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Comparison of Lifestyle Based to Traditional CVD Prediction in a Multiethnic Cohort of Non-Smoking Women

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Abstract

Background—Healthy levels of lifestyle factors can reduce risk of CVD. However, except for smoking status, often considered a traditional risk factor, their effect on cardiovascular risk prediction is unclear.

Methods and Results—We used a case-cohort design of post-menopausal non-smokers in the multiethnic Women's Health Initiative Observational Study (1587 cases and 1808 sub-cohort participants) with a median follow-up of 10 years in non-cases. Compared to non-smokers with no other healthy lifestyle factors (healthy diet, recreational physical activity, moderate alcohol use, and low adiposity), the risk of cardiovascular disease was lower for each additional factor (hazard ratio for trend 0.82; 95% CI 0.76, 0.89), with a 45% reduction in risk with all factors (95% CI 0.36, 0.84). When lifestyle factors were added to traditional risk factor models (variables from the Pooled Cohort and Reynolds risk scores), only recreational physical activity remained independently associated with risk of cardiovascular disease. The addition of detailed lifestyle measures to traditional models showed a change in the integrated discrimination improvement and continuous net reclassification improvement ($p < 0.01$ for both), but had little impact on more clinically relevant risk stratification measures.

Conclusions—While lifestyle factors have important effects on CVD risk factors and subsequent risk, their addition to established CVD risk models does not result in clear improvement in overall prediction.

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Keywords

lifestyle; risk prediction; primary prevention; cardiovascular diseases

Introduction

Healthy lifestyle factors related to diet, physical activity, smoking, and adiposity have been shown to be associated with reduced rates of cardiovascular disease (CVD), with an 83% lower risk of CVD for those with multiple healthy factors.[1] These lifestyle factors are also part of the American Heart Association's 2020 goals for cardiovascular disease reduction, which include improving rates of nonsmoking, having a body mass index (BMI) of 18.5 to <25 kg/m2, physical activity at goal levels, and pursuit of a diet consistent with current guideline recommendations as part of achieving a 20% reduction in CVD and stroke mortality.[2]

However, lifestyle factors, with the exception of smoking, have not been included in current cardiovascular risk prediction models. In development of recent Framingham risk scores, baseline BMI was assessed and found to be not significantly associated with CVD risk after adjustment for other risk factors in 10-year risk models[3] and weakly but significantly associated with 30 year risk.[4] Similar results for BMI were seen in the development of the Pooled Cohort model.[5] In the development of the Reynolds risk score, BMI, physical activity, and alcohol use were evaluated but were not found to be significantly associated with CVD risk after adjustment for traditional risk factors.[6] While some individual lifestyle factors have been evaluated, the potential improvement in risk prediction from using a combination of more detailed measures of diet, physical activity, smoking and adiposity, including measures of waist circumference, has not been assessed.

In this study we examined the association of multiple healthy lifestyle factors with incident CVD in the Women's Health Initiative Observational Study (WHI-OS), a multiethnic cohort of post-menopausal US women. We additionally examined whether lifestyle factors provide improved CVD risk performance compared to traditional risk factors, including factors used in the Pooled Cohort and Reynolds risk scores, as well as whether the combination of lifestyle and tradition risk factors improves CVD risk prediction over traditional risk factors alone.

Methods

Population Cohort

The WHI Observational Study (WHI-OS) included 93,676 post-menopausal women aged 50 to 79 at enrollment.[7] Women were recruited at 40 centers throughout the US between 1993 and 1998 and followed through 2005. Additional follow up was collected through the WHI Extension Study. All participants provided informed consent using materials approved by institutional review boards at each center.

Outcome Ascertainment

Data on self-reported outcomes through 2008 were used for this analysis. All endpoints were adjudicated through standardized medical record review.[8] Confirmation of MI used medical records, electrocardiogram readings, and cardiac enzyme and troponin levels. Strokes were defined as rapid onset of a persistent neurologic deficit attributed to a thrombotic or hemorrhagic stroke, lasting more than 24 hours and without evidence of other cause. Death certificate, medical records and other records, such as autopsy reports were used to classify the underlying cause of death. The primary endpoint used was major CVD, comprised of MI, stroke, and death from cardiovascular causes.

