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Research Article

Mortality in Relation to Changes in a Healthy Aging Index: The Health, Aging, and Body Composition Study

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Abstract

Background: Baseline scores on a Healthy Aging Index (HAI), including five key physiologic domains, strongly predict health outcomes. This study aimed to characterize 9-year changes in a HAI and explore their relationship to subsequent mortality.

Methods: Data are from the Health, Aging, and Body Composition study of well-functioning adults aged 70–79 years. A HAI, which ranges from 0 to 10, was constructed at years 1 and 10 of the study including systolic blood pressure, forced expiratory volume, digit symbol substitution test, cystatin C, and fasting glucose. The relationships between the HAI at years 1 and 10 and the change between years and subsequent mortality until year 17 were estimated from Cox proportional hazards models.

Results: Two thousand two hundred sixty-four participants had complete data on a HAI at year 1, of these 1,122 had complete data at year 10. HAI scores tended to increase (i.e. get worse) over 9-year follow-up, from (mean [SD]) 4.3 (2.1) to 5.7 (2.1); mean within-person change 1.5 (1.6). After multivariable adjustment, HAI score was related to mortality from year 1 (hazard ratio [95% confidence interval] = 1.17 [1.13–1.21] per unit) and year 10 (1.20 [1.14–1.27] per unit). The change between years was also related to mortality (1.08 [1.02–1.15] per unit change).

Conclusions: HAI scores tended to increase with advancing age and stratified mortality rates among participants remaining at year 10. The HAI may prove useful to understand changes in health with aging.

Keywords: Successful aging, Epidemiology, Mortality, Physiology.

Introduction

Comorbidity indices summarize overall burden of chronic conditions and can identify older adults with the greatest health needs (1). The Healthy Aging Index (HAI) extends this approach using five easily measured physiologic indicators sensitive to both clinical and subclinical changes in organ structure and function (2). The HAI stratifies the full range of mortality rates and may distinguish those with low from usual rates as an intermediate endpoint for longevity (3).

Many recent observations support the use of the HAI as a summary measure of physiologic aging. The HAI predicts mortality independent of chronologic age and comorbidity (2). This finding has been replicated across several samples and population subgroups, including those with minimal diagnosed comorbidity (4–6). The HAI has also

been shown to predict onset of disability in well-functioning older adults and future cardiovascular disease in adults aged 60 years and older (2,4). It has also been related to future decline in gait speed (7).

Further studies have shown heritability in HAI scores among long-lived families and identified potential genetic correlates (5,8). Most recently, HAI scores have been associated with differential metabolite profiles relevant to various age-related pathways and predictive of cardiovascular mortality (9).

These findings show potential utility for the HAI as a surrogate measure of longevity for use in future trials targeting aging (10). Before this can happen, it is vital to establish how the HAI changes with chronologic aging and to what extent these changes reflect variations in physiologic aging. A small number of studies have explored trajectories of related healthy aging measures (11,12). However, the relationships between changes in these measures and subsequent health outcomes are unclear.

This study aimed to characterize 9-year changes in the HAI in well-functioning adults aging from their 70s to their 80s. Furthermore, we sought to compare the change in HAI score to the score at a given time point as a predictor of mortality.

Methods

Participants

The Health, Aging, and Body Composition (Health ABC) Study is a prospective cohort study of 3,075 nondisabled black (41.7%) and white men and women (51.5%) from the Pittsburgh, PA and Memphis, TN areas, aged 70–79 years at baseline. Eligibility criteria included, no self-reported difficulty walking a quarter mile, climbing 10 steps, or performing mobility-related activities of daily living, no reported use of a walking aid, no history of cancer treatment in the past 3 years, and no plans to move from the area in the next 3 years. The institutional review boards of the University of Pittsburgh, the University of Tennessee, the University of California–San Francisco Coordinating Center, and the National Institute on Aging approved the study, and all participants gave informed consent.

