

# Dietary Patterns and the Odds of Carotid Atherosclerosis in Women: The Framingham Nutrition Studies<sup>1</sup>

Barbara E. Millen, Dr.P.H., R.D., FADA,\*†<sup>2</sup> Paula A. Quatromoni, D.Sc., R.D.,\* Byung-Ho Nam, Ph.D.,‡  
Catherine E. O'Horo, R.D.,\* Joseph F. Polak, M.D., M.P.H.§ and Ralph B. D'Agostino, Ph.D.‡

\*Department of Social and Behavioral Sciences, School of Public Health, †Department of Sociomedical Sciences and Division of Graduate Medical Sciences, School of Medicine, and ‡Department of Mathematics, Boston University, Boston, Massachusetts 02118; and §Department of Radiology, Brigham and Women's Hospital, Boston, Massachusetts 02115

**Background.** We prospectively examined the relationship between dietary patterns, assessed using cluster analysis and a food frequency questionnaire, and the presence of carotid artery stenosis, a subclinical marker of atherosclerotic disease.

**Methods.** Analyses were conducted among 1,423 Framingham Study women without cardiovascular disease (CVD) at baseline (1984–1988). Carotid atherosclerosis (stenosis  $\geq 25\%$ ) was measured by ultrasound 12 years later.

**Results.** Baseline differences in risk factor profiles were notable across five dietary subgroups. Compared to the more desirable profiles of women with Heart Healthy eating patterns, women who had Light Eating, High Fat, or Empty Calorie diets had higher rates of dyslipidemia and smoking and lower levels of physical activity. At follow-up, the prevalence of carotid atherosclerosis ranged from 6.8% in the Heart Health group to 17.8% in the Empty Calorie group. Compared with Heart Health women, all other groups displayed higher age-adjusted odds for carotid stenosis. In multivariate analyses, those with Empty Calorie diets had more than twofold increased odds of carotid atherosclerosis compared to Heart Health women (OR 2.28, 95% CI [1.12, 4.62];  $P < 0.05$ ).

**Conclusion.** The association among unique dietary patterns, CVD risk factor profiles, and the presence of subclinical atherosclerosis identifies candidates and strategies for preventive behavioral interventions to promote the primary prevention of heart disease. © 2002 American Health Foundation and Elsevier Science (USA)

**Key Words:** cardiovascular disease; carotid atherosclerosis; carotid artery stenosis; cluster analysis; di-

etary patterns; preventive nutrition intervention; primary prevention.

## INTRODUCTION

In a given year, about 2.5 million American women will be hospitalized for cardiovascular illnesses and over a lifetime half of the female population will die of heart disease or stroke [1,2]. One in nine females ages 45–65 years and one in three over age 65 have some form of the disease [2–4]. Despite the magnitude of this problem and the ramifications on population health, women have been underrepresented in research on cardiovascular disease (CVD) risk and management, particularly with respect to identifying ideal candidates for primary prevention and the development of interventions for CVD risk reduction [5,6].

Carotid artery stenosis, a subclinical marker of systemic atherosclerosis [7–9], predicts the development of coronary heart disease (CHD) and cerebrovascular events [7,10–17]. Increased prevalence rates for CHD and stroke are noted at levels of carotid artery stenosis above 25% [18]. About 35% of older adult women in the original Framingham cohort have carotid atherosclerosis measurements of this magnitude [19].

The assessment of carotid stenosis is possible using high-resolution B-mode ultrasonography, a noninvasive technique that is increasingly recognized as a useful indicator of subclinical cardiovascular diseases [19–23]. The technique enables the identification of potential candidates for primary prevention activities and may facilitate the evaluation of interventions aimed at delaying the development of atherosclerosis [7,22]. In this report, we examined the associations among dietary patterns, CVD risk factor profiles, and the presence of carotid atherosclerosis measured by ultrasonography at 12 years of follow-up in Framingham Offspring/Spouse women.

<sup>1</sup> This research was supported, in part, by NIH Heart, Lung, and Blood Institute Grant R01-HL-60700 and the Framingham Study Contract N01-HC-38038 (Bethesda, MD).

<sup>2</sup> To whom correspondence and reprint requests should be addressed at Department of Social and Behavioral Sciences, Boston University School of Public Health, Room 263W, 715 Albany Street, Boston, MA 02118. Fax: (617) 414-1390. E-mail: bmillen@bu.edu.

## METHODS

*Study sample.* The Framingham Study was initiated in 1948 as a longitudinal population-based study of cardiovascular disease. The original Framingham cohort consisted of 5,209 men and women, representing a two-thirds systematic sample of the residents of the town of Framingham, Massachusetts [24,25]. In 1971, some 5,124 Framingham Study offspring and their spouses were recruited to participate in the Framingham Offspring/Spouse (FOS) study [26].

Members of the FOS cohort are examined in the Framingham Study clinic about every 4 years. They participate in a standardized protocol involving a complete physical examination, laboratory tests, noninvasive diagnostic testing such as assessment of carotid artery stenosis, and updating of medical histories and other pertinent information. The data collection protocols and procedures were approved for human subjects by the Office of the Institutional Review Board at Boston University School of Medicine, Boston Medical Center. The baseline dietary and risk factor data reported here were collected among FOS women at Exam 3, between 1984 and 1988. Some 2,005 women, ages 18 to 76 years, participated in this exam (83% of eligible women). All 88 women with CVD at Exam 3 were excluded from these analyses (4.4%).

