# Chapter 2
# Challenges in Research in Nutritional Epidemiology

**David R. Jacobs, Jr.**

**Keywords** Nutritional epidemiology • Methods of dietary assessment • Dietary recall • Food frequency questionnaire • Biomarkers • Dietary patterns

## Key Points

- Diet is a complex aggregate of foods and behaviors. The food is constituted of a wide variety of intended and unintended chemicals which may act singly on human metabolism, but more likely act in groups in a synergistic fashion.
- The study of nutrition and disease in aggregates of human beings—nutritional epidemiology—is hampered by the difficulty in accurately characterizing this complex aggregate, that is, in stating what people are eating. Part of this difficulty is inherent in the large day-to-day variability in what is eaten. Another part of the difficulty relates to finding efficient and accurate ways to collect dietary information, minimizing participant burden, and maximizing utility of the data for investigators.
- Much progress has been made in nutritional epidemiology in recent years owing to the use of food frequency questionnaires, which pose little participant burden and are relatively easy to analyze. However, such data collection instruments are still characterized by high within-person variation and at the same time severely limit collection of important details about diet.
- A critical concept is whether the participant or the researcher synthesizes the dietary information, including issues such as defining the time period over which to average diet, what to do with unusual information, what constitutes a serving,

D.R. Jacobs, Jr., PhD (✉)
Division of Epidemiology and Community Health, School of Public Health,
University of Minnesota, 1300 South Second Street, Suite 300, Minneapolis, MN 55454, USA
e-mail: Jacobs@epi.umn.edu

N.J. Temple et al. (eds.), *Nutritional Health: Strategies for Disease Prevention*,
Nutrition and Health, DOI 10.1007/978-1-61779-894-8_2,

how foods are grouped (grouping fruit juice and fruit drink together, or not, for example), and what emphasis to put on brand names.
- The author speculates on protocol changes and computer technology advances that might allow more complete and accurate diet data collection.
- It is important to study foods, food groups, and food patterns as well as nutrients and other chemicals contained in food. Food is what people eat. Where many chemical constituents of a food act synergistically, an association will be found with the food but none will be found with individual constituents. The associations of food patterns with risk provide feedback to policy makers on the likely success of nutritional pronouncements.

Much has been written about the practice and challenges of research in nutritional epidemiology. For general details concerning this topic, the reader is referred to existing and extensive source materials, including *Design Concepts in Epidemiology*, edited by Margetts and Nelson [1] and *Nutritional Epidemiology* by Willett [2]. These books provide myriad technical details on the goals of nutritional epidemiology and the conduct and interpretation of studies, with discussion of potential pitfalls. This chapter focuses on two issues that are particularly challenging in nutritional epidemiology: (1) how to find out what people eat, and (2) how to think about the effect of diet on health.

## 2.1 How to Find Out What People Eat

### *2.1.1 The Nature of Dietary Information*

A full characterization of a person's diet would consist of a large number of discrete pieces of information. There are thousands of foods, prepared in myriad ways, and eaten in various amounts and combinations. Even a single "food" such as a carrot [2] or an onion [3] presents a challenge, as there are many varieties and genetic variation; growing conditions are influential in food composition. The timing and context of eating, as well as the number of meals eaten, may all contribute to metabolism of food. Willett [2] spends an entire chapter showing that actual consumption varies widely from day to day. It may take months for individual diets to settle down to a steady state average.

Each food supplies myriad chemicals. Among these chemicals, Willett [2] lists essential nutrients (vitamins, minerals, lipids, amino acids), major energy sources (fat, protein, carbohydrate, alcohol), additives (preservatives, flavorings), agricultural contaminants (pesticides, growth hormones), microbial toxins (aflatoxins), inorganic contaminants (cadmium, lead), chemicals formed in the cooking or processing of food (nitrosamines), natural toxins (natural pesticides), and other natural compounds (including DNA, enzymes, and enzyme inhibitors, many of which he says are thought of as "incidental to the human diet"). Energy content and nutrients, along with a few natural compounds, are readily available in a variety of

food tables, while assessment of the remaining categories requires specialized databases. All of these chemicals pertain to each food eaten and can be summarized over the entire diet. The complete characterization of diet, foods, and the chemicals eaten, is clearly formidable. At some point in the research process, this large volume of information must be synthesized to be used in data analysis, that is statistical variables such as food groups and nutrients must be defined based on the available information.

