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Self-rated Health and Medical Outcomes in the Women's Health Initiative: The Aging Continuum, Health, Morbidity, Mortality

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Abstract

Background: Self-rated health (SRH) predicts all-cause mortality in many studies; whereas, SRH has been inconsistently related to disease specific death, at least in part because often carefully documented cause of death is lacking.

Methods: Physician-adjudicated cardiovascular disease (CVD), cancer, and other outcomes were evaluated in the Women's Health Initiative (WHI) multi-ethnic Observational Study (OS) cohort of 93,6756 postmenopausal women, aged 50 to79 years. SRH was assessed by the RAND36 at baseline and three years later.

Results: After adjusting for confounders, compared with women reporting excellent health, the risk of all-cause death among women reporting fair/poor health was significantly higher (HR=1.91, CI 1.68, 2.16) during a 7.6 year (1.6) follow-up, as were risks of death from CVD (HR=2.12, CI 1.65, 2.71) and from cancer (HR=1.40, CI, 1.15, 1.69) but not accidental death (HR=1.39, CI 0.69, 2.76). Compared with women whose scores did not change over the initial three years of follow-up, SRH that worsened significantly was associated with higher risk of all-cause (HR=2.06), CVD (HR=1.71) and cancer (HR=2.22) mortality; whereas, women with improved SRH had significantly lower all-cause, CVD and cancer mortality risks (HR: 0.78, 0.80, and 0.79, respectively),

Conclusions: Low SRH and a decrease in SRH over three years were strongly associated with increased risks of all-cause, CVD, cancer and other cause mortality after more than 7 years of follow-up in post-menopausal women. Lower SRH was also associated with incident CVD and cancer.

Keywords: Self-reported health; Women; Mortality

Introduction

When healthy or unhealthy individuals are asked to rate their current global health status (self-rated health: SRH), low SRH has significantly predicted all-cause mortality years later in many studies [1,2]. These findings hold even after adjustment for confounders. There are numerous replications of the SRH all cause-mortality link but links to specific disease mortality and morbidity have been inconsistent. For example, using the National Death Index, SRH was strongly associated with death due to diabetes, respiratory disorders and infections, but only moderately associated with deaths due to heart disease, stroke and cancer in one study [3] whereas, SRH predicted cancer mortality, but not death from stroke or heart disease [4]. By examining a range of disease-specific outcomes, in a very large cohort, this study may provide additional insight into as SRH as a precursor to incident disease.

As a large multi-ethnic, geographically diverse, and well-characterized cohort of nearly 94,000 women the Women's Health Initiative (WHI) Observational Study (OS) provides physician adjudicated health outcomes including cause specific deaths. In addition, WHI has extensive demographic, health, physical and psychosocial measures. The present study aims to clarify the relationships of SRH with cardiovascular disease (CVD), cancer and "other" disease events and deaths. In WHI, assessment of SRH at baseline and follow-up in the cohort also allows examination of change in SRH, and predictors of SRH change. It is hypothesized that morbidity and mortality will have similar relationships to SRH and that SRH will predict endpoints occurring years later after adjustment for multiple, relevant variables. We also report mortality and morbidity relationships with the RAND36general health scale (GHS), a composite score of five questions that includes SRH.

SRH is a commonly used measure, so it is important to have a thorough understanding of its behavior, its biases, and what exactly it measures. In the WHI cohort studies that included SRH showed that participants reporting fair or poor health were nearly 12 times as likely to meet frailty criteria as those reporting excellent health [5]. In the present analysis of WHI OS participants, SRH is examined as a

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predictor of all-cause and disease-specific mortality and morbidity over a 7.6 year (s.d.=1.6) mean time span [6].

Methods

Study population

The Women's Health Initiative (WHI) Observational Study (OS) enrolled 93,676 postmenopausal women, aged 50 to 79 years, between 1994 and 1998 [7]. Details of recruitment and baseline assessments have been previously described [8]. Enrollment in the OS required likely participation for at least 3 years, absence of "serious emotional problems, mental illness, or too much stress" [9] and written informed consent, as approved by each clinical centers' Human Subjects Institutional Review Board. Less than 5% of participants (n=4452) had asked to stop follow-up or were lost to follow-up.

Assessment of Self-rated health

Measures of SRH are taken from the RAND36 [10], which have been shown to have high validity and reliability in older adults [11]. The first RAND36 item, "general self-rated health" was the primary predictor measure with the "General Health Subscale(GHS)," a combined score of 5 items that includes SRH (plus: sick easier than others, as healthy as anybody I know, expect my health to get worse, my health is excellent) was also analyzed.

Assessment of covariates and predictors

During screening (baseline) and follow-up visits three years later, cohort members completed standardized self-administered questionnaires providing information on demographics, family, reproductive and medical histories, smoking and alcohol use, personal habits, thoughts and feelings and recreational physical activity [12]. Specifically, we determined ethnicity, education, body mass index (BMI), hormone therapy (HT) use, disability (greater than one) in activities of daily living (ADL), natural parents still alive or age at death. Depressive symptoms were assessed by self-report using Burnam's 8-item scale for depressive disorders (major depression and dysthymia) [13]. This scale combines 6 questions from the Center of Epidemiologic Studies Depression Scale (CES-D) about frequency of depressive symptoms from with 2 questions from the Diagnostic Interview Schedule about symptom duration. Because the distribution of scores was highly skewed, suggesting a bimodal distribution a cut point greater than or equal to 0.06 was used to dichotomize the continuous score [14]. Physical function scores (lowest function [0] to highest [100]) were calculated from the 10-iteRAND36 physical functioning subscale. These questionnaires measured the number of chronic illnesses, and frequency of medical assessments (outside of the study) that included physical and eye exams, Pap smears, ECGs, blood pressure checks. During the baseline clinic visit and again three years later trained and certified Clinical Center staff performed anthropometric measurements. In this study, we examined white blood cell counts (WBC) from baseline blood specimens that were processed and preserved following established protocols.

