17

Nutrition Monitoring and Research Studies: Observational Studies

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Purpose

The purpose of this section is to provide an overview and examples of observational studies; specifically, cohort observational studies that incorporate nutritional assessment. After a brief review of the various types of observational studies and their corresponding purposes, a detailed description of the characteristics, advantages, and disadvantages of a cohort study is provided. Next, in order to demonstrate the use of the cohort design in the area of nutrition, a description of six cohort studies that utilized nutritional assessments is provided. Finally, selected nutrition-related publications from the six cohort examples are referenced, along with the corresponding measured nutritional variables.

Observational Studies

Epidemiology is classically known as the study of the distribution of disease in populations; however, this definition expands and often overlaps with other areas of research. We are concerned with two types of research here: clinical studies and observational studies. The primary difference between these two types of research is the randomization of subjects into groups. Clinical studies allow for the randomization of subjects into various treatment or control groups, whereas observational studies examine the subjects according to their natural selection into groups.

Observational studies include natural history studies, case-control studies, prevalence (cross-sectional or population) studies, and cohort (incidence) studies. The research question of interest would generally dictate which of the various observational studies would be used (see Table 17.1). For example, the diagnosis or prevalence of a disease would be facilitated by using the prevalence study design. Cohort studies provide the opportunity to observe populations prospectively, thereby enabling observation of incidence rates as well as prevalence rates. Risk factors and prognosis of a disease can be identified through several different types of observational studies.

TABLE 17.1

The Question and Appropriate Design

Question	Observational Studies
Diagnosis	Prevalence
Prevalence	Prevalence
Incidence	Cohort
Risk factors	Cohort, case/control, prevalence
Prognosis	Cohort, natural history

TABLE 17.2

Characteristics of a Cohort or Incidence Study

Characteristic
Selection of a study cohort WITHOUT disease
Follow study cohort over time (prospective)
Measurement of incidence and/or absolute risk (new cases developed in a time period)
Comparison of incidence in those with and without the risk factor (relative risk and attributable risk)

Cohort Studies

As noted in Table 17.1, the purpose of cohort studies is to identify the risk factors associated with a disease of interest and obtain the incidence of disease[1] and/or its prognosis. Overall, cohort studies allow the development of a disease to be described, and are therefore typically a favorite among the various types of observational studies.[2]

The defining characteristics of a cohort study are shown in Table 17.2. The first characteristic is identification of a study cohort who currently does not have the disease of interest. Any group of individuals who have either been exposed to the same occurrence, live in a defined geographic area, or have the same risk factors may be identified as a cohort.[1-3] When similar risk factors identify a cohort, a second similar cohort without the identified risk factors and the disease of interest must be obtained for comparison purposes.[2]

The second characteristic is that the study cohort(s) is followed over time. Because the study cohort(s) are disease free, the cohort(s) are followed over time to see which individuals in the cohort(s) actually develop the disease of interest.[1-4] The new cases of the particular disease which developed within a specified time period are then measured to obtain the incidence and absolute risk of the particular disease. Finally, a comparison between the incidence in those individuals who had the risk factors and those individuals who did not produce a relative risk and attributable risk of these risk factors on the development of the disease of interest.

Advantages and Disadvantages of the Cohort Studies

There are several advantages and disadvantages of using cohort studies over other types of observational studies (see Table 17.3). With respect to the advantages, cohort studies make it easier to distinguish cause from association. Because the risk factors are measured

TABLE 17.3

Advantages and Disadvantages of a Cohort Study

Advantages	Disadvantages
Easier to distinguish cause from association	Results are delayed for low incidence or long incubation
Incidence can be obtained	Large number may be needed
Multiple outcomes can be studied	Expensive in resources
Standard questions and measurements can be used	Losses may bias results
May lead to identification of variables which can be experimentally examined	Methods, criteria, and exposure status may change over time

