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# Healthy Lifestyle and Decreasing Risk of Heart Failure in Women

## 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.

**OBJECTIVES** The objectives of this study were to evaluate the effect of a combination of lifestyle factors on incident HF and to further investigate whether weighting each lifestyle factor has additional impact.

**METHODS** Participants were 84,537 post-menopausal women from the WHI (Women's Health Initiative) observational study, free of self-reported HF at baseline. A healthy lifestyle score (HL score) was created wherein 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 in which each lifestyle factor was weighted according to its independent magnitude of effect on HF. The incidence of 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 hazard ratio [HR] [95% confidence interval (CI)] 0.49 [95% CI: 0.38 to 0.62], 0.36 [95% CI: 0.28 to 0.46], 0.24 [95% CI: 0.19 to 0.31], and 0.23 [95% CI: 0.17 to 0.30] for HL score of 1, 2, 3, and 4 vs. 0, respectively). The HL score and wHL score were similarly associated with HF risk (HR: 0.46 [95% CI: 0.41 to 0.52] for HL score; HR: 0.48 [95% CI: 0.42 to 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. (J Am Coll Cardiol 2014;64:1777–85) © 2014 by the American College of Cardiology Foundation.

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**ABBREVIATIONS AND ACRONYMS**

**AHEI** = Alternative Healthy Eating Index

**BMI** = body mass index

**CHD** = coronary heart disease

**CI** = confidence interval

**HF** = heart failure

**HL score** = healthy lifestyle score

**HR** = hazard ratio

**PAR** = population attributable risk

**wHL score** = weighted healthy lifestyle score

Heart failure (HF) is a major public health concern, characterized by a high prevalence, poor clinical outcomes, and significant healthcare 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).

SEE PAGE 1786

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, examination of 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 be 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 before HF development. For example, HF in women is less associated with CHD than in 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 lifestyle factors are combined.

Accordingly, we examined whether a healthy lifestyle, as captured by a combination of high dietary quality, physical activity, healthy body mass index (BMI), and not currently smoking, is associated with risk of HF in a diverse prospective cohort of post-menopausal women from the WHI (Women's Health Initiative) 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, in 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 to 79 years at baseline) who were in overall good health and were either unwilling or ineligible to be WHI clinical trial 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 >5,000 kcal/day (n = 3,571); or were underweight (BMI ≤ 18.5 kg/m$^2$) at baseline (because of the potential for preclinical disease; n = 1,050). Those excluded were more likely ($p < 0.05$) to be nonwhite, from the South, and divorced, separated, or widowed; to have a history of hypertension or CHD at baseline; and to have lower levels of education.

**MEASURES.** We considered 4 lifestyle variables: Diet quality as measured by the Alternative Healthy Eating Index (AHEI), physical activity, BMI, and smoking. Data used to generate the AHEI were derived from the semiquantitative 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 min/week of moderate physical activity, or <75 min/week of vigorous physical activity, or equivalent combination); and active (e.g., meeting physical activity recommendations [22]: ≥150 min of moderate physical activity per week or ≥75 min 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 with a calibrated stadiometer and categorized as normal weight (18.5 ≤ BMI <25 kg/m$^2$), overweight (25 ≤ BMI ≤30 kg/m$^2$), and obese (BMI >30 kg/m$^2$).

At baseline, women reported on sociodemographic factors and medical history, including CHD (included 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-reported hospitalizations and classified by trained adjudicators using standardized methodology. Specifically, HF that required and/or occurred 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 that showed impaired left ventricular systolic or diastolic function, pulmonary edema/congestion on chest radiograph 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 left ventricular diastolic dysfunction. This method was found to have a 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 ($18.5 \leq$ BMI $<25$ kg/m$^2$) versus overweight or obese (BMI $\geq 25$ 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 an HL score that ranged from 0 (least healthy) to 4 (most healthy).

