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Healthy Lifestyle and Risk of Heart Failure in the Women's Health Initiative Observational Study

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Abstract

Background—The impact of a healthy lifestyle on risk of heart failure (HF) is not well known.

Objective—To evaluate the effect of a combination of lifestyle factors on incident HF, and further investigate whether weighting each lifestyle factor has additional impact.

Methods—Participants were 84,537 post-menopausal women from the Women's Health Initiative Observational Study, free of self-reported HF at baseline. A healthy lifestyle score (HL-score) was created, where women received 1 point for each healthy criterion met: high-scoring Alternative Healthy Eating Index, physically active, healthy body mass index, and currently not smoking. A weighted score (wHL-score) was also created where each lifestyle factor was

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weighted according to its independent magnitude of effect on HF. Incident hospitalized HF was determined by trained adjudicators using standardized methodology.

Results—There were 1,826 HF cases over a mean follow-up of 11 years. HL-score was strongly associated with risk of HF (multivariable-adjusted HR [95% CI] = 0.49 [0.38,0.62], 0.36 [0.28,0.46], 0.24 [0.19,0.31], and 0.23 [0.17,0.30] for HL-score of 1,2,3,4 vs 0, respectively]. The HL-score and wHL-score were similarly associated with HF risk (HR [95% CI] = 0.46 [0.41,0.52] for HL-score and 0.48 [0.42,0.55] for wHL-score, comparing the highest tertile to the lowest). The HL-Score was also strongly associated with HF risk among women without antecedent coronary heart disease, diabetes, or hypertension.

Conclusions—An increasingly healthy lifestyle was associated with decreasing HF risk among post-menopausal women, even in the absence of antecedent coronary heart disease, hypertension, and diabetes. Weighting the lifestyle factors had minimal impact.

Keywords

heart failure; lifestyle; cardiovascular diseases; risk factors; primary prevention

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Heart failure (HF) is a major public health concern, characterized by a high prevalence, poor clinical outcomes, and significant health care costs (1). HF primary prevention through lifestyle approaches may be more effective and less costly than secondary or tertiary prevention efforts. A healthy lifestyle, often characterized by a combination of prudent diet, regular exercise, healthy weight, and not smoking, is related to a lower risk of atherosclerotic cardiovascular diseases, such as coronary heart disease (CHD) (2) and stroke (3). Few studies, however, have focused on a healthy lifestyle in relation to HF. Healthy lifestyle factors were individually and collectively associated with a lower risk of HF among white males in the Physician's Health Study I (4), and among men and women from a large and homogenous Finnish sample (5).

Post-menopausal women and African Americans experience a greater burden of HF (6-8), and they are predicted to make up a greater proportion of future HF cases in the United States (9,10). Therefore, examining the impact of a healthy lifestyle on HF risk in these groups is of particular interest. In addition, it has been proposed that the association of healthy lifestyle factors with HF risk may largely accounted for by the development of interim CHD (4,11), as well as interim hypertension and diabetes (11-13). However, we were particularly interested in whether an association between healthy lifestyle and HF risk would be present among women without development of any of these conditions prior to HF development. For example, HF in women is less associated with CHD as compared with men (14); thus, other mechanisms are of interest. Lastly, most prior studies investigating a combination of lifestyle factors weighted each lifestyle factor equally (2-5,15). This approach assumes that each lifestyle factor has the same magnitude of effect on the outcome, and this may lead to misclassification when combining lifestyle factors.

Accordingly, we examined whether a healthy lifestyle, as captured by a combination of high dietary quality, physical activity, healthy BMI, and not currently smoking, is associated with risk of HF in a diverse prospective cohort of post-menopausal women from the Women's

Health Initiative (WHI) Observational Study, and we further assessed the additional impact of weighting each lifestyle factor according to its independent magnitude of effect on HF. We further examined the association of healthy lifestyle with HF in women with versus without antecedent CHD, African American versus non-Hispanic White women, and among women without antecedent CHD, hypertension, or diabetes.