TABLE 17.4

Factors Associated with Causality

Magnitude of the association's strength
Ability to show the association's consistency through replication
Association's identification of one risk factor to one outcome
Risk factor must precede outcome
Outcome is sensitive to different levels of risk factor
Association's logical adherence to current theory
Association's consistency with other information about the outcome
Association's correspondence to other causal associations

prior to the development of the disease of interest, temporal order is established. Temporal order is just one of eight factors associated with causality (see Table 17.4)[4] and strengthens a causal conclusion instead of simply an association between risk factors and outcome often found in other study designs.[1,4] On the other hand, the comparison of cohorts based on risk factors makes the assumption that both cohorts are similar except for the suspected risk factor. However, such an assumption rarely is completely supported and, hence restricts causal implications.[1]

Another important advantage of cohort studies is the ability to obtain the incidence of a disease which in turn can provide estimates of new incidences that preventive programs can use to identify programmatic needs and support budgetary plans.[4] Further, multiple outcomes can be studied, and standard questions and measurements can be used to compare results found in this study to previously completed studies. For example, the Framingham study[5] has provided important information on blood pressure, cholesterol, diet, eye disease, and a number of other risk factors and outcome measures. Other studies, such as the Coronary Artery Risk Development in Young Adults (CARDIA)[6] have emulated Framingham. In this study, variables were selected for inclusion in the baseline examination because of their known or suspected relationships to cardiovascular disease. The availability of multiple endpoints in the same populations further enables one to study the temporal development of the components and their interrelationships. Finally, cohort studies may permit the identification of additional variables related to specific outcome measures which can then be further examined experimentally.[3]

One of the most obvious disadvantages of the cohort studies is that length has to be adequate for development of the disease or a surrogate of the disease of interest.[1,4] For example, blood pressure and cardiovascular disease: cardiovascular disease is the ultimate outcome of interest, but the surrogate, blood pressure, is sufficiently linked to the outcome to make it a viable outcome in its own right. For these diseases or surrogates with low incidence or long incubation periods, the results are delayed. With low disease incidence rates, the sample size for each study cohort may need to be extremely large in order to make the necessary comparisons.[1,4] With both a lengthy process and large sample size,

another disadvantage is the expense associated with conducting the study.[4] The length of the study may also influence the ability to recapture all of the subjects at the end of the study. This ability to recapture the study participants depends on their geographic mobility, interest in continuing the study, and death.[4] The inability to capture all study participants may bias the results[1,2] by so-called informative censoring. In addition, the length of the study dictates other potential concerns. Methods, criteria, and exposure status may change over time. For example, environmental, cultural, or technological changes may influence the risk factors identified and the measurement of the variables under study.[2,4]

Summary of Observational Studies

Observational studies are an important part of epidemiological research, in that diseases are studied in their natural environments. Of the various types of observational studies, cohort studies provide the most valuable approach for identifying temporal relationships between risk factors and outcomes. The primary characteristic of cohort studies is that they enable the cohort (or a subgroup of them) to be identified disease-free at the beginning of the study, facilitating study of the incidence of disease. The development of the disease of interest can then be measured and compared across cohorts. Like all observational studies, cohort studies have advantages and disadvantages. The primary advantage is the cohort study's ability to distinguish cause from association, while the primary disadvantage is the cost in time, money, large sample size, and loss of subjects which can lead to substantive biases in the inferences.

The remainder of this section focuses on six selected examples of cohort studies that utilized some form of nutritional assessment (see Table 17.5). Although there are many cohort studies available and additional cohort studies that include nutritional assessments, the following examples were selected to provide a wide range of nationally recognized studies, unique uses of the cohort design, and, most importantly, different methods of collecting nutritional data. The selected examples include the following:

1. Coronary Artery Risk Development in Young Adults (CARDIA)
2. Framingham Study: Heart and Vascular Disease Program
3. Framingham Offspring and Their Spouse Study
4. The RENO (Relationship of Energy and Nutrition to Obesity) Diet-Heart Study
5. The Nurses' Health Study
6. The Health Professionals Follow-Up Study

Examples of Cohort Studies Utilizing Nutrition Assessment

Coronary Artery Risk Development in Young Adults (CARDIA)

The purpose of the CARDIA study was to identify risk factors that either contributed to or protected young adults from coronary heart disease.[6] The sample consisted of 5116 black and white men and women from four cities, who were 18 to 30 years of age.[6,10] Measurements were taken at baseline (1985 through 1986), at two years (1987 through 1988), and biannually thereafter.[7,9,10] Baseline measurements included a sociodemographic

