PART D. Section 5: Carbohydrates

Introduction

Carbohydrates (one of the three macronutrients) consist of sugars, starches, and fibers. The Institute of Medicine (IOM) (2002) set an acceptable macronutrient distribution range (AMDR) for carbohydrates of 45 to 65 percent of total calories. Thus, current dietary guidance recommends consumption of carbohydrate-containing foods, including vegetables, fruits, grains, nuts and seeds, and milk products. Carbohydrate foods are an important source of fiber and other nutrients.

Sugars and starches provide glucose, the main energy source for the brain, central nervous system, and red blood cells. Glucose also can be stored as glycogen (animal starch) in liver and muscle, or, like all excess calories in the body, converted to body fat. Dietary fibers are nondigestible forms of carbohydrates and lignin. Dietary fiber is intrinsic and intact in plants, helps provide satiety, and is important in promoting healthy laxation. Diets high in fiber also have been linked to reduced risk of diabetes, colon cancer, obesity, and other chronic diseases.

The role of carbohydrates in the diet has been the source of much public and scientific interest. These include the relationship of carbohydrates with health outcomes, including coronary heart disease (CHD), type 2 diabetes (T2D), body weight, and dental caries. The 2010 DGAC conducted NEL evidence reviews on these and other carbohydrate-related topics. The Committee also relied on evidence contained in the 2002 Dietary Reference Intakes (DRIs) report and conducted a non-NEL review of recent literature to specifically examine the relationship of carbohydrates with CHD, T2D, behavior, and cognitive performance (Colditz, 1992; Dolan, 2010; IOM, 2002; Laville, 2009; Meyer, 2000; Stanhope, 2009; Wolraich, 1995). No detrimental effects of carbohydrates as a source of calories on these or other health outcomes were reported.

The energy value of digestible carbohydrates is generally accepted as 4 calories per gram for both sugars and starches. Research suggests that high-fiber diets can cause energy losses in the feces beyond the energy contained in the fiber source that escapes fermentation (Miller, 1984) and can aid in weight control through lower energy yield. Few studies have linked carbohydrates to obesity. Indeed, observational data generally report that higher carbohydrate intake is linked to lower body weight (NHANES, 2000-2005). Aspects of carbohydrate and body weight are discussed in detail later in this section and in other sections of this report (see Question 5 for a discussion of sugar-sweetened beverages [SSB] and energy intake and body weight; ***Part D. Section 1: Energy Balance and Weight Management*** for discussions of macronutrient proportions and body weight and of SSB and body weight in children; and ***Part D. Section 2: Nutrient Adequacy*** for a discussion of added sugars as a food component over consumed in the American diet).

Carbohydrates and dental caries also are a topic of public health importance. The 2005 DGAC concluded that carbohydrate intake contributes to dental caries by providing substrate for bacterial fermentation in the mouth. A combined approach of reducing the frequency and duration of exposure to fermentable carbohydrate intake and optimal oral hygiene practices is the most effective way to reduce caries incidence. Substantive research on the relationship of carbohydrates and dental caries has not occurred since the last DGAC report, so the 2010 DGAC reaffirms the 2005 Committee's conclusion.

This section continues with background information on the nomenclature and composition of carbohydrates and provides discussion of recommended intakes of carbohydrates and their food sources. Also provided are the NEL systematic evidence-based reviews of six questions and non-NEL literature review of three questions that cover a variety of issues related to intakes of dietary carbohydrates and health.

Background on Carbohydrates

Nomenclature

Carbohydrates are subdivided into several categories, based on the number of sugar units present and the way in which the sugar units are chemically bonded to each other. These categories include sugars, starches, and fibers. Sugars are intrinsic in fruits, fluid milk, and milk products. They also are added to foods during processing, preparation, or at the table. These "added sugars" (or extrinsic sugars) sweeten the flavor of foods and beverages and improve their palatability. Sugars are also used in food preservation and to confer functional attributes, such as viscosity, texture, body, and browning capacity. They provide calories but insignificant amounts of vitamins, minerals, or other essential nutrients. The Nutrition Facts Label provides information on total sugars per serving, but does not distinguish between sugars naturally present in foods and added sugars.

Starches are made of many glucose units linked together. They are found naturally in a wide range of foods, including vegetables, cooked dry beans and peas, and grains. Most starches are broken down to sugars by digestive enzymes for use by the body, but some starches, such as those in cooked dry beans and peas and pasta, are resistant to digestive enzymes. Fibers, like starches, are made mostly of many sugar units bonded together. Unlike most starches, however, these bonds cannot be broken down by digestive enzymes and pass relatively intact into the large intestine. There, fiber can be fermented by the colonic microflora to gases such as hydrogen and carbon dioxide or it can pass through the large intestine and bind water, increasing stool weight. Although fibers are not converted to glucose, some short chain fatty acids are produced in the gut as fibers are fermented. Short chain fatty acids are absorbed and can be used for energy in the body. Fibers include both "dietary fiber," the fiber naturally occurring in foods, and "functional fibers," which are

isolated fibers that have a positive physiological effect. No analytical measures exist to separate dietary fiber and functional fiber, so the Nutrition Facts Label lists "Dietary Fiber"—which is actually total fiber.

Table D5.1 provides a summary of the carbohydrate categories, showing their chemical composition, how they are made, examples of each, and food sources.

Table D5.1. Carbohydrates: nomenclature and special issues

	Composition	Examples	Special issues	Found in
Sugars				
Monosaccharides	1 sugar unit	• Glucose • Fructose • Galactose	• Rarely found naturally in foods-except for fructose	• Apples (fructose) • Pears (fructose) • Honey (fructose)
Disaccharides	2 linked sugar units	• Sucrose (50% glucose, 50% fructose) • Lactose (50% galactose, 50% glucose) • Maltose (100% glucose-glucose bond) • High fructose corn syrup (HFCS) (generally 55% fructose –sometimes 42% fructose – varies)	• Occurs naturally in foods (sucrose, lactose) • Produced by starch digestion (maltose) • Hydrolysis of corn (HFCS)	• Fruit • Milk • Sweet potatoes
Oligosaccharides (OS)	3-10 linked sugar units	• Raffinose • Stachyose	• May cause intestinal gas	• Dry beans and peas • Onions • Breast milk • Added to food as inulin and other OS
Starches				
Polysaccharides	Many linked glucose units	• Starch • Glycogen – animal starch	• Most are broken down to glucose for absorption	• Starchy vegetables • Grains • Dry beans and peas • Nuts and seeds
		• Resistant starch	• Resistant starch does not undergo digestion in the small intestine	• Dry beans and peas • Pasta • Refrigerated cooked potatoes
Fibers				
Polysaccharides/Lignin	Many linked sugar units	• Dietary Fiber, i.e., nondigestible carbohydrates and lignin that are intrinsic and intact in plants • Functional Fiber, i.e., isolated nondigestible carbohydrates that have beneficial physiological effects in human beings • Total Fiber = Dietary Fiber + Functional Fiber	• Different chemical bonding; human enzymes cannot break bonds; pass relatively intact through upper digestive tract • Can be fermented by colonic microflora to gases and short-chain fatty acids	• Vegetables • Fruits • Whole grains • Dry beans and peas • Nuts and seeds

Recommended Intakes and Food Sources

Recommended Intakes of Sugars and Starches

In its 2002 report *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (IOM, 2002), the IOM established a Recommended Dietary Allowance (RDA) for carbohydrate of 130 grams per day for adults and children age 1 year and older. This value is based on the amount of sugars and starches required to provide the brain with an adequate supply of glucose. Although the IOM set an (Acceptable macronutrient Distribution Range (AMDR) for carbohydrate of 45 to 65 percent of total calories, it is very difficult to meet dietary fiber recommendations at the low end of this range, and high intake of total sugars (intrinsic and added) may be linked to elevated blood triglycerides. A comparison of the RDA to the AMDR shows that the recommended range of carbohydrate intake is higher than the RDA. For example, if an individual with a caloric intake of 2,000 kcal per day consumes 55 percent of calories as carbohydrate (the mid-range of the AMDR) 1,100 kcal would be from carbohydrate. This equates to 275 g carbohydrate (1 g carbohydrate = 4 kcal), well above the RDA of 130 g per day needed for brain function.

The DRI committee concluded that evidence was insufficient to set a Tolerable Upper Intake Level (UL) for carbohydrates (IOM, 2002). However, a maximal intake level of 25 percent or less of total calories from added sugars was suggested by the panel. This suggestion is based on dietary intake survey data showing that people with diets at or above this level of added sugars were more likely to have poorer intakes of important essential nutrients.

Recommended Intakes of Fiber

In its 2002 report, the IOM set an Adequate Intake (AI) value for fiber of 14g of fiber per 1,000 kcal. This value is derived from data on the relationship of fiber consumption and CHD risk, although the IOM also considered the totality of the evidence for fiber decreasing the risk of chronic disease and other health-related conditions. Consequently, the IOM fiber recommendations are highest for populations who consume the most calories, namely young males. Fiber recommendations are lower for women and the elderly. Using this method for determining recommended fiber intake for children is problematic (e.g., intake of 19 g of fiber is recommended for 2 year old children, an implausible number). Past recommendations for children were based on the age plus 5 rule (e.g., a child aged 2 years should consume 7 grams of fiber per day) (Williams, 1995).

Dietary fiber is listed on the Nutrition Facts panel, and 25 g of dietary fiber is the recommended amount in a 2,000 kcal diet. Manufacturers are allowed to call a food a "good source of fiber" if it contains 10 percent of the recommended amount (2.5 g/serving) and an "excellent source of fiber"

if the food contains 20 percent of the recommended amount (5 g/serving. Dietary fiber on food labels includes both dietary fiber and functional fiber.

Food Sources of Carbohydrates in the Diet

The amount of dietary carbohydrate that confers optimal health in humans is unknown (IOM, 2006). Adults should consume 45-65% of their total calories from carbohydrates, except for younger children who need a somewhat higher proportion of fat in their diets (IOM, 2006). Vegetables, fruits, whole grains, milk and milk products are the major food sources of carbohydrates. Grains and certain vegetables including corn and potatoes are rich in starch, while sweet potatoes are mostly sucrose, not starch (Anderson, 1982). Fruits and dark green vegetables contain little or no starch. Regular soft drinks, sugar-sweets, sweetened grains, and regular fruitades/drinks comprise 72% of the intake of added sugar (Marriott et al, 2010). Marriott et al. (2010) examined the intake of added sugars and selected nutrients from 2003-2006 National Health and Nutrition Examination Survey (NHANES) data. Thirteen percent of the population had added sugars intake of more than 25 percent of calories. The mean gram equivalent (g-eq) of added sugars intake was 83.1 g-eq/day and the food sources of added sugars were comparable to the mid-1990s. Higher added sugars intakes were associated with higher proportions of individuals with nutrient intakes below the Estimated Average Requirement (EAR), but the overall high calorie and low quality of the US diet remained the predominant issue.

Dietary fiber intake was particularly low in their analysis. With the exception of older women (51+ years), only 0 to 5 percent of individuals in all other life stage groups had fiber intakes meeting or exceeding the AI (Marriott et al, 2010). Fiber intake is closely linked to calorie intake. Thus, recommendations to reduce calorie intake will make increasing fiber intake particularly challenging (Slavin, 2008).

To reduce calories in response to the epidemic obesity crisis in the US, non-nutrient-dense carbohydrate sources, should be reduced. Because fiber has known health benefits, it is advisable to select foods high in dietary fiber, whole grain breads and cereals, legumes, vegetables, and fruit whenever possible. For more information on food sources of fiber, see ***Part D. Section 2. Nutrient Adequacy***. Typically, vegetables and fruits are not the most concentrated fiber sources, but these are important foods to encourage because they contribute important micronutrients. Similarly, milk and milk products, which contain lactose, generally do not contain fiber but these too are important because they contribute calcium, vitamin D, protein, potassium, magnesium, and riboflavin.

List of Questions

CARBOHYDRATES AND HEALTH OUTCOMES

1. What are the health benefits of dietary fiber?
2. What is the relationship between whole grain intake and selected health outcomes?
3. What is the relationship between the intake of vegetables and fruits, not including juice, and selected health outcomes?
4. What is the relationship between glycemic index or glycemic load and selected health outcomes?
5. In adults, what are the associations between intake of SSB and energy intake and body weight?

OTHER RELATED TOPICS

6. How are non-caloric sweeteners related to energy intake and body weight?
7. What is the impact of liquids versus solid foods on energy intake and body weight?
8. What is the role of carbohydrate, fiber, protein, fat, and food form on satiety?
9. What is the role of prebiotics and probiotics in health?

