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Research Article

Operationalizing Frailty in the Atherosclerosis Risk in Communities Study Cohort

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Abstract

Background: Factors that may contribute to the development of frailty in late life have not been widely investigated. The Atherosclerosis Risk in Communities (ARIC) Study cohort presents an opportunity to examine relationships of midlife risk factors with frailty in late life. However, we first present findings on the validation of an established frailty phenotype in this predominantly biracial population of older adults.

Methods: Among 6,080 participants, we defined frailty based upon the Cardiovascular Health Study (CHS) criteria incorporating measures of weight loss, exhaustion, slow walking speed, low physical activity, and low grip strength. Criterion and predictive validity of the frailty phenotype were estimated from associations between frailty status and participants' physical and mental health status, physiologic markers, and incident clinical outcomes.

Results: A total of 393 (6.5%) participants were classified as frail and 50.4% pre-frail, similar to CHS (6.9% frail, 46.6% pre-frail). In age-adjusted analyses, frailty was concurrently associated with depressive symptoms, low self-rated health, low medication adherence, and clinical biomarker levels (ie, cholesterol, hemoglobin A1c, white blood cell count, C-reactive protein, and hemoglobin). During 1-year follow-up, frailty was associated with falls, low physical ability, fatigue, and mortality.

Conclusions: These findings support the validity of the CHS frailty phenotype in the ARIC Study cohort. Future studies in ARIC may elucidate early-life exposures that contribute to late-life frailty.

Keywords: Frailty—Epidemiology—Cohort study

Frailty is a clinical syndrome characterized by vulnerability to adverse health outcomes resulting from decreased reserve and low resistance to stressors. The co-occurrence of multisystem, age-associated declines is the impetus for identifying frailty as a syndrome that includes weight loss, weakness, exhaustion, decreased physical activity, and slowness (1). Frailty is associated with a number of adverse outcomes, including hospitalizations (2) and cognitive impairment (3–5), yet little is known about risk factors in midlife, when interventions may be more effective, on risk of frailty onset in late life. The 25 plus years of follow-up in the Atherosclerosis Risk in Communities (ARIC) Study cohort present an opportunity to elucidate the association of early-life risk factors for frailty in a biracial population. Using the frailty phenotype definition, derived from the Cardiovascular Health Study (CHS) (1), our aim is to develop a frailty phenotype within the ARIC Study cohort, provide estimates of the prevalence of frail, pre-frail, and robust states of

ARIC participants, and therefore lay the groundwork for future assessments of the etiology of frailty.

Methods

Study Population

The ARIC cohort was established in 1987 as a probability sample of 15,792 men and women, aged 45–64 years (mean age: 54 years), from four US communities. Extensive physical examinations were performed at baseline and at four subsequent clinic visits. Ongoing follow-up is conducted through annual telephone interviews and surveillance of mortality and cardiovascular morbidity. The current study uses data from the fifth examination, when objective measures of frailty were first assessed (Visit 5, 2011–2013; n = 6,538). Prevalent medical conditions at Visit 5 were ascertained from self-report, prior hospitalizations, and Visit 5 physical examination. Black participants from Washington County, Maryland and Minneapolis, Minnesota (n = 25), and participants reporting Asian or American Indian/Alaskan Indian ethnicity (n = 18) were excluded due to small numbers.

Frailty Phenotype

The CHS frailty components were operationalized in ARIC (Table 1) with some modifications as required by available data and incorporating methods used in previous studies. Weight loss was defined as 10% of weight lost from Visit 4 (1996–1999) to Visit 5 (2011–2013) or Visit 5 body mass index (BMI) less than 18.5 kg/m^2 (6). The modified Baecke questionnaire assessed physical activity (7), with low physical activity defined as the lowest 20th percentile. Walking speed was measured at participants' usual pace over 4 m. Slow walking speed was defined using gender- and height-adjusted thresholds from the CHS cohort. Participants who responded "some of the time" or "most of the time" to either of the following two questions from the Center for Epidemiological Studies-Depression (CES-D) scale (8), "I felt everything I did was an effort" and "I could not get 'going'," were classified as having exhaustion. Grip strength was assessed in the participant's preferred hand using an adjustable, hydraulic grip strength dynamometer. Excluded were participants who had bilateral surgery in the hands or wrists in the previous 3 months. Low grip strength was defined as gender- and BMI-specific grip strength in the lowest 20th percentile based on established norms (1).