TABLE 17.5

Examples of Cohort Studies Utilizing Nutrition Assessments

Cohort Study	Years Conducted	Sample Studied	Outcome	Nutrition Intake Measurement
Coronary Artery Risk Development in Young Adults (CARDIA)	Baseline: 1985-1986 Year 2: 1987-1988	5116 sampled men and women blacks and whites 18-30 years old	Coronary heart disease risk factors	Baseline: Diet History Questionnaire (interview-administered) Year 2: NCI (Block) Food Frequency Questionnaire
Framingham Study: Heart and Vascular Disease Program	1949-1989	5209 sampled men and women primarily whites 30-62 years old	Cardiovascular risk factors	Semi-Quantitative Food Frequency Questionnaire (Willet)
Framingham Offspring and Their Spouse Study	1971-1988	5135 sampled men and women primarily whites 12-60 years old	Cardiovascular risk factors	24-hr dietary recall
The RENO (Relationship of Energy and Nutrition to Obesity) Diet-Heart Study	1985-1993	508 sampled men and women primarily whites 20-69 years old normal/overweight	Cardiovascular risk factors	1. 24-hr dietary recall 2. 7-Day food record 3. NCI (Block) Food Frequency Questionnaire
The Nurses' Study	1976-1996	121,700 sampled female registered nurses primarily whites 30-55 years old	Cancer risk factors	Semi-Quantitative Food Frequency Questionnaire (Willet)
The Health Professionals Follow-Up Study	1986-1994	51,529 sampled male health professionals primarily whites 40-75 years old	Heart disease and cancer risk factors	Semi-Quantitative Food Frequency Questionnaire (Willet)

questionnaire, medical (family history, current medical history, use of medications), anthropometrics (weight, height, skinfolds, and various circumferences), lab work (lipids, apolipoprotein, insulin, cotinine), blood pressure, lifestyle (treadmill test, questions on tobacco and marijuana use, nutrition intake), and psychosocial questionnaires (type A/B personality, life satisfaction, hostility, social support, and job demand or latitude).[6]

Nutrition intake was assessed with an interview-administered Diet History Questionnaire at baseline and the NCI (Block) Food Frequency Questionnaire at year two.[9,10] Reliability and validity of the Diet History Questionnaire were assessed. Reliability was measured through the correlation between a one-month test-retest method of the Diet History Questionnaire.[7,8]

The nutrient intakes and mean caloric intakes of the Diet History Questionnaire were compared to the same variables derived from 24-hour recalls,[7,8] NCI (Block) Food Frequency Questionnaire,[9] NHANES II,[7] and RDA's Body Mass Index[7] as an assessment of concurrent validity. For both reliability and validity, the Diet History Questionnaire appears to be more applicable for whites than for blacks. The relationship between diet and disease will await the results for this cohort to enter the risk period and show disease development.

Framingham Study: Heart and Vascular Disease Program

The purpose of the Framingham Study was to provide a population-based prospective examination of the development of cardiovascular disease and its risk factors.[11,12] The sample consisted of 5209 primarily white men and women between the ages of 30 to 62 years, who lived in Framingham, Massachusetts.[5,11] Measurements were taken biennially from 1949 through 1989. Measurements included blood labs, medical history, and a physical examination.[5] Additional assessments of stress, nutrition intake, and physical activity were added to the study at a later time. The latest nutrition intake was assessed through the Willet Semi-Quantitative Food Frequency Questionnaire.[11]

Framingham Offspring and Their Spouse Study

The purpose of the Framingham Offspring and Their Spouse Study was to examine the impact of genetic and familial influences on the development of cardiovascular disease and its risk factors.[12-14] The sample consisted of 5135 primarily white men and women who were 12 to 60 years of age.[12,13] Subjects were either the offspring or the offsprings' spouses of the Framingham Study participants.[12-14] Measurements were also taken biennially from 1971 through 1988.[12,14] Measurements included those similar to the original study.[12] For this study, however, nutrition intake was assessed with 24-hour recalls, one-fourth of which were collected during the weekend, and the remaining three-fourths of the subjects were collected during a weekday.[13,14]