A weighted HL score (wHL score) was also created, in which 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 could 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 that included 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 before the time of censoring, whether reported at baseline or developed during follow-up). Additional analyses were stratified on absence versus presence of antecedent CHD and African-American women versus non-Hispanic white women, as well as with restriction of 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 with SAS software version 9 (SAS Institute Inc., Cary, North Carolina).

## RESULTS

The final analytic sample included 84,537 women, with a mean age of 63.5 ± 7.3 years at baseline. General baseline characteristics are presented in Table 1. Approximately 41% of participants had

**TABLE 1 Baseline Characteristics According to the Healthy Lifestyle Score, the WHI Observational Study**

| | Healthy Lifestyle Score | | | | |
|---|---|---|---|---|---|
| | 0 (n = 1,529) | 1 (n = 19,389) | 2 (n = 27,366) | 3 (n = 24,271) | 4 (n = 11,982) |
| Age, yrs | 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/m$^2$ | 30.8 ± 5.5 | 31.3 ± 6.0 | 28.1 ± 5.4 | 25.5 ± 4.5 | 22.4 ± 1.6 |
| AHEI score | 45.1 ± 7.8 | 47.2 ± 7.5 | 53.1 ± 9.4 | 60.2 ± 9.7 | 67.4 ± 6.4 |

Values are mean ± SD or %. Categories of a given variable (e.g., race) may not necessarily add up to 100%, given that not all categories were included. *Self-reported CHD includes cardiac arrest, coronary artery bypass grafting, percutaneous transluminal coronary angiography, angina, and myocardial infarction.

AHEI = Alternative Healthy Eating Index; BMI = body mass index; CHD = coronary heart disease.

**TABLE 2 Risk of Heart Failure in Relation to Individual Lifestyle Factors, The WHI Observational Study**

| | No. of Cases | Person-Years | Crude Incidence Rate per 1,000 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) | |

*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, diabetes, and hypertension. ‡Test for linear trend.

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

normal BMI, 44% were physically active, 94% were current nonsmokers, 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 was highest for AHEI (27%; 95% CI: 15% to 39%), followed by BMI (20%; 95% CI: 10% to 29%), cigarette smoking (16%; 95% CI: 10% to 23%), and physical activity (12%; 95% CI: 4% to 20%).

A strong inverse and graded association was observed between the HL score and HF risk (Table 3). According to PAR% calculations, 35% (95% CI: 28% to 43%) of HF could theoretically be prevented if all women met all 4 healthy lifestyle criteria. When we compared the HL score and the wHL score, differences between the 2 were minimal (Figure 1). Comparing the highest versus lowest tertile, a multivariable adjusted HR of 0.46 (95% CI: 0.41 to 0.52) was observed for the regular HL score and 0.48 (95% CI: 0.42 to 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

**TABLE 3 Risk of Heart Failure in Relation to the Healthy Lifestyle Score, The WHI Observational Study**

| Healthy Lifestyle Score | No. of Cases | Person-Years | Crude Incidence Rate/ 1,000 Person-Years | Age- and Race-Adjusted HR (95% CI) | Multivariable-Adjusted* HR (95% CI) |
|---|---|---|---|---|---|
| 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) |
| 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) |

p value for trend <0.001. *Adjusted for age, race/ethnicity, marital status, education, U.S. region, and antecedent coronary heart disease, treated diabetes, and hypertension.

Abbreviations as in Table 2.