Ascertainment of outcomes

Outcomes in this report cover an average of 7.6 years' follow-up. Details of definitions, classifications of "outcomes" (diseases and causes of death), and methods of their ascertainment and documentation are published [15]. Outcomes were ascertained from questionnaires mailed annually to participants. Proxies were contacted only if participants did not respond to the mailed questionnaires or to follow-up telephone calls. This was often how death notification was obtained. Hospital records, laboratory and pathology results, death certificate information and autopsy reports were gathered according to protocol. In addition, WHI staff searched the National Death Index and obtained death certificates to determine cause of death.

Trained physician adjudicators at each site evaluated the complete information and made the decision on cause of death. These records were further evaluated and classified by Coordinating Center adjudicators with discrepancies resolved collaboratively.

Statistical analysis

Fewer than 1% of participants reported "poor" health, so we formed a combined category with the "fair" respondents to produce the primary exposure variable, baseline SRH, defined as excellent, very good, good or fair/poor health level. We analyzed baseline characteristics (age, ethnicity etc.) by level of SRH and provided age-adjusted p-values. SRH groups were further described by annualized health care utilization rates (physical and eye exams, Pap smears, ECGs, blood pressure checks). The primary statistical analysis of SRH effect was time from study enrollment to event based on the Cox regression model with time from enrollment in the OS as the time variable. Potential confounding was addressed by including age (linear), race/ethnicity, BMI (quintiles and linear), education, marital status, smoking status, alcohol consumption, menopausal hormone therapy (HT) use and depressive symptoms. Baseline hazard functions were allowed to vary by 5-year age groups, number of chronic diseases, disability, current health care provider, mammogram within 2 years of enrollment and physical functioning (quintiles). Our stratified Cox model aimed to control confounding as thoroughly as practical and ensure proportionality, without introducing sparse-data biases. We present hazard ratios (HR) and 95% confidence intervals from these Cox models and base statistical significance on a 1 degree-of-freedom test of trend. Change in SRH (year 3 minus baseline) was defined as worsened, no change, or improved. For SRH change analyses, time-to-event began at Year 3 and the Cox regression models included additional stratification on baseline SRH.

Three subgroup analyses were performed to determine whether associations of SRH and all-cause mortality were consistent across age groups, education levels, and race/ethnicity with statistical significance based on the test of interaction between SRH and these select subgroups. Additional analyses were conducted to further understand the mechanism underlying the association of SRH with mortality. Similar multivariable Cox regression models were used to determine whether incident medical events (CHD, stroke, invasive breast cancer, colorectal cancer, and hip fracture) were associated with SRH. As a post-hoc analysis, a nominal polychotomous logistic regression model with change in SRH (improve/same/worsen) as the response was regressed on change in weight and change in fruit/vegetable consumption with adjustment for age, race/ethnicity, education and height. It was hypothesized that improvements in both health behavior (e.g., consumption of fruits and vegetables) and objective measures (e.g., weight) would correspond to improved SRH.

All analyses were conducted using SAS software, version 9.2 (SAS Institute Inc, Cary, North Carolina). All statistical tests were 2-sided and P-value <0.05 was considered statistically significant.

Results

Baseline characteristics and SRH, as reported by 99% (N=93021) of OS women, which includes all variables in the analysis plan are shown

	Fair/poor		Good		Very Good		Excellent		
	N	%	N	%	N	%	N	%	P-Value[1]
Ethnicity									<0.001
White	6106	67.2	23542	79.3	32871	87.2	15067	90.9	
Black	1620	17.8	3289	11.1	2071	5.5	561	3.4	
Hispanic	822	9.0	1252	4.2	1043	2.8	391	2.4	
American Indian	97	1.1	146	0.5	120	0.3	53	0.3	
Asian/Pacific Islander	259	2.8	1003	3.4	1070	2.8	331	2.0	
Unknown	188	2.1	437	1.5	509	1.4	173	1.0	
Education									<0.001
0-8 years	608	6.8	556	1.9	278	0.7	86	0.5	
Some high school	864	9.6	1348	4.6	820	2.2	217	1.3	
High school diploma/GED	1870	20.8	5766	19.6	5641	15.1	1730	10.5	
School after high school	3357	37.4	11546	39.2	13635	36.5	5169	31.4	
College degree or higher	2286	25.4	10217	34.7	17024	45.5	9251	56.2	
Body mass index (BMI), kg/m^2									<0.001
<25	2198	24.5	9306	31.8	16636	44.6	9413	57.5	
25 - <30	2716	30.2	10251	35.0	13129	35.2	5142	31.4	
>=30	4071	45.3	9732	33.2	7515	20.2	1817	11.1	
Marital status									<0.001
Never married	466	5.2	1489	5.0	1710	4.6	689	4.2	
Divorced / Separated	1868	20.7	4634	15.7	5490	14.6	2627	15.9	
Widowed	1942	21.5	5797	19.6	6125	16.3	2267	13.7	
Presently married/Living as married	4742	52.6	17608	59.6	24184	64.5	10936	66.2	
Smoking									<0.001
Never smoked	4426	49.7	15050	51.4	19111	51.3	8176	49.8	
Past smoker	3668	41.2	12103	41.3	16099	43.2	7449	45.4	
Current smoker	816	9.2	2128	7.3	2020	5.4	796	4.8	
Alcohol									<0.001
Non/past drinker	4736	52.6	10576	35.9	9202	24.6	3346	20.3	
<1 drink/week	2532	28.1	9832	33.4	12131	32.4	4761	28.9	
1-14 drinks/week	1503	16.7	8071	27.4	14299	38.2	7442	45.1	
>14 drinks/week	225	2.5	988	3.4	1846	4.9	952	5.8	
ADL disability (>=1 limitation)									<0.001
Yes	610	6.7	558	1.9	351	0.9	115	0.7	
HT use status									
Never used	4295	47.3	12519	42.2	14456	38.4	6412	38.7	<0.001
Past user	1566	17.2	4832	16.3	5367	14.3	2070	12.5	
Current user	3227	35.5	12291	41.5	17823	47.3	8082	48.8	
Number of chronic diseases[2]									<0.001
= 0	542	6.0	4131	13.9	10340	27.4	7533	45.4	
= 1	1955	21.5	10096	34.0	15145	40.2	6238	37.6	
= 2	2916	32.1	9562	32.2	9213	24.4	2324	14.0	
= 3	2132	23.4	4376	14.7	2488	6.6	417	2.5	
= 4	1041	11.4	1204	4.1	440	1.2	59	0.4	
>=5	506	5.6	300	1.0	58	0.2	5	0.0	
Current health care provider									<0.001
Yes	8439	94.2	27935	95.1	35615	95.3	15375	93.6	
Mammogram in the last 2 years									<0.001
Yes	6925	79.6	24397	85.0	32234	87.7	14136	87.4	
Natural mother still alive									<0.001
No	7061	78.5	23002	78.1	27709	74.0	11450	69.6	
Yes	1873	20.8	6301	21.4	9512	25.4	4931	30.0	
Don't Know	57	0.6	134	0.5	199	0.5	77	0.5	
Age mother died									<0.001
<60yrs	1372	20.0	3704	16.5	4016	14.8	1557	13.9	
60-69	1050	15.3	3348	14.9	3729	13.8	1524	13.6	
70-79	1786	26.0	5737	25.6	6822	25.2	2778	24.8	
80-89yrs	1932	28.2	6814	30.4	8710	32.1	3693	32.9	
>=90yrs	717	10.5	2793	12.5	3842	14.2	1657	14.8	
Natural father still alive									<0.001

