

Research Article

# A Modified Healthy Aging Index and Its Association with Mortality: The National Health and Nutrition Examination Survey, 1999–2002

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## Abstract

**Background:** Comorbidity indices that are based on clinically recognized disease do not capture the full spectrum of health. The Healthy Aging Index (HAI) was recently developed to describe a wider range of health and disease across multiple organ systems. We characterized the distribution of a modified HAI (mHAI) by sociodemographics in a representative sample of the U.S. population. We also examined the association of the mHAI with mortality across individuals with different levels of clinically recognizable comorbidities.

**Methods:** Data are from the National Health and Nutrition Examination Survey (1999–2000, 2001–2002) on 2,451 adults aged 60 years or older. Five mHAI components (systolic blood pressure, Digit Symbol Substitution Test, cystatin C, glucose, and respiratory problems) were scored 0 (healthiest), 1, or 2 (unhealthiest) by sex-specific tertiles or clinically relevant cutoffs and summed to construct the mHAI.

**Results:** The mean mHAI score was 4.3; 20.6% had a score of 0–2, 33.2% had a score of 3–4, 31.0% had a score of 5–6, and 15.2% had a score of 7–10. Mean mHAI scores were lower in adults who were younger, non-Hispanic whites, more educated, and married/living with partner. After multivariate adjustment, per unit higher of the mHAI was associated with higher all-cause mortality (HR = 1.19, 95% CI = 1.11–1.27) and higher cardiovascular mortality (HR = 1.23, 95% CI = 1.11–1.35). Within each comorbidity category (0, 1, 2, 3, 4+), the mHAI was still widely distributed and further stratified mortality.

**Conclusions:** Substantial variation exists in the mHAI across sociodemographic subgroups. The mHAI could provide incremental value for mortality risk prediction beyond clinically diagnosed chronic diseases among elders.

**Keywords:** Aging—Mortality—Comorbidity—Epidemiology

Chronic conditions are the leading cause of disability, death, and growing healthcare expenditure in the United States (1). Between 60% and 75% of Americans aged 65 years or older have multiple chronic conditions (2); with an expanding older population, this number is predicted to rise rapidly in the near future. Numerous comorbidity indices have been developed to measure the overall health conditions among older adults and have been shown useful for predicting a wide range of outcomes (3–6). However, it is questionable whether these indices, developed based on clinically recognizable disease, can capture the full spectrum of health. Subclinical disease varies substantially among well-functioning older adults and those with no clinically recognized comorbidity (7–9) and is

associated with mortality and longevity (10,11). Therefore, identifying subclinical disease may provide additional value beyond comorbidity in distinguishing older adults who age healthily and those who do not.

Using five noninvasive tests, Newman and colleagues (12) developed the Physiological Index of Comorbidity, which described a broader range of health across multiple organ systems and identified elders with low mortality. However, one obstacle encountered when applying this tool is that some measures, such as carotid intima-media thickness and white matter grade, are not easily obtained nor frequently used in epidemiological studies. To address this limitation, Sanders and colleagues (13,14) created a Healthy Aging Index (HAI),

also called Modified Physiological Index, using surrogate tests (systolic blood pressure [SBP], forced vital capacity, cystatin C or creatinine, fasting glucose, and Digit Symbol Substitution Test [DSST] or Modified Mini-Mental Status Examination) that can be assessed more easily and are more widely available. Similar to the Physiological Index of Comorbidity, the HAI has been shown to be associated with disability and all-cause mortality (13,14). However, all previous studies focused on the marginal association between the HAI and adverse outcomes; it is unclear whether the association persists within subgroups with different levels of comorbidity.

The purpose of this study is twofold. First, we characterized the distribution of a modified HAI (mHAI; SBP, DSST, cystatin C, glucose, and respiratory problems) in the United States by sociodemographic subgroups, using a large nationally representative sample. Second, we examined the association of the mHAI with mortality across individuals with different levels of clinically recognizable comorbidities. This study would provide novel insights into the incremental value of the mHAI for mortality risk prediction beyond clinically diagnosed chronic diseases among older adults.

## Methods

### Data and Study Participants

Data are from the 1999–2000 and 2001–2002 survey cycles of the National Health and nutrition Examination Survey (NHANES), an ongoing cross-sectional study of a nationally representative sample of noninstitutionalized residents in the United States (15,16). The study population consisted of 2,451 adults who (i) aged 60 years or older, (ii) had complete data on all five mHAI components (SBP, DSST, cystatin C, serum glucose, and respiratory problems), and (iii) had information about vital status, cause of death (cardiovascular death or others), and time to death or censorship throughout the follow-up period. Compared with excluded NHANES participants, included participants were younger, were more likely to be male, of non-Hispanic white race, and married, and were healthier (Supplementary Table 1).