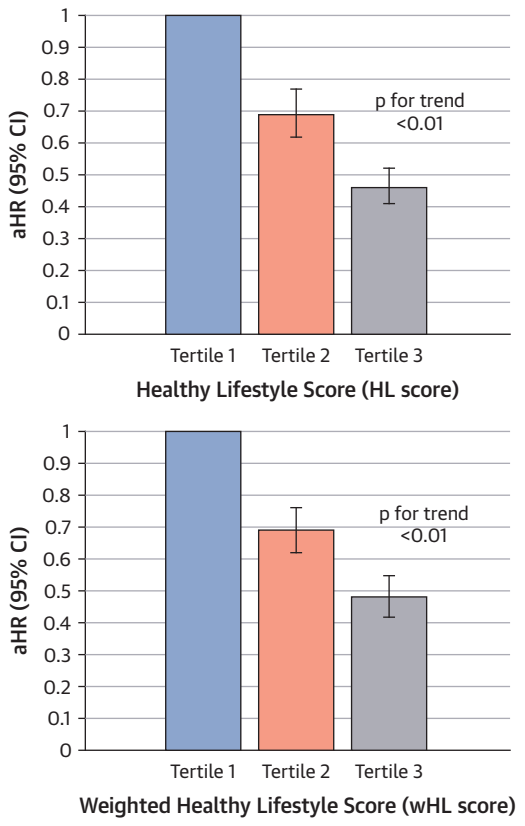



**FIGURE 1 Comparison of Nonweighted and Weighted Healthy Lifestyle Score in Relation to Heart Failure Risk**

Risk of heart failure in relation to tertiles of the healthy lifestyle score (HL score) and weighted healthy lifestyle score (wHL score), the WHI observational study. Hazard ratios were adjusted for age, race, marital status, U.S. region, education, and antecedent: coronary heart disease, hypertension and diabetes. aHR = adjusted hazard ratio; CI = confidence interval.

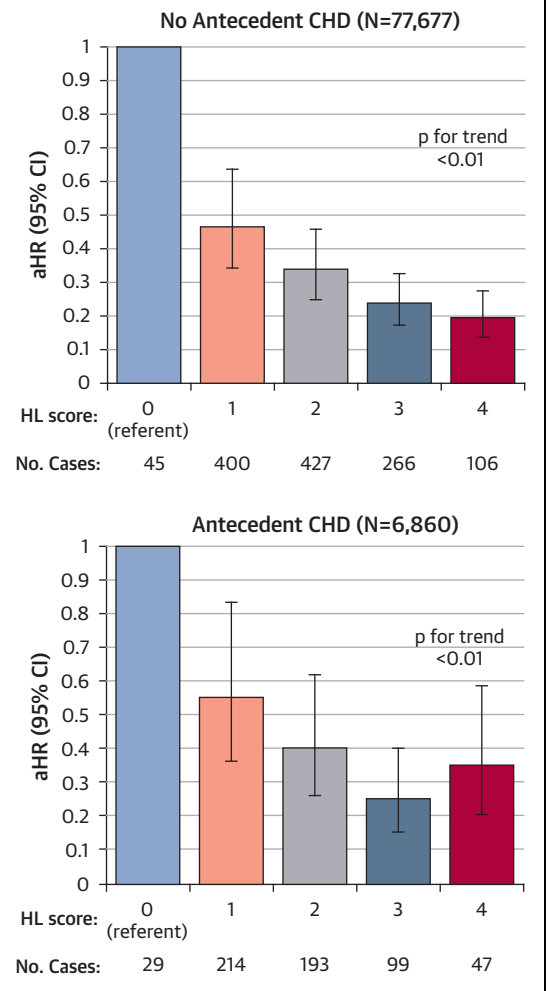



**FIGURE 2 Healthy Lifestyle and Heart Failure Risk in Women Without Versus With Antecedent CHD**

Risk of heart failure in relation to the healthy lifestyle score among women without versus with antecedent CHD, the WHI observational study. Hazard ratios were adjusted for age, race, marital status, U.S. region, education, and antecedent hypertension or diabetes. Abbreviations as in Figure 1.

risk were similar when we compared African Americans and non-Hispanic whites (Figure 4).