Methods

Study Sample

The WHI Observational Study recruited women from 40 U.S. clinical centers from 1993 to 1998. The WHI Observational Study comprised a sample of post-menopausal women (ages 50-79 at baseline) who were in overall good health and were either unwilling or ineligible to be WHI clinical trials participants (16-18). This study was approved by each center's Institutional Review Board, and the subjects provided informed consent. Women were excluded from the current analyses if they: reported a history of HF at baseline (n=897); were missing information on lifestyle factors (n=3,110); had energy intake < 600 or > 5000 kcal/day (n=3,571); or were underweight (BMI ≤ 18.5 kg/m2) at baseline (due to potential for preclinical disease; n=1,050). Those excluded were more likely ($p < 0.05$) to be non-white, from the South, divorced, separated or, widowed, to have a history of hypertension or CHD at baseline, and to have lower levels of education.

Measures

We considered four lifestyle variables: diet quality as measured by the Alternative Healthy Eating Index (AHEI), physical activity, body mass index (BMI), and smoking. Data used to generate the AHEI were derived from the semi-quantitative WHI-food frequency questionnaire (19). The AHEI is a composite numerical measure of dietary quality, based on foods and nutrients predictive of chronic disease risk (20,21) and consisting of 11 dietary components, with each scored based on a 10-point scale (0 points = least healthy; 10 points = most healthy) (12). Women also reported on their physical activity. For analyses, physical activity was categorized as inactive (e.g., no report of moderate or vigorous physical activity); somewhat active (i.e., less active than recommendations (22): < 150 minutes/week of moderate physical activity, or < 75 minutes/week of vigorous physical activity, or equivalent combination); and active (e.g., meeting physical activity recommendations (22): ≥ 150 minutes of moderate physical activity/week or ≥ 75 minutes of vigorous physical activity or an equivalent combination). Smoking status was categorized as a current, former, or never smoker. BMI was calculated from weight and height measures obtained at clinical examinations using a calibrated stadiometer, and categorized as normal weight ($18.5 \leq$ BMI <25 kg/m^2), overweight ($25 \leq$ BMI ≤ 30 kg/m^2), and obese (BMI > 30 kg/m^2).

At baseline, women reported on socio-demographic factors and medical history including CHD (includes cardiac arrest, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, angina, and myocardial infarction), diabetes, and hypertension. Race/ethnicity was self-reported as American Indian or Alaskan Native, Asian or Pacific Islander, black or African American, Hispanic/Latino, white (not of Hispanic origin), or other.

Incident hospitalized HF was ascertained yearly in WHI by medical record abstraction of self-report hospitalizations and classified by trained adjudicators using standardized methodology. Specifically, hospitalized HF requiring and/or occurring during hospitalization required physician diagnosis of new-onset or worsened congestive HF on the reported hospital admission and 1 or more of the following 4 criteria: HF diagnosed by a physician and receiving medical treatment for HF; symptoms plus documentation in the current medical record of a history of an imaging procedure showing impaired left ventricular systolic or diastolic function, pulmonary edema/congestion on chest x-ray on the current admission, dilated ventricle(s) or "poor" left ventricular or right ventricular function by echocardiography, radionuclide ventriculography, or other contrast ventriculography; or evidence of LV diastolic dysfunction. This method was found to have high (79%) agreement rate (kappa) comparing central adjudicated HF to local adjudication (23,24).

Statistical Analyses

To create a healthy lifestyles score (HL-score) for the present analyses, each lifestyle factor was dichotomized as 'healthy' versus 'unhealthy' as follows: high-scoring AHEI (quintiles 4 and 5) versus low-scoring AHEI (quintiles 1,2, 3), physically active versus somewhat active or inactive, normal BMI ($18.5 \leq \text{BMI} < 25$ kg/m^2) versus overweight or obese (BMI ≥ 25 kg/m^2), and not a current smoker versus current smoker. Women then received 1 point for every healthy criterion met, and points were summed to obtain a HL-score ranging from 0 (least healthy) to 4 (most healthy).

A weighted HL-score (wHL-score) also was created, where each dichotomous lifestyle factor was first weighted according to its independent magnitude of effect (e.g., beta coefficient adjusted for the other dichotomous lifestyle factors) on HF risk. Weighted points attained by each individual were summed to obtain a wHL-score, which ranged from 0 (least healthy) to 1.55 (most healthy). To compare the HL-scores with the wHL-scores, both were analyzed as tertiles (given that the scores can only take on a certain number of values [e.g. 0,1,2,3,or 4 for the HL-score], they could not be partitioned into quintiles).