Methodology

The Committee first reviewed the 2005 DGAC Report to inform their review process in 2010. Various topics in this section were also considered by the 2005 DGAC, including fiber (Question 1), whole grains (Question 2), vegetables and fruits (Question 3), glycemic index and load (Question 4), added sugars (Question 5), and liquids versus solids (Question 7). New questions considered by the 2010 Committee include non-caloric sweeteners (Question 6), satiety (Question 8), and prebiotics and probiotics (Question 9). NEL evidence-based systematic reviews were conducted for Questions 2 to 7. The Committee addressed the remaining topics in the DGAC report, but given limited time and resources, the systematic review methodology was not applied. Rather, the most current or representative evidence was applied. For example, the dietary fiber question was primarily answered using the 2002 DRI report (IOM, 2002) and a recent position paper on fiber from the American Dietetic Association (ADA) (Slavin, 2008). These were supplemented by an updated literature review. Questions on satiety and pre- and probiotics also were answered using a general literature search.

For each of the NEL systematic review questions in this chapter, the following general criteria applied. All study designs were originally included in the searches, but cross-sectional studies were later excluded from the review, if there was sufficient evidence from studies with stronger study designs. The Committee excluded studies that only included participants diagnosed with chronic disease, hyperlipidemia, hypertension, and related health conditions. A description of the NEL

evidence-based systematic review process is provided in ***Part C: Methodology***. Additional information about the NEL search strategies and criteria used to review each question can be found online at www.nutritionevidencelibrary.com.

Many systematic reviews and meta-analyses of primary research articles were considered by the Committee, and care was taken not to review the same study twice in the NEL evidence-based review. For most questions, systematic reviews and meta-analyses were included, and primary research articles included in the reviews were excluded. However, systematic reviews and meta-analyses were excluded from the review on glycemic index/load (Question 4) because many studies on the topic had been published since 2004 and the Committee wanted to focus their review on primary research articles.

For Questions 2, 3, 4, 5, and 7, the Conclusions expressed in the 2010 DGAC report are informed by the evidence compiled for the 2005 DGAC report, but are based primarily on the NEL evidence gathered and reviewed since 2004. As described below, for some questions, the search was extended back further to capture a larger body of evidence.

Question 2 examined the relationship between the consumption of whole grains and incidence of cardiovascular disease (CVD), T2D, and measures of adiposity. These outcomes were selected because they represent leading causes of morbidity and mortality in the US. The Committee extended this search back to 1995, so that literature reviewed by the 2005 DGAC could also be considered.

Question 3 examined the relationships between intake of vegetables and fruits, not including juice, and body weight, cardiovascular outcomes, and T2D in adults. The Committee only considered studies that directly assessed the relationship between the intake of vegetables and fruit and health outcomes; studies examining the intake of vegetables and fruits as a part of specific dietary patterns are considered in ***Part D. Section 2: The Total Diet: Combining Nutrients, Consuming Food.*** The childhood adiposity section in ***Part D. Section 1: Energy Balance and Weight Management*** provides additional information about vegetables and fruits and 100 percent juice, and ***Part D. Section 2: Nutrient Adequacy*** discusses vegetables and fruits as food groups of concern for the American population. Cancer was not considered in the NEL evidence-based systematic review because the Committee chose to address this topic using the World Cancer Research Fund/American Institute for Cancer Research report (WCRF/AICR, 2007).

Similar to 2005, the review of glycemic index/load (Question 4) included the outcomes of body weight and incidence of T2D, CVD, and cancer. Reviews for CVD and T2D were extended to January 2000 because insufficient evidence was available to draw conclusions from publications since 2004.

Although added sugars (Question 5) was considered by the 2005 DGAC, the Committee extended the search for this topic to 1990. This section of the report only considers the literature pertaining to adults (***Part D. Section 1: Energy Balance and Weight Management*** addresses SSB and childhood adiposity). The original search for this question was broad and included terms such as "added sugars," "dietary sucrose," "candy" as well as various terms for SSB. However, few studies were identified that looked at added sugars other than SSB; thus, SSB are the focus of this review. Additional information about intake of added sugars is provided in ***Part D. Section 2: Nutrient Adequacy***.

Liquids versus solids (Question 7) was considered an "unresolved issue" in 2005; therefore, the Committee extended the search for this review to January 2000. This review only included studies that compared a liquid to a solid or semi-solid form. Further, only articles that considered energy intake and/or body weight were reviewed. Although additional research on food form and appetite, hunger, and related outcomes are available, these outcomes were not addressed in this aspect of the review.

Non-caloric sweeteners (Question 6) was not considered in previous iterations of the DGAC report. The review of non-caloric sweeteners was an update to a previous systematic review conducted by the American Dietetic Association's Evidence Analysis Library on non-caloric sweeteners and energy intake and body weight. The ADA review addressed literature published from January 1985 through March 2006, and the Committee updated this search from March 2006 to present.

CARBOHYDRATES AND HEALTH OUTCOMES

Question 1: What are the Health Benefits of Dietary Fiber?

Conclusion

A moderate body of evidence suggests that dietary fiber from whole foods protects against cardiovascular disease, obesity, and type 2 diabetes and is essential for optimal digestive health.

Implications

Dietary fiber is under-consumed across all segments of the American population. The development of many risk factors that are associated with incidence of several highly prevalent chronic diseases could be reduced by increasing consumption of naturally-occurring plant-based foods that are high in dietary fiber, including whole grain foods, cooked dry beans and peas, vegetables, fruits, and nuts.

Review of the Evidence

Background

The 2002 DRIs defined dietary fiber as non-digestible carbohydrates and lignin that are intrinsic and intact in plants. Functional fiber consists of the isolated non-digestible carbohydrates that have beneficial physiological effects in human beings (IOM, 2002). Total fiber is the sum of dietary fiber and functional fiber. Since data were inadequate to determine an Estimated Average Requirement (EAR) and thus calculate a RDA for Total Fiber, an Adequate Intake (AI) was instead developed. AI was based on the median fiber intake associated with the lowest risk of CHD in prospective, cohort studies. Fiber recommendations are calculated as 14 g fiber per 1,000 kcal of usual intake, so higher fiber intakes are recommended for men compared to women. The Nutrition Facts panel suggests an intake of 25 grams of dietary fiber for a 2000 kcal diet.

Most Americans seriously under consume dietary fiber with usual intakes averaging only 15g per day (NHANES, 2005-06; NCI, 2009). Concentrated dietary fiber sources include whole grains, cooked dry beans and peas, vegetables, nuts, and dried fruits (see Table D2.16 in ***Part D. Section 2. Nutrient Adequacy***). The major sources of dietary fiber in the American diets are white flour and potatoes, not because they are concentrated fiber sources but because they are widely consumed (Slavin, 2008).

The following summary is based on a non-NEL review of the literature. It highlights conclusions from the American Dietetic Association (ADA) position paper on dietary fiber and covers other recently published findings.

Dietary Fiber and Cardiovascular Disease

The ADA published a position paper, which presents the findings of the ADA's Evidence Analysis Library systematic review on the health implications of dietary fiber (Slavin, 2008). This review found fair evidence (Grade II) that "dietary fiber from whole foods or supplements may lower blood pressure, improve serum lipids, and reduce indicators of inflammation. Benefits may occur with intakes of 12 to 33 g fiber per day from whole foods or up to 42.5 g fiber per day from supplements."

Other recent studies reported a range of cardiovascular benefits associated with dietary fiber. Demoura et al. (2009) evaluated the effect of applying the Food and Drug Administration's (FDA, 2006) definition of whole grains (see whole grain section that follows) to the strength of scientific evidence that supports whole grain health claims for CVD risk reduction. The authors concluded that when a broader whole grain definition was used, such that studies of individual whole grains (barley, oats, or rye) that did not explicitly define whole grains in the manuscript as well as studies

that added bran and germ with whole grains were included, there was sufficient evidence for a CVD health claim. Flint (2009) reported that cereal fiber was associated with reduced blood pressure in adults. The longitudinal STRIP study in children (Ruottinen, 2010) found that serum cholesterol concentrations decreased with increasing fiber intake.

Dietary Fiber and Obesity Prevention

According to the ADA position paper (Slavin, 2008), high-fiber diets provide bulk, are more satiating, and have been linked to lower body weights. Three recent prospective studies and two cross-sectional studies provide additional support for the role of dietary fiber in obesity prevention. Du et al. (2010) followed a large cohort for 6.5 years and found that total fiber and cereal fiber were inversely associated with subsequent increases in weight and waist circumference. Fruit and vegetable fiber was also inversely associated with waist circumference change, but not with weight change. Likewise, a 20-month, prospective cohort study (n=252) (Tucker and Thomas, 2009) found that for each 1g increase in total fiber consumed, weight decreased by 0.25 kg and percent body fat decreased by 0.25 percentage points. A longitudinal study of dietary intake on metabolic risk factors in Latino youth (Davis, 2009b) concluded that adolescents who increased total dietary fiber intake (3 g/1000 kcal) decreased their visceral adipose tissue (VAT), whereas adolescents who decreased in dietary (3 g/1000 kcal) and insoluble fibers increased VAT. ***Part D. Section 1: Energy Balance and Weight Management*** provides a review of dietary fiber and adiposity in children.

Dietary Fiber and Type 2 Diabetes

The ADA position paper on the health implications of dietary fiber (Slavin, 2008) concluded that limited evidence suggested that "diets providing 30 to 50g fiber per day from whole food sources consistently produce lower serum glucose levels compared to a low fiber diet." Hopping et al. (2010) examined the association between dietary fiber and T2D in a large multiethnic cohort in Hawaii over a 14-year period. Study participants in the top quintile of grain fiber intake had a 10 percent reduction in diabetes risk, while diabetes risk was reduced by 22 percent among men in the highest quintile of vegetable fiber intake.

Dietary Fiber and Bowel Health

In 2005, the DGAC examined the role of fiber in laxation and bowel health. In developed countries, chronic constipation is a common disorder for adults and children. Dietary fiber from whole foods increases stool weight and improves transit time, thereby reducing constipation (DGAC, 2005). The ADA systematic review of the health implications of dietary fiber concluded

that there was a lack of data examining the impact of fiber from whole foods on outcomes in gastrointestinal diseases. This may be due to the complexity and cost of these studies (Slavin, 2008). The 2002 DRIs recommended that dose-response studies be conducted to determine the amount of fiber that needs to be ingested to promote optimum laxation so that in the future this could form the basis for a recommendation for fiber intake and provide a basis for determining functional fibers. Few fiber supplements have been studied for physiological effectiveness, so the best advice is to consume fiber in foods (Slavin, 2008).

Question 2: What is the Relationship between Whole Grain Intake and Selected Health Outcomes?

Conclusion

A moderate body of evidence from large prospective cohort studies shows that whole grain intake, which includes cereal fiber, protects against cardiovascular disease. Limited evidence shows that consumption of whole grains is associated with a reduced incidence of type 2 diabetes in large prospective cohort studies. Moderate evidence shows that intake of whole grains and grain fiber is associated with lower body weight.

Implications

Currently most Americans are not consuming adequate amounts of whole grains, which are an important source of dietary fiber and other nutrients. Enriched and fortified grains provide important nutrients; hence, individuals are encouraged to consume grains as both fiber-rich whole grains and enriched grains. To ensure nutrient adequacy, especially for folate, individuals who consume all of their grains as whole grains should include some that have been fortified with folic acid.

Total grains servings are typically over-consumed in the US, so recommendations to consume more grains are not supported by this review. Advice should be to make more grain choices as fiber-rich whole grains, rather than eat more grains. The lack of standards for whole grain foods and measuring whole grain content of foods also make any recommendations difficult to implement.

Review of the Evidence

Background

The 2005 DGA and the FDA (2006) defined whole grains, saying: "Whole grains, as well as foods made from them, include the entire grain seed, usually called the kernel. The kernel consists of three components – the bran, germ and endosperm. If the kernel has been cracked, crushed, or flaked, then it must retain the same relative proportions as they exist in the intact grain." FDA, recognizing the benefit of whole grains, established a whole grain health claim, which includes the requirement that 51 percent or more of the product weight be a whole grain ingredient. Food manufacturers can also make factual statements about whole grains on the label of their products, such as "10 grams of whole grains," "½ ounce of whole grains," and "100% whole grain oatmeal" (FDA, 2006). There is urgent need for an international definition for whole grain and methods to measure the whole grain content of foods (Frolich & Aman, 2010).

The 2005 DGAC focused on the relationship between whole grain consumption and three health outcomes—CHD, diabetes, and obesity. The 2005 DGAC reviewed 12 prospective cohort studies to ascertain the whole grain intake levels associated with the greatest health benefit. The 2005 DGAC committee concluded that consuming at least three servings (equivalent to 3 ounce in a 2,000 calorie diet) of nutrient-rich whole grains per day can reduce the risk of diabetes and CHD and helps with weight maintenance.

For this report, the Committee reviewed literature published since June 2004 on the relationship between whole grains and three health outcomes: CVD, T2D and body weight.

Whole Grain Intake and Cardiovascular Disease

Seven articles (DeMoura, 2009; Kelly, 2007; Mellen, 2008; Brownlee, 2010; Djousse, 2007; Flint, 2009; Nettleton, 2008) met the inclusion criteria and were reviewed to determine the effect of whole grain consumption on CVD (two systematic reviews, one meta-analysis, one RCT, and three prospective cohort studies). The importance of the need for an agreed upon definition for whole grains was noted in the DeMoura et al.(2009) review. Their initial inclusion criteria required studies to explicitly state the use of the FDA definition for whole grains, 51percent of weight being whole grains, to be eligible for review. Using this standard, only two RCTs, one prospective cohort study, and one cross-sectional study were identified for review.

