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Depression and Frailty in Late Life: Evidence for a Common Vulnerability

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Abstract

Objectives: The study purpose is to estimate the correlation between depression and competing models of frailty, and to determine to what degree the comorbidity of these syndromes is determined by shared symptomology.

Methods: Data come from the 2010 Health and Retirement Study. Analysis was limited to community-dwelling participants 65 and older (N = 3,453). Depressive symptoms were indexed by the 8-item Centers for Epidemiologic Studies Depression (CESD) scale. Frailty was indexed by 3 alternative conceptual models: (a) biological syndrome, (b) frailty index, and (c) functional domains. Confirmatory factor analysis (CFA) was used to estimate the correlation between depression and each model of frailty.

Results: Each of the 3 frailty latent factors was significantly correlated with depression: biological syndrome (ρ = .68, p < .01), functional domains (ρ = .70, p < .01), and frailty index (ρ = .61, p < .01). Substantial correlation remained when accounting for shared symptoms between depression and the biological syndrome (ρ = .45) and frailty index (ρ = .56) models.

Discussion: Results indicate that the correlation of frailty and depression in late life is substantial. The association between the two constructs cannot be fully explained by symptom overlap, suggesting that psychological vulnerability may be an important component of frailty.

Keywords: Depression—Factor analysis—Frailty

Aging is often accompanied by declines and deficits in multiple bodily systems. When deficits are significant or numerous enough, physiological reserve may be compromised, rendering older adults vulnerable to adverse health outcomes as a result of stressors or minor perturbations to physical health (Clegg, Young, Iliffe, Rikkert, & Rockwood, 2013). This state of vulnerability to sudden changes in health status is termed frailty. Frailty is associated with higher incidence of adverse health outcomes such as falls, hospitalizations, and mortality (Fried et al., 2001; Rockwood et al., 2005), and may be an important predictor of complications from surgery, medication use, and other common interventions (Hubbard, O’Mahony, & Woodhouse, 2013; Makary et al., 2010). The prevalence of frailty in community-dwelling older adult populations is approximately 11%; however this estimate varies considerably depending on how frailty is defined, with estimates ranging from 4% to 59% (Collard, Boter, Schoevers, & Oude Voshaar, 2012). Among those aged 85 and older, the estimated prevalence of frailty is approximately 26%–44%.
The wide range of prevalence estimates reflects fundamental conceptual disagreements regarding the operationalization of frailty.

While there is implicit agreement that frailty is a condition conferring vulnerability to poor physical health outcomes, there is little consensus about what factors, physical or otherwise, may contribute to this vulnerability. Consequently, a range of symptoms, including biological, psychological, and sensory deficits have been incorporated into extant frailty definitions (Rothman, Leo-Summers, & Gill, 2008; Sternberg, Wershof Schwartz, Karunanathan, Bergman, & Mark Clarfield, 2011). In a community-based sample of older adults, Cigolle, Ofstedal, Tian, and Blaum (2009) compared the diagnostic overlap of three of the most widely cited frailty definitions representing three distinct conceptual approaches and operational criteria: (a) a biological syndrome model comprised of five specific physiologic symptoms (Fried et al., 2001), (b) a frailty index, characterizing frailty as a state produced by accumulated medical burdens (Rockwood et al., 2005), and (c) a functional domains model, emphasizing deficits in specific functional abilities (Strawbridge, Shema, Balfour, Higby, & Kaplan, 1998). Of the older adults found to be frail by at least one model, approximately 44% were designated as frail by at least two models and only 10% by all three (Cigolle et al., 2009). Yet despite conceptual discordance, all three operationalizations are predictive of adverse health outcomes such as falls, mortality, and hospitalizations (Bandeen-Roche et al., 2006; Rockwood et al., 2007; Strawbridge et al., 1998), suggesting that they may each be related to a more general concept of frailty as vulnerability.