We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Person-time was calculated from baseline-interview until development of HF, death, or date of last contact. The proportional hazards assumption, assessed with models including log(time)-by-covariate interaction terms, was not violated.

Analyses were initially adjusted for age and race/ethnicity, with further adjustment for education, marital status, U.S. region, and antecedent: CHD, hypertension, and diabetes ('antecedent' referring to occurrence at any point prior to censoring time, whether reported on at baseline or developed during follow-up). Additional analyses stratified on absence versus presence of antecedent CHD, African-American women versus non-Hispanic white women, as well as restricting analyses to the subgroup of women without antecedent CHD, hypertension, or diabetes.

Partial population attributable risk (PAR) calculations (25) estimated the proportion of HF that would hypothetically be prevented if all women were in the healthiest category of the

lifestyle factors or the HL-score. All Statistical analyses were conducted using SAS software version 9 (SAS Institute Inc., Cary, NC).

Results

The final analytic sample included 84,537 women, with a mean (SD) age of 63.5 (7.3) years at baseline. General baseline characteristics are presented in Table 1. Approximately 41% of participants had normal BMI, 44% were physically active, 94% were current non-smokers, and 40% had a high-scoring AHEI. Approximately 14% of women met all 4 of these healthy lifestyle criteria. There were 1,826 documented HF cases during a mean follow-up of 11 years.

After multivariable adjustment, each individual lifestyle factor was independently associated with risk of HF in an inverse and graded manner (Table 2), with the strongest associations observed for BMI and smoking. The percentage of partial PAR (95% CI) was highest for AHEI [27% (15%, 39%)], followed by BMI [20% (10%, 29%)], cigarette smoking [16% (10%, 23%)], and physical activity [12% (4%, 20%)].

A strong inverse and graded association was observed between the HL-score and HF risk (Table 3). According to PAR% calculations, 35% (28%,43%) of HF could theoretically be prevented if all women met all 4 healthy lifestyle criteria. When comparing the HL-score and the wHL-score, differences between the 2 were minimal (Figure 1). Comparing the highest versus lowest tertile, a multi-variable adjusted HR (95% CI) of 0.46 (0.41,0.52) was observed for the regular HL-score and 0.48 (0.42,0.55) for the wHL-score. Results were very similar when time-dependent lifestyle factors were used to create the HL-score and the wHL-score.

In stratified analyses, the HL-score was strongly related to HF risk in a graded manner in both women with and without antecedent CHD (Figure 2), and this was similarly observed among the subgroup of women without antecedent CHD, hypertension, and diabetes. (Figure 3). Associations of HL-score with HF risk were similar when comparing African Americans to non-Hispanic whites (Figure 4).

Discussion

In this large and diverse prospective study of post-menopausal women, an increasingly healthy lifestyle was associated with a progressively decreasing HF risk. Weighting each lifestyle factor according to its magnitude of effect on HF did not have a notable impact on the associations observed. Associations of healthy lifestyle with HF risk were also strong and graded among women without antecedent CHD, hypertension, or diabetes (Central Illustration), and similarly so among African Americans.

Smoking is currently well-known as a strong and independent risk factor for HF (26). BMI also has been shown to be strongly and independently related to HF incidence in women (11,27). Excess weight gain may increase risk of HF through increased blood pressure (28,29), insulin resistance (30,31), and elevated cholesterol levels (32), or through

mechanisms that involve inflammation (33,34), sleep apnea (35-37), or kidney disease (38-40).

Fewer studies focused on dietary pattern in relation to HF. The AHEI was recently shown to be strongly related to HF (41) and overall CVD risk (21), more so than other dietary indices (20,21). The AHEI-2010 explicitly emphasizes high intakes of whole grains, poly-unsaturated fatty acids, nuts, legumes, and low intakes of sugar-sweetened beverages, red and processed meats, and trans-fats.(12) High levels of physical activity also have been related to reduced risk of HF in previous studies and may act through beneficial effects on body weight, hypertension, diabetes, and CHD (42-45).

