Dietary Patterns and Risk of Hypertension, Type 2 Diabetes Mellitus, and Coronary Heart Disease

Matthias B. Schulze, MD, and Frank B. Hu, MD, PhD

Address
Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115, USA.
E-mail: Frank.hu@channing.harvard.edu

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Dietary pattern analysis, which reflects the complexity of dietary intake, has recently received considerable attention by nutritional epidemiologists. Two general approaches have been used to define these summary variables in observational studies. The so-called a posteriori approach builds on statistical exploratory methods, whereas the so-called a priori approach focuses on the construction of pattern variables that reflect hypothesis-oriented patterns based on available scientific evidence for specific diseases. Several studies, both observational and clinical, suggest that these measures of overall diet predict disease risk, and that its application might be especially valuable in the development of food-based dietary guidelines. In this review, we describe different patterning approaches and the available evidence regarding the relationships between dietary patterns and risk of hypertension, type 2 diabetes mellitus, and coronary heart disease.

Introduction

Cardiovascular disease (CVD) and stroke are the leading causes of death in industrialized countries [1]. In addition, the economic costs of these diseases during 2001 in the United States alone have been estimated at about $300 billion dollars [2]. Both hypertension and diabetes are major risk factors for CVD and stroke and they represent a tremendous additional economic burden in terms of health expenditures and lost productivity. Therefore, risk factors for these diseases, among them diet, have long been a focus of epidemiologic research. With regard to diet, however, the dominant approach, that of examining single nutrients or foods, is fraught with problems due to the complexity of assessing dietary intake. The high degree of intercorrelation among nutrients, as well as among foods, makes it difficult to attribute effects to single dietary components [3]. However, by attempting to separate the effects of individual nutrients, one might miss associations between diet and disease. The single-nutrient approach might not adequately account for complicated interactions and cumulative effects [4] because people do not eat isolated nutrients; they eat foods and in particular patterns [5]. In addition, in terms of public health, dietary patterns are more realistic representations of dietary intake in real life and are particularly valuable for developing food-based dietary guidelines [6]. This approach might be particularly useful in the context of prevention of CVD, hypertension, and diabetes.

Patterning Methods

Overview

Although dietary patterns can be predefined for intervention and control diets in trials, they need to be defined on the basis of available dietary data in observational studies. Two general approaches have been used to define these summary variables in observational studies [7•]. The so-called a posteriori approach uses statistical exploratory methods. Exploratory factor analysis and cluster analysis are two predominant a posteriori methods. Both might work well in identifying the major dietary patterns of a particular study population [5,7•], but independently of their relevance to any disease. On the other hand, the a priori approach focuses on the construction of pattern variables that reflect hypothesis-oriented patterns based on available scientific evidence for specific diseases. This concept of constructing an a priori pattern variable has been demonstrated to be successful for studying, for example, whether a diet score reflecting key elements of a Mediterranean diet is related to mortality in an Anglo-Celtic Australian population [8].

Exploratory factor analysis

Exploratory factor analysis is aimed at compressing the information of many variables (*eg*, food intake) into a few underlying factors by analyzing their covariance structure. For the purpose of extracting dietary patterns, factor analysis usually starts with a principal component solution. Thus, the pattern variables, called factor scores, are optimized linear combinations of the standardized food variables and are constructed to account for as much of the total variance of the food variables as possible. Optimization is attained by weighting each food variable, with the weights being equivalent to the factor loadings. Factor loadings are interpreted as the correlation coefficients between food variables and patterns [9]. The retained factor scores are perfectly uncorrelated with each other and remain so as long as the usually applied subsequent rotation procedures are orthogonal. Rotation often aims for a simple structure of the retained components, with observed variables showing either high-factor loadings with the pattern if they are measures of the latent construct or near-zero loadings if not.