A second, broader set of inclusion criteria used a minimum level of 25 percent of whole grain by dry weight to assign values for whole grains and added bran and/or germ along with whole grains. RCTs conducted with individual whole grains, such as whole grain barley, oats, and rye, were included in the broader definition group. Six RCTs found a beneficial effect of oats on CVD

outcomes and five found no significant changes. Four RCTs with barley showed reduction in plasma total cholesterol and LDL cholesterol. The authors concluded that, for the restricted assessment, while two observational studies found a significant reduction in CVD-related surrogate endpoints, there were not supporting intervention studies, and thus, insufficient evidence to support a whole grain health claim for CVD risk reduction. Using the broader definition that included added bran and/or germ along with whole grains, the authors concluded that the evidence supported a whole-grain health claim for reduced risk of CVD.

Two systematic reviews/meta-analyses found a protective effect of whole grains on CVD. Kelly et al.(2007), in a systematic review and meta-analysis of nine RCTs (eight oat, one rye), reported a significantly lower total cholesterol and LDL-cholesterol with higher whole grain (oat, rye) intake. Mellen et al.(2008), in a meta-analysis of seven prospective cohort studies, also reported a protective effect of whole grains on CVD. Mellen (2008) did not evaluate the criteria that the studies used to quantify whole grain intake. It is likely that a minimum content of 25 percent whole grain by weight, the Jacobs algorithm (AJCN 1999), was used in most cases.

More recent studies have attempted to use grams of whole grains as the measure of whole grains in foods. Flint et al. (2009) used weight of whole grain in their hypertension analysis and found that both whole grains were protective for incident hypertension.

Brownlee et al. (2010) examined markers of cardiovascular risk in a large (n=266) intervention study with high-risk participatns (BMI>25 kg/m^2). Participants who routinely consumed few whole grain products were randomized to consume 60 g whole grains/day for 8 weeks or 60 g whole grains/day for 8 weeks and then 120 g whole grains/day for 8 more weeks. Markers of CVD risk were measured at baseline, 8 and 16 weeks. Outcome data for the two intervention groups was averaged and then compared to the control group. There were no differences in fasting plasma lipid profile, indicators of inflammation, coagulation, or endothelial function.

Two prospective cohort studies examined whole grain intake and the incidence of heart failure (HF). Djousse and Graziano (2007) concluded that there was an inverse association between whole grain breakfast cereal consumption and the risk of HF. Similarly, Nettleton et al. (2008) concluded that in their large population-based cohort of the ARIC study (n = 14,153 African-American and white adults) whole-grain intake was associated with lower HF risk. The multivariate-adjusted HF risk for whole-grain intake was 0.93 ($p<0.05$) for each one serving per day increase in whole grain consumption.

Whole Grain Intake and Type 2 Diabetes

Four articles (DeMunter, 2007; Priebe, 2008; Kochar, 2008; Brownlee, 2010) were reviewed to determine the effect of whole grain consumption on the incidence of T2D. The four papers

included a systematic review/meta-analysis of six prospective cohorts, as well as a separate prospective cohort study (DeMunter, 2007), a systematic review of 12 studies (one RCT and 11 prospective cohort studies of which 5 were relevant to this question; Priebe, 2008), a randomized controlled trial (Brownlee, 2010), and a prospective cohort study (Kochar, 2008).

Both systematic reviews reported that whole grain intake was inversely associated with risk of T2D. They included a common subset of 5 prospective cohorts; one conducted a pooled analysis and the other did not. The systematic review/meta-analysis (DeMunter et al, 2007) pooled the data of six prospective cohort studies (n = 286,125 predominantly black and white male and female participants with 10,944 incident cases of T2D) and found that a two-serving-per-day increment in whole grain consumption was associated with a 21% decrease in risk of T2D after adjustment for potential confounders and BMI ($p<0.001$).

Priebe (2008), reported on five prospective cohort studies that examined the effect of whole grain foods and found an inverse association ranging from a relative risk of 0.67 to 0.79. After excluding studies that did not correct for family history of diabetes (Meyer 2000; Montonen 2003) and physical activity (Montonen 2003), the observed effect in the remaining three studies was a relative risk of 0.70, 0.73 and 0.73.

A prospective cohort study, with 19 years of follow-up, compared the highest and lowest category of ready-to-eat whole grain breakfast cereal consumption and found that the relative risk for T2D was 0.63 ($p< 0.0001$) (Kochar 2008), although the authors noted problems with their simplified food frequency questionnaire which did not collect data that would allow them to control for total energy intake and other nutrients such as fiber and magnesium.

Some randomized trials have measured biomarkers of interest in diabetes with intake of whole grains. An example is the WHOLEheart study, which found no differences in serum glucose or insulin with consumption of whole grain foods (Brownlee, 2010).

Whole Grain Intake and Body Weight

Eight studies were reviewed to examine the relationship between whole grain consumption and body weight (Harland and Garton, 2007; Williams, 2008; Behall, 2006; Katcher, 2008; Brownlee, 2010; Lutsey, 2007; McKeown, 2009; Van der Vijver, 2009). The two large systematic reviews provide evidence that whole grain intake is associated with lower body mass index (BMI) and protects against weight gain and adiposity, but did include cross-sectional studies. Pooled analysis of 15 observational studies found a difference in BMI ($p<0.0001$), reduced waist circumference ($p= 0.03$), and lower waist:hip ratio ($p=0.0001$) with higher whole grain intakes (Harland and Garton, 2007). Williams et al. (2008) examined 20 studies, including 11 studies of dietary patterns, 5 RCTs, and 4 observational studies and concluded that there was strong evidence that a diet high in whole

grains was associated with lower BMI, smaller waist circumference, and reduced risk of being overweight.

Behall (2006) compared the effects of feeding three whole-grain diets on blood pressure with weight as an ancillary outcome. Participants (n=25) consumed a controlled Step I diet for 2 weeks after which approximately 20 percent of energy was replaced with whole wheat/brown rice, barley, or half wheat-rice/half barley, for 5 weeks each. Participants lost approximately 1 kg during the study. In the RCT by Katcher et al. (2008) overweight participants (n=50) were advised to avoid whole grains foods or obtain all of their grain servings from whole grains for 12 weeks. Body weight, waist circumference, and percentage body fat decreased significantly in both groups over the study period, but there was a significantly greater decrease in percentage body fat in the abdominal region in the whole grain group compared to the refined grain group.

Three recent cross-sectional studies also found that whole grain intakes were associated with lower BMI and adiposity. Analysis of a MESA study of men and women comparing the extreme quintiles of whole grain intake found a difference in BMI (Lutsey, 2007). Similarly, McKeown et al. (2009) found that in older adults, after multivariate adjustment comparing the extreme quartiles of consumption, whole-grain intake was inversely associated with BMI percent body fat, and percent trunk fat mass measured by whole-body dual-energy X-ray absorptiometry. In the Netherlands, Van de Vijver et al. (2009) assessed the association of whole-grain and cereal fiber intake with BMI and the risk of being overweight in older adults. They reported an inverse association between whole-grain consumption and BMI. Fiber and cereal fiber intake were inversely associated with BMI in men only.

In the WHOLEheart study (Brownlee, 2010), no differences were found in BMI, percentage body fat, or waist circumference with up to 16 weeks of self-reported consumption of whole grain foods compared to refined grain foods in *ad libitum* participants.

Question 3: What is the Relationship Between the Intake of Vegetables and Fruits, not Including Juice, and Selected Health Outcomes?

Conclusion

Consistent evidence suggests at least a moderate inverse relationship between vegetable and fruit consumption with myocardial infarction and stroke, with significantly larger, positive effects noted above five servings of vegetables and fruits per day. Notwithstanding prior work on dietary patterns that emphasize vegetables and fruits, insufficient evidence published since 2004 is available to assess the independent relationship between vegetable and fruit intake and blood pressure or serum cholesterol. The evidence for an association between increased fruit and vegetable intake and lower

body weight is modest with a trend towards decreased weight gain over 5+ years in middle adulthood. No conclusions can be drawn from the evidence on the efficacy of increased fruit and vegetable consumption in weight loss diets. Limited and inconsistent evidence suggests an inverse association between total vegetable and fruit consumption and the development of type 2 diabetes. Evidence also indicates that some types of vegetables and fruits are probably protective against some cancers.

Implications

Vegetables and fruits are nutrient-dense and relatively low in calories. In order to meet the recommended intakes, Americans should emphasize vegetables and fruits in their daily food choices, without added solid fats, sugars, starches or sodium to maximize health benefits. Significant favorable associations between vegetable and fruit consumption and health outcomes appear to be linked to a minimum of five servings per day and positive linear effects may be noted at even higher consumption levels. While the impact of increased vegetable and fruit consumption per se is unclear for some chronic diseases and markers (blood lipids, glucose control, T2D, and weight loss), improvements in preventing CVD and certain cancers, especially cancers of the alimentary tract, may occur with increased consumption of these foods. Additionally, there is evidence that vegetables and fruits, when considered as part of a dietary pattern, are associated with improved weight and health outcomes (see ***Part D. Section 2: The Total Diet: Combining Nutrients, Consuming Food*** for a discussion on dietary patterns and ***Part D. Section 1: Energy Balance and Weight Management*** for a discussion on energy density).

Review of the Evidence

Background

Vegetable and fruit consumption has long been associated with good health probably due to their high vitamin, mineral, fiber, and phytochemical content, yet the research is surprisingly sparse on the documented associations between vegetables and fruits and specific health outcomes. Several mechanisms for action were hypothesized in the 2005 DGAC report, including that certain nutrients may directly improve CVD risk factors or protect against cancer, that vegetables and fruits may displace or reduce intake of saturated fat, cholesterol, and total calories, or that they may influence glucose metabolism. The study of vegetables and fruits on human health is complicated by many factors, including their large variety globally, varying dietary patterns, different effects for vegetables versus fruits, and interactions with other dietary components. However, most Americans in all age-sex groups, consume substantially fewer vegetables and fruits than is recommended.

The 2005 DGAC report noted that increased vegetable and fruit intake was associated with a reduced risk of stroke and perhaps other CVD. Moreover, the report emphasized the role of vegetables and fruits in protecting against cancer, but noted that it is difficult to distinguish the role of vegetables and fruits per se (versus their fiber content) in preventing T2D or glucose intolerance.

Additionally, vegetables and fruits were noted to have a protective effect against weight gain probably mediated through reduced calorie intake.

Since 2004, a relatively small volume of work has been published regarding vegetables and fruits. The evidence from 2004 to 2009 is summarized below.

Vegetable and Fruit Intake and Cardiovascular Disease

Evidence suggests at least a moderate inverse relationship between vegetable and fruit consumption with myocardial infarction and stroke, with significantly larger, positive effects noted above five servings of vegetables and fruits per day. This evidence is based on 12 reports, including four meta-analyses (Dauchet, 2005; Dauchet, 2006; He, 2006; He, 2007) of US and European participants; six prospective studies, four of which were conducted in the US (Genkinger, 2004; Hung, 2004; Joshipura, 2009; Tucker, 2005) and two in Japan (Nakamura, 2008; Takachi, 2008), and two international case-control studies (Galeone, 2009; Nikolic, 2008). Results varied by sex, with a significant decrease for men and women reported in all-cause cardiovascular death (Genkinger, 2004; Hung, 2004; Joshipura, 2009), for men only (Tucker, 2005), for men only in terms of vegetable intake (Nakamura, 2008), and for women only in terms of fruit intake (Nakamura, 2008). In addition, Takachi (2008) found significant results for higher fruit (but not vegetable) intake in men and women. Risk for CVD is highest at consumption levels below three servings per day, results are ambiguous at three to five servings of vegetables and fruits per day, and lowest risk is associated with consumption levels above five servings per day (Dauchet, 2006; He, 2007), suggesting a linear relationship between vegetable and fruit consumption and CHD. Overall, risk reduction for CHD was estimated to be as much as 4 percent and 11 percent for stroke alone for each serving of vegetables and fruits added per day (Dauchet, 2006).

Five studies investigating blood pressure and vegetable and fruit intake were identified in the NEL search. These included the PREMIER prospective cohort study in the US (Wang, 2008), one prospective study in Spain (Nuñez-Cordoba, 2009); cross-sectional studies in Iran (Mirmiran, 2009), Japan (Utsugi, 2008) and India (Radhika, 2008). Two studies showed no association between total vegetable and fruit intake and blood pressure (Mirmiran, 2009) and hypertension (Nuñez-Cordoba, 2009). Utsugi et al. (2008) showed a significant positive relationship with vegetable and fruit consumption and lower risk of home-measured hypertension. The Wang et al. (2008) study showed vegetable and fruit consumption was inversely associated with both systolic and diastolic blood pressure at 6 months but not at 18 months.

