

## PART D. Section 4: Protein

### Introduction

Protein is the major structural component of all cells in the body and functions as enzymes, hormones, and other important molecules. Protein is one of the major macronutrients and an important source of calories. Both protein and non-protein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM). Proteins are made of amino acids and if the amino acids are not present in the right balance, the body's ability to use protein will be affected. If amino acids needed for protein synthesis are limited, the body may break down body protein to obtain needed amino acids. Protein deficiency affects all organs and is of particular concern during growth and development. Adequate intake of high-quality protein is essential for health.

Because average protein intakes in the US are more than adequate, protein was not considered as a separate topic by past Dietary Guidelines Advisory Committees. However, the 2010 DGAC decided to focus on dietary protein for many important reasons. First, many consumers have recently adopted high-protein diets for weight loss purposes and the Committee wanted to evaluate the scientific basis of this approach. Secondly, consumer comments addressed the health benefits of vegetarian eating styles (see *Part D. Section 2: The Total Diet: Combining Nutrients, Consuming Food*) for a discussion of the nutrient adequacy of vegetarian diets). Finally, as Americans decrease total calorie intake to combat obesity, the optimal percentage of calories derived from protein in the diet may rise. The Committee wanted to review data on the use of high-protein diets and determine whether such diets limit other nutrients (see *Part D. Section 1: Energy Balance and Weight Management* for a discussion of the relationship between macronutrient proportion and body weight, including the safety aspect of high-protein diets).

### Background on Protein

#### *Nomenclature*

Protein sources vary widely in their nutritional value. The quality of a protein depends on its ability to provide the nitrogen and amino acid requirements necessary for growth, maintenance, and repair. Protein quality is determined by two factors—digestibility and amino acid profile. Amino acids can be divided into categories based on the body's ability to produce them (Table D4.1). Nine cannot be synthesized in the body and are known as indispensable, or essential, amino acids. These must be consumed in the diet. The remaining amino acids are either dispensable or conditionally indispensable. Five amino acids are dispensable, meaning that they can be produced in the body

from other amino acids or nitrogen-containing compounds. An additional six amino acids are conditionally indispensable. Under most circumstances, these amino acids can be synthesized in the body. However, in certain conditions, the body cannot synthesize adequate amounts to meet metabolic needs. Subsequently, a dietary source of the conditionally indispensable amino acids becomes necessary (IOM, 2005).

**Table D4.1. Categories of amino acids**

Essential	Conditionally essential	Non-essential
Histidine	Arginine	Alanine
Isoleucine	Cysteine	Aspartic acid
Leucine	Glutamine	Asparagine
Lysine	Glycine	Glutamic acid
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

The Recommended Dietary Allowance (RDA) for both men and women (19 years and older) is 0.80 g of good-quality protein per kilogram of body weight per day and is based on careful analyses of available nitrogen balance studies (DRI, 2006). Data were insufficient to set a Tolerable Upper Intake Level (UL) for protein or amino acids. RDAs for protein increase at certain times during the lifespan. For example, protein RDAs for children are higher on a gram per bodyweight basis than for adults: ages 1 to 3 years, 1.05 g/kg/day; ages 4 to 13 years, 0.95 g/kg/day; ages 14 to 18 years, 0.85 g/kg/day. RDAs for protein also are increased in pregnancy (1.1 g/kg/day) and lactation (1.3 g/kg/day).

The IOM-established Acceptable Macronutrient Distribution Range (AMDR) for protein is 5 to 20 percent of total calories for children ages 1 to 3 years, 10 to 30 percent of total calories for children ages 4 to 18 years, and 10 to 35 percent of total calories for adults older than age 18 years (IOM, 2002/2005). For men and women, protein typically provides about 15 percent of total calories (NCI, 2010).

As calorie intake decreases, however, it is essential to increase the percentage of calories from protein so as to consume the RDA for protein. Thus, the wide recommended range of 10 to 35 percent of total calories coming from protein for adults is based on the large range of calories consumed, which depends on physical activity and body size. For example, low-calorie, protein-sparing, modified fast diets contain mostly protein as it is necessary to get the RDA for protein. In contrast, extremely active people, such as endurance athletes, consume high-calorie diets and their

RDA for protein does not change. A lower percentage of energy from protein is therefore appropriate for them and these additional calories would typically come from carbohydrates.

The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, change nitrogen balance, alter mineral absorption, or affect chronic diseases, such as osteoporosis or renal stones.

Food allergies exist for protein foods including milk, eggs, peanuts, tree nuts, soy, fish and shellfish (DRI, 2002). Gluten-free diets are recommended for those with gluten intolerance, which limits intake of wheat and certain other grain products. Lactose intolerance, although not medically diagnosed, can limit consumption of dairy products. Care must be taken to determine the cause of the intolerance to a food product (for example, is the individual sensitive to the sugar in milk or the protein in milk) and make appropriate dietary changes. Often, children allergic to one protein source develop allergies to other protein sources. Many protein sources, including milk, wheat, or soy, must be avoided as a result. As protein allergies can be very severe, careful food selection is essential. If high-quality protein sources cannot be consumed in the diet, other options for high-quality protein sources must be explored. (See *Part D. Section 8. Food Safety and Technology*.)

### ***Food Sources of Proteins***

Diets adequate in protein can be designed in many ways and are reflected in eating patterns around the world. Since the adults (19 years and older) RDA for protein is 0.8 g/kg body weight, a 150-pound adult would require 54 grams of high quality protein daily. Three ounces (the recommended serving size) of lean meat or poultry contain about 25 grams of protein, while 1 cup of milk or yogurt contains 8 grams of protein. Cereals, grains, nuts, and vegetables contain about 2 grams of protein per serving. When protein needs are high, as during growth and development, consumption of animal products will provide both greater quantity and quality of protein than plant products. Plant products can be combined to improve protein quality, but the number of calories that must be consumed to get adequate intakes must be considered.

Thus, proteins are the most important macronutrient in the diet because they provide both essential amino acids and are a source of energy. They are particularly important during growth and development.