### Components of the Modified Healthy Aging Index

#### Systolic blood pressure

Three or four SBP measurements were taken in a seated position using a mercury sphygmomanometer in the mobile examination center. If only one SBP reading was recorded, that reading was the average. If more than one SBP reading was obtained, the first reading was excluded and the subsequent readings were used to calculate the average. We used sex-specific tertiles of the analytic sample to classify participants into three SBP categories: 0 =  $\leq 125$  mmHg for men and  $\leq 130$  mmHg for women; 1 = 125–139 mmHg for men and 130–150 mmHg for women; and 2 =  $\geq 139$  mmHg for men and  $\geq 150$  mmHg for women. Participants who reported a physician diagnosis of hypertension or were on antihypertensive medication (self-report) were coded in the unhealthiest category (score = 2).

#### Digit Symbol Substitution Test

Cognitive function was measured by the DSST, which requires response speed, sustained attention, visual spatial skills, associative learning, and memory, and is considered a more sensitive measure of dementia than the mini-mental status examination (17). Participants were classified into three DSST categories using sex-specific tertiles of the analytic sample: 0 =  $\geq 53$  for men and  $\geq 56$  for women; 1 = 38–53 for men and 39–56 for women; and 2 =  $\leq 38$  for men and  $\leq 39$  for women.

#### Cystatin C

Cystatin C was measured by the Dade Behring N Latex Cystatin C assay. Sex-specific tertiles of the analytic sample were applied to classify participants into three groups: 0 =  $\leq 0.93$  mg/dL for men and  $\leq 0.90$  mg/dL for women; 1 = 0.93–1.11 mg/dL for men and 0.90–1.09 mg/dL for women; and 2 =  $\geq 1.11$  mg/dL for men and  $\geq 1.09$  mg/dL for women.

#### Serum glucose

Random glucose measures were completed on every NHANES participant, while fasting measures were completed on only 50.7% of the analytic sample. The majority (62.0%) of the participants who took the random test fasted  $\geq 8$  hours; within-person difference between random and fasting glucose levels was minimal. We therefore used a mix of random and fasting glucose test to enhance sample size. Serum glucose was categorized based on clinically relevant cutoff points: 0 =  $\leq 100$  mg/dL, 1 = 100–125 mg/dL, and 2 =  $\geq 125$  mg/dL. Participants who reported a physician diagnosis of diabetes or used diabetes medications (self-report) were coded in the unhealthiest category (score = 2).

#### Respiratory problems

Forced vital capacity or other measures of lung function were not available in the NHANES 1999–2000 and 2001–2002 survey cycles. Therefore, pulmonary function was measured by the number of self-reported respiratory problems (cough, phlegm, wheezing, and dry cough) on most days for 3 consecutive months or more during the year. Participants were scored 0 for having no respiratory problems, 1 for one problem, and 2 for 2–4 problems. Three pulmonary function measures, including forced vital capacity, forced expiratory volume in 1 second, and peak expiratory flow, were stratified well by the number of self-reported respiratory problems (data from the NHANES 2007–2008 survey cycle; Supplementary Table 2).

All mHAI components are known risk factors for mortality (18–22). We constructed the mHAI by adding each of the five component scores to create a total score ranging from 0 (healthiest) to 10 (unhealthiest). We also categorized mHAI scores into the following: 0–2 representing the healthiest subgroup (reference), 3–4, 5–6, and 7–10 representing the unhealthiest subgroup. Cutoffs used in this study were comparable with those derived from other cohorts (Supplementary Table 3).

#### Mortality

The public-use linked mortality files were used to obtain mortality information. The National Center for Health Statistics has linked mortality data from NHANES to death certificate data in the National Death Index. Vital status and cause of death assignment are available from the date of the survey participation through December 31, 2011 based on a probabilistic match between NHANES and death certificate records from the National Death Index. All-cause mortality was defined as death from any cause. Cardiovascular mortality was defined if the cause of death was diseases of heart or cerebrovascular diseases according to the International Classification of Diseases (version 10).

