On the basis of 12 years of follow-up of 11,654 Norwegians aged 35–52 years, Njølstad et al. (1) recently reported that high density lipoprotein (HDL) cholesterol, controlled for potential confounders, was inversely associated with type 2 diabetes among women but not among men. These findings of a sex difference in HDL cholesterol as a protective factor for diabetes are consistent with an earlier study by Fagot-Campagna et al. (2) of 787 Pima Indians aged 15 years or older. Because of a high incidence of diabetes (76 men and 185 women developed diabetes during 10 years), the Pima study had greater power to find a relation between lipoproteins and diabetes. Similar to the Finnmark finding (1), HDL cholesterol was inversely related to diabetes incidence among Pima Indian women but not men, when controlled for age, body mass index, systolic blood pressure, and 2-hour glucose. In both studies, there was no effect of lipids other than HDL cholesterol on diabetes incidence when controlled for potential confounders. Replication of results in two different populations is always interesting, and we would like to comment further on these results.

Whether HDL cholesterol is directly involved in the development of type 2 diabetes is not clear. HDL cholesterol could simply be a marker for another explanatory factor, or it may act as an intermediary between a third factor and diabetes. Pima Indians were more obese, had lower HDL cholesterol levels, and were probably more insulin resistant than the Norwegians. Insulin resistance, an established risk factor for diabetes, might underlie the relation between HDL cholesterol and diabetes. Specific measures of insulin resistance were not available in the Finnmark study (1). However, Fagot-Campagna et al. (2) accounted for estimated insulin resistance, and HDL cholesterol remained protective of diabetes among Pima Indian women. Alcohol consumption and physical activity increase HDL cholesterol levels and may confound the relation between HDL cholesterol and diabetes if they are associated with diabetes. Alcohol consumption and physical activity may also explain sex differences if they are distributed differently among men and women. However, both of these studies controlled for alcohol consumption, and Njølstad et al. (1) also controlled for physical activity. The observed difference in the HDL cholesterol effect between men and women may also be due to differences in HDL subfractions between the sexes, and the subfractions themselves may have differential associations with diabetes.

A high HDL cholesterol level may reflect sex hormone balance and could explain why, in both studies, a high HDL cholesterol level was a protective factor for diabetes among women only. Both studies reported that menopause had no significant effect on the relation between HDL cholesterol and diabetes. Interestingly, another study among American Indians showed that a high HDL cholesterol level was a protective factor for diabetic nephropathy among women only, and this effect was slightly stronger before menopause than after, suggesting a sex hormone effect (3).

Results replicated in two studies from diverse populations strongly suggest that a higher HDL cholesterol level is a protective factor for type 2 diabetes among women. Alcohol consumption, physical activity, or insulin resistance may partially account for this relation, but it appears likely that sex hormones may also be involved. As Njølstad et al. (1) pointed out, an interesting implication is that the attenuated sex differences in coronary diseases among diabetic subjects may be associated with sex-related differences in diabetes determinants. Further studies should explore this intriguing link between HDL cholesterol, HDL subfractions, and type 2 diabetes but should take into account a potential effect of sex hormones.


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Three issues regarding Slattery et al.'s (1) application of factor analysis to dietary data deserve further consideration. First, one might expect the "Western" and "prudent" diets, or the "high fat/sugar dairy" and "substituter" diets, to be correlated inversely. However, the use of varimax rotation by Slattery et al. means that factors derived from the data are orthogonal, or uncorrelated. An oblique rotation would have been useful to show how correlated some of the factors are.

Second, the factor labels imply more about overall diet, lifestyle, and personality than is warranted. For example, the labels "prudent" and "substituter" imply health consciousness, while "Western" and "high fat/sugar dairy" imply the opposite. However, because factor analysis clusters foods and not persons, people can "fit into" more than one pattern. If "fitting into" a pattern is arbitrarily defined as being grouped in the fourth or fifth quintile of the factor score for the pattern, for example, then roughly 16 percent of the population would fit into both the "Western" and the "prudent" eating patterns. It is not immediately obvious that a person who eats a "Western" diet can also eat prudently. It is easier to imagine that a person who eats red meat, refined grains, and added sugar can also eat plenty of vegetables, legumes, and fresh fruit.

Finally, Slattery et al. (1) do not state explicitly how an eating-pattern approach is more useful toward public health intervention than information based on single nutrients or foods. On one hand, the implications of knowing that a "Western" diet increases the risk of colon cancer are not clear. Does the finding call for changing the whole diet, which may be less feasible than targeting single nutrients or foods? Should all the foods associated with a given pattern be targeted for population intervention? Examining eating patterns may not even deliver strikingly new knowledge. The authors essentially confirm what we already know, if only on an intuitive level: that we eat characteristic combinations of foods and that these combinations are associated with disease.

However, the simple idea of looking at eating patterns is the most valuable aspect of this research. By examining eating patterns, Slattery et al. (1) chose to study dietary "exposures" that people can relate more easily to their own diets. Findings based on single nutrients may contribute to the understanding of disease etiology, but when they are used for public health intervention they imply that targeting single nutrients is the most effective way to reduce disease risk. Studying eating patterns in epidemiologic research conveys the message that the whole diet is in fact important and worth studying. As Slattery et al. demonstrate, eating patterns may be even more strongly and consistently associated with disease than are single nutrients or foods. Descriptions of eating patterns also serve as a reminder that single nutrients and foods are not consumed together randomly, that diet has structure, and that specific dietary components consequently may be difficult to change.

By examining the association between eating patterns and risk of colon cancer, Slattery et al. (1) respond to the important question of whether the whole diet, not just some component of the diet, is associated with disease risk. Their work joins a relatively short list of other articles that have attempted to describe eating patterns by using a variety of different approaches, including principal components or factor analysis (2, 3), cluster analysis (4-6), and multiple discriminant analysis (7). These articles have examined eating-pattern associations with a variety of health correlates and outcomes, including health behaviors (8), cardiovascular risk factors (9), birth weight (10), and colon cancer (11).

Although methods of studying eating patterns are not yet widely used or accepted in nutritional epidemiology, increased interest hopefully will motivate further efforts to develop and evaluate appropriate methods to study diet measured more broadly.

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