

PART D: SCIENCE BASE

Section 6: Selected Food Groups (Fruits and Vegetables, Whole Grains, and Milk Products)

The Committee focused attention on fruits and vegetables, whole grains, and milk products because of the growing body of research linking them to health and because intake of these food groups by many Americans is far below previous recommendations. The fruit and vegetable groups are combined because they are examined together in much of the scientific literature related to health outcomes. This section addresses three major questions related to food groups and health:

1. What are the relationships between fruit and vegetable intake and health?
2. What are the relationships between whole-grain intake and health?
3. What are the relationships between milk product intake and health?

The other basic food group (meat, poultry, fish and legumes) is covered in Section 1, “Meeting Recommended Nutrient Intakes,” and fish also is covered in the “Fats” and “Food Safety” sections.

QUESTION 1: WHAT ARE THE RELATIONSHIPS BETWEEN FRUIT AND VEGETABLE INTAKE AND HEALTH?

Conclusions

Greater consumption of fruits and vegetables (5-13 servings or 2 ½- 6 ½ cups per day depending on calorie needs¹) is associated with a reduced risk of stroke and perhaps other cardiovascular diseases, with a reduced risk of cancers in certain sites (oral cavity and pharynx, larynx, lung, esophagus, stomach, and colon-rectum), and with a reduced risk of type 2 diabetes (vegetables more than fruit). Moreover, increased consumption of fruits and vegetables may be a useful component of programs designed to achieve and sustain weight loss.

Rationale

Fruits and Vegetables and Cardiovascular Disease

Overview. The conclusion related to cardiovascular disease (CVD) is based on the Committee’s review of evidence from an extensive literature view covering prospective, observational studies; other observational studies that addressed whole patterns of food consumption; and trials of the effects of fruit and vegetable consumption on blood pressure. Fruits and vegetables are associated with a reduction in CVD through a variety of mechanisms. First, they provide nutrients, such as fiber, folate, potassium, and carotenoids and other phytochemicals that may directly reduce CVD risk. Second, certain nutrients may directly improve established, diet-related CVD risk factors, such as blood pressure, hyperlipidemia, and diabetes. Third, the consumption of fruits and vegetables may lead to a reduced intake of saturated fat and cholesterol. Therefore, it is plausible to hypothesize that diets rich in fruits and vegetables should reduce the risk of CVD.

Several review articles have summarized the evidence from prospective observational studies (Bazzano et al., 2003; Law and Morris, 1998; Ness and Powles, 1997). The review by Bazzano included 10 prospective studies. In 7 of the 10 studies, an increased intake of fruits and vegetables was associated with a significant reduction in at least one CVD outcome; in pooled analyses of these studies, the relative risk of CVD (highest to lowest categories of fruit and vegetable intake) was 0.82 (95 percent CI: 0.76 to 0.89). Since then, four other major studies were published (Johnsen et al., 2003; Rissanen et al., 2003; Sauvaget et al., 2003; Steffen et al., 2003). The two studies that examined the relationship of fruit and vegetable intake with CVD mortality each documented a significant inverse relationship (Rissanen, 2003; Steffen et al., 2003). In six of the seven studies that examined the relationship of fruit and vegetable intake with stroke, there was a significant inverse relationship (Bazzano et al., 2002; Gillman et al., 1995; Johnsen et al., 2003; Joshipura et al., 1999; Rissanen et al., 2003; Steffen et al., 2003; Sauvaget et al., 2003). Only three studies examined the relationship of fruit and vegetable intake with CHD (Bazzano et al., 2002; Joshipura et al., 2001; Steffen et al., 2003); an inverse relationship was documented in only one study (Joshipura et al., 2001). In most studies, the results were attenuated in models that included CVD risk factors. This pattern of results suggests that at least part of the beneficial effects of fruit and vegetable intake is mediated through CVD risk factors. In most studies that documented a significant relationship, the general pattern of results appeared to be a progressive, inverse relationship rather than a threshold relationship.

Other observational studies have examined the relationship between whole patterns of food consumption and CVD. Often these studies use factor analysis to identify clusters of foods that are commonly consumed together. In these studies, those dietary patterns associated with a reduced risk of CVD (invariably) are rich in fruits and vegetables (Fung et al., 2001; Hu et al., 2001; Millen et al., 2004).

To date, no trial has tested the effects of increased fruit and vegetable on clinical CVD outcomes (i.e., coronary heart disease events, stroke). However, some trials have assessed the effects of fruits and vegetables on CVD risk factors. Four trials tested the effects of increased fruit and vegetable intake on blood pressure. Two of these trials documented that increased fruit and vegetable intake can lower blood pressure (Appel et al., 1997; John et al., 2002). Mean systolic blood pressure/diastolic blood pressure reductions were 2.7/1.9 mmHg and 4.0/1.5, respectively. All reductions were significant. In the two other trials, both of which were smaller or less well controlled, increased fruit and vegetable intake did not lower blood pressure (Broekmans et al., 2001; Smith-Warner et al., 2000). Finally, two trials tested the effects of fruits and vegetables in the context of multifactorial interventions on blood pressure (Appel et al., 2003; Sacks et al., 2001). In both studies, the multifactorial interventions significantly lowered blood pressure. Based on extensive research documenting that increased potassium intake reduces blood pressure (Whelton et al., 1997), at least part of the beneficial effect of increased fruit and vegetable intake on blood pressure results from increased potassium consumption. In summary, prospective observational studies have documented that increased fruit and vegetable intake is associated with a reduced risk of stroke and perhaps other cardiovascular diseases. Clinical trials have documented that an increased intake of fruits and vegetables can lower blood pressure.

Fruits and Vegetables and Cancer Prevention

Overview. The conclusion pertaining to fruit and vegetable intake and cancer prevention is based on the Committee's consideration of published evidence-based reviews focusing on the relationship between consumption of fruits and vegetables and cancer risks. These reviews were conducted by expert panels of the World Cancer Research Fund, American Institute for Cancer Research (WCRF/AICR, 1997), the National Cancer Institute (<http://cancer.gov/cancerinfo/pdq/prevention/>), and the World Health Organization (WHO) International Agency for Research on Cancer (IARC, 2003) (*IARC Handbook of Cancer Prevention on Fruits and Vegetables*). All expert panels followed a similar process of reviewing international evidence-based literature, primarily epidemiological studies including case-control and prospective cohort studies and controlled trials with meta-analyses and pooled analyses to establish the strength of the evidence.

It has now been established that cancer results from the interaction of human genes with environmental factors such as tobacco use, dietary factors including low fruit and vegetable consumption and high red meat and fat intake, and lifestyle issues such as physical inactivity and obesity (WCRF/AICR 1997). Individuals who consume diets rich in fruits and vegetables may be at lower risk for certain cancers, particularly cancers of the gastrointestinal tract. The World Health Organization International Agency for Research in Cancer (IARC) has estimated that low fruit and vegetable intake contributes to 5 to 12 percent of all cancers and up to 20 to 30 percent of upper gastrointestinal cancers that may otherwise be preventable. Therefore, the consumption of fruits and vegetables can confer protection against cancer. The phytochemical components in fruits and vegetables possess anticarcinogenic properties that influence DNA damage and repair, thus reducing mutations. These phytochemicals include antioxidants such as carotenoids and vitamin C, flavanoids, isothiocyanates, and organosulfides, as well as minerals and other bioactive compounds (Liu et al., 2003b). In addition, fruits and vegetables provide fiber, which helps decrease gut transit time and binds potential carcinogenic agents, secondary bile acids, and short-chain fatty acids (WCRF/AICR, 1997).