Cluster analysis

Cluster analysis, in contrast to factor analysis, aggregates not the observed food items, but the individuals into distinct subgroups (clusters). Although diets of individuals within the same cluster are relatively homogeneous, the diets differ between clusters. The k-means method is the most widely used clustering algorithm for defining dietary patterns [10–13] because it is particularly useful for large sample sizes. This clustering method assigns individuals to a predefined number of clusters on the basis of Euclidean distances so that distances between observations within a cluster are smaller than distances between clusters. Dietary variables should be standardized in some way, because variables with large variances tend to have a greater effect than those with small variances on the resulting clusters. Although factor analysis results in a pattern structure that is directly interpretable, further analysis is necessary to define the particular dietary profiles of the extracted clusters.

A priori patterns

The a priori approach focuses on the calculation of a graded score that describes an ideal diet with a disease-specific focus, building on previous knowledge concerning the health effects of various dietary components or even of entire diets [7•]. This approach should not be confused with exploratory attempts to explain a maximum of variance. High intercorrelation between original variables is not a prerequisite for constructing meaningful a priori pattern variables [14–16]. Patterns' scores were constructed on the basis of dietary recommendations (*eg*, the Healthy Eating Index [17–19], the Diet Quality Index [20], and the Recommended Food Score [15]) and on observed associations between single dietary components and disease [21••,22••].

Dietary Patterns and Hypertension

So far, observational studies on dietary patterns and hypertension are limited to ecologic and cross-sectional analyses. The major focus of research has been vegetarian diets. In a study of participants on a macrobiotic diet [23], individuals who consumed almost no foods of animal origin had significantly lower blood pressure than those who ate animal products more regularly. Similar affects of a vegetarian diet were observed in the Seventh-day Adventists in Australia [24] and in the United States [25]. Miller *et al.* [26] used a different a priori approach linking dietary patterns to hypertension. They calculated a diet diversity score based on the reported food intake of Saba Islanders determined from 24-hour dietary recalls and semi-quantitative food-frequency questionnaires. Those with low diet diversity—defined as the absence of one or more out of five food groups (grains and tubers, vegetables, fruits, legumes, and animal products) in the daily diet—had a fourfold greater risk of being hypertensive than did those with a high amount of diet diversity (the authors controlled for potential confounders). Only one observational study has estimated the effects of exploratory patterns on blood pressure [13]. In this cross-sectional study, 4999 individuals were assigned to six clusters by cluster analysis that was based on the reported intake of 43 food groups. No difference was found in the prevalence of hypertension between clusters.

Although numerous trials have tested the effects of single dietary components, only a few have examined the effects of overall dietary patterns (Table 1) specifically. These studies [25–29], including the landmark Dietary Approaches to Stop Hypertension (DASH) trial [28,29], primarily used plant-based diets. The DASH trial demonstrated that a diet rich in fruits and vegetables significantly reduced blood pressure in persons with and without elevated blood pressure, while holding weight constant.

Dietary Patterns and Diabetes

Most observational studies relating dietary patterns to diabetes represent cross-sectional studies using a posteriori approaches. Williams *et al.* [30] identified four patterns by factor analysis in the population-based Isle of Ely Study. Among participants without a previous diagnosis of diabetes, those identified as having diabetes on the basis of a glucose tolerance test had significantly lower intakes of fruits, vegetables, fish, and poultry compared with those participants with normal glucose tolerance. Gittelsohn *et al.* [31] related patterns derived from factor analysis to the prevalence of diabetes and impaired glucose tolerance in a Native Canadian reserve. The "vegetables" pattern showed a significant protective effect, whereas participants with a high score for the "junk-food" pattern (associated with higher intakes of French fries, chocolate, cake, canned meat, and canned fruit) showed an increased risk. Wirfalt *et al.* [13] identified six patterns by means of cluster analysis based on the energy contribution of single food items within the European Prospective Investigation into Cancer (EPIC)-Malmo study. One cluster with higher intakes of cheese, fat meat, and cake was positively associated with the risk of being hyperglycemic in men but less strongly in women. Nonsignificant inverse associations were observed for clusters that were relatively low in fat and high in fiber.