## List of Questions

### ANIMAL AND PLANT PROTEINS AND HEALTH OUTCOMES

1. What is the relationship between the intake of animal protein products and selected health outcomes?
2. What is the relationship between vegetable protein and/or soy protein and selected health outcomes?
3. How do the health outcomes of a vegetarian diet compare to that of a diet which customarily includes animal products?

### PROTEIN-RELATED FOOD GROUPS AND HEALTH OUTCOMES

4. What is the relationship between the intake of milk and milk products and selected health outcomes?
5. What is the relationship between the intake of cooked dry beans and peas and selected health outcomes?

## Methodology

For the first time, the 2010 DGAC included a chapter focusing solely on the relationship between protein and health. Most of the questions addressed here cover new topics. The Committee reviewed evidence from January 2000 to 2009. Because the 2005 DGAC reviewed the topic of milk and milk products, the 2010 Committee agreed with those recommendations and provided here only an updated review of evidence from June 2004 to 2009.

All of the questions addressed in this section were answered using a NEL evidence-based systematic review. A description of the NEL evidence-based review process can be found in **Part C: Methodology**. For each question considered in this section, the following general criteria applied. With minor exceptions noted below, 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 designs. Also original research articles included in systematic reviews or meta-analyses were not included as individual articles in the review, so as not to count the study twice. Finally, the Committee excluded studies that considered only participants diagnosed with chronic disease, hyperlipidemia, hypertension, and related health conditions. Additional information about the NEL search strategies and criteria used to review each question can be found online at [www.nutritionevidencelibrary.com/](http://www.nutritionevidencelibrary.com/).

Recent literature has begun to examine the relationship between protein and health outcomes. The Committee addressed this topic in three separate questions: animal protein products, vegetable protein, and vegetarian versus animal-based diets. Question 1 considers animal protein products, including red meat, processed meat, and poultry. Although milk and milk products are sources of animal protein, their relationship to selected health outcomes is addressed separately in Question 4. Seafood, another source of animal protein, is discussed in detail in *Part D. Section 3. Fatty Acids and Cholesterol* and in *Part D. Section 8. Food Safety and Technology*. The health outcomes considered in Question 1 were type 2 diabetes (T2D), cardiovascular disease (CVD), hypertension, body weight, and cancer. For many sections of this Report, the relationship between dietary intakes and cancer outcomes are discussed using conclusions from the World Cancer Research Fund/American Institute for Cancer Research report (WCRF/AICR, 2007). The WCRF/AICR report examined the relationship between meat and numerous types of cancer in a thorough review of the literature of various study designs with humans and animals. However, some controversy has surrounded the WCRF/AICR conclusions for red meat and colorectal cancer. Thus, the Committee decided to conduct a review parallel to other reviews in this Report and included only prospective cohort studies with humans published since 2000. In addition to colorectal cancer, prostate and breast cancers were reviewed.

Question 2 concerns the relationship of vegetable protein and selected health outcomes and was conducted to complement the Committee's review of animal protein products. Because much of the research on vegetable protein has focused on soy protein, soy protein was included in the search as a separate term. However, articles examining soy foods, rather than soy protein specifically were considered under the Committee's review of cooked dry beans and peas (Question 5). The Committee considered a variety of health outcomes in the vegetable protein search, but available evidence was sufficient to permit only a review of chronic disease, blood pressure, blood lipids, and body weight.

Question 3 considers research that directly compares health outcomes among individuals consuming a diet which customarily includes animal products to those consuming a vegetarian, including vegan, diet. The Committee recognized that additional research on this topic was published before 2000, but felt research published since 2000 represented the current plant-based dietary patterns and provided sufficient context to discuss the relationship between these dietary patterns and health. For an in-depth discussion of the relationship between various dietary patterns and health outcomes, see *Part D. Section 2: The Total Diet: Combining Nutrients, Consuming Food*.

As noted, Questions 4 and 5 address specific food groups. Milk and milk products and cooked dry beans and peas are significant protein sources in the American diet, and they also are important sources of other nutrients. Additional information about other nutrient contributions of these food

groups can be found in *Part D. Section 2: Nutrient Adequacy*. It should be noted that the Committee considered only studies that directly assessed the relationship between food group intake and health; studies examining dietary patterns that were high in a particular food group were considered as dietary patterns, not under reviews for the individual food groups. The review of milk and milk products considered bone health, cardiovascular outcomes, metabolic syndrome, T2D, and body weight. All the evidence reviews covered children and adults, except for body weight, which included only adults. The relationship between the consumption of milk and milk products and childhood adiposity is discussed in *Part D. Section 1: Energy Balance and Weight Management*. Outcomes considered in the review of cooked dry beans and peas were body weight, CVD, and T2D. Although “legumes” includes dry beans and peas as well as peanuts, peanuts were not considered in this question but are a part of the review of nuts in *Part D. Section 3: Fatty Acids and Cholesterol*.

## ANIMAL AND PLANT PROTEINS AND HEALTH OUTCOMES

### Question 1. What is the Relationship between the Intake of Animal Protein Products and Selected Health Outcomes?

#### Conclusion

Limited evidence from prospective cohort studies show inconsistent relationships between intake of animal protein products and CVD with somewhat more positive evidence for processed meats and CHD. Moderate evidence found no clear association between intake of animal protein products and blood pressure in prospective cohort studies. Limited inconsistent evidence from prospective cohort studies suggests that intake of animal protein products, mainly processed meat, may have a link to type 2 diabetes. Insufficient evidence is available to link animal protein intake and body weight. Moderate evidence reports inconsistent positive associations between colorectal cancer and the intake of certain animal protein products, mainly red and processed meat. Limited evidence shows that animal protein products are associated with prostate cancer incidence. Limited evidence from cohort studies shows there is no association between the intake of animal protein products and overall breast cancer risk. However in subgroups of breast cancer patients, limited evidence suggested a relationship between the intake of animal protein products and risk of developing breast cancer.

#### Implications

Americans may choose animal products as part of their diet based on the body of evidence showing a general lack of relationship between animal protein consumption and selected health outcomes. However, attention should be given to quantity and preparation, as some forms of meat (well done and processed) may be linked to specific cancers. In addition, animal protein products contain saturated fat and proportionately, a high calorie load, so serving sizes should be appropriate.