Review of the Evidence. In 1997, the WCRF/AICR expert panel provided key evidence that dietary protection against cancer is strongest and most consistent for diets high in vegetables and fruits, particularly in relation to cancers of the mouth and pharynx, esophagus, stomach, colon-rectum (vegetables only), and lung (WCRF/AICR 1997). The National Cancer Institute's PDQ® (Physician Data Query at <http://cancer.gov/cancerinfo/pdq/prevention/>) subsequently confirmed these findings. This database formed the basis of the NCI's National 5-A-Day Program (<http://www.5aday.gov>).

The WHO IARC published the findings of their working group's extensive review in the *IARC Handbook of Cancer Prevention on Fruit and Vegetables* (2003). The IARC Working Committee evaluated the evidence gathered on certain cancer sites in relation to intake of total fruits or total vegetables. Few of the identified studies had examined the effects of the total combined intake of fruits and vegetables. The world literature was reviewed and grouped together based on study design—either randomized-controlled trials, cohort studies, or case-control studies. The expert panel also considered the selection bias, confounding factors, measurement errors, and other variables. Human studies were included in the IARC evaluation only if the reports provided estimates of risk for total fruit or for total vegetable consumption and 95 percent confidence intervals were available. Estimates of a weighted mean of the reported

relative risks were calculated. Evidence tables have been constructed for each cancer site, and meta-analyses and pooled analyses are presented. The results of this analysis of cancer sites are published in the IARC's handbook. The IARC concluded there is evidence of cancer preventive effects with increased consumption of fruits and vegetables for cancers of the mouth, pharynx, esophagus, colon-rectum, larynx, stomach, and lung. There is inadequate evidence of a cancer-preventive effect of fruit and vegetable consumption for all other cancer sites. The number of studies, mean odd ratios, and the 95 percent confidence intervals on some of the cancer sites are listed below in Tables D4-1 and D4-2.

In addition, the preventive effects of fiber on colorectal cancer were recently demonstrated in a prospective study conducted by EPIC. Results showed that doubling total fiber intake from the current average level in most populations (about 20g per day) may reduce the risk of colorectal cancer, particularly colon cancer. About eight portions (rather than just five) of fruits and vegetables would need to be consumed per day, along with the equivalent of five slices of whole-grain bread (Riboli and Norat, 2003).

Recommendations from Other Groups. Agencies of the Federal government, preventive health organizations, and world bodies have recommended an increased intake of a variety of fruits and vegetables to 5 to 9 servings per day, or 400 to 800 g of fruits and vegetables per day (NCI website: <http://cancer.gov/cancerinfo/pdq/prevention/>, WCRF and AICR, 1997; IARC, 2003). Adherence to the AICR cancer prevention recommendations investigated in the *Iowa Women's Health Study Cohort* have substantial impact on reducing cancer incidence, with population attributable risks (avoidable risk) of 22 percent (95 percent CI, 12-30) for cancer incidence and 11 percent (95 percent CI 4-24) for cancer mortality (Cerhan et al., 2004).

Fruits and Vegetables and Type 2 Diabetes Mellitus

The conclusion relating to the relationship of fruit and vegetable intake with diabetes is based on the Committee's review of cross-sectional and prospective studies as described below. The roles of fruits and vegetables tend to be associated with those of fiber in the prevention of type 2 diabetes, making them difficult to distinguish. Dietary fiber tends to lower postprandial glucose response (Anderson and Akanji, 1991). Diets high in complex carbohydrates have been shown to protect against type 2 diabetes, and this has been ascribed in some studies to their high fiber content (Yang et al., 2003).

Review of the Evidence. Ford et al. (2000) examined whether fruit and vegetable consumption was associated with type 2 diabetes incidence in a cohort of U.S. adults age 25 to 74 years who were followed for about 20 years. After adjustment for a large number of variables, the hazard ratio for participants consuming five or more servings of fruits and vegetables per day compared with those consuming none was 0.73 for all participants, 0.53 for women, and 1.14 for men. Thus, these investigators found conflicting results in men and women. Williams and colleagues (1999) have shown that frequent intakes of raw and salad vegetables are protective against type 2 diabetes. However, in the same study, they did not find a significant association between fruits and diabetes. A subsequent study in the same cohort showed that a higher intake of both fruits and vegetables is associated with a lower risk for having glucose intolerance and undiagnosed diabetes (Williams et al., 2000). Gittelsohn et al. (1998) also

reported that a higher intake of fruits and vegetables was associated with a lower prevalence of diabetes.

In a cross-sectional study of a large population-based cohort not known to have diabetes, a report from the European Prospective Investigation into Cancer and Nutrition (EPIC) group (Sargeant et al., 2001) showed that those individuals who reported never or seldom having both fruit and green leafy vegetables had higher mean HgbA1c measurements (5.43 percent) than those who reported more frequent consumption (5.34 percent). These differences were not substantially changed after controlling for dietary fiber or for vitamin C. This lends support to the hypothesis that a high intake of fruits and green leafy vegetables may influence glucose metabolism and may contribute to the prevention of diabetes. These investigators carefully excluded participants with a diagnosis of diabetes, who may have changed their diet and lifestyle as a result of their diagnosis.

In a prospective study of middle-aged men, increased consumption of vegetables and legumes was inversely associated with 2-hour glucose level (Feskens et al., 1995). In the *Nurses' Health Study* (Colditz et al., 1992) the risk of diabetes was inversely related to vegetable but not to fruit consumption. Another longitudinal observational study of 20-year duration (Snowdon and Phillips, 1985) also reported a lower incidence of diabetes in those individuals who increased their intake of fruits and vegetables during the followup period. Some studies, however, have shown no effect (Lundgren et al., 1989; Salmeron et al., 1997a, 1997b). On the other hand, no study has found a harmful effect of fruit and vegetable consumption on the development of diabetes. Van Dam et al. (2002) reported on two major dietary patterns and the risk of type 2 diabetes in the *Male Health Professionals* study. They found that a prudent diet, characterized by a higher consumption of vegetables, fruit, fish, poultry, and whole grains, was associated with a significantly decreased risk for the development of diabetes as compared with a western diet characterized by a higher consumption of red meat, processed meat, French fries, high-fat dairy products, refined grains, and sweets and desserts.

Recommendations From Other Groups. Consistent with the above, current nutrition recommendations from the American Diabetes Association and the WHO for the prevention of type 2 diabetes encourage the consumption of carbohydrate-containing foods such as whole grains, fruits, vegetables, and low-fat milk (Franz et al., 2002; Mann et al., 2002).

Fruits and Vegetables and Weight Status

Overview. The conclusion relating to the relationship of fruit and vegetable intake with weight status is based on the Committee's review of a number of observational studies, including only two prospective studies, and several different types of trials, as described below. Fruits and vegetables are high in water and fiber content and therefore low in energy density. These types of foods also may promote satiety and decrease energy intake. Therefore, it is plausible to hypothesize that diets rich in fruits and vegetables might prevent weight gain and facilitate weight loss.