### *2.1.2 Methods of Dietary Assessment*

Two primary classes of methods have been used historically to assemble individual dietary information and synthesize it into something usable in data analysis, described in detail by Willett [2]. The first method includes dietary recalls and records. Dietary recalls are obtained by an interviewer assisting the participant to remember precisely what was eaten, usually over the past 24 h. Dietary records, on the other hand, are obtained by having the participant write down what was eaten, shortly after it was consumed; in practice, participants often wait until the end of the day to do their recording, so that the record easily transmutes to a self-administered recall. Variations in these methods include weighing foods before eating; collecting a duplicate portion of the food for subsequent chemical analysis; and recording onto partially precoded forms. Dietary recalls may differ in how intensively they inquire about different aspects of diet; for example, an interviewer may inquire deeply and pointedly, to a greater or lesser extent, for hard-to-obtain full information on such topics as alcoholic beverages drunk, salt-containing condiments used, or brand names of products eaten. Timing of eating may be obtained so that the integrity of individual meals can be maintained in the database. In both recalls and records, the data consist of a description of the food eaten and its portion size, perhaps with notes on brand names and preparation methods. The fact that a hamburger and a bun were eaten will generally be maintained in the database, but it is fairly common not to maintain whether the two were eaten as a sandwich.

The second method is a food frequency questionnaire (FFQ), characterized by asking the participant general questions about diet. A typical question would be: “Do you eat hamburgers, and if so, how often and in what portion size?” Other kinds of general questions are also common. For example, one might ask: “When you eat a hamburger, is it usually a low-fat variety?” The scope of questions may include related aspects, for example: “Do you prefer white bread or whole wheat bread?” An important aspect is that foods are often grouped: “How often do you eat apples or pears?” FFQs come in several varieties, e.g., from 12 to 250 questions, with and without information about portion size. Those that ask about portion size are called semi-quantitative FFQs. In a popular variant, the Willett-style questionnaire, a portion size is given for each food and frequency of portions is queried. In the other popular variant, the Block-style questionnaire, frequency of eating occasions is queried for each food, with a separate question about portion size. Additional

variants exist, for example in which pictures or food models are provided to facilitate food recognition and portion size estimation.

The dietary history method is closely related to the FFQ. Here, time is spent in general discussion of the diet prior to recording answers to the formal questions; this discussion is thought to improve the context of the interview and help the participant to put together the information needed. In the diet history, the close-ended questions may be general, e.g., "Do you eat red meat?," with an open-ended elicitation of foods eaten for those who answer affirmatively. The CARDIA Diet History [4–6] is of this form: 1,609 food codes or recipes were endorsed by at least one of over 5,000 participants in one of two administrations of this questionnaire through 1993. Due to expansion of the specific products supplied by industry, the number of food codes endorsed expanded dramatically in the 2005–2006 administration of this questionnaire.

It is probably a coincidence of history that the primary approach to dietary assessment used in cardiovascular disease epidemiology in most major studies through the early 1980s was 24-h recalls; used, for example, in the Lipid Research Clinics [7, 8] and Multiple Risk Factor Intervention Studies [9, 10]. Special attention was paid to translating the myriad pieces of information into energy and nutrient intake. The synthesis of the data proved quite difficult and relatively little work was done to study the associations of individual foods or food groups on long-term health outcomes. Where food grouping was done, it was done inflexibly, so only certain combinations of foods could be examined. Examination of nutrients within food groups (e.g., monounsaturated fat from plant vs. animal foods) has received little attention. In principle, the data are available for such analyses, but it is unlikely that anyone will ever have the time, money, and study connections for such purposes. In contrast, cancer epidemiologists have long used FFQs [11]. This choice may be related to the traditional use of the case–control design for rare cancers. The desired information was the diet before diagnosis, and this would not be obtainable by recording or recalling current diet. In the cancer epidemiology field, much more has been written about foods and food groups than in the cardiovascular disease epidemiology field. In contrast to analyses of dietary recall data, nutrient analyses within food groups are fairly common. On the other hand, the FFQ obtains much less information than does the recall/record method. For example, information about "yellow and green leafy vegetables" may be all that is collected; therefore, no information is obtained regarding which vegetables were eaten.