Case-cohort Design

For this study, a prospective case-cohort design was used and the project was approved by the institutional review board at Brigham and Women's Hospital. The cases and the sub-cohort were both sampled from the 60,890 WHI-OS participants with baseline blood samples, baseline clinical risk factor information, and no baseline history of myocardial infarction, stroke, revascularization, pulmonary embolism, deep vein thrombosis, peripheral vascular disease, or cancer. Non-whites were over sampled, with all cases of major CVD included for the black (n=200), Hispanic (n=53), Asian (n=55), and other/unknown ethnicity (n=55) women. The remaining cases (n=1637) were randomly sampled from the 2370 cases among white women. The sub-cohort sampling was stratified to match case distributions of race/ethnicity and 5-year age categories.

After further exclusion for baseline history of transient ischemic attack, CVD surgery, or congestive heart failure, and missing baseline lifestyle information, there were 1738 cases and a sub-cohort of 1896 participants (including 122 who were also cases) available for analysis. The primary analysis was limited to non-smokers, which included 1587 cases and 1808 sub-cohort participants (116 who were also cases).

Biomarker Measures

For the case and sub-cohort samples, blood samples collected and stored at −70 C° at the time of study entry were sent to a central lab certified by the National Heart Lung and Blood/Centers for Disease Control and Prevention Lipid Standardization Program. Total and high-density lipoprotein (HDL) cholesterol and high-sensitivity C-reactive protein (hsCRP) were measured in all samples. Additionally, hemoglobin A1c (HbA1c) was measured in participants with baseline diabetes.

Physical Activity Measures

Physical activity was assessed by self-administered questionnaire of recreational activity types. The energy expenditure associated with each activity was calculated using reported frequency and duration multiplied by intensity in metabolic equivalents (METs) from standardized classifications.[9] Weekly totals of time spent in light, moderate and vigorous physical activity were calculated for adherence to guideline recommendations.[10] Additionally, energy expenditure from all physical activity was combined into a weekly total score, which has previously been found to be predictive of CVD in the WHI-OS as well as

other populations.[11, 12] The physical activity questions were repeated for a subset of participants and the total expenditure in METs was found to have a weighted kappa of 0.77.[7]

Dietary Measures

Dietary information was collected using the WHI food-frequency questionnaire.[13] The Alternative Healthy Eating Index (AHEI) score[14], which measures adherence to US dietary guidelines was used. This score gives a maximum of 10 points for perfect adherence for each component and proportional points for less-than-perfect adherence and has previously shown to be associated with incident CVD in the WHI-OS [15] as well as other cohorts.[14] It was constructed using reported intake of vegetables (10 points for 5 servings/day), fruit (10 points for 4 serving/day), nuts and soy protein (10 points for 1 serving/day), ratio of white to red meat (10 points for a ratio of 4 or no meat), whole grains (10 points for 3 servings/day, used as a proxy for cereal fiber), *trans* fat (10 points for ≤ 0.05% of total energy, 0 points for ≥ 4%), ratio of polyunstaurated to saturated fat (10 points for ≥ 1, 0 points for ≤ 0.01), and multivitamin use (7.5 point for use, 2.5 points for non use). Alcohol use, which was originally included in the AHEI, was considered as a separate risk factor and divided into non-drinkers, ≤1 drink/day, and more than 1 drinks/day.[16, 17] A sensitivity analysis with alcohol included in the AHEI score was also performed. Alcohol and the other dietary measures from the FFQ were compared to 4 24hr recalls and a 4-day dietary log and were found to have high reliability.[18]

Adiposity Measures

Weight, height, waist circumference and hip circumference were all measured at the baseline visit. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Waist circumference (WC) was measured at the natural waist over non-binding undergarments at the end of exhalation. Previous studies in the WHI[19] and others[20] have suggested that the both BMI and WC are predictive for CVD.