Healthy Aging Index

The HAI was constructed as described previously at years 1 and 10 using markers of cardiovascular, lung, cognitive, metabolic, and kidney function (2). Kidney biomarkers were measured using different assays at year 1 compared with later years. To avoid potential interassay variability, cystatin C measured at year 3 was used for the year 1 score (13). The study also changed from desktop to handheld spirometers in year 10. Although concerns have been raised over comparability of different devices (14), the two models used in Health ABC have been found to give very similar readings (15). All components were scored from 0 to 2 from most to least healthy using tertiles or clinical cut points (2,3). Cut points for four of the components were reported previously (2), cystatin C tertiles were defined based on the year 3 data. The specific components were as follows:

- Systolic blood pressure (SBP): 0: <126 mmHg, 1: 126–142 mmHg, and 2: ≥142 mmHg.
- Forced vital capacity (FVC): men, 0: ≥3,700 mL, 1: 3,066–3,700 mL, 2: <3,066 mL; women, 0: ≥2,564 mL, 1: 2,127–2,564 mL, and 2: <2,127 mL.
- Digit Symbol Substitution Test (DSST): 0: ≥42 points, 1: 30–42 points, and 2: <30 points.
- Cystatin C: 0: ≤0.77 mg/L, 1: 0.78–0.92 mg/L, 2: >0.92mg/L
- Fasting glucose: 0: <100 mg/dL, 1: 100–126 mg/dL, 2: ≥126 mg/dL (clinical cut points suggested by the American Diabetes Association)

For the SBP and glucose components, participants with treated or self-reported diagnosed hypertension or diabetes were coded into the least healthy tertile (5). At year 10, this included cumulative reports. The five components were summed to give a score of 0–10 for each participant at each time point.

Mortality Analysis

Participants were followed up for mortality from study inception until September 30, 2014. A summary of the study design and participant flow is given in Supplementary Figure S1. Survival analyses for the year 1 HAI were conducted from the date of the year 3 visit (when cystatin C was measured). Two thousand two hundred sixty-four participants with a year 3 cystatin C measurement, complete data on the other four HAI components at year 1, and mortality follow-up were included in this analysis. One thousand three hundred fifty-nine participants returned for a health assessment at year 10; of these, 1,122 with complete data for the HAI at years 1 and 10 and mortality follow-up were included in these analyses. For the year 10, score and the change between years mortality follow-up were conducted from the date of the year 10 visit. Follow-up days were defined as days from the relevant clinic visit until date of death or date of last contact, including all 17 years of the study. Deaths were ascertained from semi-annual contacts, reports from family members or review of obituaries, and death records and adjudicated by committee from medical records, death certificate, and informant interviews. Mean follow-up time from year 3 was 10.6 years with a maximum of 15.2 years. From year 10, the mean follow-up time was 6.2 years and the maximum 8.2 years.

Covariates

Demographic covariates included age (at year 1 or 10), sex, self-reported race, study site, and education. Further health-related covariates were chosen based on prior work and known relationship to mortality from the selection of variables available at years 1 and 10 (2). These included smoking status, body mass index (BMI), and self-reported physical activity defined as kcal/kg/wk from walking, stair climbing, and chores (16,17). Twenty meter gait speed was included as a measure of functional ability and key health indicator. Prevalence of chronic health conditions was estimated at years 1 and 10 based on defined algorithms. A full description of the variables and their coding is included in Supplementary Material.

Statistical Analysis

Characteristics of the years 1 and 10 samples were summarized as mean (SD) or median (inter quartile range [IQR]) for continuous variables and frequency (%) for categorical variables. Distributions of the HAI at years 1 and 10 were explored graphically, and within-person change calculated as year 10 score–year 1 score.

The relationships between the HAI at years 1 and 10 and the change between years, and mortality were estimated from Cox proportional hazards models. The proportional hazards assumption was checked using the Schoenfeld residuals test and comparison of fitted and observed survival curves. Model 1 included demographic variables: age, sex, race, study site, and education. Model 2 additionally included BMI, smoking, physical activity, cancer, cardiovascular disease, pulmonary disease, depression, osteoporotic drug use, and hip or knee osteoarthritis, and model 3 additionally included

20 m gait speed. The full outputs from these models are included in Supplementary Tables S3–S5. Harrell's C-statistics were calculated to compare different models at year 10.

Additional sets of models were constructed entering the change jointly with (a) the year 1 score and (b) the year 10 score. This allowed us to (a) account for the relationship between the change and the initial score and (b) assess the relative importance of the change and the current score.