*Dietary assessment.* Dietary patterns were characterized using cluster analysis applied to food consumption data derived from the validated Framingham food frequency questionnaire (FFQ) [27]. In brief, the 145 food items on the FFQ were classified into 42 categories, based on similarities in nutrient content (such as vitamin-A-rich vegetables, medium-fat meats). Next, the 42 food categories were clustered using standard statistical methods (Varclus in SAS) into 13 food groupings according to similarities in frequency of consumption (number of daily servings reported) within the cohort. This procedure grouped foods according to their usual frequency of consumption, not by consumption at similar times of day, at the same meal, or in similar serving sizes. This resulted in grouping of foods that may or may not be consumed together, but rather with a similar frequency pattern. For example, women who reported a relatively higher frequency of consumption of fruits also reported a higher frequency of consumption of low-fat milk products. Finally, Ward's clustering method [28] was used to separate women into nonoverlapping groups based upon similarities in the frequency of their consumption of these food groupings.

Five clusters of women were identified through this process, each with unique dietary patterns (Table 1 and Fig. 1). Details were published previously, including differences in the mean servings of food groups and mean nutrient intake profile of each group of women [29]. Consistently, our findings support the choice of

one group of women, those with a Heart Healthy dietary pattern, as a reference group for epidemiological analyses because their eating pattern is most comparable with population-based dietary guidelines for health promotion [29–31]. We demonstrated the internal validity of the dietary pattern analysis and its ability to discriminate groups of individuals with similar dietary patterns using independently assessed nutrient intakes and heart disease risk factors [30]. We also verified the stability of the dietary patterns over time, by evaluating intake levels of key nutrients at 8 years postbaseline, and demonstrated that differences in nutrient profiles across the clusters are maintained over time.

*Assessment of carotid atherosclerosis.* Among 1,751 women who provided complete dietary data and who were free of CVD at baseline, the presence of carotid atherosclerosis was assessed at 12 years of follow-up (Exam 6, 1996–1999). Carotid ultrasound studies were obtained on 1,423 participants (81.3%). Missing measurements were exclusively due to logistic constraints at the clinic (unavailability of either the ultrasound device or the sonographer during the scheduled visit). Ultrasound imaging studies were conducted with a high-resolution linear array 5.0-MHz transducers and a color Doppler ultrasound device (Toshiba SSH-140; Toshiba Medical Systems, CA). Imaging was performed with the subject's head rotated 45° away from the side being studied, according to a standard protocol. Two grayscale images were taken at the level of the common carotid artery bulb and two additional images were obtained in the proximal 2 cm of the internal carotid artery. One image of the respective image pairs was acquired with the probe held at 45° with the horizontal. For the second image, the sonographer was instructed to position the transducer to best identify any focal lesions. All images were gated to the R-wave of an electrocardiogram and both sides of the neck were imaged. Images were directly transferred into a computer workstation through a frame-grabber board.

Color Doppler imaging and pulsed Doppler waveforms were used to evaluate blood flow velocities in the proximal internal carotid arteries. Angle-corrected Doppler velocity waveforms were acquired in the proximal internal carotid artery, at the site of highest velocity as identified on a color Doppler image. Peak-systolic velocities were measured from these tracings. A certified reader reviewed the acquired digital images and made a subjective estimate of the degree of internal carotid artery narrowing, graded as 0, 1–24, or 25–49% when Doppler-derived peak systolic velocities in the internal carotid artery were less than 150 cm/s. Internal carotid artery disease was characterized by the maximum stenosis observed on the right or left side and was categorized as 0 (no lesions), 1–24, or 25–49% (focal lesions causing a stenosis of less than 50% diam-

**TABLE 1**  
Key Features of Dietary Patterns Identified among Framingham Women

Dietary patterns	
Heart Healthy	Higher in fruits, vegetables, low-fat dairy, and other lower-fat foods including whole grains, skinless poultry, and fish; lowest in total and saturated fat content; higher in fiber and micronutrient density (calcium and folate)
Light Eating	Lower in sweets, animal and vegetable fats, and refined grains; lowest in caloric content
Wine and Moderate Eating	Lower intake of desserts; higher intake of snack foods, eggs, and wine; highest in alcohol and dietary cholesterol content with lowest calcium consumption
High Fat	Higher in sweets, animal and vegetable fats, refined grains and margarine; fewer lower-fat foods; highest in total and saturated fat content
Empty Calorie	Higher in sweetened beverages, red meats, and desserts; lower in fruits and vegetables; high in sugar, total fat, and saturated fat, lower in fiber and micronutrient density (including folate)

eter narrowing) and  $\geq 50\%$  (lesions causing 50% or more diameter stenosis). Absence of blood flow corresponded to a total occlusion.