The composite frailty variable was categorized as robust when no frailty components were present; pre-frail, if one or two of the components were present; and frail, if three or more of the component phenotypes were present. Participants with missing information on all component characteristics were classified as missing the frailty phenotype (n = 415, 6.4%), yielding an analytic sample of 6,080. In a sensitivity analysis, we assigned a frailty category for participants who were missing the frailty phenotype (n = 415), but who had at least one criterion component nonmissing. This was performed using the most prevalent frailty classification observed for the nonmissing criterion among those with a frailty classification (n = 6,080). For example, frailty of a participant with low grip strength, and all other component characteristics missing, was defined as the most prevalent frailty category observed among participants who had both nonmissing frailty phenotype and nonmissing low grip strength (Supplementary Table 3). Participants with two nonmissing component characteristics, such as slow walking speed and low grip strength, were therefore classified according to the most prevalent frailty category observed among participants who had a nonmissing frailty phenotype, nonmissing slow walking speed, and nonmissing low grip strength (Supplementary Table 4).

Outcomes

Criterion validity

We defined criterion validity of the frailty phenotype as concurrent presence of selected phenotypes signifying participant's health status. In cross-sectional analyses, we examined the association of the frailty phenotype with prevalence of low and fair self-rated health (SRH), physical and mental health status assessed from the SF-12

Table 1. Operationalization of the Frailty Construct in ARIC Cohort in Comparison With the CHS and WHAS

Characteristics of Frailty	ARIC (N = 6,080)		CHS (N = 5,317)		
Weight loss	10% of weight lost from V4 (1996–1999) to V5 (2011–2013) or BMI < 18.5 at Visit 5	20.1%	Lost > 10 lbs in last year		6.0%
Low physical activity	Gender-specific 20th percentile rank of the Baecke leisure sports activity index	14.7%	270 on an activity scale (18 items)		22.0%
Slow walking speed	Gender- and height-adjusted time in seconds used to walk 4 m Slowest speed defined as the 20th percentile of the distribution	15.1%	Walking 15 ft: Time ≥ 7 for height ≤ 159 cm Time ≥ 6 for height > 159 cm		20.0%
Exhaustion	Responded "some of the time" or "most of the time" to the following questions: *I felt everything I did was an effort* or *I could not get "going"*	10.4%	Responded "some of the time" or "most of the time" to the following questions: *I felt everything I did was an effort* or *I could not get "going"*		17.0%
Low grip strength	Gender- and BMI-specific grip strength in the lowest 20% percentile of distributions	25.4%	BMI ≤23 23.1–26 26.1–29 >29	Grip strength ≤17 ≤17.3 ≤18 ≤21	20.0%
Frailty	n = 393 (6.5%)		n = 368 (6.9%)		

Notes: ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; CHS = Cardiovascular Health Study; WHAS = Women's Health and Aging Study.

questionnaire (9), medication adherence, and multimorbidity (the presence of at least two chronic diseases). We also compared levels of clinical biomarkers (ie, white blood cell count (10), total cholesterol (11), hemoglobin (12), hemoglobin A1c [HbA1c] (13), and C-reactive protein [CRP (10)]) previously associated with frailty, across the frailty phenotypes.

Predictive validity

We examined the association of the frailty phenotype with the following outcomes assessed within 1 year of Visit 5: fatigue, falls, physical ability, and mortality.

Outcomes ascertainment

Disease status was ascertained at baseline through questionnaires administered to the participants, medical record abstraction prior to Visit 5, and from self-report of physician's diagnoses obtained during annual telephone interviews prior to Visit 5. High medication adherence was defined as a score ≥2 on the four-item Morisky Medication Adherence Measure (14). Participants' SRH was reported as "excellent," "very good," "good," "fair," or "poor." Scores for the physical and mental domains were obtained as *T*-scores standardized to the average US general population according to standard protocols (9). Participants' cognitive status at Visit 5 was assessed using the Mini-Mental State Examination (MMSE) test (15).

