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Healthy Lifestyle in the Primordial Prevention of Cardiovascular Disease Among Young Women

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ABSTRACT

BACKGROUND Overall mortality rates from coronary heart disease (CHD) in the United States have declined in recent decades, but the rate has plateaued among younger women. The potential for further reductions in mortality rates among young women through changes in lifestyle is unknown.

OBJECTIVES The aim of this study was to estimate the proportion of CHD cases and clinical cardiovascular disease (CVD) risk factors among young women that might be attributable to poor adherence to a healthy lifestyle.

METHODS A prospective analysis was conducted among 88,940 women ages 27 to 44 years at baseline in the Nurses' Health Study II who were followed from 1991 to 2011. Lifestyle factors were updated repeatedly by questionnaire. A healthy lifestyle was defined as not smoking, a normal body mass index, physical activity ≥ 2.5 h/week, television viewing ≤ 7 h/week, diet in the top 40% of the Alternative Healthy Eating Index-2010, and 0.1 to 14.9 g/day of alcohol. To estimate the proportion of CHD and clinical CVD risk factors (diabetes, hypertension, and hypercholesterolemia) that could be attributed to poor adherence to a healthy lifestyle, we calculated the population-attributable risk percent.

RESULTS During 20 years of follow-up, we documented 456 incident CHD cases. In multivariable-adjusted models, nonsmoking, a healthy body mass index, exercise, and a healthy diet were independently and significantly associated with lower CHD risk. Compared with women with no healthy lifestyle factors, the hazard ratio for CHD for women with 6 lifestyle factors was 0.08 (95% confidence interval: 0.03 to 0.22). Approximately 73% (95% confidence interval: 39% to 89%) of CHD cases were attributable to poor adherence to a healthy lifestyle. Similarly, 46% (95% confidence interval: 43% to 49%) of clinical CVD risk factor cases were attributable to a poor lifestyle.

CONCLUSIONS Primordial prevention through maintenance of a healthy lifestyle among young women may substantially lower the burden of CVD. (J Am Coll Cardiol 2015;65:43–51) © 2015 by the American College of Cardiology Foundation.

Although overall mortality rates from coronary heart disease (CHD) in the United States have declined steadily in the past 4 decades, the decline in CHD mortality rates among adults ages 35 to 54 years has slowed (1,2). Of particular concern is that the mortality rate among women ages 35 to 44 years increased on average by 1.3% (95% confidence interval [CI]: 0.2% to 2.5%) per year between 1997 and 2002, and predicted CHD risk among young adults and women has declined only modestly since

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ABBREVIATIONS AND ACRONYMS

AHEI-2010 = Alternative Healthy Eating Index-2010

BMI = body mass index

CHD = coronary heart disease

CI = confidence interval

CVD = cardiovascular disease

HR = hazard ratio

PAR% = population-attributable risk percent

then (2,3). The lack of more significant reductions in CHD incidence and mortality among younger adults may be explained in part by adverse risk factor profiles. Although hypertension rates have declined, management of hypercholesterolemia has improved, and tobacco use has diminished, these positive changes may be offset by increases in the prevalence of obesity and type 2 diabetes (2,4).

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Young women with favorable cardiovascular disease (CVD) risk profiles have a very low risk for CHD mortality compared with others (5), and recent evidence suggests that maintaining a healthy lifestyle throughout young adulthood is strongly associated with a low risk profile in middle age (6). Primordial prevention, defined as prevention of the development of clinical risk factors (7), through maintenance or adoption of a healthy lifestyle will sustain women in a low CVD risk profile and, consequently, reduce their incidence of CHD (1). Furthermore, it could reduce the substantial economic burden of the medical management of intermediate CVD-related conditions, as hypertension, diabetes mellitus, and hyperlipidemia are among the top 10 leading diagnoses for direct health expenditures in the United States (1). Finally, targeting younger women for primordial prevention of CHD may be more feasible before the development of adverse risk factor profiles common in older adults.

The purpose of this analysis was to estimate the proportion of cases of CHD and clinical CVD risk factors—diabetes, hypertension, and high cholesterol—among younger women attributable to poor adherence to a healthy lifestyle.

METHODS

STUDY POPULATION. The Nurses' Health Study II (NHSII) was established in 1989 when 116,430 registered nurses, ages 25 to 42 years, completed a baseline questionnaire that included lifestyle assessment and medical history. Follow-up biennial questionnaires were sent to participants to collect updated information on potential risk factors and newly diagnosed diseases. This study was approved by the Institutional Review Board at Brigham and Women's Hospital. Informed consent was implied by completion of the questionnaire.