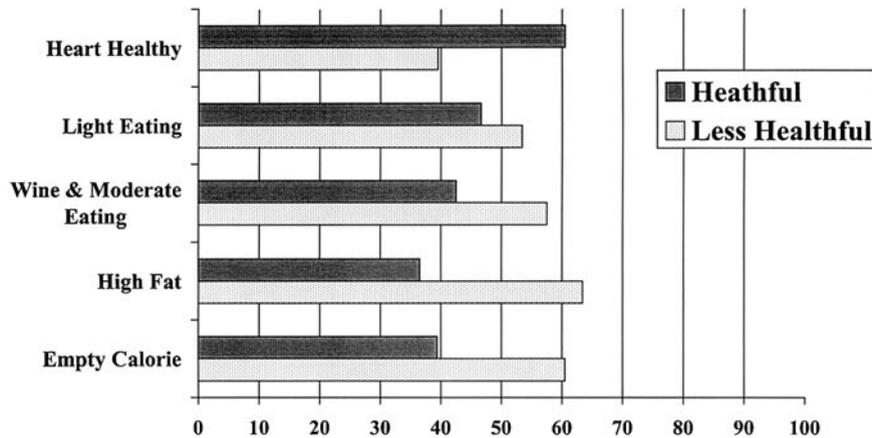
**Risk factor measurement.** CVD risk factors are routinely measured at all exams. Methods for determining risk factor status within the Framingham Study have been summarized by Cupples and D'Agostino [32] and are highlighted here. All lipid analyses were performed at the Framingham Heart Study laboratory, which participated in the Standardization Program of the Centers for Disease Control and the National Heart, Lung, and Blood Institute Lipid research clinics. Venous blood was drawn from all subjects after a 12- to 24-h fast. Total cholesterol and high-density lipoprotein cholesterol levels (HDL) were measured by automated enzymatic methods [33,34]. Diabetes was defined as a history of use of insulin or an oral hypoglycemic agent, or a fasting blood glucose level of 7.8 mmol/L (140 mg/dL) or greater. Body mass index (BMI) was calculated from height and weight values measured at the Framingham 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, use of estrogen replacement hormones, 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. Physical activity was assessed by questionnaire to determine estimates of activity in a usual day based on a 24-h history [35]. A physical activity index score ranges from 24 (total bed rest) to 120. Since physical activity was not measured at Exam 3, Exam 2 values are substituted in these analyses, adhering to the analytic approach routinely used in the Framingham Study. Family history of CVD was ascertained from the Framingham Study sequence of events file based on confirmed cases of stroke and myocardial infarction that occurred among mothers and fathers of Framingham Offspring. We had complete data on 80% of mothers and 90% of fathers of FOS women in the cohort of interest.

**Analysis.** Our major analytical objective was to determine whether dietary behavior patterns were predictive of the presence of carotid atherosclerosis at 12 years of follow-up. The endpoint of interest was carotid artery stenosis, defined by focal lesions of  $\geq 25\%$  in either the right or the left internal carotid artery, in accordance with our previously used threshold [19,36]. Age-adjusted mean levels of CVD risk factors were computed for each cluster. For continuous variables, we used the analysis of covariance procedure (GLM in SAS) [37] to compute the least square means. For dichotomous variables, age-adjusted proportions were computed using logistic regression models [38].

We examined the prospective relationship between dietary patterns and the presence of carotid atherosclerosis using the dietary pattern that most closely approximated current population dietary guidelines [31] as the reference group (the Heart Healthy dietary pattern [29]). Odds ratios were calculated using logistic regression [38]. Multivariate models considered a range of traditional CVD risk factors, including age, BMI, cigarette smoking, systolic and diastolic blood pressure, total cholesterol, LDL cholesterol, the ratio of total to HDL cholesterol, plasma triglycerides, physical activity level, menopausal status, and conditions including obesity, diabetes, and hypertension. Common CVD risk factors were introduced into multivariate analytical models and were evaluated as predictors and confounders in our model-building approach. We did not use stepwise or backward elimination methods. The final model reported here is limited to include those variables that were identified as important predictors or potential confounders of the relationship of interest.

## RESULTS

Distinct dietary patterns exist among five clusters of women in the FOS cohort. Framingham women display Heart Healthy, Light Eating, Wine and Moderate Eating, High Fat, and Empty Calorie dietary patterns. Table 1 summarizes the key features characteristic of



**FIG. 1.** Healthful<sup>a</sup> vs less healthful<sup>b</sup> daily food selections<sup>c</sup>. <sup>a</sup> Vegetables; fruits and low-fat milk; other low-fat foods; legumes, soups, and misc; meats and mixed dishes. <sup>b</sup> Refined grains, margarine, and oils; diet beverages and firm vegetable fats; sweets and animal fats; desserts; sweetened beverages; wine and cholesterol-rich foods; high-fat dairy and snack foods; fattier poultry and beer. <sup>c</sup> Proportion of daily food selections, based on standard serving sizes.

each dietary pattern, noting the relative level of intake (higher versus lower) of food selections and nutrient intake. Figure 1 provides a graphic depiction of the differences in “healthful” food consumption patterns of women in each dietary cluster. Overall, the Heart Healthy cluster is characterized by a dietary pattern consisting of more servings of lower-fat, nutrient dense food selections, fewer higher-fat, less nutritious foods, lower total and saturated fat intake, and higher fiber and micronutrient density, specifically calcium and folate. At the other end of the spectrum, the High Fat and the Empty Calorie dietary patterns are characterized by the intake of less healthful food choices, higher total and saturated fat intake, and lower micronutrient and fiber consumption. Women in the Light Eating and Wine and Moderate Eating groups display more temperate eating behaviors although with relatively fewer healthier food selections. Notably lower energy intakes were reported by women with Light Eating habits, whereas higher alcohol and cholesterol intakes and lower calcium intakes were noted among women in the Wine and Moderate Eating cluster.

