

# Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk<sup>1-3</sup>

Teresa T Fung, Eric B Rimm, Donna Spiegelman, Nader Rifai, Geoffrey H Tofler, Walter C Willett, and Frank B Hu

See corresponding editorial on page 1.

## ABSTRACT

**Background:** Although the effects of individual foods or nutrients on the development of diseases and their risk factors have been investigated in many studies, little attention has been given to the effect of overall dietary patterns.

**Objective:** Our objective was to examine the associations of 2 major dietary patterns, Western and prudent, with biomarkers of obesity and cardiovascular disease (CVD) risk.

**Design:** We used factor analysis to define major dietary patterns for a subsample of men ( $n = 466$ ) from the Health Professionals Follow-up Study by using dietary information collected from food-frequency questionnaires (FFQs) in 1994. We calculated partial correlation coefficients between pattern scores and biomarker values adjusted for age, smoking status, energy and alcohol intake, physical activity, hours of television watching, and body mass index.

**Results:** We derived 2 major dietary patterns that were generally reproducible over time. The first pattern (prudent) was characterized by higher intakes of fruit, vegetables, whole grains, and poultry. The second pattern (Western) was characterized by higher intakes of red meats, high-fat dairy products, and refined grains. Using pattern scores from 1994 and adjusting for potential confounders, we found significant positive correlations between the Western pattern and insulin, C-peptide, leptin, and homocysteine concentrations, and an inverse correlation with plasma folate concentrations. The prudent pattern was positively correlated with plasma folate and inversely correlated with insulin and homocysteine concentrations.

**Conclusion:** Major dietary patterns are predictors of plasma biomarkers of CVD and obesity risk, suggesting that the effect of overall diet on CVD risk may be mediated through these biomarkers. *Am J Clin Nutr* 2001;73:61-7.

**KEY WORDS** Dietary patterns, biomarker, cardiovascular disease, leptin, Western diet, prudent diet, Health Professionals Follow-up Study, food-frequency questionnaire

## INTRODUCTION

The traditional approach in nutritional epidemiology has focused largely on the effects of single nutrients or foods (1-3). However, nutrients and foods are consumed in combination, and

the combined effects of various nutrients and foods can be observed only when the entire eating pattern is considered. Analyzing food consumption as dietary patterns offers an additional dimension to examining the relations between diet and disease risk. Dietary patterns may also suggest a more comprehensive approach to disease prevention or treatment because the focus is on the entire diet rather than on just one food or nutrient. This approach of modifying consumption of multiple food items in the diet was used in Dietary Approaches to Stop Hypertension, a dietary pattern trial that was designed to reduce blood pressure (4).

In a previous study, we identified 2 major dietary patterns through factor analysis (5). The first, the "prudent" pattern, is characterized by a higher intake of fruit, vegetables, fish, whole grains, and legumes. The other pattern, the "Western" pattern, is characterized by a higher intake of red and processed meat, high-fat dairy products, sugar-containing beverages, sweets, and desserts. The validity of the dietary pattern measurement was reasonable; the correlations between the pattern scores generated from the food-frequency questionnaire (FFQ) and from diet records were 0.52 for the prudent pattern and 0.74 for the Western pattern. In this study, we examined the associations of these 2 major dietary patterns with biomarkers of cardiovascular disease (CVD) risk (including plasma lipids, thrombogenic factors, glycemic indicators, inflammatory markers, and leptin, folate, and homocysteine concentrations) to test the hypothesis that the prudent pattern is associated with a more favorable profile and the Western pattern with a less favorable one.

<sup>1</sup>From the Departments of Nutrition, Epidemiology, and Biostatistics, Harvard School of Public Health, Boston; the Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston; the Department of Laboratory Medicine, Children's Hospital, Harvard Medical School, Boston; and the Cardiology Department, Royal North Shore Hospital, St Leonards, Australia.

<sup>2</sup>Supported by research grants HL60712, HL35464, CA55075, and AA11181.

<sup>3</sup>Address reprint requests to TT Fung, Department of Nutrition, Simmons College, 300 The Fenway, Boston, MA 02115. E-mail: fung@simmons.edu.  
Received March 16, 2000

Accepted for publication September 7, 2000.

## SUBJECTS AND METHODS

### Study sample

The Health Professionals Follow-up Study is a prospective cohort study of 51 529 US male health professionals (dentists, optometrists, pharmacists, podiatrists, osteopathic doctors, and veterinarians) that began in 1986 to study the dietary etiologies of heart disease and cancer (6). The men were 40–75 y of age at baseline. Biennially, health information and disease status has been assessed by a self-administered questionnaire. The 466 men included in this analysis are a subset of the 18 225 male health professionals who volunteered to provide blood samples between 1993 and 1994. This subset was a random sample stratified by 7 types of reported alcohol consumption patterns (eg, light, binge, and abstaining) to examine the associations with biomarkers of CVD and diabetes in a different study. Participants were included in this study if they had not previously received a diagnosis of myocardial infarction, angina pectoris, stroke, diabetes mellitus, intermittent claudication, gastric or duodenal ulcers, gall bladder removal, liver disease, or any cancer except nonmelanoma skin cancer. The Health Professionals Follow-up Study was approved by the Human Subjects Committee of the Harvard School of Public Health.