## Review of the Evidence

Intake of animal protein products shows few links to negative health outcomes in epidemiologic studies. Most people consume protein from both animal and plant sources, making separation of protein intake into animal and plant sources difficult in epidemiologic studies. The WCRF/AICR report (WRCF/AICR, 2007) examined the relationship between meat, poultry, and eggs and a variety of different cancers including colorectal, prostate, and breast. They concluded that the evidence that red meats and processed meats are causally related to colorectal cancer is convincing. Additionally, they found that limited evidence suggests that processed meat is causally related to prostate cancer, and there was limited suggestive evidence that foods containing animal fat are associated with postmenopausal breast cancer.

In a systematic review and meta-analysis published subsequent to our review, Micha et al. (2010) examined the association between the consumption of red and processed meat and the risk of incident CHD and T2D. They found that intake of red meat was not associated with CHD or T2D. However, processed meat was associated with a 42% higher risk of CHD and 19% higher risk of T2D. Associations for total meat intake and these outcomes were intermediate.

The review provided below summarizes the evidence from literature published since 2000 related to animal protein products, specifically total meat, red meat, processed meat, poultry, and eggs, acknowledging the wide variation in how types of meat and meat products were grouped and analyzed.

### ***Animal Protein Products and Cardiovascular Disease***

Prospective cohort studies show inconsistent relationships between intake of animal protein products and cardiovascular disease. The evidence review for this question included seven articles (Djousse, 2008; Halton, 2006; Keleman, 2005; Nakamura, 2004; Nakamura, 2006; Qureshi, 2007; Sinha, 2009), which represented prospective cohorts from the US and Japan published since 2000. Regarding the relationship between the intake of total animal protein and coronary heart disease, no relationship was observed in the Nurses' Health Study (Halton, 2006) or Iowa Women's Health Study (Keleman, 2005). However, a positive association between red meat and processed meat and CVD mortality was observed in the National Institutes of Health-AARP (NIH-AARP) Diet and Health Study (Sinha, 2009), and substituting red/processed meat (combined) for carbohydrate-dense foods was positively associated with coronary heart disease (CHD) mortality in the Iowa Women's Health Study (Keleman, 2005). Studies found no association between egg intake and CVD (Djousse, 2008; Nakamura, 2006; Nakamura, 2004; Qureshi, 2007). Thus, limited information is available on this relationship, and risk may depend on type of meat or meat products consumed and the type of CVD.

### ***Animal Protein Products, Blood Pressure, and Hypertension***

No clear association was found between intake of animal protein products and blood pressure in prospective cohort studies. This conclusion is based on the review of six articles (Alonso, 2006; Miura, 2004; Steffen, 2005; Wagemakers, 2009; Wang, 2008b; Wang, 2008c) representing prospective cohorts from the US, United Kingdom, and Spain published since 2000. No relationship between intake of animal protein and hypertension was observed in the Seguimiento Universidad de Navarra (SUN) cohort in Spain (Alonso, 2006). Similarly, no association between intake of animal protein and systolic or diastolic blood pressure was observed in the PREMIER Study (Wang, 2008b), and no association between the intake of red or processed meat and systolic or diastolic blood pressure was observed in a cohort in the United Kingdom (Wagemakers, 2009).

In contrast, in the Women's Health Study (Wang, 2008c), total red meat intake was positively associated with risk of developing hypertension. In addition, each individual unprocessed and processed red meat item, including hot dogs, hamburgers, and bacon, beef or lamb as a main dish were positively associated with the risk of developing hypertension. Similarly, the CARDIA study (Steffen, 2005) found a positive association between consumption of total meat and red and processed meat (combined) and risk of developing elevated blood pressure. The Chicago Western Electric Study also showed a positive association between systolic and diastolic blood pressure and red meat, but observed no association with processed meat.

Differences in dietary assessment methodology likely affected the results in this review. Assessment methods included 24-hour recalls, 5-day diaries, diet histories, interviews, and food frequency questionnaires. Studies that used 24-hour recalls (Wang, 2008b) and 5-day diaries (Wagemakers, 2009) observed no associations between animal protein products and systolic or diastolic blood pressure.

### ***Animal Protein Products and Body Weight***

Few studies exist to link animal protein products and body weight. After applying our review criteria, only three articles (Mahon, 2007; Wagemakers, 2009; Xu, 2007) published since 2000 were identified that examined the relationship between animal protein products and body weight. Inconsistent findings were reported in a cohort of British adults (Wagemakers, 2009) on whether meat intake was associated with body mass index (BMI) and waist circumference who were studied between 1989 and 1999. Red and processed meat consumed in 1999 was significantly associated with increased BMI in women only. In a cross-sectional study in China (Xu, 2007), red meat consumption was associated with excess body weight. In the only US study found (Mahon, 2007), overweight postmenopausal women were successful in weight loss with either a meat-containing or vegetarian protein intervention. Thus, existing research is sparse and finds little link between meat



intake and body weight, and meat-containing diets work as well as calorie controlled vegetarian diets in enhancing weight loss in intervention studies.

### ***Animal Protein Products and Type 2 Diabetes***

Prospective cohort studies suggest that intake of animal protein products, mainly processed meat, may have a link to T2D, although results are not consistent. This review included seven articles (Djousse, 2009; Fung, 2004; Halton, 2008; Schulze, 2003; Song, 2004; van Dam, 2002; Vang, 2008) published since 2000 representing prospective cohorts from the US. In the three studies examining total animal protein intake, two reported a positive association with T2D (Song, 2004; Vang, 2008) and one reported no association (Halton, 2008). All five studies that reported on the relationship between the intake of processed meats and T2D reported a positive association (Fung, 2004; Schulze, 2003; Song, 2004; van Dam, 2002; Vang, 2008). Inconsistent findings were reported related to the intake of red meat and poultry. Some of the reported risk found in these studies may be attributed to obesity or weight gain, but controlling for this supported meat intake as an important risk factor for diabetes. Other dietary factors, such cereal fiber, fat, and total calories, also are strong in this relationship and the association between T2D and animal protein is attenuated when there is adjustment for these factors.