Participants first completed a validated semi-quantitative food frequency questionnaire (8) in 1991, which served as the baseline for this analysis. Women were excluded if they did not complete the food frequency questionnaire (n = 18,075), left more than 70 food items blank (n = 236), or reported energy intake of <600 or >3,500 kcal/day (n = 2,101). Women with CVD, cancer, or diabetes before 1991 (n = 4,001) or missing physical activity (n = 511) or body mass index (BMI) (n = 2,566) at baseline were excluded, leaving 88,940 women for the CHD analysis. For the analysis of clinical CVD risk factors, we additionally excluded 19,693 women with diagnoses of hypertension or hypercholesterolemia before 1991, leaving 69,247 women in the CVD analysis.

ASSESSMENT OF LIFESTYLE FACTORS. Information on weight, height (baseline only), smoking status, and physician diagnosis of disease was obtained biennially. Leisure-time physical activity (including television watching) was assessed in 1991, 1997, 2001, 2005, and 2009 with a previously validated questionnaire (9) on time per week spent on various activities over the previous year. The total hours per week spent engaged in moderate- to vigorous-intensity (≥3 metabolic equivalents) physical activity (10) was calculated.

The food frequency questionnaire was completed every 4 years beginning in 1991 (8). For each food item, participants were asked how often a specified portion was consumed during the past year. Nutrient intake was calculated by multiplying the nutrient content of each food by the frequency of intake and summed across all food items (11). All nutrients were adjusted for total energy intake by regressing nutrient intake on total energy (12).

DEFINITION OF OPTIMAL LIFESTYLE. We considered 6 factors to define optimal lifestyle: smoking, diet, physical activity, television watching, BMI, and alcohol consumption. These factors were selected on the basis of the evidence for their associations with CHD and current recommendations for CVD prevention. For each lifestyle factor, a participant received 1 point if she met the criteria for optimal and 0 points if she did not.

For smoking, the optimal group was defined as those who were not currently smoking. On the basis of current guidelines, we defined optimal physical activity as engaging in at least 2.5 h/week of moderate- to vigorous-intensity exercise (13). Because there is not yet a recommendation for TV watching, we decided a priori that optimal would be defined as 7 h/week or less (14). We defined optimal BMI as 18.5 to 24.9 kg/m^2 (15).

For alcohol, women's use was classified as optimal if they consumed an average of 0.1 to 14.9 g of alcohol per day (approximately 1 drink), which is consistent with current guidelines (16) among nonpregnant

women who choose to drink (as pregnant women should not consume alcohol). It should be noted that "optimal" in this case is with regard to cardiovascular risk, as alcohol may increase the risk for other outcomes.

For diet, we defined optimal as an Alternative Healthy Eating Index-2010 (AHEI-2010) score (17) in the top 40% of the cohort distribution (corresponding to a score ≥47) because there are no numeric targets established for the AHEI-2010 (see footnote in Table 1). The AHEI is an evidence-based measure of diet quality that is associated with low risk for chronic disease (17,18). Because we decided a priori to include alcohol as a separate factor, it is not included in the AHEI-2010 score in this analysis.

OUTCOME ASCERTAINMENT. Incident CHD. The primary end point was incident CHD, which included nonfatal myocardial infarction and fatal CHD diagnosed after the return of the 1991 questionnaire and before June 2011. Self-reported myocardial infarctions were confirmed by medical records according to World Health Organization criteria