Baseline risk factor levels of women with a Heart Healthy dietary pattern (reference group) are compared to those in the other dietary groups in Table 2. Compared with Heart Healthy women, those in the Light Eating, High Fat, and Empty Calorie groups were younger. They were also more likely to have dyslipidemia, to be current smokers with higher lifetime cigarette exposure (pack-years), and to be less physically active. Moreover, women in the Wine and Moderate Eating group had higher levels of systolic blood pressure albeit higher HDL cholesterol levels compared with Heart Healthy women. In addition, those in the Empty Calorie group had higher levels of systolic blood pressure and higher BMI. About 7% of Heart Healthy women had carotid atherosclerosis at follow-

up, compared with approximately 10% of Wine and Moderate Eating and High Fat women, 11% of Light Eating women ( $P < 0.05$ ), and 18% of Empty Calorie women ( $P < 0.05$ ).

The odds ratios for carotid atherosclerosis among women in the four comparison dietary clusters are presented in Table 3. In age-adjusted models, increased odds for subclinical atherosclerosis were observed in all groups compared to Heart Healthy women; odds were 60% higher among Light Eating women (OR 1.60, 95% CI [1.01, 2.53]) and nearly three-fold higher among those in the Empty Calorie group (OR 2.96, 95% CI [1.54, 5.68]). The addition of CVD risk factors to the model attenuated these relationships, although those with an Empty Calorie eating pattern maintained more than a doubling of the odds for subclinical disease (OR 2.28, 95% CI [1.12, 4.62]) compared to Heart Healthy women.

## DISCUSSION

Cluster analysis demonstrated the presence of five distinct dietary patterns in Framingham women that are associated cross-sectionally with cardiovascular disease risk factor profiles and with the presence of subclinical carotid atherosclerosis at 12 years of follow-up. The over twofold increase in the odds of carotid stenosis among women who display an Empty Calorie dietary pattern and, conversely, the protective benefit of a Heart Healthy dietary profile with respect to subclinical atherosclerotic disease are particularly noteworthy. The differences in cardiovascular disease risk factor profiles between women with differing dietary patterns warrant attention.

Our data are consistent with emerging literature on the relationship between dietary patterns and the development of CVD. Huijbregts *et al.* [39] applied cluster

TABLE 2

Age-Adjusted CVD Risk Factor Profiles among Clusters of Women ( $n = 1,423$ ): LS mean (95% CI)

Baseline risk factor levels	Heart Healthy ( $n = 285$ )	Light Eating ( $n = 681$ )	Wine and Moderate Eating ( $n = 51$ )	High Fat ( $n = 289$ )	Empty Calorie ( $n = 117$ )
Age (years)	49.7 (48.6, 50.9)	47.4 (48.2, 46.7)*	47.9 (45.2, 50.6)	46.7 (45.6, 47.9)*	44.4 (42.7, 46.2)*
Total cholesterol (mg/dL)	204.4 (199.9, 208.8)	210.5 (207.6, 213.4)*	202.7 (192.2, 213.3)	211.7 (207.3, 216.2)*	212.2 (205.0, 219.4)
HDL cholesterol (mg/dL)	57.8 (56.1, 59.5)	58.6 (57.5, 59.7)	62.3 (58.2, 66.3)*	54.6 (52.9, 56.3)*	53.9 (51.2, 56.6)*
Ratio of total to HDL cholesterol	3.75 (3.58, 3.91)	3.85 (3.75, 3.96)	3.41 (3.03, 3.79)	4.09 (3.92, 4.25)*	4.26 (4.00, 4.51)*
LDL cholesterol (mg/dL)	126.3 (122.1, 130.6)	130.0 (127.2, 132.7)	118.5 (108.7, 128.3)	134.8 (130.6, 139.1)*	135.3 (128.4, 142.2)*
BMI <sup>a</sup> (kg/m <sup>2</sup> )	25.0 (24.4, 25.5)	25.3 (24.9, 25.7)	25.7 (24.4, 27.1)	24.4 (23.9, 25.0)	26.2 (25.3, 27.1)*
SBP <sup>b</sup> (mm Hg)	119.7 (118.0, 121.5)	120.0 (118.9, 121.1)	126.2 (122.1, 130.2)*	118.6 (116.9, 120.3)	123.1 (120.4, 125.8)*
Current smoker (%)	16.2 (14.5, 17.9)	24.8 (23.9, 25.7)*	29.5 (22.6, 36.4)	36.6 (34.7, 38.5)*	42.9 (38.9, 46.9)*
Pack years of smoking <sup>c</sup>	6.8 (4.8, 8.8)	9.6 (8.4, 10.9)*	9.3 (4.7, 13.8)	11.6 (9.7, 13.5)*	12.8 (9.8, 15.8)*
Physical activity index <sup>d</sup>	34.6 (34.0, 35.2)	33.7 (33.3, 34.0)*	33.2 (31.8, 34.6)	33.4 (32.8, 34.0)*	33.4 (32.5, 34.3)*
Postmenopausal (%)	44.5 (41.9, 47.1)	42.6 (41.3, 44.0)	33.3 (25.2, 41.4)	47.5 (45.0, 50.0)	51.6 (46.6, 56.6)
Estrogen use (%)	6.1 (4.7, 7.4)	3.8 (3.2, 4.5)	7.6 (2.4, 12.8)	4.1 (2.9, 5.3)	4.5 (2.0, 7.0)
Diabetes <sup>e</sup> (%)	1.8 (0.7, 2.8)	2.5 (1.9, 3.0)	3.7 (0, 8.1)	1.3 (0.4, 2.3)	0.9 (0, 2.6)
Family history: father with an MI <sup>f</sup> before age 55 (%)	2.3 (1.1, 3.6)	3.1 (2.4, 3.9)	2.1 (0, 6.7)	4.4 (2.9, 5.9)	4.6 (1.8, 7.4)
Family history: father with a CVA <sup>g</sup> before age 65 (%)	5.7 (4.1, 7.4)	5.1 (4.2, 6.0)	14.6 (7.4, 21.8)	4.9 (3.4, 6.5)	7.2 (4.0, 10.5)
Family history: mother with a CVA <sup>g</sup> before age 65 (%)	4.3 (2.8, 5.7)	3.4 (2.6, 4.2)	7.2 (1.1, 13.3)	3.2 (1.7, 4.6)	3.7 (1.1, 6.3)
Follow-up prevalence Carotid atherosclerosis <sup>h</sup> (%)	6.8 (4.8, 8.8)	10.5 (9.3, 11.7)*	9.9 (1.5, 18.3)	9.8 (7.3, 12.3)	17.8 (13.2, 22.4)*