Fatigue was assessed using a custom questionnaire based on the PROMIS adult bank of fatigue questions during a telephone follow-up interview conducted approximately 1 year following Visit 5. Responses were scored using item-level calibration with standardization to the average US general population (16) (see Supplementary Material).

Within 1 year of Visit 5, ARIC participants were asked if in the previous 6 months they had experienced a fall and if so, how many. Physical ability was assessed as self-reported "difficulty in performing" household activities, meal preparation, self-care, and management of finances (17–19).

Mortality was ascertained from CMS Medicare data using the Medicare Beneficiary Summary Files for the years 2011–2013 that were linked to the ARIC Study cohort for 6,422 cohort participants (98.9%) enrolled in CMS Medicare at the time of Visit 5 (20). To ensure at least 1 year of follow-up in mortality estimates, we excluded from the assessment of mortality participants whose Visit 5 examination occurred during 2013 (n = 909).

Statistical Analysis

Baseline demographic and health characteristics were described by frailty status. Age was centered at the sample population median (75 years). Generalized linear models were used to estimate the age-adjusted cross-sectional associations between frailty status and clinical characteristics to quantify criterion and predictive validity. Cox proportional hazard models, adjusted for age, demographics, and comorbidities were fit to estimate mortality across frailty groups.

Results

The distribution of the frailty-defining criteria in ARIC compared with CHS is presented in Table 1. Low grip strength and weight loss were the most prevalent component characteristics (25.4% and 20.1%, respectively). Exhaustion was least prevalent, at 10.4%. Among the 6,080 ARIC participants at Visit 5, 393 (6.5%) were frail, 3,066 (50.4%) were pre-frail, and 2,621 (43.1%) were robust (Table 2). Frail and pre-frail participants were more likely to be older, of black race, report fair or poor SRH, have a higher prevalence of cardiovascular diseases, and report more chronic conditions compared with their robust counterparts. An increasing proportion of participants with chronic diseases other than cancer were observed in frail compared with pre-frail and robust participants. The average BMI increased from 28.3 kg/m^2 (standard deviation [*SD*]: 5.0) among the robust, to 28.9 kg/m^2 (*SD*: 5.9) among the pre-frail, to 29.7 kg/m^2 (*SD*: 7.1) among the frail. Depressive symptomology using the CES-D score also increased across the frailty categories. The prevalence of frailty increased with age and was significantly higher in women compared with men (Table 3).

Criterion Validity

In age-adjusted analyses, the proportion of participants with multimorbidity was lowest among robust and highest among frail participants (49.0% vs 75.1%; Table 4). The proportion of participants with good/excellent SRH decreased from 66.6% among the robust, to 25.8% among frail participants. The SF-12 physical and mental health aggregate scores, MMSE, and CES-D scores suggest that physical and mental health was better among robust participants than pre-frail participants, which in turn was better than that of frail participants. Frail participants also used more medications than robust participants (10.7 vs 8.6; Table 4). The proportion of participants with high medication adherence was lowest among the frail.

Predictive Validity

Participants classified as frail reported falls more frequently than did those classified as pre-frail and robust (25.0%, 16.1%, and 12.5%, respectively; Table 5). Frail participants were more likely to report limitations in physical ability (eg, meal preparation and self-care). Management of finances was not associated with frailty status. Frail participants reported a greater level of fatigue at approximately 1 year following assessment of frailty than robust participants. Sensitivity analyses, limited to those with at least 180 days of follow-up, yielded estimates similar to those observed in overall analyses. Mortality increased across frailty categories for both gender and race subgroups (Figure 1).

We observed few gender and race differences in outcomes across the frailty phenotype (Supplementary Table 1). Most notable was poorer SRH observed among women as compared with men. SRH was also significantly higher among whites than blacks; however, change in SRH across frailty categories did not differ by race. The overall proportion of those with multimorbidity, which was greater among blacks compared with whites, did not change appreciably across frailty categories.