TABLE 1 HR (95% CI) for Coronary Heart Disease by Healthy Lifestyle Factors

	Person-Years (%)	No. of Cases	Age-Adjusted HR (95% CI)	p Value for Linear Trend	MV-Adjusted HR (95% CI)*	p Value for Linear Trend
Smoking, cigarettes/day						
≥25	1.2	22	1.00	<0.001	1.00	<0.001
15–24	3.3	53	0.88 (0.54–1.46)		1.02 (0.61–1.68)	
1–14	4.5	47	0.57 (0.34–0.96)		0.75 (0.45–1.27)	
Former	25.2	116	0.21 (0.13–0.34)		0.29 (0.18–0.47)	
Never	65.8	218	0.18 (0.11–0.28)		0.23 (0.15–0.36)	
Physical activity, h/week						
<0.2	20.2	149	1.00	<0.001	1.00	0.004
0.2–0.9	15.7	86	0.86 (0.66–1.12)		1.01 (0.77–1.32)	
1–2.4	20.5	85	0.64 (0.49–0.83)		0.80 (0.61–1.06)	
2.5–4.9	19.7	67	0.52 (0.39–0.69)		0.74 (0.55–1.00)	
≥5	23.9	69	0.43 (0.32–0.57)		0.67 (0.50–0.91)	
AHEI-2010 score†						
<36	16.9	79	1.00	<0.001	1.00	0.003
36–41.9	21.1	117	1.01 (0.76–1.35)		1.15 (0.86–1.54)	
42–46.9	20.2	109	0.91 (0.68–1.22)		1.12 (0.83–1.51)	
47–52.9	20.4	85	0.67 (0.49–0.92)		0.89 (0.65–1.22)	
≥53	21.4	66	0.45 (0.32–0.63)		0.68 (0.48–0.96)	
BMI, kg/m^2						
≥35.0	9.9	97	1.00	<0.001	1.00	<0.001
30.0–34.9	12.9	86	0.69 (0.51–0.92)		0.85 (0.63–1.14)	
25.0–29.9	26.4	133	0.53 (0.41–0.69)		0.75 (0.57–0.99)	
18.5–24.9	49.2	135	0.35 (0.27–0.45)		0.58 (0.43–0.78)	
<18.5	1.5	5	0.48 (0.20–1.18)		0.72 (0.29–1.80)	
Alcohol, g/day						
0	39.7	225	1.00	<0.001	1.00	0.006‡
0.1–4.9	35.5	136	0.69 (0.56–0.86)		0.75 (0.60–0.93)	
5.0–14.9	17.9	65	0.60 (0.46–0.79)		0.73 (0.55–0.97)	
15.0–29.9	4.9	18	0.54 (0.33–0.87)		0.67 (0.41–1.10)	
≥30	2.0	12	0.81 (0.45–1.45)		0.74 (0.41–1.34)	
TV watching, h/week						
≥20.0	7.2	59	1.00	0.001	1.00	0.60
10.0–19.9	19.4	86	0.58 (0.41–0.80)		0.71 (0.51–0.99)	
5.0–9.9	27.4	124	0.62 (0.46–0.85)		0.83 (0.60–1.14)	
1.1–4.9	33.6	135	0.57 (0.42–0.77)		0.84 (0.61–1.15)	
≤1.0	12.3	52	0.58 (0.40–0.84)		0.94 (0.64–1.38)	

*The models were stratified by age (in months) and time period and included parental history of myocardial infarction before 60 years of age, aspirin use, menopausal status, postmenopausal hormone use, parity, oral contraceptive use, and history of hypertension or hypercholesterolemia at baseline. All healthy lifestyle factors were included simultaneously in the same model. †The AHEI-2010 includes 11 components: high intake of vegetables, fruits, whole grains, nuts and legumes, long-chain (n-3) fats (eicosapentaenoic acid and docosahexaenoic acid), and polyunsaturated fatty acids; moderate intake of alcohol; and low intake of sugar-sweetened beverages and fruit juice, red and processed meat, trans fat, and sodium. The AHEI-2010 score ranges from 0 to 100 (after excluding alcohol), with higher scores representing better adherence. ‡p for nonlinearity = 0.03.

AHEI = alternative healthy eating index; BMI = body mass index; HR = hazard ratio; MV = multivariable.

that included symptoms plus either diagnostic electrocardiographic changes or elevated cardiac enzymes (19). Fatal CHD was confirmed by hospital or autopsy records or if CHD was listed as the cause of death on the death certificate and evidence of previous CHD was available.

Clinical CVD risk factors. Additionally, we examined the outcome of diagnosis with at least 1 of 3 physician-diagnosed clinical CVD risk factors—type 2 diabetes, hypertension, and hypercholesterolemia—reported after the return of the 1991 questionnaire and through 2011. Type 2 diabetes was defined as a self-report of incident diabetes confirmed by a validated supplemental questionnaire using the 1997 American Diabetes Association criteria (20). Incident hypertension and hypercholesterolemia were self-reported from biennial questionnaires. The calendar year of diagnosis was recorded and used to estimate a time-to-event month assignment for the purposes of survival analysis, on the basis of the month of questionnaire return (21).

