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Dietary Patterns, Smoking, and Subclinical Heart Disease in Women: Opportunities for Primary Prevention from the Framingham Nutrition Studies

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ABSTRACT

Objectives To investigate the relationship between a heart-healthy dietary pattern and subclinical heart disease in women, and to identify potential opportunities for primary prevention.

Design Prospective analysis in which dietary patterns and cardiovascular disease (CVD) risk factors were assessed at baseline. Presence of subclinical heart disease was assessed using carotid atherosclerosis (stenosis ≥25%) measured by ultrasound at 12-year follow-up.

Subjects/Setting We studied 1,423 women in the population-based Framingham Offspring/Spouse (FOS) Study cohort, Framingham, Massachusetts. Subjects did not have CVD at baseline.

Statistical Analyses CVD risk factor differences among the dietary clusters were evaluated using analysis of covariance and logistic regression. The relationship between heart-healthy and less heart-healthy dietary patterns and the presence of subclinical heart disease at follow-up was examined using odds ratios calculated from multivariate logistic regressions; stratification by smoking status (current, former, never) was also explored.

Results Women who ate a heart-healthy diet had more favorable baseline CVD risk factor profiles. The age-adjusted odds of subclinical heart disease at follow-up was 40% lower for heart-healthy women (OR 0.60, $P=.02$). Multivariate adjustment for BMI, blood lipid levels, and blood pressure only slightly attenuated these odds. The odds remained reduced after adding pack-years of smoking to the multivariate model, but statistical significance was attenuated (OR 0.74, $P=.20$). In analyses stratified by smoking status, women who consumed a heart-healthy diet and who had never smoked had more than 80% less odds for subclinical heart disease compared with smokers whose diets were less heart-healthy (adjusted OR 0.17; $P=.0001$).

Conclusions Women who achieve a heart-healthy eating pattern, in combination with the avoidance of smoking, have a lower odds of subclinical heart disease. Among former smokers, the avoidance of smoking seemed to have somewhat more influence than diet on stenosis risk. A public health priority for women to promote the primary prevention of heart disease is the adoption of positive lifestyle behaviors, especially healthful eating (dietary patterns rich in fruits, vegetables, low-fat dairy foods, leaner protein sources, and lower in fats) and the avoidance of smoking.

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Cardiovascular disease (CVD), in particular coronary heart disease (CHD), is the leading cause of morbidity and mortality among American women, accounting for more than 500,000 deaths annually and more fatalities than from all forms of cancer and the next 16 causes of death combined (1). Over a lifetime, half of the female population will die of heart disease or stroke, and, in a given year, approximately 2.5 million American women will be hospitalized for cardiovascular illnesses (1,2). With the aging of the population, heart disease is expected to have an even greater adverse impact on wom-

en's health (1,3). Established risk factors for women other than age include elevated total cholesterol and blood pressure levels, lower high-density lipoprotein (HDL) levels, diabetes, and smoking (4), all of which may be controlled through dietary and lifestyle behaviors. The identification of ideal candidates for primary prevention and the development of effective, noninvasive interventions for CVD risk reduction are public health priorities.

Carotid artery stenosis is a subclinical marker of systemic atherosclerosis, including coronary artery disease and cerebrovascular disease (5,6). The presence and severity of carotid artery lesions are predictive of fatal and nonfatal coronary heart disease (5,7) and stroke events (8-12). Increased prevalence rates of stroke and heart disease have been documented in individuals with carotid artery lesions causing more than 25% stenosis (13). Among older adults in the Framingham cohort, the prevalence of carotid stenosis of this magnitude is estimated at 34% for women and 43% for men (14).

Carotid ultrasonography is a well-recognized, noninvasive method for estimating subclinical atherosclerosis (15,16). It enables the identification of potential candidates for primary prevention activities and facilitates the evaluation of interventions aimed at delaying the development of atherosclerosis (5,17). In this report, we examined the associations between dietary behavior patterns, CVD risk factor profiles, and the presence of subclinical heart disease, defined in terms of carotid atherosclerosis measured by ultrasonography at 12 years of follow-up in Framingham Offspring-Spouse women. We also used stratified models to examine possible interactions between diet and smoking and the risk of carotid stenosis. We hypothesized that a more healthful dietary pattern in women, alone or in combination with nonsmoking, would be associated with less risk of carotid stenosis.