Additional Measures

Personal and family medical history information was collected by questionnaire at study baseline including diabetes, family history of a premature MI (before age 55 in men or age 65 in women), smoking, anti-hypertensive use, and cholesterol-lowering medication use. Average number of cigarettes smoked per day and duration of smoking were used to construct total pack years. Resting blood pressure was measured at the baseline visit.[7]

Statistical Methods

All analysis was done in SAS 9.2 using sampling weights to account for the case-cohort design.[21–23] Our method of stratified sampling from the known distribution in the full WHI-OS cohort allowed us to estimate the characteristics of the full sample by reweighting using the sampling frequency. Population characteristics were estimated using survey procedures with inverse probability weights using Proc Surveymeans.[24] Pearson correlations were used to allow for incorporation of sampling weight. To generate survival models of risk factors and incident major CVD, hazard ratios and baseline hazards were obtained using weighted

Cox regression in Proc Phreg.[25] Asymptotic variance estimates were computed using the method of Langholz and Jiao.[26]

Smoking, one the key modifiable lifestyle factors, is already included in traditional risk prediction models. We chose to limit our primary analysis to non-smokers to more clearly assess the impact of additional lifestyle factors, with a secondary analysis examining the results in smokers as discussed below. We also did a sensitivity analysis of our results in participants without baseline diabetes.

To avoid over fitting in our sample, we chose lifestyle and demographic factors already shown to be associated with CVD in the entire WHI-OS and predictive of CVD in other cohorts. These included BMI, WC, physical activity (measured as MET-hrs/week), and AHEI diet score. A healthy lifestyle factor score, similar to that used in other cohorts[1], was created by counting the number of the following categories met: 1) non-smoker (all participants in the primary analysis); 2) BMI between 18.5 and 24.9 or WC in the bottom 2 quintiles; 3) AHEI score in top 2 quintiles; 4) 2.5 hours of moderate intensity physical activity or 75 minutes of vigorous intensity physical activity per week; and 5) alcohol consumption greater than none, but ≤1 drink per day. In further analyses, the form for individual continuous factors (AHEI diet score, physical activity, BMI and WC) was chosen by comparing discrimination as measured by the integrated discrimination improvement (IDI).[27] The IDI, which is related to an R-squared, is a measure of both prediction and model fit.[28] We generated the IDI from age and race adjusted predictions based on either sub-cohort quintiles, a linear term, a log transformation, or a linear and a quadratic term. The simplest form with no significant loss of prediction was used in subsequent models.

The selected lifestyle factors (BMI, WC, quintiles of physical activity, AHEI diet score, alcohol use) were then combined with age and race to generate the “Lifestyle model”. The “PC model” used the underlying risk factors from the Pooled Cohort (PC) risk score,[5] including age, smoking status, history of diabetes, anti-hypertensive treatment status, systolic blood pressure, total, and HDL cholesterol in addition to race, with coefficients re-estimated in our WHI-OS population. The “RRS model” used the risk factors from the Reynolds risk score (RRS),[6] including age, smoking status, family history of a premature MI, HbA1c if the participant had a history of diabetes, hsCRP, systolic blood pressure, total, and HDL cholesterol in addition to race, with coefficients re-estimated in the study population. Of note, race was not included in either the published RRS or PC scores, but was included in this analysis to take into account the multiethnic make up of the WHI-OS and to improve comparability across models. Models adding the selected lifestyle factors to the PC and RRS models were also generated.

Predictive ability was assessed continuously using change in the c-index and the integrated discrimination improvement (IDI).[27, 29] Reclassification into relevant risk categories was assessed using the net reclassification improvement (NRI) using risk categories with cut points at 5% and 7.5% 10-year risk of major CVD. The continuous NRI, which does not rely on cut-points and has been shown to be consistent with measures of association, was also calculated.[30, 31] Survival methods were used for all measures as well as reweighting to approximate the distribution in the overall cohort.[32] Calibration was assessed graphically

using deciles of predicted risk. Statistical testing of predictive ability measures was done using 1000 bootstrap samples.

Results

The distributions of lifestyle and other risk factors among non-smokers at baseline are shown in Table 1, both in the selected sample and re-weighted to approximate the population distribution. Since this analysis was limited to non-smokers, all participants had at least one healthy lifestyle factors, but only 7% of the sub cohort and 5% of cases had all 5 factors. These percentages were similar in the weighted population estimates.