STATISTICAL ANALYSIS. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina). Each eligible participant contributed person-time from the return of the 1991 questionnaire until the date of diagnosis of the first event (CHD or clinical CVD risk factor), death, or June 2011.

To obtain the best estimate of long-term dietary intake and to reduce measurement error, we used the cumulative mean of diet scores from repeated dietary assessments as described previously (12). For all other healthy lifestyle factors and covariates, we used simple updated levels of each variable in which outcomes were predicted from the most recent questionnaire. For example, events that occurred between 1991 and 1993 were examined in relation to exposures reported on the 1991 questionnaire, events occurring between 1993 and 1995 were examined in relation to exposures reported on the 1993 questionnaire, and so forth. We skipped any questionnaire cycle during which a participant was pregnant.

To examine the association between healthy lifestyle factors and CHD or clinical CVD risk factors, separate Cox proportional hazards models were used to estimate hazard ratios (HRs) of each outcome (CHD or clinical CVD risk factor). The models were stratified by age (in months) and time period and adjusted for parental history of myocardial infarction before 60 years of age, aspirin use, menopausal status, postmenopausal hormone use, parity, and oral contraceptive use. Additionally, the models for CHD included history of hypertension or hypercholesterolemia at baseline. Tests for linear trend were computed using category medians, except for smoking, for which an ordinal variable was used. Statistical significance was defined as $p < 0.05$. We also examined possible nonlinear relations between healthy lifestyle factors and each outcome nonparametrically with restricted cubic splines (22).

To estimate the proportion of CHD and clinical CVD risk factors attributable to poor adherence to a healthy lifestyle, we calculated the population-attributable risk percent (PAR%), an estimate of the percent of cases in this population that would not have occurred if all women had been in the optimal group, assuming a causal relationship (23). To allow valid calculation of the PAR%, pooled logistic regression models were used with age and time period included explicitly in the model.

RESULTS

During 20 years of follow-up, 456 women had documented incident CHD, and 31,691 reported physician diagnoses of 1 or more clinical CVD risk factors (n = 2,749 with diabetes, n = 16,978 with hypertension, and n = 23,971 with hypercholesterolemia). The mean age of the population at baseline was 37.1 ± 4.5 years, whereas the mean age at diagnosis of CHD was 50.3 ± 5.9 years and the mean age at diagnosis with a clinical CVD risk factor was 46.8 ± 6.2 years.

ASSOCIATION BETWEEN HEALTHY LIFESTYLE FACTORS AND CHD AND CLINICAL CVD RISK FACTORS. In multivariable-adjusted analyses (**Table 1**), not smoking, higher physical activity, higher AHEI-2010 diet score, and lower BMI were associated with lower risk for CHD (p for linear trend <0.01 for each). The relationship with alcohol was J shaped, with the lowest risk being among women with alcohol intake of 15.0 to 29.9 g/day. Television watching was not significantly associated with CHD after adjusting for the other healthy lifestyle factors. Similar results were seen for clinical CVD risk factors: not smoking, higher physical activity, higher AHEI-2010 score, lower BMI, and not watching television were each associated with lower risk for a diagnosed clinical CVD risk factor (diabetes, hypertension, or hypercholesterolemia) (p for linear trend < 0.001 for each; **Table 2**). Again, the association with alcohol intake appeared J shaped, with the lowest risk among women who reported 5.0 to 14.9 g/day (p for nonlinearity <0.0001).

When the healthy lifestyle factors were collapsed into binary categories of optimal versus not optimal, each lifestyle factor remained significantly associated with lower risk for incident CHD (except television watching) and diagnosis with a clinical CVD risk

TABLE 2 HR (95% CI) of Diagnosis With a Clinical CVD Risk Factor (Diabetes, Hypertension, or Hypercholesterolemia*) by Healthy Lifestyle Factors