## DISCUSSION

In this large and diverse prospective study of postmenopausal 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 have focused on dietary pattern in relation to HF. The AHEI recently was shown to be

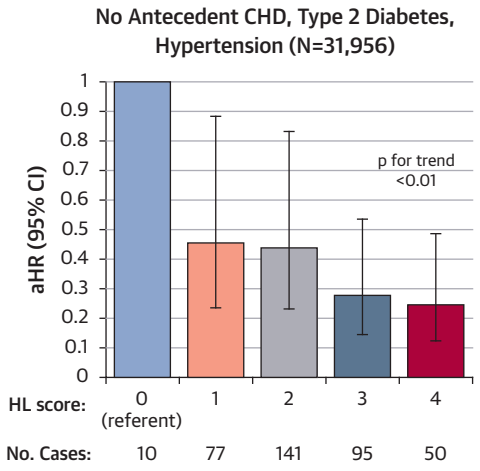



**FIGURE 3 Healthy Lifestyle and Heart Failure Risk in Women Without Antecedent CHD, Hypertension, or Diabetes**

Risk of heart failure in relation to the healthy lifestyle score among women without antecedent CHD, hypertension, and diabetes, the WHI observational study. Hazard ratios were adjusted for age, race, marital status, U.S. region, and education. Abbreviations as in Figure 1.

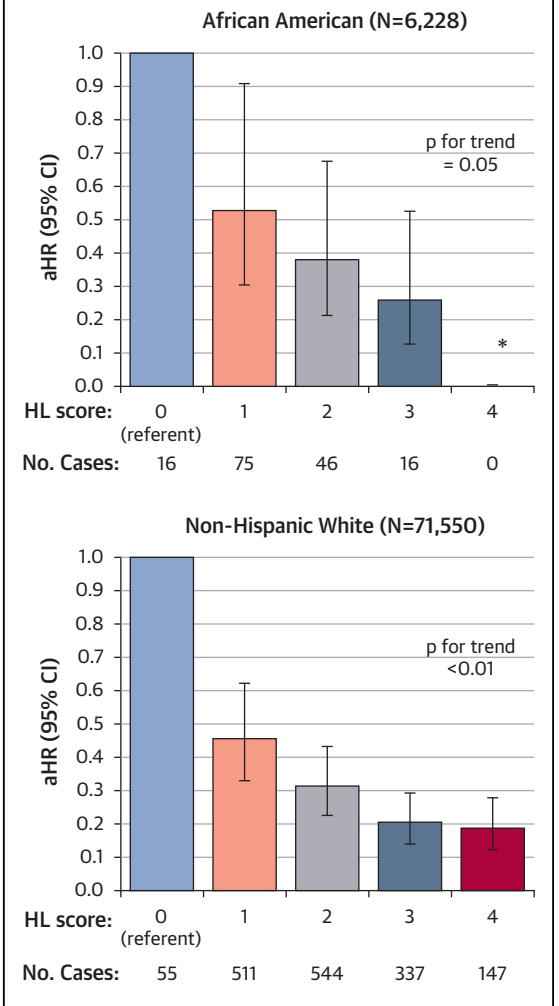



**FIGURE 4 Healthy Lifestyle and Heart Failure Risk in African Americans Versus Non-Hispanic Whites**

Risk of heart failure in relation to the HL score among African Americans versus non-Hispanic whites, the WHI observational study. Hazard ratios were adjusted for age, race, marital status, U.S. region, education, and antecedent hypertension and diabetes. *HR could not be calculated due to 0 heart failure cases in this category. Abbreviations as in Figure 1.

strongly related to HF (41) and overall cardiovascular disease risk (21), more so than other dietary indexes (20,21). The AHEI-2010 explicitly emphasizes high intakes of whole grains, polyunsaturated fatty acids, nuts, and 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, which suggests that the adoption of an overall healthy lifestyle in which 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 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 left ventricular systolic dysfunction, one-third of cases are not defined by underlying CHD but rather by nonischemic 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, a healthy lifestyle was strongly related to risk of HF among both African Americans and non-Hispanic whites.

