associated with depressive symptoms. Association between chronic conditions and depression was mediated by disability.
Hybels	2001	USA *n* = 4162 62% women Age range: 65–105 years 66% White; 34% Black	Modified ADL index Weighted sum of chronic health conditions	CES-D	Functional limitations were associated with both sub-syndromal and severe depression syndrome.
Jang	2002	USA *n* = 406 52% women	Katz ADL index IADL index	GDS	Disability status was associated with depression. This relationship was moderated by sense of mastery.

First author	Year	Sample characteristics	Measure of frailty	Measure of depression	Main findings
		Age range: 60–84 years	Physical Performance Scale		
		98% White	Functional Health Scale		
Cummings	2003	USA	ADL and IADL indices	CES-D	Functional impairment was not significantly associated with depression after accounting for social support and religiosity.
		n = 568			
		81% women			
		Mean age: 70.7 years (SD: 6.7)			
		68% White; 32% Black			
Stek	2004	Netherlands	GARS	GDS	Functional limitations were associated with elevated depressive symptoms.
		n = 500			
		63% women			
		Mean age: 85 years			
		Racial composition unknown			
Jang	2006	USA	Physical Performance Scale	CES-D	Functional disability was associated with depressive symptoms. This association was mediated by health perceptions.
		n = 230			
		59% women			
			Functional Health Scale		
		Age range: 60–92 years			
		100% Asian			
Wada	2008	Japan	History of falling	GDS	History of falling was positively associated with depressive symptoms.
		n = 1261			
		58% women	ADL index		
		Mean age: 75.4 years (SD: 7.2)			
		100% Asian			
Depression as determinant, frailty as outcome					
Prince	1997	United Kingdom	OARS impairment scale	SHORT-CARE	Depression was positively associated with functional impairment, disability, and physical handicap.
		n = 654			
		Age range: 65–98 years	SHORT-CARE		
		61% women	London Handicap Scale		
		Racial composition unknown	Modified Katz scale		
Blyth	2008	Australia	Cardiovascular Health Study	GDS	Depression was significantly associated with pain. The association between pain and frailty was significantly

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First author	Year	Sample characteristics	Measure of frailty	Measure of depression	Main findings
			Frailty Index		attenuated after adjusting for depression.
		n = 1705			
		100% men			
		Mean age: 76.9 years (SD: 5.5)			
		Racial composition unknown			
Deshpande	2008	Italy	SAFE	CES-D	Fear of falling was positively associated with depressive symptoms, physical weakness and slowness, and reduced activities. Depression modified the relationship between fear of falling and activity restriction.
		n = 848			
		55% women	FICSIT-4		
		Mean age: 75.9 years (SD: 6.4)	Repeated chair stand		
		Racial composition unknown	Dynamometer		
Hajjar	2009	USA	Gait speed	CES-D	The confluence of depressive symptoms, slowness, and poor executive function describe a common phenotype that is associated with functional decline.
		n = 580			
		64% women	Trail Making Test Part B		
		Mean age: 77.8 years (SD: 0.2)	Hopkins Verbal Learning Test		
		80% White, 14% Black			
Chang	2010	USA	Cardiovascular Health Study Frailty Index	GDS	Depressive symptoms were significantly associated with frailty status.
		n = 620			
		100% women			
		Age range: 70–79 years			
		80% White; 20% Black			
Chen	2010	Taiwan	Cardiovascular Health Study Frailty Index	CES-D	Depressive symptoms were significantly associated with frailty status.
		n = 2238			
		49% women			
		Age range: 65–103 years			
		100% Asian			

ADLs, activities of daily living (e.g., hygiene, dressing, eating, toileting, basic mobility); IADLs, instrumental activities of daily living (e.g., keeping appointments, using the telephone, traveling, preparing meals, shopping, housework, managing medications, managing finances); GARS, Groningen Activity Restriction Scale; OARS, Older Americans Resources and Services; SAFE, Survey of Activities and Fear of Falling in the Elderly; FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques; CES-D, Centers for Epidemiologic Studies—Depression Scale; GDS, Geriatric Depression Scale; SHORT-CARE, Comprehensive Assessment and Referral Evaluation—Short Form.