The relationships of the individual lifestyle components to CVD, after adjustment for age and race, are shown in Table 2. Optimal weight had the strongest association with CVD risk (HR 0.69). Increasing numbers of healthy lifestyle components also have a relationship with CVD risk, as shown in Table 3. Compared to the reference group of 1 factor (non-smoking), the risk of CVD was lower for each additional factor (HR trend 0.82; 95% CI: 0.76, 0.89) and the presence of all 5 risk factors was associated with a 45% lower risk (HR 0.55; 95% CI: 0.36, 0.84). After adjustment for PC components or RRS components, having all 5 factors was associated with a 20% lower risk of CVD. Results for the white and black participants separately showed similar patterns (Supplemental Table 1), with a crude reduction of risk of 75% for black participants with all 5 factors and 44% for white participants (HR trend 0.85 and 0.81, respectively). Results became less stable and were attenuated in black participants after adjustment for traditional risk factors.

Weighted correlation coefficients between the lifestyle factors and both traditional factors and other lifestyle variables are shown in Supplemental Table 2. The strongest correlation between lifestyle and traditional factors was waist circumference and HDL cholesterol (−0.32).

Hazard ratios for CVD risk for mutually adjusted lifestyle factors are shown in Table 4. After additional adjustment for age and race, the only lifestyle factors with hazard ratios that were not statistically significant were BMI, AHEI score and alcohol use >1 drinks/day. However, after additional adjustment for PC or RRS components, only physical activity remained independently associated with risk of CVD. Hazard ratios for all variables included in each model are shown in Supplemental Table 3.

Predictive values were compared for models with lifestyle factors, the PC and RRS models alone and a combined model with both lifestyle factors and the PC or RRS factors, as shown in Table 5. Calibration plots for the lifestyle alone and lifestyle plus PC and RRS models are shown in Supplemental Figure 1. The model with age, race and lifestyle factors had lower predictive ability on all measures than all of the other models (PC, PC and lifestyle, RRS, and RRS and lifestyle). However, adding the lifestyle factors to both the PC and RRS models did result in a statistically significant continuous NRI (0.09, $p < 0.001$ for both) and IDI (0.004, $p < 0.01$ for both). The categorical NRI and change in the c-statistic were small and not statistically significant for the addition of lifestyle factors to either the PC or RRS models. The reclassification tables for the PC and RRS models alone compared with the

addition of lifestyle factors are shown in Supplemental Table 4. When achievement of the recommended physical activity level alone was added to the RRS and PC models, the change in the c-statistic, categorical NRI, and IDI were non-significant, but the continuous NRI was 0.14 ($p = 0.001$) for both models.

Our subgroup analysis by age at baseline of 65 years or older produced similar results to the overall study (Supplemental Table 5). Results were also similar when smoking status was included as both the lifestyle and traditional factor models and pack years were added to the lifestyle factors. Similarly to the main results, only physical activity remained significantly associated with CVD risk in all models; the highest quintile of pack years remained significant after adjustment for PC components but not RRS components. The addition of lifestyle factors including pack years to the RRS or PC models (Supplemental Table 5) resulted in statistically significant changes to the c-index, IDI and continuous NRI, though no significant changes to the categorical NRI were observed. Similar results were also seen for participants without diabetes at baseline. Using an AHEI score including alcohol consumption in the full sample generated similar results to the main analysis, showing no association with CVD risk after adjustment for traditional risk factors.

Discussion

This study examined the association between healthy lifestyle factors and CVD risk in a multi-ethnic cohort of post-menopausal US women. In this cohort, having a greater number of healthy lifestyle factors was associated with a decrease in CVD risk. We also found that the while traditional risk factors showed superior performance in predicting CVD risk to lifestyle factors alone, adding lifestyle factors does offer improvement in overall model performance, as evidenced by the improvement of the IDI and continuous NRI. However, that improvement is small in relation to CVD risk prediction based on traditional factors alone and does not have a significant effect on classification into established clinical absolute risk categories, as shown in the non-significant categorical NRI of 0.02 or less as compared to increases of closer to 0.1 for the addition of blood pressure and smoking to similar models.[33]