An example of a local effort that addresses this issue is the foods and nutrient database maintained in the Department of Nutrition at the University of Oslo, which has long had a food grouping code for each food. Therefore, foods analysis has been available independent of the nature of the method of dietary data collection. Such analysis has been performed fruitfully, also allowing diet pattern analysis to take place [12]. Further, partially addressing this issue, the Nutrition Coordinating Center in the early 2000s added a food grouping system with 166 food subgroups in its Nutrition Data System for Research (NDS-R) diet analysis system (University of Minnesota, Minneapolis, MN, http://www.ncc.umn.edu/index.html, accessed May 6, 2011). The CARDIA database added these for its diet history data in 1985–1986,

1992–1993, and 2005–2006, which has enabled substantial food group analyses. Nevertheless, a great number of details in the CARDIA diet database remain inaccessible, primarily for reasons of cost in pulling those data (other than the preformulated food group) from those massive databases.

### *2.1.3 Ability to Represent Usual Diet*

Two major conceptual differences exist between the recall/record and FFQ methods. The first relates to representativeness of usual diet. The strength of the recall/record method is that it can collect accurate and detailed information about actual consumption of particular meals. However, the particular day or meal is rarely of interest in nutritional epidemiology. It is well agreed that a single day's recall or record is inadequate as a representation of typical intake [2]. The general experience has been that the recall/record method has not worked well in studies of diet and chronic disease outcomes. Nevertheless, multiple days of recalls or records can represent the typical diet quite accurately, as in the Framingham Children's Study [13, 14]. However, it is rare for large studies to undertake more than one or possibly 2 days of recalls.

The FFQ class of methods, in contrast, asks about the typical dietary pattern during a longer time frame, typically the past year. Many studies have found associations of nutrients and/or food groups with chronic disease outcomes using this method [15]. An even more powerful method uses repeated FFQ assessments during follow-up in a cohort study [16]. When the typical diet is not changing greatly over several years, averaging results from repeated FFQ assessments can be quite powerful.

### *2.1.4 Who Synthesizes Dietary Information?*

The second major conceptual difference between the recall/record and FFQ methods relates to how the myriad dietary details get synthesized into data analytic variables. This refers to the acts of summarizing, as an average, or otherwise characterizing, such as eating or not, discounting or upweighting unusual days or periods, dealing with unusual items, setting defaults for portion size and other aspects that are not specifically known, such as in restaurant eating, making fine distinctions, such as between fruit, fruit juice, and fruit drink, focusing on brand names, or not, and how to deal with waste. In the recall/record method, a huge database is created with near infinite flexibility. The researcher is responsible for putting this information together in a manner that is usable in data analysis. In practice, this synthesis is often limited to energy and nutrient intake analysis; however, it is quite possible that the inherent flexibility of this method may be better utilized in coming years as computer technology continues to improve; for example, as indicated above

this has occurred in the interactions between the Nutrition Coordinating Center and the CARDIA study.

In the FFQ class of methods, the participant synthesizes the information. Much potential detail, and therefore flexibility, is lost, but the vastly reduced amount of information collected tends to make it a small job to create arbitrary combinations of food and nutrient variables. It seems likely that the investigators' formal synthesis of multiple recalls or records would be more accurate than the participant's informal synthesis. However, especially if the investigators' synthesis never gets done, the participant's synthesis is not without merit, despite variability in synthetic capability across participants and difficulty in defining typical patterns. For example, if a person actually drank 20 glasses of milk in a month, including one stretch of 5 days in which 10 of the glasses were drunk, one might say that the typical pattern is two-thirds glass per day. A recall could easily be done on a day when no milk or two glasses were drunk, thus getting the wrong answer, but it is easy for a person to summarize their pattern into something like a glass every other day.

Some cleverness may be needed in the FFQ mode to get at nutritional concepts with which the public is less familiar, such as whole grain bread. A prime example is the use by Willett of the term "dark bread" to elicit breads that were most likely to have at least moderate whole grain content. Although "dark bread" is a somewhat oblique reference, asking directly about whole grain bread might not have been well understood by participants, and most breads containing a substantial amount of whole grain are darker than American white bread. Dark bread is oblique due to exceptions popular in the US, including pumpernickel cooked with molasses and rye bread made with refined rye. Despite these potential problems, the reference to "dark bread" succeeded in eliciting breads that were inversely associated with coronary heart disease mortality in the Iowa Women's Health Study [15]. Another interesting Willett innovation in an attempt to get at an important detail, and also used in the Iowa Women's Health Study, was the additional query of the brand name of the usual breakfast cereal eaten [15]. Despite the fact that many people eat more than one breakfast cereal, this detail provided the ability to categorize brands, a great boon in the study of whole grains and health. Similarly, the CARDIA Diet History was innovative in that it intended to blend recall and synthesis. It asked for the last 30 days of typical intake, recent enough for some level of recall to assist the participant in synthesizing. It also allowed tremendous detail in the participant's self-assessment of typical intake by prompting the participant with 100 general food categories (e.g., eggs), then asking the participant to name all foods consumed within each category. The question, "How often do you eat at fast food restaurants?," while not specifically asking about foods consumed, falls within the FFQ type of query. It has been used fruitfully in finding, for example, that fast food intake appears to promote obesity and insulin resistance [17–19], while eating at "slow food restaurants" does not have the same effect [17, 18].

