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Gender Differences in the Construct Overlap of Frailty and Depression: Evidence from the Health and Retirement Study

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Abstract

OBJECTIVES—To determine the degree of diagnostic overlap between frailty and depression and investigate whether gender differences in symptom endorsement influence this overlap.

DESIGN—Cross-sectional latent class analysis.

SETTING—Data come from the 2008 wave of the Health and Retirement Study, a nationally-representative longitudinal survey of health characteristics among older adults.

PARTICIPANTS—Community-dwelling adults aged 65 and older completing a general health questionnaire and consenting to physical measurements (N=3,665).

MEASUREMENTS—Frailty was measured using criteria developed in the Cardiovascular Health Study and depressive symptoms were measured using the 8-item Center for Epidemiologic Studies Depression scale.

RESULTS—Frailty and depression were best modelled as two distinct but highly correlated constructs with 3-classes and 4-classes of symptom response respectively. Measurement overlap was high among both men and women. Approximately 73% of individuals with severe depressive symptoms, and 86% of individuals with primarily somatic depressive symptoms, were categorized as concurrently frail. The degree of construct overlap between depression and frailty did not significantly vary by gender, but women were significantly more likely to endorse all frailty and depressive symptoms.

CONCLUSION—Measures of depression and frailty identify substantially overlapping populations of older men and women. More frequent endorsement of depressive symptoms, but not differential endorsement of somatic symptoms may contribute to the higher prevalence of

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frailty among women. The symptom of exhaustion is particularly important to the correlation between these two conditions. Findings will inform efforts by clinicians and researchers to refine the definition of geriatric syndromes like frailty and to develop effective interventions.

INTRODUCTION

Frailty, a syndrome characterized by vulnerability to morbidity and mortality in later life, affects approximately one in 10 older adults, and is an important predictor of disability, falls, hospitalization and mortality (1-3). One principal justification for denoting frailty as a discrete geriatric syndrome is that it provides a useful way for clinicians to identify vulnerable older adults in time to delay or prevent disability (4-6). However, lack of consensus about the symptoms that define frailty as a distinct syndrome limits the ability to clinically identify affected individuals and develop meaningful approaches to treatment (3, 7).

The criteria proposed by Fried and colleagues define frailty as a syndrome of five biologic deficits which are thought to operate distinctly from comorbidity, disability, or disease (4, 7, 8). Previous research supports the existence of a syndrome characterized by co-occurrence of these deficits (9); however, other symptoms, particularly psychological symptoms, may also be relevant to the definition of frailty. Indeed, alternative definitions of this construct have included cognitive (10) and sensory (11) domains (7, 12). However, these different conceptual models have only limited agreement in identifying whether an individual is frail or not, which limits the application of this construct in clinical care (3, 13).

The refinement of the definition of frailty is additionally complicated by the potential inability of current operational schema to discriminate frailty from other geriatric syndromes, particularly depression (14). Like frailty, depression is a common condition among older adults and shares symptoms, putative causes, and potential consequences with frailty (15). Predictably, the two conditions are highly comorbid, but the reasons for their co-occurrence are unclear (16, 17). Older adults with depression are more likely than younger adults to endorse somatic depressive symptoms (e.g., sleep disturbances, fatigue (18)), suggesting that frailty and depression may be correlated due to shared symptom profiles. These two conditions may also represent alternate manifestations of a more general vulnerability to functional decline which increases with age (19).

Latent class analysis is a method for identifying distinct subgroups of individuals based on their patterns of symptom endorsement. It is a useful technique for identifying clinical syndromes, particularly in cases where there is no consensus regarding case definition, or in instances where there is potential overlap between syndromes (e.g., depression and frailty). Finally, there has been little research on the role of gender in the correlation between depression and frailty. Women are more likely to be identified as frail, regardless of the criteria used, and tend to accumulate more physiological deficits with age (1). Likewise, depressive symptoms, particularly somatic symptoms, are more common among women (20).