Though the majority of frailty definitions focus primarily on physical and biological indicators of vulnerability, it is important to consider the risk of adverse health outcomes associated with mental health disorders (Katz, 1996). Like frailty, depression among older adults has been described in terms of diminished reserve capacity, representing a lack of resources to respond to stressors (de Jonge et al., 2004; Katz, 2004). For example, de Jonge and colleagues hypothesized that poor adjustment following somatic insult among depressed older adults may reflect inadequate psychological and social coping mechanisms, referring to depression as a form of “psychosocial frailty” (de Jonge et al., 2004). Depression also shares many symptoms, risk factors, and consequences with frailty. For example, physical inactivity and fatigue are criteria used to define both frailty and depression (Katz, 2004; Mezuk, Edwards, Lohman, Choi, & Lapane, 2012). Depression likewise predicts higher mortality and disability (Fauth, Gerstorf, Ram, & Malmberg, 2012; Saint Onge, Krueger, & Rogers, 2014; Schulz et al., 2000)—outcomes typically used to validate frailty definitions. The two concepts are understandably difficult to disentangle. Previous work has shown that common measures of frailty and depression produce highly overlapping classification of afflicted individuals, even when correcting for chance categorical overlap (Lohman, Dumenci, & Mezuk, 2014; Mezuk, Lohman, Dumenci, & Lapane, 2013). It is not clear to what extent this overlap holds across different definitions of frailty or to what extent it is determined by shared symptoms.

There are numerous potential explanations for the concordance of frailty and depression. First the two conditions may be linked as mutually reinforcing processes of decline. For example, depression is associated with declines in muscle strength and decreased physical activity among older adults (Rantanen et al., 2000; Stieglitz, Schniter, von Rueden, Kaplan, & Gurven, 2014), while functional limitations and medical comorbidity are in turn associated with higher risk of depression (Blazer, 2003). The two conditions may also be alternate manifestations of a common underlying process such as vascular degeneration. Vascular diseases and vascular ageing have been implicated in increased risk of sarcopenia, frailty, and depression (Alexopoulos et al., 1997; Newman et al., 2001). While the theoretical mechanisms responsible for the comorbidity of frailty and depression remain to be explored, the consistency of comorbidity across diverse study populations suggests that comorbidity should not be ignored but instead be an important consideration in study design (Katz, 2004; Mezuk et al., 2012).

Arguably, the comorbidity of frailty and depression is similar to the comorbidity between common mental disorders (e.g., depression and anxiety) and presents similar challenges to research design (Beekman et al., 2000; Mezuk et al., 2012). In epidemiologic studies of frailty, typical strategies for addressing this comorbidity are: (a) excluding individuals who meet criteria for depression, (b) including individuals without regard for comorbid depression, and (c) statistical adjustment. These strategies are problematic and may potentially lead to incorrect inferences regarding these conditions (Krueger, 1999). For instance, excluding depressed individuals from a study of frailty would yield a sample of frail individuals who are nonrepresentative of frail older adults and, importantly, who are less severely impaired (Clark, Watson, & Reynolds, 1995; Krueger, 1999). On the other hand, ignoring comorbidity in this context would make it difficult to determine whether outcomes were related to frailty, depression, or the interaction of the two (Clark et al., 1995; Krueger, 1999). As the validity of frailty models is often tied to prediction of poor health outcomes (Fried et al., 2001; Rockwood et al., 2007), this problem would conceivably impact the comparative effectiveness of alternative frailty definitions. Finally, while statistically controlling for comorbid depression in regression models would allow investigation of the independent and interacting effects of these two conditions, it would not account for the inherent measurement error introduced when indexing latent constructs (e.g., depression and frailty) by observed symptoms.

In order to provide clarity to the discussion of comorbidity between depression and frailty and to inform future attempts to refine the definition of frailty, this study aimed...
to determine the correlation (i.e., comorbidity) between these two conditions conceived as latent dimensional factors. Using data from a large population-based sample of older adults, this study applied confirmatory factor analysis (CFA) to overcome analytical limitations of prior studies. By modeling frailty and depression as extreme points on continua of physical and psychological functioning, the CFA approach avoids categorization of these two conditions according to unreliable, and somewhat arbitrary, diagnostic symptom thresholds. In separate analyses, we examined the correlation between depression and each of the three frailty definitions described earlier. We were interested in answering the following questions: Is correlation between depression and frailty consistent across different models of frailty? To what extent can correlation be explained by shared symptomology between depression and competing frailty models? Which sociodemographic factors influence correlation between depression and frailty? We hypothesized that the correlation of frailty and depression would be substantial across all frailty definitions but that characteristics related to correlation would vary considerably based on different frailty-specific and shared criteria.