The relationships between changes in the individual HAI components and mortality were modeled adjusting for the full set of covariates and for the year 10 score for that component.

All analyses were conducted using Stata version 14.1.

Results

The mean (SD) age of the sample at year 1 was 73.6 (2.8) years, 51.4% were female, 38.4% were black, and 44.9% were educated above secondary level (Table 1). At year 10, the mean age of these participants was 82.1 (2.7), 50.5% had post secondary education, and 32.7% were black (Table 1). At year 1, they represented a healthier subset of the full sample with better scores on the HAI components (except SBP and fasting glucose) and lower levels of chronic disease (Table 1). As expected with increasing age, the prevalence of chronic disease was generally higher and scores on the HAI components generally poorer at year 10.

The HAI was relatively normally distributed at both years 1 and 10 (Figure 1A). In the matched years 1 and 10 sample, there was a shift from mainly lower scores at year 1 to higher scores at year 10 (Figure 1A). Within-person change in the HAI was approximately normally distributed around a mean of 1.5, with about three-quarters of the sample increasing their score over time (Figure 1B). Participants with lower scores tended to have greater increases, while those with high scores remained more stable (Figure 1C).

Less than 10% of participants decreased their scores over time on any one component (Supplementary Table S1). Consistent with previous reports of limited cross-sectional correlations between the HAI components (2,3), correlations between component changes were low (–0.0461 to 0.1071, Supplementary Table S2).

A total of 1,436 deaths occurred during up to 15.2 years follow-up from year 3. Four hundred ninety-seven occurred after the year 10 assessment in the remaining sample. The mortality gradient across the range of the HAI was similar at years 1 and 10 (Figure 2), increasing from 33 events per 1,000 person-years in participants with HAI scores ≤2 to 90 events per 1,000 person-years in participants with scores of 7–10 at year 1 and from 33 to 100 across this range at year 10 (Table 2). This graded relationship remained after adjustment for demographic factors at both years (hazard ratio [HR; 95% confidence interval, CI] for the highest [7–10] vs lowest [0–2] scores = 2.58 [2.10–3.18] at year 1 and 2.75 [1.68–4.48] at year 10). HRs (95% CI) per unit higher HAI were 1.18 (1.14–1.21) at year

Table 1. Description of Participants at Years 1 and 10

	Full Sample	Year 10 Sample	
	Year 1	Year 1	Year 10
N	2,264	1,122	1,122
HAI and components			
HAI score	4.8 (2.2)	4.3 (2.1)	5.7 (2.1)
Systolic blood pressure, mmHG, mean (*SD*)	135.4 (20.5)	135.3 (20.1)	135.0 (19.0)
Forced vital capacity, mL, mean (*SD*)	2890.9 (824.2)	2974.3 (800.1)	2606.8 (789.3)
Digit symbol substitution test, points, mean (*SD*)	36.5 (14.4)	39.9 (13.6)	34.5 (14.1)
Serum cystatin C*, mg/dL, mean (*SD*)	0.89 (0.28)	0.84 (0.18)	0.96 (0.33)
Serum fasting glucose, mg/dL, mean (*SD*)	103.8 (33.7)	101.1 (29.9)	100.8 (24.5)
Covariates			
Age, years, mean (*SD*)	73.6 (2.8)	73.1 (2.7)	82.1 (2.7)
Female, *n* (%)	1,164 (51.4)	594 (52.9)	–
Black race, *n* (%)	870 (38.4)	367 (32.7)	–
Pittsburgh site, *n* (%)	1,172 (51.8)	599 (53.4)	–
Post secondary education, *n* (%)	1,013 (44.9)	567 (50.5)	–
Body mass index, kg/m^2, mean (*SD*)	27.3 (4.7)	27.3 (4.6)	27.1 (4.8)
Physical activity†, kcal/kg/wk, median (IQR)	10.5 (3.5–24.3)	12.2 (4.2–26.2)	3.8 (0.5–11.6)
20 m gait speed, m/s, mean(*SD*)‡	1.3 (0.3)	1.4 (0.3)	1.0 (0.2)
Current smoker, *n* (%)	210 (9.3)	69 (6.2)	37 (3.3)
Cancer, *n* (%)	381 (16.9)	167 (14.9)	276 (24.6)
Cardiovascular disease, *n* (%)	592 (26.7)	250 (22.7)	368 (32.8)
Pulmonary disease, *n* (%)	242 (10.8)	90 (8.1)	144 (13.0)
Depression (CES-D ≥ 10), *n* (%)	114 (5.1)	33 (3.0)	145 (13.4)
Osteoporotic drug, *n* (%)	101 (4.5)	49 (4.4)	166 (14.8)
Hip or knee osteoarthritis, *n* (%)	253 (11.3)	134 (12.1)	346 (31.0)
Hypertension§, *n* (%)	1,124 (50.0)	520 (46.6)	776 (69.2)
Diabetes§, *n* (%)	325 (14.4)	125 (11.2)	185 (16.5)