The US results support the work reviewed in the 2005 DGAC report, but the international studies do not. The variation in results may be due to differences between these international

population samples and typical American patterns in baseline consumption levels of vegetables and fruits, types of vegetables and fruits consumed, and overall dietary patterns.

Blood lipids are traditionally used as an intermediate indicator or marker for CVD. The evidence testing the effect of vegetable and fruit intake on blood lipids is sparse, but suggests an associative trend between an increased consumption of vegetables and fruits with lower total and LDL-blood cholesterol levels. The evidence is based on three reports since 2004, including one limited trial (Kelley, 2006) and two cross-sectional studies (Mirmiran, 2009; Radhika, 2008). The trend is apparent for total and LDL-cholesterol, and persists even after adjustment for education, physical activity, and fat intakes. However, significance occurs only when the highest levels of vegetable and fruit intake are compared to the lowest levels of intake and the mechanisms of action are unknown.

Vegetable and Fruit Intake and Body Weight

A modest association with decreased weight gain over 5 or more years in middle adulthood has been reported with increased vegetable and fruit. However, based on current studies, no conclusions can be drawn about the efficacy of increasing vegetable and fruit consumption in achieving weight loss nor can any distinction be made about the relative influence of fruits versus vegetables on weight status.

The review of evidence regarding weight gain and vegetable and fruit consumption was based on11 studies (Bes-Rastrollo, 2006; Buijee, 2009; Davis, 2006; Fujioka, 2008; Goss, 2005; He, 2004; Ortega, 2006; Radhika, 2008; Tanumibardjo, 2009; Vioque, 2008; Xu, 2007). These studies were conducted around the globe and varied considerably in length of observation. Two of the RCTs (Fujioka, 2008; Ortega, 2006) collected data at an endpoint of only 6 weeks; a third RCT evaluated participants at 3, 12, and 18 months. All indicated small, but significant, and nonsustainable weight loss over time with an intensive addition of vegetables and fruits to the diet. Similar results showing weak inverse relationships between vegetable and fruit consumption and weight gain were noted in the prospective (Buijsee, 2009; He, 2004; Vioque, 2008), case control (David, 2006) and cross-sectional studies (Bes-Rastrollo, 2006; Goss, 2005; Radhika, 2008) that followed participants over a longer time. The evidence is insufficient to ascertain the value of vegetable and fruit consumption in weight loss diets.

Vegetable and Fruit Intake and Type 2 Diabetes

In a review of five articles describing prospective cohort studies, the evidence is inconsistent but suggests an inverse association between the development of T2D and total vegetable and fruit

consumption (Liu, 2004), a direct association with potato (french fry) consumption (Halton, 2006b), and no significant effect of tomato-based products (Wang, 2006). Another study indicated that total vegetables as well as vegetable subgroups, but not fruit, may have a preventive effect (Villegas, 2008). Conversely, the Nurses' Health Study (Bazzano, 2008) indicated no association between T2D risk and total vegetable and fruit consumption, but total fruit and green leafy vegetables were inversely associated. The number of vegetable and fruit servings in these five studies ranged from about 2.5 servings to more than 10 servings per day and sample sizes were large in all five cohort studies ranging from 35,000 to 84,000 participants (Bazzano, 2008; Halton, 2006b; Liu, 2004; Villegas, 2008; Wang, 2006). The effect size was variable ranging from a multivariate relative risk of 0.82 (Bazzano, 2008) to 1.04 (Wang, 2006) and 1.21 (Halton, 2006b) when comparing lowest quintiles to highest quintiles. However, the evidence is insufficiently strong to draw firm conclusions.

Vegetable and Fruit Intake and Cancer

The DGAC chose not to conduct an independent systematic review of vegetables and fruits and cancer due to the comprehensive and recent report by the WCRF/AICR (2007). The DGAC chose instead to review the WCRF/AICR findings (see summary Table D4.2 at the end of the chapter). Types of cancer examined by the WCRF/AICR Panel include cancers of the esophagus, stomach, colorectum, pancreas, liver, prostate, cervix, endometrium, ovary, breast, skin, and mouth, pharynx, larynx, and nasopharynx. Broadly speaking, there is no general agreement on classification of vegetables and fruits to drive comparisons in the research questions. The WCRF/AICR Panel examined the evidence by starchy and non-starchy vegetables. In their analysis, starchy vegetables were combined with cereal grains, roots, tubers and plantains. The non-starchy vegetables were categorized into subtypes (cruciferous, allium [e.g., garlic], green leafy, tomatoes, and white or pale vegetables) and whether they are eaten in raw (salad) or cooked forms. Studies also were separated by whether the conclusions were based on vegetable intakes alone or vegetables and fruits combined. In addition, evidence was examined in vegetables and fruits containing certain micronutrients, including folate, carotenoids (spinach, kale, butternut squash, pumpkin, red bell pepper, carrots, tomatoes, cantaloupe and sweet potatoes), lycopene (tomatoes), other flavinoids or phytochemicals, vitamin C and other vitamins.

The WCRF/AIRC Panel found that non-starchy vegetables as a group as well as non-starchy vegetables and fruits in combination had a significant and consistent protective effect against cancer of the mouth, pharynx, and larynx, as well as esophageal cancer at least among the highest consumers of vegetables and fruits. Some studies suggested a dose response. Cruciferous vegetables, green leafy vegetables, and tomatoes did not have a significant association for these cancers as a

separate exposure, but 16 of 18 cohort studies of carrot consumption indicate a statistically significant effect. Raw vegetables show a consistent association (16 of 16 case-control studies) with decreased risk of esophageal cancer. A decreased risk of stomach cancer was associated with green-yellow vegetables, but not with green, leafy vegetables, tomatoes, or white or pale vegetables. Data about an association with nasopharyngeal cancer are too sparse and the data relating non-starchy vegetables to colorectal cancer are too inconsistent to draw a firm conclusion. Limited evidence suggests that non-starchy vegetables protect against lung, ovarian, and endometrial cancers. The evidence is sparse but fairly consistent that allium vegetables (such as onions, garlic, leeks, and chives) probably protect against stomach and colorectal cancer and that carrots may protect against cervical cancer.

In their analysis, the WCRF/AICR Panel combined starchy vegetables with other starchy plant foods, including grains, tubers (including potatoes), plantains (excluding bananas), and roots, recognizing that these foods have to be prepared or cooked in some way to make them edible. The panel concluded that all foods in the starchy vegetable group as well as starchy vegetables and fruits in combination have an insubstantial effect on the risk of any cancer.

According to the WCRF/AICR Panel, fruits as a group, including fruit subtypes, show consistent evidence suggesting that they protect against mouth, pharynx, larynx, and esophageal cancer, though most of the studies are case-control designs. The evidence for a protective effect of fruits on lung cancer is convincing with a dose-response relationship. Evidence linking fruits to nasopharyngeal cancer, pancreatic cancer, colorectal, and liver cancer is too sparse and/or inconsistent to draw conclusions.

Micronutrients in vegetables and fruits that have been studied for risk of cancer include beta-carotene and lycopene, folate, Vitamin C, Vitamin D, Vitamin E, quercetin, pyridoxine, and selenium (see ***Part D. Section 2: Nutrient Adequacy*** for additional information on folate and health outcomes). Foods containing carotenoids probably protect against cancers of the mouth, pharynx, larynx, and esophagus as well as lung cancer with a dose-response relationship, but they are unlikely to have a substantial effect on prostate cancer or non-melanoma skin cancer. Foods containing folate probably protect against pancreatic cancer. A substantial amount of consistent evidence indicates that foods containing lycopene, especially cooked tomato products, probably protect against prostate cancer.

Studies about the effect of dietary vitamin E show non-significant decreased risk of esophageal and prostate cancer and much of the evidence is of poor quality. A sparse amount of evidence for foods containing selenium suggest this mineral may protect against lung cancer and stomach cancer, whereas a substantial amount of data indicate it may protect against colorectal cancer, but these studies are from case-control designs only.

Part of the healthful effect of vegetables and fruits, including protection against cancer risk, may be due to the effect of phytochemicals. Technically, phytochemicals are not essential to the diet, so no daily requirement has been established for them, but they are bioactive and there may be as many as 100,000 different compounds. Future research will require assessment of these compounds and the possible mechanisms that may be associated with health. Only then can the amounts needed for a public health effect be noted, both in foods and in herbs and spices.

Question 4: What is the Relationship between Glycemic Index or Glycemic Load and Body Weight, Type 2 Diabetes, Cardiovascular Disease, and Cancer?

Conclusion

Strong and consistent evidence shows that glycemic index and/or glycemic load are not associated with body weight and do not lead to greater weight loss or better weight maintenance. Abundant, strong epidemiological evidence demonstrates that there is no association between glycemic index or load and cancer. A moderate body of inconsistent evidence supports a relationship between high glycemic index and type 2 diabetes. Strong, convincing evidence shows little association between glycemic load and type 2 diabetes. Due to limited evidence, no conclusion can be drawn to assess the relationship between either glycemic index or load and cardiovascular disease.

Implications

When selecting carbohydrate foods, there is no need for concern with their glycemic index or glycemic load. What is important to heed is their calories, caloric density, and fiber content.

Review of the Evidence

Background

There has been a great deal of interest as to whether glycemic index and glycemic load can predict the risk of chronic disease. The Committee felt that the question should be investigated further by looking at any new data available since the 2005 DGAC Report. The glycemic index is a classification system proposed to quantify the relative blood glucose response to consumption of carbohydrate-containing foods. Operationally, it is the area under the curve for the increase in blood glucose after the ingestion of a set amount of carbohydrate in a food (e.g., 50 g) during the 2-hour postprandial period, relative to the same amount of carbohydrate from a reference food (white bread or glucose) tested in the same individual under the same conditions and using the initial blood glucose concentration as a baseline.

The glycemic load is an indicator of the blood glucose response or insulin demand that is induced by total carbohydrate intake. It is calculated by multiplying the weighted mean of the dietary glycemic index of the diet of an individual by the percentage of total energy from carbohydrate.

Glycemic Index or Load and Body Weight

Current evidence shows that the glycemic index and/or glycemic load are not associated with body weight and do not lead to greater weight loss or better weight maintenance. Evidence from RCTs shows no difference between high glycemic index and low glycemic index diets on weight loss in studies longer than 8 weeks. Evidence from fewer RCTs show the same for high glycemic load versus low glycemic load. The Committee reviewed 22 studies published since 2005. Of these, 13 were RCTs, two were prospective cohort studies, and seven were cross-sectional studies.

Seven RCTs compared high versus low glycemic index or high versus low glycemic load in a reducing diet protocol. Of these, two studies (Abete, 2008; de Rougemont, 2007) showed a significant weight loss difference of 2.3 kg and 0.8 kg after 8 and 5 weeks with a greater drop in the low glycemic index diet. The other five RCTs (Phillipou, 2009; Pittas, 2005; Raatz, 2005; Sichieri, 2007; Sloth, 20004) showed no difference in weight loss in much longer studies lasting from 16 to 76 weeks. Three RCTs (Ebbeling, 2007; Maki, 2007; Pereira, 2004) compared low glycemic load diets versus low-fat diets. They did not show any differences in weight loss between the diets. One RCT (Pal, 2008) compared the effect of a high glycemic index versus low glycemic index breakfast and found no difference in weight after 3 weeks. One RCT (McMillan-Price, 2006) compared four diets, two of which were high carbohydrate and two were high protein, with either high or low glycemic index. No difference in weight loss was found with any of the diets over 12 weeks. In summary, the RCTs overwhelmingly report no difference between low and high glycemic index diets in achieving weight loss during reducing diet programs or maintenance diet programs. The data on glycemic load are less numerous but report similar results.

Two prospective cohort studies also examined this issue (Deienlein, 2008; Hare-Bruun, 2006). The first was a gestational diabetes study that found glycemic load not to be associated with gestational weight gain or weight gain ratio. The second followed normalweight participants for 6 years and showed no significant association between glycemic load and change in weight in either men or women. It showed no association between glycemic index and change in weight in men, but did show an association of glycemic index with lower weight gain in women. These studies suggest that in men there is no relation between either glycemic index or load and weight, and in women there is no relation of glycemic load and weight, but a possible relation of glycemic index and weight.

Seven cross-sectional studies also have been carried out, comprising a total of 21,231 participants, both children and adults. Of these, six (Hui, 2006; Lau, 2006; Liese, 2005; Mendez, 2009; Milton, 2007; Nielsen, 2005) showed no association between glycemic index or load and weight or BMI. One study (Murakami, 2007) did show a positive correlation between glycemic index and glycemic load with BMI in young lean Japanese women. These cross-sectional studies support the conclusion that glycemic index or load and weight are not associated.