Methods
Sample
This study is based on data from the 2010 wave of the Health and Retirement Study (HRS), a prospective survey of older adults, designed to collect longitudinal information on the health and finances of older Americans. The HRS employs a multi-stage probability sample of U.S. households to produce a nationally representative sample of adults aged 51 and older (Heeringa & Connor, 1995). Self-reported information regarding demographics, chronic health conditions, daily activities, disability status, and other health determinants are collected at baseline and at subsequent 2-year intervals. Beginning in 2004, a randomly selected subset of HRS respondents participated in enhanced face-to-face interviews which included objective assessment of walking speed, hand strength, weight, height, and other physical measures (Crimmins et al., 2008).

A total of 22,034 respondents participated in the 2010 HRS wave, of whom 10,938 were 65 or older at the time of interview and were considered eligible for the study. The primary analytical sample was restricted to respondents who were selected for enhanced face-to-face interviews. Because respondents aged 64 and younger were not asked to perform walking speed tasks necessary to assess frailty status, they were excluded from analysis. Respondents were also excluded if they were interviewed by proxy (N = 847) or resided in a nursing home (N = 462). Of the community-dwelling, nonproxy respondents, 4,035 were selected for and consented to enhanced face-to-face interviews and physical measures. The primary analytical sample was restricted to 3,453 respondents who completed or attempted physical measures tasks (Supplementary Figure 1).

Measures
Frailty
Biological syndrome
The biological syndrome model of frailty was operationalized using five criteria proposed by Fried and colleagues (2001) in the Cardiovascular Health Study (CHS): low weight, physical inactivity, exhaustion, weakness, and slowness. Low weight was defined as a loss of 10% or more in BMI since the previous (2008) wave or a current BMI <18.5 kg/m^2. Physical activity was calculated as the average frequency of three activity intensities (mild, moderate, and vigorous) weighted by average metabolic equivalency of task (MET) scores: mild (1–3 MET), moderate (4–6 MET), and vigorous (7–10 MET). Participants were considered physically inactive if they scored in the lowest 20% of average physical activity. Exhaustion was specified using two items from the Center for Epidemiologic Studies-Depression (CESD) indicating difficulty feeling motivated to perform daily activities (Supplementary Table 1). Strength was assessed using the average of two measurements of dominant hand grip strength as measured by dynamometer. Weakness was defined as strength below BMI- and gender-specific thresholds established in the CHS. Slowness was defined as having a walking speed measured over a 2.5-m distance below gender- and height-specific cut-points established in the CHS (Fried et al., 2001). Participants were considered as meeting criteria for weakness or slowness if they attempted the corresponding physical measures but were unable to complete. Participants who did not attempt physical measures due to lack of appropriate facilities or equipment or due to recent surgery were assigned missing values for those physical measures.

Frailty index
As originally conceived, the frailty index is a count of 70 clinical deficits, including presence of diseases, difficulties in daily activities, and other physical and neurological signs and symptoms (Rockwood et al., 2005). A frailty index score is calculated as the ratio of present deficits to total possible deficits (e.g., FI = 20/70 = .29). Subsequent analyses have demonstrated that frailty indices composed of 30–40 deficits have comparable predictive validity to the full index when deficits are selected based on predetermined criteria (Searle, Mitnitski, Gahbauer, Gill, & Rockwood, 2008). Selection criteria for deficit inclusion are: (a) a deficit must generally accumulate with age, (b) a deficit must be related to health status in a biologically plausible way, (c) a deficit must not become saturated (i.e., universally prevalent) at an early age, and (d) the deficits together must represent a range of bodily systems (Searle...
Using variables available in the HRS, the current study reproduced 35 of the original 70 deficits satisfying these selection criteria (Supplementary Table 2). Each deficit was considered either present (1) or absent (0).

