*Review Article*

# Identification of diet-disease relations through dietary pattern approach:
# A review

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## Abstract

Recently, diet-disease relations have been recommended to be looked for through dietary pattern approach rather than traditional approach (nutrient or food-oriented approach). Dietary pattern analysis allows consideration of the entire diet, rather than individual foods or ingredients. This approach can be particularly useful when traditional analyses in nutritional epidemiology cannot move beyond weak associations. The dietary pattern approach is more realistic than the food-based or nutrient approach, in that inter-correlations and biological interactions between foods and nutrients confound the associations of a single food or nutrient with a certain chronic disease. Several studies provide evidence supporting use of the dietary pattern approach in nutritional epidemiology. Most of these studies indicate that empirically derived food intake patterns by statistical methods are related to chronic diseases. This review aims to provide more detailed information about the methods of measurement, advantages and disadvantages of the dietary pattern approach and to assess whether major dietary patterns are related to the prevalence of metabolic syndrome and insulin resistance.

**KEYWORDS:** Dietary patterns, factor analysis, cluster analysis, diet, dietary assessment.

The traditional focus of nutrition science on the amount and distribution of nutrients is being replaced by a focus on a combination of nutrients and food components (i.e. fat, saturated fat, cholesterol, fiber) and foods (i.e. fish, vegetables, fruits, low-fat dairy products). The possibility of many undiscovered compounds in foods, and the enormity of interactions among food components are now recognized.[1-3] As a result, looking at the whole dietary pattern has been considered by nutrition investigators in an attempt to capture a snapshot of the entire diet. Due to co-linearity among food and nutrient intakes, using the dietary pattern multivariate approach can resolve concerns about confounding factors and interactions of foods and nutrients.[1,4,5] Furthermore, the dietary pattern approach reflects individuals' dietary behaviors and therefore can provide more detailed information about nutritional etiology of chronic diseases.[6] Nutritional interventions using the dietary pattern approach have achieved favorable and positive changes in the diet.[7,8] Such changes have resulted in more reductions in blood pressure than by nutrient supplementation in clinical trials.[9,10] Finally, dietary pattern analysis helps us to make recommendations for the general population because understanding dietary patterns appear to be easier than the nutrient or food-based approach.[11]

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## Assessment of dietary patterns

One method of describing the overall diet is to assess the agreement of an individual's diet with pre-defined dietary standards. This approach is based on our previous knowledge about the health or disease promoting effects of dietary components, and is thus referred to as a priori. It involves the use of a graded score to assess an individual's diet against our best estimation of an ideal diet, which is usually based on scientific evidence regarding diet-disease relationships and current dietary recommendations.[4] Examples include a scoring system derived from studies of food groups, individual food items and nutrients in relation to common diseases in the population,[12] and the healthy eating index[13] which is a short measure defining how well a diet conforms to the US dietary guidelines. Necessarily, a priori approaches are limited by current scientific knowledge of diet-disease relationships.

Factor analysis and cluster analysis detect dietary patterns from existing data with no prior assumptions of health or disease relationships and are referred to as a posteriori. Factor analysis is a well-established statistical method used both to aggregate the variables and to categorize these variables into factors.

The long-established conventional practice in nutritional epidemiology was to examine the contribution of nutrients or foods for risks of chronic diseases.[4,14,15] The great majority of studies conducted in the field of human nutrition have investigated diet-disease relationships by focusing on nutrients, foods or food groups in relation to chronic disease.[16-20] A major disadvantage of these studies, however, is that individuals who differ in the intake of a particular nutrient usually also differ in intake levels of other nutrients, which may either enhance or diminish the effect of the first nutrient. Controlling for the effects of correlated micro- or macronutrients in multivariate statistical analysis addresses this issue in part, but the results are often contaminated by problems of multicollinearity and confounding by association.[21]

Over the past 20 years, an approach has been recommended by a number of nutrition experts to deal with the complex interrelationship of the wide variety of foods and nutrients. This approach known as dietary pattern analysis was first suggested by Jacobson and Stanton. DPA or food patterning has emerged as an approach for examining the associations between dietary patterns and chronic disease conditions.[4] This involves the process of examining how foods are grouped together by consumption patterns in an individual's overall diet. Subsequently, the relationships of the identified dietary consumption patterns to various sociodemographic, psychological and behavioral lifestyle risk factors are examined within the context of determining chronic disease outcomes.[22-24]