The purpose of this study is two-fold: 1) To assess the extent of diagnostic overlap between frailty and depression among a nationally representative sample of older adults; and 2) To explore gender differences in the depression-frailty diagnostic overlap.

METHODS

Data and Sample Characteristics

Data for this study come from the 2008 wave of The Health and Retirement Study (HRS), an ongoing, nationally-representative prospective survey of adults aged 51 and over (21). Respondents are interviewed every two years, and beginning in 2004, a random subset was selected at each wave to participate in enhanced face-to-face interviews. The enhanced interviews include objective measures of physical characteristics such as height, weight, gait speed, strength, and other indicators of physical functioning (22).

A total of 17,217 respondents were interviewed in the 2008 wave. Respondents were ineligible to participate in enhanced physical measurement interviews if they were currently residing in a nursing home (n=460) or interviewed by proxy (n=1,140). Of the 6,931 respondents who consented to enhanced interviews, 4,552 were aged 65 and over. The current study is restricted to the 3,665 respondents aged 65 and over who completed or attempted physical performance measures required to determine frailty status. Respondents who completed the physical performance measures were more likely to be women ($t=3.44$, $p<.001$), white ($t=8.36$, $p<.001$), currently married ($t=6.50$, $p<.001$) and more educated ($t=5.68$, $p<.001$) compared to those excluded.

Measures

Frailty—Frailty was modeled using criteria from the Cardiovascular Health Study (CHS), which includes deficits in five areas: low weight, physical inactivity, exhaustion, weakness, and slowness (8). To the extent possible, operationalization of these criteria approximated or replicated CHS criteria. *Low weight* was defined as a self-reported or calculated loss of 10% or more in BMI since the previous (2006) wave or as a current BMI $<18.5 \text{ kg/m}^2$. Physical activity was calculated as the average frequency of three activity intensities weighted according to average metabolic equivalency of task (MET) scores (mild: 1-3 MET, moderate: 3-6 MET, and vigorous 6-10 MET); *physical inactivity* was defined as being in the lowest 20% on the physical activity score stratified by gender. In the CHS, exhaustion was indicated by endorsement of one of two items from the Center for Epidemiologic Studies – Depression (CESD) scale. Because the goal of this study is to examine the degree of diagnostic overlap between depression and frailty, we did not use items from the CESD to indicate frailty. We instead defined *exhaustion* as self-report of persistent or troublesome fatigue or exhaustion within the past two years. *Weakness* was defined as having dominant hand grip strength below gender- and BMI-specific cut-points as established in the CHS (8). *Slowness* was defined as a speed $<.762 \text{ m/s}$ for women $>159 \text{ cm}$ or men $>173 \text{ cm}$ tall, and as $<.653 \text{ m/s}$ for women $>159 \text{ cm}$ or men $>173 \text{ cm}$ tall, measured on a 2.5-meter course (8, 9). Individuals who attempted but were unable to complete physical tests for health reasons were considered as meeting the corresponding frailty criteria.

Depression—Depressive symptoms were ascertained using the 8-item CESD(23, 24). The CESD assesses the presence or absence of eight depressive symptoms over the previous week; positive items were reverse-coded. The CESD has moderate agreement with major depression as assessed using the Composite International Diagnostic Interview (CIDI). In the HRS specifically, the CESD has a sensitivity of .71 and specificity of .79 compared to the CIDI-assessed MD (23, 24).

Covariates—Demographic characteristics, self-rated health, and disability status were assessed by self-report. Cognitive functioning was assessed using a summary index (range: 0-35) (25).

Analysis

The bivariate associations between depressive symptoms and demographic characteristics, health indicators, disability status, and the five frailty indicators were examined using t-tests for continuous variables and Fisher's exact tests for categorical variables.