Note. The significantly higher rate of paternal history of CVA in the Wine and Moderate Eating cluster noted here may be an artifact of the small number of women in this cluster, with 6 cases of a positive family history arising among only 41 women; statistical significance may be due to chance.

<sup>a</sup> BMI, body mass index.

<sup>b</sup> SBP, systolic blood pressure.

<sup>c</sup> Pack-years smoking defined as number of cigarettes smoked per day multiplied by total years of smoking.

<sup>d</sup> Physical Activity Index was measured at Exam 2.

<sup>e</sup> Diabetes defined as a history of use of insulin or an oral hypoglycemic agent, or a fasting blood glucose level of 7.8 mmol/L (140 mg/dL) or greater.

<sup>f</sup> Myocardial infarction, defined as MI recognized with diagnostic electrocardiogram (ECG); or MI recognized without diagnostic ECG but with transaminase and history; we could not estimate maternal history for this variable due to the small numbers of MI events among women in the cohort.

<sup>g</sup> Cerebrovascular accident (stroke), defined as CVA including atherothrombotic infarction, transient ischemic attack, cerebral embolism, intracerebral hemorrhage, subarachnoid hemorrhage, other CVA, or questionable CVA.

<sup>h</sup> Defined as stenosis of the left or right carotid artery of  $\geq 25\%$ .

\* Means are significantly different from the mean in the Heart Healthy cluster ( $P < 0.05$ ).

analysis to a dietary history methodology and characterized four dietary patterns. In their cross-sectional analyses, a healthy diet was associated with more favorable levels of cardiovascular risk factors. Similarly, a longitudinal analysis carried out by Farchi *et al.* [40] demonstrated differences in overall mortality rates between clusters of men aggregated on the basis of dietary patterns. While these observations are important, we note that neither of these studies was conducted in women, nor did they consider the relationships among dietary behaviors, other modifiable risk factors, and specific cardiovascular disease outcomes. More recently, however, Stampfer *et al.* [41]

reported that prudent eating behavior, when considered in conjunction with nonsmoking behavior and physical activity, reduces risk for coronary heart disease in women.

To determine whether the manifestation of CVD was driving the relationship we observed between dietary patterns and carotid atherosclerosis, we carried out additional analyses excluding all 54 women (3.8% of the sample) who developed CVD during the 12 years of follow-up. Those analyses were consistent with the findings reported here and confirm the increased age-adjusted odds for stenosis among women with Light Eating dietary patterns, the over twofold increased

TABLE 3

Odds Ratio for Carotid Atherosclerosis<sup>a</sup> with Heart Healthy as the Referent Group (*N* = 1,423) OR (95% CI)

	Heart Healthy ( <i>n</i> = 285)	Light Eating ( <i>n</i> = 681)	Wine and Moderate Eating ( <i>n</i> = 51)	High Fat ( <i>n</i> = 289)	Empty Calorie ( <i>n</i> = 117)
Age-adjusted	1.0	1.60 (1.01, 2.53)*	1.49 (0.57, 3.89)	1.49 (0.87, 2.56)	2.96 (1.54, 5.68)**
Multivariate-adjusted <sup>b</sup>	1.0	1.39 (0.86, 2.32)	1.34 (0.45, 3.48)	1.01 (0.55, 1.87)	2.28 (1.12, 4.62)*

<sup>a</sup> Stenosis of the left or right carotid artery,  $\geq 25\%$ .<sup>b</sup> Adjusted for age, systolic blood pressure, body mass index, the ratio of total to HDL cholesterol, and pack-years smoking.\* *P* < 0.05.\*\* *P* < 0.01.

odds associated with the Empty Calorie diet, and the protective aspects of the Heart Healthy eating pattern.