### Blood collection and assessment of biomarkers

Blood samples, preferably fasting, were requested and collected in EDTA-containing tubes and returned to our laboratory via overnight courier on ice packs in insulated containers. Of all the blood samples received, >95% arrived within 24 h of the blood draw. On arrival, <15% were slightly hemolyzed, <3% were moderately hemolyzed, <1% were lipemic, and <0.5% were not cooled. They were centrifuged at  $700 \times g$  for 15 min at room temperature, dispensed as aliquots on ice, and stored in liquid nitrogen ( $-150^\circ\text{C}$ ).

Lipids and lipoproteins were measured by using a Hitachi 911 analyzer (Roche Diagnostics, Indianapolis) at a laboratory certified by the Centers for Disease Control and Prevention–National Heart, Lung, and Blood Institute Lipid Standardization Program. Total plasma cholesterol (CV in our laboratory: 1.7%) and triacylglycerol (CV in our laboratory: 1.8%) were measured enzymatically. HDL cholesterol was measured by a colorimetric assay from Roche Diagnostics (CV at the concentrations of our samples: 1.7%) and LDL cholesterol (CV in our laboratory: <3.1%) by a direct method from Genzyme Corporation (Cambridge, MA). Apolipoprotein A-I measurement was based on an immunonephelometric assay with a CV <5% in our laboratory. Lipoprotein(a) and C-reactive protein were assayed with latex-enhanced immunotechniques that had CVs <6%. The detection threshold for C-reactive protein was 0.15 mg/L. Insulin and C-peptide were measured by radioimmunoassay (Linco Research, St Charles, MO). This assay allows accurate assessment with little or no proinsulin and C-peptide cross-reactivity; the CV we obtained was <10%. Glycated hemoglobin ( $\text{Hb A}_{1c}$ ) was measured with turbidometric immunoinhibition in red cells by using a Hitachi 911 analyzer. Our CVs for  $\text{Hb A}_{1c}$  values of 0.056 and 0.096 were <2.5%. Fibrinogen was measured by the Clauss method with a CV of 2.6%. Factor VII antigen, tissue-type plasminogen activator (tPA) antigen, and the von Willebrand factor were measured by enzyme-linked immunoassay; the respective CVs were 3.0%, 5.5%, and 8.8%. Leptin was measured by a radioimmunoassay (Linco

Research; the intraassay CV was 4.3% and the interassay CV was 8.3%). Folate was measured by immunoassay (Abbott Laboratories, Abbott Park, IL) with CVs of 7.7% for 1.1 nmol/L and 1.9% for 35.8 nmol/L. Homocysteine was measured by HPLC with fluorometric detection; the intralaboratory CV was 3.3% for 7  $\mu\text{mol/L}$  and 2.9% for 12  $\mu\text{mol/L}$ .

### Dietary assessment

Participants completed a semiquantitative FFQ every 4 y beginning in 1986 that consisted of  $\approx 130$  items. Standard portion sizes were listed with each food and 9 frequency choices from “almost never” to “ $\geq 6$  times/d” were given. The selected frequency choice for each food was then converted to a daily intake; for example, “1 serving/wk” was converted to 0.14 serving/d. The validity and reproducibility of the FFQ was described elsewhere (7, 8).

### Assessment of other variables

Cigarette smoking and body weight were assessed biennially. Body mass index (BMI), a measurement of obesity, was calculated for each 2-y cycle as weight (kg)/height<sup>2</sup> (m). The weekly number of hours spent watching television or videotapes was assessed biennially starting in 1988. Every 2 y between 1986 and 1994, men in the cohort provided the weekly time spent on 10 common leisure-time physical activities such as walking, swimming, and tennis. These were summed for each individual and expressed as metabolic equivalent hours (METs) (9).

### Statistical analysis

Details of the food groupings and factor analysis used to generate the dietary patterns were described elsewhere (5). Briefly, foods from the 1994 FFQ were classified into 42 food groups on the basis of nutrient profiles or culinary use. Foods that did not fit into any of the groups or that may represent distinctive dietary behaviors were considered as food groups on their own (eg, pizza, tea, and beer). Factor analysis (principal component) was performed (10) and factor scores were rotated by using varimax rotation. The resulting factor scores for the Western and prudent dietary patterns were therefore standardized and not correlated with each other. We also repeated our analysis, eliminating the breakfast cereal food group by classifying ready-to-eat cereals as either whole-grain or refined-grain cereals on the basis of criteria set by Jacobs et al (11) and adding them to those groups; however, the results did not change materially.

Factor scores for each FFQ year (1986, 1990, and 1994) for both dietary patterns were calculated for each individual by using food intake information from the particular FFQ year. We calculated partial correlation coefficients for factor scores and log-transformed biomarker values adjusted for age, alcohol intake, smoking status (never, past, current smoker of  $\leq 14$  cigarettes/d, and current smoker of  $\geq 14$  cigarettes/d), physical activity in METs/wk, total energy intake, and hours of television watching/wk. We also adjusted for BMI and vitamin E and multivitamin supplement use in secondary analyses. BMI may be an intermediate factor in the causal pathway of dietary patterns and coronary heart disease; therefore, we did not adjust for it in the main analyses. To correct for attenuation of correlation coefficients due to random within-person variation in biomarker measures, we used biomarker values obtained in 1997 from 82 men in this sample to calculate the ratio of within- to between-person variation for each biomarker (12).