Latent class analysis (LCA) was used to investigate the construct overlap between frailty and depression. LCA assumes the existence of an underlying categorical latent variable (i.e. frailty and/or depression) which explains the correlation between a set of observed symptoms(26). LCA is used to identify discrete subgroups (called classes) of individuals who share similar symptom endorsement patterns. LCA estimates two types of parameters: 1) the proportion of the population belonging to a particular class (unconditional probabilities); and 2) probability of symptom endorsement given membership in a class (conditional probabilities). Observations in all LCA models were weighted to account for the complex sampling design of the HRS (22).

We compared a series of LCA models in which two separate latent variables representing frailty and depression were indicated by symptoms from the CHS criteria and CESD respectively. Each of these models specified different numbers of classes for each of the two latent variables representing depression and frailty. The explanatory strengths of these models were compared using goodness-of-fit statistics including Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and sample-size adjusted Bayesian Information Criterion (BIC_N), for which smaller numbers indicate better relative fit.

To examine differences in frailty and depression classes by gender, we performed a multiple group LCA(27). To summarize, first, the analytic steps described above were repeated among men and women separately to determine whether the number of latent classes was similar by gender. Second, we evaluated whether the prevalence of each class (i.e., unconditional probabilities) and symptom endorsement patterns (i.e., conditional probabilities) differed across gender by comparing the fit of a model constraining these parameters to be equal for men and women with a model without these constraints. The final, best-fitting model was used to compare symptom endorsement profiles across gender. All latent class models were estimated using Mplus software (30).

RESULTS

The characteristics of the analytic sample stratified by gender and depression status are shown in Table 1. Individuals who reported experiencing at least 4 CESD symptoms were significantly more likely to be women, have less education, and be unmarried. Elevated depressive symptoms were also associated with presence of functional disability, lower cognitive performance scores, poorer self-rated health, and higher likelihood of endorsing all frailty criteria. Women were more likely to endorse all frailty criteria.

Measurement Invariance by Gender

In overall and gender-specific analyses, the model achieving the best fit to the data was one in which depression and frailty were represented by separate but correlated latent variables, with depression described by four latent classes (low, moderate, somatic, and severe) and frailty described by three latent classes (low, moderate frailty, and frailty with exhaustion).

In a multiple-group LCA, we evaluated whether there were significant differences in class membership and symptom endorsement patterns by gender. Models allowing for variability in symptom endorsement probability by gender produced comparable fit to models constraining these probabilities to be equal ($BIC_N = 39493.57$ and $BIC_N = 39486.44$ respectively), indicating that men and women were equally likely to endorse particular symptoms given their membership in a particular class.

Class Characteristics

Figures 1a and 1b present class proportions and symptom endorsement probabilities for the best-fitting model. Conditional probabilities (that is, the probability of symptom endorsement given membership in a particular class) of the four depression subgroups were similar by gender (Figure 1a). Among both men and women, three distinct classes of depression characterized by low, moderate and high endorsement of all criteria were apparent. The fourth class, *somatic depression*, was characterized by endorsement of restless sleep, lack of motivation, and feeling activities were an effort. Women were more likely than men to be in the moderate or severe depression classes. Frailty conditional probabilities were also similar by gender (Figure 1b). The criterion of *exhaustion* distinguished the two classes with the greatest symptom endorsement; the criterion of low BMI did not discriminate between frailty classes among either men or women, as shown by similar conditional probabilities for all three classes. As described above, the characteristics of the frailty and depression classes (e.g., conditional probabilities) did not vary by gender. However, as shown by Figures 1a and 1b, women were more likely to belong to the moderately frail or frail with exhaustion classes, as well as to the somatic, moderate and severe depression classes, relative to men. For example, 16.4% of women were in the moderately frail class, as compared to only 9.5% of men.

Table 2 summarizes class overlap of frailty and depression. Among those in the low depression class, only 13.2% were classified in the moderate frailty class, and 0% were in the frailty with exhaustion class. Among those in the somatic depression class, 23.3% were classified as moderately frail and 63.2% were classified as the frailty with exhaustion.