No	8118	90.3	26730	90.7	33601	89.7	14281	86.7	
Yes	627	7.0	2170	7.4	3261	8.7	1944	11.8	
Don't Know	248	2.8	557	1.9	596	1.6	243	1.5	
Age father died									<0.001
<60yrs	1816	23.2	5538	21.3	6342	19.3	2602	18.6	
60-69	1726	22.0	5531	21.3	6874	20.9	2786	19.9	
70-79	2221	28.4	7425	28.6	9322	28.4	4057	29.0	
80-89yrs	1666	21.3	5857	22.6	8004	24.4	3521	25.2	
>=90yrs	405	5.2	1615	6.2	2314	7.0	1004	7.2	
	Fair/poor		**Good**		**Very Good**		**Excellent**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**P-Value**
Age at screening	64.2	7.6	64.4	7.4	63.5	7.3	62.1	7.2	<0.001
Physical functioning construct, BL	54.1	25.3	75.2	20.2	86.6	14.6	93.3	10.3	<0.001
Depressive symptoms	4.3	3.4	2.7	2.6	2.0	2.2	1.6	2.0	<0.001
White blood cell (Kcell/ml)	6.8	13.5	6.4	13.4	6.0	10.2	6.0	16.0	<0.001
General health construct, BL	41.1	14.6	64.5	12.2	80.2	9.9	93.3	9.1	<0.001

[1]Test of association between self-rated health and baseline characteristic adjusted for age.
[2]Includes CHD (MI, angina, CABG/PTCA), CHF, stroke, treated diabetes, history of cancer, arthritis, hypertension (medication or high blood pressure), 2 or more falls 12 months prior to enrollment, emphysema, and hip fracture after age 55.

Table 1: Baseline Characteristics by self-Rated Health at Baseline: Women's Health Initiative Observational Study (n=93676).

in table 1. At baseline, women reporting fair/good, good, and very good or excellent SRH numbered 9092, 29669, 37684 and 16576 respectively.

Participants with better SRH were slightly younger (p<0.001), with a mean age of 62.1 years (excellent health) and 64.2 with fair or poor SRH. SRH was significantly associated with ethnicity. Visual examination of these ethnicity data suggested that Black and Hispanic women had proportionally more fair/poor than excellent SRH responses than did White women. Current smoking and alcohol abstinence both tended to be more frequent among those reporting fair/poor SRH than excellent SRH. Women with poorer SRH reported more chronic illnesses and they had parents with shorter life spans (Table 1). There was a modest positive association between parents' age at death and SRH. There were large differences in self-reported chronic illnesses at baseline, i.e. only 6% of women reporting fair/poor health had no chronic illnesses compared with 45% of women reporting excellent health. Overall, a small number of participants reported having a disability that interfered with activities of daily living (ADL). However, less than 1% of women reporting very good and excellent health had ADL interference compared with 6% of women with fair/poor health. The RAND36 physical functioning and general health scales (GHS) indicated large differences across SRH groups. Depressive symptoms, though uncommon, were associated with poorer SRH. White blood cell counts were also slightly higher with lower SRH. Women with higher SRH completed more routine health screening exams that were measured in WHI than those with lower SRH (Table 2). Fair/poor SRH was associated with 13-15% lower rates of annual mammogram and Pap test completion compared to very good or excellent SRH. However, reporting of an ECG was 9 to 11% more frequent in women with fair/poor than very good or excellent SRH. A prior history of health related problems did not appear to be related to this difference. Regular physical exams were only slightly less frequent in lower SRH groups and the proportion of women having a current health care provider was similar and non-linear across SRH groups. White blood cell count (WBC) was included as a covariate in a sensitivity analysis. There was no appreciable attenuation in risk; HR(fair/poor vs. excellent) in table 3a changed from 1.91 to 1.89, 2.12 to 2.06, 1.40 to 1.39, 1.39 to 1.32, and 2.77 to 2.76 for total death, CVD death, cancer death, accidental death and other death respectively.