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Table 2

Community-based cohort studies of the relationship between frailty and depression

First author	Year	Sample characteristics	Length of follow-up	Measure of frailty	Measure of depression	Main findings
Frailty as determinant, depression as outcome						
Kennedy	1991	USA *n* = 1577 82% women Age range: 65+ years Racial composition unknown	2 years	Number of medical conditions ADL index Use of formal support services	CES-D	Poorer health status and use of formal support services were associated with greater persistence of depressive symptoms.
Ormel	2002	Netherlands *n* = 753 72% women Mean age (F): 73 years (SD: 7.6) Mean age (M): 71 years (SD: 8.7) Racial composition unknown	2 years	GARS	HADS	Disability had a stronger relationship with worsening depressive symptoms than depression had on worsening disability.
Taylor	2004	USA *n* = 3876 65% women Mean age: 73.2 years (SD: 6.4) 46% White;	10 years	ADL and IADL indices	CES-D	Trajectories of increasing disability were significantly associated with trajectories of increasing depressive symptoms.

First author	Year	Sample characteristics	Length of follow-up	Measure of frailty	Measure of depression	Main findings
		54% Black				
Yang	2005	USA *n* = 1300 63% women Mean age: 71.1 years (SD: 5.1) 46% White; 54% Black Modified Rosow-Breslau Health Scale for the Aged	3 years	ADL and IADL indices Nagi Physical Performance scale	CES-D	Onset and persistence of disability were significantly associated with increases in depressive symptoms.
Schieman	2007	USA *n* = 898 50% women Age: 65+ years 52% White; 48% Black	2 years	ADL index	Hopkins Symptom Checklist	Functional limitations predicted increases in depressive symptoms at follow-up.
Gayman	2008	USA *n* = 1495 54% women Mean age: 57 years (SD: 17) 24% White; 24% Cuban; 22% non-Cuban Hispanics; 30% Black	3 years	ADL and IADL indices Physical mobility	CES-D	Functional limitations predicted increases in depressive symptoms; depression only weakly predictive of increases in functional limitations.
Chang	2009	USA *n* = 671 100% women	3 years	ADL index	GDS	Incident disability significantly predicted depressive symptoms at the time of disability onset.

First author	Year	Sample characteristics	Length of follow-up	Measure of frailty	Measure of depression	Main findings
		Age: 65+ years 72% White; 27% Black				Among those without depression, disability was not significantly associated with depressive symptoms 6 months post-disability onset.
Depression as determinant, frailty as outcome						
Buchner	1996	USA *n* = 152 Age range: 65–85 years 55% women 94% White	6months	Gait speed Lower body strength SF-36	CES-D	Worsening of depressive symptoms was significantly associated with gait slowing.
Strawbridge	1998	USA *n* = 574 Age range: 65–102 years 57% women 82% White	29 years	Impairments in physical, nutritive, cognitive, and sensory functioning	18-item depressive symptom scale	Depressive symptoms associated with greater likelihood of frailty at follow-up.
Vaillant	1998	USA *n* = 237 100% men Mean age: 75 years (SD: 2) Racial composition unknown	55 years	Medical examination Physical limitations	IMDDS	Depression was associated with lower likelihood of experiencing no physical limitations at follow-up.
Hebert	1999	Canada *n* = 504 60% women Mean age: 79.9 years	3 years	Functional Autonomy Measurement System	GDS	Depression was not significantly predictive of functional decline at follow-up.

First author	Year	Sample characteristics	Length of follow-up	Measure of frailty	Measure of depression	Main findings
		(SD: 3.9) Racial composition unknown				
Rantanen	2000	USA *n* = 2275 100% men Age range: 71–92 years 100% Asian	3 years	Hand grip strength Body weight	CES-D	Depressive symptoms were associated with a steeper decline in grip strength over time, particularly among low-weight men.
Sarkisian	2000	USA *n* = 6632 100% women Mean age: 73 years (SD: 4.9) Racial composition unknown	4 years	ADL index	GDS	Depressive symptoms were significantly associated with greater functional decline at follow-up.
Mehta	2002	USA *n* = 5697 64% women Mean age: 77 years (SD: 5.5) 86% White; 10% Black	2 years	ADL index	CES-D	Depressive symptoms were significantly predictive of incident functional impairment but not worsening functional impairment.
Ostir	2004	USA *n* = 1558 61% women Mean age:	7 years	Modified Cardiovascular Health Study Frailty Index	CES-D	Positive affect was negatively associated with incidence of frailty.