### 2.1.5 *Can Accurate Dietary Information Be Obtained?*

A great deal of progress has been made in understanding the relationship of diet with chronic disease, based mostly on FFQs. Nevertheless, validation studies of FFQs against 1–4 weeks of food diaries are somewhat discouraging. It is difficult for most people to summarize their diet accurately. There are several reasons for this including: that such summarization requires considerable quantitative ability; that most people simply eat, without making habitual summaries of what they are eating; that diet varies considerably and what is typical for the past month might be different from what is typical for the past year; and that the researchers' questions might not be the optimal formulation for eliciting particular dietary facts. Criterion measures have revealed correlations in the range of 0.3–0.6 between the two methods [5, 20–22]. The resulting within-person error leads to serious problems in interpretation of dietary data [1, 2, 23, 24].

Certain data analytic and interpretive approaches can be helpful. Cautious statements and consistency checks are called for. For example, an assertion that a nutrient is related to incident disease will be stronger if all the foods that contain the nutrient are individually also related to that disease, given that different foods contain different mixes of nutrients [2]. Conversely, if an apparent relationship of disease with a nutrient exists only for a single food that was eaten often and is high in the nutrient, that would be more consistent with the concept that the food, not the nutrient, is causally related to incident disease. Then the causal pathway might rely on a synergy of the components of the food or on a different single nutrient. An example of this type of finding was that phosphorous from dairy, but not from other sources, was related to future hypertension [25]. While this type of finding could reflect synergy of some type, other possible explanations include selective misclassification of the nutrient across the food groups (e.g., phosphate may be preferentially underestimated for processed foods) or introduction of new confounding. Meta-analysis showing consistency of findings across studies can also be helpful [26, 27]. Nevertheless, the FFQ method appears to have intrinsic limitations in how precisely it can define individual intake. Among possibilities for improvement of the FFQ method are increasing precision and innovation of questions; repeated administrations of the questionnaire with averaging to reduce the influence of within-person variation in intake; and enhancing dietary awareness of participants, for example by encouraging or requiring the participant to keep informal dietary records for a few days prior to filling out the questionnaire or by giving advance instruction in portion size determination.

A single recall or record does not accurately represent typical dietary information because of intrinsic day-to-day variation [2]. In contrast, in the Framingham Children's Study the clarity of findings in only 95 children with repeated diet assessments is impressive [13, 14], but they obtained many more diet records than is typical of studies in nutritional epidemiology. The detail obtained from many dietary records is seductive from the research perspective. This approach, in its flexibility for the researcher, far outstrips the already successful studies, for example at Harvard

and the University of Minnesota, that have relied on FFQs. The multiple diet record method is a powerful cohort study design indeed that obtains unlimited accurate dietary characterization and follow-up for many different chronic disease outcomes. However, even with added power from such a large number of diet records, it is probable that thousands of participants would be needed in studies of remote and rare chronic disease outcomes. In most practical epidemiological situations, the possibilities are limited for obtaining four to twelve 24-h diet records per year in the assembly line fashion that would be needed for a cohort study of a chronic disease. Given present methodologies it is unlikely that many studies will achieve this standard. Nevertheless, we can dream.

The success of the internet and the surge in computer power means that one might optimistically hope for better methods in the future. In particular, one could imagine widespread collection of self-administered dietary information on the internet, with full software including help and dialog boxes that would simulate the support currently given by an interviewer. Thus the dietary collection instrument could even be a mixture of recall and synthesis. The open-ended methods of the CARDIA Diet History might be helpful, combined with some aspects of artificial intelligence. Branching logic for finding food codes could be employed, similar to that currently used by the NDS-R, a "Windows-based software package incorporating a time-tested, highly accurate database with an up-to-date interface," released in 1998 by the Nutrition Coordinating Center of the University of Minnesota [28]. One could even envision questionnaires filled out over the telephone, with automated voice prompts to assist in accuracy. As questionnaires accrued, the foods database could automatically expand in line with what was reported by participants. Thus a participant could repeatedly and at their convenience do a 24-h recall or report typical intake over the past week with verbal or online prompts that help find correct food codes and pointed questions to help improve the quality of the information obtained.