The RENO (Relationship of Energy and Nutrition to Obesity) Diet-Heart Study

The purpose of the RENO Diet-Heart Study was to examine prospectively over a five year period the behavioral patterns with respect to weight between normal-weight and mildly to severely obese individuals.[15] The sample consisted of 508 healthy primarily white men and women between the ages of 20 to 69. Subjects were stratified by gender, weight (overweight and normal weight), and five age decades. Measurements were taken over an eight year period (1985 through 1993). Measurements included history questionnaires (weight, activity, health, and demographics), anthropometrics, energy expenditure, laboratory analyses, blood pressure, pulse, weight and dieting measures, activity data (Caltrac Monitors and activity diary), nutrition intake and attitudes, cancer questionnaire, and psychosocial questionnaires (general wellbeing, depression, cohesion, locus of control, hostility inventory, social support, perceived stress).[16]

Nutrition intake was assessed through several measures. The first nutrition assessment was the 24-hour dietary recalls measured at years one and five.[17] The NCI (Block) Food Frequency Questionnaire[18] was used to measure nutrition intake at years two, three, and five. Finally, a seven-day food record that collected information about the day, time, location, and the amount and type of food eaten was measured at years one, three, and five.[19,20]

The Nurses' Health Study

Initially, the purpose of the Nurses' Health Study was to examine the relationship between oral contraceptives and breast cancer.[21,22] The study was then expanded to examine other female-related cancers, lung cancer, and life-style factors such as diet and exercise.[21,22] The sample consisted of 121,700 registered female nurses who were 30 to 55 years of age.[21,22]

Selected from 11 states, nurses were chosen because they were expected to be more accurate in reporting the incidence of diseases and lifestyle factors, and in addition were expected to have higher participation and retention rates.[21-23]

Measurements were requested biennially from 1976 to 1996. Unique to this study, the study researchers did not have personal contact with the nurse participants; instead, all contact was maintained through the mail. That is, study participants were required to mail in their bodily samples, anthropometric information, and the various questionnaires.[21-25] Only when a participant was nonresponsive to mailing in measurements were telephone interviews conducted. Measurements included basic demographics, medical history including the use of medications, blood and toenail samples, anthropometrics, lifestyle factors such as diet, exercise, and cigarette smoking, and quality of life and social support questionnaires.[21,22] In order to confirm the presence of a specified outcome (e.g., cancer, myocardial infarction, diabetes, or fractures), medical chart reviews were conducted when participants indicated an outcome's existence.[21,23,25] Nutrition intake was measured with Willett's semi-quantitative food frequency questionnaire, which assessed the consumption frequency of specified portions of food within the last year.[21,23-25] In 1980, the food frequency questionnaire identified only 61 common foods,[21] while the 1984, 1986, 1990, and 1994 measures were expanded to include 120 common foods, and both vitamin and mineral supplementations.[23]

The Health Professionals Follow-Up Study

The purpose of the Health Professionals Follow-Up Study was to examine the relationship between diet and two chronic diseases: heart disease and cancer.[26] The sample consisted of 51,529 primarily white male health professionals 40 to 75 years of age.[25-27] The health professions included dentists, optometrists, osteopaths, pharmacists, podiatrics, and veterinarians.

Measurements were taken biennially from 1986 through 1994.[25-27] Similar to the Nurses' Health Study, the measures were all self-administered, mailed, and the outcome identifications were verified through medical chart reviews.[25,27-29] The measurements included demographics, medical history, anthropometrics (height, weight, body mass index), chronic disease risk factors (heart disease and cancer in particular), and lifestyle factors such as diet, physical activity, cigarette smoking, and alcohol use.[26-30]

Nutrition intake was assessed with Willett's 131-item semi-quantitative food frequency questionnaire used as the expanded version in the Nurse's Health Study.[25,28] As in the Nurse's Health Study, the food frequency questionnaire assessed the consumption frequency of specified portions of food within the last year.[25,28,30] Nutrition intake was assessed in 1986 and 1990.[27]

Selected nutrition-related publications from the aforementioned studies and their respective measured nutrient variables are shown in Table 17.6.