Functional domains
Strawbridge and colleagues (1998) define frailty as functional impairment in at least two of four domains: physical, nutritive, cognitive, and sensory. In the current study, impairment in each domain was designated as present (1) or absent (0) according to operational criteria proposed for use with HRS data (Cigolle et al., 2009; Supplementary Table 3). Impairment in physical functioning was defined as having persistent dizziness or lightheadedness, experiencing at least one fall in the prior 2 years, or having difficulty lifting or carrying weights over 10 pounds. Impairment in nutritive functioning was defined as a loss of 10% or more in BMI since the previous (2008) wave or a current BMI <18.5 kg/m². Cognitive functioning was assessed using a 35-point composite measure of mental status, reasoning and memory task performance developed in the HRS (Blaum, Ofstedal, & Liang, 2002; Ofstedal, Fisher, & Herzog, 2005). Impairment in cognitive functioning was defined as a score of 10 or less (corresponding with lowest 10% of HRS respondents) on this measure. Sensory impairment was defined as having fair/poor self-rated vision despite use of corrective lenses or fair/poor hearing despite use of a hearing aid.

Depression
Current depressive symptoms (referred to hereafter as “depression”) were measured using the eight-item CESD scale (Turvey, Wallace, & Herzog, 1999). Respondents are asked to indicate whether they have experienced any of the following symptoms much of the time during the previous week: (a) felt depressed, (b) felt activities were efforts, (c) had restless sleep, (d) felt happy, (e) felt lonely, (f) enjoyed life, (g) felt sad, and (h) felt unmotivated. Positive symptoms (i.e., feeling happy and enjoying life) were reverse-coded. Although the CESD is not intended to be a diagnostic tool for major depression, it has been shown to have moderate agreement (sensitivity = .71; specificity = .79) compared to the Composite International Diagnostic Interview (CIDI), a structured instrument for assessment of major depression (Steffick, 2000; Turvey et al., 1999).

Sociodemographic Characteristics
Other variables included in the analysis were sex (male = 0; female = 1), race (dummy variables for white, black, and other), years of education (12 or more years = 0; fewer than 12 years = 1), primary health insurance provider (dummy variables indicating private, Medicare, and Medicaid insurance), marital status (dummy variables for currently married/partnered, separated/divorced, never married, and widowed), and household income (categorized in quartiles). Age was considered as categorical (dummy variables for 65–74 years, 75–84 years, and 85 or greater) to allow for potential nonlinear relationships between age and depressive or frailty symptoms.

Analysis
Single- and two-latent variable CFA models were used to evaluate the correlation between depression and frailty. CFA is an appropriate method for assessing correlation between latent factors that are not directly observable and which are imperfectly measured by presence of observable symptoms (Joreskog, 1969; Mulaik, 2009). In CFA, constraints are imposed a priori on the number of latent factors, the variables used to indicate the factors, and the relationships between variables in the model (Joreskog, 1969; Mulaik, 2009). Latent factors are conceived as dimensional traits, existing on a continuum rather than as categorical diagnoses. In the current study, indicators of the latent frailty factor were determined by the dichotomous symptoms from each of the three models described above, while depression was indicated by items from the CESD. Two types of CFA model were fit: (a) single-factor models in which a single latent factor was indicated by both frailty items and depression items from the CESD; (b) correlated two-factor models in which separate frailty and depression factors were each defined by their respective indicator variables (Figure 1). In cases where frailty and depression share symptoms by definition (i.e., the symptom “exhaustion” in the biological syndrome model of frailty, as described earlier), the shared indicator variables were allowed to cross-load on (i.e., serve as indicators of) each factor (Figure 1). Models allowing cross-factor loading were compared with models in which shared symptoms indicated only a single factor in order to evaluate the role of shared symptoms in the correlation between frailty and depression.