**TABLE 1**

Factor-loading matrix for the 2 major dietary patterns identified from the 1986, 1990, and 1994 food-frequency questionnaires

| Foods or food groups             | 1986                       |                            | 1990                       |                            | 1994                       |                            |
|----------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
|                                  | Prudent diet<br>(factor 1) | Western diet<br>(factor 2) | Prudent diet<br>(factor 1) | Western diet<br>(factor 2) | Prudent diet<br>(factor 1) | Western diet<br>(factor 2) |
| Other vegetables                 | 0.73                       | — <sup>1</sup>             | 0.74                       | —                          | 0.70                       | —                          |
| Leafy vegetables                 | 0.63                       | —                          | 0.70                       | —                          | 0.65                       | —                          |
| Yellow and orange vegetables     | 0.48                       | —                          | 0.50                       | —                          | 0.62                       | —                          |
| Cruciferous vegetables           | 0.48                       | —                          | 0.59                       | —                          | 0.60                       | —                          |
| Legumes                          | 0.50                       | —                          | 0.55                       | —                          | 0.60                       | —                          |
| Tomatoes                         | 0.60                       | —                          | 0.50                       | —                          | 0.51                       | —                          |
| Fruit                            | 0.22                       | —                          | 0.44                       | —                          | 0.50                       | -0.39                      |
| Fish                             | 0.46                       | —                          | 0.39                       | —                          | 0.40                       | —                          |
| Olive oil                        | NA <sup>2</sup>            | NA                         | 0.53                       | —                          | 0.35                       | —                          |
| Garlic                           | 0.45                       | —                          | NA                         | NA                         | 0.35                       | —                          |
| Fruit juices                     | —                          | —                          | 0.18                       | —                          | 0.31                       | -0.16                      |
| Poultry                          | 0.39                       | -0.15                      | 0.45                       | —                          | 0.31                       | —                          |
| Salad dressings                  | 0.39                       | —                          | 0.46                       | —                          | 0.26                       | 0.23                       |
| Tea                              | —                          | —                          | —                          | —                          | 0.16                       | —                          |
| Red meats                        | —                          | 0.61                       | —                          | 0.63                       | —                          | 0.64                       |
| Processed meats                  | —                          | 0.58                       | —                          | 0.67                       | —                          | 0.62                       |
| French fries                     | —                          | 0.36                       | —                          | 0.49                       | —                          | 0.54                       |
| Eggs                             | —                          | 0.40                       | —                          | 0.54                       | —                          | 0.52                       |
| High-fat dairy products          | —                          | 0.45                       | —                          | 0.47                       | —                          | 0.47                       |
| Butter                           | —                          | 0.23                       | —                          | 0.34                       | —                          | 0.45                       |
| Coffee                           | —                          | 0.22                       | —                          | 0.25                       | —                          | 0.35                       |
| Beer                             | —                          | —                          | —                          | 0.17                       | —                          | 0.35                       |
| Added salt                       | NA                         | NA                         | —                          | 0.43                       | —                          | 0.33                       |
| Mayonnaise                       | —                          | 0.39                       | —                          | 0.31                       | —                          | 0.31                       |
| Refined grains                   | 0.25                       | 0.34                       | —                          | 0.36                       | 0.24                       | 0.30                       |
| Cream soups                      | 0.36                       | 0.18                       | —                          | 0.36                       | —                          | 0.26                       |
| Liquor                           | —                          | 0.20                       | —                          | —                          | —                          | 0.24                       |
| Pizza                            | —                          | 0.19                       | —                          | 0.17                       | —                          | 0.22                       |
| Low-sugar beverages              | —                          | —                          | —                          | —                          | —                          | —                          |
| Margarine                        | —                          | 0.39                       | —                          | 0.40                       | —                          | —                          |
| Whole grains                     | 0.25                       | —                          | 0.23                       | -0.20                      | 0.16                       | -0.26                      |
| Low-fat dairy products           | —                          | 0.50                       | —                          | —                          | —                          | —                          |
| Desserts                         | —                          | 0.20                       | —                          | 0.33                       | —                          | 0.26                       |
| Snacks                           | 0.16                       | 0.33                       | —                          | 0.17                       | —                          | —                          |
| Potatoes other than French fries | 0.22                       | 0.35                       | 0.21                       | 0.34                       | 0.16                       | —                          |
| Condiments                       | 0.25                       | 0.34                       | —                          | 0.19                       | —                          | 0.18                       |
| Breakfast cereals                | —                          | —                          | —                          | -0.20                      | —                          | -0.32                      |
| Nuts                             | —                          | 0.24                       | —                          | 0.15                       | —                          | —                          |
| Water                            | —                          | —                          | —                          | —                          | 0.25                       | —                          |
| Organ meats                      | —                          | 0.19                       | —                          | —                          | —                          | —                          |
| Sugar-containing beverages       | —                          | 0.31                       | -0.18                      | 0.24                       | —                          | —                          |
| Wine                             | 0.35                       | -0.18                      | 0.25                       | —                          | 0.19                       | —                          |
| Other soups                      | 0.37                       | 0.22                       | NA                         | NA                         | NA                         | NA                         |

<sup>1</sup> Absolute values <0.15 were excluded from the table for simplicity.<sup>2</sup> Not applicable because the particular item was not on that year's food-frequency questionnaire.

From this we calculated the corrected correlation coefficient by using the following equation:

$$\text{Corrected correlation coefficient} = (\text{uncorrected coefficient}) \times \sqrt{(1 + \lambda/k)} \quad (1)$$

where  $k$  is the number of repeated measurements ( $k = 2$  in this case) and  $\lambda$  is the ratio of within- to between-person variation.