### ***Animal Protein Products and Colorectal Cancer***

Inconsistent positive associations have been reported between colorectal cancer and the intake of certain animal protein products, mainly red and processed meat. This review included 13 studies (Chao, 2005; Cross, 2007; English, 2004; Flood, 2003; Jarvinen, 2001; Kojima, 2004; Larsson, 2005; Lee, 2009b; Norat, 2005; Oba, 2006; Sato, 2006; Wei, 2004; Wu, 2006) representing prospective cohorts from the US, Europe, Australia, Finland, Japan, China, and Sweden published since 2000. In studies examining total meat intake, none reported a relationship with overall colorectal cancer risk (Flood, 2003; Jarvinen, 2001; Lee, 2009b; Oba, 2006; Sato, 2006) or risk associated with specific subsites (Lee, 2009b; Sato, 2006; Wu, 2006).

However, more varied results were reported for red and processed meats. For example, in the NIH-AARP Diet and Health Study, positive associations between red meat and processed meat and colorectal cancer were observed (Cross, 2007). However, no associations were observed between red or processed meats and colorectal cancer in the Breast Cancer Detection Demonstration Project (Flood, 2003). The European Prospective Investigation into Cancer and Nutrition (EPIC) study observed no association between red meat and colorectal cancer, but did observe a positive association for processed meat. Further risk may vary depending on subsite. Some studies found a

relationship with rectal cancer and red meat intake (Chao, 2005; English, 2004), while others found no association (Kojima, 2004; Larsson, 2005; Lee, 2009b; Wei, 2004; Wu, 2006).

Studies also report inconsistent results for the intake of poultry and colorectal cancer at various subsites, with studies reporting a positive association (Jarvinen, 2001; Kojima, 2004; Sato, 2006), no association (Flood, 2003; Lee, 2009b; Norat, 2005; Wu, 2006), or an inverse association (Chao, 2005; English, 2004; Larsson, 2005).

In general, the studies showed no consistent findings on type of meat or meat product and colorectal cancer. Little information also is available about how much meat is consumed, and the association may differ depending on amount as well as the way it is cooked. Further, although it has been suggested that animal protein products have a different effect in different sites of the colon and rectum, no consistent findings are available. Future studies should consider the subsite of the cancer.

### ***Animal Protein Products and Prostate Cancer***

Little evidence is available that animal protein products are associated with prostate cancer incidence. The Committee reviewed six articles (Cross, 2005; Koutros, 2008; Michaud, 2001; Park, 2007; Rodriguez, 2006; Rohrmann, 2007) examining the relationship between animal protein products and incidence of prostate cancer published since 2000. All of the studies represented prospective cohorts from the US. Most studies reported no association between total, red, processed, or white meat consumption, meat-cooking method and risk of total prostate cancer, incident cancer, or advanced disease. However, in the Health Professionals Follow Up Study (Michaud, 2001), positive associations between metastatic prostate cancer and red and processed meats were observed. Also, in the Cancer Prevention Study (Rodriguez, 2006), red meat (including processed red meat) and cooked processed meats were positively associated with prostate cancer in Black, but not White, men. Rohrmann and colleagues (2007) reported a positive association between the intake of processed meat and total and advanced prostate cancer but did not observe relationships between cancer and other animal protein products.

Mixed results were observed regarding the level of doneness of meat. Well and very well done meat were associated with prostate cancer in the Prostate, Lung, and Colorectal and Ovarian (PLCO) Screening Trial (Cross, 2005) and the Agricultural Health Study (Koutros, 2008), but level of doneness was not related to cancer risk in the Multiethnic Cohort Study (Park, 2007) or Cancer Prevention Study (Rodriguez, 2006). Thus, cohort studies of animal protein products and prostate cancer since 2000 show little link between total meat intake and prostate cancer although there may be a link between processed meat products as well as well done meat and prostate cancer.

### ***Animal Protein Products and Breast Cancer***

Cohort studies show little association between intake of animal protein products and overall breast cancer risk. However, in premenopausal and estrogen receptor positive individuals, meat intake may alter risk of certain types of breast cancer. This review included six studies published since 2000 (Cho, 2006; Ferrucci, 2009; Fung, 2005; Kabat, 2009; Linos, 2008; Taylor, 2007). Results were often reported based on menopausal status (premenopausal or postmenopausal) and/or estrogen receptor status (positive or negative). In the Nurses' Health Study (Cho, 2006), overall, there was no association between total meat intake and risk of breast cancer. However, there was a positive association for ER (estrogen receptor)+/PR (progesterone receptor)+ breast cancer and no association for ER-/PR-. Similarly, they reported positive associations between ER+/PR+ breast cancer and individual red and processed meats, but not for ER-/PR-. Ferrucci et al. (2009) found a stronger association between red meat intake and ER+/PR+ breast cancer compared to negative receptor status in the PLCO Screening Trial.

In additional analyses from the Nurses' Health Study, Linos et al. (2008) found a positive association between premenopausal breast cancer and red meat, and this relationship was stronger among estrogen receptor positive participants. In the UK Women's Cohort Study (Taylor, 2007), positive associations between total meat and premenopausal and postmenopausal breast cancer were observed. Non-processed meat also was positively associated with premenopausal breast cancer. However, postmenopausal but not premenopausal breast cancer was associated with the intake of red meat and processed meat. Thus, results are conflicting and future research should further investigate the relationship between the intake of animal protein products and breast cancer specifically related to menopausal and receptor status.

## **Question 2: What is the Relationship between Vegetable Protein and/or Soy Protein and Selected Health Outcomes?**

### **Conclusion**

Few studies are available, and the limited body of evidence suggests that vegetable protein does not offer special protection against type 2 diabetes, coronary heart disease, and selected cancers. Moderate evidence from both cohort and cross-sectional studies show that intake of vegetable protein is generally linked to lower blood pressure. Moderate evidence suggests soy protein may have small effects on total and low density lipoprotein cholesterol in adults with normal or elevated blood lipids, although results from systematic reviews are inconsistent. A moderate body of consistent evidence finds no unique benefit of soy protein on body weight. A limited and inconsistent body of evidence shows that soy protein does not provide any unique benefits in blood pressure control.