Risk of death from any cause over the period of 6-9 years (mean 7.6) of follow-up was negatively associated with baseline SRH (Table 3a). The fully adjusted model took into account factors that were significantly related to SRH, including age, ethnicity, education, marital status, smoking, alcohol use, hormone therapy, disability, depression and BMI. After adjustment for these confounders, the risk of death among women reporting fair/poor health was nearly double that of women reporting excellent health over the average of 7.6 years' follow-up (HR = 1.91, 1.68, 2.16). The all-cause death rate did not differ significantly between "very good" and excellent SRH. Risk of CVD death was more than two-fold higher in women reporting fair/poor health, and cancer death was 40% higher. The "other" medical death category was nearly tripled with fair/poor SRH. Also, these deaths from causes other than CVD and cancer, in fully adjusted models, differed between very good and excellent SRH by 20%. Accidental death was not associated with SRH. In subgroup analyses, the association of SRH with all-cause mortality was not modified by race/ethnicity (p-int=0.94), age (p-int = 0.13), or education (p-int = 0.53), and the risk associated with "fair/poor" SRH was similar among diverse groups. For example, the HR (95% CI), comparing fair/poor to excellent SRH was 1.81(1.64, 2.00) among Whites and 1.87(1.45, 2.43) among Blacks.

Results of analyses using the RAND36 General Health Subscale are shown in table 3b. The pattern of relationships with death was similar to that for the single SRH item, with lowest quintile and two lowest quintiles being significantly associated with all-cause, CVD, cancer and "other" mortality compared with the best health category, while accidental death was not significantly associated with SRH.

SRH was significantly associated with incident CHD, stroke and hip fractures with participants reporting "fair/poor" SRH experiencing approximately 50% higher risk of incident CHD, stroke, and hip fracture over the follow-up period compared with those reporting "excellent," SRH with hazard ratios (95% CI) of 1.7 (1.38, 2.11), 1.46 (1.17,1.82), and 1.41 (1.06, 1.88), respectively. In contrast, SRH was not associated with invasive breast cancer or colorectal cancer (Table 4).

The screening (baseline) surveys were repeated at year 3 of the study by 90% (n=82031) of women who were not lost to follow-up or death (n=91130). Results of analyses of difference score (i.e. the baseline score minus the score at year 3) categorized as improved, no change or worse, are presented in table 5a. Compared with women who did not change SRH over the three-year period, when SRH declined

Exam/tests/procedure	Excellent	Very Good	Good	Fair/Poor
Mammogram	71.0%	70.4%	66.1%	58.4%
Pap smear	56.6%	54.1%	48.8%	41.4%
ECG	30.8%	33.2%	37.4%	42.1%
ECG among women with no prior history of CHD[4] or CHF	30.6%	32.6%	36.0%	39.3%
ECG among women with no prior history of CHD or CHF or other heart conditions[5]	30.4%	32.1%	35.3%	38.1%
Mammogram*	70.7%	70.4%	66.2%	59.4%
Physical exam or check up*	74.4%	75.4%	73.5%	69.7%
Blood Pressure Check*	81.4%	83.2%	81.9%	79.2%
Eye exam*	63.4%	64.0%	62.7%	59.7%

[3]Cumulative number of exams, tests, or procedures divided by cumulative follow-up time
[4]MI, angina, CABG/PTCA
[5]Cardiac catheterization, carotid endarterectomy/angioplasty, atrial fibrillation, aorticaneurysm
*Data on these procedures were not collected prior to 1997. Mammograms utilization rates provided to illustrate that there is no discernable selection bias.

Table 2: Annualized Health Care (exams/tests/procedures) Utilization Rates[3].

	Min Adjust[6]					Full Adjust[7]		
Cause of Death by Self-Rated Health	**Event**	**AnnPer**	**HR**	**95% CI**	**P-trend[8]**	**HR**	**95% CI**	**P-trend**
Total Death			<0.001					<0.001
Fair/Poor	1405	(2.18%)	4.02	(3.63, 4.46)		1.91	(1.68, 2.16)	
Good	2340	(1.06%)	1.84	(1.67, 2.02)		1.27	(1.14, 1.41)	
Very Good	1842	(0.64%)	1.23	(1.11, 1.35)		1.08	(0.97, 1.19)	
Excellent	606	(0.47%)	1.00			1.00		
CVD Death			<0.001					<0.001
Fair/Poor	493	(0.77%)	5.97	(4.86, 7.34)		2.12	(1.65, 2.71)	
Good	725	(0.33%)	2.33	(1.91, 2.84)		1.30	(1.04, 1.62)	
Very Good	431	(0.15%)	1.26	(1.03, 1.55)		1.01	(0.81, 1.25)	
Excellent	130	(0.10%)	1.00			1.00		
Cancer Death			<0.001					<0.001
Fair/Poor	386	(0.60%)	2.10	(1.80, 2.46)		1.40	(1.15, 1.69)	
Good	977	(0.44%)	1.51	(1.32, 1.72)		1.19	(1.03, 1.38)	
Very Good	935	(0.32%)	1.16	(1.02, 1.32)		1.06	(0.93, 1.22)	
Excellent	336	(0.26%)	1.00			1.00		
Accidental Death			0.01					0.40
Fair/Poor	32	(0.05%)	2.08	(1.22, 3.56)		1.39	(0.69, 2.76)	
Good	55	(0.02%)	0.92	(0.57, 1.48)		0.82	(0.47, 1.41)	
Very Good	52	(0.02%)	0.76	(0.47, 1.21)		0.69	(0.42, 1.14)	
Excellent	27	(0.02%)	1.00			1.00		
Other Death			<0.001					<0.001
Fair/Poor	460	(0.71%)	7.97	(6.31, 10.07)		2.77	(2.09, 3.66)	
Good	538	(0.24%)	2.59	(2.06, 3.26)		1.55	(1.20, 2.00)	
Very Good	391	(0.14%)	1.59	(1.25, 2.00)		1.33	(1.04, 1.70)	
Excellent	101	(0.08%)	1.00			1.00		