Factor analysis is a statistical method used both to reduce the number of variables and to categorize the variables into factors.[25] This method does not assess the association of independent variables to dependent variables; instead, it evaluates the associations among several dependent variables to detect something new regarding the independent variable.[25] Therefore, findings from factor analysis are not based on current knowledge; instead, they are more hypothetical than when the researcher directly evaluates independent variables.

Principal component analysis is the method of factor analysis that has been used to define dietary patterns because the principal components of a correlation matrix are mathematical functions of the observed variables. The central concept of principal components analysis is summarization of a large number of variables that can be replaced by a small number that still represents the whole.[25] Results of a principal components analysis include a factor loading matrix, which comprises the dietary patterns (i.e. factors) for the entire sample, and a factor score for each individual, which is derived by summing the individual intakes of the food items weighed by standardized scoring coefficients for each dietary pattern factor.

Therefore, each individual has a score for each factor or dietary pattern.

The other exploratory multivariate method used to describe dietary patterns is cluster analysis. While factor analysis aggregates food groups based on their correlation with one another, cluster analysis aggregates individuals based on the similarity of diets. The purpose is to sort people into relatively uniform groups (i.e. clusters), so that members of each cluster have dietary intakes similar to one another, but not similar to the dietary intakes of members of other clusters.[26]

The ability of cluster analysis to separate individuals to distinct groups is an advantage over factor analysis in which an individual may score high on more than one factor and thus the results may be more difficult to interpret. Another advantage of cluster analysis is that it can be used for different kinds of similarity indices, such as rating of the similarity Likert scale responses, whereas principal component analysis can be applied to correlation matrices. Cluster analysis is not designed to recognize unique characteristics of correlation matrices. For instance, factor analysis can detect the directionality of correlations (-1 to 1) and any alterations in the signs of the factor loadings without changing anything else in the PCA output, whereas negative correlations totally alter the cluster analysis output. Furthermore, the PCA method can identify other characteristics of correlation matrices that cluster analysis cannot. This is due to treating the associations as similarity measures, rather than correlations, in cluster analysis.[26]

Both factor and cluster analysis have distinctive features, so the study question at hand must guide the decision regarding which technique to use. Each method has the ability to uncover associations and structure that are both sensible and useful, even though not previously apparent. The results can help the classification scheme of dietary patterns.

### Advantages of dietary pattern analysis
Assessment of the total diet by any method has several advantages over single nutrient analy-sis. We have many examples of known interactions between nutrients (e.g. enhanced calcium absorption in the presence of vitamin D).[27] Moreover, dietary intake is inherently complex with the possibility of unknown components in foods that may interact with known nutrients or as yet other unknown food components. Similarly, single nutrient effects may be small, but their cumulative effect may be beneficial (or harmful) to human health. Dietary pattern analysis incorporates all nutrient interactions in the diet and makes investigators able to detect diet-disease relations without having any idea about the exact responsible nutrient or food.[28] Furthermore, identification of separate effects of nutrients or foods is very difficult due to the huge correlation between these components. For example, other beneficial compounds found in high fiber foods such as antioxidants and other phytochemicals confound conclusions from early studies regarding dietary fiber intake. Likewise, dietary intakes of nutrients may be confounded by dietary patterns. For instance, supplementation with beta-carotene in prospective trials failed to affect risk of chronic disease, while intake of fruits and vegetables as rich sources of beta-carotene were associated with reduced risk of disease in observational studies. Such beneficial effects of fruits and vegetables can partially be attributed to other beneficial constituents of these healthy foodstuffs. For example, the high content of fiber, folate, flavonoids, plant sterols, magnesium and potassium can explain such effects to some extent.[29]

The diet as a whole in free-living populations must be considered in assessing diet-disease relations and the effects of dietary recommendations because the addition or deletion of certain foods within a diet tends to displace other foods. There is a move toward inclusive food-based recommendations in the prevention of chronic diseases; however, the addition of all foods thought to be beneficial may lead to excess energy intake.[30] While most dietary recommendations aim to have less healthy foods replaced by healthy foods in the diet, it is critical to examine the entire dietary

pattern in order to determine the actual effects of dietary changes. Additionally, certain foods (e.g. eggs) may contain both beneficial (i.e. essential amino acids, unsaturated fats, foliate, other B vitamins) and detrimental nutrients (i.e. saturated fat and cholesterol) and thus the individual nutrient effects may actually cancel each other out.