Sensitivity Analyses

Analyses conducted using the definition of frailty that minimized the amount of participants with missing frailty classification yielded estimates of concurrent and predictive validity that were similar to those obtained using the original frailty construct (data not shown). The definition of frailty created within ARIC was therefore robust to approximately 6.4% of data missingness.

Discussion

In this study, we validated a version of the CHS frailty phenotype, modified to data available in a biracial older population of ARIC Study cohort participants, and demonstrated nearly identical

Table 2. Baseline Demographic and Health Characteristics; the ARIC Study 2011–2013

Characteristic	Overall	Robust	Pre-Frail	Frail	*p* Value
N	6,080 (100%)	2,621 (43.1%)	3,066 (50.4%)	393 (6.5%)	
Age, y					<.001
66–74	2,887 (47.5)	1,536 (58.6)	1,230 (40.1)	121 (30.8)	
75–84	2,786 (45.8)	1,016 (38.8)	1,558 (50.8)	212 (53.9)	
85+	407 (6.7)	69 (2.6)	278 (9.1)	60 (15.3)	
Gender, % male	2,526 (41.5)	1,195 (45.6)	1,198 (39.1)	133 (33.8)	<.001
Race, % black	1,383 (22.7)	508 (19.4)	776 (25.3)	99 (25.2)	<.001
ARIC Study center					<.001
Forsyth	1,300 (21.4)	535 (20.4)	679 (22.1)	86 (21.9)	
Jackson	1,287 (21.2)	484 (18.5)	713 (23.3)	90 (22.9)	
Minneapolis	1,819 (29.9)	919 (35.1)	821 (26.8)	79 (20.1)	
Washington County	1,674 (27.5)	683 (26.1)	853 (27.8)	138 (35.1)	
Self-rated health					<.001
Excellent	986 (16.3)	604 (23.1)	366 (12.1)	16 (4.1)	
Very good	2,216 (36.7)	1,139 (43.5)	992 (32.8)	85 (21.7)	
Good	2,091 (34.6)	741 (28.3)	1,190 (39.3)	160 (40.8)	
Fair	676 (11.2)	131 (5.0)	435 (14.4)	110 (28.1)	
Poor	71 (1.2)	4 (0.2)	46 (1.5)	21 (5.4)	
Prevalent disease					
CHD	893 (14.9)	309 (12.0)	508 (16.9)	76 (19.7)	<.001
Heart failure	991 (16.3)	294 (11.2)	564 (18.4)	133 (33.8)	<.001
Stroke	235 (3.9)	56 (2.1)	148 (4.8)	31 (7.9)	<.001
Atrial fibrillation	453 (7.5)	134 (5.1)	266 (8.7)	53 (13.5)	<.001
Diabetes	1,973 (33.1)	673 (25.9)	1,124 (37.9)	176 (45.1)	<.001
Hypertension	4,472 (74.4)	1,827 (70.2)	2,330 (77.1)	315 (81.8)	<.001
Arthritis	2,599 (42.7)	1,031 (39.3)	1,352 (44.1)	216 (55.0)	<.001
Cancer	197 (3.2)	75 (2.9)	110 (3.6)	12 (3.1)	.30
Number of chronic conditions					<.001
0	670 (11.0)	379 (14.5)	278 (9.1)	13 (3.3)	
1	1,930 (31.7)	957 (36.5)	888 (29.0)	85 (21.6)	
2	2,129 (35.0)	859 (32.8)	1,123 (36.6)	147 (37.4)	
3–4	1,286 (21.1)	417 (15.9)	735 (24.0)	134 (34.1)	
≥5	65 (1.0)	9 (0.3)	42 (1.4)	14 (3.6)	
Ever-drinker	4,633 (78.7)	2,138 (82.5)	2,211 (76.2)	284 (72.4)	<.001
Ever-smoker	3,310 (58.8)	1,408 (58.0)	1,692 (60.0)	210 (55.1)	.11
BMI, mean (*SD*)	28.6 (5.7)	28.3 (5.0)	28.9 (6.1)	29.7 (7.1)	<.001
CES-D, median (IQR)	2 (1, 5)	2 (1, 3)	3 (1, 5)	4 (2, 8)	<.001

Notes: ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; CES-D = Center for Epidemiological Studies-Depression; CHD = coronary heart disease; IQR = interquartile range; *SD* = standard deviation.