We included 466 men without missing values for biomarkers except for insulin. The 197 individuals who reported food consumption within 6 h of having blood drawn were excluded from the analysis of insulin, C-peptide, and triacylglycerol concentrations. All  $P$  values are two-tailed.

## RESULTS

The 2 major dietary patterns identified by using factor analyses were qualitatively similar across time (1986, 1990, and 1994) (Table 1). Because the pattern scores were standardized, the mean and SD for both the prudent and Western pattern were 0 and 1, respectively. The prudent pattern was characterized by a higher intake of fruit, vegetables, poultry, fish, whole grains, and legumes and the Western pattern by higher intakes of red meat, processed meat, French fries, eggs, high-fat dairy products, sweets, and refined grains. The correlations between 1986 and 1990 were 0.65 for the prudent pattern and 0.70 for the Western pattern. The correlations between 1990 and 1994 were 0.67 for

**TABLE 2**Age- and energy-adjusted mean lifestyle characteristics by quintile of prudent and Western diet scores from the 1994 food-frequency questionnaire<sup>1</sup>

|                                   | Prudent diet (factor 1)           |                      |                     |             | Western diet (factor 2) |                      |                     |             |
|-----------------------------------|-----------------------------------|----------------------|---------------------|-------------|-------------------------|----------------------|---------------------|-------------|
|                                   | Q1: -1.2 <sup>2</sup><br>(n = 93) | Q3: -0.2<br>(n = 94) | Q5: 1.6<br>(n = 93) | P for trend | Q1: -1.2<br>(n = 93)    | Q3: -1.1<br>(n = 94) | Q5: 1.5<br>(n = 93) | P for trend |
| BMI (kg/m <sup>2</sup> )          | 21.7 ± 1                          | 21.3 ± 1             | 23.5 ± 1            | 0.49        | 22 ± 1                  | 21 ± 1               | 25 ± 1              | 0.12        |
| Activity (METs/wk) <sup>3</sup>   | 27 ± 4                            | 36 ± 3               | 43 ± 4              | 0.03        | 43 ± 3                  | 38 ± 3               | 27 ± 4              | 0.01        |
| Television viewing (h/wk)         | 11 ± 1                            | 9 ± 1                | 7 ± 1               | 0.07        | 7 ± 1                   | 10 ± 1               | 13 ± 1              | 0.0003      |
| Smokers (%)                       | 14 ± 3                            | 5 ± 2                | 1 ± 3               | 0.01        | 0 ± 2                   | 4 ± 2                | 19 ± 3              | <0.0001     |
| Vitamin E supplement users (%)    | 25 ± 5                            | 44 ± 5               | 58 ± 5              | 0.003       | 56 ± 5                  | 38 ± 5               | 29 ± 6              | 0.004       |
| Multivitamin supplement users (%) | 57 ± 5                            | 57 ± 5               | 49 ± 5              | 0.51        | 57 ± 5                  | 46 ± 5               | 47 ± 6              | 0.03        |

<sup>1</sup> $\bar{x} \pm SE$ .<sup>2</sup>Quintile of diet score (1, 3, or 5) and median score.<sup>3</sup>Metabolic equivalent hours per week; 1 MET is defined as the energy expenditure of an average adult sitting quietly for 1 h.

the prudent pattern and 0.69 for the Western pattern. The correlations between 1986 and 1994 were 0.58 for both the prudent and Western patterns.

The 2 dietary patterns were correlated with other lifestyle variables (**Table 2**). Individuals who had higher prudent diet scores also exercised more, watched less television, used more vitamin E supplements, and were less likely to smoke than were those with lower prudent diet scores. In contrast, those who scored high on the Western dietary pattern tended to exercise less, watch more television, and use fewer vitamin supplements and were more likely to smoke compared with those who scored low on the Western pattern.

The means and SEs for various CVD biomarkers across quintiles of dietary pattern factor scores are presented in **Table 3**. Plasma lipoprotein(a) concentration was lower with higher Western pattern scores. In contrast, triacylglycerol concentration was lower with higher prudent pattern scores and was higher with higher Western pattern scores. A lower insulin concentration was observed with a higher prudent pattern score, and

C-peptide was greater with a greater Western pattern score. Plasma leptin and homocysteine concentrations were higher with higher Western diet scores, and plasma folate concentration was greater with greater prudent pattern scores but lower with higher Western pattern scores.

The correlations of log-transformed biomarker values and the 2 pattern scores from 1994 are shown in **Table 4**. The corrected correlation coefficients were slightly stronger than the uncorrected ones. We observed moderately high intraclass correlations with most of the biomarkers (many  $\approx 0.7$ ). Therefore, the corrected correlations were not substantially different from the uncorrected ones. We observed significant positive correlations between the Western pattern and tPA antigen (0.19,  $P < 0.01$ ), fasting insulin (0.32,  $P < 0.01$ ), C-peptide (0.31,  $P < 0.01$ ), leptin (0.28,  $P < 0.0001$ ), C-reactive protein (0.22,  $P < 0.0001$ ), and homocysteine (0.23,  $P < 0.01$ ) after adjusting for various potential confounders. In addition, a significant inverse correlation was observed between plasma folate ( $-0.39$ ,  $P < 0.0001$ ) and the Western pattern. In contrast, inverse correlations were observed