Finally, it has been suggested that interventions based on total diet approaches are easier to implement. The position of the American Dietetic Association is that "healthful eating messages to the public should emphasize the total diet, or overall pattern of food eaten, rather than any one food or meal".[31] Assessing dietary patterns that reflect actual consumption can facilitate understanding dietary changes and may also help to translate the findings into practical public health recommendations.[32] Two notable clinical trials have set precedents not only in demonstrating that dietary patterns can have a remarkable beneficial effect on important risk factors for cardiovascular disease, but also in their ability to persuade subjects to adopt and comply with new dietary habits.[33,34]

*Limitations of dietary pattern approach*
Like all nutrition investigations, the validity of dietary pattern analysis depends on the dietary assessment method. Dietary recalls, food records, or food frequency questionnaires (FFQ) are generally used to assess dietary intake.[35] FFQs require subjects to recall their usual intake of food items or food group from a list of foods for a given period of time. Because the FFQ gathers less information regarding specific foods, cooking methods and portion size than 24-hour dietary recalls or food records, the quantification of nutrient intake is not considered as accurate.[35] This retrospective method of dietary assessment inherently has some measurement errors like possible under- and over-reporting of general food intake,[36] or selective under- or over-reporting of certain foods,[37] or both. Validation studies comparing FFQs with repeated dietary recalls generally show correlations in the range of 0.4 to 0.7 for

most foods and nutrients.[21,38] In validation studies comparing FFQs with biomarkers of nutrient intake, plasma triacylglycerol, vitamin C, and carotenoid concentrations also correlate similarly with food frequency estimates of both macronutrients[39] and micronutrients.[40] FFQs have been shown to correlate moderately well with 24-hour urinary nitrogen (r = 0.21-0.29) and urinary potassium (r = 0.32-0.34), even though 7-day food diaries provided better estimates of nitrogen and potassium intakes.[41] However, the FFQ is easier to administer and less costly to analyze, and because it is designed to assess usual intake, most large epidemiological studies have utilized food frequency questionnaires.[42-44]

In the dietary pattern approach, the researcher has to make arbitrary decisions and establish judgments at several stages of the process, which may yield biased results regarding the selection of the variables that participate in the analysis, the number of retained factors and factor interpretation. Generally, all statistical methods that have been used for data reduction have limitations. For example, using factor analysis for dietary data reduction has been criticized for its subjectivity in nature and difficulty in replicating the results in other populations.[45] However, similar dietary patterns derived by factor analysis have been observed in different populations. It is also inappropriate to analyze the relationship between nutrients and disease through dietary pattern analysis, since this analysis is not specific for such purposes. Most dietary pattern analyses have not considered participants' dietary behaviors, while the inclusion of eating behaviors such as meal and snack patterns in dietary pattern analysis has been recommended.[46]

*Validity and reliability of dietary patterns*
Dietary patterns resulting from a factor analysis of FFQ items have been validated against dietary patterns derived from food records.[38] Hu et al[38] assessed the validity and repeatability of dietary patterns identified by factor analysis by comparing results from the FFQ administered twice, 1 year apart, and two 1-