Review of the Evidence. A relatively large number of observational studies have examined the relationship between fruit and vegetable consumption and weight (Bazzano et al., 2002; Drapeau et al., 2004; Nicklas, 2003; Flood et al., 2002; Gillman et al.; 1995; Kobayashi et al.,

2002; LaForge et al., 1994; Lahti-Koski et al., 2002; Lin and Morrison, 2002; Liu et al., 2000; 2001; Patterson et al., 1990; Rissanen et al., 2003; Serdula et al., 1996; Terry et al., 2001; Trudeau et al., 1998; Williams et al., 1999). However, most are cross-sectional studies, which limit causal inferences. Drapeau et al. (2004) reported that increases in the consumption of whole fruits in a cohort of 248 volunteers followed for approximately 6 years was associated with a lower increase in body weight with time. Only two prospective studies examined the relationship between fruit and/or vegetable consumption and change in BMI. In one study, Kahn and colleagues (1997) followed 35,156 men and 44,080 women who participated in the *Cancer Prevention Study II* of the American Cancer Society. Over the course of 10 years, those men and women in the highest quintile of vegetable intake (> 19 servings per week) experienced a significant decrease in BMI (that is, a decline of 0.11 kg/m² in men and 0.10 kg/m² in women). Another prospective study (Field et al., 2003) assessed the effects of fruit and vegetable intake on changes in BMI over the course of 3 years of followup in 8,203 girls and 6,715 boys, age 9 to 14 years. In this study, neither fruits nor fruit juices predicted changes in BMI. Vegetable intake was inversely associated with BMI change in boys but not girls. This effect in boys was diminished and no longer statistically significant once total calories were included in the model. These findings suggest that the protective effect of vegetables was mediated through reduced calorie intake rather than the vegetables per se.

As reviewed by Rolls and colleagues (2004), several different types of trials have assessed the effects of increased fruit and vegetable intake on weight. In two uncontrolled studies, *ad libitum* provision of a traditional Native Hawaiian diet, which is rich in fruits and vegetables, led to reduced weight in overweight Hawaiians. Several small trials that advised persons to increase fruit and vegetable consumption but did not advise them to lose weight documented no net effect on weight (see Table 4 from Rolls et al., 2004). Trials that advised persons to increase fruit and vegetable consumption and also to decrease fat intake, again without giving advice to lose weight, tended to show weight maintenance or net weight loss (see Table 4 from Rolls et al., 2004). Of interest is one trial that specifically tested the effects of fruits and vegetables on weight over 1 year (Djuric et al., 2002). In this randomized 2 by 2 factorial trial that tested the effects of

(1) increased fruit and vegetable intake and (2) reduced fat intake, alone or combined, participants were counseled to maintain their energy intake while they made the dietary changes relevant to their assigned group. The group assigned to increase their fruit and vegetable group without reducing fat intake increased fruit and vegetable consumption from about 4 to 11 servings per day and increased their energy intake by approximately 170 kcal per day. This group increased their weight by 4 pounds. Those assigned to the reduced fat group alone reduced their weight by 11 pounds, while those assigned to both increased intake of fruits and vegetables and reduced fat had no change in weight. In aggregate, these data indicate that in the absence of advice to lose weight, increased fruit and vegetable intake by itself does not lead to weight loss.

Most relevant are those trials that attempted weight loss through increased fruit and vegetable consumption, often combined with reduced calorie intake, typically with a focus on decreased fat intake. The largest and longest study to examine this issue documented the effects of a cardiovascular risk reduction intervention that attempted to improve blood pressure and lipid control (Stamler and Dolecek, 1997). In this trial, 6,248 men were advised to lose weight.

Several dietary changes predicted sustained weight loss, including greater intakes of fruit and vegetables.

Another clinical trial, PREMIER (Appel et al., 2003), tested the effects of two different behavioral intervention programs to lower blood pressure, in part through weight loss. One intervention emphasized calorie reduction, reduction in fat intake to < 30 percent energy, and increased physical activity. The other intervention emphasized the DASH diet, which is rich in fruits and vegetables and further reduced fat intake (< 25 percent energy). After 6 months of intervention, mean intake of fruit and vegetable intake was nearly 8 servings per day in the group that received advice on the DASH diet but only about 5 servings per day in the other group. Corresponding net weight loss was 12.8 lb and 10.8 lb, respectively, but the difference between the groups was not statistically significant ($p=0.08$). Two uncontrolled studies documented that a low-fat, low-energy density diet that allowed unlimited intake of fruits and vegetables led to sustained weight loss. In the first study with an average followup period of 17 months (Weinsier et al., 1982), 44 percent of individuals continued to lose weight and 92 percent remained below their baseline weight. A similar pattern was evident in the second study by this group with 25 months of followup (Fitzwater et al., 1991).

Overall, available data suggest that increased consumption of fruits and vegetables may be a useful component of programs designed to achieve and sustain weight loss. However, there are limited data that increased consumption of fruits and vegetables prevent weight gain in the first place.

Intakes of Fruits and Vegetables

Daily servings of fruits and vegetables for individuals 2 years of age and older remained similar from an average total of 4.5 servings in 1989–1991 to 4.9 servings in 1994–1996; they decreased slightly to 4.7 servings in 1999–2000. (NCI website: <http://cancer.gov/cancerinfo/pdq/prevention/>) Daily vegetable intake increased from 3.2 to 3.4 servings, then decreased to 3.2 servings. On average, total vegetable intake included 0.3 servings of dark green/deep yellow vegetables, 1.4 servings of starchy vegetables (primarily fried potatoes) and 1.5 servings of tomatoes and other vegetables. Fruit intake increased from 1.3 to 1.5 servings over the same time frame. Neither trend is considered statistically significant. Vegetable consumption tends to increase as individuals age, but fruit consumption is highest among the very young and oldest individuals in the population. Individuals of lower education and income levels tend to eat fewer servings of vegetables and fruit than do those with more education and higher income. According to national surveys, African Americans tend to have the lowest intakes of fruits and vegetables among ethnic and racial groups (USDA, 2004; HHS, 2004).

QUESTION 2: WHAT ARE THE RELATIONSHIPS BETWEEN WHOLE-GRAIN INTAKE AND HEALTH?

Conclusion

Consuming at least 3 servings (equivalent to 3 ounces) of whole grains per day can reduce the risk of diabetes and coronary heart disease (CHD) and helps with weight maintenance. Thus,

daily intake of 3 ounces of whole grains per day is recommended, preferably by substituting whole grains for refined grains.

Rationale

Overview. The conclusion is based on the Committee's review of scientific evidence from 46 published papers pertaining to coronary heart disease, diabetes, and obesity. The recommended number of whole grain servings is based on evidence presented in 12 large prospective studies, which are presented in Appendix G3.