We note that the attenuation of the association between the Light Eating dietary pattern and carotid atherosclerosis when CVD risk factors were added to the multivariate model suggests that the influence of this dietary profile may be modulated through biological factors, in particular plasma lipid levels. Also, because the number of women who displayed the Wine and Moderate Eating pattern was relatively small (*n* = 51), a more precise estimate of relationships between this dietary pattern and health outcomes would require a larger subgroup with similar eating practices.

It appears important to further investigate the fairly dramatic baseline CVD risk factor profile but only modest increased odds for carotid stenosis among women with the High Fat dietary pattern. This observation is somewhat inconsistent with what might be anticipated. We note, however, that the High Fat dietary subgroup is in fact different from the Empty Calorie cluster in terms of food consumption behavior and nutrient intake profiles. The Empty Calorie group displays the most extreme profile; it is not only high in fat content but also highest in sugar and lowest in micronutrient density. The comprehensive nature of nutritional risk in this subgroup appears particularly important and has been confirmed by our previous analyses demonstrating a higher level of overall dietary risk in this subgroup of women [30,42]. Smoking and BMI profiles are also more extreme in Empty Calorie cluster compared with the High Fat subgroup, further supporting their likelihood for increased CVD risk.

Interest in carotid artery stenosis as a clinical marker of atherosclerotic disease has been peaked for two reasons: the simplicity of its measurement and its potential role in guiding the development and evaluation of primary preventive interventions. This technique is noninvasive, inexpensive, and safe and can be performed repeatedly, thus allowing investigators to demonstrate the increased risk for the development of coronary heart disease [7,10] and ischemic events [11–15] associated with carotid stenosis. Results of a Finnish study indicated that the presence of  $\geq 20\%$  carotid

stenosis increased the relative risk of incident myocardial infarction by almost sevenfold among men [7].

Our findings have important implications for designing preventive nutrition interventions. They characterize the dietary behaviors of distinct subgroups of women in the population that can be targeted in health promotion campaigns and behavioral interventions. These data indicate that individuals in a population have markedly different behavioral profiles and need different messages that are tailored to focus on specific aspects of eating behavior to promote successful modification of risk. This feature is clear, even among Heart Healthy women who would benefit from continued improvements in their dietary behavior to further lower their total fat intake and from ongoing reinforcement to sustain the positive behaviors they have already adopted. Nutrition promotion messages for this subgroup of women are equally as important, yet dramatically different, from messages that would be relevant to women in other dietary clusters. Dietary patterns may also be useful to screen for women with particularly problematic eating practices, such as those with the Empty Calorie and Light Eating profiles, who may be more prone to subclinical cardiovascular diseases because of their dietary choices and other aspects of their lifestyle profile (including smoking behavior).

Several successful interventions that have focused on dietary patterns for CVD risk reduction have recently emerged in the clinical literature. In the Dietary Approaches to Stop Hypertension trial, investigators witnessed the importance of the combined effects of foods and their constituent nutrients on lowering blood pressure levels among both normotensive and hypertensive men and women [43,44]. Similarly, Gambera *et al.* [45] demonstrated the effectiveness of a food-based behavioral intervention to reduce BMI, total cholesterol levels, and low-density lipoprotein levels in adult men and women. As well, patients with a history of coronary events experienced improved body weight and serum lipid levels and a reduction in the percentage diameter of coronary artery stenosis after participating in the Lifestyle Heart Program [46–48].

It is a potential limitation that our observations were

established in a cohort of women, the majority of whom are white residents of a western Boston suburban community. It should be noted, however, that the models for cardiovascular disease risk that have been formulated in the Framingham study have been repeated and confirmed in domestic and international populations [49–52]. Our data encourage further research on the relationships among dietary patterns, subclinical cardiovascular diseases, and other health outcomes.

It is a further potential limitation that our findings related to dietary patterns do not distinguish the relative influence of specific dietary components (such as individual fatty acids) on stenosis at follow-up. Nonetheless, the recent literature [30,39–43] discusses the confounding inherent in single-nutrient approaches and advocates for the improved understanding of the relationships between dietary patterns and health outcomes. Such information is believed to be critical for the future development of sound public health nutrition policies and behavioral interventions for risk reduction and health promotion.

This research points to the importance of understanding the distinctive dietary behaviors and CVD risk factor profiles of adult women. Further, it highlights the potential usefulness of these dietary profiles in preventive medicine practice, particularly for screening and the development of intervention strategies which target dietary patterns for the primary prevention of cardiovascular diseases. We demonstrated the distinct CVD risk factor profiles of five nonoverlapping subgroups of Framingham women and the particularly problematic baseline risk profiles associated with Light Eating, High Fat, and Empty Calorie diets. The longitudinal findings underscore the cardioprotective nature of a Heart Healthy dietary pattern and the detrimental impact, particularly of the Light Eating and Empty Calorie diets on the presence of subclinical atherosclerotic disease. The identification of women who are candidates for primary prevention and the development of behavioral interventions tailored to their unique dietary patterns, lifestyle behaviors, and CVD risk profiles offer considerable opportunity in preventive medicine.

