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Research Article

Racial, Ethnic, and Socioeconomic Differences in a Deficit Accumulation Frailty Index in the Multiethnic Cohort Study

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Abstract

Background: Frailty status has been sparsely studied in some groups including Native Hawaiians and Asian Americans.
Methods: We developed a questionnaire-based deficit accumulation frailty index (FI) in the Multiethnic Cohort (MEC) and examined frailty status (robust, FI 0 to <0.2, prefrail, FI 0.2 to <0.35, and frail FI ≥ 0.35) among 29 026 men and 40 756 women.
Results: After adjustment for age, demographic, lifestyle factors, and chronic conditions, relative to White men, odds of being frail was significantly higher (34%–54%) among African American, Native Hawaiian, and other Asian American men, whereas odds was significantly lower (36%) in Japanese American men and did not differ in Latino men. However, among men who had high school or less, none of the groups displayed significantly higher odds of prefrail or frail compared with White men. Relative to White women, odds of being frail were significantly higher (14%–33%) in African American and Latino women, did not differ for other Asian American women and lower (14%–36%) in Native Hawaiian and Japanese American women. These racial and ethnic differences in women were observed irrespective of education. Risk of all-cause mortality was higher in prefrail and frail men than robust men (adjusted hazard ratio [HR] = 1.69, 1.59–1.81; HR = 3.27, 3.03–3.53); results were similar in women. All-cause mortality was significantly positively associated with frailty status and frailty score across all sex, race, and ethnic groups,
Conclusions: Frailty status differed significantly by race and ethnicity and was consistently associated with all-cause mortality. The FI may be a useful tool for aging studies in this multiethnic population.

Keywords: Deficit accumulation frailty index, Education, Mortality, Multiethnic

Frailty is defined as a state of increased vulnerability to adverse health outcomes resulting from aging-related reduction in physiological reserve capacity across multiple systems (1,2). Many operational definitions of frailty have been used in studies of mortality, hospitalizations, disability, falls and other health endpoints (3–5). Two frequently used ways to assess frailty are the "Fried"/frailty phenotype (FP) (1) and the Rockwood Frailty index (FI) (6). The Fried/FP is a measure of physical frailty based on 5 characteristics: grip strength,

slow walking speed, low physical activity, exhaustion and unintentional weight loss where poor performance in 1 or 2 characteristics is defined as prefrail, and having 3 or more characteristics as frail (1). Rockwood FI, a deficit accumulation index, is calculated based on self-reported questionnaire items on physical functioning, symptoms, comorbidities, and mental well-being. This score counts the number of health deficits observed for individuals; the greater the number of health deficits, the greater the perceived level of frailty (7,8). The FI is a ratio of the number of deficits present relative to the total number of deficits considered (at least 30 considered in most studies) and has been applied in population-based studies (9–11)).

Despite a rich literature on frailty and health using the above 2 mentioned measures, only a handful of studies have examined racial, ethnic, and socioeconomic disparities in frailty and compared frailty prevalence between African American and White (12–16) and between Hispanic and White adults (14–17). In the Cardiovascular Health Study (CHS) (12) and the National Health and Aging Trends (NHAT) study (15), relative to Whites, African American adults had a ~50% higher odds of frailty after adjusting for sex, education, income, body size, and chronic conditions. However, in the Women's Health and Aging Study (WHAS), African American race was not a correlate of frailty when either education or income was adjusted for but there was a significant 3-fold increased odds of frailty among those with less than a high school degree compared with those with a high school degree or more (13). Despite the modest sample size of African American women in the WHAS ($n = 175$), these results suggest that additional studies by sex and socioeconomic status (SES) may help to elucidate racial and ethnic disparities in frailty. Results on frailty in Hispanics compared with Whites are also limited. Although the odds of frailty was ~60% higher among Hispanic adults than Whites in the NHAT study (15), results from the San Antonio Longitudinal Study of Aging (SALSA) showed that the higher frailty prevalence in Hispanics relative to Whites was observed when the frailty criteria were standardized to the pooled height and body mass index (BMI) of Whites and Hispanics but was eliminated when ethnic-specific height and BMI were applied to determine frailty (17). Given that racial and ethnic differences in frailty may be related to SES (education, income, neighborhood factors), differences in health status, BMI, as well as the interplay between race, ethnicity, sex, and other factors (13,17–21), further investigation of racial and ethnic differences in frailty separately in men and women and with consideration of education, neighborhood SES (nSES), and other lifestyle factors is warranted. Frailty prevalence in other major racial and ethnic groups, such as Native Hawaiian and Asian American groups, are largely not known. Although the Women's Health Initiative Observation Study investigated racial and ethnic differences in frailty status using a modified FP definition, few details were provided on the 1 233 Asian Americans/Pacific Islanders who were included in the analysis (16). In a study of frailty index conducted in Hawaii (22), only men of Japanese descent were included, precluding comparisons with other racial and ethnic groups.

To address gaps in our knowledge of risk of frailty status in major racial and ethnic groups in the United States compared with Whites, we report here a deficit accumulation frailty index developed in the Multiethnic Cohort (MEC) study, an ongoing, long-term prospective study of older adults in Hawaii and California (23). In the fifth follow-up survey of the MEC (2012–2016), ~70 000 participants responded to a geriatric assessment which provided the necessary information to develop the MEC frailty index (FI) (see below). Thus, our first study objective was to examine variation in the FI across diverse and understudied ethnic groups with attention to demographic, social, lifestyle and disease factors that may influence this variation. Specifically, we examined cross-sectionally the prevalence of robust, prefrail and frail among African American (2 430 men, 5 563 women), Latino American (6 049 men, 7 757 women), Native Hawaiian (1 963 men, 2 998 women), Japanese American (9 225 men, 11 574 women), other Asian American of Filipino, Chinese, and Korean ethnicities (1 265 men, 2 451 women), and White American (8 094 men, 10 413 women). We estimated the odds of prefrail and frail in each race and ethnic group relative to Whites with adjustment for age, demographic factors, and key baseline lifestyle factors in a stepwise manner. Our second objective was to evaluate the validity of the FI by examining its performance in predicting all-cause mortality, cardiovascular (CVD) and cancer-specific mortality after 7 years of follow-up by race/ethnicity, sex, age, and other lifestyle, social, and disease factors. Thus, using a deficit accumulation frailty index, we provide new information on how frailty operates within diverse multiethnic populations of older men and women.

Method

Study Population

The MEC was established between 1993 and 1996, enrolling 96 810 men and 118 441 women, aged 45–75 years and included African American, Latino American, Native Hawaiian, White, Japanese, and other Asian American including Filipino, Chinese, and Korean (23). At cohort entry, participants completed a 26-page mailed questionnaire that assessed demographics, anthropometry, smoking, alcohol use, medical history, diet, physical activity, and reproductive history (among women).