#### Covariates

Sociodemographic characteristics were collected using computer-assisted interview in the home. Sex (male or female), age (60–64, 65–69, 70–74, 75–79, 80–84, or 85+ years), race/ethnicity (non-Hispanic white, non-Hispanic black, other Hispanics,

Mexican American, or other), education (<high school, high school/equivalent, or >high school), and marital status (married/living together, widowed, divorced/separated, or never married) were self-reported. Smoking status was categorized as current, former, or never smokers. Body mass index (BMI) was calculated as body weight (kilograms) divided by height (meters) squared and was categorized as underweight (BMI < 18.5), normal (BMI = 18.5–24.9), overweight (BMI = 25.0–30.0), or obese (BMI > 30). Underweight and normal categories were collapsed due to small sample sizes. Physical activity was assessed based on self-report of four leisure-time activities (walking or bicycling, tasks around home/yard, average level of physical activity such as lifting and climbing stairs, and muscle strengthening activities) in the past 30 days, weighted by the metabolic equivalent score provided by the NHANES. An index of chronic conditions was created as the sum of the following self-reported physician diagnosed diseases: coronary heart disease, congestive heart failure, heart attack, angina, stroke, hypertension, diabetes (excluding borderline diabetes), cancer or malignancy, liver condition, arthritis, and osteoporosis. Based on the sample distribution, the index of comorbidities was categorized as 0, 1, 2, 3, and 4 or more.

**Statistical Analysis**

We first compared the characteristics between the analytic sample (N = 2,451) and the excluded participants who had one or more mHAI components missing (n = 1,252). Then, we estimated the mean mHAI scores and the relative frequencies of four mHAI categories (0–2, 3–4, 5–6, and 7–10) among all participants in the analytic sample. We also identified the mean mHAI scores and the distribution of the mHAI categories by age, sex, race/ethnicity, education, and marital status. Subsequently, we used linear regression to identify the multivariable associations of these sociodemographic characteristics along with behavioral and health factors (smoking status, BMI, physical activity, and count of comorbidities) with the mHAI.

We calculated the death rates across four categories of the mHAI (0–2, 3–4, 5–6, or 7–10). We also estimated the death rates across the mHAI categories for participants reporting 0, 1, 2, 3, and 4+ comorbidities, respectively, and for those who are in each of the six age categories (60–64, 65–69, 70–74, 75–79, 80–84, or 85+ years). Cox proportional hazards models were used to determine the associations of the mHAI with all-cause and cardiovascular mortality. The mHAI was modeled both continuously and in categories (0–2, 3–4, 5–6, or 7–10) with 0–2 being the reference. Age, count of comorbidities, sociodemographics (sex, race/ethnicity, marital status, and education), and behavioral characteristics (current smoker, former smoker, BMI, and physical activity) were included in the multivariable models. We used c-statistic to compare the discrimination between the mHAI, chronologic age, and comorbidity. We also evaluated the incremental discrimination of the mHAI beyond chronologic age and comorbidity.

We conducted several supplementary analyses. First, we examined the association of the mHAI with cancer mortality using Cox models. We also explored whether the mHAI could explain racial/ethnic differences in mortality by including an interaction term between the mHAI and race/ethnicity.

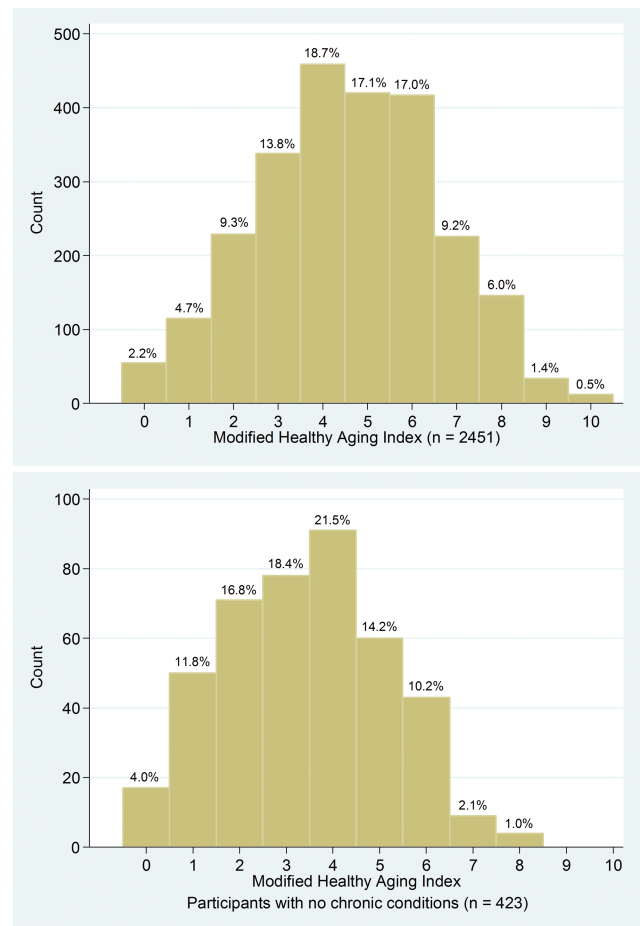
Complex, multistage, probability sampling design of the NHANES was appropriately accounted for by specifying the sampling weight (4-year weight provided by the NHANES), strata, and primary sampling unit parameters. All tests were two-sided with a

significance level of *p* less than .05. All analyses were performed using Stata 13.1 (StataCorp, College Station, TX).