The influence of sociodemographic characteristics on latent factors was estimated using multiple indicator, multiple cause (MIMIC) structural equation models (Muthén, 1989). MIMIC models allow for estimation of the influence of covariate characteristics such as age, sex, and race on latent variables. MIMIC models contain at least two components: (a) a measurement component relating indicator symptoms to the latent variables, and (b) a regression component, regressing latent variables on the covariates. When the correlation between frailty and depression was high (i.e., >.60), correlated factor models were equivalently re-expressed as second-order factor models in which a higher-order factor was postulated to represent the correlation between frailty and depression subfactors. MIMIC models were used in these cases to estimate the influence of covariate factors on the second-order factor representing correlation (Figure 2).
evaluate differences in covariate influence by age, we fit MIMIC models separately for participants aged 75–84 (N = 1,262) and participants aged 85 and older (N = 355; Supplementary Tables 4 and 5).

Sensitivity analyses were conducted to evaluate the potential influence of excluding individuals with missing or incomplete physical measures data (N = 582) from primary analysis. Missing values for slow gait speed and weakness were imputed using multiple imputation for categorical variables as implemented in Mplus. Results from analysis of the average of 20 imputed datasets are presented in Supplementary Tables 6 and 7. Results of the multiple imputation analyses were similar to analyses using data for participants with complete physical measures data (N = 3,453), and so only results from the analytic sample are hereafter reported.

Analyses were performed using MPlus Version 7 (Muthén & Muthén, Los Angeles, CA). Participant-level data were weighted according to HRS sample weights, accounting for probability of selection into the primary sample and physical measures sub-sample. Model fit was assessed using standard fit criteria: comparative fit index (CFI), Tucker-Lewis index (TLI), and root mean square error of approximation (RMSEA). Values of CFI >.90, TLI >.90, and RMSEA <.06 were taken to indicate adequate model fit (Hu & Bentler, 1999).

**Results**

**Sample Characteristics**

Table 1 shows the demographic and health characteristics of the analytic sample. Participants with a self-reported history of depression were more likely to be female, white, to have a household income in the lowest quartile, to be widowed or separated, and to be Medicaid beneficiaries. Participants with a history of depression were significantly more likely to be frail according to diagnostic criteria for each of the three frailty models. Comparing individuals with a history of depression to those without, the odds of being considered frail at the time of interview were approximately twice as high according to the biological syndrome and functional domains definitions. According to the frailty index model, the odds of being frail at time of interview were approximately four times as high for those with a history of depression.

**CFA Models of Depression and Frailty**

Results from CFA models of depression and the three models of frailty are shown in Table 2. When depression and frailty were conceived as a single latent factor (indicated by symptoms of both depression and frailty), the biological syndrome and functional domains definitions fit the data adequately, while the frailty index fit the data poorly.
according to prespecified model fit criteria. Correlated two-factor models provided better fit to the data than single factor models according to all three definitions. Correlation between frailty and depression latent variables was substantial for each of the three frailty definitions with correlations of 0.68 (95% confidence interval [CI]: 0.65–0.72) for the biological syndrome, 0.61 (95% CI: 0.59–0.63) for the frailty index, and 0.70 (95% CI: 0.66–0.74) for the functional domains definition.

Because the biological syndrome and frailty index models explicitly share symptoms with the CESD, a third set of CFA models was estimated allowing cross-loading of items on both frailty and depression factors. Allowing shared symptoms to serve as indicators of both frailty and depression significantly improved fit indices of both models. Correlation between frailty and depression decreased in the shared-symptom models for the biological syndrome (from 0.68 to 0.43) and for the frailty index (from 0.61 to 0.56) definitions, suggesting that shared symptoms determine some, but not all, of the comorbidity between the constructs.

MIMIC Models of Depression and Frailty

The size of correlations between depression and the three frailty models suggested that frailty and depression could be re-specified as subfactors of a second-order latent factor representing their correlation (Figure 2). MIMIC models were fit to estimate the influence of sociodemographic covariates on this correlation. Regression coefficients from MIMIC models are displayed in Table 3. Compared to men, women had significantly higher average factor level for each of the three frailty definitions (Biologic syndrome: \( \beta = 0.10, 95\% \text{ CI } 0.07–0.14 \); Frailty index: \( \beta = 0.15, 95\% \text{ CI } 0.11–0.20 \); Functional domains: \( \beta = 0.07, 95\% \text{ CI } 0.03–0.10 \)). Likewise, older age, lower education, being widowed or separated, having lower income, and being a Medicaid beneficiary were associated with higher levels of the second-order latent factors for each frailty definition. The influence of race was inconsistent by frailty definition. Minority participants had higher average levels of comorbid disorder according to the functional domains and biological syndrome definitions; however there were no significant racial differences according to the frailty index. Covariate influence on the higher order latent factors suggests that these characteristics predict not only greater levels of frailty and depression but also their comorbidity.