Geriatric Ascertainment and Construction of a Frailty Index

Follow-up questionnaires were mailed about every 5 years to update select exposures or assess new exposures. As described previously (24), in the 5th follow-up questionnaire (Qx5) that was administered in 2012–2016, a geriatric assessment was conducted and included 21 items related to physical function, validated questions on social network and isolation, symptoms, and history of 22 chronic conditions that were diagnosed by a physician and reported by the respondent. Following the algorithm developed by Rockwood (9), 39 health items covering 4 domains were included in the frailty index (FI): 15 questions on physical functioning, 13 questions on mood, depression, 4 questions on persistent symptoms including shortness of breath, dizziness, fatigue, and falling, self assessment of eyesight and hearing, 9 chronic conditions (heart disease, stroke, diabetes, arthritis, emphysema, cancers, glaucoma/cataracts, high blood pressure, osteoporosis), and BMI assessed at Qx5 (Table 1). Other chronic conditions that were asked at Qx5 but were not included in FI were adjusted for as covariates in our analyses (see below). Each of the 39 items were scored between 0 and 1, where 0 indicates the absence of the deficit and 1 the presence of deficit. A frailty score was calculated for each participant by dividing the sum of the health deficit scores by the total deficits measured. This resulted in a score of between 0 (no deficits) to 1 in our FI. Participants were then assigned to one of the following frailty status based on their FI score: robust (<0.2), prefrail (0.2 to <0.35), and frail (0.35 to 1.0). We did not calculate a

Table 1. Variables Included in Frailty Index (FI) Among 71 283 MEC Participants

	Physical Functioning, Symptom, Social Network, and Chronic Conditions	Score 1		Score 0.5		Score 0			
		N	%	*N*	%	*N*	%	*N*	%
		Cannot Do		Some Difficulty		No Problem		Missing	
1	Taking bath/showering*	978	1.4	6 301	8.8	63 582	89.2	422	0.6
2	Dressing	975	1.4	12 687	17.8	57 204	80.2	417	0.6
3	Get in and out of bed	480	0.7	8 169	11.5	62 304	87.4	330	0.5
4	Walk across a room	914	1.3	4 941	6.9	64 948	91.1	480	0.7
5	Rising from chair	1 065	1.5	2 832	39.7	41 089	57.6	797	1.1
6	Lifting/carrying weights 10 lb	7 005	9.8	17 423	24.4	46 232	64.9	623	0.9
7	Feeding yourself	346	0.5	2 658	3.7	67 923	95.3	356	0.5
8	Walk one block	5 362	7.5	13 087	18.4	51 934	72.9	900	1.3
9	Use toilet, getting up and down	470	0.7	7 333	10.3	63 128	88.6	352	0.5
10	Climbing stairs	6 235	8.7	16 667	23.4	47 650	66.8	731	1.0
11	Shopping for groceries	5 033	7.1	5 653	7.9	60 193	84.4	404	0.6
12	Pulling or pushing	7 511	10.5	18 249	25.6	44 818	62.9	705	1.0
13	Prepare meals	4 935	6.9	4 584	6.4	61 311	86.0	453	0.6
14	Take medicine	1 676	2.4	2 795	5.9	66 351	93.1	458	0.6
15	Handle own money	3 841	5.4	4 195	5.9	62 755	88.0	492	0.7
		Yes				No		Missing	
16	Shortness of breath while awake†	8 480	11.9			62 212	82.3	591	0.8
17	Persistent dizziness or lightheaded	7 558	10.6			62 306	87.4	1 419	2.0
18	Severe fatigue or exhaustion	8 459	11.9			60 584	84.5	2 240	3.1
19	Falling down	12 139	17.0			57 652	80.9	1 492	2.1
20	Feel depressed	8 832	12.4			61 247	85.9	1 204	1.7
21	Feel everything was effort	14 591	20.6			54 743	76.8	1 849	2.6
22	Feel sleep was restless	19 668	27.7			50 199	70.4	1 416	2.0
23	Feel could not get going	9 838	13.8			59 571	83.6	1 874	2.6
24	Feel lonely	8 882	12.5			59 400	83.3	3 001	4.2
25	Did not enjoy life	5 766	8.1			62 639	87.9	2 878	4.0
26	Feel sad	10 713	15.0			57 435	80.6	3 135	4.4
27	Did not feel happy	7 344	10.3			60 749	85.2	3 190	4.5
		Yes				No		Missing	
28	Heart disease	7 201	10.1			62 205	87.3	1 877	2.6
29	Stroke	4 844	6.8			63 634	89.3	2 805	3.9
30	Diabetes	15 651	22.0			54 247	76.1	1 385	1.9
31	Arthritis	29 858	41.9			40 017	56.1	1 408	2.0
32	Emphysema, COPD, asthma	10 570	14.8			58 059	81.4	2 654	3.7
33	Cancers/leukemia	8 217	11.5			63 066	88.5	0	0
34	Glaucoma, cataracts	31 689	44.5			38 085	53.4	1 509	2.1
35	High blood pressure	46 229	64.9			24 361	34.2	693	1.0
36	Osteoporosis	14 479	20.3			54 725	76.8	2 079	2.9
		Poor		Fair or Good		Excellent		Missing	
37	Eyesight‡	2 650	3.7	59 906	66.2	8 174	11.5	553	0.8
38	Hearing‡	5 055	7.1	51 359		12 134	17.0	1 735	2.4
		Obese or Underweight		Overweight		Healthy Weight		Missing	
39	Body mass index§	15 595	21.9	24 357	34.2	30 521	42.8	810	1.1

Notes: COPD = chronic obstructive pulmonary disease.

*Items 1 to 15 were coded as 1 if cannot do or do not do; 0.5 for some difficulty, and 0 if no difficulty.

†Items 16 to 36: Yes = score 1, and No = score 0.

‡Poor sight (or poor hearing) = score 1, Fair sight (hearing) score = 0.75, good hearing (sight) score = 0.25, excellent hearing (sight) score = 0. For eyesight, there were 23 382 (32.8%) fair, 36 524 (51.2%) good. For hearing, there were 23 811 (33.4%) fair and 28 548 (40.0%) good.

§BMI > 30 (obese) or BMI < 18.5 (underweight) = score 1, BMI > 25 to ≤30 (overweight) = score 0.5, BMI > 18.5 to ≤25 (healthy weight) = score 0.

frailty score for 1 501 participants (1 001 women and 500 men) with more than 20% missing variables.

Mortality Outcome Ascertainment

The primary outcome was all-cause mortality, assessed using state death records and the National Death Index. All-cause mortality included deaths from CVD, cancer, as well as deaths from other causes, including accidents and suicides. All death linkages were complete through December 2019 for all participants. Participants with no recorded deaths as of this date were censored. Cancer deaths were identified by using International Classification of Diseases, Ninth Revision codes 140–208 or Tenth Revision codes C00–C97. CVD deaths included acute myocardial infarction (410, I21), other heart diseases (411, 413–414, 425–429, I20, I22–I24, I42–I52), and stroke (430–438, I60-I69). During an average of 6.8 ± 2.2 years of follow-up of MEC respondents with information on the frailty index (29 026 men, 40 756 women), there were 10 523 deaths (5 218 men, 5 305 women).