HAI = Healthy aging index.

*From year 3.

†kcal/kg/wk from walking, stairs, and chores.

‡From 2 minute walk at year 1 (*n* = 2,029).

§From self-reported diagnosis or medication use.

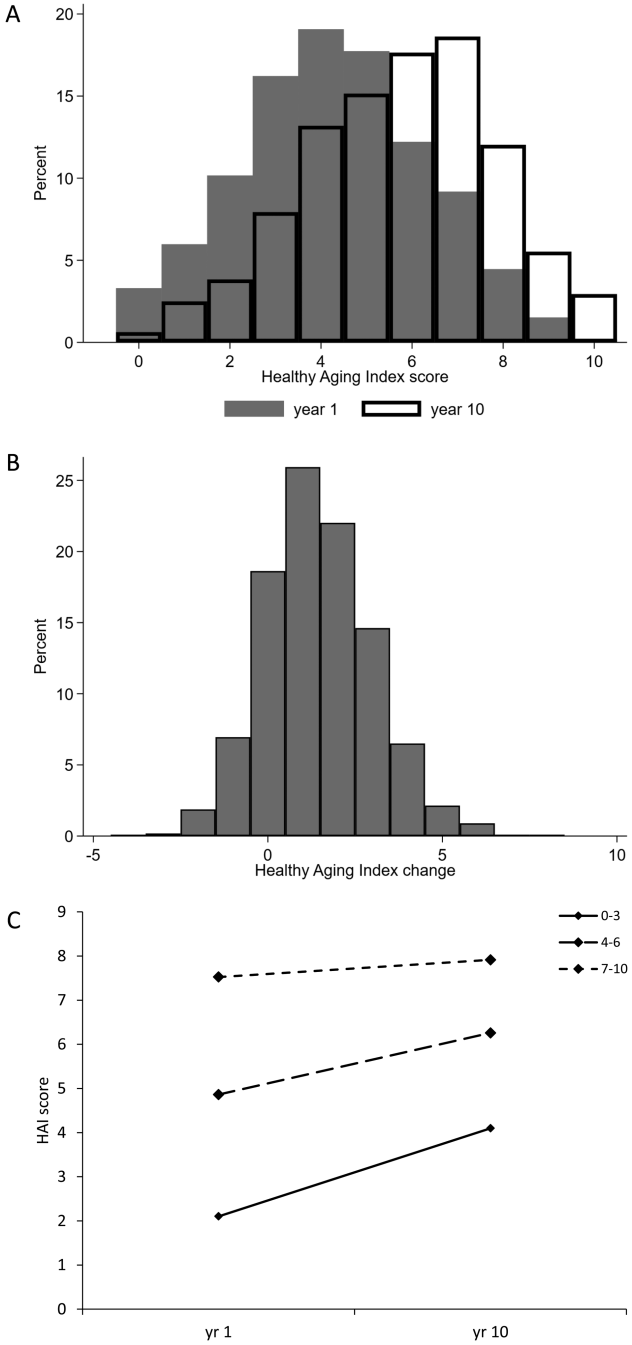

Figure 1. Summaries of changes in a healthy aging index (HAI) over 9 years. (**A**) Distribution of the HAI at years 1 and 10. (**B**) Distribution of the change in HAI scores. (**C**) Mean changes in HAI by baseline score.