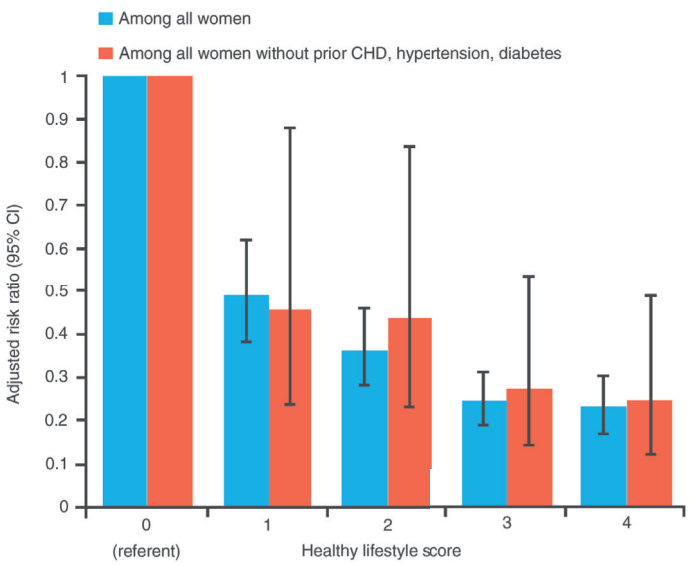
**PRIOR LITERATURE.** Two prior studies examined a combination of lifestyle factors in relation to HF. Normal body weight, not smoking, regular exercise, moderate alcohol intake, and consumption of fruits, vegetables, and breakfast cereals were individually and collectively associated with lower lifetime 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 the WHI. Our investigation was the first, to the best of our knowledge, to report on the association of healthy lifestyle with risk of HF among a diverse group of U.S. 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

HF 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 HF 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 suggests that multicomponent lifestyle interventions, in which several healthy lifestyle habits are promoted simultaneously, 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.




**CENTRAL ILLUSTRATION Healthy Lifestyle and Risk of Heart Failure in the WHI Observational Study**

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

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## 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 implemented effectively in routine clinical practice and at the population level in order to reduce the incidence of heart failure in both men and women.

## REFERENCES

**1.** Krum H, Abraham WT. Heart failure. Lancet 2009;373:941–55.

**2.** Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. N Engl J Med 2000;343:16–22.

**3.** Chiuve SE, Rexrode KM, Spiegelman D, Logroscino G, Manson JE, Rimm EB. Primary prevention of stroke by healthy lifestyle. Circulation 2008;118:947–54.

**4.** Djoussé L, Driver JA, Gaziano JM. Relation between modifiable lifestyle factors and lifetime risk of heart failure. JAMA 2009;302:394–400.

**5.** Wang Y, Tuomilehto J, Jousilahti P, et al. Lifestyle factors in relation to heart failure among Finnish men and women. Circ Heart Fail 2011;4:607–12.

**6.** Alexander M, Grumbach K, Remy L, Rowell R, Massie BM. Congestive heart failure hospitalizations and survival in California: patterns according to race/ethnicity. Am Heart J 1999;137:919–27.

**7.** Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the Multi-Ethnic Study of Atherosclerosis. Arch Intern Med 2008;168:2138–45.

**8.** Eaton CB, Abdulbaki AM, Margolis KL, et al. Racial and ethnic differences in incident hospitalized heart failure in postmenopausal women: the Women's Health Initiative. Circulation 2012;126:688–96.

**9.** Lloyd-Jones D, Adams RJ, Brown TM, et al. Executive summary: heart disease and stroke statistics–2010 update: a report from the American Heart Association [published correction appears in Circulation 2010;121:e259]. Circulation 2010;121:948–54.

**10.** Yancy CW. Heart failure in African Americans. Am J Cardiol 2005;96:3i–12i.

**11.** Kenchaiah S, Sesso HD, Gaziano JM. Body mass index and vigorous physical activity and the risk of heart failure among men. Circulation 2009;119:44–52.