Table 1. Trials on dietary patterns and hypertension, type 2 diabetes mellitus, or coronary heart disease

Study / year	Study population	Dietary intervention	Main findings
Hypertension			
Rouse *et al.* [25] / 1983	59 healthy men and women aged 25–63 y	Vegetarian diet	Significant fall of systolic (5–7 mm Hg) and diastolic BP (2–3 mm Hg) with vegetarian diet
Margetts *et al.* [27] / 1986	58 men and women aged 30–64 y with mild untreated hypertension	Vegetarian diet	A 5-mm Hg fall of systolic BP with vegetarian diet, no significant effect on diastolic BP
Appel *et al.* [28] / 1997	459 men and women aged >22 y with systolic BP <160 and diastolic BP 80–95 mm Hg	“Fruit and vegetable” diet + “combination” diet (rich in fruits, vegetables and low-fat milk products)	Significant lower BP with “fruit and vegetable” diet (2.8 mm Hg systolic and 1.1 mm Hg diastolic) as well as with “combination” diet (5.5 mm Hg systolic and 3.0 mm Hg diastolic)
Type 2 diabetes mellitus			
Pan *et al.* [33] / 1997	577 men and women with IGT	25% to 30% energy from fat; specific advice on cereal, vegetable, meat, milk, and oil intake	Diet intervention was associated with a 31% reduction in risk of developing diabetes
Tuomilehto *et al.* [34] / 2001	522 men and women aged 40–65 y with IGT	Weight reduction; <30% energy from fat; frequent intake of whole-grain products, vegetables, fruits, low-fat milk and meat products, soft margarines and vegetable oils; physical activity	58% reduction in incidence of diabetes in the intervention group
Diabetes Prevention Program Research Group [35] / 2002	3234 men and women aged >25 y with IGT	7% weight reduction through healthy diet and 150 min/wk of physical activity	58% reduction in incidence of diabetes in the intervention group
Coronary heart disease			
Singh *et al.* [41] /1992	505 MI patients	Low-fat diet rich in fruits, vegetables, nuts, and grain products	Lower risk of cardiac events (RR of 0.60; 95% CI, 0.31–0.75) and cardiac mortality (RR of 0.58; 95% CI, 0.34–0.83) in intervention group
de Lorgeril *et al.* [42••] / 1999	423 MI patients aged <70 y	Mediterranean diet enriched with alpha-linolenic acid	Lower risk for cardiac death or nonfatal MI with Mediterranean diet (RR of 0.28; 95% CI, 0.15–0.53)

BP—blood pressure; IGT—impaired glucose tolerance; MI—myocardial infarction; RR—relative risk.

There are two prospective cohort studies linking dietary patterns to type 2 diabetes mellitus. In one study, carried out within the Health Professionals Follow-up Study, van Dam *et al.* [32] examined the associations between two exploratory patterns derived from factor analysis and the risk of diabetes mellitus. The "prudent" pattern (characterized by higher consumption of vegetables, fruits, fish, poultry, and whole grains) was associated with a modest risk reduction, whereas the "Western" pattern (characterized by higher consumption of red meat, processed meat, French fries, high-fat dairy products, refined grains, and sweets and deserts) was associated with an increased risk for type 2 diabetes mellitus. In the Nurses' Health Study, Hu *et al.* [22••] found that a pattern score based on the intake of cereal fiber, polyunsaturated fatty acids, trans fatty acids, and glycemic load (which reflects the effect of diet on the blood glucose level) was strongly associated with diabetes incidence (Fig. 1). Women within the highest quintile of the pattern score had a relative risk (RR) of 0.49 (95% CI, 0.42 to 0.56) compared with women in the lowest quintile.

Several randomized trials have tested dietary patterns in conjunction with exercise as an intervention in the prevention of diabetes (Table 1). Pan *et al.* [33] reported on a Chinese trial with 577 subjects who had impaired glucose tolerance (IGT). Participants in the diet-intervention group were prescribed a diet with a specific fat content and with individual goals for cereal, vegetables, meat, milk, and oil intake. During 6 years of follow-up, the progression from