[6]Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups.
[7]Adjusted for age (linear), race/ethnicity, BMI (quintiles and linear), education, marital status, smoking status, alcohol consumption HT use and depressive symptoms. Baseline hazard functions were allowed to vary by 5-year age groups, number of chronic diseases, disability, current health care provider, mammogram within 2 years of enrollment and physical functioning (quintiles).
[8]From a multivariable Cox proportional hazards models

Table 3a: Multivariable adjusted Risk of Death Associated with Self-Rated Health at Baseline.

there was a two-fold increased risk of subsequent all-cause mortality (2.06 HR 1.89, 2.23) whereas improved scores lowered risk of death (0.78 HR, 0.70, 0.87). These relationships were statistically significant in fully adjusted models including baseline SRH score as a possible confounding variable. As with baseline SRH, accidental death was not associated with change in SRH. A post-hoc analysis demonstrated that participants who lost weight were more likely to report improved SRH than lower SRH; OR (95%CI) = 1.07 (1.05, 1.09) for a decrease of 5 lb. per year (15 lb. difference between baseline and year 3). Participants who ate more "healthful" foods were also more likely to report improved SRH than lower SRH; OR (95%CI)* = 1.06 (1.04, 1.08) for an increase of 0.5 serving of fruits/vegetables per year (1.5 serving difference between baseline and Y3).

Change in the General Health Subscale of the RAND36 produced similar results to those for SRH (Table 5b).

Discussion

In this large multi-ethnic U.S. cohort of postmenopausal women, aged 50 to 79 years, at baseline, who were then followed for an average of 7.6 years in the WHI Observational Study, participants' self-rating of their health (self-rated health: SRH) was a strong predictor of all-

	Min Adjust[9]					Full Adjust[10]		
Cause of Death by General Health	**Event**	**AnnPer**	**HR**	**95% CI**	**P-trend**	**HR**	**95% CI**	**P-trend**
Total Death			<0.001					<0.001
1st quintile (Worst)	1978	(1.65%)	2.72	(2.50, 2.96)		1.41	(1.27, 1.56)	
2nd quintile	946	(1.00%)	1.62	(1.47, 1.78)		1.14	(1.02, 1.26)	
3rd quintile	1216	(0.79%)	1.32	(1.21, 1.44)		1.05	(0.96, 1.16)	
4th quintile	1061	(0.69%)	1.22	(1.11, 1.34)		1.07	(0.97, 1.18)	
5th quintile (Best)	927	(0.52%)	1.00			1.00		
CVD Death			<0.001					<0.001
1st quintile (Worst)	677	(0.56%)	3.61	(3.06, 4.24)		1.41	(1.16, 1.72)	
2nd quintile	270	(0.29%)	1.75	(1.44, 2.12)		1.01	(0.82, 1.24)	
3rd quintile	339	(0.22%)	1.51	(1.26, 1.81)		1.05	(0.87, 1.27)	
4th quintile	251	(0.16%)	1.15	(0.95, 1.40)		0.94	(0.77, 1.14)	
5th quintile (Best)	225	(0.13%)	1.00			1.00		
Cancer Death			<0.001					0.05
1st quintile (Worst)	634	(0.53%)	1.75	(1.54, 1.98)		1.23	(1.05, 1.43)	
2nd quintile	390	(0.41%)	1.32	(1.14, 1.51)		1.06	(0.91, 1.23)	
3rd quintile	553	(0.36%)	1.16	(1.02, 1.32)		1.01	(0.88, 1.15)	
4th quintile	546	(0.36%)	1.23	(1.09, 1.40)		1.11	(0.98, 1.27)	
5th quintile (Best)	490	(0.27%)	1.00			1.00		
Accidental Death			0.05					0.91
1st quintile (Worst)	43	(0.04%)	1.63	(1.02, 2.61)		1.06	(0.59, 1.91)	
2nd quintile	20	(0.02%)	1.00	(0.57, 1.76)		0.84	(0.46, 1.54)	
3rd quintile	35	(0.02%)	1.01	(0.62, 1.65)		0.85	(0.50,1.45)	
4th quintile	31	(0.02%)	0.93	(0.56, 1.53)		0.88	(0.52, 1.48)	
5th quintile (Best)	34	(0.02%)	1.00			1.00		
Other Death			<0.001					<0.001
1st quintile (Worst)	582	(0.48%)	4.44	(3.69, 5.34)		1.77	(1.41, 2.21)	
2nd quintile	243	(0.26%)	2.38	(1.93, 2.94)		1.47	(1.17, 1.85)	
3rd quintile	264	(0.17%)	1.59	(1.29, 1.95)		1.17	(0.94, 1.46)	
4th quintile	217	(0.14%)	1.36	(1.10, 1.69)		1.16	(0.93, 1.44)	
5th quintile (Best)	164	(0.09%)	1.00			1.00		

[9]Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups.
[10]Adjusted for age (linear), race/ethnicity, BMI (quintiles and linear), education, marital status, smoking status, alcohol consumption, HT use and depressive symptoms. Baseline hazard functions were allowed to vary by 5-year age groups, number of chronic diseases, disability, current health care provider, mammogram within 2 years of enrollment and physical functioning (quintiles).

Table 3b: Multivariable adjusted Risk of Death Associated with RAND36 General Health Subscale at Baseline.