A requisite for exploiting this type of ambitious scheme would be correspondingly simple-to-use programs to extract nutrients, foods, food groups, and food group-specific nutrients. The researcher would require package programs to assemble the data, to formulate and reformulate food groups, and to compute nutrient values. As new information comes along, it could be added to the food table, to simplify study of novel compounds.

These schemes are perhaps dreamlike, but maybe not completely out of the question. Who would have imagined only a few years ago the internet, or, to cite one important application, millions of journal abstracts and articles themselves available at the touch of a few computer keystrokes? Or, for that matter, "telephones" that are really personal computers with highly specialized "apps" that enable highly individualized and detailed participant contact. In the near term, however, it is most likely that nutritional studies of chronic disease outcomes will continue to be based on the FFQ class of methodologies, bolstered by findings from short-term human and animal studies and the native ingenuity of the scientists doing the research.

Willett [2] comments on another method that has promise, but also pitfalls: correlation of food intake with biomarkers. A biomarker is a chemical measured in

some biological sample, commonly blood or urine, but others as well, for example feces, hair, toenails, cheek cells, adipocytes, and skin scrapings. Minerals reside in toenails, which grow over several months; therefore this measure represents an average intake over several months. This technique has been used in studies on the relationship between selenium status and risk of cancer [29]. Urinary nitrogen is a marker of nitrogen and therefore protein intake. Sodium and potassium intake are mirrored quite rapidly (over ~2 days) in urinary sodium and potassium. Serum carotenoids and ascorbic acid are highly responsive to both dietary and supplemental intake of the same substances. Freedman and coworkers have suggested methods for combining biomarker and diet information to improve accuracy [30, 31]. Nevertheless, biomarkers have limitations as indicators of dietary intake. Each tissue and substance has its own half life and metabolism. Some tissues store substances, and some utilize them rapidly. The amount of a substance in blood may not be representative of its occurrence throughout the body. Substances may be maintained homeostatically, or may be partially under dietary and partially under homeostatic control. There may be changes in nutrients consumed prior to storage, for example, elongation of fatty acids. For all these reasons, biomarkers are rarely perfect representations of intake. An example of this is the imperfect relationship between serum carotenoids and total antioxidant intake [32]. Furthermore, biomarkers tell us nothing about dietary behaviors. Still, biomarkers have a future in dietary assessment. Research should continue to identify and better understand biomarkers in relation to dietary intake.

## 2.2 What Element of Diet Should Be Studied?

In Sect. 2.1.1, following Willett [2], the kind of chemicals that are dietary components was cited. The number and kind of such components present a very complex picture. Diet can also be described in terms of food, food groups, or dietary patterns. The early history of nutrition research focused primarily on chemicals, with some justification according to Willett. The existence of deficiency diseases such as scurvy (ascorbic acid), rickets (vitamin D), beriberi, pellagra, and neural tube defects (B vitamins) points to one class of nutritional problems. Willett cites a model of Mertz [33] that begins with death and deficiency disease at sufficiently low level of a nutrient, complemented by similarly severely reduced function at levels that are sufficiently high. Also in the model is reduced function at modestly reduced or elevated levels of the nutrient. Willett calls this "subclinical dysfunction," a view much in line with the slow, mostly subclinical development of diseases such as cancer and cardiovascular disease. There is also a broad plateau at highest function across a wide range of intake of the nutrient.

Willett [2] further thinks that the focus on major energy sources is justified because they are quantitatively important in the diet and manifestly vary markedly across human populations. These focuses on nutrients have led to the development of extensive tables of energy and of these dietary chemicals. Furthermore, there is

a strong tendency among basic scientists toward reductionism: the belief that worthwhile knowledge consists of simple pathways linking single nutrients to bodily function and pathogenesis [34, 35], what Willett calls "linkage to our fundamental knowledge of biology." An excellent example is the protective association of folate with neural tube defects [36], as is improvement in insulin function and metabolic control in diabetics with supplemental magnesium [37]. Much remains to be studied regarding the composition of foods. The tabulated nutrient composition of a food does not fully describe the physiological effect of that food, whether because of differential bioavailability or unknown constituents. There are thousands of untabulated or unidentified compounds in foods, including many phytochemicals. Additionally, a relatively undeveloped aspect of diet characterization is that of food function. For example, Blomhoff and colleagues [32, 38] analyzed thousands of food samples for their total antioxidant content, measured as the molar content of donatable electrons using the ferric reducing ability of plasma, FRAP; those data are available as a dietary exposure measure. A similar functional assessment in the idea stage is the ability of a given food to prevent cell proliferation in in vitro incubation with cancer cells, A la work by Eberhardt et al. [39].