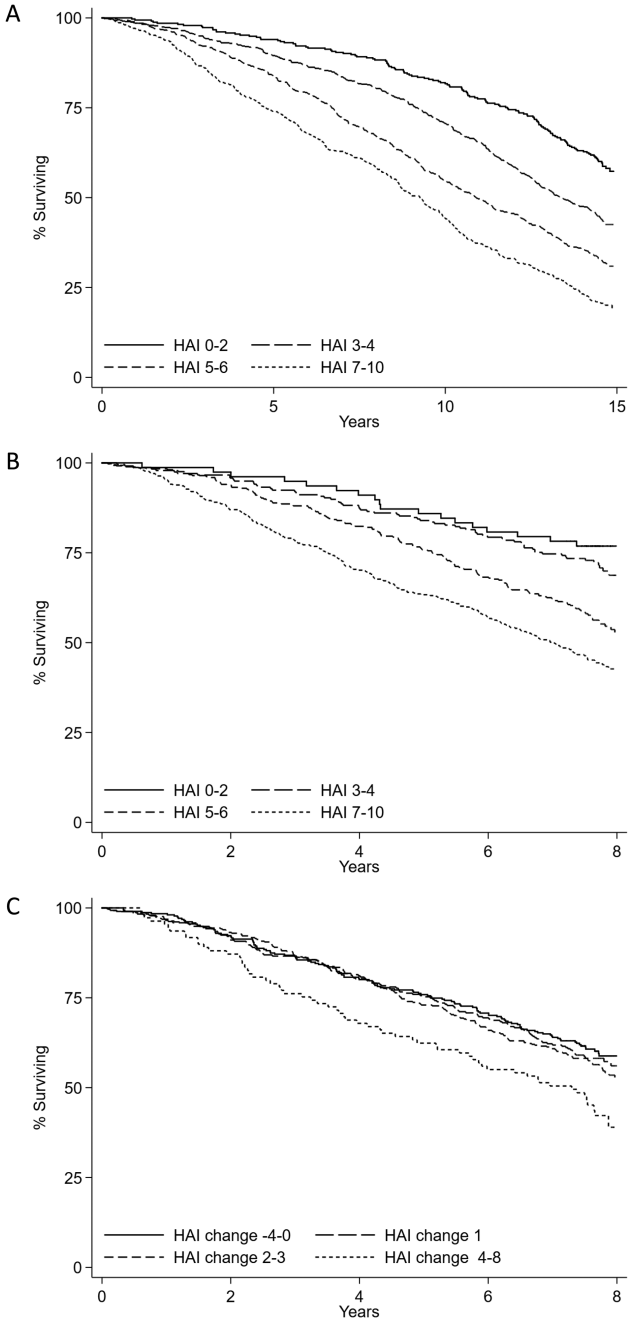

Figure 2. Kaplan–Meier survival curves for healthy aging index (HAI) scores for year 1, year 10, and the change between years. (**A**) Mortality by HAI score from year 1. (**B**) Mortality by HAI score from year 10. (**C**) Mortality by HAI change score between years.

1 and 1.23 (1.17–1.29) at year 10. The relationships between the HAI and mortality tended to be slightly stronger after adjustment for chronic conditions and health behaviors (Table 2). This was due to the inclusion of BMI, which was positively related to several HAI components and negatively related to mortality. Further adjustment for gait speed slightly reduced the strength of relationships (Table 2).

The change in the HAI between years was also related to mortality (HR [95% CI] = 1.08 [1.02–1.15] per unit increase in change score in the full models). Participants with the greatest increase had the highest mortality: HR (95% CI) = 1.55 (1.11–2.16) in those gaining ≥4 points in the full models. Adjustment for the year 1 score increased the effect size for the change (HR [95% CI] = 1.19 [1.11–1.27] per unit increase in the full models).