Similarly, those in the severe depressive subgroup (8.6%) were likely to endorse frailty symptoms, with approximately 71% classified as moderately frail or frail with exhaustion.

DISCUSSION

The primary finding of this study is that frailty and depression identify highly-overlapping populations of older adults. The overlap between depression and frailty was greatest for the somatic and severely depressed subgroups; nearly three-quarters of the individuals in the severe depression class were categorized in either the moderately frail or frail with exhaustion classes, compared to only 12% of individuals in the low depression class. This indicates that current approaches to operationalizing frailty and depression syndromes are poor at discriminating between these two conditions among older adults. We also found no evidence that the measurement of these constructs differs by gender. That is, the higher prevalence of frailty among older women is not driven by gender differences in the measurement of depression (and vice versa).

A key implication of these findings is that investigations of the determinants, course, and consequences of frailty should not be examined in isolation from those of depression. Because of the substantial construct overlap in these two conditions, to examine them in isolation would be to misattribute risk factors, treatment outcomes, and consequences to only one condition when both are relevant. This replicates recent work from our group that demonstrated substantial construct overlap between frailty, as defined by CHS criteria, and depression syndrome, as defined by the Diagnostic Interview Schedule (DIS) (14). The consistency of overlap between CHS-defined frailty and two different operationalizations of depression syndrome (DIS and CESD) suggests that the association between these two constructs may be explained in part by an underlying conceptual overlap or a common underlying factor, rather than features of the measurement tool. Our findings are consistent with the hypothesis that the co-occurrence of frailty and depression may be indicative of some common pathology, such as vascular damage to the brain, in line with a recent proposition by Hajjar and colleagues (28). Vascular depression, a subtype of depression characterized by slowness, fatigue and muscular weakness, has been suggested as a prodromal state or early warning sign of frailty (29). In support of this hypothesis, we found that individuals in the somatic depression class were highly likely to be considered frail, with 85% of individuals categorized in the moderate or frail with exhaustion classes. In addition to shared pathology, there are other mechanisms that may explain the depression-frailty relationship. Lakey and colleagues found that antidepressant use predicted incident frailty among older women independent of depressive symptoms (30).

Our findings should be interpreted in light of study limitations. First, while the CESD asks respondents to report depressive symptoms in the previous week, some frailty criteria describe changes (e.g., weight loss) or represent average measures (e.g. physical activity). These differences may have inflated the concurrence of depression and frailty. Second, the resulting classes from LCA are dependent on the specific metrics used to operationalize frailty and depression syndromes. The CESD, a short symptom inventory, may not evaluate all the depressive symptoms that are relevant to identify all meaningful subgroups. Lastly, although analyses were weighted according to sampling probabilities, only a subsample was

selected for the enhanced face-to-face interviews with physical measurements. Strengths of this study include the large, nationally-representative sample and use of LCA to empirically determine syndrome classes. We were also able to examine whether gender differences in the prevalence of depression and frailty were due to measurement inconsistencies, one of the first efforts of this kind.

There is substantial construct overlap between depression and frailty among older adults. The symptom of exhaustion is particularly important to the correlation between these two conditions. These findings can inform efforts by clinicians and researchers to refine the definition of geriatric syndromes like frailty. Finally, future research should examine whether the co-occurrence of depression and frailty is due to a shared pathology, and whether there are distinct implications of this comorbidity for risk of disability and mortality.

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a. Probability of endorsing specific CESD symptoms according to subtype of depression and gender

b. Probability of endorsing specific frailty symptoms according to subtype of frailty and gender

Figure 1.

a: This figure illustrates the probability of endorsing each of the 8 CESD symptoms for individuals in each of the four depressive subtype groups (severe depression, moderate depression, somatic depression, and low symptoms). The results for the four depression subtypes are plotted separately for women (FEM) and men (MALE). The percentages in the legend refer to the prevalence of each specific depressive subtype within each gender group.

b: This figure illustrates the probability of endorsing each of the 5 frailty symptoms for individuals in each of the three frailty subtype groups (frail/exhaustion, moderate frailty, and low symptoms). The results for the three frailty subtypes are plotted separately for women (FEM) and men (MALE). The percentages in the legend refer to the prevalence of each specific frailty subtype within each gender group.