Whole grains and foods made from them consist of the entire grain seed, usually called the kernel. The kernel is made of three components—the bran, the germ and the endosperm. If the kernel has been cracked, crushed, or flaked, then it must retain nearly the same relative proportions of bran, germ, and endosperm as the original grain to be called whole grain (AACC et al., 2004). In the grain-refining process, most of the bran and some of the germ is removed, resulting in the loss of dietary fiber (also known as cereal fiber), vitamins, minerals, lignans, phytoestrogen, phenolic compounds and phytic acid (Slavin, 2003). Most refined grains are then enriched with thiamin, riboflavin, iron and niacin to restore these nutrients to levels found in the grain prior to refining. Enriched refined grains products are required by law to be fortified with folic acid, but whole-grain foods are not required to be fortified with folic acid. (ANON, Federal Register, 1996). However, food manufacturers may fortify whole-grain foods where regulations permit the addition of folic acid. Currently, a number of ready-to-eat whole-grain breakfast cereals are fortified with folic acid.

Important grains in the U.S. diet include wheat, rice, maize, and oats. The average intake of whole grains is less than 1 serving per day; less than 10 percent of Americans consume 3 servings per day (Cleveland et al., 2000). In a study of whole-grain consumption by U.S. children and adolescents using data from the 1994–1996 *Continuing Survey of Food Intake by Individuals* (CSFII), the average whole-grain intake ranged from 0.8 servings per day for preschool-aged children to 1.0 servings per day for adolescents (Harnack et al., 2003). Ready-to-eat cereals, corn or tortilla chips, and yeast breads were the major sources of whole grains (30.9 percent, 21.7 percent and 18.1 percent respectively).

Whole Grains and Risk of Coronary Heart Disease

Whole-grain intake has been found to be consistently associated with a reduction in the risk of CHD among both men and women (see Appendix G3) (Jacobs et al., 1998; 1999; Jensen et al., in press 2004; Liu et al., 1999, 2002; Pietinen et al., 1996; Rimm et al., 1996; Steffen et al., 2003). Collectively, the studies suggest a 20 to 30 percent reduced risk of CHD with 3 or more servings of whole grain foods per day. For example, in the *Nurses' Health Study*, which documented 761 cases of CHD in 75,521 women, increased whole-grain intake was associated with decreased risk of CHD. Women in the highest quintile of intake had a relative risk of 0.51 ($P < 0.0001$) compared to those in the lowest quintile (Liu et al., 1999). In the *Iowa Women's Health Study* (Jacobs et al., 1998), which involved 34,492 postmenopausal women followed for 6 years, a greater intake of whole grain was associated with a reduced risk of CHD death (RR = 0.67 comparing the highest quintile to the lowest quintile of intake). In the *Health Professionals Study* (all men) (Jensen et al., in press 2004), men in the highest quintile for whole-grain intake

had a RR of 0.64 for CHD compared to those in the lowest quintile of whole-grain intake. Although adjustment for potential confounders and risk factors for CHD other than BMI attenuated this association (Hazard Ratio (HR) = 0.82; P for trend = 0.01), each 20 g increment in whole-grain consumption corresponded to a 6 percent reduction in CHD risk (Jensen et al., in press 2004).

Certain studies base their evaluation of the strength of the relationship between whole-grain intake and reduced risk of CHD on the consumption of specific food groups or foods that are high in whole grains. For example, *The Adventist Health Study* (Fraser et al., 1992) reported an inverse association between intake of whole wheat bread and risk of myocardial infarction in 31,208 Seventh-Day Adventists (RR=0.56 for nonfatal myocardial infarction in those consuming whole wheat compared to white bread). Whole-grain bread intake also has been associated with a reduced incidence of CHD (Jacobs et al., 2001). Similarly, intake of breakfast cereals with a high whole-grain content also has been associated with a reduced incidence of CHD (Liu et al., 2003a).

Fiber and the Observed Protective Effect of Whole Grain. Because dietary fiber is an important component of whole grains, and the fiber content is greatly reduced when grains are refined, the literature on fiber and CHD also is applicable to the protective role of whole grains against CHD (See “Rationale” for Question 1 on fiber and CHD above). In brief, intake of high fiber foods has been independently associated with reduced incidence of ischemic heart disease and stroke (Humble et al., 1993; Khaw and Barrett-Connor, 1987; Pietinen et al., 1996; Rimm et al., 1996; Wolk et al., 1999).

Mozaffarian et al. (2003) determined whether fiber consumption from fruit, vegetable, and cereal sources (including whole grains and bran) is associated with incident cardiovascular disease in elderly persons. During 8.6 years of followup in 3,588 men and women age 65 years or older at baseline, cereal fiber consumption was inversely associated with incident CVD ($P = 0.02$). The relative risk was 0.79 in the highest quintile of intake compared with the lowest quintile. Neither fruit fiber intake nor vegetable fiber intake were associated with CHD incidence (Mozaffarian et al., 2003). This finding of a protective effect of fiber from cereals, but not from fruits or vegetables, is consistent with results from other studies (Pietinen et al., 1996; Rimm et al., 1996; Wolk et al., 1999) and supports the importance of whole-grain consumption as protective against CHD risk.

A number of studies assessing the relationship between whole-grain consumption and risk of CHD have evaluated the relationship of fiber intake and CHD risk in the same population. For example, the report on the *Nurses' Health Study* (Liu et al., 1999) evaluated whether the association of whole-grain intake with CHD risk could be attributed to its constituents (e.g., dietary fiber, folate, vitamin B₆, and vitamin E) or if something other than the micronutrient and fiber content of the whole grain was correlated with the protective effect. When the investigators adjusted for these protective factors, the significant inverse relationship of whole-grain intake to CHD risk was still evident. They suggest that this implies either a synergistic effect of the protective factors in whole grains or an effect from other substances, as yet unidentified, in whole grains. When the investigators for the *Health Professionals Study* looked at bran (a component of whole grain) and CHD risk, they found that the inverse association of bran and

CHD was even stronger than that for whole grain. The HR of CHD among men with the highest intake of added bran was 0.70 compared to that among men with no intake of added bran ($P < 0.001$) (Jensen et al., in press 2004). The authors conclude that their study supports the reported beneficial association of whole-grain intake and CHD, and it suggests that the bran component of whole grains could be a key factor in this relationship. However, the inverse relationship between whole-grain consumption remained after adjusting for bran intake.

In the *Cardiovascular Health Study* (a population-based, multicenter study with 3,588 men and women age 65 or older), cereal fiber consumption was inversely associated with CHD ($P = 0.02$). Risk was 21 percent lower in the highest quintile of intake, compared with the lowest quintile. In similar analyses, neither fruit fiber intake ($P = 0.98$) nor vegetable fiber intake ($P = 0.95$) was associated with incidence of CHD (Mozaffarian et al., 2003).

Physiological Basis for a Relationship Between Whole-Grain Intake and Decreased Risk of CHD. Although well-conducted prospective cohort studies are important and valuable in determining associations between nutrient intake and risk of disease, there is more confidence in these results when they are supported by biologically plausible mechanisms for the observed effect. One potential mechanism by which whole grains may decrease risk of CHD is through their antioxidant content (Decker et al., 2002). Vitamin E is present in whole grains but removed in the refining process and not added back in the enriching process. Similarly, selenium is present in whole grains but not enriched grains (Miller et al., 2001). Other bioactive compounds in whole grains include lignans, phytoestrogens, phytosterols, and digestive enzyme inhibitors. Although it is difficult to sort out the beneficial effects of whole grains independent of some of their constituents such as fiber and antioxidants, Slavin makes a case that whole-grain consumption is protective beyond what would be predicted if the protection found with the individual compounds were simply additive (Slavin et al., 2001; Slavin, 2003).