**Results**

**Distribution of the mHAI**

The mHAI was approximately normally distributed with very few participants scoring 0 or 10 (Figure 1). The mean mHAI score in adults aged 60 years or older was 4.3 (SD = 2.1); 20.6% had a score of 0–2, 33.2% had a score of 3–4, 31.0% had a score of 5–6, and 15.2% had a score of 7–10 (Table 1). Substantial variation existed in the mHAI score across sociodemographic subgroups. The mean mHAI scores were lower (healthier) in adults who were younger, non-Hispanic whites, more educated, and married/living together with partner. For example, only 1.0% of adults aged 85 years or older, 6.3% of non-Hispanic blacks, and 9.3% of adults without a high school degree had mHAI scores in the 0–2 category (healthiest). After multivariable adjustment, advanced age, male gender, racial/ethnic minorities, low education, being not married, current smoking status, overweight or obese BMI, physical inactivity, and number of comorbidities were associated with a higher (unhealthier) mHAI score (Supplementary Table 4).



**Figure 1.** Distribution of the modified Healthy Aging Index among all participants and participants with no comorbidities; National Health and Nutrition Examination Survey, 1999–2002.

**Table 1.** Distribution of the Modified Healthy Aging Index by Sociodemographics of 2,451 Participants Aged 60 Years or Older, National Health and Nutrition Examination Survey, 1999–2002

	Subgroup (%)	Modified Healthy Aging Index (%)				
		Mean (95% CI)	0–2 Healthy	3–4	5–6	7–10 Unhealthy
All sample		4.3 (4.2, 4.5)	20.6	33.2	31.0	15.2
Age (years) <sup>***</sup>						
60–64	25.9	3.3 (3.1, 3.5)	37.1	38.8	17.1	6.9
65–69	21.9	3.9 (3.7, 4.2)	25.9	35.6	26.6	11.9
70–74	20.2	4.4 (4.2, 4.6)	17.6	35.7	32.2	14.5
75–79	15.4	5.1 (4.9, 5.3)	7.0	31.1	40.2	21.8
80–84	10.8	5.3 (5.1, 5.6)	5.7	23.8	48.0	22.4
85+	5.7	6.1 (5.8, 6.4)	1.0	12.3	50.0	36.8
Sex						
Female	56.6	4.3 (4.1, 4.5)	21.1	32.5	30.7	15.8
Male	43.4	4.3 (4.2, 4.5)	20.0	34.1	31.4	14.5
Race/ethnicity <sup>***</sup>						
Non-Hispanic White	83.8	4.2 (4.0, 4.4)	22.3	33.6	29.6	14.5
Non-Hispanic Black	6.7	5.2 (5.0, 5.4)	6.3	30.2	38.8	24.7
Mexican American	2.7	4.6 (4.4, 4.8)	15.8	34.2	33.7	16.3
Others	6.8	4.6 (4.4, 4.9)	16.1	29.8	39.8	14.2
Education <sup>***</sup>						
>High school	41.6	3.7 (3.5, 3.9)	29.3	35.2	25.5	10.0
High school	29.0	4.3 (4.1, 4.6)	19.7	36.1	29.0	15.3
<High school	29.4	5.1 (5.0, 5.3)	9.3	27.4	40.8	22.5
Marital status <sup>***</sup>						
Married/living together	64.4	4.0 (3.8, 4.1)	25.3	36.3	26.6	11.6
Divorced/separated	24.2	4.4 (4.1, 4.7)	18.0	28.4	34.7	18.8
Never married	8.9	4.6 (4.2, 5.0)	9.7	24.9	40.8	24.6
Widowed	2.5	5.1 (4.9, 5.4)	16.3	37.6	31.5	14.6

Note: CI = confidence interval.

<sup>\*\*\*</sup> $p < .001$  for comparisons within each variable (weighted means and proportions).