Statistical Analyses

The FI was constructed for 69 782 of 71 283 MEC participants (Table 1) who were included in subsequent analyses. Similar to previous studies (9), scores of 0 to <0.2 were classified as robust, 0.2 to <0.35 as prefrail, and 0.35 to 1 as frail. FI scores were standardized to have the same distribution by age (<70, 70–74, 75–79, 80–84, 85–89, ≥90), race, and ethnicity as the MEC population. Age, race, and ethnicity-standardized prevalence of prefrail and frail by other covariates were examined, and they included education, nSES—a composite measure based on principal component analyses of 7 census-based indicators of SES from census data: education, median household income, percent living 200% below poverty level, percent blue-collar workers, percent older than 16 years in workforce without job, median rent, and median house value (25), smoking status, BMI, physical activity, chronic conditions (see listing in Table 1), and energy-adjusted diet quality measured by the alternate Mediterranean diet score (26) assessed at baseline.

Polytomous logistic regression models were used to characterize the odds of prefrail and frail versus robust in each race and ethnic group relative to White by sex to allow comparison with published literature (12–16). We conducted analyses adjusting for (a) age only (Model 1), (b) adding demographic factors (education, nSES, marital status; Model 2), (c) adding baseline lifestyle factors (smoking, Mediterranean diet score, alcohol, physical activity), BMI (<25, 25–30, ≥30 kg/m^2), and chronic conditions (0, 1, 2–3, 4+; Model 3), and (d) adding chronic conditions assessed in Qx5 that were not already included in the FI (Model 4; skin cancer-not melanoma, Alzheimer's disease, other dementia, polyps of intestines, Crohn's disease, ulcerative colitis, osteoporosis, gallbladder removal, ulcer, chronic heartburn, asthma, chronic lung disease, Parkinson's disease, and enlarged prostate (men only)—the count of these conditions was coded as 0, 1, 2–3, 4+). We did not adjust for BMI at Qx5 since this was part of the FI. In addition, to explore the potential modifying effect of education, we investigated race and ethnic disparities in the odds of prefrail and frail separately by low (high school or less) versus high (some college or college graduate) education. We used Cox proportional hazard regression to estimate the multivariable hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality in relation to FI in men and women, by race and ethnicity, age group, education, nSES, as well as baseline smoking status, BMI, chronic conditions and Mediterranean diet score. We included potential risk factors for covariate adjustment: racial and ethnic group, age (<70, 70–74, 75–79, 80–84, 85+), nSES at baseline (Q1–Q5), and education at baseline (5 categories), and other baseline variables including smoking (status and pack-years), alcohol (none, >0 to <12, 12 to <24, ≥24 g/d), moderate to vigorous physical activity (<2.5, 2.5 to <5, 5 to <7, 7 to <14, ≥14 h/wk), BMI (<25, 25-<30, ≥30 kg/m^2), Mediterranean diet score (energy adjusted, 0–2, 3, 4, 5, 6–9), and chronic conditions (0, 1, 2–3, 4+). For women, the models were additionally adjusted for age at menarche (≤12, 13–14, >14 years), number of children (0, 1, 2–3, 4+), baseline menopausal status, and use of menopausal hormones as these factors may influence the prevalence and pathophysiology of frailty (27). Analyses were performed using SAS 9.4 statistical software (SAS Institute, Cary, NC).

Results

Prevalence of Prefrail and Frail and Determinants of Frailty

The FI was developed on 29 026 male and 40 756 female participants in the MEC, ages 60–99 years old (Table 1). The mean FI score was 0.16 (*SD* 0.11) in men and 0.19 (*SD* 0.13) in women. The slope of the FI in relation to age was 0.032 (*SE* 0.0007) in men versus 0.036 (*SE* 0.0006) in women ($p < .01$). Table 2 shows in men, the age-adjusted mean FI score was highest in African Americans (0.18) and Latinos (0.18), intermediate in Native Hawaiians (0.17) and other Asian Americans (0.17), and lowest in Whites (0.15) and Japanese Americans (0.14). *p*-Values for all groups compared with Whites were <.0001 except for Japanese Americans for which the *p*-value was .03. When we further adjusted for education, these patterns largely remained. The higher FI scores in African American, Latino American, Native Hawaiian, and other Asian American men relative to White men were clearest for men in their 70s as these differences narrowed for men in the 80s. Japanese American men in their 80s significantly showed lower FI scores than White men in their 80s (Table 2). In analysis among women, Latinos and African Americans displayed higher mean FI scores than Whites in each age group but for Native Hawaiians, the higher FI scores were mainly observed in women <80 years old. Other Asian American women showed comparable mean FI scores as White women, whereas Japanese American women displayed lower FI scores (Table 2). Results also showed that relative to White men, higher FI scores in African American and Latino men were mainly observed among those with higher education (some college or college graduate) but did not differ between men with high school education or less. The higher FI scores in Native Hawaiian men were observed across all education levels.

Racial and ethnic differences by frailty status, robust (FI 0 < 0.2), prefrail (0.2 to <0.35), and frail (≥0.35; Table 3) showed similar patterns of FI as a continuous variable. In total, 22.2% of MEC participants were classified as prefrail and 10.3% as frail; this was higher in women (24.4% prefrail, 12.0% frail) than in men (19.2% prefrail, 7.9% frail). The largest sex difference in frailty status was found in Latino Americans and African Americans and the smallest difference in Native Hawaiians and other Asian Americans. Prevalence of prefrail and frail also differed by education, nSES, and other lifestyle factors after adjusting for age and race and ethnicity. Frailty prevalence was 4–6 times higher among those with 4 + vs 0 chronic conditions, ~2.5–3 times higher for obese vs normal BMI, ~2.5 times higher among those with less education (high school or less) than

Table 2. Mean (*SD*) Frailty Index (FI) Score by Age Group and Race/Ethnicity in Men and Women

