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

Robert Brunner*, Marcia L. Stefanick, Aaron K. Aragaki, Shirley A.A. Beresford, F. Allan Hubbell, Andrea LaCroix, Dorothy S. Lane, Stephen R. Rapp, Monika M. Safford, Nazmus Saquib, Nelson B. Watts and Nancy Fugate Woods

1University of Nevada School of Medicine, Reno, NV, USA
2Stanford Prevention Research Center, Stanford University School of Medicine, Stanford, CA, USA
3WHI Clinical Coordinating Center, Seattle, WA, USA
4University of Washington, Seattle, WA, USA
5University of California, Irvine, Chao Family Comprehensive Cancer Center, CA, USA
6Department of Psychiatry and Behavioral Medicine, Wake Forest School of Medicine, Winston-Salem, NC, USA
7Department of Preventive Medicine, Stony Brook, New York, USA
8University of Alabama, Birmingham, AL, USA
9Prevention Research Center, School of Medicine, Stanford University, Stanford, CA, USA
10Mercy Health Osteoporosis and Bone Health Services, Cincinnati OH, USA
11Biobehavioral Nursing, University of Washington, Seattle, WA, USA

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 93,675 postmenopausal women, aged 50 to 79 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 RAND36 general 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
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 Burnum’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 | P-Value |
|----------------------|-----------|------|-----------|-----------|---------|
|                      | N  | %   |  N  | %   |  N  | %   |  N  | %   | <0.001 |
| **Ethnicity**        |    |     |    |     |    |     |    |     |        |
| White                | 6106| 67.2| 23542| 79.3| 32871| 87.2| 15067| 90.9| <0.001 |
| 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/m²** |     |     |    |     |    |     |    |     | <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| 556  | 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** |     |     |    |     |    |     |    |     | <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 |
| 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 |
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 constructs (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 poorer SRH. Women with higher SRH completed more routine health care provider was similar and non-linear across SRH groups. Fair/poor SRH was associated with 13-15% lower rates of SRH responses than did White women. Current smoking and 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(1.43, 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.

| 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                               | 246  | 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                                    | 1728 | 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  |

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

1Test of association between self-rated health and baseline characteristic adjusted for age.
2Includes 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.
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-
### Table 3b: Multivariable adjusted Risk of Death Associated with RAND36 General Health Subscale at Baseline.

| Cause of Death by General Health | Min Adjust<sup>a</sup> | Full Adjust<sup>b</sup> |
|----------------------------------|------------------------|------------------------|
| 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, 1.00)        | 1.00 (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, 1.00)        | 1.00 (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, 1.00)        | 1.00 (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, 1.00)        | 1.00 (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, 1.00)        | 1.00 (1.00, 1.00) |

<sup>a</sup>Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups.

<sup>b</sup>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 3c: Adjudicated Risk of Death by Self-Rated Health.

| Adjudicated outcome by Self-Rated Health | Min Adjust<sup>c</sup> | Full Adjust<sup>d</sup> |
|----------------------------------------|------------------------|------------------------|
| Event                                  | AnnPer                 | HR                     | 95% CI                  | P-trend | 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, 1.00)        | 1.00 (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, 1.00)        | 1.00 (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 (1.00, 1.00)        | 1.00 (1.00, 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, 1.00)        | 1.00 (1.00, 1.00) |
Table 4: Multivariable adjusted Risk of Adjudicated Outcomes Associated with Self-Rated Health at Baseline.

| Cause of Death by Change in Self-Rated Health | Min Adjust<sup>14</sup> | Full Adjust<sup>15</sup> |
|---------------------------------------------|-------------------------|--------------------------|
|                                             | Event | AnnPer | HR | 95% CI | P-trend<sup>16</sup> | HR | 95% CI | P-trend |
| **Total Death**                             |       |        |    |        |                        |    |        |        |
| 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**                               |       |        |    |        |<sup>0.006</sup> |<sup><0.001</sup>|        |        |
| 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**                            |       |        |    |        |<sup><0.001</sup> |<sup><0.001</sup>|        |        |
| 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**                             |       |        |    |        |<sup><0.001</sup> |<sup><0.001</sup>|        |        |
| 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) |  |

<sup>14</sup>Adjusted for age (linear) and race/ethnicity. Baseline hazard functions were allowed to vary by 5-year age groups.
<sup>15</sup>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.
<sup>16</sup>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).

| Cause of Death by Change in General Health | Min Adjust<sup>17</sup> | Full Adjust<sup>18</sup> |
|-------------------------------------------|-------------------------|--------------------------|
|                                            | Event | AnnPer | HR | 95% CI | P-trend<sup>19</sup> | HR | 95% CI | P-trend |
| **Total Death**                            |       |        |    |        |                        |    |        |        |
| 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|        | 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**                              |       |        |    |        |<sup><0.001</sup> |<sup><0.001</sup>|        |        |
| 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**                           |       |        |    |        |<sup><0.001</sup> |<sup><0.001</sup>|        |        |
| 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 |        |  |
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 to 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 three-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 lengths, 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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