METHODS

Participants

The Framingham Study was initiated in 1948 as a longitudinal population-based study of cardiovascular disease. The original Framingham cohort represented a two-thirds systematic sample of residents in Framingham, MA (18,19). In 1971, some 5,124 Framingham Study offspring and their spouses were recruited to participate in the Framingham Offspring/Spouse (FOS) study (20).

Members of the FOS cohort are examined in the Framingham Study clinic on average every 4 years. They participate in a standardized protocol involving a complete physical exam, laboratory tests, noninvasive diagnostic testing, and updating of medical histories and other pertinent information. At certain exams, detailed dietary data are collected.

The baseline dietary and risk factor data reported here were collected among FOS women at Exam 3, between 1984 and 1988; 2,005 women, age range 18 to 76 years, participated in this exam (83% of eligible women). All 88 women with CVD at baseline were excluded from these analyses (4.4%). The institutional review board at Boston University Medical Center approved this study. All participants provided informed consent.

Dietary Patterns

The semiquantitative Framingham food frequency questionnaire (FFQ) was completed by 1,828 women (91% of Exam 3 participants). Dietary patterns were characterized using cluster analysis applied to food consumption data derived from the FFQ. Both the FFQ and the cluster analysis were validated in the FOS (21-23). Details of the cluster analysis methodology and the identification of dietary clusters among Framingham women were described previously (22-24). Further, we validated our analytical method (22,23), and verified that these dietary patterns are relatively stable over time and that the distinct differences in nutrient intake observed at baseline are maintained (23). The use of analytical approaches that capture the individual's dietary pattern, alone or in combination with other modifiable behaviors, to evaluate relationships between nutritional status and chronic disease risk have been recently recommended as innovative (25) because of their focus on overall food and nutrient intake rather than single dietary markers of risk.

In brief, we identified five distinct groups of Framingham women, each with unique dietary patterns that displayed differing food group consumption and nutrient intake levels (22-24). The heart-healthy dietary pattern, compared with the other four dietary patterns, most closely approximated current dietary guidelines (24). It was characterized by higher consumption of foods that are typically recommended for health promotion (vegetables, fruits, whole grains, leaner protein sources, lower-fat dairy products, and fewer dietary fats) and was lower in dietary lipids (total and saturated fat), higher in micronutrients (vitamins B-6, E, C, and folate), and higher in total dietary fiber (24). In this report, we examine the relationship between subclinical heart disease and the heart-healthy dietary pattern, in comparison with the other less heart-healthy dietary patterns observed among FOS women.

Assessment of Subclinical Heart Disease

Among 1,751 women who provided complete dietary data and who did not have CVD at baseline, presence of subclinical heart disease was assessed at 12 years of follow-up (Exam 6, 1996-1999). Carotid artery ultrasound studies were obtained on 1,423 participants (81.3%). Missing measurements were exclusively due to logistic constraints at the clinic (unavailability of the ultrasound device or the sonographer during the scheduled visit). Reliability studies were ongoing during data acquisition.

Carotid artery imaging was conducted using previously published methods (9). A certified image reader reviewed color Doppler digital images of both sides of the neck and made a subjective estimate of the degree of internal carotid artery narrowing, graded as 0%, 1% to 24%, or 25% to 49%. Internal carotid artery disease was characterized by the maximum stenosis observed on the right or left side and was categorized as 0% (no lesions), 1% to 24% or 25% to 49% (focal lesions causing a stenosis of less then 50% diameter narrowing), and 50% or more (lesions causing 50% or more diameter stenosis). Absence of blood flow corresponded to a total occlusion.

CVD Risk Factor Measurements

CVD risk factors are routinely measured at all Framingham exams (26). All lipid analyses were performed at the Framingham Study laboratory, which participates in the Standardization Program of the Centers for Disease Con-