## REFERENCES

1. American Heart Association. 1999 Heart and Stroke Statistical Update. Dallas: American Heart Association, 1998.
2. Chiamvimonvat V, Sternberg L. Coronary artery disease in women. *Can Fam Physician* 1998;44:2709–17.
3. Giardina EG. Call to action: cardiovascular disease in women. *J Womens Health* 1998;7:37–43.
4. Ginsini GF, Micheli S, Prisco D, Abbate R. Menopause and risk of cardiovascular disease. *Thromb Res* 1996;84:1–19.
5. Keller KB, Lemberg L. Coronary artery disease—ignored in women or inherently more lethal in women. *Am J Crit Care* 1998;7:77–9.
6. Redberg RF. Coronary artery disease in women: understanding the diagnostic and management pitfalls. *Medscape Womens Health* 1998;3:1–14.
7. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. *Atheroscler Thromb* 1991;11:1245–9.
8. Salonen JT. Is there a continuing need for longitudinal epidemiological research? The Kuopio ischaemic heart disease risk factor study. *Ann Clin Res* 1988;20:46–50.
9. Selhub J, Jacques PF, Boston AG, D'Agostino RB, Wilson PW, Belanger AJ, *et al*. Association between plasma homocysteine concentrations and extracranial carotid-artery stenosis. *N Engl J Med* 1995;332:286–91.
10. Kuller LH, Shemanski L, Psaty BM, Borhani NO, Gardin R, Haan MN, *et al*. Subclinical disease as an independent risk factor for cardiovascular disease. *Circulation* 1995;92:720–6.
11. Autret A, Saudeau D, Bertrans PH, Pourcelot L, Marchal C, de Boisvilliers S. Stroke risk in patients with carotid stenosis. *Lancet* 1987;1:888–90.
12. Ogren M, Hedblad B, Isacson S, Janzon L, Jungquist G, Lindell S. Ten year cerebrovascular morbidity and mortality in 68 year old men with asymptomatic carotid stenosis. *BMJ* 1995;310:1294–8.
13. Longstreth WT Jr, Shemanski L, Lefkowitz D, O'Leary DH, Polak JF, Wolfson SK Jr. Asymptomatic internal carotid artery stenosis defined by ultrasound and the risk of subsequent stroke in the elderly: the Cardiovascular Health Study. *Stroke* 1998;29:2371–6.
14. Inzitari D, Eliasziw M, Gates P, Sharpe BL, Chan RKT, Mel-drum HE, *et al*. The causes and risk of stroke in patients with asymptomatic internal-carotid-artery stenosis. *N Engl J Med* 2000;342:1693–1700.
15. Molloy J, Markus HS. Asymptomatic embolization predicts stroke and TIA risk in patients with carotid artery stenosis. *Stroke* 1999;30:1440–3.
16. Mansour M, Ashraf, Littooy FN, Watson WC, Blumofe KA, Heilizer TJ, *et al*. Outcome of moderate carotid artery stenosis in patients who are asymptomatic. *J Vasc Surg* 1999;29:217–27.
17. European Carotid Surgery Trialists' Collaborative Group. Risk of stroke in the distribution of an asymptomatic carotid artery. *Lancet* 1995;345:209–12.
18. O'Leary KH, Polak JF, Kronmal RA, Kittner SJ, Bond G, Wolfson SK Jr, *et al*. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. *Stroke* 1992;23:1752–60.
19. Selhub J, Jacques PF, Boston AG, D'Agostino RB, Wilson PW, Belanger AJ, *et al*. Relationship between plasma homocysteine, vitamin status and extracranial carotid-artery stenosis in the Framingham Study population. *J Nutr* 1996;126:1258s–65s.
20. AbuRahma AF, Pollack JA, Robinson PA, Mullins D. The reliability of color duplex ultrasound in diagnosing total carotid artery occlusion. *Am J Surg* 1997;174:185–7.
21. Modaresi KB, Cox TCS, Summers PE, Jarosz JM, Verma H, Taylor PR, *et al*. Comparison of intra-arterial digital subtraction angiography, magnetic resonance angiography and duplex ultrasonography for measuring carotid artery stenosis. *Br J Surg* 1999;86:1422–6.
22. Kuller L, Borhani N, Furberg C, Gardin J, Manolio T, O'Leary D, *et al*. Prevalence of subclinical atherosclerosis and cardiovascular disease and association with risk factors in the Cardiovascular Health Study. *Am J Epidemiol* 1994;139:1164–79.
23. Wilson PW, Hoeg JM, D'Agostino RB, Silbershatz H, Belanger AM, Poehlmann H, *et al*. Cumulative effects of high cholesterol levels, high blood pressure, and cigarette smoking on carotid stenosis. *N Engl J Med* 1997;377:516–22.
24. Dawber TR. The Framingham Study. The epidemiology of ath-