Given that certain lifestyle factors show stronger associations with risk of disease than others, simply adding the lifestyle factors when combining them may lead to misclassification due to heterogeneous people having the same HL-score. However, we found that the relative weighting of lifestyle factors did not have any impact on associations of healthy lifestyle with HF risk, suggesting that adopting an overall healthy lifestyle where these healthy lifestyle habits are integrated is optimal.

A large proportion of HF incidence is accounted for by antecedent CHD (46,47), and lifestyle factors are thought to increase risk of HF largely through development of CHD as an intermediate endpoint (4,11). In our analyses, however, the association between healthy lifestyle and HF risk was strong and graded, even among women without antecedent CHD. These findings are consistent with previous studies showing that smoking, BMI, and physical activity are strongly associated with HF risk independent of the presence or absence of CHD or other atherogenic risk factors for HF (11,13,26). Thus, healthy lifestyle factors may act on HF through other mechanisms. For example, obesity may impact HF risk through renal insufficiency (38-40). In addition, HF in the elderly, and particularly among elderly women, is more commonly characterized by impaired diastolic function but preserved left ventricular (LV) systolic function, and the vast majority of HF patients with preserved systolic function do not have a defined myocardial disease but rather a clinically significant impairment of diastolic function (47,48). Even in HF characterized by LV systolic dysfunction, one-third of cases are not defined by underlying CHD, but rather by non-ischemic causes (48). Similarly, the association of healthy lifestyle with risk of HF risk remained strong even after further exclusion of women with antecedent hypertension and diabetes. Finally, healthy lifestyle was strongly related to risk of HF among both African Americans and non-Hispanic whites.

Prior literature

Two prior studies examined a combination of lifestyle factors in relation to HF. Normal body weight, not smoking, regular exercise, moderate alcohol intake, and consumption of fruits, vegetables and breakfast cereals were individually and collectively associated with lower lifetime risk of HF among male physicians. Lifetime risk of HF was 21% and 10% in men with 0 versus ≥ 4 healthy lifestyle factors, respectively (4). Smoking, BMI, physical activity, and vegetable intake also were individually and collectively associated with risk of HF in both men and women from a large, homogenous Finnish sample (5), with an inverse association observed between number of healthy lifestyle factors and HF risk.

Strengths and Limitations

Strengths of this study include the large sample size, prospective design, and the racial, socioeconomic, and geographic diversity within WHI. Our investigation was the first, to our knowledge, to report on the association of healthy lifestyle with risk of HF among a diverse group of US women. In addition, we took into account the relative magnitude of impact of each lifestyle factor. Finally, a thorough follow-up of HF cases using comprehensive criteria and standardized methodology used in WHI ensures satisfactory case ascertainment (23).

Several limitations should also be noted. The ascertainment of HF was based on initial self-report, and this may have led to some HF cases being missed. Similarly, hospitalization was used to identify incident HF, and exclusion of outpatient diagnoses of HF may have underestimated mild or transient cases of HF.

Conclusions

Heart failure remains a costly disease, with approximately two-thirds of costs reported to come from hospitalizations (9). Despite improved medical and surgical management, mortality after onset of heart failure remains high (49,50). In parallel, the prevalence of healthy habits (with the exception of smoking abstinence) is generally low among middle-aged and older women in the United States (51). We observed that an overall healthy lifestyle was strongly protective against HF among post-menopausal women, even in the absence of antecedent CHD, hypertension, and diabetes. This suggests that a healthy lifestyle is beneficial for protection against HF over and above its benefits in lowering risk for these clinical intermediates. Evidence from randomized trials suggest that multi-component lifestyle interventions, where several healthy lifestyle habits are simultaneously promoted, are successful in increasing healthful habits and decreasing cardiovascular disease risk (52-55)—in some cases, even more so than clinical treatment (56). Therefore, prevention strategies that place a higher emphasis on the combination and integration of healthy lifestyle habits may be of most benefit.

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Abbreviations

AHEI	Alternative Healthy Eating Index
BMI	body mass index
CHD	coronary heart disease
HF	heart failure
HL-score	healthy lifestyle score

wHL-score	weighted healthy lifestyle score

Perspectives

Competency in Medical Knowledge

In the Women's Health Initiative Observational Study, a healthy lifestyle was associated with a substantially lower risk of developing heart failure, even among women without coronary disease, hypertension or diabetes.