Most of the individual lifestyle factors were associated with incident CVD in the expected direction after adjustment for age and race. Increasing BMI and WC were associated with increasing CVD risk, as seen in the WHI cohort[19] and in the combined results from multiple studies by the Emerging Risk Factors Collaboration.[20] Physical activity, even at low levels, was associated with decreased risk of CVD as seen in the WHI cohort and similar cohorts.[34] Moderate alcohol use was also associated with a decreased risk of CVD which is consistent with the findings in the full cohort and with previous reports of a U-shaped relationship.[16, 17] The AHEI diet score was not associated with CVD risk in this study, despite being associated with CVD risk in the full WHI cohort[15] and other studies.[14] In our results this seemed to be primarily due to the correlation with physical activity, which was not adjusted for in previous studies.

Once adjusted for the traditional risk factors, many of the associations with lifestyle factors were diminished, partially due to traditional risk factors, such as diabetes and high blood

pressure, being in the causal pathway from lifestyle to CVD. However, our findings are consistent with previous studies showing some increase in CVD prediction with the addition of individual lifestyle factors. Sacco and colleagues showed improvement in CVD risk prediction by adding waist circumference, alcohol consumption and physical activity to traditional risk factors.[35] Improved estimation of CVD risk with the addition of physical activity to traditional risk factors has also been suggested by Arsenault and colleagues in the EPIC-Norfolk study, though they did not assess prediction performance directly.[36] The NOMAS study also found an increase in the c-statistic for CVD death of 0.736 to 0.748 in women when BMI, physical activity, and psychological distress were added to more traditional risk factors, though a formal test of the improvement was not provided.[37] Additionally, Faeh and colleagues found increased risk prediction when BMI was exchanged for cholesterol in the traditional risk model.[38] Different measurement of lifestyle factors may also affect the results. Our measurements of physical activity are based on self-report and more accurate measures, such as accelerometer data or fitness testing, might improve prediction further, as suggested by Gupta and colleagues.[39] More accurate measures of diet which are less reliant on self-report may also affect the results, though the AHEI score has been shown to be predictive in the larger cohort[15] and other studies.[14] Similarly, while more accurate adiposity measures may provide additional predictive value, BMI and WC remain, in combination, the suggested measures for population health[40]

Our study does have important limitations. Our models were not tested on an external validation sample and our estimates of predictive ability for each model may be slight overestimates. However, we did not use data-driven methods to optimize the selection of lifestyle factors for predictive ability in our study. Instead, the pre-specified lifestyle factors have been shown to be predictive of CVD in multiple cohorts, reducing the risk of overestimation of effect, and are part of current prevention guidelines. The WHI-OS does not include any men, limiting our ability to generalize from the results. However, the relationship between healthy lifestyle factors and CVD has been similar in men and women in previous studies.

Improvements in lifestyle factors, especially physical activity and adiposity, have been shown to reduce traditional cardiovascular risk factors,[41–43] and are thus intrinsically important to reducing overall cardiovascular risk over the long term. Observational evidence suggests that healthy lifestyles are also associated with increased overall lifespan[44] and lifestyle modifications remain part of recommended clinical practice.[45] However, since some of the influence of lifestyle factors is captured by measures of traditional risk factors, they do not appear to improve prediction over the traditional models. This was quantified most recently for BMI, with blood pressure, cholesterol and diabetes mediating the CVD risk associated with higher BMI,[46] and the Emerging Risk Factors Collaboration finding that BMI and WC did not improve CVD risk prediction when added to traditional risk factors alone or in combination.[47] Whether a risk prediction score that includes lifestyle information would be useful to patients or physicians in motivating behavior change will require further research.