### Association of the mHAI With Mortality

Over an average 9.1 years of follow-up, 925 deaths occurred (241 from cardiovascular diseases); the overall death rate was 38.9 per 1,000 person-years. Rates of all-cause mortality for adults with a mHAI score of 0–2 (healthiest), 3–4, 5–6, and 7–10 (unhealthiest) were 13.0, 26.6, 53.9, and 87.8 per 1,000 person-years, respectively (Table 3). The association of the mHAI with mortality persisted in multivariable adjusted models. Per unit higher of the mHAI was associated with a higher all-cause mortality (hazard ratio [HR] = 1.19, 95% confidence interval [CI]: 1.11–1.27) and higher cardiovascular mortality (HR = 1.23, 95% CI: 1.11–1.35). Adults in the unhealthiest mHAI category (score: 7–10) had a more than threefold higher risk of all-cause mortality and a more than fivefold greater risk of cardiovascular mortality than those who were in the mHAI healthiest category (score: 0–2). There was a much weaker association of the mHAI with cancer mortality. Per unit higher of the mHAI was related to a 5% higher risk of cancer mortality; adults with a mHAI score of 7–10 had a 38% higher cancer mortality than those having a score of 0–2. However, none of these associations reached statistical significance. Results of interaction analysis showed that the association of race/ethnicity with mortality outcomes was not modified by the mHAI.

The mHAI alone predicted death substantially better than the number of comorbidities alone ( $c$ -statistic: 0.71 vs. 0.61,  $p < .001$ ). Addition of the mHAI significantly improved the discrimination for death of both age only model ( $c$ -statistic: 0.75 to 0.79,  $p$  for comparison  $< .001$ ) and model including age and number of comorbidities ( $c$ -statistic: 0.77 to 0.79,  $p$  for comparison  $< .001$ ). Moreover, the mHAI alone explained 20.8% of the association of age with

mortality, whereas addition of number of comorbidities alone only attenuated the association by 6.5% (Supplementary Table 5). The extent of attenuation was more pronounced among participants with more advanced age.

### Association of the mHAI With Mortality Across Comorbidity

Death rates for adults with 0, 1, 2, 3, and 4+ comorbidities were 24.0, 28.3, 37.3, 59.6, and 69.2 per 1,000 person-years, respectively (Table 3). Compared with the mHAI, comorbidities captured a narrower range of mortality (24.0 to 69.2 vs. 13.0 to 87.8). Within each comorbidity category, the mHAI scores were widely distributed and further stratified mortality in both unadjusted and multivariate-adjusted models. Among 423 adults who reported no comorbidities, the distribution of the mHAI was slightly right-skewed (Figure 1); 32.6% had a mHAI score of 0–2, 40.0% had a score of 3–4, 24.4% had a score of 5–6, and 3.1% had a score of 7–10. Within this subgroup, death rates associated with an mHAI score of 0–2, 3–4, 5–6, and 7–10 were 9.0, 25.9, 51.5, and 56.7 (per 1,000 person-years), respectively (Figure 2). After multivariate adjustment, per unit higher of the mHAI was related to a HR of 1.21 for mortality (95% CI: 1.01–1.45).

### Association of the mHAI With Mortality Across Age

Death rates increased steadily with age, ranging from 16.3 per 1,000 person-years among adults aged 60–64 years to 143.3 per 1,000 person-years among those aged 85 years or older (Supplementary Table 6). Within each age group, death rates

**Table 2.** Association of the Modified Healthy Aging Index With Mortality Among Participants Aged 60 Years or Older, National Health and Nutrition Examination Survey, 1999–2002