	Person-Years (%)	No. of Cases	Age-Adjusted HR (95% CI)	p Value for Linear Trend	MV-Adjusted HR (95% CI)†	p Value for Linear Trend
Smoking, cigarettes/day						
≥25	1.1	411	1.00	<0.001	1.00	<0.001
15–24	3.3	1,109	0.94 (0.84–1.05)		1.01 (0.90–1.13)	
1–14	4.8	1,445	0.81 (0.73–0.91)		0.92 (0.83–1.03)	
Former	24.2	8,365	0.83 (0.75–0.92)		0.95 (0.86–1.05)	
Never	66.5	20,361	0.80 (0.72–0.88)		0.91 (0.82–1.00)	
Physical activity, h/week						
<0.2	18.0	7,015	1.00	<0.001	1.00	<0.001
0.2–0.9	15.6	5,125	0.91 (0.88–0.95)		0.98 (0.94–1.01)	
1–2.4	21.0	6,662	0.87 (0.84–0.90)		0.98 (0.94–1.01)	
2.5–4.9	20.7	6,046	0.77 (0.75–0.80)		0.93 (0.90–0.96)	
≥5	24.7	6843	0.68 (0.66–0.70)		0.88 (0.85–0.91)	
AHEI-2010 score						
<36	17.7	5,446	1.00	<0.001	1.00	<0.001
36–41.9	21.6	6,950	0.92 (0.89–0.96)		0.95 (0.91–0.98)	
42–46.9	20.0	6,576	0.89 (0.86–0.92)		0.93 (0.90–0.97)	
47–52.9	19.8	6,514	0.84 (0.81–0.88)		0.91 (0.88–0.95)	
≥53	20.8	6,205	0.72 (0.69–0.74)		0.83 (0.80–0.86)	
BMI, kg/m^2						
≥35.0	5.9	3,840	1.00	<0.001	1.00	<0.001
30.0–34.9	9.5	5,231	0.82 (0.79–0.86)		0.85 (0.82–0.89)	
25.0–29.9	24.3	9,729	0.61 (0.59–0.63)		0.65 (0.62–0.67)	
18.5–24.9	58.3	12,637	0.36 (0.35–0.37)		0.39 (0.38–0.41)	
<18.5	2.0	254	0.23 (0.21–0.27)		0.26 (0.23–0.29)	
Alcohol, g/day						
0	38.5	12,788	1.00	<0.001	1.00	0.07‡
0.1–4.9	36.7	10,945	0.89 (0.87–0.91)		0.94 (0.91–0.96)	
5.0–14.9	18.5	5,469	0.79 (0.76–0.81)		0.90 (0.87–0.93)	
15.0–29.9	4.6	1,659	0.83 (0.79–0.87)		0.96 (0.91–1.01)	
≥30	1.8	830	1.06 (0.99–1.14)		1.17 (1.09–1.26)	
TV watching, h/week						
≥20.0	5.8	2,399	1.00	<0.001	1.00	<0.001
10.0–19.9	18.2	6,486	0.89 (0.85–0.93)		0.99 (0.94–1.03)	
5.0–9.9	27.5	8,787	0.80 (0.77–0.84)		0.94 (0.90–0.99)	
1.1–4.9	35.0	10,422	0.74 (0.71–0.78)		0.92 (0.88–0.97)	
≤1.0	13.6	3,597	0.64 (0.60–0.67)		0.85 (0.80–0.89)	

*Total number of cases = 31,691; diabetes n = 2,749, hypertension n = 16,978, hypercholesterolemia n = 23,971. †The models were stratified by age (in months) and time period and included parental history of myocardial infarction before 60 years of age, aspirin use, menopausal status, postmenopausal hormone use, parity, and oral contraceptive use. All healthy lifestyle factors were included simultaneously in the same model. ‡p for nonlinearity <0.001.

CVD = cardiovascular disease; other abbreviations as in Table 1.

factor in multivariable-adjusted models including all lifestyle factors simultaneously (Table 3). Among women in the optimal category for all 6 lifestyle factors, comprising approximately 5% of the study population, the HR for CHD was 0.08 (95% CI: 0.03 to 0.22) and for the presence of ≥1 clinical CVD risk factor was 0.34 (95% CI: 0.30 to 0.38), compared with women not in the optimal category for any lifestyle factor.

PAR% FOR CHD AND CLINICAL CVD RISK FACTORS. Table 3 additionally provides the PAR% for each healthy lifestyle factor separately as well as all 6 factors combined. For women in the optimal category for all 6 lifestyle factors, the PAR% for CHD was 72.7% (95% CI: 39.1% to 89.2%), suggesting that almost three-quarters of all confirmed CHD events in this cohort of younger women could have been prevented if all women were in the optimal group. For diagnosis of at least 1 clinical CVD risk factor, the PAR% was 46.1% (95% CI: 42.7% to 49.3%). As a sensitivity analysis, we restricted cases of incident hypertension and hypercholesterolemia only to participants also reporting medication use, and the PAR% was 52.7% (95% CI: 48.7% to 56.5%).