	African American	Japanese American	Latino American	Native Hawaiian	Other Asian American	Whites
N men	2 430	9 225	6 049	1 963	1 265	8 094
Age (*SD*)	78.6 (7.7)	77.0 (7.9)	78.0 (6.6)	73.5 (6.7)	76.5 (6.7)	75.5 (7.1)
Mean FI						
All ages	0.18 (0.12)	0.14 (0.10)	0.18 (0.12)	0.17 (0.12)	0.17 (0.12)	0.15 (0.11)
<70	0.15 (0.12)	0.11 (0.08)*	0.14 (0.11)	0.15 (0.12)	0.13 (0.10)	0.11 (0.09)
70 to 74	0.17 (0.11)	0.12 (0.08)*	0.15 (0.11)	0.16 (0.12)	0.15 (0.10)	0.13 (0.10)
75 to 79	0.17 (0.12)	0.14 (0.10)*	0.17 (0.11)	0.18 (0.12)	0.17 (0.11)	0.15 (0.11)
80 to 84	0.18 (0.12)	0.16 (0.10)	0.19 (0.12)	0.19 (0.12)	0.18 (0.12)*	0.17 (0.12)
85 to 89	0.20 (0.13)*	0.18 (0.12)	0.21 (0.13)	0.22 (0.13)*	0.23 (0.14)	0.19 (0.12)
≥90	0.23 (0.14)*	0.22 (0.13)	0.26 (0.15)*	0.26 (0.15)*	0.25 (0.17)*	0.25 (0.14)
By education, mean† (*SD*)						
≤High school	0.20 (0.005)*	0.17 (0.003)	0.19 (0.002)*	0.29 (0.005)	0.20 (0.007)*	0.20 (0.004)
Some college	0.19 (0.003)	0.16 (0.001)	0.17 (0.002)	0.19 (0.003)	0.18 (0.004)	0.16 (0.002)
Graduate or more	0.17 (0.005)	0.14 (0.002)	0.17 (0.004)	0.16 (0.007)*	0.17 (0.007)*	0.15 (0.002)
By neighborhood SES (nSES)‡ (*SD*)						
Low nSES	0.19 (0.003)	0.16 (0.002)	0.19 (0.002)	0.21 (0.004)	0.18 (**0.004**)*	0.17 (0.002)
High nSES	0.17 (0.004)	0.15 (0.001)*	0.17 (0.002)	0.18 (0.003)	0.18 (**0.004**)	0.16 (0.002)
***N* women**	**5 563**	**11 574**	**7 757**	**2 998**	**2 451**	**10 413**
Age (*SD*)	78.1 (7.9)	77.7 (8.0)	77.5 (6.7)	73.5 (7.1)	75.7 (7.1)*	75.8 (7.4)
All ages	0.22 (0.13)	0.16 (0.11)	0.22 (0.14)	0.18 (0.12)	0.17 (0.12)*	0.17 (0.13)
<70	0.17 (0.12)	0.12 (0.08)	0.17 (0.12)	0.16 (0.11)	0.13 (0.10)*	0.13 (0.10)
70 to 74	0.19 (0.12)	0.13 (0.09)	0.19 (0.13)	0.18 (0.12)	0.14 (0.09)*	0.14 (0.11)
75 to 79	0.21 (0.13)	0.15 (0.10)	0.22 (0.14)	0.19 (0.12)	0.18 (0.11)*	0.17 (0.12)
80 to 84	0.23 (0.13)	0.17 (0.10)	0.24 (0.14)	0.20 (0.12)*	0.21 (0.13)*	0.21 (0.13)
85 to 89	0.25 (0.13)*	0.20 (0.12)	0.27 (0.15)	0.23 (0.14)*	0.23 (0.13)*	0.24 (0.14)
≥90	0.28 (0.14)*	0.27 (0.15)*	0.33 (0.16)	0.27 (0.15)*	0.28 (0.16)*	0.28 (0.15)
By education, mean (*SD*)						
≤High school	0.25 (0.003)	0.19 (0.002)	0.24 (0.002)	0.23 (0.004)*	0.21 (0.005)*	0.22 (0.003)
Some college	0.22 (0.002)	0.17 (0.001)	0.23 (0.002)	0.20 (0.003)	0.18 (0.003)*	0.19 (0.002)
Graduate or more	0.19 (0.004)	0.16 (0.002)	0.21 (0.005)	0.19 (0.006)*	0.18 (0.005)*	0.18 (0.002)
By neighborhood SES (nSES)‡ (*SD*)						
Low nSES	0.23 (0.002)	0.18 (0.002)	0.24 (0.002)	0.21 (0.003)	0.21 (**0.004**)*	0.20 (0.002)
High nSES	0.20 (0.003)	0.17 (0.001)	0.22 (0.003)	0.20 (0.003)	0.20 (**0.003**)*	0.19 (0.001)

Notes: SD = standard deviation.

*p-Values > .05; no asterick are shown for $P < .05$.

†Adjusted for age at Qx5 (<70, 70–74, 75–79, 80–84, 85–89, ≥90) by proc surveyfreq method.

‡Low education (high school or less), high education (some college or college graduate), low nSES (Q1, Q2, Q3), and high nSES (Q4, Q5).

those with higher education, ~2 times higher in the lowest quintiles of nSES vs highest quintile, ~60% higher among lowest vs highest physical activity group; 20%–30% higher in current smokers than never smokers, and ~25%–40% higher in those with lowest diet quality (0–2) versus highest quality (6–9) (Table 3).

Odds of Prefrail and Frail Compared With Whites

We evaluated whether frailty disparities by race and ethnicity may be explained by demographic (education, nSES, marital status; Model 2), baseline lifestyle factors (Model 3) and Qx5 chronic conditions (Model 4; Table 4). Relative to White men, age-adjusted odds of prefrail and frail were significantly higher for African American, Latino American, Native Hawaiian, and other Asian American men but significantly lower for Japanese American men (Model 1). After further adjusting for education, nSES, and marital status, the higher odds were attenuated but remained significantly elevated in all groups except for Latino men (Model 2). After adjustment for baseline lifestyle factors that included smoking, alcohol intake, diet, physical activity, baseline BMI, and chronic conditions (Model 3), the higher odds of prefrail was statistically significant for African American men (1.15, 95% CI 1.02–1.20) and the higher odds of prefrail (OR 1.19) and frail (OR 1.28) remained significant for other Asian American men relative to White men. In the last model, when chronic conditions at Qx5 were also considered (Model 4), relative to White men, African American, Native Hawaiian men, and other Asian American men displayed significantly higher odds of frail (respective odds 1.34, 95% CI 1.12–1.60; 1.35, 95% CI 1.11–1.65; and 1.54, 95% CI 1.22–1.94) and prefail compared with White men. The odds of prefrail and frail did not differ significantly between Latino and White men, whereas the decreased odds of frail and prefrail in Japanese American men remained (Model 4; Table 4).