Translational Outlook

Further research is required to determine whether a comprehensive lifestyle modification approach can be effectively implemented in routine clinical practice and at the population level, in order to reduce the incidence of heart failure in both men and women.

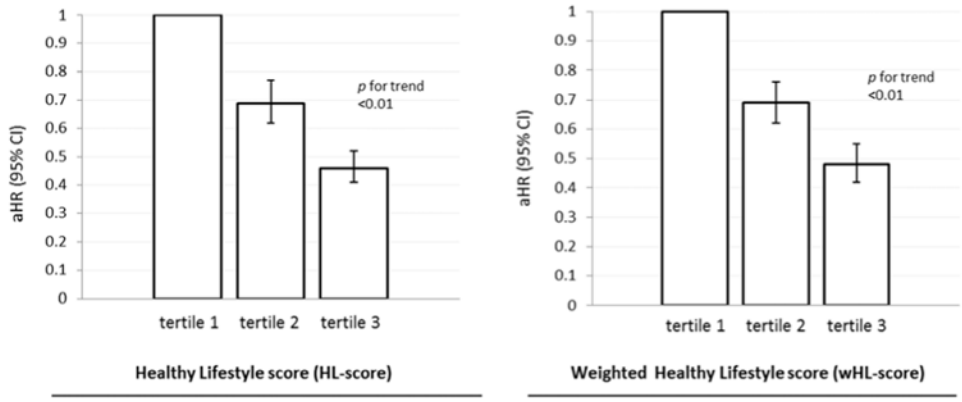


Figure 1. Comparison of Non-weighted and Weighted Healthy Lifestyle Score in relation to Heart Failure Risk

Risk of heart failure in relation to tertiles of the healthy lifestyle score and weighted healthy lifestyle score, Women's Health Initiative Observational Study.

HRs adjusted for age, race, marital status, US region, education, and antecedent: CHD, hypertension and diabetes.

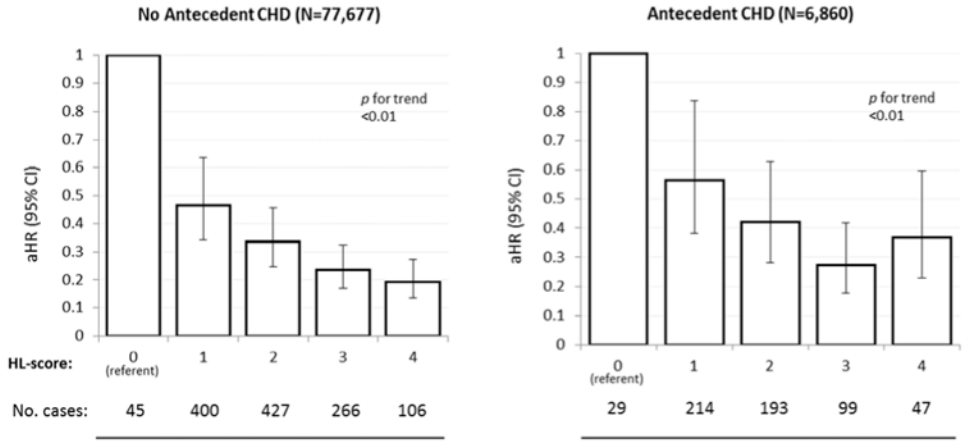


Figure 2. Healthy Lifestyle and Heart Failure Risk in Women Without vs. With Antecedent CHD

Risk of heart failure in relation to the healthy lifestyle score among women without versus with antecedent CHD, Women's Health Initiative Observational Study. Abbreviations: CHD, coronary heart disease; HL-score, healthy lifestyle score. HRs adjusted for age, race, marital status, US region, education, and antecedent hypertension or diabetes.