## Implications

Our review indicated that intake of vegetable protein is generally linked to lower blood pressure, but this could be due to other components in plant foods, such as fiber, or other nutrients. Individual sources of vegetable protein have no unique health benefits so choice of plant protein sources can come from a wide range of plant-based foods. Consumption of plant proteins of lower quality is generally fine as long as calorie needs are met and effort is made to complement the incomplete vegetable proteins. Consumption of lower-quality or incomplete protein is of greater concern when protein needs are high. Thus, consumption of lower-quality vegetable protein must be carefully considered during pregnancy, lactation, and childhood. Additionally, recommendations to lower calorie intake to combat obesity by increasing plant-based food intake must be linked to cautionary messages to maintain protein total intake of sufficient quality at recommended levels.

## Review of the Evidence

### *Background*

Smit et al. (1999) estimated intakes of animal plant protein intake in US adults, based on the Third National Health and Nutrition Examination Survey, 1988–1999. The main protein source in the American diet is animal protein (69%). Meat, fish, and poultry protein combined contributed the most to animal protein (42%), followed by dairy protein (20%). Grains (18%) contributed the most to plant protein consumption. Results found that the percentage of total energy from protein was similar among race-ethnicities and between men and women, their sources of protein were different. But, typically animal protein provides about 70 percent of the protein in the American diet.

In epidemiologic studies, food frequency questionnaires are often used to assess dietary intake and protein-rich foods are often divided into vegetable and animal sources. Most people consume both types of protein, so this division is often complicated (see Question 3 for a discussion of protein and vegan eating patterns). Additionally, sources of vegetable protein are typically also associated with intake of dietary fiber and other potentially beneficial phytonutrients, thereby confounding true, isolated comparisons of protein type.

Soy protein has been the focus of much published research. Based on earlier studies reporting that large intakes of soy protein (25 g) were required to lower serum lipid in the US, the US Food and Drug Administration established a health claim stating that 25 grams per day of soy protein will lower serum lipids, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides without lowering high-density lipoprotein (HDL) cholesterol (FDA approves health claim labeling for foods containing soy protein. JADA 2000;100:292). No statement regarding isoflavone content or form of soy protein was issued.

The existing health claim for soy requires that each food contain at least 6.25 g of soy protein, based on the need for 25 grams of soy protein to show significant lowering of serum total

cholesterol and LDL-cholesterol. Soy foods that meet the 6.25 g level include 4 oz. of whole soybeans, 8 oz. of soy milk, 3.5 oz. soy flour, 8 oz. textured soy protein, 4 oz. tofu, and 4 oz. tempeh (FDA approves health claim labeling for foods containing soy protein. JADA 2000; 100:292).

### ***Vegetable Protein and Chronic Disease***

Few studies are available, and the limited data collectively suggests that vegetable protein does not offer special protection against T2D, coronary heart disease (CHD), and selected cancers. This conclusion was based on seven studies, including six prospective cohort studies (Halton, 2006; Keleman, 2005; Halton, 2008; Sluijs, 2010; Song, 2004; Lee, 2009a) and one ecological study (Nagata, 2000). Five studies addressed vegetable protein (Halton, 2006; Keleman, 2005; Halton, 2008; Sluijs, 2010; Song, 2004) and two studies focused on soy protein (Lee, 2009a; Nagata, 2000). Five of the seven studies only included women (Halton, 2006; Keleman, 2005; Halton, 2008; Song, 2004; Lee, 2009a).

Three studies examined the relationship between vegetable protein and CHD. In the Nurses' Health Study, no association was found with vegetable protein intake and risk of CHD (Halton, 2006). In the Iowa Women's Health Study, intake of vegetable protein in the highest quintile decreased CHD mortality by 30 percent with isocaloric substitution of vegetable protein for carbohydrate (Keleman, 2005). An ecological study in Japan found no relationship between the intake of soy protein and heart disease mortality (Nagata, 2000).

Three studies examined the relationship between vegetable protein intake and the risk of T2D. No association was found with vegetable protein intake in the Nurses' Health Study (Halton, 2008), Women' Health Study (Song, 2004), or the Dutch cohort of the EPIC study (Sluijs, 2010).

Substituting vegetable protein for carbohydrate or animal protein did not affect risk for cancer and was not associated with all-cause mortality in the Iowa Women's Health Study (Keleman, 2005). In the Shanghai Women's Health Study, vegetable protein was protective against premenopausal but not postmenopausal breast cancer, although only soy protein intake was evaluated (Lee, 2009a). Small protective effects of soy protein were found in men against stomach cancer in the Japanese ecological study (Nagata, 2000). However, intake of soy protein was not associated with breast, prostate, or lung cancer mortality in this study, and intake of soy protein increased colorectal cancer mortality (Nagata, 2000).

In summary, few studies have examined the relationship of vegetable protein intake and chronic diseases and the results from prospective studies report no relationship to diabetes, most cancers and all-cause mortality. Results are inconsistent for CHD.

### ***Vegetable Protein and Blood Pressure among Adults without Hypertension***

Intake of vegetable protein is associated with lower blood pressure. This conclusion is based on the review of six studies, including four prospective observational and two cross-sectional studies (Alonso, 2006; Elliott, 2006; Stamler, 2002; Steffen, 2005; Umesawa, 2009; Wang, 2008b). Alonso et al. (2006) reported in the SUN cohort in Spain that vegetable protein intake was associated with less hypertension. In the Chicago Western Electric Study, intake of vegetable protein was linked to lower systolic and diastolic blood pressure (Stamler, 2002). In the CARDIA study, an inverse relationship between the consumption of plant foods and elevated blood pressure was observed (Steffen, 2005). In the PREMIER Trial, plant protein had a beneficial effect on blood pressure and was associated with a lower risk of hypertension at 6 months, but not at 18 months (Wang, 2008b). Cross-sectional studies (Elliott, 2006; Umesawa, 2009) also report lower systolic and diastolic blood pressure links to vegetable protein intake.