prevalence rates of frailty in the ARIC Study cohort as was reported among CHS participants 15 years earlier. We anticipate the frailty assessment in the ARIC cohort will provide unique opportunities to shed light on important contributors to late-life frailty. Although most studies on the frailty syndrome have been conducted in older adults, ARIC provides a detailed characterization of this cohort since midlife. Consistent with other studies, the prevalence of frailty was higher among older participants, women, and blacks. Low grip strength was the most prevalent frailty component, followed by weight loss and slowness. The frailty phenotype, originally developed in the CHS cohort (1), has been previously validated (1,2,21) but requires further validation in several distinct populations to determine its utility in predicting the risk of long-term adverse health outcomes. The frailty phenotype was validated in the present study by examining its associations with clinical characteristics and physiological markers previously found to be associated with frailty.

In age-adjusted cross-sectional analyses, frailty was associated with presence of depressive symptoms, low SRH, comorbidity burden, low medication adherence, and clinical biomarker levels (ie, total cholesterol, HbA1c, white blood cell count, C-reactive protein, and hemoglobin). Across all frailty phenotypes, blacks reported lower SRH than whites. There is extensive literature to suggest that SRH is an important predictor of adverse health outcomes, including coronary heart disease (22) and mortality (23). These observed racial differences in SRH may be attributable to access to health care (24) and may contribute to observed differences in frailty prevalence by race subgroups.

Predictive validity of the frailty phenotype was demonstrated through associations with participant's ability to perform functional tasks, including housekeeping, meal preparation, and self-care within 1 year of frailty assessment. In a critical test of predictive validity, frailty in ARIC was observed to be associated with a higher risk of mortality that did not differ by gender or race.

Our findings were similar to observations from other population-based cohorts of older adults, underscoring the utility of the CHS definition of frailty in ARIC. Compared with the Women's Health and Aging Study (WHAS) (6), a population-based observational cohort of older women, we observed a lower prevalence of frailty in ARIC women (11.3% vs 6.5%); this could be explained by WHAS sampling, which included a broader representation of the

disabled through targeted recruitment and lower susceptibility to healthy volunteer effects. It is also important to note that WHAS participants were all women, who are at a higher risk of disability compared with men (25). Compared with the Women's Health Initiative (WHI) (2), a prospective study of women aged 50–79, the prevalence of frailty in ARIC was also lower (16.3% vs 6.5%). The prevalence of frailty in the National Health and Aging Trends Study (NHATS) was similar to that of WHI (15%), which is higher than that of ARIC (6.5%). Similar to ARIC, frailty in NHATS was more prevalent among individuals of older ages, women, and racial/ethnic minorities; however, NHATS reported a higher incidence of falls among the frail (21). Differences across these cohorts are to be expected considering the distinct component measures that may not be identical to those in CHS. However, similar estimates of the prevalence of frailty in CHS and ARIC and associations with health status, incident outcomes, and biomarkers, despite heterogeneity in some measurements, age cohorts, and geographical catchment areas, support the validity of the frailty construct.

Table 3. Prevalence of Frailty in the ARIC Cohort, by Age and Race/Gender Subgroups

Race/Gender Subgroups	All Ages	Age Strata (y)		
		66–74	75–84	85+
Total cohort				
Total cohort	*n* = 6,080	*n* = 2,887	*n* = 2,786	*n* = 407
n (% frail)	393 (6.5)	121 (4.2)	212 (7.6)	60 (14.7)
Total women	*n* = 3,554*	*n* = 1,737*	*n* = 1,590*	*n* = 227
n (% frail)	260 (7.3)	89 (5.1)	139 (8.7)	32 (14.1)
Total men	*n* = 2,526	*n* = 1,150	*n* = 1,196	*n* = 180
n (% frail)	133 (5.3)	32 (2.8)	73 (6.1)	28 (15.6)
Whites only				
Total whites	*n* = 4,697	*n* = 2,129	*n* = 2,245	*n* = 323
n (% frail)	294 (6.3)	85 (4.0)	159 (7.1)	50 (15.5)
White women	*n* = 2,623†	*n* = 1,232†	*n* = 1,221†	*n* = 170
n (% frail)	190 (7.2)	62 (5.0)	102 (8.4)	26 (15.3)
White men	*n* = 2,074	*n* = 897	*n* = 1,024	*n* = 153
n (% frail)	104 (5.0)	23 (2.6)	57 (5.6)	24 (15.7)
Blacks only				
Total blacks	*n* = 1,383	*n* = 758	*n* = 541	*n* = 84
n (% frail)	99 (7.2)	36 (4.7)	53 (9.8)	10 (11.9)
Black women	*n* = 931	*n* = 505	*n* = 369	*n* = 57
n (% frail)	70 (7.5)	27 (5.3)	37 (10.0)	6 (10.5)
Black men	*n* = 452	*n* = 253	*n* = 172	*n* = 27
n (% frail)	29 (6.4)	9 (3.6)	16 (9.3)	4 (14.8)