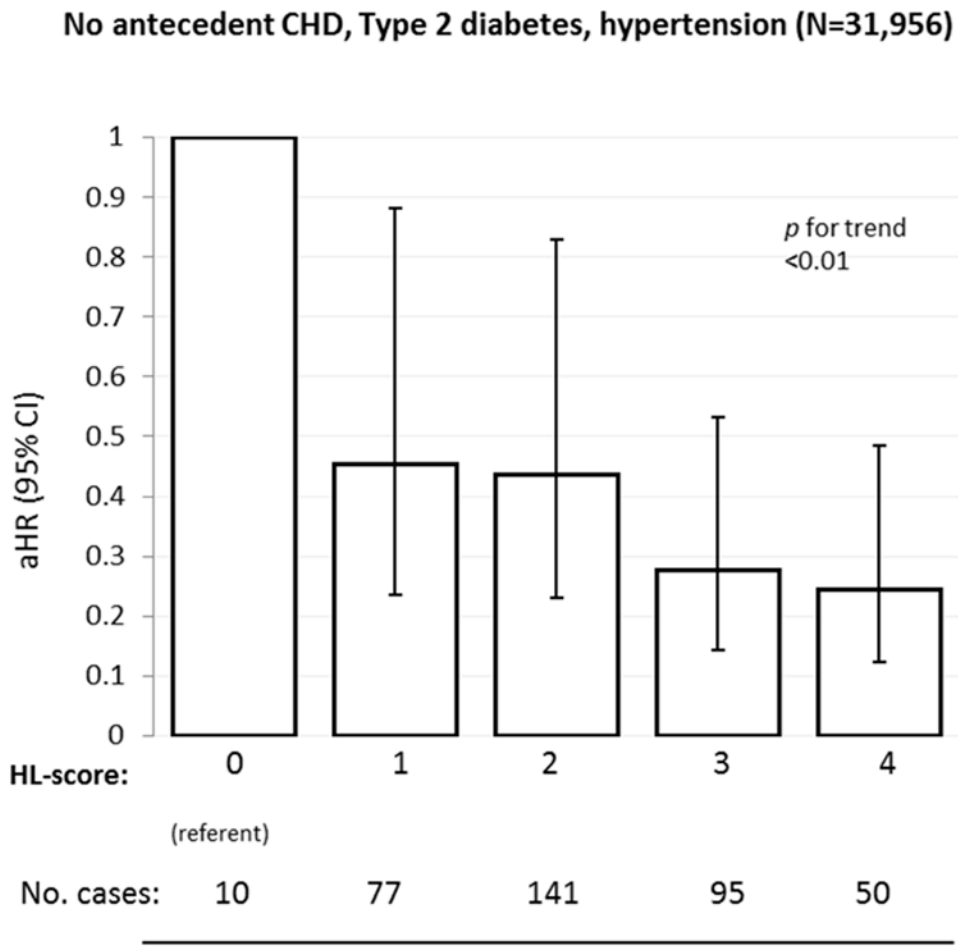


Figure 3. Healthy Lifestyle and Heart Failure Risk in Women Without Antecedent CHD, Hypertension, or Diabetes

Risk of heart failure in relation to the healthy lifestyle score among women without antecedent CHD, hypertension, and diabetes, Women's Health Initiative Observational Study.

Abbreviations: HL-score, healthy lifestyle score. HRs adjusted for age, race, marital status, US region, and education.