Inclusion of the year 10 score and the change in the same model attenuated the relationship with the change with little effect on the year 10 score relationship (HR [95% CI] = 0.98 [0.92–1.05] for the change and HR [95% CI] = 1.21 [1.14–1.29] for the year 10 score in the full models). C-statistics for the unadjusted year 10 score and change score models were 0.62 and 0.53 (Supplementary Table S6). For the combined year 10 score and change model, it was 0.62. The

Table 2. Hazard Ratios for Mortality by Healthy Aging Index Scores From Years 1 and 10 and the Change Between Years

	Events/1,000 Person-Years	Model 1	Model 2	Model 3
HAI score year 1				
Mortality from years 3–17 (*N* = 1,436/2,264)				
HR per unit index		1.18 [1.14, 1.21]	1.19 [1.15, 1.23]	1.17 [1.13, 1.21]
HAI score				
0–2 (*n* = 138/333)	33	1	1	1
3–4 (*n* = 384/677)	49	1.39 [1.14, 1.69]	1.42 [1.16, 1.74]	1.39 [1.13, 1.71]
5–6 (*n* = 502/737)	67	1.91 [1.57, 2.33]	1.94 [1.59, 2.38]	1.81 [1.46, 2.24]
7–10 (*n* = 412/517)	90	2.58 [2.10, 3.18]	2.70 [2.17, 3.36]	2.45 [1.94, 3.08]
HAI score year 10				
Mortality from years 10 to 17 (*N* = 497/1,122)				
HR per unit index		1.23 [1.17, 1.29]	1.24 [1.18, 1.31]	1.20 [1.14, 1.27]
HAI score				
0–2 (*n* = 18/78)	33	1	1	1
3–4 (*n* = 70/237)	43	1.24 [0.74, 2.09]	1.39 [0.80, 2.41]	1.39 [0.80, 2.40]
5–6 (*n* = 163/368)	70	1.95 [1.19, 3.20]	2.26 [1.34, 3.84]	2.05 [1.21, 3.47]
7–10 (*n* = 246/439)	100	2.75 [1.68, 4.48]	3.18 [1.87, 5.39]	2.66 [1.57, 4.52]
HAI change years 1–10				
Mortality from years 10 to 17 (*N* = 497/1,122)				
HR per unit change		1.09 [1.03, 1.16]	1.08 [1.02, 1.14]	1.08 [1.02, 1.15]
HAI change score				
−4 to 0 (*n* = 124/311)	63	1	1	1
1 (*n* = 125/291)	69	1.13 [0.88, 1.45]	1.18 [0.91, 1.53]	1.24 [0.95, 1.61]
2–3 (*n* = 186/411)	73	1.15 [0.91, 1.44]	1.13 [0.89, 1.44]	1.24 [0.97, 1.59]
4–8 (*n* = 62/109)	102	1.77 [1.30, 2.41]	1.62 [1.17, 2.25]	1.55 [1.11, 2.16]
HAI change years 1–10 and score at year 1				
HR per unit change		1.21 [1.14, 1.29]	1.21 [1.13, 1.30]	1.19 [1.11, 1.27]
HR per unit year 1 score		1.24 [1.17, 1.30]	1.27 [1.19, 1.35]	1.21 [1.14, 1.29]
HAI change years 1–10 and score at year 10				
HR per unit change		0.98 [0.92, 1.04]	0.95 [0.89, 1.02]	0.98 [0.92, 1.05]
HR per unit year 10 score		1.24 [1.17, 1.30]	1.27 [1.19, 1.35]	1.21 [1.14, 1.29]

HAI = Healthy aging index; HR = Hazard ratio.

Model 1: age, sex, site, race, education.

Model 2: Model 1 + BMI, smoking, physical activity, cancer, cardiovascular disease, pulmonary disease, depression, osteoporotic drugs and hip or knee osteoarthritis.

Model 3: Model 2 + gait speed.

C-statistic for the model containing the year 10 score and all covariates was 0.7 and for a model containing all covariates without the HAI was 0.69.

One issue in constructing a HAI is whether to count known diagnoses of hypertension and diabetes as the highest score. Using the values for glucose and SBP without additionally scoring the condition gave lower average scores at years 1 and 10 and a slightly reduced mean change score of 1.1 points. Mortality estimates were similar when these conditions were adjusted for in the full models, instead of including in the HAI (HR [95% CI] per unit = 1.13 [1.09–1.17] for year 1; 1.18 [1.11–1.25] for year 10; and 1.07 [1.01–1.14] for the change).