Possible Confounders With Respect to Whole-Grain Intake and CHD Incidence. Compared with low consumers of whole-grain foods, high consumers may smoke less, exercise more, and be more likely to use supplements of multivitamins. Thus, whole-grain intake may be just a proxy for a healthy lifestyle. However, when any of these known confounders have been evaluated, the inverse relationship between whole-grain consumption and risk of CHD (although attenuated) still remains statistically significant (Jensen et al., in press 2004; Liu et al., 1999). Moreover, in the studies that have evaluated fiber as a confounder, whole-grain intake has still remained protective against CHD (Liu et al., 2000). In fact, an argument could be made that the beneficial effects observed with cereal fiber are really due to whole grains rather than to the fiber *per se*, since it is probable that the cereal fiber intake is closely reflective of the whole-grain intake. Studies that focus on whole grain or on cereal fiber as the exposure measurements are, therefore, often measuring approximately the same entity (Mozaffarian et al., 2003). In addition, problems specific to measuring whole-grain intake may hinder accurate interpretation of results. For example, often participants are asked how much dark bread they ate; but the whole grain content of many dark breads is very low.

Whole Grains and Risk of Type 2 Diabetes

As with whole grains and CHD, major prospective epidemiological studies show an inverse relationship between whole-grain consumption and the risk of type 2 diabetes. Three prospective

studies in large numbers of men and women examined the relationship of whole-grain or cereal-fiber intake with the risk of type 2 diabetes. Each study used a mailed food frequency questionnaire as well as self-reported diabetes diagnosis. Risk of incident diabetes was 21 to 27 percent lower for those in the highest quintile of whole-grain intake and 30 to 36 percent lower in the highest quintile of cereal-fiber intake, each compared to the lowest quintile (Liu et al., 2000; Salmeron et al., 1997a, 1997b.). Risk reduction persisted after adjustment for the healthier lifestyle found among habitual whole-grain consumers.

Similarly, in the *Iowa Women's Health Study*, approximately 100,000 post-menopausal women were sampled and followed for 6 years. Meyer et al. (2000) examined the relationship of baseline intake of carbohydrate, fiber, and grains on the incidence of diabetes in this large cohort of women. Total grain, whole grain, total fiber, cereal fiber, and dietary magnesium intakes all showed strong inverse associations with incidence of diabetes after adjustment for potential nondietary confounding variables. Multivariate-adjusted relative risks of diabetes were 1.0, 0.99, 0.98, 0.92, and 0.79 ($P= 0.0089$) for whole grains and 1.0, 0.81, 0.82, 0.81, and 0.67 ($P= 0.0003$) for total fiber. Women who consumed the most whole grains (>17.5 servings per week) had a 21 percent lower risk of diabetes compared with those with the lowest intakes of whole grains (<3 servings per week) (Meyer et al., 2000). There was no significant effect of refined grains, or of fruits and vegetables.

Fung et al. (2001) examined prospectively the associations between whole- and refined-grain intake and the risk of type 2 diabetes among a large cohort of men in the *Health Professionals Follow-Up Study*. After adjustment for age; physical activity; cigarette smoking; alcohol consumption; family history of diabetes; and fruit, vegetable and energy intakes; the relative risk of diabetes was 0.58 ($P= <0.0001$) comparing the highest with the lowest quintile of whole-grain intake. Intake of refined grains was not significantly associated with the risk of type 2 diabetes

Whole-grain consumption was associated with a reduced risk of type 2 diabetes in the *Finnish Mobile Clinic Health Examination Survey* (Montonen et al., 2003). This survey consists of a cohort of 2,286 men and 2,030 women during a 10-year followup. The relative risk between the highest and lowest quartiles of whole-grain consumption was 0.65; $P= 0.02$.

In summary, the four prospective studies (*Iowa Women's Health*, *Nurses' Health*, *Health Professionals Follow-Up Study* and the *Finnish Mobile Clinic Health Examination Survey*) all show a risk reduction for type 2 diabetes of 20 to 30 percent. For an excellent review on whole grains and risk of diabetes, see Murtaugh et al. (2003).

Physiological Basis for a Relationship Between Whole-Grain Intake and Decreased Risk of Diabetes. The results of the four epidemiological studies that used diabetes as the end point are supported by other studies using intermediate markers for diabetes. For example, plasma glucose and insulin values may supply information on mechanisms by which whole grains exert their protective effect. The Committee examined evidence of the relationship of whole-grain consumption to glucose and insulin levels included in a recent review (Murtaugh et al., 2003). Briefly, in one cohort of 3,627 individuals age 18 to 30 (the *CARDIA* study) whole-grain consumption was assessed at years 0 and 7 and compared to insulin values at

year 10 (Pereira et al., 1998). Whole-grain consumption was inversely related to fasting insulin values.

In a feeding study, Pereira et al. (2002) tested whether or not whole-grain consumption improves insulin sensitivity in overweight and obese adults. When whole-grain products replaced refined-grain products, fasting insulin decreased by 10 percent over 6 weeks. In the *Framingham Offspring Study* (McKeown et al., 2002), whole-grain consumption in the highest quintile (13 to 64 servings per week) was associated with a significant decrease in fasting insulin compared to the lowest whole-grain consumption (0 to 1.5 servings per week) after adjusting for known confounders ($P=0.01$). This relationship was no longer significant after adjusting for total fiber. Also, whole-grain consumption has been inversely associated with BMI (McKeown et al., 2002), which is an independent risk factor for diabetes and CHD (See section below). The American Diabetes Association has concluded that some evidence supports the role of whole grain or dietary fiber in reducing the risk of type 2 diabetes (Franz et al., 2002).

Is the Observed Protective Effect of Whole Grain Due to Its Fiber Content? Some of the published epidemiologic studies have found an inverse association between fiber intake and the occurrence of type 2 diabetes (Hu et al., 2001; Meyer et al., 2000; Montonen et al., 2003; Salmeron et al., 1997a, 1997b). For example, in the *Nurses' Health Study*, Salmeron et al. reported on fiber intake and its relationship to diabetes. The risk reduction was similar to that of whole-grain intake in the same cohort (a 28 percent risk reduction from the highest to the lowest quintile of fiber intake) (Salmeron et al., 1997a). However, the source of fiber appears to be important, as cereal fiber but not fruit or vegetable fiber intake has been inversely associated with risk for diabetes in several studies (Salmeron et al., 1997b).

In the *Health Professionals Follow-Up Study* (Hu et al., 2001), the risk of developing diabetes did not decrease with higher total fiber intakes, but a risk reduction of 30 percent was observed in the highest quintile of cereal-fiber intake (median 10.2 g per day) compared to the lowest quintile (median intake 1.14 g per day). Again, as in the *Nurses'* cohort, cereal fiber but not fruit or vegetable fiber intake was associated with the protective effect. Similarly, in the *Finnish Mobile Clinic Survey* (Montonen et al., 2003), cereal fiber intake also was associated with a reduced risk of type 2 diabetes. The relative risk between the extreme quartiles of cereal fiber intake was 0.39; $p=0.01$. The authors conclude that the similar result for cereal fiber intake and whole-grain intake suggests that the whole grain association is due to cereal fiber intake.