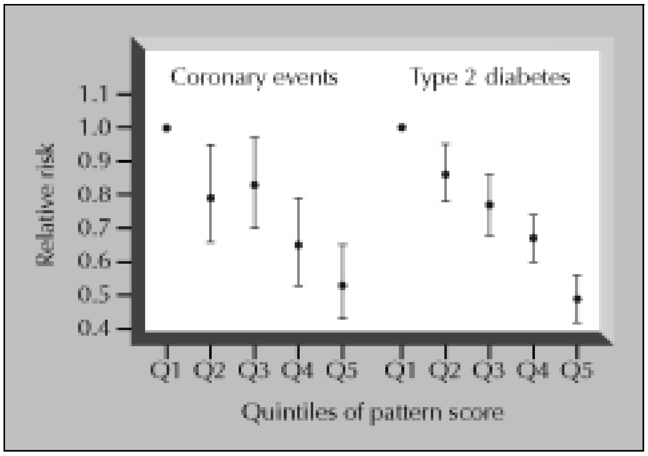

Figure 1. Relative risk of coronary events and type 2 diabetes mellitus in the Nurses' Health Study [21••,22••] by quintiles (Q) of dietary pattern score. Relative risk of coronary events adjusted for age, time periods, presence or absence of a parental history of myocardial infarction before the age of 60 years, menopausal status and use of postmenopausal hormones, presence or absence of a history of hypertension, and presence or absence of a history of high cholesterol. Relative risk of diabetes mellitus adjusted for age, time periods, presence or absence of a parental history of diabetes, menopausal status, and use of postmenopausal hormones.

IGT to diabetes was reduced by 46% in the dietary intervention group. In the Finnish Diabetes Prevention Study [34], 522 persons with IGT were randomly assigned to either a control group or an intervention group in which each individual received counseling aimed at reducing their weight, total intake of fat, and intake of saturated fat and increasing their intake of fiber and their physical activity. The intervention resulted in an overall risk reduction of 58%. The most recent results from the multicenter Diabetes Prevention Program [35] in 3234 US adults with IGT indicated that weight loss through a healthy low-energy and low-fat diet and physical activity reduced the incidence of diabetes over a period of about 3 years by 58%. In both the Diabetes Prevention Study and the Diabetes Prevention Program, it remains unclear what the effect of the dietary patterns is independent of weight loss or physical activity.

Dietary Patterns and Coronary Heart Disease

Few studies have investigated relationships between dietary patterns and biochemical markers of risk of coronary heart disease (CHD) [10,36]. Fung *et al.* [37] examined the relationship between two major eating patterns and biochemical markers of CHD and obesity in the Health Professionals Follow-up Study. For the "Western" pattern, positive correlations were found for tissue plasminogen activator antigen, fasting insulin, C-peptide, leptin, C-reactive protein, and homocysteine, and a negative correlation was found for folate. The "prudent" pattern was positively correlated with plasma folate and inversely correlated with insulin and homocysteine concentrations.

A growing number of studies have examined dietary pattern associations with CHD morbidity [18,19,21••,38••,39] and mortality [15,16,40]. Exploratory factor analysis was used to derive major dietary patterns in the Nurses' Health Study [39] and the Health Professionals Follow-up Study [38••]. In both studies, a "prudent" pattern, rich in vegetables, fruits, legumes, whole grains, fish and poultry significantly lowered CHD risk. In the Health Professionals Follow-up Study, the RR comparing the highest with the lowest quintile of pattern score was 0.70 (95% CI, 0.56 to 0.86), whereas the corresponding RR in the Nurses' Health Study was 0.76 (95% CI, 0.60 to 0.98). In contrast, a "Western" diet pattern (high in red meat, processed meat, refined grains, sweets and desserts, French fries, and high-fat dairy products) found in both studies was positively associated with CHD incidence. The RR comparing the highest with the lowest quintile of pattern score were 1.64 (95% CI, 1.24 to 2.17) in the Health Professionals Follow-up Study and 1.46 (95% CI, 1.07 to 1.99) in the Nurses' Health Study.