Foods themselves should also be studied even if that does not immediately lead to additional knowledge of specific biological pathways. Foods are what people eat; findings regarding foods are directly applicable to people's diets. Most importantly, it is quite likely that there are synergies among food constituents and between foods [34, 35]; studies of individual chemical constituents may never find the relevant pathways because they are more complex than the researchers imagined. In a nondeficiency state, despite findings that foods containing antioxidants are associated with better long-term health, consumption of isolated nutrients or chemicals does not fare so well. The most striking example is that of supplementary β-carotene, which has been administered in several large, long-term clinical trials, with the effect of increasing disease [40]. Higher antioxidant nutrient intake was associated with more diabetic retinopathy in one study [41]. Other provocative examples from the author's observational work include that supplemental vitamin C in diabetics was associated with increased coronary heart disease [42], and that supplemental iron in association with breakfast cereal intake (which is often fortified with supplemental iron) was associated with an increased rate of distal colon cancer [43].

These findings are supportive of the concept that food synergies are important: the compounds in question are part of foods that appear to be healthy, but do not work outside their food matrix. The food matrix arises from a living organism consisting of thousands of compounds with checks and balances among those compounds to maintain homeostasis and life by preventing the action of any one compound from getting out of control. It is likely that some of this multiplicity of function is retained during human metabolism of the food. For example, whole grain breakfast cereals are associated with reduced risk of chronic disease [14, 44, 45], as are fruits and vegetables [46], which are high in β-carotene and vitamin C, among a wide variety of phytochemicals. The concept of food synergy is discussed at greater length in Chap. 14.

In a very simple example of food synergy, vitamin E functions as an antioxidant by accepting electrons, after which it exists in an oxidized state, that is, as a pro-oxidant. To reduce the risk that it will cause damage, it must be reduced, which is done by vitamin C. The vitamin C is then oxidized and must be reduced, and so on until the cycle reaches an end. One important in vitro study was suggestive of the influence of balancing substances in food by showing that cell proliferation in a cancer cell line was much lower when incubated with apple or apple skin than it was when incubated with an amount of isolated vitamin C that had an equivalent total antioxidant capacity [39].

A final aspect of diet that has been successfully studied is food patterns. Dietary patterns have been discovered using factor analysis. For example, Hu et al. [47, 48] identified a "prudent" pattern associated with reduced incidence of cardiovascular disease and a "Western" pattern associated with increased incidence. Many other authors have followed a similar strategy, generally finding support for the general prudent pattern [49]. The association of a food pattern with incident disease is suggestive of a synergy between foods. There has been much advice about a diet that has potential to prevent chronic disease; the lower risk associated with the "prudent" pattern suggests that many people have apparently taken that advice and that the advised diets do have merit in risk reduction.

## 2.3 Summary

Two particularly challenging issues in nutritional epidemiology were discussed in editorial fashion. Concerning how to find out what people eat, nutritional epidemiologists use variants of two basic methods. In the first, the participant records or recalls extensive detail about recent intake. The investigator then synthesizes this information into analytically usable variables. This method does not represent typical diet well unless multiple recalls/records are obtained. In the second method, the participant synthesizes his/her dietary information by responding to general questions about diet, such as how often a particular class of foods is eaten. This method does determine the typical diet, but fails to obtain details that are necessary for many types of analysis. It is hoped that advances in technology will enable simpler and more extensive collection and processing of dietary intake data.

Concerning how to think about the effect of diet on health, I suggest that simple nutrient pathways are inadequate for a full understanding of diet. It is proposed that considerable attention be paid to the foods and food patterns that people eat, as well as to the relationships of these foods and food patterns with disease outcomes.

## References

1. Margetts BM, Nelson M, editors. Design concepts in nutritional epidemiology. Oxford: Oxford University Press; 1997.
2. Willett W. Nutritional epidemiology. 2nd ed. New York: Oxford University Press; 1998.