Glycemic Index or Glycemic Load and Type 2 Diabetes

Evidence is mixed as to whether there is an association between a high glycemic index and T2D. Little evidence suggests that a high glycemic load is associated with T2D. This conclusion is based on 10 longitudinal prospective observational studies published since 2000 (Barclay, 2007; Halton, 2008; Hodge, 2004; Krishnan, 2007; Mosdol, 2007; Sahyoun, 2008; Schulz, 2006; Schulze, 2004; Stevens, 2002; Villegas, 2007). No RCTs were reported. Of the 10 prospective observational studies, glycemic index was positively associated with T2D in five reports (Halton, 2008; Krishnan, 2007; Schulz, 2006; Schultze, 2006; Villegas, 2007). Four other longitudinal studies reported no association of glycemic index with T2D (Barclay 2007; Mosdol 2007; Sahyoun 2008; Steven 2002). One longitudinal study reported an inverse association (Hodge, 2004).

Of the 10 prospective observational studies, one study reported a significant, positive association between glycemic load and risk of T2D during 20 years of follow-up in comparison of extreme deciles (Halton, 2008). Six studies found no relationship (Barclay, 2007; Hodge, 2004; Krishnan, 2007; Sahyoun, 2008; Schulz, 2006; Stevens, 2002). Two studies found an inverse association (Mosdol, 2007; Villegas, 2007).

Glycemic Index or Glycemic Load and Cardiovascular Disease

Although the evidence for an association between high glycemic index or high glycemic load and CVD is more negative than positive, the evidence available is inadequate to come to a firm conclusion on this question.

Eight reports have been published since 2000 (Beulens, 2007; Kaushik, 2009; Levitan, 2007; Liu, 2000; Halton, 2006a; Oh, 2005; Tavani, 2003; van Dam, 2000). Of these, three are from the same Nurses' Health Study. After 10 years of follow-up, Liu et al. (2000) reported glycemic index was associated with CVD. A high glycemic load was associated with CVD in women with a BMI greater than 23 but not with a BMI less than 23 kg/m2. After 20 years of follow-up, Halton (2006a) reported both a high glycemic index and load to be associated with CVD. Oh (2005) reported on the associations between dietary carbohydrate, glycemic index, glycemic load, and stroke. They found no

association between glycemic index and stroke. They found a positive association between glycemic load and total stroke in women with a BMI greater than 25 but not in those with a BMI less than 25 kg/m2.

Five other reports are available. Of these, Beulens (2007) found a positive trend for an association between glycemic load and stroke, but not for glycemic index and stroke. He found a positive trend between glycemic index and CHD and between glycemic load and CHD only for women with a BMI greater than 25 kg/m2.

Kauschik (2009) found an association between both glycemic index and glycemic load and death from stroke. Levitan (2007) found no association between glycemic index or glycemic load with myocardial infarction, ischemic stroke, or all-cause mortality. van Dam (2000) found no association of either glycemic index or glycemic load and CHD.

One case-control study (Tavani, 2003) reported on the relation between glycemic index and glycemic load and the risk of non-fatal acute myocardial infarction. No significant association was found.

Glycemic Index or Glycemic Load and Cancer

The epidemiological evidence for an association between glycemic index or load and cancer is overwhelmingly negative. Twenty-eight reports have been published since 2005. Of these, 20 are prospective longitudinal observation studies, one is a cross-sectional observation study, five are case-control studies, and two are case-cohort studies.

Of the 20 prospective longitudinal observational studies, 18 studied the association between glycemic index and cancer. One showed a very weak positive association between glycemic index and total cancer risk (George, 2009), while thirteen studies found no association between glycemic index and specific types of cancer including pancreatic (Heinen, 2008; Johnson, 2005; Nothlings, 2007; Patel, 2007; Silvera, 2005), breast (Giles, 2006; Lajous, 2008; Sieri, 2007; Silvera, 2005), endometrial (Cust, 2007; Larsson and Friberg, 2007) stomach (Larsson, 2006), and ovarian (Silvera, 2007) cancers. Varying results were found for colorectal cancer with no association reported in three studies (Larsson, 2007; McCarl, 2006; Michaud, 2005) and an inverse association reported by Strayer et al. (2007).

Of the 20 prospective longitudinal observational studies, all studied the association between glycemic load and cancer. Two showed a positive association for total cancer (George, 2009) and ovarian cancer (Silvera, 2007). However, most studies reported no association between glycemic load and cancer, including pancreatic (Heinen, 2008; Johnson, 2005; Nothlings, 2007; Patel, 2007; Silvera, 2005), breast (Giles, 2006; Lajous, 2008; Sieri, 2007; Silvera, 2005), endometrial (Cust, 2007; Larsson

and Friberg, 2007), and stomach (Larsson, 2006) cancers. Similar to glycemic index, there were mixed results regarding the relationship between glycemic load and colorectal cancer with five studies finding no association (Kabat, 2008; Larsson, 2007; McCarl, 2006; Michaud, 2005; Strayer, 2007) and one study reporting an inverse association (Howarth, 2008).

The two case-cohort studies reported no association of either glycemic index or load with pancreatic (Kabat, 2008) or colorectal (Weijenberg, 2008) cancers. Similarly, one cross-sectional observational study showed no association between either glycemic index or load and colorectal adenomas (Flood, 2006a).

The five available case-control reports reported mixed results. Of these, three found glycemic index to be significantly associated with prostate (Augustin, 2004), gastric (Bertuccio, 2009), and thyroid (Randi, 2008) cancers, and two found no association with breast cancer (Lajous, 2005; McCann, 2007). Similarly, three found glycemic load to be significantly associated with cancer of the breast (Lajous, 2005), prostate (Bertuccio, 2009), or thyroid (Randi, 2008) and found no association for breast (McCann, 2007) and prostate (Augustin, 2004) cancers.

Question 5: In Adults, What Are the Associations between Intake of Sugar-sweetened Beverages and Energy Intake and Body Weight?

Conclusions

Limited evidence shows that intake of sugar-sweetened beverages is linked to higher energy intake in adults. A moderate body of epidemiologic evidence suggests that greater consumption of sugar-sweetened beverages is associated with increased body weight in adults. A moderate body of evidence suggests that under isocaloric controlled conditions, added sugars, including sugar-sweetened beverages, are no more likely to cause weight gain than any other source of energy.

Implications

Added sugars, as found in sugar-sweetened beverages (SSB), are not different than other extra calories in the diet for energy intake and body weight. Thus, reducing intake of all added sugars, including sucrose, corn sweetener, fructose, high fructose corn syrup, and other forms of added sugars, is a recommended strategy to reduce calorie intake in Americans. Intake of caloric beverages, including SSB, sweetened coffee and tea, energy drinks, and other drinks high in calories and low in nutrients should be reduced in consumers needing to lower body weight. While still moderate, recent evidence is stronger than prior evidence available to assess the relationship between sugar-sweetened beverages and increased body weight.

Review of the Evidence

Background

The 2005 DGAC asked the following question: "What is the significance of added sugars intake to human health?" Their conclusion was, "Compared with individuals who consume small amounts of foods and beverages that are high in added sugars, those who consume large amounts tend to consume more calories but smaller amounts of micronutrients. Although more research is needed, available prospective studies suggest a positive association between the consumption of SSB and weight gain. A reduced intake of added sugars (especially SSB) may be helpful in achieving recommended intakes of nutrients and in weight control."

The role of dietary sugars in the current obesity epidemic is much debated, with many opposing views. A review by Saris (2003) concluded that the fat content of the diet is the most important contributor to overconsumption of calories and that the carbohydrate content, regardless of carbohydrate type, is relatively benign, with little evidence for direct negative effects of dietary sugar on body weight. Another recent review by the same group (van Bakk, 2008) concluded that there is insufficient evidence that an exchange of sugar for non-sugar carbohydrates in the context of a reduced fat *ad libitum* diet or energy-restricted diet results in lower body weight. They also noted that observational studies suggest a possible relationship between consumption of SSB and body weight, but that current supporting evidence from RCTs of sufficient size and duration was insufficient to support a difference between liquid and solid sugar intake in bodyweight control.

Most reviews have asked the question whether intake of SSB is linked to obesity. As described by Olsen and Heitmann (2009), the prevalence of obesity has increased in the past 30 years, and at the same time consumption of soft drinks has increased sharply. They reviewed the literature on calorically-sweetened beverages and obesity, relative to adjustment for energy intake. No cross-sectional studies were included. They concluded that a high intake of calorically-sweetened beverages can be regarded as determinant for obesity. However, there seems to be no support for an association between intake of calorically-sweetened beverages and obesity as mediated through increased energy intake, suggesting that alternative biological explanations should be explored. Other studies that examined obesity risk and intake of SSB in adults in US as measured with CSFII and NHANES datasets found no association between obesity risk and sugar intake (Sun, 2007).

Intake of SSB and adiposity was reviewed by Bachman et al. (2006). They described four mechanisms to explain the possible association between sweetened beverages and increased overweight or obesity, including excess caloric intake, glycemic index and glycemic load, lack of effect of liquid calories on satiety, and displacement of milk. They report inconsistent results across studies. The strongest support was for the excess caloric intake hypothesis, but the findings were not conclusive. They suggest that assigning possible links between sweetened beverage consumption and

adiposity requires research that compares and contrasts specific mechanisms, especially in populations at risk of obesity, while controlling for likely confounding variables.

Based on these existing reviews, the 2010 DGAC asked the questions whether intake of SSB was related to energy intake and body weight in adults. The Committee included systematic reviews and primary research studies in the NEL review. Because studies with stronger methodology were available in 2010, the Committee excluded cross-sectional studies. However, some of the systematic reviews included in the NEL review considered cross-sectional studies. The Committee therefore places more confidence in the reviews that excluded cross-sectional studies in our conclusions.

Methodological Challenges

Sugar is a ubiquitous term, but one that is not easy to define and measure. Analytical methods can measure total sugar in foods and nutrient databases and Nutrition Facts labels include values for total sugars. Added sugars are typically calculated values and can be added to dietary assessment tools in nutrition studies. As described by Ruxton et al. (2010), exact definitions of sugar are often omitted from studies, making it difficult to determine exactly what was under investigation. This hinders the ability to compare studies. Studies can report specific sugars—sucrose, glucose, fructose, or just say "sugar" to mean mono- and disaccharides. "Total sugars" means all dietary sugars whether added or naturally occurring. "Sugar-containing" is thought to mean foods and beverages that contain sugar. In epidemiologic studies, it is often easier to assess intake of SSB as these can be counted in food frequency instruments. This tends to be non-specific because fruit-ades, fruit punches, sport drinks, energy drinks, and juices that are not 100 percent juices may or may not be counted in these systems.

Two studies in the United Kingdom used non-milk extrinsic sugars (NMES) and reported an inverse relationship between NMES and BMI (Gibson, 2007a; Gibson, 2007b) though no relationship was found between body weight status and sugar intake in a New Zealand population (Parnell, 2008). Thus, assessment of "added sugars" or "extrinsic sugar" is challenging because no analytical methods exist with which to measure sugars added to foods. Additionally, studies use different techniques to assess added sugars intake. Reliable and standardized measures of exposure to added sugars are necessary to draw meaningful conclusions. Currently, the best assessments involve counting frequency of intake of SSB in epidemiologic studies.

Sugar-Sweetened Beverages and Energy Intake

To answer this question the Committee reviewed one meta-analysis (Vartanian, 2007) and four trials (Flood, 2006b; Reid, 2007; Soenen, 2007; Stookey et al., 2007) published since 1990. Vartanian

et al. (2007) conducted a meta-analysis that examined the association between soft drink consumption and various health outcomes, including energy intake. It should be noted that this analysis included some unpublished data as well as cross-sectional studies. However, they conducted separate analyses based on study design and outcomes. Of the 88 studies in the review, three longitudinal studies and 11 experimental studies examined the relationship between soft drink consumption and energy intake in adults. Although effect size was small, the authors concluded that there was a clear positive association between soft drink intake and energy intake.

Two additional primary studies also support a relationship between the intake of SSB and increased energy intake. Flood et al. (2006b) examined the impact of beverage type (cola, diet cola, or water) and size (12 or 18 fluid ounces) on intake at an *ad libitum* lunch. Energy intake from food consumed at lunch did not differ across conditions. However, when the energy from beverages was added to the energy consumed from food, mean total energy intake at lunch was greater when regular cola was served as compared to the other beverages, regardless of portion size.

Reid et al. (2007) compared the effects of supplementary soft drinks sweetened with sucrose or aspartame added to the diet over 4 weeks on dietary intake in normal-weight women. Participants consumed four 250 ml bottles of drink per day. Sucrose supplements provided 430 kcal/d and aspartame supplements provided less than 20 kcal/d. For those consuming the sucrose drink, daily energy intake was higher during the intervention phase than at baseline; women consuming the SSB consumed about 200 kcal more energy each day.

Stookey et al. (2007) compared four weight loss diets and predicted that replacing sweetened caloric beverages with water would save 200 kcal per day over 12 months. Although weight loss might be expected due to lower energy intake, the study by Stookey et al.(2007) was not an intervention trial and thus did not measure change in body weight.