Summary

This section has focused on the benefits of the cohort study and has provided examples of several studies that have used this form of design. There are certainly other forms that can be utilized to assess the impact of diet on disease or health. The value of

TABLE 17.6

Selected Nutrition-Related Publications from the Six Cohort Examples

Reference	Nutrient Variables
Slattery, M.L., Dyer, A., Jacobs, D.R., Jr., Hilner, J.E., Cann, B.J., Bild, D.E., Liu, K., McDonald, A., Van Horn, L., Hardin, M. (1994). A comparison of two methods to ascertain dietary intake: The CARDIA Study. *J Clin Epidemiol*, 47, 701-711.	Total kcals, macronutrients, and selected micronutrients by gender and race.
Liu, K., Slattery, M., Jacobs, D. Jr., Cutter, G., McDonald, A., Van Horn, L., Hilner, J.E., Caan, B., Bragg, C., Dyer, A., Havlik, R. (1994). A study of the reliability and comparative validity of the CARDIA dietary history. *Ethnicity & Disease*, 4, 15-27.	Total kcals, macronutrients, and selected micronutrients by gender and race.
Bild, D.E., Sholinsky, P., Smith, D.E., Lewis, C.E., Hardin, J.M., Burke, G.L. (1996). Correlates and predictors of weight loss in young adults: The CARDIA Study. *Int J Obesity*, 20, 47-55.	Baseline caloric and fat intake, change in caloric and fat intake at year 2 by gender and race.
Tucker, K.L., Selhub, J., Wilson, P.W.F., Rosenberg, I.H. (1996). Dietary intake pattern relates to plasma folate and homocysteine concentrations in the Framingham Heart Study. *Hum Clin Nutr*, 126, 3025-3031.	Folate intake, ranking of dietary contributors to folate intake by gender and age (67-95 years old). Folate intake through supplements and breakfast cereals, orange juice, green leafy vegetables.
Posner, B.M., Cupples, L.A., Franz, M.M., Gagnon, D.R. (1993). Diet and heart disease risk factors in adult American men and women: The Framingham Offspring-Spouse nutrition studies. *Int J Epidemiol*, 22, 1014-1025.	Total kcals, macronutrients, and selected micronutrients by gender. Ranking of dietary contributors to total fat, saturated fat, cholesterol, calories, carbohydrate, protein, oleic acid, and linoleic acid.
Posner, B.M., Cupples, L.A., Gagnon, D., Wilson, P.W.F., Chetwynd, K., Felix, D. (1993). Healthy People 2000: the rationale and potential efficacy of preventive nutrition in heart disease: The Framingham Offspring-Spouse study. *Arch Intern Med*, 153, 1513-1556.	Total kcals, macronutrients, and selected micronutrients by gender.
Dodds, M.P., Silverstein, L.J. (1997). The 24-Hour Dietary Recall, in S. St. Jeor (Ed.). *Obesity Assessment: Tools, Methods, Interpretations*, New York: Chapman and Hall. RENO Diet-Heart Study	Total kcals, macronutrients, and selected micronutrients by gender and weight status. Total kcals, macronutrients, and selected micronutrients by BMI and age.
Scott, B.J., Reeves, R.B. (1997). Seven Day Food Records. In S. St. Jeor (Ed.). *Obesity Assessment: Tools, Methods, Interpretations*, New York: Chapman and Hall. RENO Diet-Heart Study	Total kcals, macronutrients, and selected micronutrients by gender and weight status.
Benedict, J.A., Block, G. (1997). Food Frequency Questionnaires, in S. St. Jeor (Ed.). *Obesity Assessment: Tools, Methods, Interpretations*, New York: Chapman andHall. RENO Diet Heart Study	Total kcals, macronutrients, and selected micronutrients by gender and weight status. Total kcal, macronutrients, and selected micronutrients by BMI and age.
Silverstein, L.J., Scott, B.J., St. Jeor, S.T. (1997). Eating Patterns, in S. St. Jeor (Ed.). *Obesity Assessment: Tools, Methods, Interpretations*, New York: Chapman and Hall. RENO Diet Heart Study	Number of foods per day, caloric density, number of meals per day and number of eating incidents per day by age group. Number of foods per day, caloric density, eating incidents per day, calories per eating incident, percent fat and total calories by gender and weight status. Breakfast eating variables by gender and weight status.