Table 1
Sample characteristics stratified by depressive symptom levels and gender: The 2008 Health and Retirement Study

	Overall (N = 3665)	High Depressive Symptoms ^b (N = 403)	Low Depressive Symptoms (N = 3262)	Women (N=2,093)	Men (N=1,572)
Demographics					
Female	55.5	67.0	54.0	---	---
Race					
White	90.8	88.3	91.1	89.8	91.9
Black	6.2	7.4	6.1	7.1	5.2
Other	3.0	4.3	2.9	3.1	2.9
Age (years)	74.6 (6.8)	74.9 (7.1)	74.6 (6.8)	74.7 (7.1)	74.5 (6.5)
Education (years)	12.4 (3.1)	11.1 (3.4)	12.6 (3.0)	12.2 (2.9)	12.6 (3.3)
Married	56.0	41.8	57.9	41.9	73.6
Currently Employed (PT/FT)	10.2	6.8	10.6	7.5	13.5
Health Indicators					
Cognitive Total	21.8 (4.9)	19.5 (5.6)	22.1 (4.7)	22.0 (4.6)	21.5 (4.6)
Any IADL disability	12.4	32.1	9.9	13.6	11.0
Any ADL disability	14.9	40.4	11.6	15.6	14.0
Self-rated health (poor/fair)	25.8	63.5	20.9	25.7	25.9
CESD 4 Symptoms	---	---	---	13.81	8.49
Frailty Criteria (present)					
Low BMI	6.7	9.1	6.4	8.3	4.8
Exhaustion	15.9	46.4	12.0	18.7	12.4
Slow movement	30.9	48.8	28.6	35.9	24.8
Weakness	29.6	42.7	28.6	33.6	26.0
Low energy expenditure	21.9	41.0	19.4	23.7	19.7
Intermediate frail ^c	45.6	52.7	44.7	48.8	41.7
Frail ^c	9.3	26.5	7.1	11.5	6.5

^a Values are weighted using the HRS physical measures subsample weight

^b High depressive symptoms defined as 4 symptoms on the CES-D.

^c Based on Fried et al. (2001) criteria. Frail = endorse 3 or more frailty criteria. Intermediate frail = endorse 1 or 2 frailty criteria.

Table 2

Prevalence of frailty (low, moderate, and frail/exhaustion) according to depression symptom subgroup

	Total	Women	Men
	3,665	2,093	1,572
Depression subgroup			
Low depressive symptoms	66.3%	61.0%	74.4%
<i>Low symptoms</i>	86.8%	88.7%	84.2%
<i>Moderate Frail</i>	13.2%	11.4%	15.8%
<i>Frail - exhaustion</i>	0.0%	0.0%	0.0%
Moderate depressive symptoms	11.3%	13.5%	7.3%
<i>Low symptoms</i>	57.0%	62.3%	80.5%
<i>Moderate Frail</i>	38.2%	36.5%	11.5%
<i>Frail - exhaustion</i>	4.9%	1.3%	8.0%
Somatic depression	13.9%	15.2%	12.7%
<i>Low symptoms</i>	13.4%	15.3%	9.1%
<i>Moderate Frail</i>	23.3%	23.5%	30.3%
<i>Frail - exhaustion</i>	63.2%	61.2%	60.6%
Severe depression	8.6%	10.3%	5.5%
<i>Low symptoms</i>	27.2%	20.3%	48.4%
<i>Moderate Frail</i>	1.7%	3.88%	0.4%
<i>Frail - exhaustion</i>	71.1%	75.8%	51.2%

Estimates derived from the best-fitting model with four depression classes and three frailty classes (BIC=36535.95;BIC_N=36351.65).

Class membership is based on estimated posterior probabilities.