		All-cause mortality ( <i>n</i> = 925 died)		
		Unadjusted	Adjusted for age and chronic conditions	Multivariable adjusted <sup>a</sup>
Events per 1,000 person-years (95% CI)		HR (95% CI)	HR (95% CI)	HR (95% CI)
Per unit of the mHAI		1.36 (1.31, 1.42)	1.21 (1.14, 1.27)	1.19 (1.11, 1.27)
mHAI categories				
0–2 (healthiest)	13.0 (9.8, 17.6)	Ref.	Ref.	Ref.
3–4	26.6 (22.9, 31.0)	2.10 (1.50, 2.94)	1.58 (1.11, 2.24)	1.63 (1.07, 2.50)
5–6	53.9 (48.2, 60.4)	4.42 (3.29, 5.95)	2.41 (1.70, 3.41)	2.34 (1.56, 3.50)
7–10	87.8 (76.5, 100.9)	7.56 (5.56, 10.3)	3.50 (2.37, 5.16)	3.27 (2.05, 5.24)
		Cardiovascular mortality <sup>b</sup> ( <i>n</i> = 241 died)		
		Unadjusted	Adjusted for age and chronic conditions	Multivariable adjusted <sup>a</sup>
Events per 1,000 person-years (95% CI)		HR (95% CI)	HR (95% CI)	HR (95% CI)
Per unit of the mHAI		1.48 (1.37, 1.60)	1.28 (1.17, 1.40)	1.23 (1.11, 1.35)
mHAI categories				
0–2 (healthiest)	1.9 (0.8, 5.4)	Ref.	Ref.	Ref.
3–4	5.2 (3.8, 7.3)	2.86 (1.16, 7.12)	2.15 (0.90, 5.13)	2.31 (0.85, 6.28)
5–6	13.8 (11.1, 17.3)	7.90 (3.25, 19.17)	4.17 (1.66, 10.52)	4.03 (1.47, 11.04)
7–10	25.0 (18.8, 33.9)	15.00 (5.74, 39.17)	6.37 (2.44, 16.58)	5.32 (1.78, 15.96)
		Cancer mortality <sup>c</sup> ( <i>n</i> = 195 died)		
		Unadjusted	Adjusted for age and chronic conditions	Multivariable adjusted <sup>a</sup>
Events per 1,000 person-years (95% CI)		HR (95% CI)	HR (95% CI)	HR (95% CI)
Per unit of the mHAI		1.12 (1.05, 1.20)	1.05 (0.96, 1.15)	1.05 (0.95, 1.15)
mHAI categories				
0–2 (healthiest)	6.4 (4.3, 10.1)	Ref.	Ref.	Ref.
3–4	6.7 (5.0, 9.4)	1.06 (0.59, 1.92)	0.93 (0.50, 1.72)	1.06 (0.52, 2.16)
5–6	11.1 (8.6, 14.5)	1.78 (1.10, 2.90)	1.36 (0.77, 2.42)	1.38 (0.69, 2.76)
7–10	11.2 (7.8, 16.7)	1.86 (1.07, 3.22)	1.31 (0.70, 2.44)	1.38 (0.68, 2.79)

Note: CI = confidence interval; HR = hazard ratio; mHAI = modified Healthy Aging Index.

<sup>a</sup>Adjusted for age, sex, race (non-Hispanic white, non-Hispanic Black, Mexican American, others), education (<high school, high school or equivalent, >high school), marital status (married/living with partner, divorced/separated, widowed, never married), smoking status (current, former, never), physical activity, body mass index (<25.0, 25.0–30.0, >30.0), and count of chronic conditions including coronary heart disease, congestive heart failure, heart attack, angina, stroke, hypertension, diabetes (excluding borderline diabetes), cancer or malignancy, liver condition, arthritis, and osteoporosis. <sup>b</sup>Died due to disease of heart or cerebrovascular diseases. <sup>c</sup>Died due to malignant neoplasms.

were further discriminated by the mHAI. For example, among adults aged 60–64 years, death rates for those in the unhealthiest mHAI category (score: 7–10) were more than 5 times higher than that of individuals who were in the healthiest mHAI category (score: 0–2).

### Discussion

Using nationally representative data from the NHANES, we found approximately 1 in 5 U.S. adults aged 60 years or older were classified in the healthiest category of the mHAI (score: 0–2). Substantial variation existed in the mHAI across sociodemographics. The mHAI scores were lower (healthier) in adults who were younger, non-Hispanic whites, more educated, and married/living together with partner. Current smoking status, low levels of physical activity, and being overweight or obese were potential behavioral risk factor for the mHAI.

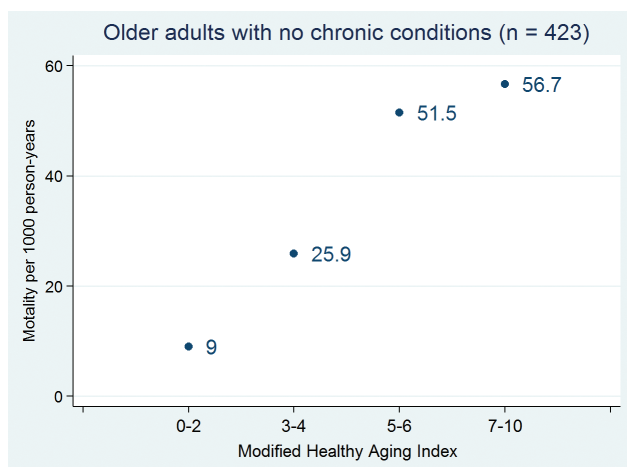
We found that the mHAI was strongly associated with all-cause and cardiovascular mortality, independent of age, diagnosed comorbidities, sociodemographics, and health behaviors in older adults. Notably, the mHAI identified a gradient of mortality risk, even among those at the low risk end of the spectrum. These findings are in line with previous studies, suggesting that the HAI was valuable in predicting death among the elderly adults and was especially useful for identifying elders with low mortality risk (13,14,23). The strengths of associations reported in different cohorts were comparable with our results; the hazard ratio for adults with highest index scores (7–10) compared with those with lowest index scores (0–2) was 3.27 in the present study and ranged from 2.62 to 3.50 in other cohorts (13,14,23). Our findings provided evidence supporting reproducibility of the association of the HAI with mortality in a nationally representative sample and demonstrated the feasibility of using surrogate indicator of pulmonary function to construct the HAI. It is also worth mentioning that addition of the mHAI in the