Conclusions

Healthy lifestyle factors were associated with CVD risk in this multiethnic cohort of postmenopausal women. Addition of these factors to traditional risk scores, especially physical activity, improved the overall fit of the prediction models but did not improve clinically relevant risk stratification as measured by the NRI. While inclusion of lifestyle factors, especially physical activity, in risk prediction models may provide a cohesive message about the importance of a healthy lifestyle, their additional value in risk prediction remains unclear.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Comparison of baseline characteristics among non-smokers in the sampled cases, sub-cohort, and weighted to the WHI-OS non-smoking population *

	Sample		Weighted to Population¶	
	Subcohort (n=1,808)	**Cases (n=1,587)**	**Cohort (N=50,577)**	**Cases (N=2,138)**
Age (years)	69 (63, 73)	69 (64, 73)	62 (56, 68)	69 (64, 73)
Race				
White	83%	84%	86%	88%
Black	9%	8%	6%	6%
Other	8%	8%	8%	6%
BMI (kg/m2)	26 (23, 29)	27 (24, 31)	26 (23, 30)	27 (24, 31)
Waist circumference (cm)	83 (75, 92)	85 (77, 96)	83 (75, 92)	85 (77, 95)
Physical activity (MET-hrs/week)	11 (4, 20)	8 (3, 18)	10 (3, 20)	8 (2, 17)
AHEI score	35 (29, 42)	35 (29, 41)	35 (29, 42)	35 (29, 41)
Alcohol use				
Never	41%	45%	40%	44%
≤1 drink/day	47%	42%	47%	43%
>1 drinks/day	13%	13%	13%	13%
Number of healthy lifestyle factors				
1	11%	15%	12%	15%
2	29%	34%	27%	34%
3	33%	29%	31%	29%
4	20%	17%	22%	17%
5	7%	5%	8%	6%
Anti-hypertensive medication use	26%	38%	22%	37%
Cholesterol-lowering medication	9%	10%	7%	9%
Diabetes	4%	10%	3%	10%
Family history of early MI	18%	22%	18%	22%
Systolic Blood pressure (mmHg)	128 (117, 140)	134 (122, 148)	123 (114, 135)	133 (122, 148)
Total cholesterol (mg/dL)	226 (201, 257)	225 (198, 251)	225 (201, 257)	225 (198, 251)
HDL (mg/dL)	54 (45, 66)	49 (40, 60)	55 (46, 67)	49 (40, 60)
hsCRP (mg/L)	2.3 (1.0, 4.9)	2.9 (1.3, 5.9)	2.3 (1.0, 5.1)	2.9 (1.4, 5.8)
HbA1c % (if diabetic)	6.9 (6.2, 7.7)	7.5 (6.6, 9.0)	6.9 (6.0, 7.7)	7.5 (6.6, 8.9)

* median (25^{th} percentile, 75^{th} percentile) for continuous variables, percent for categorical

¶ Using the sampling weights from the case-cohort design

Table 2

Hazard ratios and 95% confidence intervals for incident CVD by individual healthy lifestyle components* weighted to the WHI-OS non-smoking population

	Weighted Percent in Subcohort	Adjusted for age and race	
		HR (95% CI)	P value
Optimal weight	58%	0.69 (0.60, 0.80)	<0.001
Healthy diet	48%	0.86 (0.75, 0.98)	0.002
Recommended physical activity	34%	0.78 (0.67, 0.91)	<0.001
Moderate alcohol	47%	0.83 (0.72, 0.95)	<0.001

* The healthy lifestyle components were defined as 1) non-smoker (all participants by inclusion criteria); 2) optimal weight: BMI between 18.5 and 24.9 or WC in bottom 2 quintiles; 3) healthy diet: AHEI score in top 2 quintiles; 4) adequate physical activity: ≥ 2.5 hours of moderate intensity physical activity or ≥ 75 minutes of vigorous intensity physical activity per week; and 5) Moderate alcohol: alcohol consumption greater than none, but <1 drink per day. The reference group for each component was all other participants.

Table 3

Hazard ratios and 95% confidence intervals for incident CVD by healthy lifestyle score weighted to the WHI-OS non-smoking population*

Healthy Lifestyle Score	Sample N	Unadjusted	Adjusted for PC components	Adjusted for RRS components
1	432	Reference	Reference	Reference
2	1019	0.95 (0.76, 1.01)	1.04 (0.81, 1.33)	0.97 (0.76, 1.27)
3	1015	0.78 (0.58, 1.04)	0.83 (0.65, 1.07)	0.79 (0.62, 1.02)
4	604	0.57 (0.42, 0.78)	0.81 (0.62, 1.06)	0.78 (0.59, 1.02)
5	209	0.55 (0.36, 0.84)	0.80 (0.56, 1.14)	0.80 (0.56, 1.15)
Trend		0.82 (0.76, 0.89)	0.92 (0.85, 0.98)	0.92 (0.85, 0.98)

*The healthy lifestyle score was created by counting the number of the following categories met: nonsmoker (all participants by inclusion criteria); optimal weight; healthy diet; adequate physical activity; and moderate alcohol use.