**12.** Chiuve SE, Fung TT, Rimm EB, et al. Alternative dietary indices both strongly predict risk of chronic disease. J Nutr 2012;142:1009–18.

**13.** Horwich TB, Fonarow GC. Glucose, obesity, metabolic syndrome, and diabetes relevance to incidence of heart failure. J Am Coll Cardiol 2010;55:283–93.

**14.** Nieminen MS, Harjola VP, Hochadel M, et al. Gender related differences in patients presenting with acute heart failure: results from EuroHeart Failure Survey II. Eur J Heart Fail 2008;10:140–8.

**15.** van Dam RM, Li T, Spiegelman D, Franco OH, Hu FB. Combined impact of lifestyle factors on mortality: prospective cohort study in US women. BMJ 2008;337:a1440.

**16.** The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. Control Clin Trials 1998;19:61–109.

**17.** Hays J, Hunt JR, Hubbell FA, et al. The Women's Health Initiative recruitment methods and results. Ann Epidemiol 2003;13 Suppl:S18–77.

**18.** Langer RD, White E, Lewis CE, Kotchen JM, Hendrix SL, Trevisan M. The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures. Ann Epidemiol 2003;13 Suppl:S107–21.

**19.** Patterson RE, Kristal AR, Tinker LF, Carter RA, Bolton MP, Agurs-Collins T. Measurement characteristics of the Women's Health Initiative food frequency questionnaire. Ann Epidemiol 1999;9:178–87.

**20.** McCullough ML, Feskanich D, Stampfer MJ, et al. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. Am J Clin Nutr 2002;76:1261–71.

**21.** McCullough ML, Willett WC. Evaluating adherence to recommended diets in adults: the Alternate Healthy Eating Index. Public Health Nutr 2006;9:152–7.

**22.** U.S. Department of Health & Human Services. 2008 Physical Activity Guidelines for Americans. Washington, DC: U.S. Department of Health & Human Services, 2008. ODPHP publication No. U0036.

**23.** Curb JD, McTiernan A, Heckbert SR, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol 2003;13:S122–8.

**24.** Heckbert SR, Kooperberg C, Safford MM, et al. Comparison of self-report, hospital discharge codes, and adjudication of cardiovascular events in the Women's Health Initiative. Am J Epidemiol 2004;160:1152–8.

**25.** Wand H, Spiegelman D, Law M, Jalaludin B, Kaldor J, Maher L. Estimating population attributable risk for hepatitis C seroconversion in injecting drug users in Australia: implications for prevention policy and planning. Addiction 2009; 104:2049–56.

**26.** He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. Arch Intern Med 2001;161:996–1002.

**27.** Kenchaiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. N Engl J Med 2002; 347:305–13.

**28.** Stamler R, Stamler J, Riedlinger WF, Algera G, Roberts RH. Weight and blood pressure: findings in hypertension screening of 1 million Americans. JAMA 1978;240:1607–10.

**29.** Stamler J. Epidemiologic findings on body mass and blood pressure in adults. Ann Epidemiol 1991;1:347–62.

**30.** Ferrannini E, Natali A, Bell P, Cavallo-Perin P, Lalic N, Mingrone G. Insulin resistance and hypersecretion in obesity: European Group for the Study of Insulin Resistance (EGIR). J Clin Invest 1997;100:1166–73.

**31.** Abbasi F, Brown BW Jr., Lamendola C, McLaughlin T, Reaven GM. Relationship between obesity, insulin resistance, and coronary heart disease risk. J Am Coll Cardiol 2002;40:937–43.

**32.** National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report (published correction appears in Obes Res 1998;6:464). Obes Res 1998;6 Suppl 2: 51S–209S.

**33.** Bahrami H, Bluemke DA, Kronmal R, et al. Novel metabolic risk factors for incident heart failure and their relationship with obesity: the MESA (Multi-Ethnic Study of Atherosclerosis) study. J Am Coll Cardiol 2008;51:1775–83.