	Min Adjust[11]					Full Adjust[12]		
Adjudicated outcome by Self-Rated Health	**Event**	**AnnPer**	**HR**	**95% CI**	**P-trend[13]**	**HR**	**95% CI**	**P-trend**
CHD					<0.001			<0.001
Fair/Poor	524	(0.83%)	3.98	(3.33, 4.77)		1.71	(1.38, 2.11)	
Good	1058	(0.48%)	2.46	(2.09, 2.90)		1.47	(1.23, 1.76)	
Very Good	675	(0.23%)	1.38	(1.17, 1.64)		1.11	(0.93, 1.32)	
Excellent	187	(0.14%)	1.00			1.00		
Stroke					<0.001			<0.001
Fair/Poor	366	(0.58%)	2.50	(2.08, 3.00)		1.46	(1.17, 1.82)	
Good	788	(0.36%)	1.64	(1.39, 1.92)		1.18	(0.98, 1.41)	
Very Good	637	(0.22%)	1.17	(1.00, 1.38)		1.02	(0.86, 1.22)	
Excellent	208	(0.16%)	1.00			1.00		
Invasive Breast Cancer					0.57			0.22
Fair/Poor	308	(0.49%)	1.03	(0.89, 1.20)		1.09	(0.91, 1.30)	
Good	1098	(0.50%)	1.06	(0.95, 1.18)		1.09	(0.97, 1.23)	
Very Good	1419	(0.50%)	1.06	(0.96, 1.18)		1.07	(0.96, 1.19)	
Excellent	580	(0.46%)	1.00					
Colorectal Cancer					0.01			0.17
Fair/Poor	106	(0.17%)	1.50	(1.13, 2.00)		1.20	(0.85, 1.70)	
Good	329	(0.15%)	1.42	(1.13, 1.78)		1.26	(0.98, 1.62)	
Very Good	346	(0.12%)	1.25	(1.00, 1.56)		1.18	(0.94, 1.49)	
Excellent	120	(0.09%)	1.00			1.00		

Hip Fracture					<0.001			0.02
Fair/Poor	184	(0.29%)	2.32	(1.84, 2.94)		1.41	(1.06, 1.88)	
Good	414	(0.19%)	1.36	(1.11, 1.66)		1.10	(0.87, 1.38)	
Very Good	382	(0.13%)	1.07	(0.88, 1.31)		0.99	(0.80, 1.22)	
Excellent	139	(0.11%)	1.00			1.00		

[11]Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups and prior history of disease (i.e., depending on given outcome, prior history of MI, stroke, invasive breast cancer, colorectal cancer or hip fracture after 54 years of age).
[12]Adjusted for age (linear), race/ethnicity, BMI (quintiles and linear), education, marital status, smoking status, alcohol consumption, HT use and depressive symptoms. Baseline hazard functions were allowed to vary by 5-year age groups, number of chronic diseases, disability, and current health care provider, mammogram within 2 years of enrollment, physical functioning (quintiles), and prior history of disease.
[13]From a multivariable Cox proportional hazards models.

Table 4: Multivariable adjusted Risk of Adjudicated Outcomes Associated with Self-Rated Health at Baseline.

	Min Adjust[14]					Full Adjust[15]		
Cause of Death by Change in Self-Rated Health	**Event**	**AnnPer**	**HR**	**95% CI**	**P-trend[16]**	**HR**	**95% CI**	**P-trend**
Total Death					<0.001			<0.001
Worsened	1360	(1.44%)	1.64	(1.52, 1.77)		2.06	(1.89, 2.23)	
No Change	1880	(0.84%)	1.00			1.00		
Improved	594	(0.89%)	1.09	(0.98, 1.20)		0.78	(0.70, 0.87)	
CVD Death					0.006			<0.001
Worsened	345	(0.37%)	1.37	(1.18, 1.58)		1.71	(1.46, 2.01)	
No Change	553	(0.25%)	1.00			1.00		
Improved	174	(0.26%)	1.13	(0.94, 1.35)		0.80	(0.66, 0.97)	
Cancer Death					<0.001			<0.001
Worsened	619	(0.66%)	1.87	(1.68, 2.09)		2.22	(1.97, 2.51)	
No Change	773	(0.35%)	1.00			1.00		
Improved	227	(0.34%)	0.99	(0.85, 1.16)		0.79	(0.66, 0.93)	
Accidental Death					0.85			0.37
Worsened	28	(0.03%)	1.27	(0.78, 2.07)		1.45	(0.84, 2.52)	
No Change	47	(0.02%)	1.00			1.00		
Improved	21	(0.03%)	1.43	(0.83, 2.48)		1.06	(0.57, 1.96)	
Other Death					<0.001			<0.001
Worsened	338	(0.36%)	1.66	(1.43, 1.93)		2.29	(1.93, 2.71)	
No Change	455	(0.20%)	1.00			1.00		
Improved	149	(0.22%)	1.11	(0.91, 1.35)		0.69	(0.55, 0.85)	

[14]Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups.
[15]Adjusted for age (linear), race/ethnicity, BMI (quintiles and linear), education, marital status, smoking status, alcohol consumption, HT use and depressive symptoms. Baseline hazard functions were allowed to vary by 5-year age groups, number of chronic diseases, disability, and current health care provider, mammogram within 2 years of enrollment, physical functioning (quintiles), and self-rated health at baseline.
[16]From a multivariable Cox proportional hazards model.

Table 5a: Multivariable adjusted Risk of Death (after three years of follow-up) Associated with Change in Self-Rated Health (Year 3 - Baseline).