Possible Confounders With Whole-Grain Intake and Risk of Type 2 Diabetes. Salmeron et al. (1997a; 1997b) found that diets with a high glycemic load and low cereal fiber content were positively associated with the risk of type 2 diabetes mellitus among both adult males and females in the United States (Salmeron et al., 1997a, 1997b). This finding suggests that total glycemic load may be a confounding factor. One study reported a positive relationship between fiber intake and the incidence of diabetes, but this study was retrospective and involved 242 individuals with diagnosed diabetes and 460 individuals without a prior diagnosis. More weight is given to the prospective studies since diet intake is assessed prior to rather than after disease occurrence. It is possible that individuals change their diets after they have been diagnosed with a disease (Marshall et al., 1991).

Whole Grains and Obesity, Weight Gain, Body Mass Index

Several studies have investigated the effect of whole-grain consumption on weight and body mass index (BMI) (often as a secondary analysis in a larger study). For a recent review of these studies see Koh-Banerjee, 2003. In the *Nurses' Health Study*, BMI did not vary appreciably across quintiles of whole-grain intake (Liu et al., 1999). In a later report on this same cohort, (Liu et al., 2003b), women who consumed more whole grains consistently weighed less than did women who consumed less whole grains ($P < 0.0001$). In the *Iowa Women's Health Study*, whole-grain intake was inversely correlated with body weight and fat distribution (Jacobs et al., 1998). In the *Health Professionals Follow-Up Study* (Koh-Banerjee, in press 2004), an increase in whole-grain intake was inversely associated with long-term weight gain (P for trend < 0.0001). A dose-response relation was observed, and for every 40 g increment in whole grains from all foods, weight gain was reduced by 0.49 kg. Independent of whole grains, changes in cereal and fruit fiber inversely predicted weight gain. In the *Coronary Artery Risk Development in Young Adults (CARDIA)* study, whole-grain intake was inversely related to BMI at 7-year followup of the participants (Pereira et al., 1998). In the *Framingham Offspring Study*, diets rich in whole grains were inversely associated with BMI and with the waist:hip ratio (McKeown et al., 2002). BMI values at the lowest whole-grain intake level averaged 26.9; at the highest whole-grain intake level the average BMI was 26.4 ($P = 0.06$). Weight was 1 to 2 kg higher among those with the lowest intake of whole grain than among those in the upper 20 percent of whole-grain intake.

Since whole grains also are high in fiber, the relationship of fiber intake to BMI is pertinent. In cross-sectional observational studies, fiber has been inversely associated with body weight (Alfieri et al., 1995) and body fat (Nelson et al., 1996; Miller et al., 1994). In a longitudinal study (the *CARDIA* study), macronutrient and fiber intakes were examined in relation to 10-year weight gain (Ludwig et al., 1999). Fiber had a strong negative association with weight gain, whereas fat had no association. Those in the lowest quintile of fiber intake (< 5 g per 1000 kcal per day) gained an average of 8 pounds more than those in the highest quintile (> 12 g per 1000 kcal per day). Fiber was inversely associated with BMI at all levels of fat intake, and the results were not explained by dietary fat intake. In the *Nurses' Health Study* (Liu et al., 1999), women in the highest quintile of dietary fiber intake had a 49 percent lower risk of major weight gain. Over a period of 12 years, those with the greatest increase in intake of dietary fiber gained an average of 1.52 kg less than did those with the smallest increase in intake of dietary fiber ($P = < 0.0001$). Again, as shown with whole-grain intake and risk of CHD or diabetes, an important component of the whole grain appears to be the fiber content.

Whole Grains and Cancer

A meta-analysis of 40 studies on gastrointestinal cancers found a 21 percent to 43 percent lower cancer risk with high intakes of whole grains compared to low intakes (Jacobs et al., 1998). In a recently reported case-control study on the relationship between frequency of consumption of whole-grain foods and cancer risk in Italy, there was a reduced risk of several cancers. The odds ratios for the highest intake category of whole-grain cereal consumption compared to the lowest category were 0.3 to 0.5 for upper digestive tract and respiratory neoplasms and colon (La Vecchia et al., 2003). A separate case-control study with 952 incident cases of rectal cancer compared with 1,205 population-based controls found that whole-grain intake had a reduced risk for rectal cancer (odds ratio of 0.69) and refined grain intake had a direct association with increased risk of rectal cancer (1.42) (Slattery et al., 2004). In addition, an inverse relationship

between cereal and cereal fiber intake and colon cancer incidence was reported in 24 studies although 7 other studies did not see this effect (Jacobs et al., 1998). The data on dietary fiber intake and colon cancer are inconsistent. Although between country studies generally show a protective effect of high fiber intake (Boyle et al., 1985), this is not true for within country studies. For example, two large prospective cohort studies in the United States, the *Nurses' Health Study* (Fuchs et al., 1999) and the *Physician's Follow-Up Study* (Giovannucci, 1994) do not show a protective effect of fiber intake against colon cancer. Most importantly, the three clinical intervention trials with colon polyp recurrence as an end point also failed to show a protective effect against this surrogate marker for colon cancer (Alberts et al., 2000; Bonithon-Kopp et al., 2000; Schatzkin et al., 2000). There are many reasons for the discrepancy among these different types of studies. Therefore, the overall benefits of whole-grain intake or any of its constituents (such as cereal fiber or fiber *per se*) and the incidence of colon cancer remain an unresolved issue and further research is needed.

Amount of Whole Grains To Consume

A recent report on the *Health Professionals Follow Up Study* (Jensen et al., in press 2004) confirms the results of previous individual studies and meta-analyses of servings of whole grain foods or products with whole-grain content above 25 percent (Anderson et al., 2000; Fraser et al., 1992; Jacobs et al., 1998, 1999; Liu et al., 1999; Steffen et al., 2003). In this report, the beneficial effects for whole-grain consumption are greatest for a daily whole-grain intake above approximately 30 g, regardless of the food source. In the *Iowa Women's Health Study* the protected quintile for ischemic heart disease was an average of 3.2 whole-grain servings per day (Jacobs et al., 1998). Taken collectively, there are strong and consistent data primarily from prospective cohort studies that whole-grain intake is protective against CHD incidence. The protected quintile of intake appears to be approximately three servings (equivalent to three ounces) of whole grains per day (See Appendix G3 Whole Grains and Chronic Disease Risk). There is good evidence that whole-grain intake may be protective against type 2 diabetes, and this evidence is supported by measurements of intermediate endpoints such as blood glucose and insulin concentrations. There is suggestive evidence from a number of secondary analyses, that whole-grain intake may protect against weight gain and help with weight maintenance although the concept that whole-grain intake represents a healthy lifestyle cannot be excluded as a confounder. Children and adolescents should strive to consumer primarily whole grains rather than refined grains.

QUESTION 3: WHAT ARE THE RELATIONSHIPS BETWEEN MILK PRODUCT INTAKE AND HEALTH?