While MIMIC model results for participants aged 75–85 were similar to those of the full analytic sample (Supplementary Table 6), differences among participants aged 85 and older are notable (Supplementary Table 7). Whereas low income was a consistent predictor of comorbid disorder in the total sample, income had no significant
influence among the oldest old. Instead, being a widow (Biologic syndrome: $\beta = 0.19$, 95% CI 0.08–0.30; Frailty index: $\beta = 0.28$, 95% CI 0.15–0.40; Functional domains: $\beta = 0.22$, 95% CI 0.10–0.34) and being a Medicaid beneficiary (Biologic syndrome: $\beta = 0.18$, 95% CI 0.04–0.32; Frailty index: $\beta = 0.47$, 95% CI 0.29–0.65; Functional domains: $\beta = 0.27$, 95% CI 0.11–0.43) were the strongest predictors of the second-order latent factor.

**Discussion**

This study examined the correlation between frailty and depression using three conceptually distinct definitions of frailty and a latent variable approach. Regardless of definition, frailty was substantially associated with depression, with correlation coefficients ranging from 0.61 to 0.70 in correlated factor models. The association between these two constructs remained substantial when accounting for shared symptomology and the influence of demographic covariates. Furthermore, we found that sociodemographic factors such as age, gender, low income, and marital status were consistent predictors of correlation for each frailty definition. The consistency of our findings across conceptually discordant frailty models suggests that frailty and depression, as commonly defined in epidemiologic research, may describe similar concepts. Despite focus on physical and functional indicators of vulnerability frequent in frailty models, our results indicate

**Table 1. Sample Characteristics by Self-Reported History of Depression**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall ($n = 3,453$)</th>
<th>Lifetime depression ($n = 462$)</th>
<th>No lifetime depression ($n = 2,991$)</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weighted % or Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>74.2 (6.8)</td>
<td>72.7 (6.5)</td>
<td>74.4 (6.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female</td>
<td>54.3</td>
<td>71.5</td>
<td>51.5</td>
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<tr>
<td>Race</td>
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<td></td>
<td></td>
<td>.063</td>
</tr>
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<td>White</td>
<td>89.2</td>
<td>92.1</td>
<td>88.7</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>7.5</td>
<td>4.9</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3.3</td>
<td>3.0</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Education (&gt;12 years)</td>
<td>47.0</td>
<td>48.2</td>
<td>46.5</td>
<td>.512</td>
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<td>Household income</td>
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<td>26.8</td>
<td>18.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>$19,000–37,000</td>
<td>26.3</td>
<td>27.5</td>
<td>26.1</td>
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<tr>
<td>$37,000–69,000</td>
<td>28.8</td>
<td>26.7</td>
<td>29.1</td>
<td></td>
</tr>
<tr>
<td>$69,000+</td>
<td>25.4</td>
<td>19.1</td>
<td>26.4</td>
<td></td>
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<tr>
<td>Marital status</td>
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<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Married/partnered</td>
<td>63.7</td>
<td>52.5</td>
<td>65.5</td>
<td></td>
</tr>
<tr>
<td>Separated/divorced</td>
<td>10.6</td>
<td>14.5</td>
<td>9.9</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>2.8</td>
<td>2.5</td>
<td>2.9</td>
<td></td>
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<tr>
<td>Widowed</td>
<td>22.9</td>
<td>30.4</td>
<td>21.7</td>
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<tr>
<td>Health insurance (primary)</td>
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<tr>
<td>Medicaid</td>
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<td>7.9</td>
<td>4.3</td>
<td>.004</td>
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<tr>
<td>Private</td>
<td>21.8</td>
<td>20.7</td>
<td>21.9</td>
<td>.182</td>
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<tr>
<td>Frailty definitions</td>
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<tr>
<td>Biological syndrome</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Frail</td>
<td>10.8</td>
<td>20.7</td>
<td>9.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intermediate</td>
<td>51.3</td>
<td>58.8</td>
<td>50.1</td>
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<tr>
<td>Nonfrail</td>
<td>37.9</td>
<td>20.5</td>
<td>40.7</td>
<td></td>
</tr>
<tr>
<td>Frailty index</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frail</td>
<td>24.2</td>
<td>51.2</td>
<td>20.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intermediate</td>
<td>27.5</td>
<td>27.2</td>
<td>27.5</td>
<td></td>
</tr>
<tr>
<td>Nonfrail</td>
<td>48.3</td>
<td>22.6</td>
<td>52.4</td>
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<tr>
<td>Functional domains</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frail</td>
<td>20.6</td>
<td>31.7</td>
<td>18.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intermediate</td>
<td>38.8</td>
<td>44.7</td>
<td>37.8</td>
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<tr>
<td>Nonfrail</td>
<td>40.6</td>
<td>23.6</td>
<td>43.3</td>
<td></td>
</tr>
</tbody>
</table>