3. Yang J, Meyers KJ, van der Heide J, Liu RH. Varietal differences in phenolic content and antioxidant and antiproliferative activities of onions. J Agric Food Chem. 2004;52:6787–93.
4. McDonald A, Van Horn L, Slattery M, et al. The CARDIA dietary history: development, implementation, and evaluation. J Am Diet Assoc. 1991;91:1104–12.
5. Liu K, Slattery M, Jacobs Jr DR, et al. A study of the reliability and comparative validity of the CARDIA dietary history. Ethn Dis. 1994;4:15–27.
6. Liu K, Slattery M, Jacobs DR Jr. Is the dietary recall the method of choice in black populations? Ethn Dis. 1994;4:12–4 (letter to the editor).
7. Prewitt TE, Haynes SG, Graves K, Haines PS, Tyroler HA. Nutrient intake, lipids, and lipoprotein cholesterols in black and white children: the Lipid Research Clinics Prevalence Study. Prev Med. 1988;17:247–62.
8. Dennis BH, Zhukovsky GS, Shestov DB, Davis CE, Deev AD, Kim H, et al. The association of education with coronary heart disease mortality in the USSR Lipid Research Clinics Study. Int J Epidemiol. 1993;22:420–7.
9. Dolecek TA, Johnson RL, Grandits GA, Farrand-Zukel M, Caggiula AW. Nutritional adequacy of diets reported at baseline and during trial years 1–6 by the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr. 1997;65 (1 Suppl):305S–13.
10. Dolecek TA, Stamler J, Caggiula AW, Tillotson JL, Buzzard IM. Methods of dietary and nutritional assessment and intervention and other methods in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr. 1997;65(1 Suppl):196S–210.
11. Graham S, Mettlin C, Marshall J, Priore R, Rzepka T, Shedd D. Dietary factors in the epidemiology of cancer of the larynx. Am J Epidemiol. 1981;113:675–80.
12. Lockheart MS, Steffen LM, Rebnord HM, et al. Dietary patterns, food groups and myocardial infarction: a case-control study. Br J Nutr. 2007;98:380–7.
13. Singer MR, Moore LL, Garrahie EJ, Ellison RC. The tracking of nutrient intake in young children: the Framingham Children's Study. Am J Public Health. 1995;85:1673–7.
14. Moore LL, Singer MR, Bradlee ML, et al. Intake of fruits, vegetables, and dairy products in early childhood and subsequent blood pressure change. Epidemiology. 2005;16:4–11.
15. Jacobs DR, Meyer KA, Kushi LH, Folsom AR. Whole grain intake may reduce risk of coronary heart disease death in postmenopausal women: The Iowa Women's Health Study. Am J Clin Nutr. 1998;68:248–57.
16. Willett WC, Stampfer MJ, Manson JE, et al. Intake of trans fatty acids and risk of coronary heart disease among women. Lancet. 1993;341:581–5.
17. Pereira MA, Kartashov AI, Ebbeling CB, et al. Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. Lancet. 2005;365:36–42. Erratum in Lancet. 2005;365:1030.
18. Duffey KJ, Gordon-Larsen P, Jacobs Jr DR, Williams OD, Popkin BM. Differential associations of fast food and restaurant food consumption with 3-y change in body mass index: the Coronary Artery Risk Development in Young Adults Study. Am J Clin Nutr. 2007;85:201–8.
19. Duffey KJ, Gordon-Larsen P, Steffen LM, Jacobs Jr DR, Popkin BM. Regular consumption from fast food establishments relative to other restaurants is differentially associated with metabolic outcomes in young adults. J Nutr. 2009;139:2113–8.
20. Munger RG, Folsom AR, Kushi LH, Kaye SA, Sellers TA. Dietary assessment of older Iowa women with a food frequency questionnaire: nutrient intake, reproducibility, and comparison with 24-hour dietary recall interviews. Am J Epidemiol. 1992;136:192–200.
21. Willett WC, Sampson L, Browne ML, et al. The use of self-administered questionnaire to assess diet four years in the past. Am J Epidemiol. 1988;127:188–99.
22. Feskanich 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.
23. Fraser GE. Diet, life expectancy, and chronic disease. New York: Oxford University Press; 2003. p. 265–76.