TABLE 3 HR (95% CI) of Diagnosis With a Clinical CVD Risk Factor (Diabetes, Hypertension, or Hypercholesterolemia) or CHD by Optimal Lifestyle Factor Status

		CHD (n = 456)			Clinical CVD Risk Factor (n = 31,691)		
	Definition of Optimal	Person-Years at Optimal Level (%)	MV-Adjusted HR (95% CI)*	PAR% (95% CI)	Person-Years at Optimal Level (%)	MV-Adjusted HR (95% CI)*	PAR% (95% CI)
Smoking	Not currently smoking	91.0	0.29 (0.23-0.35)	19.2 (13.6-24.6)	90.7	0.97 (0.93-1.00)	0.4 (0.1-0.8)
Physical activity	≥2.5 h/week	43.7	0.72 (0.58-0.88)	20.0 (7.4-32.0)	45.4	0.88 (0.85-0.90)	8.2 (6.8-9.6)
AHEI-2010 score	AHEI-2010 score ≥47	41.8	0.69 (0.57-0.85)	19.5 (8.1-30.4)	40.6	0.90 (0.88-0.92)	5.4 (4.0-6.8)
BMI	18.5-24.9 kg/m^2	49.2	0.68 (0.55-0.84)	22.9 (10.2-34.9)	58.3	0.54 (0.53-0.55)	29.8 (28.6-31.0)
Alcohol	0.1-14.9 g/day	53.4	0.77 (0.64-0.93)	12.6 (3.1-21.8)	55.2	0.91 (0.89-0.93)	4.6 (3.5-5.7)
TV watching	≤7 h/week	45.9	1.04 (0.86-1.26)	—	48.6	0.91 (0.89-0.93)	5.9 (4.6-7.2)
All 6 factors	—	4.6	0.08 (0.03-0.22)	72.7 (39.1-89.2)	5.4	0.34 (0.30-0.38)	46.1 (42.7-49.3)

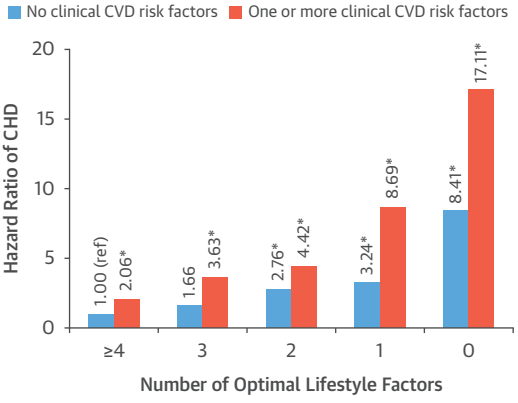
*The models were stratified by age (in months) and time period and included parental history of myocardial infarction before 60 years of age, aspirin use, menopausal status, postmenopausal hormone use, parity, and oral contraceptive use. For CHD, the model also includes history of hypertension or hypercholesterolemia at baseline. All healthy lifestyle factors were included simultaneously in the same model.

CHD = coronary heart disease; PAR% population-attributable risk percent; other abbreviations as in Tables 1 and 2.

LIFESTYLE FACTORS AND CHD RISK IN WOMEN WITH AND WITHOUT CLINICAL CVD RISK FACTORS. Figure 1 shows the association between the number of optimal lifestyle factors and CHD among women with no clinical CVD risk factors and women with 1 or more risk factors. Overall, for a given number of optimal lifestyle factors, women with 1 or more clinical CVD risk factors (diabetes, hypertension, or hypercholesterolemia) were at higher risk for CHD compared with women with no risk factors. However, even among women diagnosed with CVD risk factors, adherence to 4 or more healthy lifestyle factors was associated with a substantially lower risk for CHD (HR: 2.06; 95% CI: 1.20 to 3.52) compared with adherence to zero healthy lifestyle factors (HR: 17.11; 95% CI: 9.29 to 31.52) (p for difference on the basis of Wald test <0.001). Additionally, the PAR% for all lifestyle factors combined was slightly higher in women with at least 1 clinical CVD risk factor (71.1%; 95% CI: 36.3% to 88.5%) compared with women with no CVD risk factors (64.9%; 95% CI: 24.6% to 86.1%) (Online Table 1).