week diet records among a subset of subjects in the Health Professional Follow-up Study.[38] They identified two major dietary patterns which they label "prudent" and "western". The prudent pattern was characterized by a higher intake of vegetables, fruits, legumes, whole-grains and fish, whereas the western pattern was characterized by a higher intake of processed meat, red meat, butter, high-fat dairy products, egg, and refined grains. The correlations between the FFQ and the diet records (0.45 to 0.74) for the two patterns and the correlations between factor scores and plasma biomarkers, which were in the expected directions, indicated great validity and reliability of food intake patterns identified by factor analysis. Khani et al[47] indicated that identification of dietary patterns by factor analysis is valid and reproducible. Similar studies are available validating dietary patterns derived from cluster analysis by comparing nutrient or biochemical profiles between the clusters.[48,49] In a study of 1828 adult women who participated in the Framingham Offspring-Spouse study, Millen et al[49] have identified five distinct dietary patterns by the use of cluster analysis. Patterns rich in fruits, vegetables, grains, low-fat dairy, and lean protein foods resulted in higher nutrient density assessed by 3-d food records. Patterns rich in western food items have lower nutrient density. Those with greater adherence to Empty Calorie pattern had lower compliance with clinical risk factor guidelines as compared with other groups. They came to the conclusion that cluster analysis is an accurate method to identify dietary patterns. The internal validity of a dietary pattern analysis for characterizing dietary exposures in epidemiological research has also been reported by other investigators.[50]

The reproducibility of dietary patterns across populations, however, has not been examined and doing so brings up the subjective nature of factor analysis. In conducting factor analysis, the researcher must decide which variables to enter into the correlation matrix. A bias in either the inclusion or exclusion of certain variables can cause problems.[25] Although dietary patterns would not be expected to be uniform across all populations, the use of factor analysis has been criticized because of its subjective nature.[45] However; the similarity of findings among different populations would help investigators of nutritional epidemiology to use this method in their future studies.

*Major dietary patterns in the Middle East*
Overall, data on dietary patterns from developing countries are scarce. Therefore, one of the major aims of the present study is to encourage nutrition investigators in the region to use this approach in the identification of diet-disease relations. Studying the associations between major food intake patterns and risk of chronic diseases is particularly important in Middle-Eastern countries due to the high prevalence of a Middle-Eastern pattern of obesity in these populations, which makes them very susceptible to increased risk of obesity-related co-morbidities.[51] Besides different patterns of obesity, dietary intakes of Middle Eastern populations have their own unique characteristics: large portion sizes with high intakes of refined grains[52] (like white rice and bread) and hydrogenated fats[53] and more percentage of energy from carbohydrates.[51] With these features, factor or cluster analysis might provide different dietary patterns in this region as compared to those reported from other parts of the world. From the Middle-Eastern countries, Esmaillzadeh et al found three empirically derived dietary patterns among Tehrani female teachers by the use of factor analysis based on data from a food frequency questionnaire.[51,54,55] Three dietary patterns have been extracted and labeled as healthy, western and traditional by the investigators. Further analysis showed a significant relationship between these major dietary patterns and metabolic syndrome and insulin resistance and also with inflammatory biomarkers.

The patterns extracted in our study were similar to those found in earlier studies on adult populations. In the dietary validation study of the Health Professional's Follow-up Study, Hu et al[38] identified two major dietary

patterns named "Prudent" (including vegetables, fruits, legumes, whole-grain and fish) and "Western" (including processed meat, red meat, butter, high-fat dairy products, eggs and refined-grain). Similar dietary patterns were found in the Nurses Health Study[56] and other studies that included American women.[57] Khani et al,[47] investigating the participants of Swedish Mammography Cohort, reported three major dietary patterns labeled "Healthy" (high in vegetables, fruits, fish, poultry, tomato, cereal, and low-fat dairy products), Western (processed meat, meat, refined grains, sweets, and fried potatoes) and "Drinker" (beer, wine and liquor, snacks). The "Healthy" and "Western" patterns found in the current study are very similar to the "Prudent" and "Western" patterns reported by Hu et al[38] and are comparable to the "Healthy" and "Western" patterns reported by Khani et al.[47] However, it should be kept in mind that patterns are comparable only if the food groups and the factor loadings relating to their magnitudes are similar. Since the patterns are extracted from the data collected from studied populations, the results are not expected to be reproduced in populations with different food habits.

As major dietary patterns differ according to sex, race, and cultural situations,[35] we recommend nutrition scientists in each country to identify major dietary patterns in their own country. These dietary patterns can be stressed when educating people to modify their lifestyle for reducing chronic disease risk.