All HAI components were related to mortality from years 1 and 10 in all models, except SBP at year 10 (Supplementary Table S7). However, of the change scores at year 10, only changes in DSST and cystatin C were related to mortality (HR [95% CI] = 1.53 [1.33–1.75] and 1.14 [1.01–1.29] per unit increase in change score in demographic adjusted models, Table 3). These relationships were not greatly affected by adjustment for health covariates (Table 3). As for the overall change score, adjustment for year 1 score strengthened relationships with DSST (1.79 [1.54–2.09]), Cystatin C (1.30 [1.13–1.50]), and FVC (1.26 [1.08–1.47]) in demographic models (not shown). Adjustment for the year 10 scores attenuated the relationship with cystatin C and reduced the relationship with DSST (1.22 [1.03–1.46]). Changes in SBP and glucose did not clearly relate to mortality in any models (Table 3).

Discussion

Scores on a HAI increased at least 1 point over 9 years in 72% of adults aged in their 70s at baseline. The HAI score was related to mortality from years 1 and 10. The change in HAI was also related to mortality, especially when accounting for differences in baseline score. Although, this relationship could be attenuated by adjustment for year 10 score.

Some limitations of this study should be acknowledged. There was missing data for the HAI components at both years 1 and 10; substantial attrition due to mortality and other causes occurred before year 10, and not all remaining participants could complete a health assessment. This limits the generalizability of findings to less healthy older adults. Survival and other biases introduced from missing data might be expected to lead to underestimation of the relationship between HAI and mortality from year 10 and to limit variation in change scores. It was only possible to construct a full HAI at 2 time points, and cystatin C from year 3 had to be used for the year 1 score, limiting the scope of analyses possible. These limitations are balanced by important strengths of prospective measurement of the HAI, long-term follow-up for repeat measurements and mortality and well-validated assessments of outcomes and confounding variables.

Table 3: Changes in Healthy Aging Index Components and Mortality

HAI component	Events/1,000 Person-Years	Model 1	Model 2	Model 3
Mortality from years 10 to 17 (*N* = 497/1,122)				
SBP				
HR per unit change		0.90 [0.79, 1.02]	0.90 [0.79, 1.03]	0.87 [0.75, 1.00]
Change score				
−1/−2 (*n* = 28/61)	77	1	1	1
0 (*n* = 351/772)	74	1.02 [0.69, 1.50]	0.97 [0.64, 1.46]	0.77 [0.48, 1.24]
1 (*n* = 81/191)	67	0.86 [0.55, 1.32]	0.96 [0.61, 1.52]	0.78 [0.47, 1.29]
2 (*n* = 37/98)	58	0.81 [0.50, 1.34]	0.70 [0.42, 1.18]	0.54 [0.30, 0.96]
FVC				
HR per unit change		1.08 [0.94, 1.24]	1.08 [0.94, 1.25]	0.96 [0.82, 1.13]
Change score				
−1/−2 (*n* = 21/45)	75	1	1	1
0 (*n* = 265/591)	73	1.07 [0.69, 1.69]	0.97 [0.61, 1.55]	0.82 [0.51, 1.32]
1 (*n* = 175/421)	66	1.05 [0.66, 1.66]	0.98 [0.61, 1.58]	0.74 [0.45, 1.23]
2 (*n* = 36/65)	96	1.56 [0.90, 2.70]	1.40 [0.79, 2.51]	0.94 [0.51, 1.76]
DSST				
HR per unit change		1.53 [1.33, 1.75]	1.41 [1.21, 1.63]	1.22 [1.03, 1.46]
Change score				
−1/−2 (*n* = 20/82)	35	1	1	1
0 (*n* = 275/669)	64	1.74 [1.10, 2.74]	1.87 [1.14, 3.08]	1.71 [1.04, 2.82]
1 (*n* = 178/336)	92	2.44 [1.54, 3.89]	2.45 [1.47, 4.05]	1.88 [1.10, 3.21]
2 (*n* = 24/35)	150	4.64 [2.56, 8.42]	3.63 [1.86, 7.08]	2.51 [1.23, 5.11]
Cystatin C				
HR per unit change		1.14 [1.01, 1.29]	1.15 [1.01, 1.31]	1.04 [0.90, 1.21]
Change score				
−1/−2 (*n* = 43/99)	72	1	1	1
0 (*n* = 279/665)	67	0.96 [0.69, 1.32]	0.96 [0.68, 1.34]	0.85 [0.60, 1.21]
1 (*n* = 136/287)	76	1.08 [0.77, 1.53]	1.10 [0.77, 1.58]	0.89 [0.60, 1.32]
2 (*n* = 39/71)	103	1.50 [0.97, 2.31]	1.48 [0.93, 2.36]	1.10 [0.66, 1.84]
Glucose				
HR per unit change		1.01 [0.88, 1.17]	1.02 [0.87, 1.19]	0.86 [0.72, 1.03]
Change score				
−1/−2 (*n* = 41/89)	74	1	1	1
0 (*n* = 342/793)	70	0.96 [0.69, 1.33]	1.08 [0.74, 1.56]	0.98 [0.67, 1.42]
1 (*n* = 99/206)	78	1.00 [0.69, 1.44]	1.12 [0.75, 1.69]	0.84 [0.54, 1.30]
2 (*n* = 15/34)	69	1.00 [0.55, 1.82]	0.96 [0.50, 1.85]	0.60 [0.29, 1.20]