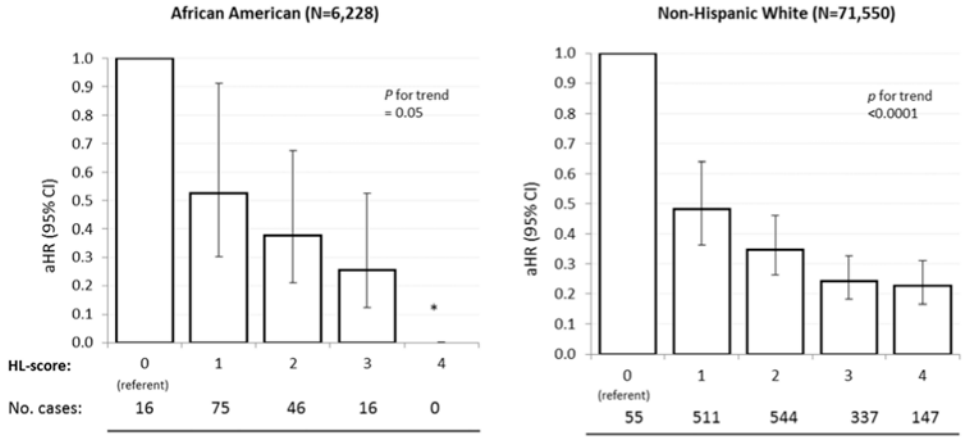
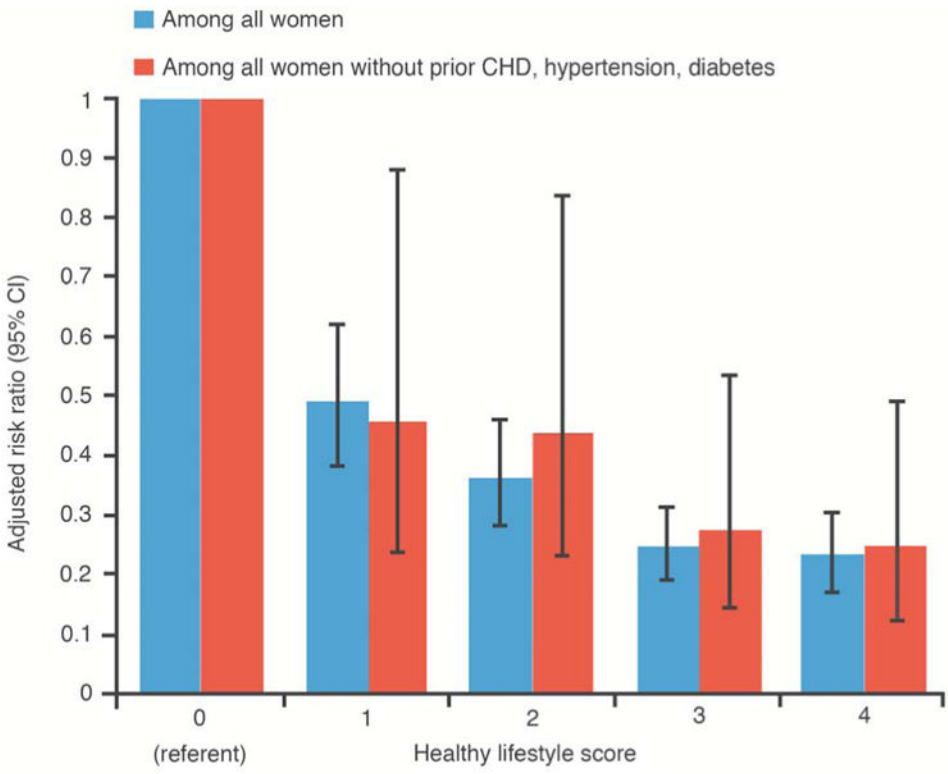


Figure 4. Healthy Lifestyle and Heart Failure Risk in African-Americans vs. Non-Hispanic Whites

Risk of heart failure in relation to the healthy lifestyle score among african americans versus non-hispanic whites, Women's Health Initiative Observational Study. Abbreviations: HL-score, healthy lifestyle score. HRs adjusted for age, race, marital status, US region, education, and antecedent hypertension and diabetes. *HR could not be calculated due to 0 heart failure cases in this category.



Central Illustration. Healthy Lifestyle and Risk of Heart Failure in the Women's Health Initiative

An overall healthy lifestyle is strongly associated with lower risk of heart failure among post-menopausal, even in the absence of coronary heart disease (CHD), hypertension, or diabetes.

Table 1

Baseline Characteristics According to the Healthy Lifestyle Score, Women's Health Initiative Observational Study