	Min Adjust[17]					Full Adjust[18]		
Cause of Death by Change in General Health	**Event**	**AnnPer**	**HR**	**95% CI**	**P-trend[19]**	**HR**	**95% CI**	**P-trend**
Total Death					<0.001			<0.001
Worsened >10	1214	(1.59%)	2.02	(1.82, 2.26)		1.95	(1.74, 2.19)	
Worsened 5 to 10	901	(0.95%)	1.21	(1.08, 1.36)		1.16	(1.03, 1.31)	
No change	515	(0.72%)	1.00					
Improved 5 to 10	671	(0.79%)	1.05	(0.93, 1.19)		0.94	(0.83, 1.07)	
Improved > 10	419	(0.83%)	1.20	(1.05, 1.37)		0.93	(0.80, 1.07)	
CVD Death					<0.001			<0.001
Worsened >10	307	(0.40%)	1.57	(1.29, 1.92)		1.53	(1.23, 1.89)	
Worsened 5 to 10	256	(0.27%)	1.03	(0.84, 1.27)		1.02	(0.82, 1.27)	
No change	162	(0.23%)	1.00			1.00		
Improved 5 to 10	200	(0.24%)	1.01	(0.81, 1.26)		0.90	(0.71, 1.13)	
Improved > 10	116	(0.23%)	1.04	(0.81, 1.34)		0.76	(0.58, 0.99)	
Cancer Death					<0.001			<0.001
Worsened >10	542	(0.71%)	2.33	(1.97, 2.75)		2.26	(1.90, 2.69)	
Worsened 5 to 10	376	(0.39%)	1.31	(1.10, 1.56)		1.27	(1.06, 1.52)	
No change	209	(0.29%)	1.00			1.00		

Improved 5 to 10	287	(0.34%)	1.12	(0.93, 1.35)		1.05	(0.86, 1.27)	
Improved > 10	167	(0.33%)	1.18	(0.95, 1.46)		1.03	(0.83, 1.29)	
Accidental Death					0.48			0.16
Worsened >10	26	(0.03%)	1.55	(0.78, 3.06)		1.56	(0.77, 3.15)	
Worsened 5 to 10	22	(0.02%)	1.08	(0.54, 2.18)		1.11	(0.54, 2.28)	
No change	14	(0.02%)	1.00			1.00		
Improved 5 to 10	21	(0.02%)	1.24	(0.61, 2.52)		0.98	(0.46, 2.08)	
Improved > 10	11	(0.02%)	1.13	(0.50, 2.58)		0.96	(0.40, 2.27)	
Other Death					<0.001			<0.001
Worsened >10	313	(0.41%)	2.14	(1.72, 2.67)		1.97	(1.56, 2.49)	
Worsened 5 to 10	224	(0.24%)	1.24	(0.98, 1.56)		1.11	(0.87, 1.42)	
No change	120	(0.17%)	1.00			1.00		
Improved 5 to 10	141	(0.17%)	0.92	(0.71, 1.19)		0.75	(0.57, 0.98)	
Improved > 10	108	(0.21%)	1.30	(0.99, 1.71)		0.85	(0.64, 1.13)	

[17]Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups
[18]Adjusted for age (linear), race/ethnicity, BMI (quintiles and linear), education, marital status, smoking status, alcohol consumption, HT use and depressive symptoms. Baseline hazard functions were allowed to vary by 5-year age groups, number of chronic diseases, disability, current health care provider, mammogram within 2 years of enrollment, physical functioning (quintiles), and self-rated health at baseline.
[19]From a multivariable Cox proportional hazards model

Table 5b: Multivariable adjusted Risk of Death (after three years of follow-up) associated with change in the RAND36 General Health Subscale (Year 3 - Baseline).

cause, CVD and cancer mortality after adjusting for known risk factors and important confounding variables. SRH was significantly associated with cardiovascular and fracture endpoints, but not with cancer. Approximately 15% of the women who rated their health as fair or poor at baseline died during the subsequent 7.6 years of follow-up compared with 3.6% of women who rated their health as excellent at study outset. Other studies report SRH relationships with total mortality of similar magnitude [16,17]. Absolute numbers have varied by age, health of the cohort and plus other demographic and health factors.

Poor/fair baseline SRH or worsening of SRH (compared to no change) from baseline to 3 years later was strongly associated with all-cause, as well as CVD- and total cancer specific mortality. Baseline SRH and changes in SRH were also strongly related to "other" deaths (i.e. not CVD or cancer), but not to accidental deaths. Both SRH and GHS were strongly associated with prediction of all cause or disease-specific mortality. In situations where patient burden is a concern, SRH can be ascertained with a single question.

Improvement in SRH (compared with no change) resulted in about a 20% lower risk of death from both CVD and cancer consistent with research by others addressing improvement in SRH [18-22]. Future research might consider how health behavior changes and/or improvements in modifiable intermediate health measures (e.g. better blood pressure control) may improve SRH as an intermediary to reduced mortality. Post-hoc analysis showed that improved SRH coincided with weight loss and increased fruit and vegetable consumption. Of possible relevance to these observations, Shirom et al. [23] found that improved SRH scores were associated with an improvement in HDL-C and triglyceride levels.

Several other studies that have differentiated the relationship of SRH with cancer death from all cause mortality have reported a significant linear relationship between SRH and cancer mortality in men and women combined [24,25]. In the Zutphen Study [26] and the Brazilian "EPOCA" Research Project on Population Aging and Cancer [25], SRH was a significant predictor of cancer death in men. In contrast, in Epic II, the association between poor self-reported physical functional health and cancer mortality was relatively weak and was not significant after exclusion of deaths in the first 2 years [27].