DSST = Digit Symbol Substitution Test; FVC = Forced Vital Capacity; HAI = Healthy aging index; HR = Hazard ratio; SBP = Systolic blood pressure.

Model 1: age, sex, site, race, education.

Model 2: Model 1 + BMI, smoking, physical activity cancer, cardiovascular disease, pulmonary disease, depression, osteoporotic drugs, hip or knee osteoarthritis and gait speed.

Model 3: Model 2 + year 10 score for that component.

The HAI has been shown to stratify mortality rates in several samples of people aged 60 years and older (4,6,8). Here, we confirm it performs similarly in the older sample (mean age 82 years) remaining at year 10 of Health ABC. This effect was independent of known comorbidity and functional ability. Adding the HAI did not greatly increase the C-statistic for the full model. However, there is a limit to the classification accuracy achievable in epidemiologic studies of complex outcomes, and even apparently strong predictors may not increase these statistics for detailed models (18).

The raw change in HAI score was more modestly related to subsequent mortality. Survival bias is a partial explanation, with participants experiencing rapid increases in score not surviving to the second assessment. Additionally, interpreting change in longitudinal studies is complex. The change partly reflects the initial score, and the relevance of the change score is contextual with a small increase in a high score likely to capture a more serious or "later" decline in health than a similar increase from a lower score. The availability of only 2 time points is particularly problematic as it is not possible to separate "true" change processes from variations due to measurement error (and therefore regression to the mean), without at least a 3rd time point to estimate a trend. Adjustment for the initial score provides some accounting for these factors. After adjustment, the strength of relationship between the change and mortality reached a level comparable with the scores at year 1 or 10.

Our results overall show the HAI scores tend to increase with chronologic age, and variation in the change is related to subsequent mortality. These findings suggest the HAI is sensitive to physiologically relevant changes in health in aging, further supporting its utility as a measure of physiologic aging. However, adjustment for the year 10 score attenuated the relationship between the change and mortality. This implies, at least with respect to mortality prediction, an individual's trajectory to their current score adds little prognostic information to the score itself. Clinically, this suggests a current measurement in itself would give a useful indication of possible health risks in cases where a longer history is unavailable.

Of the HAI components, only changes in DSST and cystatin C were related to mortality, and only the DSST relationship remained after adjustment for year 10 score. Baseline measures of these variables have

been identified as strong predictors of mortality in Health ABC (19). This heterogeneity of the change in HAI at the component level further helps to explain the more modest relationship with mortality for the total change score. Blood pressure and glucose are extensively treated in this age group, making it more difficult to assess changes. The implications of these measures may also be different at advanced ages (20).

Future studies may usefully explore strategies to refine the HAI to optimally capture change, for example by focusing on the most informative components or through component weighting by mortality rates or functional ability (5,21). Another important area is to analyze changes across larger numbers of time points. In addition to mean changes, this will allow derivation of indices of variability and classification of groups following different health trajectories to more completely capture the heterogeneity of health changes in aging (22–25).

In summary, HAI scores tended to increase with advancing age and predicted mortality from a given time point, supporting the utility of the HAI as a summary measure of health in aging. Future studies to further characterize changes in the HAI and their relationships to health outcomes are warranted.

Supplementary Material

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

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