Notes: ARIC = Atherosclerosis Risk in Communities.
*$p < .05$ for significant difference between women and men.
†$p < .05$ for significant difference between white women and white men.

The role of multimorbidity in the etiology of frailty remains unclear, with some studies supporting the accumulation of deficits as a reliable marker of the frailty construct (26), while others suggesting comorbidity, disability, and frailty overlap (27), but are distinct constructs. Prior data from WHAS suggest increased risk of frailty with a higher number of dysregulated physiologic patterns (28). In WHI and CHS, the prevalence of greater chronic conditions increased across frailty categories as the number of chronic diseases reached ≥3. In ARIC, 75% of frail participants had two or more chronic conditions; however, the prevalence of multimorbidity across the frailty groups differed by only 1%–2%, supporting the observation that frailty overlaps with, but is not fully explained by chronic disease (27).

Strengths and Limitations

The informative ARIC cohort is a large study of older adult men and women, allowing for assessment of gender and racial differences in the prevalence of frailty. The availability of data since midlife (29) is unique and may elucidate important factors associated with frailty in late life. Many of the other larger cohorts have been primarily in older women (2,6) with small proportions of blacks (1) and could not adequately examine frailty by clinically and socially meaningful subgroups.

Validity and reliability of the multifactorial frailty construct rely on the strengths and weaknesses of its components. These component characteristics in the ARIC cohort were highly correlated (data not shown). Frailty components derived from self-report (ie, exhaustion, low physical activity) are subject to lower reliability compared with that of the objectively measured components (ie, walking speed). Our measure of weight loss, estimating 10% weight lost during the

Table 4. Baseline Cross-Sectional Association of the Frailty Phenotype With Study Participant Characteristics; the ARIC Study Cohort 2011–2013

Characteristic	Robust (*n* = 2,621)	Pre-Frail (*n* = 3,066)	Frail (*n* = 393)
Overall			
Self-rated health, % good or excellent (95% CI)	66.6 (64.7, 68.4)	44.8 (43.1, 46.6)*	25.8 (21.0, 30.5)*
SF-12 physical aggregate score (*SD*)	49.9 (0.6)	44.2 (0.7)*	36.4 (0.7)*
SF-12 mental aggregate score (*SD*)	56.3 (0.1)	54.8 (0.1)*	52.1 (0.1)*
MMSE (*SD*)	28.0 (0.5)	27.0 (0.6)*	26.3 (0.6)*
CES-D (*SD*)	2.4 (0.1)	3.6 (0.1)*	5.3 (0.1)*
% with >2 chronic conditions (95% CI)	49.0 (47.2, 50.1)	62.0 (60.2, 63.7)*	75.1 (70.2, 79.9)*
Total cholesterol, mmol/L (*SD*)	4.8 (0.1)	4.7 (0.07)	4.5 (0.1)*
White blood cell count, mg/L (*SD*)	5.7 (0.1)	6.1 (0.1)*	6.5 (0.1)*
CRP, mg/L (*SD*)	3.5 (0.3)	4.6 (0.4)*	5.9 (0.4)*
HbA1c, % (95% CI)	5.7 (0.1)	6.1 (0.1)*	6.1 (0.1)*
Hemoglobin, g/dL (*SD*)	13.6 (0.1)	13.1 (0.1)*	12.7 (0.1)*
Self-reported number of medications used (*SD*)	8.6 (0.02)	9.8 (0.02)*	10.7 (0.02)*
Medication adherence, % high (95% CI)	62.5 (60.6, 64.4)	58.5 (56.8, 60.3)	57.4 (53.6, 62.2)*