*Biological syndrome: frail = 3 or more symptoms; intermediate = 1 or 2 symptoms.*

*Frailty index: frail = index score >.25; intermediate = index score >.15.*

*Functional domains: frail = 2 or more symptoms; intermediate = 1 symptom.*
that psychological vulnerability, as reflected by depression, may be an inherent component of what it means to be frail. Future attempts to refine the definition of frailty should consider incorporating depressive symptoms rather than treating depression as a categorically separate disorder.

This study provides valuable insights regarding the measurement and definition of frailty and helps to synthesize disconnected lines of research in geriatrics and psychiatry. One key finding is that the strong correlation exhibited between frailty and depression is not unique to a single definition of frailty and cannot be fully explained by shared symptomology. Indeed, the functional domains model, which shares no symptoms with the CESD, was the most highly correlated with depression. While there are a number of distinct components used to define frailty (Sternberg et al., 2011), researchers generally agree that it is fundamentally a state of vulnerability to adverse physical health events (Clegg et al., 2013). Yet despite a large body of research demonstrating depression as a risk factor for poor physical health, mortality, and disability (Blazer, 2003; Fauth et al., 2012; Saint Onge et al., 2014), depressive symptoms are seldom incorporated in models of frailty (Sternberg et al., 2011). The exclusion of depression likely limits the prognostic value of current frailty definitions (Rothman et al., 2008), and disregards the complex relationships between physical and mental health among older adults (Katz, 1996).

The three models of frailty presented in this study offer different conceptual views of its place within the development of disability and poor health. The biological syndrome model, for instance, defines frailty as a distinct antecedent of disease and disability (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004); while the functional domains and frailty index models consider disease and disability to be components of frailty (Rockwood et al., 2005; Strawbridge et al., 1998). Nonetheless, the current study demonstrates that there is potential common ground between models of frailty and depression, highlighted by characteristics that predict their comorbidity. For example, the strongest predictors of comorbid depression and frailty were variables related to personal and environmental resources such as less educational attainment, lower income, and Medicaid insurance coverage. Among the oldest group of participants, widowhood, representing a potential lack of social support (Sullivan & Fenelon, 2014), was also a consistent predictor of higher levels of disorder. These results underscore that frailty is a multifactorial condition, determined both by physical deficits and by presence/lack of psychological and social resources to cope with stressors (Ament et al., 2012). In accordance with the description of depression as “psychosocial frailty” (de Jonge et al., 2004), depression may thus serve to exacerbate physical frailty not because it is associated with any particular disease process or frailty model, but because it represents a lack of psychological and social coping resources.