To determine if major dietary patterns identified by factor or cluster analysis are associated with chronic disease risk, we reviewed the studies that have assessed the association of these dietary patterns with insulin resistance and metabolic syndrome. However, most studies have evaluated the association of major dietary patterns with other chronic diseases. But as our aim was not to review the studies that assessed the associations between major dietary patterns and chronic disease risk, we bring here just two chronic diseases as examples to show that dietary patterns are associated with chronic disease risk. Our previous report has reviewed the association between major dietary patterns and chronic disease risk.[58]

### Major dietary patterns and metabolic syndrome

The metabolic syndrome is clustering of metabolic abnormalities in one person. The prominent core abnormalities for this syndrome seems to be abdominal adiposity and insulin resistance.[59] The criteria for diagnosing the metabolic syndrome has not been unanimously agreed.[60] The definition suggested by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) is currently in use with minor modifications.[61] Individuals affected by this syndrome are more likely to have risk of coronary heart disease, stroke, peripheral vascular disease and type 2 diabetes.[62,63] The metabolic syndrome is highly prevalent in both developed[64-66] and developing countries.[67-69]

Several studies have reported the association between empirically derived dietary patterns and the metabolic syndrome. In the framework of the Framingham Offspring Study,[70] higher prevalence of the metabolic syndrome has been reported among women with the "empty calorie" dietary pattern and lower prevalence among women with "wine and moderate eating" dietary pattern. In a cross sectional study among British adults,[71] a food pattern characterized by high consumption of fruits and vegetables and low consumption of processed meat and fried foods was inversely associated with features of the metabolic syndrome. However, the limitation of this study was lack of statistical adjustment for physical activity that is associated with dietary patterns.[72] In the Malmö Diet and Cancer Cohort,[73] features of the metabolic syndrome were more prevalent among women with the "white-bread" dietary pattern and less prevalent among women with "milk-fat" pattern. All studies mentioned above have been reviewed by Boxter et al[74] in a recent review article. There is just one report[75] available assessing the association of major dietary patterns and

the metabolic syndrome among adolescents; in which the Korean investigators have found three major dietary patterns (namely Korean traditional, western and modified) among 944 adolescents aged 10-19 years. They found that abdominal obesity was highly prevalent in Western group (16.0%) than that in the Korean traditional (9.76%) or the modified (9.75%) cluster. The Western group had also the highest prevalence of elevated triglyceride levels and abnormal glucose homeostasis. No significant difference was seen in the prevalence of the metabolic syndrome across dietary patterns' clusters. It should be taken into account that all the mentioned studies have used cluster analysis to identify dietary patterns and it has remained unknown until most recently whether dietary patterns identified by factor analysis are also associated with metabolic syndrome. Factor analysis and cluster analysis are statistically different procedures and each one identifies dietary patterns with different food compositions.[76] Some evidence supports that individuals' dietary patterns would be best represented using factor analysis.[76,77] Our recent studies[51,54,55,78] among Tehrani female teachers identified three major dietary patterns using factor analysis: the healthy dietary pattern (high in fruits, vegetables, tomatoes, poultry, legumes, tea, fruit juices and whole grains), the western dietary pattern (high in refined grains, red meat, butter, processed meat, high-fat dairy products, sweets and desserts, pizza, potatoes, eggs, hydrogenated fats, soft drinks and low in other vegetables and low-fat dairy products) and the traditional dietary pattern (high in refined grains, potato, whole-grains, tea, hydrogenated fats, legumes and casserole). After controlling for potential confounders, individuals in the highest quintile of healthy dietary pattern score had a lower odds of the metabolic syndrome (OR = 0.61; 95% CI: 0.30-0.79, p for trend < 0.01) than those in the lowest quintile. Compared to those in the lowest quintile, women in the top quintile of western dietary pattern score had greater odds of metabolic syndrome (1.68; 1.10, 1.95, p for trend < 0.01). Higher consumption

