The recent paper by Hoffmann et al. (1) raises a very important methodological issue in nutritional epidemiologic research. The investigation of dietary patterns in disease risk analyses is a necessary step away from the reductionist approach of studying single nutrients as disease predictors. The suggestion of Hoffmann et al. to substantially improve the hitherto-applied statistical procedures in dietary pattern analysis by employing a method that uses an actual data set and prior knowledge about nutrient-disease relations is to be greatly appreciated. However, I would like to comment on some further limitations of that approach which were not sufficiently considered in the article.

The main criticism raised about dietary quality scores, an approach to the characterization of food-related effects on health and disease, was that they focus on selected aspects of diet—based on prior knowledge—but do not take the correlation structure of food and nutrient intake into account. In contrast, principal-components analysis is a factor analysis of the actual data to derive dietary patterns but does not incorporate prior knowledge of nutrient-disease relations. Although Hoffmann et al. convincingly argue that reduced rank regression (RRR) overcomes these limitations, this is only partly true.

RRR uses disease-specific response variables to determine combinations of foods that explain a maximum amount of response variation. Two prerequisites here might not be present in all instances. First, there needs to be a clear picture of the underlying biologic mechanism relating nutrients or dietary factors to the development of a specific disease. Second, data on the nutrient or dietary factor must be available in food composition tables. The case of fruit and vegetable intake and the glycemic effect of foods on blood glucose and insulin levels illustrates these issues very well.

A high fruit and vegetable intake has been found to be protective against many diseases (2, 3). However, this protective effect has been ascribed to a range of different nutrients and nonnutritive components in fruits and vegetables that could be independently or jointly responsible for the apparent reduction in disease risk. Given this lack of clarity, RRR cannot be any more informative than a dietary factor defined a priori, such as fruit and vegetable intake per se. In addition, the majority of constituents in fruits and vegetables are not listed in food and nutrient databases; therefore, no maximization of the response variation is possible. Similarly, physiologic responses to food intake, such as the glycemic response to foods containing carbohydrates, can only be accounted for in a very limited way, if at all, in food and nutrient databases.

Both of these aspects might be important predictors of the risk of developing type 2 diabetes mellitus (4, 5). Since they cannot be considered adequately in dietary pattern analysis like the suggested RRR, the resulting patterns, as presented by Hoffmann et al. (1), have only limited meaning.

RRR does not overcome the limited knowledge about the relations among food intake, dietary factors, and disease risk. If the underlying biologic mechanisms remain to be elucidated, RRR can only work on the basis of current knowledge or hypotheses. This is quite often the case and is not an extreme case, as Hoffmann et al. (1) stated in their Discussion section. Therefore, the results can only provide answers within the current theoretical framework.

**REFERENCES**


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**THE AUTHORS REPLY**

We thank Dr. Kroke for her comments (1) on the application of reduced rank regression (RRR) in nutritional epidemiology. We agree that using nutrients as response variables in RRR requires both adequate data from food composition tables and prior knowledge of an association between nutrient intake and disease. However, we do not agree that a clear picture of the underlying biologic mechanism is a prerequisite for RRR analysis. For deriving disease-related patterns, the RRR method is already more powerful than principal-components analysis if variation in intake of the selected nutrients is more relevant for disease development than the unspecified variation in intake of all foods. This weaker assumption seems to be fulfilled for the ratio of poly-