TABLE 17.6 *(Continued)*

Selected Nutrition-Related Publications from the Six Cohort Examples

Reference	Nutrient Variables
Colditz, G.A. (1995). The Nurses' Health Study: A cohort of U.S. women followed since 1976. *JAMWA*, 50, 40-63.	Selected macronutrients and selected micronutrients by breast cancer, CHD/stroke, colon cancer, fracture, diabetes, and other diseases. Fruits and vegetables by CHD/stroke, red meat by colon cancer, and caffeine by fractures.
Hu, F.B., Stampfer, M.J., Manson, J.E., Ascherio, A., Colditz, G.A., Speizer, F.E., Hennekens, C.H., Willett, W.C. (1999). Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. *Am J Clin Nutr*, 70, 1001-1008. The Nurses' Health Study	Saturated fat consumption over ten years. Saturated fat top 5 contributors. Saturated fat consumption by coronary heart disease risk factors. Red meat, white meat, high-fat and low-fat dairy consumption by coronary heart disease.
Liu, S., Willett, W.C., Stampfer, M.J., Hu, F.B., Franz, M., Sampson, L., Hennekens, C.H., Manson, J.E. (2000). A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in U.S. women. *Am J Clin Nutr*, 71, 1455-1461. The Nurses' Health Study	Selected macronutrients, selected micronutrients, and selected food sources by glycemic load. Energy-adjusted dietary glycemic load by CHD. Energy-adjusted total carbohydrate, type of carbohydrate and glycemic index by CHD.
Michels, K.B., Giovannucci, E., Joshipura, K.J., Rosner, B.A., Stampfer, M.J., Fuchs, C.S., Colditz, G.A., Speizer, F.E., Willett, W.C. (2000). Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. *J Nat Cancer Inst*, 92, 1740-1752. The Nurses' Health Study and The Health Professionals' Follow-Up Study	Frequency of fruit and vegetable intake by colorectal cancer age-standardized risk factors. Selected categories of fruit and vegetables by relative risk of colon cancer and rectal cancer. Selected categories of fruits and vegetables stratified by vitamin supplement useage by relative risk of colon cancer.
Van Dam, R.M., Huang, Z., Giovannucci, E., Rimm, E.B., Hunter, D.J., Colditz, G.A., Stampfer, M.J., Willett, W.C. (2000). Diet and basal cell carcinoma of the skin in a prospective cohort of men. *Am J Clin Nutr*, 71, 135-141. The Health Professionals' Follow-Up Study	Demographics related to nutrient intake, energy-adjusted dietary fat intake by relative risk of basal cell carcinoma of the skin, energy-adjusted intake of select micronutrients and relative risk of basal cell carcinoma of the skin.
Platz, E.A., Willett, W.C., Colditz, G.A., Rimm, E.B. (2000). Proportion of colon cancer risk that might be preventable in a cohort of middle-aged U.S. men. *Cancer Causes and Control*, 11, 579-588. The Health Professionals' Follow-Up Study	Mean alcohol intake, mean red meat intake, mean folic acid intake by colon cancer risk factors.
Giovannucci, E., Rimm, E.B., Colditz, G.A., Stampfer, M.J., Ascherio, A., Chute, C.C., Willett, W.C. (1993). A prospective study of dietary fat and risk of prostate cancer. *J Nat Cancer Inst*, 85, 1571-1579. The Health Professionals' Follow-Up Study	Fat intake by cancer-free members and by relative risk of prostate cancer. Levels of fat from various animal sources by relative risk of advanced prostate cancer.
Giovannucci, E., Rimm, E.B., Wolk, A., Ascherio, A., Stampfer, M.J., Colditz, G.A., Willett, W.C. (1998). Calcium and fructose intake in relation to risk of prostate cancer. *Cancer Res*, 58, 442-447. The Health Professionals' Follow-Up Study	Low and high intake of total calcium, total fructose, fruit fructose and non-fruit fructose by age-standardized selected characteristics. Total calcium intake and total fructose intake by total, advanced and metastatic prostate cancer.