### ***Soy Protein and Blood Pressure among Adults without Hypertension***

Some data suggest soy protein may lower blood pressure in adults with normal blood pressure. This conclusion is based on review of three RCTs (He, 2005; Liao, 2007; Teede, 2002), one prospective cohort study (Yang, 2005), and one cross-sectional study (Pan, 2008) published since 2000. All studies were published outside of the US. He et al. (2005) and Teede et al. (2002) conducted RCTs that included 40 g of soy protein consumed per day over 3 months. In both studies, participants receiving soy protein supplementation experienced a significant decrease in systolic blood pressure and diastolic blood pressure compared to the control groups. Liao et al. (2007) did not observe significant changes in systolic blood pressure or diastolic blood pressure among participants consuming soy protein as the only protein source versus a control diet with animal and plant protein for 8 weeks. The groups consumed an isocaloric diet providing 1200 kcal per day.

In the Shanghai Women's Health Study, systolic blood pressure and diastolic blood pressure were lower in women who consumed 25 g or more of soy protein per day than in women consuming less 2.5 g per day (Yang, 2005). In cross-sectional analyses of the Nutrition and Health of Aging Population Project in China, soy protein intake and elevated blood pressure were inversely associated in men, but not women (Pan, 2008); median soy protein in quartile 1 and quartile 4 of this study were 3 g per day and 16 g per day, respectively. Thus, while data suggest that vegetable protein plays a role in blood pressure, the data specifically for soy protein are limited and inconsistent. Soy protein does not appear to have any unique benefits in blood pressure control.

### ***Soy Protein and Body Weight***

Soy protein had no advantage over other proteins when consumed in isocaloric studies on body weight as based on one systematic review (Cope, 2008) and three primary citations (Liao, 2007; McVeigh, 2006; Pan, 2008). Cope et al. (2008) completed a systematic review including 91 international references with data from in vitro, animal, epidemiologic, and clinical studies evaluating the relationship between soy foods, including soy protein, and weight loss. The authors reported that studies with overweight and obese individuals suggest that soy, as a source of dietary protein, may be used to achieve significant weight loss. However, there is no convincing evidence to show whether soy protein is better than other protein sources to achieve weight loss when prescribed in isocaloric levels.

Three additional studies identified in the NEL review support the conclusion by Cope et al. (2008). No differences in weight loss were found when a soy diet was compared to a traditional low-calorie diet (McVeigh, 2006). Pan et al. (2008) examined the effect of soy protein on risk of metabolic syndrome in a cross-sectional study of older Chinese individuals and found no differences in body weight. Liao et al. (2007) conducted a randomized, controlled trial with obese adults, examining the effect of soy protein on weight loss in obese adults and found no effect. Thus, studies consistently find no unique benefit of soy protein with weight loss.

### ***Soy Protein and Blood Lipids among Adults without Hyperlipidemia***

Soy protein may have small effects on total and LDL-cholesterol in adults with normal or elevated blood lipids, although systematic reviews report inconsistent results. This conclusion is based on four meta-analyses (Harland, 2008; Reynolds, 2006; Weggemans, 2003; Zhan, 2005) and consideration of an additional randomized, controlled trial (Liao, 2007) and a cross-sectional study (Pan, 2008). Results from the meta-analyses are somewhat inconsistent. Harland et al. (2008) concluded that 25 grams of soy protein lowered total cholesterol, LDL cholesterol, and triglycerides, with no change in HDL-cholesterol in adults without hyperlipidemia. Reynolds et al. (2006) suggested that soy protein supplementation (20 to >61 g/d) lowered total cholesterol, LDL-cholesterol, triglycerides, and actually increases HDL cholesterol. Zhan et al. (2005) concluded that soy protein with isoflavones lowered total cholesterol, LDL-cholesterol, triglycerides and had no effect on HDL-cholesterol. In contrast, Weggemans et al. (2003) reported that soy-associated isoflavones and soy protein have no effect on either LDL-cholesterol or HDL-cholesterol. However, unlike others, this review compared soy protein with isoflavones only with studies in which control groups consumed dairy or other animal protein sources. The role of isoflavones in lowering lipids is discussed in many of these reviews, but it remains unclear whether the protein in

soy-associated substances (isoflavones, other phytonutrients or substitution for animal protein) cause lipid lowering.

Liao et al. (2007) reported a significant decrease in total cholesterol and LDL cholesterol in their weight loss study with soy protein, but no changes in triglycerides or HDL cholesterol were observed. A cross-sectional study in China (Pan, 2008) found no relationship between soy protein intake and elevated triglycerides. Overall, conclusions suggest that soy protein may have small effects on total and LDL cholesterol in adults with normal or elevated blood lipids but neither the etiology nor the potential importance of isoflavones in this relationship have been clarified.

### **Question 3: How Do the Health Outcomes of a Vegetarian Diet Compare to that of a Diet which Customarily Includes Animal Products?**

#### **Conclusion**

Limited evidence is available documenting that vegetarian diets protect against cancer. However, it suggests that vegetarian, including vegan, diets are associated with lower BMI and blood pressure. Vegan diets may increase risk of osteoporotic fractures. The effect of vegetarian diets on cardiovascular disease, stroke, and mortality are discussed further in *Part B. Section 2: The Total Diet: Combining Nutrients, Consuming Food*.

#### **Implications**

Most people consume diets containing both animal and plant foods. Few studies exist on the nutritional or health status of vegetarians and/or vegans. Individuals who restrict their diet to plant foods may be at risk of not getting adequate amounts of certain indispensable amino acids because the concentration of lysine, sulfur amino acids, and threonine are sometimes lower in plant than in animal food proteins. Nutrients of concern on vegan diets include calcium, iron, B<sub>12</sub>, zinc, and long-chain *n*-3 fatty acids. Vegetarian diets that include complementary mixtures of plant proteins can provide the same quality of protein as that from animal protein. Education is needed for those designing diets containing complementary proteins for consumers switching to a more plant-based diet. Additionally, individuals consuming vegetarian, particularly vegan, diets should ensure adequate intake of all nutrients.

#### **Review of the Evidence**

##### ***Background***

The nitrogen requirement for adults eating high-quality plant food proteins is not significantly different than animal protein or protein from a mixed diet. Most consumers eat protein from a variety of sources and few cohort studies include enough vegetarians or vegans to draw any conclusions. Also, many self-described vegetarians consume milk products or eggs or even consume



processed foods that contain animal protein. Thus, there is limited accurate data to answer questions about health differences between vegetarians and non-vegetarians.