Soenen and Westerterp-Platenga (2007) examined the satiating effects of HFCS and sucrose in comparison with milk and a diet drink. In this trial, participants completed four test sessions that included an *ad libitum* meal served after one of four beverages: one containing sucrose, one HFCS, one milk, and one a diet drink. All four drinks were isovolumetric (800 mL). The energy drinks were isocaloric. Test meal energy intake was lower after consumption of preloads containing sucrose or HFCS or milk (with no differences between the energy-containing preloads) compared to the diet drink preload. Total energy intake (preload + meal) with the energy-containing preloads was significantly higher than total energy intake with the diet drink preload. During the meal, energy intake from the beverage was partly compensated for. However, compensation for energy intake from the preloads containing sucrose, HFCS, or milk did not differ significantly and ranged from 30 percent to 45 percent. This study indicated that although energy intake was higher following the drinks sweetened with HFCS and sucrose compared to a diet drink preload, energy intakes were not

different than the milk preload, indicating that the added sugar did not have a unique effect on energy intake.

Sugar-Sweetened Beverages and Body Weight

The Committee addressed this question by reviewing four systematic reviews (Gibson, 2008; Malik, 2006; Ruxton, 2010; Vartanian; 2007), four RCTs (Raben, 1997; Reid, 2007; Stanhope, 2009; Surwit, 1997), and three prospective observational studies (Chen, 2009; Dhingra, 2007; Palmer, 2008).

The studies included in the systematic reviews did not use consistent methods to evaluate added sugars. Typical search terms were soft drinks, SSB, liquid sugar, and soda. The systematic reviews used different criteria to review the literature, and three reviews (Gibson, 2008; Malik, 2006; Vartanian, 2007) included cross-sectional studies, as there were limited prospective studies on the topic. Malik et al. (2006), attempted a meta-analysis, but the degree of heterogeneity among study designs made a more qualitative assessment necessary. Vartanian et al. (2007) attempted to separate out the effects in different study designs. Studies with experimental designs (five studies) showed no association with added sugar intake for body weight for adults. Significant relationships were found in longitudinal studies (three studies) for a relationship between added sugar intake and body weight, although the effect size was small. Similarly, Malik et al. (2006) concluded that epidemiologic and experimental data indicated a greater consumption of SSB is associated with weight gain and obesity. In contrast, Gibson (2008) reviewed six longitudinal and one intervention study with adults and concluded that SSB are a source of energy, but that little evidence showed that they are any more obesogenic than any other source of energy. In a recent review, Ruxton et al. (2010) concluded that recent evidence does not suggest a positive association between BMI and sugar intake. However, some studies, specifically on sweetened beverages, highlight a potential concern in the relation to obesity risk. The methods used for these systematic reviews varied and may explain the discrepancies in results.

The four trials included in the NEL review varied greatly in design. In general, when calorie intake was controlled, there were no differences in weight gain when participants consumed diets with a higher percent of calories from added sugars compared to diets with a lower percent of intake from added sugars (Raben, 1997; Stanhope, 2009; Surwit, 1997). When energy intake was not controlled, Reid et al. (2007) found a non-significant trend for weight gain among normal-weight women consuming four regular soft drinks per day compared to those consuming diet soft drinks. In a trial by Stanhope et al. (2009) that included 25 percent of energy from beverages sweetened with glucose or fructose, weight gain was observed when participants consumed self-selected diets in an outpatient setting.

The Committee also reviewed three prospective studies. Lower consumption of soft drinks was linked to weight loss in the PREMIER study (Chen, 2009). A reduction in SSB intake of one serving per day was associated with a weight loss of approximately 0.5 kg at 6 months and 18 months, and a significant dose-response trend between change in body weight and change in SSB intake also was observed. Over a mean follow-up of 4 years in the Framingham Heart Study (Dhingra, 2007), consumption of one or more soft drinks per day was associated with increased odds of developing obesity and increased waist circumference compared to drinking none.

Palmer et al. (2008) included sugar-sweetened soft drinks and fruit drinks in their analysis of T2D in a prospective cohort study of African-American women. Participants gained weight during the study, but the lowest mean weight gain occurred among those who decreased their consumption of soft drinks.

Thus, there are mixed results on this topic. RCTs report that added sugars are not different from other calories in increasing energy intake or body weight. Prospective studies report some relationship with SSB and weight gain, but it is not possible to determine if these relationships are merely linked to additional calories, as opposed to added sugars per se. The systematic reviews in this area are also inconsistent, probably based on different measures used to determine added sugars intake or intake of SSB.

OTHER RELATED TOPICS

Question 6: How are Non-caloric Sweeteners Related to Energy Intake and Body Weight?

Conclusion

Moderate evidence shows that using non-caloric sweeteners will affect energy intake only if they are substituted for higher calorie foods and beverages. A few observational studies reported that individuals who use non-caloric sweeteners are more likely to gain weight or be heavier. This does not mean that non-caloric sweeteners cause weight gain rather that they are more likely to be consumed by overweight and obese individuals.

Implications

The replacement of sugar-sweetened foods and beverages with sugar-free products should theoretically reduce body weight. Yet many questions remain, as epidemiologic studies show a positive link with use of nonnutritive sweeteners and BMI. Additionally, whether use of low calorie sweeteners is linked to higher intake of other calories in the diet remains a debated question.

Review of the Evidence

Background

Replacing sugar with low-calorie sweeteners is a common strategy to facilitate weight control (Bellisle, 2007). Intense sweeteners help lower energy density of beverages and foods, which should result in lower energy intakes. Mattes and Popkin (2008) estimate that 15 percent of the US population ingests nonnutritive sweeteners, but that percentage is increasing. Concern about negative effects of diet soft drink consumption on energy intake came from animal studies that suggested an increased food intake and weight gain following prolonged exposure to saccharin-sweetened yogurt (Swithers, 2008). This study suggested that artificial sweeteners "uncouple" a relationship between sweet taste and energy, which promoted the rats to consume more food and gain weight.

The use of non-caloric sweeteners has increased greatly over the past three decades while the incidence of obesity also has risen. Thus, cross-sectional studies suggest that intake of non-caloric sweeteners is positively associated with increased obesity. If non-caloric sweeteners are used as substitutes for higher energy yielding sweeteners, they have the potential to aid in weight management, but whether they will be effective in this regard is not found in existing literature.

The DGAC answered this question using a partial NEL review. The ADA Evidence Analysis Library conducted a search from January 1985 through March 2006 on the question, "In adults, does using foods or beverages with non-nutritive sweeteners (saccharin, aspartame, acesulfame-K, sucralose, neotame) in a calorie-restricted or *ad libitum* diet affect energy balance?" (ADA, 2009).

For adults, the conclusion was, "Using non-nutritive sweeteners in either a calorie restricted or *ad libitum* diet will affect overall energy balance only if the non-nutritive sweeteners are substituted for higher calorie food and beverages (Grade II)." For children, they concluded, "Studies do not support that the use of non-nutritive sweeteners causes weight gain. If non-caloric beverages, including non-nutritive sweeteners, are substituted for SSB, there is a potential for energy savings in adolescents (Grade III)."

Additionally, ADA conducted a review of aspartame and body weight in 2008 that included articles reviewed in 2006. In this review, they asked the question, "In adults, does aspartame affect energy balance (weight)?" The conclusion was "Use of aspartame by individuals consuming a hypocaloric diet may be associated with increased weight loss. In some cases aspartame did not affect weight loss (Grade I)."

Non-Caloric Sweeteners and Energy Intake and Body Weight

If non-caloric sweeteners are substituted for higher-calorie food or beverages, they are associated with weight loss. Observational studies find that individuals who use non-caloric sweeteners are more likely to gain weight or be heavier. This does not support that non-caloric sweeteners cause weight gain only that they are more likely to be used by overweight and obese individuals. The ADA EAL review of non-nutritive sweeteners in both adults and children served as the foundation for this review. This conclusion also is based on review of one meta-analysis (de la Hunty et al., 2006), a randomized crossover study (Flood, 2007), and a prospective cohort study (Fowler et al., 2008) published since 2006.

The meta-analysis by de la Hunty et al. (2006) supports a significant reduction in energy intakes with aspartame compared with all types of control diets except when aspartame was compared with non-sucrose controls such as water. For body weight, the analysis was conducted in three stages: (1) used all weight outcomes including follow-up weights, (2) excluded studies in which the control group gained weight and (3) excluded follow-up periods. A significant reduction in weight was seen for all three analyses. The combined effect was approximately a 3 percent reduction in body weight. The authors concluded that using foods and drinks sweetened with aspartame instead of sucrose results in a significant reduction in both energy intakes and body weight. Further, using foods and drinks sweetened with aspartame instead of those sweetened with sucrose is an effective way to maintain and lose weight.

In a prospective cohort study, Fowler et al. (2008) reported a significant positive dose-response relationship between baseline artificially-sweetened beverage consumption and incidence of overweight/obesity, incidence of obesity, and BMI change; however, this association does not establish causality.

Flood et al. (2006b) examined the impact of beverage type (cola, diet cola, or water) and size (12 or 18 fluid ounces) on intake at an *ad libitum* lunch. Participants consumed significantly more energy at lunch when cola was provided versus diet cola or water.

Question 7: What is the Impact of Liquid Versus Solid Foods on Energy Intake and Body Weight?

Conclusion

A limited body of evidence shows conflicting results about whether liquid and solid foods differ in their effects on energy intake and body weight except that liquids in the form of soup may lead to decreased energy intake and body weight.

Implications

In general, if total calorie content is held constant, there is little support for any effects on energy intake and body weight due to the calories consumed either as liquid or solid. Some studies suggest that whole foods may be more satiating than liquid foods. Food structure, specifically a whole food (apple, carrots), plays a role in satiety and decreasing food intake at subsequent meals, yet fiber added to a drink is not effective in reducing food intake at subsequent meals. Soup as a preload decreases food intake at a subsequent meal. Thus, Americans are advised to pay attention to the calorie content of the food or beverage consumed, regardless of whether it is a liquid or solid. Calories are the issue in either case.

Review of the Evidence

Background

The 2005 DGAC asked the question "What is the evidence to support caloric compensation for liquid versus solids foods?" They concluded that this was an unresolved issue and that evidence on whether liquid and solid foods differ in their effect on calorie compensation was conflicting.

The 2010 DGAC conducted a NEL review and examined literature from 2000 to present, comparing liquids to solid or semi-solid forms. In addition to examining the role of food form on energy intake and body weight, Question 8 includes additional information on food form and satiety.

Liquids versus Solids and Energy Intake and Body Weight

No consistent relationships have been reported between the form of a food and energy intake and body weight. This review included 12 studies with no consistent experimental designs. One study examined liquid calories to solid calories in the PREMIER trial (Chen, 2009). Six of the studies were crossover trials that investigated the impact of a preload before breakfast (Stull, 2008) or lunch (Almiron-Roig, 2004; Flood-Obbagy, 2009; Mattes, 2009; Mourao, 2007; Tsuchiya, 2006) on *ad libitum* intake of a meal. An additional crossover trial (Moorhead, 2006) examined the intake of carrots in various forms with a meal rather than as a preload. DiMeglio et al. (2000) conducted a longer term crossover trial that included two, 4-week interventions with daily consumption of liquid (caffeine-free soda) or solid (jelly beans) food. Finally, three studies (Rolls, 2005; Flood, 2007; Bertrais, 2001) examined soup as the liquid form.

No standard protocol has been established to answer this question, and information on food form and consumption of liquid is not collected in prospective cohort trials. Most of the available evidence to answer this question is from preload studies, in which meals are controlled for total calories and macronutrient content, and then satiety is measured for 3 hours after the meal.

Subsequent food intake is then measured by consumption of a buffet lunch and food intake for 24 hours may then be calculated.

In the one prospective study, Chen et al. (2009) examined beverage consumption in the PREMIER study at baseline, 6 months, and 18 months. Analyses considered changes in volume, calorie intake, and percentage of calories from beverages both overall and from seven categories (SSB; diet drinks; milk; 100percent juices; coffee and tea with sugar; coffee and tea without sugar or with artificial sweeteners; and alcoholic beverages). A reduction of 100 kcal per day in liquid calorie intake was associated with an approximate 0.25 kg weight loss at 6 and 18 months. In comparison, a reduction in solid calorie intake by 100 kcal/day was associated with a less than 0.1 kg weight loss at 6 and 18 months. Reductions in liquid calorie intake had a stronger effect on weight loss than did a reduction in solid calorie intake, but the difference was statistically significant only at 6 months. A significant dose-response trend between change in body weight and change in liquid calorie intake was observed at 6 and 18 months.

Consumption of solid food compared to juice in a controlled caloric load may decrease energy intake at a subsequent meal. Flood-Obbagy and Rolls (2009) examined how consuming preloads of apples in different forms (apple, applesauce, and apple juice with and without added fiber) influenced energy intake of a meal. Study participants consumed fewer calories at lunch after consuming apples compared to equal calories as applesauce, apple juice, or apple juice with added fiber. In a similar study, whole carrots were associated with less calorie intake for the remainder of the day compared to carrot juice or a carrot juice cocktail that contained all the nutrients in carrots (Moorhead, 2006).