Given the impact of education on frailty prevalence, we further investigated these patterns in men separately by education level (Supplementary Table 1). In analyses restricted to men with low education, age-adjusted prevalence of prefrail and frail in African American, Latino, and Other Asian American men were comparable to those of White men. Native Hawaiian men displayed higher age-adjusted odds of prefrail (1.33, 95% CI 1.06–1.67) and frail (1.23, 95% CI .92–1.64) than White men, but the odds were attenuated and were not significant with adjustment for baseline demographic and other lifestyle factors (Model 3). The lower age-adjusted odds of prefrail and frail among Japanese American men remained after

Table 3. Frequency Distribution of Frailty Status (Robust, Prefrail, Frail)* by Demographic and Baseline Lifestyle Factors among MEC Participants

	Men				Women			
	N	% Robust FI 0 to <0.2	% Prefrail FI 0.2 to <0.35	% Frail FI ≥0.35 to 1.0	*N*	% Robust FI 0 to <0.2	% Prefrail FI 0.2 to <0.35	% Frail FI ≥0.35 to 1.0
Age and race standardized†	29 026	72.9	19.2	7.9	40 756	63.6	24.4	12.0
By age group, race adjusted								
<70	6 501	84.0	12.4	3.6	9 220	79.1	15.7	5.2
70 to 74	5 653	81.2	14.3	4.5	7 830	74.4	18.8	6.8
75 to 79	6 308	74.4	18.8	6.8	8 654	65.3	23.8	10.9
80 to 84	5 043	67.9	22.6	9.5	6 963	55.7	30.2	14.1
85 to 89	3 623	59.0	28.1	12.9	5 091	45.9	34.0	20.1
90+	1 898	46.3	31.0	22.7	2 998	33.1	36.6	30.3
By race, age-adjusted								
African American	2 430	61.5	25.7	12.8	5 563	46.7	33.7	19.6
Japanese American	9 225	75.4	18.4	6.2	11 574	68.4	23.0	8.6
Latino American	6 049	66.3	22.8	10.9	7 757	51.0	29.4	19.6
Native Hawaiian	1 963	67.9	22.2	9.9	2 998	63.9	24.8	11.4
Other Asian Americans	1 265	69.0	21.1	9.9	2 451	67.6	22.4	10.0
Whites	8 094	75.9	17.3	6.8	10 413	66.5	23.0	10.5
Education†								
High school or less	7 909	62.0	24.7	13.3	13 732	51.9	29.8	18.3
Some college/graduate	15 202	74.6	18.6	6.8	19 815	68.2	22.5	9.3
Graduate and more	5 693	80.6	14.5	4.9	6 868	72.0	20.0	8.0
Missing	222	70.5	20.6	8.9	341	59.9	23.9	16.3
Neighborhood SES (nSES)†								
Q1 (low)	3 307	66.6	22.5	10.9	5 254	54.8	27.8	17.4
Q2	5 070	68.8	20.9	10.2	7 666	59.0	25.7	15.2
Q3	5 939	71.8	20.1	8.1	8 521	62.0	26.3	11.8
Q4	5 634	72.8	19.8	7.4	8 011	64.2	24.1	11.6
Q5 (high)	8 856	77.7	16.1	6.1	11 045	70.0	21.4	8.6
Missing	220	63.1	26.8	10.1	259	55.0	24.9	20.1
Education and nSES†,‡								
Low education, low nSES	5 256	60.8	25.4	13.8	9 045	49.7	29.6	20.6
Low education, high nSES	2 592	64.3	23.5	12.2	4 604	55.6	30.0	14.4
High education, low nSES	8 924	74.3	18.5	7.1	12 184	66.3	24.1	9.5
High education, high nSES	1 814	78.2	16.4	5.5	14 326	71.5	20.1	8.4
Missing	440	67.0	23.6	9.4	597	58.0	24.3	11.7
Smoking status								
Never	10 529	77.2	16.1	6.7	24 223	65.3	23.3	11.3
Former	14 387	70.8	20.8	8.4	11 544	62.7	25.0	12.3
Current	3 870	67.9	21.8	10.3	4 479	57.7	28.3	14.0
Missing	240	68.0	23.1	8.9	510	53.7	27.1	19.2
Baseline chronic conditions§								
0	9 103	82.5	13.1	4.4	13 317	75.8	17.9	6.3
1	10 092	75.5	17.8	6.7	14 514	65.9	24.5	9.7
2 to 3	8 425	63.5	25.1	11.4	11 047	51.9	30.1	18.0
4+	1 406	48.0	33.1	18.9	1 878	27.7	37.3	35.0
Baseline BMI kg/m^2†								
<25	10 416	79.7	14.7	5.6	20 365	72.4	19.8	7.8
25 to 30	14 073	72.8	19.5	7.7	12 456	60.1	26.9	13.0
>30	4 492	57.2	28.6	14.2	7 774	43.8	33.8	22.4
Missing	45	65.1	28.6	6.3	161	45.1	23.1	31.8
Moderate/vigorous physical activity								
<2.5 h/wk	4 428	64.7	23.3	12.0	6 478	53.5	28.3	18.2
2.5 to <5 h/wk	4 736	71.6	20.1	8.3	9 169	62.9	24.9	12.1
5 to <7 h/wk	5 389	73.7	18.8	7.5	8 472	64.5	24.3	11.2
7 to <14 h/wk	7 691	75.7	17.6	6.7	8 579	68.7	21.9	9.4
≥14 h/wk	6 782	74.3	18.4	7.3	8 058	64.4	24.2	11.4
Baseline Mediterranean diet score†								
0 to 2	4 905	70.4	20.3	9.3	7 149	59.0	26.9	14.1
3	5 143	71.6	20.5	7.9	7 513	61.4	25.5	13.1
4	5 939	71.6	19.6	8.8	8 702	63.9	24.2	11.9
5	5 484	73.6	19.0	7.4	7 836	66.3	22.6	11.1
6 to 9	6 751	76.6	17.1	6.2	8 394	67.3	23.2	9.4

*Frailty index (FI) categorized as robust (FI 0 to <0.2), prefrail (FI 0.2 to <0.35), and frail (FI ≥0.35 to 1.0).

†Adjusted for race, ethnicity and age at Qx5 (<70, 70–74, 75–79, 80–84, 85–89, ≥90) by proc surveyfreq method.

‡Low education (high school or less), high education (some college or college graduate), low nSES (Q1, Q2, Q3), high nSES (Q4, Q5).

§Chronic conditions asked at baseline are as follows: high blood pressure, heart attack/angina, diabetes, tuberculosis, gout, polyps of intestines, partial removal of stomach, gallstones, gallbladder removal, asthma/hay fever, glaucoma, cataract surgery, colon or rectal surgery, stomach cancer, melanoma, other skin cancer, breast cancer, vasectomy, enlarged prostate, and prostate cancer (men only), cervix cancer, other uterine cancer (women only).