of traditional dietary pattern was only associated with abnormal glucose homeostasis (1.19; 1.04, 1.59). In another recently-published cross-sectional study among more than 3000 adult men and women in Greece, Panagiotakos et al[79] identified six major dietary patterns by using factor analysis. These patterns explained 56% of the total variation in dietary intakes. They concluded that a dietary pattern characterized by high intakes of cereals, fish, legumes, vegetables, and fruits was independently associated with reduced levels of clinical and biological markers linked to the metabolic syndrome, whereas a dietary pattern highly loaded with meat and alcohol showed the opposite association. Besides the association of posteriori dietary patterns with the metabolic syndrome reviewed above, several studies have assessed the association of a priori dietary patterns with this syndrome; most recent ones are the inverse association between adherence to 2005 Dietary Guidelines to Americans and also adherence to the Mediterranean dietary pattern (both assessed by creating an index) and the metabolic syndrome.[80,81] Therefore, it seems that both posteriori and a priori dietary patterns are significantly associated with the risk of metabolic syndrome.

*Major dietary patterns and insulin resistance*
Insulin resistance has been reported as a basis for clustering of metabolic abnormalities of the metabolic syndrome. Few studies have investigated the dietary determinants of insulin resistance and particularly the association between dietary patterns and insulin resistance has received little attention. While some studies have considered this association as their main objective,[82] others have reported it as an accessory finding.[83, 84] In a cross-sectional study on 980 multi-ethnic adults aged 40-69 years, Liese et al[82] showed that individuals with the "white bread" pattern (identified by cluster analysis as being high in white breads, tomatoes, cheese, dried beans, eggs, meats, fats, oils and beer) had worse levels of insulin sensitivity, while the "dark bread" (with high intakes of dark-bread and high-fiber cereal, rice and

pasta, cruciferous vegetables, other vegetables, potatoes, low-fat milk, fish, nuts, seeds and tofu) and "wine" patterns (with high intakes of wine and mixed drinks) ranked best with regard to insulin sensitivity compared to the other patterns identified. Higher scores on the "western" dietary pattern (identified by factor analysis) were associated with higher insulin levels in the Health Professionals Follow-up Study.[83] The same results have also been observed in the NHANES III.[84] All studies reviewed above are reported from the US and limited data are available in this area from other countries. This could be a huge concern because the association between diet and insulin resistance is race-dependent.[85] In a study from South Ireland,[86] investigators have identified three major dietary patterns among 1018 adult men and women by using cluster analysis: Irish traditional pattern, healthy dietary pattern and a pattern composed of high alcohol and convenience foods. Further analysis showed that those in the healthy pattern cluster had lower scores of HOMA-IR as compared to the other clusters. The prevalence of insulin resistance among individuals in the healthy cluster was significantly lower as compared to the other clusters. Among Iranian people, we showed that after controlling for potential confounders, individuals in the highest quintile of healthy dietary pattern score had a lower odds of insulin resistance (0.51; 0.24, 0.88, p for trend<0.01) than those in the lowest quintile. Compared to those in the lowest quintile, women in the top quintile of western dietary pattern score had greater odds of insulin resistance (1.26; 1.00, 1.78, p for trend < 0.01). We

found no significant association between Iranian traditional dietary pattern and insulin resistance.[55] As evident from the studies reviewed here, empirically derived dietary patterns are significantly associated with the risk of insulin resistance.

## Conclusion
As mentioned above, the traditional focus of nutrition science on the amount and distribution of nutrients is being replaced by a combinational focus on nutrients and food components and foods. There are many unknown nutritious and non-nutritious compounds in foods that may interact with other foods or nutrients. Therefore, the dietary pattern approach that considers the whole diet has received considerable attention in recent years. Previous studies showed that this approach provides a valid and reliable method for identifying diet-disease relations. They also showed that the dietary patterns extracted from factor or cluster analysis are significantly associated with chronic disease risk. However, some investigators believe that in assessing dietary patterns other factors such as time, number of meals and snacks should also be taken into account. Anyway, considering few data available from the Middle East region in this field on the one hand and high prevalence of non-communicable diseases on the other hand, it is recommended that nutrition scientists in the region focus on existing dietary patterns in their population and assess the association of these patterns with prevalent chronic diseases. The dietary pattern approach can also be emphasized in lifestyle modification programs.

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