**TABLE 3**Age- and energy-adjusted mean biomarker values by quintile of prudent and Western diet scores in 1994<sup>1</sup>

| Biomarker                              | Prudent diet (factor 1) |               |               |             | Western diet (factor 2) |               |               |             |
|--|-------------------------|---------------|---------------|-------------|-------------------------|---------------|---------------|-------------|
|  | Q1: -1.17 <sup>2</sup>  | Q3: -0.15     | Q5: 1.56      | P for trend | Q1: -1.16               | Q3: -1.14     | Q5: 1.49      | P for trend |
| Cholesterol (mmol/L)                   | 6.3 ± 0.1               | 6.5 ± 0.1     | 6.4 ± 0.1     | 0.64        | 6.1 ± 0.1               | 6.5 ± 0.1     | 6.5 ± 0.1     | 0.12        |
| HDL cholesterol (mmol/L)               | 1.5 ± 0.1               | 1.6 ± 0.1     | 1.6 ± 0.1     | 0.81        | 1.5 ± 0.1               | 1.6 ± 0.1     | 1.6 ± 0.1     | 0.74        |
| LDL cholesterol (mmol/L)               | 3.8 ± 0.1               | 3.9 ± 0.1     | 3.9 ± 0.1     | 0.63        | 3.7 ± 0.1               | 4.0 ± 0.1     | 3.8 ± 0.1     | 0.29        |
| Total cholesterol:HDL cholesterol      | 4.3 ± 0.1               | 4.2 ± 0.1     | 4.3 ± 0.1     | 0.63        | 4.4 ± 0.1               | 4.3 ± 0.1     | 4.3 ± 0.1     | 0.94        |
| Triacylglycerols (mmol/L) <sup>3</sup> | 1.7 ± 0.2               | 1.9 ± 0.2     | 2.0 ± 0.2     | 0.56        | 2.0 ± 0.2               | 2.3 ± 0.2     | 1.5 ± 0.2     | 0.14        |
| Apolipoprotein A-I (g/L)               | 1.5 ± 0.03              | 1.5 ± 0.03    | 1.5 ± 0.03    | 0.65        | 1.5 ± 0.03              | 1.6 ± 0.03    | 1.6 ± 0.03    | 0.03        |
| Lipoprotein(a) (μmol/L)                | 1.0 ± 0.2               | 1.1 ± 0.1     | 1.4 ± 0.2     | 0.31        | 1.4 ± 0.2               | 1.0 ± 0.1     | 1.0 ± 0.2     | 0.03        |
| Fibrinogen (μmol/L)                    | 5.5 ± 0.01              | 5.5 ± 0.01    | 5.4 ± 0.01    | 0.61        | 5.4 ± 0.01              | 5.5 ± 0.01    | 5.5 ± 0.02    | 0.06        |
| von Willebrand factor                  | 1.51 ± 0.07             | 1.48 ± 0.06   | 1.52 ± 0.07   | 0.48        | 1.45 ± 0.07             | 1.54 ± 0.06   | 1.54 ± 0.07   | 0.44        |
| Factor VII antigen                     | 1.01 ± 0.012            | 0.99 ± 0.011  | 0.98 ± 0.012  | 0.20        | 0.98 ± 0.01             | 1.02 ± 0.01   | 0.99 ± 0.01   | 0.07        |
| tPA antigen (ng/L)                     | 129 ± 5                 | 120 ± 5       | 110 ± 5       | 0.13        | 99 ± 5                  | 120 ± 5       | 140 ± 5       | <0.0001     |
| Insulin (pmol/L) <sup>3</sup>          | 62.9 ± 7.3              | 70.7 ± 7.0    | 90.7 ± 7.9    | 0.54        | 82.8 ± 7.7              | 70.8 ± 7.0    | 63.5 ± 8.1    | 0.21        |
| C-peptide (nmol/L) <sup>3</sup>        | 0.52 ± 0.05             | 0.65 ± 0.05   | 0.82 ± 0.06   | 0.65        | 0.78 ± 0.05             | 0.65 ± 0.05   | 0.54 ± 0.06   | 0.29        |
| Glycated hemoglobin                    | 0.057 ± 0.001           | 0.057 ± 0.001 | 0.058 ± 0.001 | 0.57        | 0.057 ± 0.001           | 0.058 ± 0.001 | 0.058 ± 0.001 | 0.76        |
| Leptin (ng/L)                          | 6741 ± 504              | 6310 ± 482    | 6431 ± 509    | 0.75        | 5277 ± 487              | 6331 ± 472    | 8941 ± 525    | <0.0001     |
| C-reactive protein (mg/L)              | 2.4 ± 0.3               | 1.6 ± 0.3     | 1.8 ± 0.3     | 0.17        | 1.7 ± 0.3               | 1.9 ± 0.3     | 2.5 ± 0.3     | 0.04        |
| Homocysteine (μmol/L)                  | 16.5 ± 0.6              | 14.7 ± 0.5    | 14.0 ± 0.6    | 0.03        | 13.9 ± 0.6              | 15.4 ± 0.5    | 16.8 ± 0.6    | 0.004       |
| Folate (nmol/L)                        | 18.4 ± 0.8              | 19.3 ± 0.8    | 20.3 ± 0.8    | 0.34        | 21.4 ± 0.8              | 18.3 ± 0.7    | 17.2 ± 0.8    | 0.007       |

<sup>1</sup> $\bar{x} \pm SE$ . tPA, tissue-type plasminogen activator.<sup>2</sup>Quintile of diet score (1, 3, or 5) and median score.<sup>3</sup>Values for those who had fasted <6 h were excluded.