Table 4. Relative Odds of Prefrail and Frail Versus Robust* in African American, Latino American, Native Hawaiian, Japanese American, and Other Asian American Relative to Whites, in Men and Women

	Model 1 Age	Model 2 +Education, +nSES + Marital Status†	Model 3+ Baseline Smoking, Alcohol, Diet, Physical Activity, Body Mass Index, Chronic Conditions†	Model 4 + Qx5 Chronic Conditions‡
African American men (1 577 R, 581 PF, 272 F) vs White men (6 186 R, 1 374 PF, 534 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.42 (1.26–1.59)	1.22 (1.08–1.37)	1.15 (1.02–1.30)	1.23 (1.08–1.39)
Frail	1.55 (1.32–1.82)	1.20 (1.02–1.42)	1.11 (0.93–1.32)	1.34 (1.12–1.60)
Latino men (4 059 R, 1 356 PF, 634 F) vs White men (6 186 R, 1 374 PF, 534 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.34 (1.23–1.46)	1.05 (0.96–1.16)	1.04 (0.94–1.14)	1.07 (0.97–1.19)
Frail	1.55 (1.37–1.76)	1.03 (0.90–1.29)	1.00 (0.86–1.15)	1.11 (0.96–1.29)
Native Hawaiian men (1 343 R, 430 PF, 190 F) vs White men (6 186 R, 1 374 PF, 534 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.64 (1.45–1.86)	1.37 (1.20–1.56)	1.08 (0.95–1.24)	1.16 (1.02–1.33)
Frail	2.05 (1.71–2.45)	1.54 (1.28–1.85)	1.10 (0.91–1.34)	1.35 (1.11–1.65)
Japanese American men (7 136 R, 1 586 PF, 503 F) vs White men (6 186 R, 1 374 PF, 534 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	0.90 (0.83–0.98)	0.84 (0.78–0.92)	0.82 (0.75–0.89)	0.85 (0.78–0.92)
Frail	0.68 (0.60–0.78)	0.62 (0.54–0.70)	0.58 (0.50–0.66)	0.64 (0.56–0.74)
Other Asian American men (879 R, 264 PF, 122 F) vs White men (6 186 R, 1 374 PF, 534 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.31 (1.12–1.52)	1.16 (1.00–1.35)	1.19 (1.01–1.39)	1.26 (1.08–1.48)
Frail	1.56 (1.26–1.93)	1.28 (1.03–1.60)	1.28 (1.02–1.60)	1.54 (1.22–1.94)
Women				
African American women (2 897 R, 1 728 PF, 938 F) vs White women (6 989 R, 2 356 PF, 1 068 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.59 (1.48–1.72)	1.34 (1.23–1.45)	1.09 (1.00–1.19)	1.12 (1.03–1.22)
Frail	1.79 (1.61–1.98)	1.37 (1.23–1.52)	1.00 (0.89–1.13)	1.14 (1.01–1.28)
Latino women (4 041 R, 2 247 PF, 1 469 F) vs White women (6 989 R, 2 356 PF, 1 068 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.54 (1.43–1.65)	1.21 (1.12–1.30)	1.13 (1.04–1.23)	1.14 (1.05–1.24)
Frail	2.22 (2.02–2.43)	1.44 (1.31–1.59)	1.26 (1.13–1.41)	1.33 (1.19–1.48)
Native Hawaiian women (1 932 R, 732 PF, 334 F) vs White women (6 989 R, 2 356 PF, 1 068 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	1.28 (1.16–1.42)	1.10 (1.00–1.23)	0.88 (0.79–0.97)	0.90 (0.81–1.01)
Frail	1.42 (1.24–1.62)	1.10 (0.96–1.27)	0.76 (0.65–0.88)	0.86 (0.74–1.00)
Japanese American women (8 208 R, 2 499 PF, 867 F) vs White women (6 989 R, 2 356 PF, 1 068 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	0.77 (0.72–0.82)	0.76 (0.71–0.82)	0.85 (0.79–0.91)	0.87 (0.80–0.93)
Frail	0.54 (0.49–0.59)	0.53 (0.46–0.56)	0.59 (0.52–0.66)	0.64 (0.57–0.72)
Other Asian American women (1 676 R, 539 PF, 236 F) vs White women (6 989 R, 2 356 PF, 1 068 F)				
Robust	1.00	1.00	1.00	1.00
Prefrail	0.95 (0.85–1.06)	0.94 (0.81–1.05)	1.04 (0.92–1.17)	1.06 (0.94–1.19)
Frail	0.93 (0.80–1.09)	0.91 (0.78–1.07)	0.99 (0.84–1.17)	1.07 (0.90–1.27)

Notes: F = frail, PF= prefrail, R = robust.

*Frailty index (FI) was categorized as robust (FI 0 to <0.2), prefrail (FI 0.2 to <0.35), and frail (FI ≥ 0.35 to 1.0). Polytomous logistic regression analyses were used to compare relative odds of prefrail and frail in each race and ethnic group relative to Whites. Covariates were added in each of the models as specified.

†Details of these covriates are given in Table 3.

‡Qx5 chronic conditions that were adjusted are: skin cancer(not melanoma), polyps of intestines, Crohn's disease, ulcerative colitis, gallbladder removal, ulcer, chronic heartburn, Alzheimer's disease, other dementia, Parkinson's disease, and enlarged prostate (men only).

adjustment for the various covariates (Models 3 and 4). Among men with high education, the higher age-adjusted odds of prefrail (OR ranged from 1.21 to 1.49) and frail (OR ranged from 1.36 to 1.97) in African American, Latino American, Native Hawaiian, and other Asian American men relative to White men remained significant in the fully adjusted models (Supplementary Table 1).

Relative to White women, African American women displayed higher age-adjusted odds of prefrail (OR 1.59) and frail (OR 1.79; Model 1), but these odds were attenuated with adjustment for demographic factors (OR 1.34, 1.37; Model 2) and were further reduced but remained marginally significant (OR 1.12, 1.14) in a fully adjusted model (Model 4; Table 4). For Latino women, the age-adjusted odds of 1.54 (prefrail) and 2.22 (frail) were also attenuated but remained significantly elevated (OR 1.14, 1.33; Model 4). For Native Hawaiian women, the higher age-adjusted odds (OR 1.28, 1.42) were not only eliminated but the odds became lower (OR 0.90, 0.86) than White women in a fully adjusted model (Model 4). For Japanese women, the lower age-adjusted odds of prefrail (OR

0.77) and frail (OR 0.54) remained statistically significant (OR 0.87, 0.64, respectively; Model 4). Other Asian American women did not show significant differences in age-adjusted odds of prefrail and frail than White women, and this remained in the fully adjusted models (Model 4). Unlike the analyses in men, racial/ethnic differences in frailty relative to White women were similar for women with low education and those with high education. The racial and ethnic differences in frailty were slightly weakened when we adjusted for reproductive and hormonal factors (data not shown).

Frailty and All-Cause Mortality

Table 5 shows the HRs during an average of 6.8 years of follow-up, with 5 218 deaths in men and 5 305 deaths in women. Compared with men who were robust (<0.2), the risk of all-cause mortality was significantly higher for men who were classified as prefrail (0.2 to <0.35; HR 1.69, 95% CI 1.59–1.81) or frail (≥0.35; HR 3.27, 95% CI 3.03–3.53); the corresponding HRs in women were 1.83 (95% CI 1.71–1.96) for prefrail and 3.31 (95% CI 3.07–3.57) for frail. For each 0.1 increase in FI score, the respective HRs for all-cause mortality in men and women were 1.43 (95% CI 1.40–1.46) and 1.42 (95% CI 1.39–1.44). The HR for each 0.1 increase in FI score was higher for men ages ≤74 (HR 1.52, 95% CI 1.45–1.61) than men ages 75–84 (HR 1.49, 95% CI 1.44–1.54) or ages 85+ (HR 1.41, 95% CI 1.37–1.45; Phet 2df < 0.0001) (Supplementary Table 2). Results were similar in women; the HRs were 1.58 (95% CI 1.50–1.66), 1.46 (95% CI 1.42–1.51), and 1.40 (95% CI 1.37–1.44) for ages ≤74, 75–84, and ≥85, respectively.