prospective observational studies relative to cross-sectional studies, where incidence cannot be estimated, only prevalence, must be weighted against the real difficulty in obtaining funding for them. Many such studies today are either sponsored by the government through direct funding via a contract, or as add-ons to multicenter clinical trials. It is difficult to convince funding sources that observational studies, especially in disease areas where a good deal of information already exists, are worth the investment. Thus, sometimes adding components to existing studies such as a clinical trial can be done to gather prospective information. However, in this type of observation add-on, care must be taken to consider generalizability due to the eligibility criteria in the primary study.

References

1. Monsen ER, Cheney CL. *J Am Diet Assoc* 88: 1047; 1988.
2. Friedman GD. *Primer of Epidemiology*, McGraw-Hill, New York, 1987.
3. Zolman JF. *Biostatistics: Experimental Design and Statistical Inference*, Oxford University Press, New York, 1993.
4. Slome et al. *Basic Epidemiological Methods and Biostatistics: A Workbook*, Wadsworth Health Sciences Division, Monterey, 1982.
5. Dawber TR. *The Framingham Study: The Epidemiology of Atherosclerotic Disease*, Harvard University Press, Cambridge, 1980.
6. Friedman, GD, et al. *J Clin Epidemiol* 41: 1105; 1988.
7. McDonald A, et al. *J Am Diet Assoc* 91: 1104; 1991.
8. Liu K, et al. *Ethnicity Disease* 4: 15; 1994.
9. Slattery ML, et al. *J Clin Epidemiol* 47: 701; 1994.
10. Bild DE, et al. *Int J Obesity* 20: 47; 1996.
11. Tucker KL, et al. *Hum Clin Nutr* 126: 3025; 1996.
12. Kannel WB, et al. *Am J Epidemiol* 110: 281; 1979.
13. Posner BM, et al. *Int J Epidemiol* 22: 1014; 1993.
14. Posner BM, et al. *Arch Intern Med* 153: 1993.
15. St. Jeor ST, Dyer AR. In *Obesity Assessment: Tools, Methods, Interpretations*, St Jeor ST, Ed, Chapman and Hall, New York, 1997, ch. 1.
16. St. Jeor ST, Ed, *Obesity Assessment: Tools, Methods, Interpretations*, Chapman and Hall, New York, 1997.
17. Dodds MP, Silverstein LJ. In *Obesity Assessment: Tools, Methods, Interpretations*, St Jeor ST, Ed, Chapman and Hall, New York, 1997, ch. 17.
18. Benedict JA, Block G. In *Obesity Assessment: Tools, Methods, Interpretations*, St Jeor ST, Ed, Chapman and Hall, New York, 1997, ch. 19.
19. Scott BJ, Reeves RB. In *Obesity Assessment: Tools, Methods, Interpretations*, St Jeor ST, Ed, Chapman and Hall, New York, 1997, ch. 18.
20. Silverstein LJ, Scott BJ, St Jeor ST. In *Obesity Assessment: Tools, Methods, Interpretations*, St Jeor ST, Ed, Chapman and Hall, New York, 1997, ch. 22.
21. Colditz GA. *JAMWA* 50: 40; 1995.
22. Colditz GA, Coakley E. *Int. J. Sports Med* 18: S162; 1997.
23. Hu FB, et al. *Am J Clin Nutr* 70: 1001; 1999.
24. Liu S, et al. *Am J Clin Nutr* 71: 1455; 2000.
25. Michels KB, et al. *J Natl Cancer Inst* 92: 1740; 2000.
26. Rimm EB, et al. *The Lancet* 338: 464; 1991.
27. Van Dam RM, et al. *Am J Clin Nutr* 71: 135; 2000.
28. Giovannucci E, et al. *J Natl Cancer Inst* 85: 1571; 1993.
29. Platz EA, et al. *Cancer Causes Control* 11: 579; 2000.
30. Giovannucci E, et al. *Cancer Res* 58: 442; 1998.