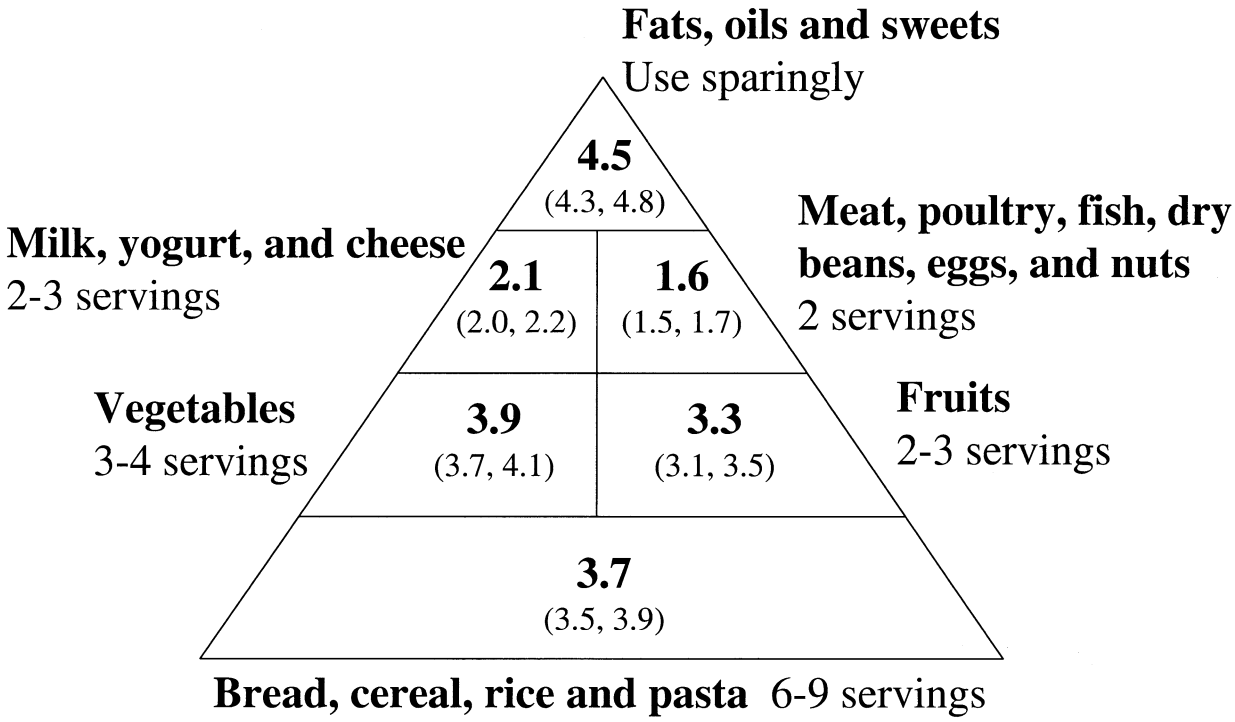

Figure 1. Mean daily servings (95% CI) consumed by women following the heart-healthy dietary pattern, compared with Food Guide Pyramid guidelines for adult women.

trol and the National Heart, Lung and Blood Institute Lipid Research Clinics. Venous blood was drawn from all subjects after a 12- to 24-hour fast. Total cholesterol and HDL cholesterol levels were measured by automated enzymatic methods (27,28). Body mass index (BMI) was calculated from height and weight values measured at the clinic. Blood pressure was determined by duplicate measurements on the subject's left arm using a mercury sphygmomanometer with the subject in a sitting position. Cigarette smoking and menopausal status were self-reported. Pack-years of cigarette smoking was defined as the number of packs of cigarettes smoked per day multiplied by the total number of years a person smoked. This variable factors in smoking duration as well as level of cigarette consumption. Physical activity was assessed by questionnaire and a physical activity index was calculated (29).

Analysis

Our primary objective was to determine whether heart-healthy, compared with less-heart-healthy, dietary patterns were related to the presence of subclinical heart disease at 12 years of follow-up. The endpoint of interest was the presence of subclinical heart disease assessed by carotid artery stenosis, defined by focal lesions of 25% or more in either the right or left internal carotid artery, in accordance with our previously used threshold (4,14).

For descriptive purposes, age-adjusted mean levels of baseline CVD risk factors were computed for the dietary clusters. Analysis of covariance was used for calculating the least squares means of continuous variables using the SAS procedure PROC GLM (30). For categorical variables, age-adjusted means were computed using age-adjusted logistic regression (PROC LOGISITC) (30) and the standard errors of the age-adjusted means were calculated using the Delta theorem (31).

We then examined the relationship between the dietary patterns and the presence of subclinical heart disease at follow-up, using women who consumed a less-heart-healthy diet as the reference group. Odds ratios were calculated using logistic regression. Because smoking behavior is known to be a major risk factor for the development of carotid stenosis (32), and noting that there were differences in the smoking behaviors of women in the two dietary groups, an a priori decision was made to stratify the analyses by baseline smoking status (current, former, never). Multivariate models considered a range of CVD risk factors including age, BMI, systolic and diastolic blood pressure, total cholesterol, low-density lipoprotein (LDL) cholesterol, the total-to-HDL cholesterol ratio, plasma triglycerides, physical activity level, menopausal status, and conditions including obesity, diabetes, and hypertension. The final model reported here is limited to those variables that were identified as important predictors or potential confounders of the relationship of interest.