First author	Year	Sample characteristics	Length of follow-up	Measure of frailty	Measure of depression	Main findings
		71.9 years				
		(SD: 5.7)				
		100% Mexican				
		American				
Woods	2005	USA	3 years		CES-D	
		n = 40657		Modified Cardiovascular Health Study Frailty Index		Depressive symptoms were significantly associated with incident frailty.
		100% women				
		Age range:				
		65–79 years				
		86% White;				
		6.5% Black				
Avlund	2006	Finland & Denmark	5 years	Lower Limb T-Scale	CES-D	Depressive symptoms were significantly associated with feelings of tiredness performing daily activities at baseline but did not predict onset of tiredness at follow-up.
		n = 546				
		55% women		Muscle strength		
		Age range:		Forced expiratory volume		
		75–80 years				
		100% White				
Avlund	2006	Finland and Denmark	5 years	PADL-H Scale	CES-D	Depressive symptoms were associated with onset of disability, independent from feelings of tiredness.
		n = 419				
		61% women				
		Mean age:				
		75 years				
		100% White				
Han	2006	USA	2 years	ADL and IADL scales	CES-D	Declines in depressive symptoms were associated with better self-rated health at follow-up among both disabled and non-disabled older people.
		n = 6771				
		Age range:				
		65+ years				
		Gender and racial		Self-rated health		
		composition				
		unknown				

First author	Year	Sample characteristics	Length of follow-up	Measure of frailty	Measure of depression	Main findings
Atkinson	2007	USA *n* = 2349 52% women Mean age: 75.6 years (SD: 2.9) 63% White; 37% Black	3 years	3MS CLOX1 EXIT15 Gait speed	CES-D	Depressive symptoms mediated the relationship between cognitive functioning and gait speed change.
Xue	2007	USA *n* = 599 100% women Age: 65+ years 71% non-Black; 29% Black	3 years	Cardiovascular Health Study Frailty Index	GDS	Depressive symptoms were not significantly associated with incident frailty but were associated with increased frailty-free mortality.
Barry	2009	USA *n* = 754 65% women Age: 70+ years >90% White	9 years	ADL index	CES-D	Depressive symptoms predicted degree of mild and severe disability at follow-up.
Park-Lee	2009	USA *n* = 954 100% women Mean age: 81.2 years (SD: 3.7) 87% White	4 years	Modified Cardiovascular Health Study Frailty Index	CES-D [Positive affect subscale]	Positive affect was associated with lower incidence of frailty, independent from depressive symptoms.

ADLs, activities of daily living (e.g., hygiene, dressing, eating, toileting, basicmobility); IADLs, instrumental activities of daily living (e.g., keeping appointments, using the telephone, traveling, preparing meals, shopping, housework, managing medications, managing finances); GARS, Groningen Activity Restriction Scale; OARS, Older Americans Resources and Services; SAFE, Survey of Activities and Fear of Falling in the Elderly; FICSIT, Frailty and Injuries Cooperative Studies of Intervention Techniques; 3MS, Modified Mini-Mental Status Examination; CLOX1, Executive Clock-Drawing Task; EXIT15, Executive Interview; SF-36, Short-Form Health Survey; PADL-H Scale, Physical Activities of Daily Living—Help Scale; CES-D, Centers for Epidemiologic Studies—Depression Scale; GDS, Geriatric Depression Scale; SHORT-CARE, Comprehensive Assessment and Referral Evaluation—Short Form; DPHS, Depression Homogenous Subscale; DPDS, Depression Diagnostic Subscale; HADS, Hospital Anxiety and Depression Scale; HADS, Hospital Anxiety and Depression Scale; IMDDS, Indicators of Major Depressive Disorder Scale.