- erosclerotic disease. Cambridge (MA): Harvard Univ. Press, 1980.
25. D'Agostino RB, Kannel WB. Epidemiological background and design: the Framingham Study. *Proceedings of the ASA Sesquicentennial*. 1988–1989:707–18.
  26. Kannel WB, Feinleib M, McNamara PM, Garrison RJ, Costal W. An investigation of coronary heart disease in families: the Framingham Offspring Study. *Am J Epidemiol* 1979;110:281–90.
  27. Posner BM, Martin-Munley SS, Smigelski C, Cupples LA, Cobb JL, Schaefer E, *et al*. Comparison of techniques for estimating nutrient intake—the Framingham Study. *Epidemiology* 1992;3:171–7.
  28. Ward JH. Hierarchical grouping to optimize an objective function. *J Am Stat Assoc* 1963;58:236–44.
  29. Millen BE, Quatromoni PA, Gagnon DR, Cupples LA, Franz MM, D'Agostino RB. Dietary patterns of men and women suggest targets for health promotion: the Framingham Nutrition Studies. *Am J Health Promot* 1996;11:42–53.
  30. Quatromoni PA, Copenhafer DL, Demissie S, D'Agostino RB, O'Horo CE, Nam BH, *et al*. The internal validity of a dietary pattern analysis. *The Framingham Nutrition Studies*. *J Epidemiol Community Health* 2002;56:381–8.
  31. U.S. Department of Agriculture. *The food guide pyramid. Home and Garden Bulletin No. 252*. Hyattsville (MD): Human Nutrition Information Service, August 1992.
  32. Cupples LA, D'Agostino RB. Some risk factors related to the annual incidence of cardiovascular disease and death using pooled repeated biennial measurements: Framingham Heart Study, 30-year follow-up. In: Kannel WB, Wolf PA, Garrison RJ, editors. *The Framingham Study, an epidemiological investigation of cardiovascular disease*. Washington: Dept. of Health and Human Services; 1987. [NIH Publication No. 87-2703. (NTIS PB87-177499)].
  33. McNamara JR, Schaefer EJ. Automated enzymatic standardized lipid analyses for plasma and lipoprotein fractions. *Clin Chem Acta* 1987;166:1–8.
  34. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-magnesium precipitation procedure for quantification of high-density lipoprotein cholesterol. *Clin Chem* 1982;28:1379–82.
  35. Kannel WB, Sorlie P. Some health benefits of physical activity. *The Framingham Study*. *Arch Intern Med* 1979;139:857–61.
  36. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;97:1837–47.
  37. SAS Institute, Inc. *SAS user's guide, version 6, vol 1 and 2, 4th ed*. Cary (NC): SAS Institute, 1989.
  38. SAS/STAT Software. *Changes and enhancement for release 6.12*. Cary (NC): SAS Institute, 1996.
  39. Huijbregts PPCW, Feskens EJM, Kromhout D. Dietary patterns and cardiovascular risk factors in elderly men: the Zutphen Elderly Study. *Int J Epidemiol* 1995;24:313–20.
  40. Farchi G, Mariotti S, Menotti A, Seccareccia F, Torsello S, Fidanza F. Diet and 20-y mortality in two rural population groups of middle-aged men in Italy. *Am J Clin Nutr* 1989;50:1095–103.
  41. Stampfer MJ, Hu FB, Manson JE, *et al*. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000;343:16–22.
  42. Millen BE, Quatromoni PA, O'Horo CE, Dimissie S, D'Agostino RB, Copenhafer DL. Validation of a dietary pattern approach for evaluating nutritional risk. *The Framingham Nutrition Studies*. *J Am Diet Assoc* 2001;101:187–94.
  43. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, *et al*. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 1997;336:1117–24.
  44. Svetkey LP, Simons-Morton D, Vollmer WM, Appel LJ, Conlin PR, Ryan DH, *et al*. Effects of dietary patterns on blood pressure: subgroup analysis of the Dietary Approaches to Stop Hypertension (DASH) randomized clinical trial. *Arch Intern Med* 1999;159:285–93.
  45. Gambera PJ, Schneeman BO, Davis PA. Use of the food guide pyramid and US dietary guidelines to improve dietary intake and reduce cardiovascular risk in active-duty Air Force members. *J Am Diet Assoc* 1995;95:1268–73.
  46. Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, *et al*. Can lifestyle changes reverse coronary heart disease? *Lancet* 1990;336:129–33.
  47. Gould KL, Ornish D, Kirkeeide R, Brown S, Stuart Y, Buchi M, *et al*. Improved stenosis geometry by quantitative coronary arteriography after vigorous risk factor modification. *Am J Cardiol* 1992;69:845–53.
  48. Gould KL. *Coronary artery stenosis and reversing atherosclerosis, 2nd ed*. New York: Oxford Univ. Press, 1999:395–474.
  49. Gordon T, Garcia-Palmieri MR, Kagan A, Kannel WB, Schiffman J. Differences in coronary heart disease in Framingham, Honolulu and Puerto Rico. *J Chron Dis* 1974;27:329–44.
  50. McGee D, Gordon T. *The Framingham Study applied to four other U.S. based epidemiological studies of cardiovascular disease (Section No. 31)*. Bethesda (MD): U.S. Dept. of Health, Education, and Welfare, NIH, 1976:76–1083.
  51. Brand RJ, Rosenman RH, Scholtz RI. Multivariate prediction of coronary heart disease in the Western Collaborative Group Study compared to the findings of the Framingham Study. *Circulation* 1976;53:348–55.
  52. Leaverton PE, Sorlie PD, Kleinman JC, Dannenberg AL, Ingster-Moore L, Kannel WB, *et al*. Representativeness of the Framingham risk model for coronary heart disease mortality; a comparison with a national cohort study. *J Chron Dis* 1987;40:775–84.