RESULTS

Figure 1 depicts the food consumption profile of women in the heart-healthy cluster, in relation to food intake guidelines of the Food Guide Pyramid (33). Heart-healthy women consumed adequate amounts of fruits, vegetables, and dairy products. They used fats, oils, and sweets sparingly and did not overindulge in sources of dietary protein. Consumption of breads, cereals, and grains seems to be less than recommended, and thus identifies increasing

Table 1. Age-adjusted distribution of CVD risk factors at baseline among heart-healthy and less-heart-healthy women (n=1,423)[a]

	Heart-healthy women (n=285)	Less-heart-healthy women (n=1,138)	*P*
Risk factor	← *LS mean±standard error* →		
Age (y)	49.7±0.6	47.0±0.3	.0001
Total cholesterol, mmol/L	5.29±0.06	5.46±0.03	.02
(mg/dL)	204.4±2.28	210.6±1.15	
LDL-C[d], mmol/L	3.27±0.06	3.40±0.03	.05
(mg/dL)	126.4±2.17	131.2±1.09	
HDL-C[e], mmol/L	1.50±0.02	1.48±0.01	.67
(mg/dL)	57.7±0.87	57.3±0.44	
Total-to-HDL cholesterol ratio	3.75±0.08	3.93±0.04	.048
BMI[f] (kg/m^2)	25.0±0.3	25.2±0.2	.49
Systolic blood pressure (mm Hg)	119.8±0.9	120.2±0.4	.63
Current smoker (%)	16.7±2.6	30.0±1.3	.0001
Former smoker (%)	42.1±1.0	30.3±0.3	.0002
Never (non)-smoker (%)	41.1±1.0	39.5±0.3	.6142
Pack-years smoking[b]	6.8±1.0	10.4±0.5	.0012
Subclinical heart disease (%) (at follow-up)[c]	6.9±0.7	11.0±0.3	.02

[a]Analysis of covariance was used for calculating the least square means of continuous variables; Age-adjusted logistic regression was used to calculate age-adjusted means for categorical variables (reference 30). Standard errors for categorical variables were calculated using the Delta theorem (reference 31).
[b]Defined as number of cigarettes smoked per day multiplied by total years of smoking.
[c]Defined as maximum stenosis of the left or right carotid artery that is equal to or exceeds 25%; measured at 12-year follow-up.
[d]LDL-C=low-density lipoprotein cholesterol.
[e]HDL-C=high-density lipoprotein cholesterol.
[f]BMI=body mass index.

Table 2. Odds ratios for subclinical heart disease[a] among heart-healthy women (n=285), compared with less-heart-healthy women (n=1,138)

	Heart-healthy cluster	
Models	**Odds ratio (95% CI)**	***P* value**
Age-adjusted	0.60 (0.38, 0.92)	.02
Age, SBP[b], BMI[c]-adjusted	0.61 (0.38, 0.94)	.03
Age, SBP, BMI, total/HDL-C[d]–adjusted	0.65 (0.41, 1.01)	.06
Age, SBP, BMI, total/HDL-C, pack-years–adjusted[e]	0.74 (0.45, 1.17)	.20

[a]Stenosis of the left or right carotid artery, ≥25%.
[b]SBP=systolic blood pressure.
[c]BMI=body mass index.
[d]HDL-C=high-density lipoprotein cholesterol.
[e]Defined as number of cigarettes smoked per day multiplied by total years of smoking.

consumption of whole grains as a behavioral target of importance for these women. Women with less-heart-healthy dietary patterns had lower daily mean intakes of most food groups (vegetables, 2.7 servings; breads, 3.0 servings; fruits, 1.9 servings; milk, 1.4 servings; and meat, 1.5 servings) but higher intakes of fats (5.6 servings). As previously published (24), our estimates of consumption from both the grains and protein food groups underestimate actual intake because of the inability to completely sort out servings of these foods from mixed dishes and combination food items surveyed on the food frequency questionnaire.