TABLE 4

Pearson partial correlation coefficients for dietary patterns and log-transformed biomarker values, uncorrected and corrected for variation in biomarker values, from the 1994 food-frequency questionnaire<sup>1</sup>

| Biomarker                         | Prudent pattern    |                    | Western pattern    |                    | Prudent pattern<br>(also adjusted for BMI) |                    | Western pattern<br>(also adjusted for BMI) |                    |
|-----------------------------------|--------------------|--------------------|--------------------|--------------------|--|--------------------|--|--------------------|
|                                   | Uncorrected        | Corrected          | Uncorrected        | Corrected          | Uncorrected                                | Corrected          | Uncorrected                                | Corrected          |
| Cholesterol                       | -0.03              | -0.04              | 0.03               | 0.04               | -0.06                                      | -0.07              | 0.04                                       | 0.05               |
| HDL cholesterol                   | -0.04              | 0.04               | 0.06               | 0.07               | -0.05                                      | -0.06              | 0.16 <sup>2</sup>                          | 0.17 <sup>2</sup>  |
| LDL cholesterol                   | -0.03              | -0.04              | 0.04               | 0.05               | -0.07                                      | -0.08              | 0.05                                       | 0.06               |
| Total cholesterol:HDL cholesterol | 0.01               | 0.02               | -0.04              | -0.04              | 0.009                                      | 0.009              | -0.12 <sup>3</sup>                         | -0.13 <sup>3</sup> |
| Triacylglycerol <sup>4</sup>      | -0.08              | -0.09              | -0.08              | -0.09              | -0.08                                      | -0.09              | -0.10                                      | -0.11              |
| Apolipoprotein A-I                | -0.03              | -0.04              | 0.03               | 0.04               | -0.04                                      | -0.05              | 0.08                                       | 0.11               |
| Lipoprotein(a)                    | 0.10 <sup>3</sup>  | 0.10 <sup>3</sup>  | -0.07              | -0.07              | 0.08                                       | 0.08               | -0.07                                      | -0.07              |
| Fibrinogen                        | -0.005             | -0.006             | 0.12               | 0.15               | 0.007                                      | 0.009              | 0.06                                       | 0.07               |
| von Willebrand factor             | -0.03              | -0.04              | 0.09               | 0.11               | 0.002                                      | 0.003              | 0.05                                       | 0.06               |
| Factor VII antigen                | -0.004             | -0.005             | 0.02               | 0.03               | 0.003                                      | 0.004              | 0.04                                       | 0.04               |
| tPA antigen                       | -0.08              | -0.1               | 0.17 <sup>2</sup>  | 0.19 <sup>2</sup>  | -0.07                                      | -0.09              | 0.09                                       | 0.10               |
| Insulin <sup>4</sup>              | -0.16 <sup>3</sup> | -0.25 <sup>3</sup> | 0.20 <sup>2</sup>  | 0.32 <sup>2</sup>  | -0.16 <sup>2</sup>                         | -0.25 <sup>2</sup> | 0.17 <sup>2</sup>                          | 0.28 <sup>2</sup>  |
| C-peptide <sup>4</sup>            | 0.12               | 0.16               | 0.23 <sup>2</sup>  | 0.31 <sup>2</sup>  | 0.12                                       | 0.16               | 0.20 <sup>2</sup>                          | 0.28 <sup>2</sup>  |
| Glycated hemoglobin               | -0.01              | -0.01              | 0.03               | 0.04               | 0.001                                      | 0.001              | -0.051                                     | -0.06              |
| Leptin                            | -0.05              | -0.06              | 0.26 <sup>5</sup>  | 0.28 <sup>5</sup>  | -0.03                                      | -0.03              | 0.09                                       | 0.09               |
| C-reactive protein                | -0.06              | -0.06              | 0.19 <sup>5</sup>  | 0.22 <sup>5</sup>  | -0.05                                      | -0.06              | 0.11                                       | 0.12               |
| Homocysteine                      | -0.14 <sup>2</sup> | -0.20 <sup>2</sup> | 0.16 <sup>2</sup>  | 0.23 <sup>2</sup>  | -0.13 <sup>2</sup>                         | -0.19 <sup>2</sup> | 0.13 <sup>3</sup>                          | 0.18 <sup>3</sup>  |
| Folate                            | 0.23 <sup>5</sup>  | 0.28 <sup>5</sup>  | -0.32 <sup>5</sup> | -0.39 <sup>5</sup> | 0.25 <sup>5</sup>                          | 0.31 <sup>5</sup>  | -0.29 <sup>5</sup>                         | -0.36 <sup>5</sup> |

<sup>1</sup>*n* = 466. tPA, tissue-type plasminogen activator. Correlation coefficients adjusted for age (<50, 51–54, 55–59, 60–64, or ≥65y), smoking status [never, past, current (1–14 cigarettes/d), current (≥14 cigarettes/d)], physical activity [metabolic equivalent hours (METs) in quintiles: ≤10.6/wk, 10.7–20.6/wk, 20.7–37/wk, 37.1–57.1/wk, or >57.1/wk], total energy [in quintiles: <6372 kJ (1523 kcal), 6376–7891 kJ (1524–1886 kcal), 7895–9088 kJ (1887–2172 kcal), 9092–10710 (2173–2560 kcal), or >10710 kJ], television watching (in quintiles: ≤1.5 h/wk, 1.6–5 h/wk, 5.1–8.5 h/wk, 8.6–15.5 h/wk, or >15.5 h/wk), and total alcohol (none, 0.1–10 g/d, 10.1–20 g/d, or >20 g/d).