Table 5 also shows risk association patterns with all-cause mortality by race and ethnicity. In each race/ethnic group, compared with men who were robust, risks ranged from 1.44 to 1.93 for men who were prefrail, and from 2.59 to 4.19 for men who were frail. Although the HR associations were significant in all sex, race, and ethnic groups, the magnitude of the associations varied. In men, the HR for each 0.1 increase in FI was highest in Whites (HR 1.56, 95% CI 1.50–1.62) and lowest in African Americans (HR 1.33, 95% CI 1.26–1.41; *p* heterogeneity < .0001). Similarly in each race and ethnic group among women, compared with robust women, the ranges of HR were 1.29–2.32 for prefrail and 2.47–4.47 for frail. In women, the HR for each 0.1 increase in FI was highest in Native Hawaiian women (HR 1.60, 95% CI 1.48–1.73) and lowest in African American women (HR 1.32, 95% CI 1.26–1.39; Table 5).

We tested the longer-term utility of FI in predicting overall mortality by excluding deaths (1 875 in men, 1 801 in women) that occurred within 2 years after MEC participants responded to the 5th follow-up survey. The HR for each 0.1 increase in frailty index score was reduced but remained statistically significant; the HR was 1.34 (95% CI 1.30–1.37) in men and 1.36 (95% CI 1.33–1.39) in women. We also investigated the FI–mortality associations in various subgroups including education, nSES, smoking status, Mediterranean diet score, BMI, and number of chronic conditions at baseline and Qx5. FI score was consistently associated with significantly higher overall mortality in each of these subgroup analyses (Supplementary Table 2), underscoring its utility. In addition, FI was significantly associated with CVD-specific mortality in men and women and across race and ethnic groups; the magnitude of HR estimates were similar to the HRs for all-cause mortality. Based on 1 404 cancer deaths in men and 1 347 in women, the HR for each 0.1 increase in FI was also significantly increased (respective HR 1.29, 95% CI 1.23–1.35; 1.23, 95% CI 1.18–1.29; Supplementary Table 3).

Discussion

To the best of our knowledge, this is one of the first studies to investigate the characteristics and utility of a deficit accumulation frailty index in multiethnic populations which included large numbers of older African American, Japanese American, Latino American, Native Hawaiian, other Asian American, and White Americans, addressing calls to eliminate disparities and address health inequities (28,29). Previous studies of frailty seldom included Native Hawaiians and Asian Americans, and our results identified noteworthy frailty differences between these groups and Whites. We evaluated whether racial and ethnic differences in frailty may be explained by differences in demographic, lifestyle factors, BMI, and history of chronic conditions. Our results suggest that adjustment for these covariates substantially affected the magnitude of frailty differences by race and ethnicity, but these changes were not uniform and varied by sex and education level. Our results also demonstrate the utility of FI as a categorical (robust, prefrail, frail) and a continuous marker for risk; it is strongly associated with overall mortality across all 12 sex, race, and ethnic groups after adjustment for relevant covariates. The characteristics of the FI by age and sex are consistent with findings from previous studies of older adults (9–11,30). African American, Latino American, and Native Hawaiian men in their 70s showed significantly higher frailty prevalences than White men, but these differences diminished with increasing age. In the CHS, the higher frailty prevalence in African Americans relative to Whites also declined in older age groups (12). Allostatic load has been associated with frailty (31), and studies of allostatic load have reported flattening of allostatic-load-related risks at the oldest ages (32,33). In contrast, the generally lower prevalence of frailty in Japanese American men and women relative to Whites suggests that there may be other beneficial lifestyle factors practiced by Japanese Americans. To the best of our knowledge, the Honolulu-Asia Aging Study (HAAS) was the only previous study that investigated frailty in Japanese Americans over 6 waves of evaluations spanning 1991–2009. Based on an accumulation frailty index in the HAAS, the mean FI for Japanese American men was 0.14 in Wave 1 (average age 77.9) and 0.22 in Wave 7 (average age 90.9) (22). Our findings of FI of 0.11 (*SD* 0.08) for Japanese American men ages <70 and 0.22 (0.13) for those ages 90 or older are consistent with the results in HAAS. Frailty patterns by race and ethnicity in women were generally comparable to the patterns in men except the lower prevalence in Japanese American women was more consistently observed and the higher prevalence in Latino women than White women was observed in every age group. High frailty prevalence in Latinos have been reported in some studies that used Fried/frailty phenotype definition (16,34).

In the recent national NHAT study that was based on Fried/frailty phenotype (15), results based on 1 646 African Americans (39.9% men) and 441 Hispanics (44.2% men) showed higher odds of frail in African Americans (1.46, 95% CI 1.21–1.76) and Hispanics (1.56, 95% CI 1.20–2.03), compared with Whites after adjustment for sex, income (or education), BMI, chronic conditions, and region in the United States. The odds of 1.34 (95% CI 1.12–1.60) for frail observed among African American men in the MEC is comparable to the adjusted odds in the NHAT, but our result of 1.14 (95% CI 1.01–1.28) in African American women is lower. Similarly, our results of higher odds of frailty in Latino women (1.33, 95% CI 1.19–1.48) is comparable to the NHAT result, but our finding of 1.11 (95% CI .96–1.29) in Latino men is weaker. In the SALSA, higher odds of frailty in Hispanics relative to Whites was only observed in unadjusted analyses, and the difference was

Table 5. Hazard Ratio Association* Between Frailty Status (Robust, Prefrail, Frail) and All-Cause Mortality by Race and Ethnic Groups, in Men and Women, Multiethnic Cohort (2012–2019)