**Table 3.** Death Rates by the Modified Healthy Aging Index and Comorbidities Among Participants Aged 60 Years or Older, National Health and Nutrition Examination Survey, 1999–2002

Number of Comorbidities	mHAI Score	N (%) in Each Category	Death Events	Death Per 1,000 Person-Years (95% CI)	Unadjusted	Multivariable Adjusted <sup>a</sup>
					HR (95% CI)	HR (95% CI)
0	Continuous				1.44 (1.26, 1.64)	1.21 (1.01, 1.45)
	0–2	138 (32.6%)	17	9.0 (5.1, 17.2)	Ref.	Ref.
	3–4	169 (40.0%)	43	25.9 (18.6, 37.0)	2.94 (1.36, 6.34)	2.13 (0.78, 5.78)
	5–6	103 (24.4%)	52	51.5 (36.7, 72.7)	6.10 (2.67, 13.90)	2.85 (0.87, 9.32)
	7–10	13 (3.1%)	7	56.7 (22.5, 143.1)	6.72 (2.31, 19.54)	1.51 (0.31, 7.39)
	Total	423	119	24.0 (19.5, 29.9)		
1	Continuous				1.51 (1.37, 1.66)	1.28 (1.13, 1.44)
	0–2	163 (23.1%)	23	13.5 (8.8, 21.7)	Ref.	Ref.
	3–4	286 (40.5%)	58	19.5 (14.5, 26.8)	1.49 (0.82, 2.71)	1.36 (0.72, 2.56)
	5–6	205 (29.0%)	91	50.3 (39.8, 64.0)	4.01 (2.25, 7.14)	1.99 (1.06, 3.73)
	7–10	53 (7.5%)	37	126.2 (93.6, 171.7)	11.57 (6.28, 21.29)	5.05 (2.52, 10.12)
	Total	707	209	28.3 (24.1, 33.3)		
2	Continuous				1.36 (1.26, 1.46)	1.24 (1.11, 1.38)
	0–2	67 (10.1%)	11	14.6 (7.4, 32.0)	Ref.	Ref.
	3–4	216 (32.5%)	56	26.3 (19.9, 35.4)	1.82 (0.77, 4.27)	1.70 (0.81, 3.58)
	5–6	265 (39.9%)	107	43.3 (34.7, 54.3)	3.08 (1.40, 6.76)	2.38 (1.14, 4.99)
	7–10	117 (17.6%)	76	83.0 (64.2, 107.4)	6.16 (2.89, 13.11)	3.69 (1.58, 8.58)
	Total	665	250	37.3 (32.3, 43.2)		
3	Continuous				1.14 (1.06, 1.23)	1.07 (0.94, 1.22)
	0–2	20 (5.7%)	6	27.6 (11.5, 79.3)	Ref.	Ref.
	3–4	77 (21.8%)	30	42.2 (29.1, 62.8)	1.57 (0.54, 4.55)	0.99 (0.26, 3.80)
	5–6	147 (41.6%)	79	68.1 (54.8, 85.3)	2.57 (1.03, 6.43)	1.47 (0.46, 4.69)
	7–10	109 (30.9%)	66	73.6 (55.7, 97.8)	2.78 (1.05, 7.33)	1.44 (0.36, 5.80)
	Total	353	181	59.6 (51.0, 69.9)		
4+	Continuous				1.21 (1.10, 1.33)	1.18 (1.01, 1.37)
	0–2	11 (3.6%)	2	19.2 (2.4, 619.0)	Ref.	Ref.
	3–4	49 (16.2%)	19	42.4 (27.1, 68.5)	2.30 (0.49, 10.74)	2.10 (0.47, 9.41)
	5–6	117 (38.6%)	63	67.0 (51.8, 87.5)	3.82 (0.93, 15.73)	2.49 (0.56, 10.95)
	7–10	126 (41.6%)	82	96.3 (74.8, 124.4)	5.65 (1.33, 23.95)	3.94 (0.82, 18.93)
	Total	303	166	69.2 (58.5, 82.1)		

Note: CI = confidence interval; HR = hazard ratio; mHAI = modified Healthy Aging Index.