<sup>2</sup>*P* < 0.01.

<sup>3</sup>*P* < 0.05.

<sup>4</sup>*n* = 269 because nonfasting values were excluded.

<sup>5</sup>*P* < 0.0001.

between the prudent pattern and fasting insulin ( $-0.25$ ,  $P < 0.05$ ) and homocysteine ( $-0.20$ ,  $P < 0.01$ ); a positive correlation was observed with folate ( $0.28$ ,  $P < 0.0001$ ) and lipoprotein(a) ( $0.10$ ,  $P < 0.05$ ). No significant correlation was found between the prudent pattern score and plasma lipids and apolipoproteins. Among thrombogenic factors, only tPA antigen showed a consistent positive correlation with the Western pattern score, but this was no longer significant after adjustment for BMI. The associations between dietary pattern scores and log-transformed biomarker values were not substantially altered after additional adjustment for BMI or supplemental vitamin use. Averaged long-term analysis using pattern scores from 1986 to 1994 provided similar results.

## DISCUSSION

Using dietary data collected from FFQs, we observed 2 major dietary patterns that we previously called prudent and Western. Individuals in our sample who scored high on the prudent diet ate more vegetables, fruit, whole grains, fish, and poultry and had a healthy lifestyle in general. On the other hand, those who had high Western diet scores tended to eat more red meat, refined grains, snacks, high-fat foods such as French fries, full-fat dairy products, eggs, beer, and liquor. Their lifestyles also tended to be less healthy than those of individuals who mainly adhered to the prudent diet. We observed significant associations between dietary pattern scores and several plasma biomarkers. In particular, the Western diet was significantly and positively correlated

with HDL cholesterol, tPA antigen, homocysteine, fasting insulin and C-peptide, leptin, and C-reactive protein and negatively associated with folate. The prudent pattern was inversely associated with fasting insulin and homocysteine and positively associated with folate concentration. Because the 2 patterns were not correlated, individuals with a high Western pattern score did not necessarily have a low prudent pattern score. Therefore, the 2 patterns may act in concert.


The use of dietary patterns for examining associations with biomarkers of obesity and CVD risk has several advantages over focusing on individual nutrients or foods. Any synergistic effect between nutrients or foods may be more easily detected and the results can be more easily translated into practical advice for the public. We identified 2 dietary patterns similar in content to the Western and prudent patterns identified by Slattery et al (13) in 1997. The composition of the 2 patterns in our study remained consistent over time.

The associations between the various biomarkers and diet patterns were, in general, in the expected directions. The prudent pattern was more associated with a favorable biomarker profile, including lower fasting insulin, lower homocysteine, and higher folate concentrations. The higher concentrations of HDL cholesterol associated with a high Western pattern score could be related to the higher total fat content and lower carbohydrate content identified with this pattern (14). We observed a positive correlation between lipoprotein(a) and the prudent pattern, which is lower in saturated fats than the Western pattern, before adjustment for BMI. Although, in general, diet is not considered

to alter lipoprotein(a) concentrations substantially (15), some studies have shown a reduction in lipoprotein(a) concentration with higher saturated fat intake or an increase in fruit and vegetable intakes (16, 17). At the same time, the lower intake of leafy vegetables and legumes in the Western pattern diet probably resulted in a lower intake of folate. A higher folate intake, either by food or supplement, has been shown to lower homocysteine concentrations (18, 19). Consequently, we observed a positive association for homocysteine concentration and an inverse association for folate with the Western diet pattern. Predictably, a high prudent diet score was also associated with a lower homocysteine concentration. We observed an inverse association between fasting insulin and the prudent pattern diet and a positive association with the Western pattern diet. The higher intake of vegetables and whole grains from the prudent diet, as opposed to higher intakes of refined grains in the Western diet, may lead to a lower glycemic and insulinemic response (20). The Western pattern diet contains several foods high in total fat; higher intakes of fat, especially saturated and *trans* fats, may be associated with a higher fasting insulin concentration (21, 22).

Substantial evidence has accumulated on the relations of plasma homocysteine and glycemic response to the risk of CVD (23–25). Because the influence of diet on CVD and obesity may be mediated through these plasma biomarkers, dietary patterns may act as predictors of CVD and obesity as well. In a recent study that used dietary data from the entire Health Professionals Follow-up Study cohort, we found a positive association between the Western pattern diet and incidence of coronary heart disease and an inverse association with the prudent pattern diet (26). Slattery et al (13) found that the Western pattern diet was associated with an increased risk of colon cancer and the prudent pattern diet with a lower risk. Randall et al (27) identified 3 dietary patterns that were associated with colon cancer in men. The “traditional” pattern was characterized by potatoes, beef, and cabbage; the “snack” pattern by cookies, pastries, and candies; and the “high-fat” pattern by eggs and processed meat. The Western pattern identified in the present study is similar to the combination of Randall et al’s patterns.