Conclusion

Consuming three servings (equivalent to 3 cups) of milk and milk products each day can reduce the risk of low bone mass and contribute important amounts of many nutrients. Furthermore, this amount of milk product consumption may have additional benefits and is not associated with increased body weight. Therefore, the intake of three cups of milk products per day is recommended.

Rationale

Overview. The first part of the conclusion is based on the Committee's review of scientific evidence pertaining to nutrient adequacy, improving bone health, and reducing the risk of insulin resistance syndrome. Depending on the study reviewed, milk product intake was assessed by milk (1 serving = 1 cup) and sometimes included other dairy products such as yogurt (1 serving = 1 cup) and cheese (1 serving = 1.5 oz). The conclusion regarding milk products and weight is supported by the Committee's systematic review of the scientific evidence including two randomized clinical trials that addressed the question directly; four randomized controlled trials that addressed other questions; two longitudinal, case-control studies of milk group consumption and body weight and fatness; and seven observational studies that reported a secondary analysis of data collected for another purpose.

Many of the health benefits associated with milk consumption may be attributable to the component nutrients including calcium, potassium, magnesium, vitamin D, and vitamin A. The extent to which components unique to milk products play a role in promoting health such as the nature of milk proteins or conjugated linoleic acid (see Question 3 in Section 4, "Fats") are not well understood from the current literature.

Milk Products and Overall Nutrient Adequacy

Milk product consumption has been associated with overall diet quality and adequacy of intake of many nutrients including calcium, potassium, magnesium, zinc, iron, riboflavin, vitamin A, folate, and vitamin D for children and younger and older adults (Ballow et al., 2000; Barger-Lux et al., 1992; Devine et al., 1996; Foote et al., 2004; Johnson et al., 2002; Weinberg et al., 2004). Increasing the quartile of milk product intake was associated with increased intakes of all micronutrients studied except vitamin C among 17,959 participants in CSFII 1994-1996 (Weinberg et al., 2004). One cross-sectional study in young adults showed that the greatest benefit in intakes of vitamins and minerals was observed in those consuming three or more servings of milk products compared to those consuming two servings or less (Ranganathan et al., in press 2004). Choosing a variety of foods within the dairy food group was strongly associated with improved nutrient adequacy among 4,969 men and 4,800 women participating in CSFII 1994-1996 (Foote et al., 2004). Milk product and calcium intake in childhood shows a moderate degree of tracking with age (Whelton et al., 1997; Dwyer et al., 1989; Teegarden et al., 1999; Skinner et al., 2003). That is, those who consume milk regularly as children are more likely to do so as adults. Trends in consumption show a decline in milk intake, suggesting that milk has been displaced by other beverages. For example, in the *Bogalusa Heart Study*, (Nicklas et al., 2003b), the proportion of 10-year-old children consuming milk declined from 1972 to 1994. During the same period, the children's consumption of sweetened beverages including soft drinks, sweetened coffee, and fruit-flavored drinks increased. Fluid milk consumption was negatively related to soft drink consumption in boys and girls (McGartland et al., 2003; Whiting et al., 2001). Soft drink consumption negatively affected bone mineral accrual in the adolescent girls in both studies.

Milk Products and Bone

Because milk products are the major sources of calcium in the diets of Americans, low intake of milk products is associated with low calcium intake. The Institute of Medicine based the

Adequate Intakes (AIs) for calcium on maximizing calcium retention and optimizing bone health (IOM, 1997). Studies relating calcium intake and bone health were reviewed by the Institute of Medicine (IOM, 1997) and by Heaney (2000). For dietary guidance, this Committee evaluated studies specifically on milk and other milk products. All 7 of the randomized, controlled trials and 25 of 34 observational studies showed a positive relationship between the intake of milk products and bone mineral content or bone mineral density in one or more skeletal sites (see Appendix G3). Bone mineral density is a strong predictor of fracture. Therefore, it is a biomarker for the disease of osteoporosis.

In older adults, the strongest outcome measure for bone health is fracture incidence. Five of the eight observational studies using fracture as an end point found milk product consumption significantly associated with reduced fracture risk. Randomized, controlled trials are less confounded, but they are of insufficient duration to use fracture as an end point.

In studies of all age groups, the magnitude of the effect of milk product consumption on bone is at least as good as that obtained with calcium supplement trials. However, calcium supplements and milk products have not been compared in the same trial to determine if milk products offer more benefits than does calcium alone. Trials using milk, foods fortified with dairy calcium, or calcium supplements have demonstrated a comparable and important increase in skeletal mass in younger subjects and reduction in loss of skeletal mass in older subjects. In trials using milk or foods fortified with calcium extracted from milk, followup showed that the increase in skeletal mass was maintained after the intervention ceased (Bonjour et al., 2001; Ghatge et al., 2001). However, the increase in skeletal mass was not maintained following the interventions that used calcium supplements (Lee et al., 1996; Slemenda et al., 1997). This comparison suggests that skeletal benefits of dairy calcium persist longer than those derived from calcium supplements.

The intake of milk products is especially important to bone health during childhood and adolescence. Using data from 3251 Caucasian women from NHANES III, low intake (<1 serving of milk per week compared to >1 serving per day) during childhood and adolescence was associated with less hip bone mass in adulthood ($P<0.04$), and low milk intake during childhood was associated with a two-fold greater risk of fracture ($P<0.05$) (Kalkwarf et al., 2003). This association was not apparent in black women in NHANES III (Opotowsky and Bilezikian, 2003).

Milk Products and Insulin Resistance Syndrome

In a limited number of studies, the consumption of milk products has been related to a decreased risk of insulin resistance syndrome (IRS), otherwise known as syndrome X or the metabolic syndrome. IRS, which is characterized by obesity, insulin resistance, and hyperinsulinemia, leads to glucose intolerance, dyslipidemia, hypertension, and impaired fibrinolytic capacity. Thus, IRS leads to an increased risk for type 2 diabetes and cardiovascular disease (Reaven, 1993). While 22 percent of the U.S. adult population is estimated to have IRS (Ford et al., 2000), currently there are no standard diagnostic criteria and no treatment (Roth et al., 2002). In some studies, higher milk product consumption has been associated with decreased risk of IRS components, including coagulopathy (Mennen et al., 1999), coronary artery disease (Ness et al., 2001), stroke, and hypertension. In a cross-sectional analysis of men and women ages 30 to 64

years, Mennen et al. (2000) demonstrated that greater than 1 serving per day of milk products was associated with a 40 percent lower risk of IRS only in men.

Perhaps the largest study to examine the relationship of milk and IRS is the *Coronary Artery Risk Development in Adults* (CARDIA), a study of 3157 black and white adults age 18 to 30 years. In this prospective observational study, milk product consumption was inversely associated with the 10-year cumulative incidence of IRS among those individuals who were overweight (Pereira, 2002). Each additional serving of milk products was associated with a 21 percent lower odds of IRS (odds ratio, 0.79; 95 percent CI, 0.7 to 0.88). Three or more servings of milk products per day had the most benefit.