Mourao et al. (2007) investigated the independent effect of food form on appetite and energy intake in lean and obese adults using high carbohydrate, fat, or protein food stimuli. Treatments were matched beverage and solid food forms: high carbohydrate (watermelon and watermelon juice); high protein (cheese and milk); high fat (coconut meat and coconut milk). Participants consumed the entire test food as part of an *ad libitum* meal. Regardless of the predominant energy source, the beverage form elicited a weaker compensatory dietary response than the matched solid food form. The authors concluded that inclusion of a caloric beverage in a lunch meal led to greater daily energy intake compared to customary intake or days where a solid version of the same food was ingested. This occurred regardless of the primary energy source, and there was no clear indication that the lean and obese differ in this regard.

Stull et al. (2008) assessed the effect of liquid versus solid meal replacements on appetite and subsequent food intake in healthy older adults. After an overnight fast, participants consumed meal replacement products as either a liquid or as a solid (bar) followed by *ad libitum* oatmeal. Participants consumed more calories from oatmeal after the liquid versus solid meal replacement product.

Other studies suggest that food form may affect food intake, although inconsistent study designs make it difficult to compare results. DiMeglio and Mattes (2000) examined the differential effects of matched liquid (soda) and solid (jelly beans) carbohydrate loads on diet and body weight. Participants were assigned to one of two dietary load conditions (solid: 450 kcal serving of jelly beans; liquid: 450 kcal serving of caffeine-free soda) for 4 weeks, followed by a 4 week washout period and subsequent participation in the other condition for 4 weeks. During the solid load condition, participants compensated for some of the energy in the test foods by reducing free-feeding intake such that the overall compensation score was 118 percent. However, when the liquid load was included in the diet, no compensation was observed, resulting in a compensation score of -17 percent. The authors concluded that liquid carbohydrate promotes positive energy balance, whereas a comparable solid carbohydrate elicits dietary compensation; further, body weight and BMI increased only with the liquid load.

In contrast, both Mattes and Campbell (2009) and Almiron-Roig et al. (2004) found no differences in subsequent food intake when they compared solid food to liquids in studies well controlled for macronutrients and calories. Mattes and Campbell (2009) assessed the effects of apple food form (apple, applesauce, apple juice) and timing of eating events (meal or snack) on appetite and daily energy intake. There were no treatment effects on daily energy intake.

Almiron-Roig et al. (2004) compared the impact on energy intakes of equal-energy preloads (300 kcal) of regular cola or fat-free cookies presented either 2 hour or 20 minutes before a tray lunch. Liquid or solid form had no impact on energy intakes during the test meal. Similarly, physical form had no effect when the sum of the energy intake of breakfast, preload, and lunch was considered.

In another crossover trial (Tsuchiya, 2006) participants consumed 200-kcal preloads: semisolid peach yogurt with peach pieces, peach yogurt homogenized to liquid form, peach syrup and water, or a milk-based peach and apricot beverage followed by an *ad libitum* lunch. No significant differences in energy intakes were detected across the four conditions, either for lunch alone or for total energy consumed from breakfast, preload, and lunch.

Liquids in soup may have different effects as studies find that daily soup consumers have lower daily energy intake than those who consume little soup (Bertrais, 2001), and soup pre-loads reduce food intake at a subsequent meal (Flood, 2007). Rolls et al. (2005) tested the effect on weight loss of a diet incorporating one or two servings per day of foods equal in energy but differing in energy density. Participants followed an energy-restricted diet in a 1-year trial (6-month weight loss and 6-month weight maintenance); participants were randomized to one of four intervention groups. Participants were instructed to consume daily: one serving of soup, two servings of soup, or two servings of dry snack foods. Participants in the fourth group were not provided with any specific

food to consume (comparison group). There were no significant differences in reported energy intake among the intervention groups at any time points. All four groups showed significant weight loss at 6 months that was well maintained at 12 months. The magnitude of weight loss, however, differed by group. At 1 year, weight loss in the comparison (8.1 ± 1.1 kg) and two-soup (7.2 ± 0.9 kg) groups was significantly greater than that in the two-snack group (4.8 ± 0.7 kg); weight loss in the one-soup group (6.1 ± 1.1 kg) did not differ significantly from other groups. The authors concluded that on an energy-restricted diet, consuming two servings of low energy-dense soup daily led to 50 percent greater weight loss than consuming the same amount of energy as high energy-dense snack food.

When macronutrient content of a liquid food and a solid food is balanced, there are few data that food form affects energy intake. These studies are difficult to design and conduct as the form of the food cannot be blinded (i.e., participants know that they are eating apples or drinking apple juice). In the acute studies of food intake, efforts are made to control variables, including the time allowed to consume the test food, but it is difficult to generalize these results to the eating environment of real life.

Food structure may play a role in food intake. Whole foods, such as apples and carrots, play a role in satiety and decrease food intake at a subsequent meal. When a non-viscous fiber was added to apple juice, the fiber-enriched apple juice was not as effective as the apple in reducing food intake at a subsequent meal. Thus, factors besides the fiber in whole foods may affect energy intake, including food structure and chewing.

The data with soup as a preload are often in conflict with other data on liquid calories. In a 1-year weight loss trial, consumption of two servings of soup per day led to greater weight loss than consuming the same amount of energy from two snack foods. Soup preload significantly reduced test meal and total meal energy intake in one study. Thus, the studies with soup as a liquid calorie source suggest that specific liquid calories can be an aid to weight loss and that liquid calories from soup result in reduced intake at a subsequent meal.

Question 8: What is the Role of Carbohydrate, Fiber, Protein, Fat, and Food Form on Satiety?

Conclusion

Many factors affect satiety and most studies are conducted in laboratory settings to control for variables. Thus results may not be generalized to the more complicated eating environment of the outside world. Foods high in dietary fiber generally are more satiating than low fiber foods, although some fibers added to drinks have little impact on satiety. Overall, small changes in the macronutrient content of the diet do not significantly alter satiety.

Implications

Intakes of caloric preloads, whether carbohydrate, protein, or fat, typically increase satiety. Protein and carbohydrate may be more satiating than fat, although studies are not consistent. Dietary fiber, especially from whole foods, appears to enhance satiety in studies. Not all fibers added to beverages or foods are equally satiating. In fact, some functional fibers show no effect on satiety.

Review of the Evidence

Background

Satiation and satiety are part of the body's appetite control system and are involved in limiting energy intake. Benelam (2009) summarized satiation, satiety, and their effects on eating behavior in an extensive literature review. Satiation is the process that causes one to stop eating, while satiety is the feeling of fullness that persists after eating, suppressing further consumption. Satiation and satiety are controlled by a cascade of factors that begin when a food is consumed and continues as it enters the gastrointestinal tract and is digested and absorbed. As food moves down the digestive tract, signals are sent to the brain, and gut hormones are produced that affect energy balance in a variety of ways, including slowing gastric emptying, acting as neurotransmitters, and reducing gastrointestinal secretions. These effects are proposed to influence satiety. The terms satiety and satiation are often used differently in the literature and many methods to measure each exist.

Interest in satiety and its role in obesity prevention are great, so the 2010 DGAC examined satiety's relationship between carbohydrate, fiber, protein, and fat using a non-NEL literature review.

The most common study design for satiety studies uses a test preload in which variables of interest are carefully controlled. Generally, participants rate aspects of their appetite sensations, such as fullness or hunger, at intervals and then, after a predetermined time interval, a test meal at which energy intake is measured. Longer-term studies typically provide foods or drinks of known composition to be consumed *ad libitum* and use measures of energy intake and/or appetite ratings as indicators of satiety. Satiety tests are often conducted with liquids where differences in macronutrient content are more easily formulated. Other studies use muffins or bars. However, it is difficult to formulate and blind products that vary greatly in the content of fiber, protein, fat, and carbohydrate.

Measurement of satiety is complicated because many internal signals also influence appetite, such as bodyweight, age, sex, habitual diet, exercise, and dietary restraint. These acute studies are typically done in laboratory settings where variables can be controlled. It is extremely difficult to conduct satiety studies in free-living individuals, so most studies are conducted in a laboratory setting. Usually visual analogue scales are used to monitor hunger, fullness, and motivation to eat.

Studying the effects of one variable in food or drink while keeping others constant is inherently difficult, especially if researchers do not want the differences to be obvious to participants. Adding fiber to foods decreases energy density and often palatability, both of which can affect satiety (Slavin and Green, 2007).

External factors that affect satiety include palatability, variety, portion size, sleep, physical activity, television viewing and other distractions, and social situations (Benelam, 2009).

Macronutrients have no consistent differences in satiety, although general statements are often given that protein is most satiating, followed by carbohydrate, and then fat. Recent studies on the relationship between macronutrients, fiber, and satiety are summarized below.

Carbohydrate and Satiety

The carbohydrate content of foods and drinks is diverse and includes digestible carbohydrates and fiber. In the 1950s, the glucostatic theory of appetite regulation was developed by Mayer (1953), who hypothesized that blood glucose levels determined appetite, initiating energy intake when low and causing satiety when increased. Glucose levels do affect satiety and thus intake of calories as carbohydrate must be controlled and balanced in satiety studies.

Both glucose and fructose preloads have been found to reduce subsequent energy intake and no consistent differences are found when comparing the two (Anderson, 2003). A number of studies have investigated whether drinks sweetened with HFCS compared with sucrose have different effects on satiety, and a significant difference between the two types of sweetener has not been found (Soenen, 2007). Alfenas and Mattes (2005) concluded that under controlled conditions, the glycemic index of foods does not affect satiety or energy intake. RCTs comparing low and high glycemic index diets find no differences in weight loss (Aston et al., 2008; Das et al., 2007).

Fiber and Satiety

Fiber includes a wide range of compounds and although fiber generally affects satiety, not all fibers are equally effective in changing satiety (Slavin and Green, 2007). Typically a large dose of fiber is required, such as 10 grams or more in a serving of food (an amount not naturally occurring in a single serving of food). Viscous fibers, such as guar gum, oat bran, and psyllium, are generally more effective, although insoluble fibers that survive gut transit, such as wheat bran and cellulose, also are known to alter satiety.

Willis et al. (2009) compared the satiety response when four different muffins were fed at breakfast. Resistant starch and corn bran had the most positive impact on satiety, whereas polydextrose had little effect and behaved like the low-fiber muffin. Generally, whole foods that

naturally contain fiber are satiating. Flood-Obbagy and Rolls (2009) compared the effect of fruit in different forms on energy intake and satiety at a meal. Results showed that eating apple reduced lunch energy intake by 15 percent compared to control. Fullness ratings differed significantly after preload consumption, with apple being the most satiating, followed by applesauce, then apple juice, then the control food. The addition of a pectin fiber to the apple juice did not alter satiety.

Other fibers added to drinks do change satiety. Pelkman et al. (2007) added low doses of a gelling pectin-alginate fiber to drinks and measured satiety. The drinks were consumed twice a day over 7 days and energy intake at the evening meal was recorded. The 2.8 g dose of pectin alginate caused a decrease of 10 percent in energy intake at the evening meal. Thus, it generally found that high-fiber foods are more satiating and that certain isolated fibers affect satiety while others are not effective. Clinical studies are needed to assess the effectiveness of isolated fibers on satiety as there are no measures of fiber chemistry (solubility, structure, etc) that can predict fiber's effect on satiety.

Protein and Satiety

It is generally accepted that at sufficiently high levels, protein has a stronger effect on satiety than equivalent quantities of energy from carbohydrate or fat. Differences in study design make it difficult to pinpoint the optimum dose or percentage of energy needed to observe significant effects of protein on satiety. Anderson and Moore (2004) suggest that at least 50 grams of protein in a food or meal is necessary to see a significant effect on satiety, but note that information is insufficient to describe a dose-response relationship.

Other factors have been considered as potential mechanisms for protein's effect on satiety. Westerterp-Plantenga et al. (2007) described the relationship between diet-induced thermogenesis and satiety. Additionally, the role of ketosis as an explanation for the satiating effect of protein has been offered, although studies find inconsistent results for fullness and prospective food consumption when low and high protein diets are compared (Johnstone, 2008).

Fat and Satiety

Dietary fat affects satiety by slowing gastric emptying, stimulating the release of satiating gut hormones and suppressing the release of ghrelin (Little et al., 2007). Still, most reviews find that the effect of fat on satiety is weaker than that of either protein or carbohydrate (Benelam, 2009). Bell and Rolls (2001) compared the effects of meals containing different amounts of fat that were matched at different levels of energy density. When energy density was matched, the fat content of the diets did not affect energy intake, indicating that it was the energy density and not the fat content that influences satiety. In free-living individuals, high-fat foods have a higher energy density than

high-protein or high-carbohydrate foods. The palatability of high fat foods also may contribute to overconsumption of calories.