Notes: All analyses adjusted for age centered at the sample population median (75 y). ARIC = Atherosclerosis Risk in Communities; CES-D = Center for Epidemiological Studies-Depression; CI = confidence interval; CRP = C-reactive protein; HbA1c = hemoglobin A1c; MMSE = Mini-Mental State Examination; *SD* = standard deviation.
*$p < .05$ for significant difference compared to robust (referent group).

Table 5. Predictive Validity of the Frailty Phenotype; the ARIC Study Cohort 2011–2013 (age-adjusted estimates)*

	Robust (n = 2,576)	Pre-Frail (n = 2,996)	Frail (n = 385)
Percent reported experiencing a fall	12.5	16.1	25.0
Physical ability (percent with no difficulty in performing tasks)			
Physical mobility	58.8	46.1	28.7
Housekeeping	87.1	76.7	52.4
Meal preparation	97.2	92.8	84.7
Self-care	96.4	92.5	85.4
Managing finances	98.7	97.4	93.6
Fatigue score†	43.2 (7.5)	46.3 (8.4)	51.2 (9.0)

Notes: All estimates, except the fatigue score, adjusted for age centered at the sample population median (75 y), race, BMI, LDL cholesterol, prevalent heart failure, prevalent CHD, diabetes, hypertension, cigarette smoking status. ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; CHD = coronary heart disease; IQR = interquartile range; LDL = low-density lipoprotein.

*Outcomes assessed at time of ARIC post-Visit 5 telephone follow-up interview. Median time from date of Visit 5 to date of telephone interview: 481 days (IQR 299, 569).

†Population-based normative scoring of a PROMIS fatigue questionnaire.

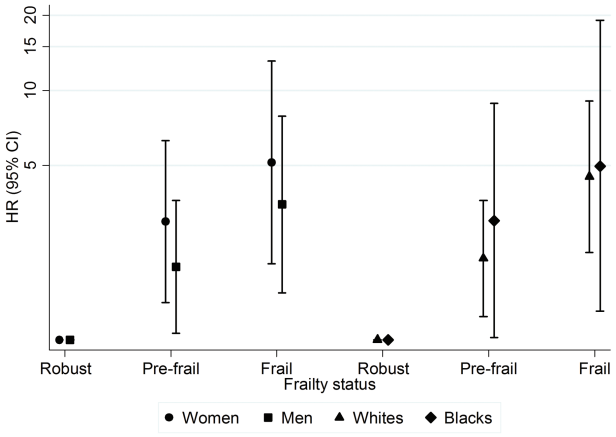

Figure 1. Mortality across frailty phenotype, by gender and race subgroups.

almost 15 years between ARIC Visits 4 and 5, did not capture the "unintentional" weight loss. Similarly to WHAS, ARIC participants were also categorized as having significant weight loss if their BMI was less than 18.5 kg/m^2. Our definition of low physical activity was based on the Baecke questionnaire and its comparison with physical activity assessments in CHS, WHAS, and WHI is not known. Despite these differences, the frailty measure in ARIC appears quite robust. Across the three frailty categories, missingness was low (<4%) for all variables examined with respect to criterion and predictive validity, except medication use, the missingness of which was 6% among the pre-frail and 5.6% among the frail. Using factor analyses, we confirmed the loading of the five frailty component variables onto one factor, suggesting that correlations between component criteria did not bias our assessment of the criterion and predictive validity of the frailty construct.

In summary, based on extant literature on the conceptualization of frailty across several cohorts, we concluded that this phenotype is stable across different study populations, the utility of the frailty construct is high, and it can be used to predict the risk of adverse health outcomes (30). As a result, it has strong potential to assist with risk stratification in the clinical setting. As an important element of aging, future work may consider adding measures of cognitive and social function to the frailty definition.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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