When we stratified by age, the PAR% for CHD was 66.5% (95% CI: 12.0% to 90.2%) for all 6 factors among women <50 years of age and 78.5% (95% CI: 26.8% to 95.1%) among women ages 50 years and older. Finally, we examined the association between the lifestyle factors and each of the clinical CVD risk factors separately (Online Table 2). The PAR% for all 6 lifestyle factors combined was 92.9% (95% CI: 87.6% to 96.0%) for diabetes, 57.0% (95% CI: 52.8% to 60.9%) for hypertension, and 40.0% (95% CI: 35.5% to 44.3%) for hypercholesterolemia.

FIGURE 1 Hazard Ratios for Coronary Heart Disease According to Number of Optimal Lifestyle Factors Among Women With No CVD Risk Factors and 1 or More Risk Factors

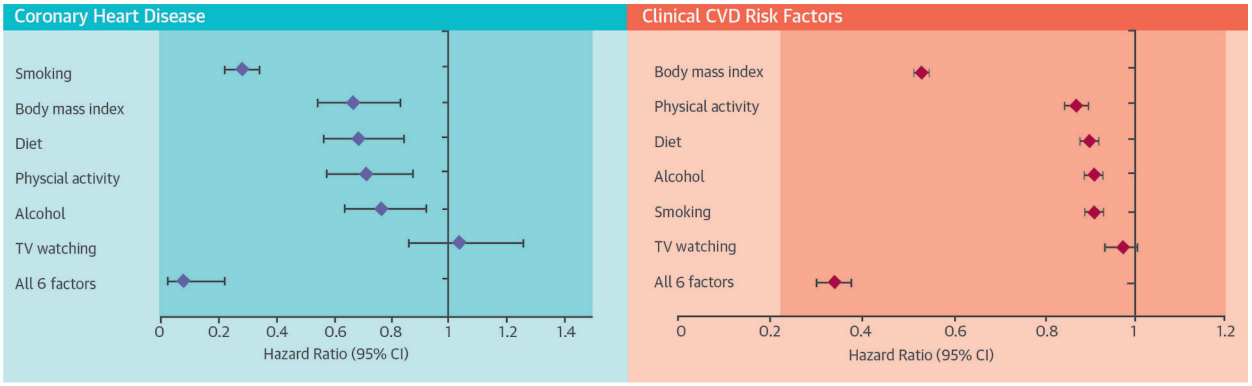


The models were stratified by age and period and included parental history of myocardial infarction, aspirin use, menopausal status, postmenopausal hormone use, parity, and oral contraceptive use. *Values significant at p = 0.05. P for interaction = 0.48. CI = confidence interval; CVD = cardiovascular disease.

DISCUSSION

In this large, prospective study of young United States women, adhering to a healthy lifestyle was associated with decreased risk for incident CHD as well as decreased risk for diagnosis with 1 or more clinical CVD risk factors, including type 2 diabetes, hypertension, and hypercholesterolemia (**Central Illustration**). Women who engaged in all 6 healthy lifestyle choices had a 92% lower risk for CHD and a 66% lower risk for a clinical CVD risk factor. If these associations are causal, more than 70% of CHD and nearly one-half of CVD risk factor diagnoses in this cohort may have been prevented if all women had been in the optimal category for all 6 lifestyle factors. Thus, even among young women, healthy lifestyle plays an important role in the primordial prevention of CHD.

CENTRAL ILLUSTRATION **Hazard Ratios (95% CI) for Coronary Heart Disease or Diagnosis With a Clinical CVD Risk Factor (Diabetes, Hypertension, or Hypercholesterolemia) for Optimal Levels of Lifestyle Factors**



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The models were stratified by age (in months) and time period and included parental history of myocardial infarction before 60 years of age, aspirin use, menopausal status, postmenopausal hormone use, parity, and oral contraceptive use. For coronary heart disease, the model also included history of hypertension or hypercholesterolemia at baseline. All healthy lifestyle factors were included simultaneously in the same model. CVD = cardiovascular disease.

This study is timely given recent indications that the CHD mortality rate in women ages 35 to 44 years may not be declining as it is in other groups (2). Furthermore, there is limited evidence regarding associations between modifiable lifestyle factors and CHD in young women. Existing evidence for CHD risk factors in young women comes primarily from small case-control studies and is limited to oral contraceptive use (24), smoking (25), diabetes (25), hypertension (25), alcohol (26), and coffee (27).