24. Schatzkin A, Kipnis V. Could exposure assessment problems give us wrong answers to nutrition and cancer questions? J Natl Cancer Inst. 2004;96:1564–5.
25. Alonso A, Nettleton JA, Ix JH, et al. Dietary phosphorus, blood pressure, and incidence of hypertension in the atherosclerosis risk in communities study and the Multi-Ethnic Study of Atherosclerosis. Hypertension. 2010;55:776–84.
26. Pereira MA, O'Reilly E, Augustsson K, et al. Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies. Arch Intern Med. 2004;164:370–6.
27. Knekt P, Ritz J, Pereira MA, et al. Antioxidant vitamins and coronary heart disease risk: a pooled analysis of 9 cohorts. Am J Clin Nutr. 2004;80:1508–20.
28. http://www.ncc.umn.edu. Accessed 11 May 2011.
29. Zhuo H, Smith AH, Steinmaus C. Selenium and lung cancer: a quantitative analysis of heterogeneity in the current epidemiological literature. Cancer Epidemiol Biomarkers Prev. 2004;13:771–8.
30. Freedman LS, Tasevska N, Kipnis V, et al. Gains in statistical power from using a dietary biomarker in combination with self-reported intake to strengthen the analysis of a diet-disease association: an example from CAREDS. Am J Epidemiol. 2010;172:836–42.
31. Freedman LS, Kipnis V, Schatzkin A, Tasevska N, Potischman N. Can we use biomarkers in combination with self-reports to strengthen the analysis of nutritional epidemiologic studies? Epidemiol Perspect Innov. 2010;7:2.
32. Svilaas A, Sakhi AK, Andersen LF, et al. Intakes of antioxidants in coffee, wine, and vegetables are correlated with plasma carotenoids in humans. J Nutr. 2004;134:562–7.
33. Mertz W. The essential trace elements. Science. 1981;213:1332–8.
34. Messina M, Lampe JW, Birt DF, et al. Reductionism and the narrowing nutrition perspective: time for reevaluation and emphasis on food synergy. J Am Diet Assoc. 2001;101:1416–9.
35. Jacobs DR, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. Am J Clin Nutr. 2003;78 Suppl 3:508S–13.
36. Stover PJ. Physiology of folate and vitamin B12 in health and disease. Nutr Rev. 2004;62 (6 Pt 2):S3–12; discussion S13.
37. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in Type 2 diabetic subjects: a randomized double blind controlled trial. Diabetes Care. 2003;26:1147–52.
38. Halvorsen BL, Holte K, Myhrstad MC, et al. A systematic screening of total antioxidants in dietary plants. J Nutr. 2002;132:461–71.
39. Eberhardt MV, Lee CY, Liu RH. Antioxidant activity of fresh apples. Nature. 2000;405: 903–4.
40. Clarke R, Armitage J. Antioxidant vitamins and risk of cardiovascular disease. Review of large-scale randomised trials. Cardiovasc Drugs Ther. 2002;16:411–5.
41. Mayer-Davis EJ, Bell RA, Reboussin BA, Rushing J, Marshall JA, Hamman RF. Antioxidant nutrient intake and diabetic retinopathy: the San Luis Valley Diabetes Study. Ophthalmology. 1998;105:2264–70.
42. Lee DH, Aaron R, Folsom AR, Harnack L, Halliwell B, Jacobs DR. Does supplemental vitamin C increase cardiovascular disease risk in women with diabetes? Am J Clin Nutr. 2004;80:1194–200.
43. Lee DH, Jacobs DR, Folsom AR. A hypothesis: interaction between supplemental iron intake and fermentation affecting the risk of colon cancer. The Iowa Women's Health Study. Nutr Cancer. 2004;48:1–5.
44. Jacobs DR, Gallaher DD. Whole grain intake and cardiovascular disease: a review. Curr Atheroscler Rep. 2004;6:415–23.
45. Liu S, Sesso HD, Manson JE, Willett WC, Buring JE. Is intake of breakfast cereals related to total and cause-specific mortality in men? Am J Clin Nutr. 2003;77:594–9.
46. Key TJ, Schatzkin A, Willett WC, Allen NE, Spencer EA, Travis RC. Diet, nutrition and the prevention of cancer. Public Health Nutr. 2004;7(1A):187–200.

47. Hu FB, Rimm E, 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.
48. 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.
49. Newby PK, Tucker KL. Empirically derived eating patterns using factor or cluster analysis: a review. Nutr Rev. 2004;62:177–203.

http://www.springer.com/978-1-61779-893-1

Nutritional Health
Strategies for Disease Prevention
Temple, N.J.; Wilson, T.; Jacobs, Jr., D.R. (Eds.)
2012, XXII, 562 p., Hardcover
ISBN: 978-1-61779-893-1
A product of Humana Press