Our study was conducted in predominantly white men. Dietary patterns may differ between sex, ethnic, and cultural groups. Although a prior study found no significant difference in eating patterns between men and women, the associations found in this study should be tested in other populations (13). In addition, dietary patterns may change over time because of changing preferences and food availability. Because our analyses were constrained to healthy people, the identified patterns may not apply to people with chronic diseases. An advantage of our study is that we had repeated measurements of biomarkers in 82 individuals to adjust correlation coefficients for random within-person variation. We also had repeated dietary information over 8 y with which we were able to show that dietary patterns were qualitatively similar across time, indicating high reproducibility of the method in our study. Although the use of factor analysis generates patterns based on available data without an a priori focus, the patterns generated fit well into the commonly recognized Western and prudent eating habits. However, because these patterns are based simply on behavioral patterns, they do not necessarily represent optimal patterns. Nevertheless, our data do show that these 2 major patterns predict obesity and CVD risk factors. Also, the addition or deletion of any 1 or 2 food groups from either dietary pattern would not likely have much effect on the general pattern of findings.

In conclusion, we found that the prudent pattern diet is correlated with a more favorable biomarker profile and the Western pattern diet with a less favorable biomarker profile for CVD. This supports the use of such patterns to evaluate disease risk and, potentially, to serve as guidelines for healthful food consumption. 

## REFERENCES

1. Kwiterovich POJ. The effect of dietary fat, antioxidants, and pro-oxidants on blood lipids, lipoproteins, and atherosclerosis. *J Am Diet Assoc* 1997;97:S31–41.
2. Klor HU, Hauenschild A, Holbach I, Schnell-Kretschmer H, Stroh S. Nutrition and cardiovascular disease. *Eur J Med Res* 1997;2:243–57.
3. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 1997;20:545–50.
4. Zemel MB. Dietary pattern and hypertension: the DASH study. *Nutr Rev* 1997;55:303–8.
5. Hu FB, Rimm EB, Smith-Warner SA, et al. Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. *Am J Clin Nutr* 1999;69:243–9.
6. Rimm EB, Giovannucci EL, Willett WC, et al. A prospective study of alcohol consumption and the risk of coronary disease in men. *Lancet* 1991;338:464–8.
7. Feskanih D, Rimm EB, Giovannucci EL, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. *J Am Diet Assoc* 1993;93:790–6.
8. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol* 1992;135:1114–26.
9. Ainsworth B, Haskell W, Leon A, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* 1993;25:71–80.
10. Kim J-O, Mueller CW. Factor analysis: statistical methods and practical issues. Newbury Park, CA: Sage Publications, 1978.
11. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women’s Health Study. *Am J Clin Nutr* 1998;68:248–57.
12. Willett WC. *Nutritional epidemiology*. 2nd ed. New York: Oxford University Press, 1998.
13. Slattery ML, Boucher KM, Caan BJ, Potter JD, Ma K-N. Eating patterns and risk of colon cancer. *Am J Epidemiol* 1998;148:4–16.
14. Katan MB. Effect of low-fat diets on plasma high-density lipoprotein concentrations. *Am J Clin Nutr* 1998;68(suppl):573S–6S.
15. MacKinnon LT, Hubinger L, Lepre F. Effects of physical activity and diet on lipoprotein(a). *Med Sci Sports Exerc* 1997;29:1429–36.
16. Jenkins DJ, Popovich DG, Kendall CW, et al. Effect of a diet high in vegetables, fruit, and nuts on serum lipids. *Metab Clin Exp* 1997;46:530–7.
17. Sanders TA, Oakley FR, Miller GJ, Mitropoulos KA, Crook D, Oliver MF. Influence of n–6 versus n–3 polyunsaturated fatty acids in diets low in saturated fatty acids on plasma lipoproteins and hemostatic factors. *Arterioscler Thromb Vasc Biol* 1997;17:3449–60.
18. Brouwer IA, van Dusseldorp M, Thomas CMG, et al. Low-dose folic acid supplementation decreases plasma homocysteine concentrations: a randomized trial. *Am J Clin Nutr* 1999;69:99–104.
19. Brouwer IA, van Dusseldorp M, West CE, et al. Dietary folate from vegetables and citrus fruit decreases plasma homocysteine concentrations in humans in a dietary controlled trial. *J Nutr* 1999;129:1135–9.
20. Wolever TMS, Bolognesi C. Prediction of glucose and insulin response of normal subjects after consuming mixed meals varying

- in energy, protein, fat, carbohydrate and glycemic index. *J Nutr* 1996;126:2807–12.
21. Marshall JA, Bessesen DH, Hamman RF. High saturated fat and low starch and fibre are associated with hyperinsulinaemia in a non-diabetic population: the San Luis Valley Diabetes Study. *Diabetologia* 1997;40:430–8.
  22. Storlien LH, Baur LA, Kriketos AD, et al. Dietary fats and insulin action. *Diabetologia* 1996;39:621–31.
  23. Ridker PM, Manson JE, Buring JE, Shih J, Matias M, Hennekens CH. Homocysteine and risk of cardiovascular disease among postmenopausal women. *JAMA* 1999;281:1817–21.
  24. Eikelboom JW, Lonn E, Genest J Jr, Hankey G, Yusuf S. Homocyst(e)ine and cardiovascular disease: a critical review of the epidemiologic evidence. *Ann Intern Med* 1999;131:363–75.
  25. Haffner SM. Epidemiology of insulin resistance and its relation to coronary artery disease. *Am J Cardiol* 1999;84:11J–4J.
  26. Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study of major dietary patterns and risk of coronary heart disease in men. *Am J Clin Nutr* 2000;72:912–21.
  27. Randall E, Marshall JR, Brasure J, Graham S. Dietary patterns and colon cancer in Western New York. *Nutr Cancer* 1992;18:265–76.