To our knowledge, this is the first study to investigate the association between lifestyle factors and risk for both clinical CVD risk factors and incident CHD. Focusing on primordial prevention through healthy lifestyle could importantly address the economic burden of the medical management of clinical CVD risk factors (1,7) as well the substantial health care costs of subsequent CHD, stroke, eye disease, and premature death (1,4,7,28,29). In the American Heart Association's 2020 Impact Goals, ideal cardiovascular health is characterized by 7 health metrics (1), including 4 health (lifestyle) behaviors (not smoking, physical activity, diet, normal body weight) and 3 health (risk) factors (optimal total cholesterol, blood pressure, and fasting blood glucose in the absence of drug treatment). On the basis of data from the National Health and Nutrition Examination Survey 2009-2010, among adults 20 to 39 years of age, 32.2% had total cholesterol ≥200 mg/dl, 35.7% had blood pressure ≥120/80 mm Hg, and 26.5% had fasting blood glucose ≥100 mg/dl. The percentages of subjects who do not have ideal levels of these risk factors rise to 63.2%, 59.3%, and 46.0%, respectively, among adults 40 to 59 years of age (1). Previous evidence suggests that approximately 70% of incident CVD can be explained by elevated levels of risk factors (30). Our data suggest that adhering to 4 healthy lifestyle behaviors, with the addition of light drinking and possibly limited television, would substantially decrease the burden of both CVD risk factors and CHD among young women in the United States.

We found that healthy lifestyle was equally important in preventing CHD among women who had already developed at least 1 clinical CVD risk factor. This is an important public health message and consistent with previous work among men, whose healthy lifestyle prevented the majority of CHD events, even among those already taking medications for hypertension and hypercholesterolemia (31).

Strengths of our study include the prospective design, minimal loss to follow-up, detailed information on a large number of lifestyle factors collected multiple times during follow-up, and the large number of self-reported physician-diagnosed clinical CVD-related conditions and confirmed CHD cases despite the relatively young age of study participants.

STUDY LIMITATIONS. As in any observational study, the possibility of residual confounding cannot be eliminated; however, we were able to adjust for many known risk factors. Our study population, consisting of predominantly white nurses, is not representative of the general population. Thus, we cannot

necessarily generalize our results to other populations with different educational levels, incomes, or distributions of race and ethnicity. Nonetheless, the prevalence of CVD risk factors in this cohort (7.1% with diabetes, 32.7% with hypertension, and 46.7% with hypercholesterolemia) is very similar to that of women in the United States population (1). Additionally, when we examined the association between healthy lifestyle and clinical CVD risk factors within racial subgroups, the PAR% was similar for Hispanic and Asian women and higher for African-American women, although CIs for these estimates were wide and overlapping because of limited power. The healthy lifestyle factors examined in this study were self-reported; however, this method of data collection has been validated for many factors, including physical activity (9), diet (8,32), alcohol (33), and weight (34). Furthermore, measurement error would be nondifferential with respect to subsequent disease status and likely results in an underestimate of the true effect. Hypertension and hypercholesterolemia were also self-reported, possibly resulting in misclassification of these outcomes. However, reporting of hypertension and hypercholesterolemia has previously been found to be fairly reliable in this and a similar population (35,36), with 94% of self-reported cases of hypertension and 86% of self-reported cases of hypercholesterolemia confirmed by medical records.

CONCLUSIONS

A healthy lifestyle was associated with significant reductions in the incidence of CHD and clinical CVD risk factors, including diabetes, hypertension, and hypercholesterolemia, in this population of young women at baseline. Adhering to a healthy lifestyle similar to that used here for CHD prevention in young women has been found to be associated with a lower risk for several diseases in middle-aged and older women, including CHD (37,38), stroke (39), sudden cardiac death (40), diabetes (41), and cancer (38,42). Thus, promoting adherence to a healthy lifestyle has the potential to not only substantially reduce the burden of CHD and CVD-related conditions but could be a simple, but important, strategy to lower overall morbidity and premature death in young and middle-aged women. Primordial prevention provides enormous potential for future reductions in CHD rates in young women.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Preventing the development of clinical risk factors through a healthy lifestyle can reduce the incidence of diabetes, hypertension, and hypercholesterolemia and reduce the incidence of coronary artery disease in young women, just as a healthy lifestyle can prevent coronary disease in women with these risk factors.

TRANSLATIONAL OUTLOOK: More work is needed to identify the most effective strategies to encourage patients to adopt or maintain a healthy lifestyle.

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KEY WORDS coronary disease, diabetes, epidemiology, hypercholesterolemia, hypertension, risk factors

APPENDIX For supplemental tables, please see the online version of this article.