Three servings of low-fat milk products were a part of the DASH combination diet (see Section D1 for a description of this diet), which significantly lowered blood pressure (one component of IRS) in adults. In two controlled feeding studies (Appel et al., 1997; Sacks et al., 2001), the DASH diet—which is rich in fruits and vegetables (8 to 10 servings per day) and low-fat milk products (3 servings per day) and reduced in saturated and total fat—lowered systolic blood pressure by 5.5 mmHg and diastolic blood pressure by 3 mmHg in comparison to a typical American diet. The effect of increased fruits and vegetables alone (without the milk product component and other aspects of the DASH diet) was approximately half as large (-2.7 mmHg systolic and -1.9 mmHg diastolic blood pressure). In the PREMIER trial, there was no significant blood pressure difference between two lifestyle interventions, one of which emphasized milk products as well as other features of the DASH diet (Appel et al., 2003). However, participants in this behavioral intervention study did not fully meet nutrient goals of the DASH diet; approximately 60 percent of the participants consumed the amount of milk products prescribed, and only one-third consumed the prescribed amounts of fruits and vegetables.

An analysis of 10 prospective cohort studies relating milk intake at baseline to vascular disease events showed a pooled estimate of relative odds of 0.84 (95 percent CI, 0.78-0.90) for any vascular event and 0.87 (0.74 to 1.03) for ischemic heart disease (Elwood et al., 2004b). Elwood and colleagues (2004a) followed 2,403 men every 5 years for 20 to 24 years, obtaining data on milk intake and incidence of ischemic stroke. The hazard ratio for ischemic stroke in those who consumed 2 or more cups of milk per day, compared to those who did not consume milk, was 0.64 (0.39 to 1.06). The ratio was 0.37 (0.15 to 0.90) in those who had experienced a prior vascular event. Blood pressure was slightly ($P<0.02$) lower in the men who consumed milk. This emerging role of the relationship between milk product consumption and IRS and its components is provocative. More research is warranted to better understand the role of milk products and their constituents.

Milk Products and Weight Management

Randomized Clinical Trials Addressing the Question. Two randomized clinical trials evaluated the effects of calcium or milk products on body weight and/or body fat loss (Summerbell et al., 1998; Zemel et al., 2004). Both of these relatively small trials found a significant negative relationship between calcium/milk group intake and body weight or fat.

Summerbell studied 45 subjects randomized to a control energy-restricted diet, a milk-only diet, or a milk plus one selected food diet. Only 31 subjects finished the trial, and it is not clear that the three dietary treatments were eucaloric. Zemel et al. (2004) randomized 32 subjects to an energy-restricted diet, an energy-restricted diet plus 800 mg supplemental calcium, or a high-milk products (1,200 to 1,300 mg of calcium per day) energy-restricted diet for 24 weeks. Subjects on the high-milk products diet lost 70 percent more weight than those on the standard diet.

Secondary Analyses of Data From Other Randomized Controlled Trials. Four groups evaluated the relationship between milk group or calcium intake and body weight in randomized controlled trials designed to address other questions. Energy intakes were not controlled in any of these four trials. Barr and co-workers (2000) evaluated the impact of milk group consumption on cardiovascular risk factors and found that subjects in the milk group gained significantly more weight (0.6 kg) than the control group in the 12-week study. However, the net gain was less than anticipated from the increased energy intake from milk products (Barr et al., 2000). To evaluate the relationship between calcium and bone health, Davies et al. (2000) re-evaluated the data from a randomized trial of 216 women who received 1,200 mg of supplemental calcium per day for 3.9 years. Both the calcium-supplemented and control groups lost weight, but the calcium-supplemented group lost significantly ($P < 0.025$) more (0.346 kg per year) weight than the placebo group. Stamler and Dolecek (1997) evaluated the relationship between food intakes and body mass in 6,289 adults participating in the *Multiple Risk Factor Intervention Trial* (MRFIT). Greater weight loss was associated with greater reductions in medium-fat and high-fat milk products. The overall effect, however, was due to consuming a diet with lower energy density; there was no specific effect of dietary calcium. Also, in the *Trials of Hypertension Prevention* (TOHP) study, Yamamoto and co-workers (1995) found no effect of supplemental calcium (1 g per day) on BMI in 698 healthy men and women with high-normal diastolic blood pressure (80 to 89 mm Hg) participating in the trial. Energy intakes were not controlled in these four trials.

Longitudinal, Case-Control Studies in Children. Two longitudinal, case-control studies of milk group consumption and body weight and fatness have been done in children (Carruth and Skinner, 2001; Phillips et al., 2003). Carruth and Skinner found that the mean longitudinal calcium intake of preschool children from 24 to 60 months of age was associated with lower body fat at 70 months. However, Phillips et al (2003) found no evidence that milk group consumption was associated with the BMI z-score or the percentage of body fat in 178 nonobese girls followed from premenarche to 4 years postmenarche.

Observational Studies. Observational studies of the relationship between increased milk group consumption or increased calcium in the diet and body weight or body fat also have been done. The results of those studies are mixed (Buchowski et al. 2002; Davies, et al. 2000; Drapeau et al., 2004; Jacqmain et al., 2003; Lin, et al. 2000; Lovejoy et al., 2001; Melanson et al., 2003; Pereira et al., 2002). None of the observational studies were designed with the intention of studying the relationship between milk group intake or calcium consumption and either body weight or composition. Instead, the papers report a secondary analysis of data collected for another research question. Heterogeneity in methodologies used to measure body composition and dietary intake along with differences in the number and type of variables used

as covariates and the manner in which calcium intake is expressed (i.e., energy-adjusted or protein-adjusted) may account for the divergent results.

Recommendations from Other Groups. A recommendation of 3 servings milk products per day (See Table D1-13) is consistent with recommendations from other authoritative groups (American Academy of Pediatrics, 2001; American Heart Association, 2004; National Medical Association, 2004). Mean intake of milk products is much lower than this, and only about 28 percent of men and 15 percent of women consume 2 servings in a day

Milk Products Summary. Taken collectively, there is strong and consistent evidence that the intake of milk products is protective against osteoporosis and limited evidence that milk product intake protects against IRS. The protected quintile of intake appears to be approximately 3 servings of milk or milk products per day. The possible reduction of the incidence of IRS with higher milk product consumption may be partially or mostly related to the calcium content of milk products.

None of the studies show that milk group consumption is associated with an increase in body weight. Since adults and children benefit from including milk products in the amounts suggested in the revised USDA food intake pattern -- both for bone health and for lowering the risk of several diseases -- milk products are recommended as part of the overall dietary pattern. There is no evidence that milk products should be avoided because of concerns that these foods are fattening. Because of the lack of large-scale, randomized trials or controlled feeding studies designed explicitly to test the effect of milk group intake or calcium consumption on body weight and the limitations of the studies reported above, at this time there is insufficient evidence on which to base a more definitive statement regarding the intake of milk products and management of body weight.

SUMMARY

The main message from these reviews is that an increased intake of fruits and vegetables (2 ½ to 6 ½ cups; equal to 5 to 13 servings depending on caloric needs), and the consumption of approximately 3 ounces of whole grains daily promotes health and reduces the risk of chronic diseases. In addition, the daily consumption of approximately three cups of nonfat or low-fat milk or the equivalent from other milk products can reduce the risk of low bone mass. All these foods make important nutrient contributions. There is no evidence that the recommended amounts of milk products increases body weight. The DASH diet, which is consistent with the recommendations made here, has been demonstrated to have beneficial effects on health (see Section D1).

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Table D6-1.

Table D6-2.