The baseline CVD risk factor profiles of women who consumed a heart-healthy diet were different from those women whose diets were less heart-healthy (Table 1). Heart-healthy women were older, had lower total and LDL cholesterol levels and total-to-HDL cholesterol ratios, were less likely to be current smokers, and had lower lifetime (pack-years) cigarette exposure compared with women whose diets were less heart-healthy. Only 7% of heart-healthy women had subclinical heart disease at follow-up, compared with 11% in all other women.

The age-adjusted and multivariate odds ratios for subclinical heart disease among heart-healthy women compared with those whose diets were less heart-healthy are shown in Table 2. In age-adjusted analyses, heart-healthy women were 40% less likely to have subclinical CVD compared with those whose diets were less heart-healthy (age-adjusted OR 0.60, $P=.02$). After adjusting for systolic blood pressure and BMI, heart-healthy women continued to display lower odds for subclinical heart disease (adjusted OR 0.61; $P=.03$). Adding the total-to-HDL cholesterol ratio to the model only slightly attenuated the odds ratio (OR 0.65; $P=.06$). The addition of smoking behavior to the model substantially attenuated the estimate of odds (OR 0.74; $P=.20$).

Table 3. Odds Ratio (95% CI) for subclinical heart disease by baseline dietary pattern and smoking status (N=1,421)

		Age-adjusted		Multivariate-adjusted[a]	
Dietary Cluster, Smoking Status	**n**	**OR (95%CI)**	***P***	**OR (95%CI)**	***P***
Less heart-healthy, current smoker	345	1.0		1.0	
Less heart-healthy, former smoker	345	0.28 (0.17, 0.46)	.0001	0.34 (0.21, 0.57)	.0001
Less heart-healthy, never smoker	447	0.30 (0.19, 0.46)	.0001	0.33 (0.21, 0.53)	.0001
Heart-healthy, current smoker	45	0.45 (0.17, 1.04)	.078	0.56 (0.21, 1.34)	.2165
Heart-healthy, former smoker	120	0.34 (0.17, 0.63)	.009	0.41 (0.20, 0.79)	.0103
Heart-healthy, never smoker	120	0.15 (0.06, 0.31)	.0001	0.17 (0.07, 0.36)	.0001

[a]Adjusted for age, systolic blood pressure, body mass index, and total-to-HDL-cholesterol ratio.

In Table 3, we present the age-adjusted and multivariate-adjusted odds ratios for subclinical heart disease after stratifying heart-healthy women and those with less heart-healthy dietary patterns according to baseline smoking status (current, former, never). The reference group for these analyses was women who had less heart-healthy diets and were current smokers. The complete avoidance of smoking was associated with dramatically lower odds in both dietary groups (67% to 85% lower odds; $P=.0001$). Former smokers had statistically significantly lower odds of developing carotid stenosis (59% to 66% lower odds), regardless of dietary pattern ($P<.01$). There were also apparent benefits of a heart-healthy diet among women who smoked. Current smokers who consumed a heart-healthy diet had a 44% lower odds of developing carotid stenosis, albeit the group was small (n=45), and the statistical significance of the results were attenuated on age and multivariate adjustment ($P=.078$ and $P=.2165$, respectively). Women who consumed a heart-healthy diet and who had never smoked had the overall lowest odds of subclinical heart disease. Compared with women in the reference group, women who consumed a heart-healthy diet and who had never smoked had a greater than 80% lower odds of carotid stenosis (multivariate-adjusted OR 0.17; $P=.0001$).

DISCUSSION

Framingham women with a heart-healthy dietary pattern exhibited more favorable CVD risk factor profiles at baseline and lower prevalence rates of subclinical heart disease, as measured by carotid atherosclerosis, at 12 years of follow-up compared with women whose diets were less heart-healthy at baseline. The heart-healthy dietary pattern, alone or in combination with the avoidance of smoking, was associated with lowered odds for subclinical cardiovascular disease and multivariate adjustment for BMI, blood pressure, and lipid levels attenuated these relationships only slightly.

Our data are consistent with newly emerging literature on the relationship between dietary patterns and other modifiable lifestyle risk factors and the development of CVD. In the Zutphen Elderly Study (34), a more healthful dietary pattern was associated with more favorable levels of cardiovascular risk factors compared with other dietary patterns of elderly men. Among men in the Health Professionals cohort and women in the Nurses Health Study, a prudent eating pattern, similar to our heart-healthy pattern, was associated with reduced CVD risk (35,36).