**34.** Vasan RS, Sullivan LM, Roubenoff R, et al. Inflammatory markers and risk of heart failure in elderly subjects without prior myocardial infarction: the Framingham Heart Study. Circulation 2003;107:1486–91.

**35.** Vgontzas AN, Tan TL, Bixler EO, Martin LF, Shubert D, Kales A. Sleep apnea and sleep disruption in obese patients. Arch Intern Med 1994;154:1705–11.

**36.** Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.

**37.** Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001;163:19–25.

**38.** Chae CU, Albert CM, Glynn RJ, Guralnik JM, Curhan GC. Mild renal insufficiency and risk of congestive heart failure in men and women > or =70 years of age. Am J Cardiol 2003;92:682–6.

**39.** Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D. Predictors of new-onset kidney disease in a community-based population. JAMA 2004;291:844–50.

**40.** Kenchaiah S, Gaziano JM, Vasan RS. Impact of obesity on the risk of heart failure and survival after the onset of heart failure. Med Clin North Am 2004;88:1273–94.

**41.** Belin RJ, Greenland P, Allison M, et al. Diet quality and the risk of cardiovascular disease: the Women's Health Initiative (WHI). Am J Clin Nutr 2011;94:49–57.

**42.** Hu FB, Sigal RJ, Rich-Edwards JW, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. JAMA 1999;282:1433–9.

**43.** Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341: 650–8.

**44.** Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE–a randomized controlled study. Arch Intern Med 2004;164:31–9.

**45.** Weinstein AR, Sesso HD, Lee IM, et al. Relationship of physical activity vs body mass index with type 2 diabetes in women. JAMA 2004; 292:1188–94.

**46.** Gheorghiade M, Bonow RO. Chronic heart failure in the United States: a manifestation of coronary artery disease. Circulation 1998;97: 282–9.

**47.** Gottdiener JS, Arnold AM, Aurigemma GP, et al. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. J Am Coll Cardiol 2000;35:1628–37.

**48.** Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. J Am Coll Cardiol 2005;46:e1–82.

**49.** Gillum RF. Epidemiology of heart failure in the United States. Am Heart J 1993;126:1042–7.

**50.** Schocken DD, Benjamin EJ, Fonarow GC, et al. Prevention of heart failure: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Clinical Cardiology, Cardiovascular Nursing, and High Blood Pressure Research; Quality of Care and Outcomes Research Interdisciplinary Working Group; and Functional Genomics and Translational Biology Interdisciplinary Working Group. Circulation 2008;117: 2544–65.

**51.** Schoenborn CA, Adams PE. Health behaviors of adults: United States, 2005-2007. Vital Health Stat 10 2010;245:1–132.

**52.** Hayashi T, Farrell MA, Chaput LA, Rocha DA, Hernandez M. Lifestyle intervention, behavioral changes, and improvement in cardiovascular risk profiles in the California WISEWOMAN project. J Womens Health (Larchmt) 2010;19: 1129–38.

**53.** Keyserling TC, Samuel Hodge CD, Jilcott SB, et al. Randomized trial of a clinic-based, community-supported, lifestyle intervention to improve physical activity and diet: the North Carolina enhanced WISEWOMAN project. Prev Med 2008;46:499–510.

**54.** Khare MM, Carpenter RA, Huber R, et al. Lifestyle intervention and cardiovascular risk reduction in the Illinois WISEWOMAN Program. J Womens Health (Larchmt) 2012;21:294–301.

**55.** Stoddard AM, Palombo R, Troped PJ, Sorensen G, Will JC. Cardiovascular disease risk reduction: the Massachusetts WISEWOMAN project. J Womens Health (Larchmt) 2004;13: 539–46.

**56.** Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403.

**KEY WORDS** cardiovascular diseases, heart failure, lifestyle, primary prevention, risk factors