Although our findings are consistent with the hypothesis that a common vulnerability factor contributes to the correlation between depression and frailty, there are several parallel processes and alternative explanations that may also be relevant. For example, evidence suggests that depression may lead to decreased physical activity, fatigue, and loss of muscle mass among older adults, which in turn may lead to further withdrawal from activity and depressed mood (Blazer, 2003; Rantanen et al., 2000; Stiegltz et al., 2014). Although few studies have attempted to empirically test alternative explanations of comorbidity, one notable exception by Paulson and Lichtenberg (2013) examined the longitudinal, bi-directional associations between depressive symptoms and frailty. The authors found that depressive symptoms, particularly those concurrent with cerebrovascular disease, predicted incidence of frailty and subsequent mortality, but that frailty symptoms did not predict onset of depression. The authors concluded that vascular depression may be a prodromal sign of frailty (Paulson & Lichtenberg, 2013). Similarly, evidence suggests that vascular disease and vascular ageing may be important predictors of frailty, depression, and other geriatric syndromes (Alexopoulos et al., 1997; Newman et al., 2001). While such a “common cause” hypothesis could potentially explain associations between depression and frailty, vascular changes likely
account for depression and frailty among only a subset of individuals.

Regardless of the true mechanisms determining the relationship between these two constructs, acknowledgment of psychosocial sources of frailty is informative for future studies of the predictors of health decline and disability in later life. Determining whether depression therapies (e.g., antidepressant medications, behavioral activation therapy) may prevent or mitigate frailty symptoms would not only be clinically significant but would provide important information about the mechanisms determining comorbidity. More comprehensive collection of physical and functional measures within depression treatment trials can inform such questions. Similarly, research is needed to determine whether frailty status can be used to inform appropriate treatment options for late-life depression. Individuals with both frailty and depression may benefit from more comprehensive interventions, for instance, that combine antidepressant treatment with exercise and nutritional interventions (Brown et al., 2014). Finally, findings from this study regarding the interaction of several demographic factors, such as widowhood, age, and race/ethnicity, deserve further study.

These findings should be interpreted in light of study strengths and limitations. First, the HRS is among the largest, most well-characterized cohorts of older adults. Because of the breadth of this data source we were able to compare multiple definitions of frailty and to estimate associations among a diverse and representative population of older adults. This study is among the first, to our knowledge, to investigate the association between depression and multiple models of frailty using a common data source. Consistency of results across multiple definitions of frailty indicates that our inferences regarding the nature of the relationship between depression and frailty are analytically and conceptually robust. Also, our latent variable modeling approach accounted for the measurement error inherent in the study of syndromes like depression and frailty. This methodology is well-suited for the analysis of the discriminant properties of syndromes like frailty for which there is no consensus definition.

We also note study limitations. First, our operationalizations of frailty were approximate replications of the measurement schema proposed by their original developers. Although care was taken to closely reproduce the elements of each definition, the extent to which the indicators do not capture the intended construct may introduce
error in the results. Nevertheless, these operationalizations of frailty have been successfully applied in past studies of frailty and were found to be consistent with the original definitions (Cigolle et al., 2009). Second, the analytic sample was restricted to community-dwelling adults aged 65 and older who were selected for and completed physical measures, limiting generalizability of study findings. Exclusion of participants with missing physical measures may have introduced selection bias. We believe this bias is minimal, however, because models estimated using multiple imputation of missing physical measures produced similar results to the restricted analytic sample. Lastly, the measure of depression used in this study, the CESD, is not designed to approximate clinician diagnosis of major depression. Nonetheless, the CESD is among the most widely used scales for the measurement of depressive symptoms in epidemiologic research, and therefore its association with frailty has significance for research. Furthermore, the CESD has been shown to produce moderate diagnostic agreement with more structured instruments for the assessment of major depression (Steffick, 2000; Turvey et al., 1999).

In conclusion, our results demonstrate a significant and consistent correlation between frailty and depression among older adults, which is not fully explained by definitional differences, symptom overlap, or sociodemographic covariates. Given that comorbidity of physical and mental disorders is common in late life, future research should continue to explore reasons for comorbidity and the implications of comorbidity in predicting adverse health outcomes.

Supplementary Material
Please visit the article online at http://gerontologist.oxfordjournals.org/ to view supplementary material.

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