	All Men		African American		Japanese American		Latino American		Native Hawaiian		Other Asian American		White	
	Deaths (D)	HR (95% CI)	#D	HR (95% CI)	#D	HR (95% CI)	#D	HR (95% CI)	#D	HR (95% CI)	#D	HR (95% CI)	#D	HR (95% CI)
Robust (0 to <0.2)	2 556	1.00	303	1.00	798	1.00	507	1.00	168	1.00	95	1.00	685	1.00
Prefrail (0.2 to <0.35)	1 543	1.69 (1.59–1.81)	184	1.58 (1.30–1.91)	457	1.73 (1.54–1.95)	315	1.44 (1.25–1.67)	111	1.60 (1.24–2.06)	68	1.88 (1.34–2.62)	408	1.93 (1.69–2.20)
Frail (0.35 to 1)	1 119	3.27 (3.03–3.53)	135	2.59 (2.08–3.22)	279	3.49 (3.02–4.04)	270	2.85 (2.43–3.33)	81	2.88 (2.15–3.85)	55	3.46 (2.41–4.95)	299	4.19 (3.61–4.87)
p Trend		<.0001		<.0001		<.0001		<.0001		<.0001		<.0001		<.0001
Per 0.1 unit		1.43 (1.40–1.46)		1.33 (1.26–1.41)		1.48 (1.42–1.54)		1.35 (1.30–1.41)		1.37 (1.27–1.48)		1.46 (1.33–1.60)		1.56 (1.50–1.62)
Phet vs Whites				<0.0001		0.39		0.0008		0.24		0.78		
	All Women		**African American**		**Japanese American**		**Latino American**		**Native Hawaiian**		**Other Asian American**		**White**	
Robust (0 to <0.2)	1 753	1.00	281	1.00	468	1.00	277	1.00	134	1.00	92	1.00	501	1.00
Prefrail (0.2 to <0.35)	1 837	1.83 (1.71–1.96)	326	1.41 (1.19–1.67)	506	2.32 (2.03–2.65)	348	1.75 (1.48–2.06)	120	1.74 (1.34–2.27)	58	1.29 (0.91–1.83)	479	1.80 (1.58–2.06)
Frail (0.35 to 1)	1 715	3.31 (3.07–3.57)	316	2.47 (2.06–2.94)	383	4.47 (3.85–5.20)	402	2.79 (2.36–3.30)	122	3.91 (2.96–5.18)	78	3.74 (2.65–5.29)	414	3.34 (2.89–3.86)
p Trend		<.0001		<.0001		<.0001		<.0001		<.0001		<.0001		<.0001
Per 0.1 unit		1.42 (1.39–1.44)		1.32 (1.26–1.39)		1.56 (1.50–1.62)		1.34 (1.29–1.39)		1.60 (1.48–1.73)		1.50 (1.36–1.64)		1.41 (1.36–1.46)
Phet vs Whites				0.05		0.0006		0.30		0.33		0.05		

Notes:

*Adjusted for race and ethnic group (analysis for all men or all women), age, nSES at baseline (Q1 to Q5), education at baseline (5 categories), smoking density, alcohol (none, <12, <24 g/d), moderate physical activity (<2.5, 2.5 to <5, 5 to <7, 7 to <14, ≥14 h/wk), baseline chronic conditions (0, 1, 2 to 3, 4+) and baseline BMI (<25, 25 to <30, ≥30). In addition, age at menarche (≤12, 13 to 14, >14), #children (0, 1, 2 to 3, 4+), menopausal status, and use of menopausal hormones were adjusted in women.

eliminated after adjustment for various covariates (35). Modest sample sizes of Hispanics in the previous studies and the heterogeneity of Hispanics in terms of country of origin and generation in the US likely contributed to some of the differences in results. We were able to adjust for additional factors including neighborhood SES, marital status, alcohol intake, diet quality, and physical activity. These factors, in combination, likely explained some of the frailty differences between race and ethnicity relative to Whites. Our results suggest that frailty differences by race and ethnicity varied by education level (Supplementary Table 1), highlighting that education and socioeconomic status likely play key roles in the multifactorial causes of frailty (13,15,19,36). We did not see clear differences in frailty among men with less education, suggesting that those in the low education group uniformly face challenges associated with poverty and that it may be difficult to distinguish racial and ethnic differences. However, the significantly higher odds of frailty in African American and Latino men with high education compared with White men may be related to the wide distribution in income, access to resources and other factors among high education group across race and ethnicity as shown by their differences in odds of frailty even after careful adjustment for the main covariates. Thus, the proportion of men with low education was not only higher among African American (27%), Native Hawaiian (36%), Latino American men (53%), relative to White men (13%) in the MEC, but those in the high education group also experienced a higher odds of frailty.

Adding to published studies on frailty index as a predictor of mortality (37), the FI measure displayed significant associations with all-cause mortality across age groups and 6 major race and ethnic groups of men and women. Published literature on frailty index/phenotype and mortality are lacking in Native Hawaiians and limited in African Americans (38), Japanese Americans (22), and Latinos (39). Although the UK Biobank study reported weak evidence that the FI–mortality association was modified by ethnicity, less than 5% of its cohort participants were of ethnicities other than Whites (10). In contrast, results in the MEC suggest that there may be considerable racial and ethnic differences in the FI mortality associations. Our results also suggest slightly stronger associations in younger than older ages, which has been reported in some studies (10,11,37). Although we did not observe any overall differences in the HR associations by sex, our results in Whites are consistent with meta-analysis results (30) and additional studies of Whites in the United Kingdom (10) and the Netherlands (11), suggesting a higher HR estimate in White men than in White women. However, our results indicate that sex differences in mortality association may be nonuniform by race and ethnicity and longer follow-up will be needed to confirm these results in the MEC. Finally, our results showed significant associations between FI and risk of CVD mortality and cancer-specific mortality, adding to limited previous studies on FI and cause-specific mortality (40–43).

The present study has several important strengths. First, we had a large sample size of men and women, representing major race and ethnic groups in the United States, which allowed comparisons of frailty prevalence and mortality associations relative to White men and White women, which have served as comparison groups in published studies. Second, while few covariates were available in many previous studies (37), we included key relevant lifestyle covariates in our analyses and potential confounding effects were considered carefully. Third, we were able to conduct numerous subgroup analyses to evaluate consistency in our results as well as explore potential modifying factors, and added new information not only on all-cause mortality but also on cause-specific mortality. However, there are also a few limitations. Frailty was not assessed in 1 501 MEC participants because of missing data on 7 or more items, and this subgroup tended to be older, with less education, and were non-Whites. Frailty was measured using only one scale, which included 39 items that were self-reported and all the items were weighted equally. Our information on lifestyle covariates were limited to variables of later adult life and influences of earlier life or genetic factors associated with frailty were not considered. In terms of individual SES, we only had information on highest education and neighborhood SES and lacked information on income. Finally our analyses on overall mortality were based on older adults from ~ages 70s to 90s with few younger adults and the results were based on a relatively short period of follow-up.

In conclusion, the FI was consistently associated with all-cause mortality and cause-specific mortality in all sex, race, and ethnic groups and provides further evidence of the value of an accumulation-deficit approach to examining frailty in older adults. We encourage further research on frailty in other cohorts that include diverse race/ethnic groups and have the needed variables to construct a deficit accumulation FI applying the method of Searle and Rockwood (9).

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki, and the informed consent and study protocol were approved by the Institutional Review Boards at the University of Southern California; University of Hawaii, and University of California, San Francisco.

Conflict of Interest

None declared.

Acknowledgments

The authors of this manuscript certify that they comply with the ethical guidelines for authorship and publishing in the *Journal of Gerontology, Series A: Biological Sciences and Medical Sciences*.

Data Availability

Statement: Data requests can be submitted to Multiethnic Cohort Online Request System (https://www.uhcancercenter.org/for-researchers/mec-data-sharing).

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