Table 4

1 Standard Deviation Hazard ratios and 95% confidence intervals for incident CVD for mutually adjusted lifestyle factors weighted to the WHI-OS population of non-smokers

	Additionally adjusted for age and race		Additionally adjusted for PC components		Additionally adjusted for RRS components	
	HR (95% CI)	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
BMI	1.00 (0.89, 1.14)	0.96	0.96 (0.83, 1.11)	0.59	0.98 (0.84, 1.13)	0.74
Waist circumference	1.22 (1.08, 1.38)	0.001	1.02 (0.88, 1.19)	0.80	0.99 (0.85, 1.16)	0.90
Physical activity quartiles						
0–1.4 MET-hrs/week	Reference		Reference		Reference	
1.5–5.5 MET-hrs/week	0.77 (0.61, 0.98)	0.03	0.72 (0.56, 0.93)	0.01	0.72 (0.56, 0.92)	0.01
5.6–11.7 MET-hrs/week	0.71 (0.56, 0.90)	0.004	0.69 (0.53, 0.89)	0.004	0.68 (0.53, 0.88)	0.003
11.8–21.0 MET-hrs/week	0.67 (0.52, 0.84)	0.001	0.66 (0.51, 0.86)	0.001	0.67 (0.52, 0.86)	0.002
21.1 + MET-hrs/week	0.66 (0.52, 0.84)	0.001	0.67 (0.51, 0.87)	0.002	0.65 (0.50, 0.85)	0.002
AHEI score	0.98 (0.92, 1.07)	0.84	0.97 (0.90, 1.05)	0.50	0.98 (0.91, 1.06)	0.66
Alcohol use						
Never	Reference		Reference		Reference	
≤1 drink/day	0.86 (0.73, 1.00)	0.05	0.93 (0.79, 1.10)	0.40	0.92 (0.78, 1.08)	0.31
>1 drinks/day	0.94 (0.75, 1.18)	0.61	1.12 (0.87, 1.42)	0.38	1.10 (0.85, 1.41)	0.47

Table 5

Comparisons between CVD risk predictions based on lifestyle factors, traditional factors and combined models weighted to the WHI-OS population of non-smokers

New Model	New Model c-statistic	Reference Model	Reference Model c-statistic	Change in c-statistic	IDI	Continuous NRI	NRI
Lifestyle + PC *	0.779	PC	0.776	0.003 (0.10)	0.004 (0.006)	0.14 (<0.001)	0.01 (0.25)
Lifestyle + RRS **	0.777	RRS	0.775	0.002 (0.10)	0.004 (0.004)	0.15 (<0.001)	−0.004 (0.73)
Lifestyle + PC	0.779	Lifestyle	0.743	0.035 (<0.001)	0.026 (<0.001)	0.46 (<0.001)	0.10 (<0.001)
Lifestyle + RRS	0.777	Lifestyle	0.743	0.034 (<0.001)	0.029 (<0.001)	0.41 (<0.001)	0.09 (<0.001)
PC	0.776	Lifestyle	0.743	0.033 (<0.001)	0.023 (<0.001)	0.32 (<0.001)	0.09 (<0.001)
RRS	0.775	Lifestyle	0.743	0.032 (<0.001)	0.025 (<0.001)	0.40 (<0.001)	0.09 (<0.001)

Each row provides the results for a comparison between a reference (or old) model and a new model.

* The PC model included age, history of diabetes, anti-hypertensive treatment status, and the natural logarithms of systolic blood pressure, total, and HDL cholesterol in addition to race, with coefficients re-estimated in the study population.

** The RRS model included age, family history of a premature MI, HbA1c if the subject had a history of diabetes, and the natural logarithms of hsCRP, systolic blood pressure, total, and HDL cholesterol in addition to race with coefficients re-estimated in the study population.