Food Form and Satiety

The physiological effects of solids versus liquids are covered in Question 7, but the satiety effects of liquid diets will be described here. Overall, inconsistent evidence suggests that energy from liquids is less satiating than energy from solids (Benelam, 2009). Soups appear to have a particularly satiating effect, which may be due to their lower energy density. Mattes (2005) has suggested that soups are seen as part of a meal and consumed in response to hunger, compared with drinks, which are consumed to address thirst or to accompany foods. The impact of intense sweeteners on satiety and energy intake, as reviewed by Drewnowski and Bellisle (2007), is mixed, with some studies finding increases in appetite and/or energy intake, some decreases, but most finding no significant effects. Differences in study design make it difficult to reach any overall conclusions about the effect of intense sweeteners on satiety, but it seems that intense sweeteners do not enhance satiety.

Thus, many factors affect satiety and most studies are conducted in laboratory settings to control for variables. Therefore, results may not be generalized to the more complicated eating environment of the outside world. Foods high in dietary fiber generally are more satiating than low-fiber foods, although some fibers added to drinks have little impact on satiety. Overall, small changes in the macronutrient content of the diet are unlikely to significantly alter satiety.

Question 9: What is the Role of Prebiotics and Probiotics in Health?

Conclusion

Gut microflora play a role in health, although the research in this area is still developing. Foods high in prebiotics (wheat, onions, garlic) may be consumed, as well as food concentrated in probiotics (yogurt), within accepted dietary patterns.

Implications

The lack of epidemiologic studies that support a role for changes in gut microflora and health outcomes limits any specific dietary recommendations in this area. Foods high in prebiotics and probiotics are linked to health benefits. For example, fiber is a prebiotic linked to health benefits. Many probiotic-containing foods, such as dairy foods, also are linked to health benefits and are recommended for inclusion in the diet.

Review of the Evidence

Evidence that the intestinal microbiota is linked with overall health is emerging (Davis, 2009b). The adult human gut contains 100 trillion microbial organisms, which are referred to as the microbiota. Although the importance of the microbiota has been accepted for diseases of the large intestine, it is now thought that the microbiota play a role in obesity control and other chronic diseases such as autism. Because of these new ideas, consumer interest in altering the microbiota is high.

Prebiotics are defined as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health (De Vrese, 2008). Oligosaccharides such as fructo-oligosaccharides and galacto-oligosaccharides are generally accepted as prebiotics and are often added to infant formula and other food products.

Probiotics are defined viable microorganisms, sufficient amounts of which reach the intestine in an active state and thus exert positive health effects (De Vrese, 2008). Synbiotics are combinations of both probiotics and prebiotics. The idea to suppress and displace harmful bacteria in the intestine by orally administered "beneficial" ones and thus improve microbial balance, health, and longevity has been around for more than a century. Tissier (1906) recommended the administration of bifidobacteria to infants suffering from diarrhea, claiming that bifidobacteria supersede the putrefactive bacteria causing the disease. He showed the bifidobacteria were predominant in the gut of breast-fed infants, the rationale for adding prebiotics to infant formula. Nobel Prize winner Elie Metchnikoff (1907) also suggested that intake of lactobacilli-containing yogurt results in reduction of toxin-producing bacteria in the gut which increased longevity in the host.

For this review, we completed a non-NEL review since 2004 of systematic reviews on prebiotics and probiotics and health. We conclude that the importance of the gut microbiota is an important emerging area of research, but not enough research is available to make dietary recommendations for either prebiotics or probiotics. All prebiotics are dietary fibers, but not all dietary fibers are prebiotics. Recommended intakes of dietary fiber can provide prebiotics to the diet. Also, recommended foods, such as yogurt, are probiotics, so by observing guidelines for dairy food consumption and picking yogurt or other fermented dairy products, probiotics will be included in the diet.

Some of the proposed health benefits of prebiotics and probiotics include reduction in diarrhea incidence, improvements in gut health, elimination of allergies, and prevention of infections. It is accepted that the gut microflora have a potential role in immune function, but studies showing an improvement in immunity with consumption of either prebiotics or probiotics are limited. Despite the continued interest in enhancing the gut environment, there are no cohort studies where fecal

samples have been collected and higher levels of bifidobacteria or lactobacillus in feces linked to improved health status.

A systematic review of randomized controlled trials evaluating the relationship between probiotics and constipation concluded that until more data are available, the use of probiotics for the treatment of constipation should be considered investigational (Chmielewska and Szajerska, 2010). Probiotics may play a role in preventing and treating acute diarrhea in both children and adults, although results are inconsistent (Cummings, 2009). A systematic review and meta-analysis of probiotics in the treatment of irritable bowel syndrome found that probiotics could potentially play a role in irritable bowel syndrome treatment, but results of trials are inconsistent and many questions remain on the type of probiotics, dose, and whether certain subgroups of patients are more likely to benefit from probiotics (Hoveyda, 2009).

The effect of prebiotics on immune function, infection and inflammation was reviewed (Lomax and Calder, 2009a). Again, results are mixed in human trials. Ten trials involving infants and children have mostly reported benefits on infectious outcomes, while in 15 adult trials, little effect was seen. A similar review was conducted on probiotics (Lomax and Calder, 2009b). Overall, the data are mixed with large species and strain differences of probiotic treatments influencing results.

Thus, the DGAC believes that the gut microbiota do play a role in health, although the research in this area is still developing. No recommendations for intake of prebiotics or probiotics for the American people can be made, although foods high in prebiotics (wheat, onions, garlic) should be consumed, as well as food concentrated in probiotic (yogurt).

Chapter Summary

Healthy diets are high in carbohydrates. Accepted Macronutrient Distribution Ranges (AMDR) for carbohydrates are 45 to 65 percent from carbohydrates. A maximal intake level of 25 percent or less of total energy from added sugars is suggested, based on trends indicating that people with diets at or above this level of added sugars are more likely to have poorer intakes of important essential nutrients. Active Americans should consume diets at the high end of the AMDR range (65%) while Americans on low calorie diets will need to consume diets at the low end of the range (45%). Usually proteins will replace carbohydrate on low calorie diets.

Americans should choose fiber-rich foods such as whole grains, vegetables, fruits, and cooked dry beans and peas as staples in the diet. Dairy products are also a nutrient-dense source of carbohydrates in the diet and provide high quality protein, vitamins, and minerals.

Carbohydrates are the primary energy source for active people. Sedentary people, including most Americans, should decrease consumption of caloric carbohydrates to balance energy needs and

attain and maintain ideal weight. The high-energy, non-nutrient-dense carbohydrate sources that should be reduced to aid in calorie control include SSB, desserts, including grain-based desserts, grain products, and other carbohydrate foods and drinks that are non-nutrient-dense.

Needs for Future Research

1. Develop and validate carbohydrate assessment methods. Explore and validate new and emerging biomarkers to elucidate alternative mechanisms and explanations for observed effects of carbohydrates on health.

   Rationale: Studies of carbohydrates and health outcomes on a macronutrient level are often inconsistent or ambiguous due to inaccurate measures and varying food categorizations and definitions. The science cannot progress without further advances in both methodology and theory.

2. Develop definitions for whole grain foods and criteria for whole grain foods that can be universally accepted.

   Rationale: At present, there is no consistent way that whole grain foods are defined and determined. Without clear definitions for whole grain foods, it is difficult to compare research studies examining the effectiveness of various whole grains on biomarkers of interest in CVD, diabetes, and obesity. Clear definitions would also help consumers identify foods that can help them meet the Dietary Guidelines recommendation.

3. Conduct intervention and research studies with strong designs that include sufficient sample sizes over time and specific measures of vegetable and fruit intake, including specific types of vegetables and fruits, overall dietary patterns, exercise, sex, and other confounding factors to evaluate the impact of consuming vegetables and fruits on health.

   Rationale: Rigorous methods of assessing dietary intake are needed along with rigorous measures of outcomes. Strong designs that control for confounding variables will provide deeper insight into the effect vegetables and fruits have on health. Plausible mechanisms for these effects also need to be studied in depth. Traditional markers, such as blood lipids, while useful for risk factor assessment, appear to have limited explanatory value.

4. Conduct long-term, randomized controlled trials to resolve whether use of nonnutritive sweeteners can actually aid weight loss or prevention of weight gain.

   Rationale: Currently available data are insufficient to recommend non-nutritive sweeteners as an aid to weight loss, except on a theoretical basis for calorie reduction.

5. Develop standardized assessment tools to determine accurate intake of added sugars.

   Rationale: This is challenging because carbohydrate methods are also limited as total carbohydrate is measure "by difference." Unless efforts are made to define and measure

carbohydrates and carbohydrate fractions with potential health benefits, it will be difficult to determine if different carbohydrates types have different health effects.

6. Develop innovative methods to evaluate "food form" as a variable in food intake studies for the field to progress.

   Rationale: Unless macronutrients are carefully controlled, it is not possible to answer the question on how does food form affect energy intake. These questions will remain unless RCTs are conducted that measure differences in exposure to different carbohydrates (glucose, fructose, sucrose) and different forms (liquid, solid, whole food).

7. Develop methods for use in epidemiologic studies to measure accurately or quantify intake of liquids, either caloric or non-caloric.

   Rationale: There has been an increase in the number of beverages available, and it would be valuable to know how these beverages are contributing to satiety, energy intake, and body weight. Drinks can include a wide range of macronutrients, artificial sweeteners, and are difficult to assess with food frequency instruments. The type of drinks consumed now includes sport drinks, designer coffees and teas, smoothies and juices, and carbonated beverage with different sugars or artificial sweeteners.

8. Determine whether the effects of vegetables and fruits in the overall dietary pattern are due to displacement of other foods in the diet or to the action of vegetables and fruits per se on specific health outcomes.

   Rationale: The mechanism(s) of action for the effects of vegetables and fruits have not been determined and, therefore, may vary for different health outcomes. The observed effects could be a simple displacement of these foods with other foods that cause poorer outcomes or vegetables and fruits may contribute specific benefits or a combination of the above may explain the observations made thus far in the literature. Only further research can provide more definitive answers.

9. Identify whether a progressive, inverse relationship of fruits and vegetable consumption exists with the prevention of chronic disease(s) or whether there is a threshold effect that may vary depending on factors such as disease, sex, and dietary pattern.

   Rationale: The evidence suggests that there may be a threshold effect of vegetables and fruits, at least within the American dietary pattern, but further research is needed to verify this hypothesis and to test whether the threshold varies among a variety of dietary patterns and/or among the specific variety of vegetables and fruits consumed.

Table D4.2. Vegetables,[1] fruits,[1] pulses (legumes), nuts, seeds, herbs, spices, and the risk of cancer

In the judgment of the Panel, the factors listed below modify the risk of cancer. Judgments are graded according to the strength of the evidence.

	Decreases Risk Exposure	Decreases Risk Cancer site	Increases Risk Exposure	Increases Risk Cancer site
Convincing				
Probable	**Non-starchy vegetables[1]**	**Mouth, pharynx, larynx Oesophagus Stomach**		
	Allium vegetables[1]	**Stomach**		
	Garlic[1]	**Colorectum**		
	Fruits[1]	**Mouth, pharynx, larynx Oesophagus Lung Stomach**		
	Foods containing folate[2]	**Pancreas**		
	Foods containing carotenoids[2]	**Mouth, pharynx, larynx Lung**		
	Foods containing beta-carotene[2]	**Oesophagus**		
	Foods containing lycopene[2 3]	**Prostate**		
	Foods containing Vitamin C[2 4]	**Oesophagus**		
	Foods containing selenium[2 5]	**Prostate**		
Limited—suggestive	Non-starchy vegetables[1]	Nasopharynx Lung Colorectum Ovary Endometrium	Chilli[1]	Stomach
	Carrots[1]	Cervix		
	Fruits[1]	Nasopharynx Pancreas Liver Colorectum		
	Pulses (legumes)[7]	Stomach Prostate		
	Foods containing folate[2]	Oesophagus Colorectum		
	Foods containing pyridoxine[2 8]	Oesophagus		
	Foods containing vitamin E[2 6]	Oesophagus Prostate		
	Foods containing selenium[2 5]	Lung Stomach Colorectum		
	Foods containing quercetin[2]	Lung		
Substantial effect on risk unlikely	Foods containing beta-carotene[9]: prostate; skin (non-melanoma)			

[1]Judgements on vegetables and fruits do not include those preserved by salting and/or pickling.
[2]Includes both foods naturally containing the constituent and foods which have the constituent added (see chapter 3.5.3).
[3]Mostly contained in tomatoes and tomato products. Also fruits such as grapefruit, watermelon, guava, and apricot.
[4]Also found in some roots and tubers—notably potatoes. See chapter 4.1.
[5]Also found in cereals (grains) and in some animal foods. See chapters 4.1 and 4.3.
[6]Also found in plant seed oils. See chapter 4.5.
[7]Including soya and soya products.
[8]Vitamin B6. Also found in cereals. See chapter 4.1.
[9]The evidence is derived from studies using supplements and foods containing beta-carotene: see chapter 4.10.
For an explanation of all the terms used in the matrix, please see chapter 3.5.1, the text of this section, and the Glossary.
Source: World Cancer Research Fund/American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective, Washington, DC: AICR 2007.

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