In general, plant proteins are less digestible than animal proteins, but digestibility can be improved with certain processing methods and food preparation techniques. Vegetarians typically consume less protein than non-vegetarians and Hadded et al. (1999) found that 10 of 25 vegan women had potentially inadequate intakes.

Most available evidence relates to the nutritional content and health effects of the average diet of well-educated vegetarians living in Western countries (Key, 2006). Vegetarian diets are rich in carbohydrates, *n*-6 fatty acids, dietary fiber, carotenoids, folic acid, vitamin C, vitamin E, and magnesium and relatively low in protein, saturated fat, *n*-3 fatty acids, vitamin B<sub>12</sub>, and zinc. Vegans have particularly low intakes of vitamin B<sub>12</sub>, iron and calcium. Most data find little differences in major causes of death or all-cause mortality when comparing vegetarians with non-vegetarians from the same population (Key, 2006b). Animal protein intake was linked to greater muscle mass index in a Finnish study (Aubertin-Leheudre & Adlercreutz, 2009) and there is concern about protein intake during growth and development. Nutrients of concern on vegan diets include calcium, iron, B<sub>12</sub>, zinc, and long-chain *n*-3 fatty acids. Because some vegetarian diets are low in protein, calcium, and other nutrients, research has examined the relationship between plant-based diets and bone health. It is possible to consume complementary plant proteins and have an adequate intake of protein, but education is needed on how to design adequate diets.

We examined studies published since January 2000 with no limits to study design to address these questions. Few cohort studies were available and there were no randomized, controlled trials. A limitation of this area is the small number of vegans and semi-vegetarians in the cohorts studied. For a more in-depth discussion of vegetarian and vegan eating patterns, including review of articles published before 2000 and using additional search strategies, see ***Part B. Section 2: The Total Diet: Combining Nutrients, Consuming Food.***

### ***Health Outcomes of a Vegetarian Diet Compared to a Diet which Customarily Includes Animal Products***

Eighteen studies published since 2000 were reviewed that represented eight countries (Alewaeters, 2005; Appleby, 2002; Appleby, 2007; Baines, 2007; Chen, 2008; Dos Santos Silva, 2002; Grant, 2008; Hung, 2006; Key, 2009a; Key, 2009b; Newby, 2005; Nakamoto, 2008; Rosell, 2006; Spencer, 2003; Teixeira, 2007; Thorpe, 2008; Wang, 2008d; Yen, 2008). Most studies in this review were of a weaker design, including cross-sectional and case-control studies. Only five articles were prospective cohort studies and no RCTs were identified. Six articles provided results from the EPIC study from the United Kingdom, and four studies were conducted in Taiwan. Other countries

represented were the US, Australia, Japan, Sweden, Belgium, and Brazil. Vegetarian diets varied greatly among countries, and classifications of plant-based diets were inconsistent among studies. However, all studies compared the health outcomes observed between individuals who regularly consumed animal products to those who occasionally, rarely, or never consumed animal products.

In the EPIC cohort, vegetarian, particularly vegan, diets were associated with lower BMI and lower levels of obesity than diets that included meat (Spencer, 2003). Similar results were found in the Swedish Mammography Cohort (Newby, 2005). Rosell et al. (2006) reported on 5-year changes in weight in the EPIC cohort by dividing participants into groups based on their eating patterns. Specifically, they examined whether participants maintained the same diet (e.g., vegan) over time, or reverted from a vegan or vegetarian diet to a diet containing meat, or converted from eating meat to a vegetarian or vegan diet. Among those who had not changed their eating patterns over time, the largest weight gain was seen in meat-eaters. The smallest weight gain was observed in participants who converted to a vegetarian or vegan diet, and the highest weight gains were among participants classified as reverted, but mean weight gains were not different than weight gains in meat eaters.

Meat eaters had the highest prevalence of hypertension and vegans the lowest in the EPIC cohort (Appleby, 2002), and vegetarians had lower blood pressure than omnivores in small studies in Taiwan (Chen, 2008) and Brazil (Teixeira, 2007). Studies from Taiwan and Brazil also showed improvement in cardiovascular biomarkers, such as total cholesterol, between individuals consuming vegetarian compared to omnivorous diets (Chen, 2008; Teixeira, 2007; Yen, 2008).

Vegans were found to have a higher risk of fractures than vegetarians and meat eaters in the EPIC cohort, which was related to the lower mean calcium intake in this group (Appleby, 2007). However, those on a vegetarian diet in Taiwan did not differ from non-vegetarians in bone mineral density or risk of osteoporosis (Wang, 2008d). In a review of women from the Adventist Health Study (Thorpe, 2008), greater intake of foods rich in protein, whether from animal or plant sources, was associated with reduced wrist fractures.

Data on cancer are inconsistent with one recent study finding more colorectal cancer in vegetarians compared to meat eaters (Key, 2009a). However, the risk of female breast, prostate, ovarian, and lung cancer were not significantly different between vegetarians and non-vegetarians.

Overall, Key and colleagues (2009b) found no differences in mortality rates between vegetarians and non-vegetarians in the EPIC cohort.

## PROTEIN-RELATED FOOD GROUPS AND HEALTH OUTCOMES

### Question 4: What is the Relationship Between the Intake of Milk and Milk Products and Selected Health Outcomes?

#### Conclusion

Strong evidence demonstrates that intake of milk and milk products provide no unique role in weight control. Moderate evidence indicates that the intake of milk and milk products is linked to improved bone health in children. Limited evidence suggests a positive relationship between the intake of milk and milk products and bone health in adults, but results are inconsistent due to variability in outcomes considered. Moderate evidence shows that intake of milk and milk products are inversely associated with cardiovascular disease. A moderate body of evidence suggests an inverse relationship between the intake of milk and milk products and blood pressure. Moderate evidence shows that milk and milk products are associated with a lower incidence of type 2 diabetes in adults. Limited evidence is available showing intake of milk and milk products are associated with reduced risk of metabolic syndrome. Insufficient evidence is available to assess the relationship between intake of milk and milk products and serum cholesterol levels.