Besides exploratory patterns, several studies have evaluated whether a priori patterns predict CHD risk. In both the Nurses' Health Study [19] and the Health Professionals Follow-up Study [18], the Healthy Eating Index (HEI), a measure of how well diets conform to the US Department of Agriculture Dietary Guidelines for Americans, was associated with a modest reduction in CVD risk. The HEI consists of 10 equally weighted components measuring adherence to serving recommendations for grains, vegetables, fruits, milk, and meat, as well as measuring intake of total fat, saturated fat, cholesterol, sodium, and diet diversity. The RRs comparing the highest with the lowest quintile of pattern score were 0.86 (95% CI, 0.72 to 1.03) in the Nurses' Health Study and 0.72 (95% CI, 0.60 to 0.88) in the Health Professionals Follow-up Study. Although these modest effects suggest that improvements to the HEI may be warranted, the observed trend is consistent with the study by Kant *et al.* [15], who found a diet-quality index based on the number of recommended foods to be a strong predictor of CHD and stroke mortality, and the study by Osler *et al.* [16], who found a pattern rich in whole-grain bread, fruits, and vegetables to be negatively associated with cardiovascular mortality. Meanwhile, Stampfer *et al.* [21••] demonstrated that a pattern score reflecting a diet low in trans fatty acids and glycemic load, high in cereal fiber, marine omega-3 fatty acids, and folate and with a high ratio of polyunsaturated to saturated fat strongly predicted the risk of CHD in the Nurses' Health Study (Fig. 1).

Only two randomized trials have examined the effect of dietary patterns on CVD, both conducted among patients with existing myocardial infarction (Table 1). Singh *et al.* [41] observed a decreased risk of cardiac events and total mortality in patients with recent myocardial infarction who followed a diet rich in fruits, vegetables, nuts, and grain products. The diet resulted in a decrease in both blood lipid concentration and body weight. In the Lyon Diet Heart

Study, de Lorgeril *et al.* [42••] found that a Mediterranean-type diet rich in alpha-linolenic acid reduced the rate of recurrence after a first myocardial infarction over a period of 46 months. In comparison with the control group, the Mediterranean-type diet group had a RR of cardiac death and non-fatal myocardial infarction of 0.28 (95% CI, 0.15 to 0.83).

Methodologic Issues in Dietary Pattern Analysis

Exploratory approaches to defining dietary patterns involve some subjectivity in the analytical process. This includes the consolidation of food items into food groups, the number of factors or clusters to be retained, or the applied rotation method in factor analysis [43]. Although McCann *et al.* [44] reported that the choice of food groups had only a small impact on the observed associations, more sensitivity analyses are needed to examine whether these decisions affect the reproducibility of results.

Moreover, only a few attempts have been undertaken to insure the internal validity of identified pattern structures. Hu *et al.* [45] tested the validity and reproducibility of patterns based on factor analysis in the Health Professionals Follow-up Study. In addition, Cronbach's [46] coefficient alpha or confirmatory factor analysis [9] can be sued to test the goodness of fit of the extracted factor structures. So far, these two methods have hardly been used [31,47].

Another concern of the a posteriori approach is that the patterns extracted in one population may not be reproducible in other populations [5,43]. Indeed, somewhat different dietary patterns have been generated in various populations with different cultures and eating habits [16,31,38••,47,48], which makes the observed associations across studies difficult to compare. Moreover, in multicenter studies such as the EPIC Study [49], pooled analyses require the same pattern variables for all centers, which may be difficult to retain with exploratory factor or cluster analysis across the centers.

On the other hand, the a priori approach offers the possibility of constructing pattern variables based on existing scientific evidence. The evidence for constructing these patterns might come from observational or clinical studies on individual nutrients or foods [7•], although dietary pattern analysis still considers the effect of the overall diet rather than that of single nutrients. This approach is unlikely to enhance biologic understanding of diet-disease relationships, but can be useful for making dietary recommendations.

Conclusions

Dietary pattern analysis is an analytical approach that reflects the complexity of dietary exposure. This approach might be useful, especially if many dietary components are relevant for a disease, as it accounts for complicated interactions and cumulative effects. This may be particularly important for CHD, hypertension, and diabetes mellitus, for which multiple dietary components are established risk factors. Evidence is increasing from both observational and clinical studies that plant-based dietary patterns, which are rich in fruits, vegetables, and whole grains, are useful for preventing a large proportion of these diseases in populations accustomed to a Western diet. Dietary pattern analysis is seen as a useful approach to the development and evaluation of food-based dietary guidelines.

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