Recent literature has also demonstrated that the relationships between traditional CVD risk factors, including smoking, increased blood pressure, and abnormal lipid levels, on the development of subclinical heart disease (carotid artery stenosis) (32). However, the observation here that a heart-healthy eating pattern in Framingham women is associated with lower risk for subclinical CVD in women who formerly smoked or never smoked is a relatively unique finding. These observations are consistent with available literature on the combined influences of lifestyle behaviors on heart disease outcomes. Stampfer et al (37) recently demonstrated that the women in the Nurses Health Study who exhibited prudent eating behavior, nonsmoking status, and higher physical activity levels had lower risks for CHD at 14 years of follow-up.

Women who consumed a heart-healthy diet and who had never smoked had the overall lowest odds of subclinical heart disease.

Interest in carotid artery stenosis as a marker of atherosclerotic vascular disease has been piqued for two reasons: the simplicity of its measurement and its potential role in guiding the development of, and possibly the evaluation of, primary preventive interventions. Measurement of carotid stenosis is possible using high-resolution B-mode ultrasonography, a technique that is now recognized as a useful indicator of subclinical CVD (14,26,32). Though measuring carotid atherosclerosis is well-accepted as a practical indicator for subclinical CVD (5,7-11), little is known about the combined impact of modifiable lifestyle behaviors (such as smoking, eating habits, and physical activity) over time on the extent of carotid atherosclerosis. In fact, to our knowledge, no other studies have prospectively observed the prevalence of carotid stenosis measured over 12 years within population subgroups with unique dietary and behavioral profiles.

We carried out analyses in which we excluded 54 women (3.8% of the sample) in whom CVD developed. Of these 54 women, 22 (41%) had carotid atherosclerosis at follow-up. Analyses excluding these 54 women were consistent with those reported here and confirm that dietary behavior patterns, alone and in combination with smok-

ing behavior, are associated with the presence of asymptomatic CVD in women. Thus, the manifestation of CVD does not seem to drive the observed relationship between dietary patterns, smoking, and subclinical heart disease.

We note that generalizing these observations within Framingham women may be limited to the white population because of the low proportion of minorities in the FOS cohort. Nonetheless, these findings emphasize the importance of additional research that explores the association between dietary patterns and health outcomes in more diverse populations.

CONCLUSIONS

- Nutrition professionals need to recognize the importance of heart-healthy eating behavior in the primary prevention of CVD and should advocate with their professional colleagues for preventive nutrition interventions in healthy clients as well as those who have subclinical heart disease.
- A heart-healthy dietary pattern is associated with lower risk for subclinical heart disease, particularly when combined with the cessation and avoidance of smoking. Nutrition professionals should assess the dietary patterns and smoking status of their clients and counsel them about methods to promote heart-healthy eating behaviors. Among smokers, smoking cessation should be explored and combined with dietary intervention strategies.
- Our findings also suggest several important public health messages for women, which include: a) significantly lower odds of subclinical heart disease is associated with a heart-healthy dietary pattern; b) the combination of a heart-healthy dietary pattern and avoidance of smoking is associated with the lowest odds of subclinical CVD; and c) smokers, including those who cannot or do not quit, seem to achieve some level of benefit by making dietary behavior changes toward heart-healthy eating. These messages need to be included in health campaigns to reduce CVD risk in women.
- The heart-healthy dietary pattern (characterized by higher consumption of vegetables, fruits, whole grains, leaner protein sources, and lower-fat dairy products; lower intake of dietary fats; and higher nutrient density, specifically vitamins B-6, E, C, and folate) is achievable for women and can be modeled and evaluated in health promotion campaigns and tailored behavioral interventions. The benefit of this dietary pattern alone, but particularly in combination with the complete avoidance of smoking, is noteworthy and should be promoted. The specific features of the less healthful dietary patterns (higher intakes of visible fats and lower fruit, vegetable, whole grain, dairy and micronutrient consumption) also offer discrete targets for preventive behavioral interventions to reduce CVD risk.
- To achieve national goals related to healthful aging, nutrition professionals need to extend the emerging research on population dietary patterns and the relationships between dietary patterns, adverse health outcomes, and overall health promotion in women (22-24,38). Professionals also need to use innovative strategies to incorporate the key features of population dietary patterns (22-24,39) in planning preventive nutrition interventions (40). Given the major impact of CVD on morbidity and mortality of women, further research is needed to establish the feasibility and benefits of total dietary and lifestyle approaches in primary prevention and long-term CVD risk reduction (40-42).

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