<sup>a</sup>Adjusted for age, sex, race (non-Hispanic white, non-Hispanic Black, Mexican American, others), education (<high school, high school or equivalent, >high school), marital status (married/living with partner, divorced/separated, widowed, never married), smoking status (current, former, never), physical activity, and body mass index (<25.0, 25.0–30.0, >30.0).



**Figure 2.** Death events across the modified Healthy Aging Index among 423 participants with no chronic conditions; National Health and Nutrition Examination Survey, 1999–2002. 95% confidence interval was (5.1, 17.2) for adults with an index score of 0–2, (18.6, 37.0) for adults with a score of 3–4, (36.7, 72.7) for adults with a score of 5–6, (22.5, 143.1) for adults with a score of 7–10.

age-only model attenuated the association of chronologic age with death by over 20%. These findings suggest that the mHAI may serve as a biomarker of aging, according to several widely accepted criteria for qualifying a biomarker of aging (24,25).

We found that the mHAI was more strongly associated with cardiovascular mortality than all-cause mortality. We also discovered that the mHAI was relatively not useful for stratifying risk of cancer mortality. A plausible explanation is that older adults with high subclinical disease burden may be at an increased risk of developing clinical cardiovascular events but not cancer that may lead to death. This is supported by results of a recent study, where McCabe and colleagues (23) found that the HAI was associated with increased risk of cardiovascular disease (eg, myocardial infarction and stroke) among adults aged 60 years or older from the Framingham Offspring Study.

The mHAI discriminated older adults into a wider range of mortality risk compared with comorbidity and was particularly valuable in identifying elders with very low risk of death and the potential to survive to very old age. In addition, the mHAI was able to further stratify mortality risk among apparently healthy adults with no clinically diagnosed diseases. Most of the existing research on determinants of exceptional longevity and healthy aging has focused on

cardiovascular and genetic risk factors (26–30). The mHAI, which measures subclinical disease burden, may provide a supplementary explanation of the variation in mortality risk and survival among clinically healthy older adults. Our findings highlight the importance of the mHAI in capturing heterogeneity in health status beyond clinically recognizable diseases in old age.

Our study has several strengths. We characterized the distribution of a mHAI across sociodemographic subgroups using a nationally representative sample where racial/ethnic minorities are well represented. In addition, we identified several potential behavioral risk factors of the mHAI. Moreover, we found an association of the mHAI with mortality across adults with different burden of clinical disease (count of comorbidities) and in different age groups.

This study is not without limitations. First, we used self-reported respiratory problems as a surrogate for forced vital capacity because no objective measurements of pulmonary function were available in the NHANES 1999–2000 or 2001–2002 cycles. Spirometry was only administered in the NHANES 2007–2008, 2009–2010, and 2011–2012 cycles where the DSST was not assessed and good surrogates for cognitive function were not available. Second, to ensure appropriate sample size, we did not exclude participants who had the random glucose test and used a mix of random and fasting glucose test instead. However, most of the participants fasted over 8 hours before the test, which largely reduced misclassification. We also compared the glucose levels between participants who had the random test and those who had the fasting test, and the difference was minimal. Third, all five mHAI components were only measured once; these measures may vary over time, leading to misclassification. Future research needs to characterize the trajectories of the mHAI or the HAI and examine their relation to adverse outcomes. Lastly, we were unable to establish a causal relation between behavioral risk factors and the mHAI because the NHANES is cross-sectional in design. Future research utilizing longitudinal design may elucidate the dynamic relationship between a broader range of modifiable risk factors and the mHAI.

In summary, among a nationally representative cohort of community-dwelling adults aged 60 years or older, we found that the mHAI was strongly associated with all-cause and cardiovascular mortality and was useful for discriminating elders with low mortality and potentially defining a healthy aging group. The association persisted among adults with different number of comorbidities and of different ages. Moreover, we found that adults with minimal impairment across multiple organ systems (mHAI score: 0–2) were not common among the young-old and the old-old and were rare among the oldest-old. Future research needs to identify and depict the behavioral and psychosocial profiles of these exceptionally healthy older adults. Such an endeavor may provide us a better understanding of pathways leading to optimal aging.

## Supplementary Material

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

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## Conflict of Interest

The authors have no conflicts of interest and no financial associations to disclose.

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