	Healthy lifestyle score				
	0	**1**	**2**	**3**	**4**
	(n =1,529)	**(n =19,389)**	**(n =27,366)**	**(n =24,271)**	**(n =11,982)**
Age in years, mean (SD)	60.5 (6.9)	63.2(7.3)	63.7 (7.3)	63.8 (7.3)	63.6 (7.4)
African American, %	18.8	12.5	8.0	4.5	2.0
Hispanic/Latino, %	5.1	5.1	3.9	2.6	1.6
Non-Hispanic white, %	73.2	79.1	84.1	88.2	90.8
Less than High school, %	10.1	8.1	5.1	2.7	1.1
Never married, %	5.6	4.7	4.7	4.5	4.3
Divorced/separated, %	27.7	17.3	15.3	14.2	13.6
history of diabetes, %	6.5	6.6	4.2	2.5	1.1
History of hypertension, %	37.3	43.6	35.4	27.9	19.9
History of CHD*, %	7.8	6.8	5.7	4.7	3.6
BMI (kg/m2), mean (SD)	30.8 (5.5)	31.3 (6.0)	28.1 (5.4)	25.5 (4.5)	22.4 (1.6)
AHEI score, mean (SD)	45.1 (7.8)	47.2 (7.5)	53.1 (9.4)	60.2 (9.7)	67.4 (6.4)

abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index; CHD, coronary heart disease

*Self-reported CHD includes cardiac arrest, CABG, PTCA, angina, and MI

Categories of a given variable (e.g. race) may not necessarily add up to 100%, given that not all categories were included

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Table 2

Risk of Heart Failure in Relation to Individual Lifestyle Factors, Women's Health Initiative Observational Study

	No. of cases	Person-years	Crude Incidence rate/1000 person-years	Model 1* HR (95% CI)	*P* value for trend‖	Model 2† HR (95% CI)	*P* value for trend‡
AHEI							
Quintile 1	499	178,032	2.80	Referent		Referent	
Quintile 2	411	183,884	2.24	0.83 (0.73,0.95)		0.85 (0.74,0.97)	
Quintile 3	350	188,254	1.86	0.76 (0.66,0.87)	<0.001	0.81 (0.70,0.93)	0.001
Quintile 4	321	191,496	1.68	0.72 (0.62,0.83)		0.76 (0.65,0.88)	
Quintile 5	245	194,954	1.26	0.60 (0.51,0.70)		0.61 (0.52,0.73)	
Physical Activity							
Inactive	386	117,311	3.29	Referent		Referent	
Somewhat active	614	285,095	2.15	0.77 (0.67,0.87)	0.008	0.77 (0.67,0.87)	0.06
Active	826	534,214	1.55	0.66 (0.58,0.75)		0.69 (0.61,0.79)	
BMI							
BMI ≥ 30 kg/m^2	752	223,128	3.37	Referent		Referent	
25 ≤ BMI ≤ 30 kg/m^2	557	322,941	1.72	0.50 (0.45,0.56)	0.008	0.56 (0.50,0.63)	0.1
18.5 ≤ BMI < 25 kg/m^2	517	390,552	1.32	0.43 (0.38,0.48)		0.51 (0.45,0.57)	
Smoking							
Current smoker	174	52,182	3.33	Referent		Referent	
Past smoker	820	407,776	2.01	0.52 (0.44,0.62)	<0.001	0.56 (0.47,0.66)	<0.001
Never smoker	832	476,663	1.75	0.42 (0.35,0.49)		0.46 (0.39,0.55)	

abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index

*Model 1 adjusted for age, race/ethnicity, and all other healthy lifestyle factors

†Model 2 adjusted for model 1 covariates, marital status, education, U.S. region, and antecedent: coronary heart disease, treated diabetes, and hypertension

‡test for linear trend

Table 3

Risk of Heart Failure in Relation to the Healthy Lifestyle Score, Women's Health Initiative Observational Study

Healthy lifestyle score	No. of cases	Person-years	Crude Incidence rate/1000 person-years	Age and race-adjusted HR (95% CI)	Multivariable-adjusted* HR (95% CI)	*P* value for trend
0	74	15,099	4.90	Referent	Referent	
1	614	204,287	3.01	0.45 (0.35,0.57)	0.49 (0.38,0.62)	
2	620	300,462	2.06	0.30 (0.24,0.38)	0.36 (0.28,0.46)	< 0.001
3	365	276,654	1.32	0.19 (0.15,0.25)	0.24 (0.19,0.31)	
4	153	140,121	1.09	0.17 (0.13,0.22)	0.23 (0.17,0.30)	

*Adjusted for age, race/ethnicity, marital status, education, U.S. region, and antecedent: coronary heart disease, treated diabetes, and hypertension