Lower health ratings have been more strongly associated with mortality for adults with higher education and/or higher income relative to their lower SES counterparts [28], and a number of studies have reported that SRH is a much stronger predictor of mortality in Whites than Blacks [29] with differences in the distribution of scores associated with ethnic origin [30]. As we report here, SRH was significantly higher in Whites than in other ethnicities ($P<0.001$) in the WHI OS cohort; however, our subgroup analyses found that the association between SRH and all-cause mortality was not modified by race (1.81 among Whites and 1.87 among Blacks). In addition, the association between SRH and all-cause mortality was not modified by age (p-int = 0.13), or education (p-int = 0.53) in our study, demonstrating the value of considering SRH in diverse groups. In recent work, Black respondents' SRH did not differ, on average, from White respondents if health-care status, health behaviors and social status were controlled [31].

Studies have reported that SRH at one point in time has substantial predictive power for medical care utilization but not necessarily for utilization of preventive health tests [32]. We found that WHI participants with higher SRH were more likely to complete routine health screening exams (Pap test, mammogram) than those with poorer SRH. In the lower SRH groups, rates of ECG were higher and regular physical exams were slightly less frequent. The proportion of women having a current health care provider was similar across SRH levels. Prior history of health problems did not appear to be related to predictive differences among SRH groups, although women with poorer SRH reported having more chronic illnesses.

A few studies have shown a modest relationship of family history to SRH [33]; however, a 10-year longer increment of parental life-span was associated with an approximate 0.20 reduction in the adjusted odds ratio for offspring having fair, poor, or very poor SRH [34]. Parental life span might impact how one rates their health as well as affecting important cardiovascular risk factors [35]. In WHI, SRH was significantly lower in women who reported that their parents had shorter life-spans.

While most studies have reported that SRH predicts mortality, an understanding of the many factors that contribute to the perception of one's own health remains unclear. A succinct conceptualization of the issue states that "self-rated health is a deceptively simple variable that likely measures a great deal more than disease burden" [36]. One explanation is that self-rated health is a relatively inclusive measure encompassing multiple psychosocial factors [37]. Among those factors,

we found that SRH varies by age, race/ethnicity and education. The presence of serious medical conditions lowers average SRH [3], and controlling for medical conditions determined by clinical exam or physician diagnosis, reduced the predictive power of SRH in some [38], though not all studies [39-41].

When SRH and other indicators of well-being are measured concurrently, physical functioning is more strongly associated with SRH than mental health or social functioning [42,43]. Nevertheless, with depression SRH, is lower [44], and adjustment for depression attenuates the strength of the relationship with mortality [44,45]. Subjective well-being, also measured by a single item ("overall feeling of well-being during the past month"), has been associated with adverse clinical outcomes in much the same way as SRH [45]. The latter study argued that subjective well-being and SRH are modestly correlated but are not predicted by the same factors and do not predict outcomes to the same extent because subjective well-being assesses the interplay between perceived health and chronic life stresses. Self-efficacy and internal locus of control also predict mortality and are positively correlated with SRH. Self-efficacy significantly predicts mortality after controlling for SRH [46].

Other studies have examined change in SRH with disease incidence and mortality [47]. Some studies have suggested that SRH change is a stronger predictor of mortality than SRH at baseline [17] and others have not [48]. In WHI, worsening SRH doubled the risk of subsequent all-cause mortality compared with women whose scores did not change over the three-year period, and improved scores were associated with approximately 25% lowered risk of death compared with no change. This relationship was statistically significant in a fully adjusted model that included baseline SRH score as a possible confounder, suggesting that change in SRH and the cause of the change may be important to consider in future studies.

In our study, with higher white blood cell count SRH was lower (current clinical relevancy is not being asserted), similar to a finding that inflammatory activity, assessed by IL-6 and hs CRP levels, was associated with exhaustion and SRH in CHD women [49]. SRH may be sensitive to processes such as chronic inflammation implicated in CHD and cancer through multiple psychological and physiological pathways. This hypothesis suggests clinical consideration of poor self-reported physical health as an indicator of important underlying conditions that may have not yet been diagnosed and this indicator is not represented in traditional risk assessment.

Strengths of this WHI study include the population size and detailed history, race/ethnic and geographical diversity, low drop-out rates, verified medical event endpoints, long-term follow-up and non-fatal medical event. WHI is one of the few studies to look at cause-specific mortality and prospective changes in SRH. Most studies of SRH and mortality have involved relatively short follow-up (usually no more than five years). Longer follow-up periods, such as one study's 13-year period [47], can be helpful in determining the extent to which SRH is a measure that adds to mortality prediction by disease burden alone. Furthermore, important variables, including SRH itself, may change over the course of a long follow-up period. As follow-up duration lengthens, SRH stability cannot be assumed.

Limitations of the study are that it included older women only, so the results may not apply to men or younger adults, and the study was not specifically designed to directly assess psychosocial, personality or cognitive factors that may influence the self-assessment of health. The general effectiveness of SRH as a "predictor" is supported by the Norfolk-Epic Study 1 finding a relationship with all cause mortality in both young and old [42]; in Epic 2, the relationship was stronger in women than men [43]. Future research might consider how to improve the predictive power of SRH. For example, combining spouse-rated and self-rated health has been shown to predict mortality better than using SRH alone [50]. It is also important to continue to explore the association of mortality with interactions of SRH and clinical, biological and physiological states [51].

How do our findings relating healthy habits to SRH relate to improved health outcomes over time? Adopting a healthier lifestyle, with exercise, healthy eating, recommended bodyweight and smoking cessation, which would improve physical functioning, may be beneficial, even in old age as was supported in post-hoc analyses. How SRH changes is not well understood. The hypothesis that individuals with low SRH may benefit from targeted preventive interventions, such as management of known risk factors and increased uptake of positive lifestyle behaviors should be tested. How SRH scores might interact with traditional risk factor scores should be explored. Our study results and the literature review suggest that addressing self-efficacy and negative affect should occur in concert with working to change health habits, especially those related to physical functioning.

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