#### Implications

Currently, many children and adults are not consuming adequate amounts of milk and milk products. NHANES 2005-2006 reported that the mean consumption of calcium does not meet the recommended Dietary Reference Intakes for any age group older than age 12. Research since 2004 shows that the under-consumption of milk and milk products may lead to an increase in cardiovascular disease and type 2 diabetes, as well as an increased risk for poor bone health and related diseases.

Consumption of the recommended daily amounts of low-fat or fat-free milk and milk products (2 cups for children ages 2 to 8 years, 3 cups for those ages 9 years and older) should be promoted. It is especially important to establish milk drinking in young children, as those who consume milk as children are more likely to do so as adults. Those who choose not to consume milk and milk products should include other foods in the diet that contain the nutrients provided by the milk and milk products group, protein, calcium, potassium, magnesium, Vitamin D, and Vitamin A.

#### Review of the Evidence

##### ***Background***

In addition to providing protein, milk and milk products are a source of many important nutrients, including calcium, potassium, magnesium, vitamin D, and vitamin A (DGAC, 2005; p. 183). This topic is further discussed in *Part D. 2 Nutrient Adequacy*. Previous research, as reviewed by the 2005 DGAC, has established the positive relationship between milk and milk products and bone mineral content or bone mineral density. Also milk product consumption has been linked with overall diet quality and the adequacy of many nutrients (DGAC, 2005, p. 183).

Calcium maintains the strength and density of the bones, with 99 percent of the calcium in the body found in bones and teeth. Bone undergoes constant remodeling, a process in which existing bone is broken down and replaced with new bone. Without sufficient calcium in the diet, there is inadequate formation of new bone, resulting in osteoporosis or other bone disease. (IOM, 1997) When dietary intake of calcium is too low, the body will draw upon the calcium stored in the bones which can lead to low bone mass.

Some of the most bioavailable sources of calcium are in milk and milk products. Calcium also is found in dark green vegetables, whole grains, beans and soy protein, but it is not as well absorbed due to the oxalic or phytic acid found in these foods. Other foods may be fortified with calcium and numerous calcium supplements are available. However, calcium naturally occurring in foods is the recommended source. Absorption of calcium varies based on a number of factors, such as the amount consumed at any one time, the age of the individual, and other foods consumed including dietary fiber, phytic acid, and oxalic acid. Calcium status is also affected by the intake of vitamin D, phosphorus, and protein. Vitamin D is especially important in the absorption of calcium.

Dietary guidance has recommended reduction in dairy fats because of they contain high levels of saturated fats and cholesterol. In general, studies show that the higher the saturated fat intake is, the higher the serum total and LDL-cholesterol concentrations will be. Serum total and LDL-cholesterol concentrations have a positive linear relationship with the risk of CHD or mortality from CHD. Fat-free dairy products are devoid of saturated fats, but still contain protein, calcium, and the other nutrients found in milk products.

The WCRF/AICR report (WCRF/AICR, 2007) examined the relationship between milk and dairy products and the risk of cancer. The WCRF/AICR Panel concluded that milk probably protects against colorectal cancer, and limited evidence suggests that milk protects against bladder cancer. There is limited evidence suggesting that high consumption of milk and dairy products is a cause of prostate cancer.

The relationship between milk intake and weight management was reviewed in 2005 and it was reported that there was insufficient data to conclude that milk and milk products have an impact on weight. However the importance of milk and milk products in the diet was emphasized. The review provided below provides an update to the literature reviewed by the 2005 DGAC, focusing on studies published since 2004 that have examined milk and milk products and their impact alone on health outcomes.

### ***Milk and Milk Products and Bone Health***

Research since 2004 indicates that the intake of milk and milk products is linked to improved bone health in children. Results in adults are mixed. The conclusion reached for this question is

based on a review of three systematic reviews or meta-analyses (Alvarez-Leon, 2006; Huncharek, 2008; Kanis, 2005), three primary research studies conducted since the reviews (Budek, 2007; Kristensen, 2005; McCabe, 2004), one longitudinal study (Rockell, 2005), one case-control study (Konstantynowicz, 2007), and one cross-sectional study (Al-Zahrani, 2006), all published since 2004.

The results of the systematic reviews and meta-analyses are inconsistent when children and adults are considered together. In a meta-analysis focused on children, Huncharek et al. (2008) examined the relationship between dairy and calcium intake and bone mineral content. Their review of 21 studies concluded that increased dairy/calcium intake, with or without vitamin D supplementation, results in significantly higher total body and lumbar spine bone mineral content among children with low baseline intakes of dairy, calcium, and/or vitamin D. In a small, short-term study among prepubertal boys consuming equal amounts of protein, Budek et al. (2007) found that a high intake of milk, but not meat, decreased bone turnover. However, the relevance of reduced turnover for peak bone mass is unclear.

A longitudinal study conducted in New Zealand (Rockell, 2005), assessed 2-year changes in bone and body composition in young children with a history of prolonged milk avoidance. The authors concluded that young milk avoiders demonstrated persistent height reduction, overweight, and osteopenia at the ultradistal radius and lumbar spine over 2 years of follow-up.

Alvarez-Leon et al. (2006) reviewed literature on the associations between the consumption of dairy products and health outcomes, including two review papers on bone health. They concluded that there is weak evidence of the protective capacity of dairy products on bone health, noting that limitations in studies examining this relationship make it difficult to make firm conclusions about the effect of dairy products on bone health.

Kanis et al. (2005) reviewed six prospectively studied cohorts from European, Australian and Canadian research. They examined calcium intake, measured by milk consumption, and its association with the risk of fracture. They found no significant relationship between low intake of calcium and fracture risk. This study did not include other sources of dietary calcium besides milk and did not account for variations in vitamin D intake or sunlight exposure. Therefore, the authors caution that these findings should not be misinterpreted as suggesting that calcium is not causally related to fracture risk nor that calcium does not play a role in fracture prevention.

Results from three intervention studies supported the role of dairy products in bone health. McCabe et al. (2004) found that calcium supplementation protected study participants from bone loss and that higher dairy product consumption was associated with greater hip bone mineral density in men, but not in women. In a small study of Caucasian males who replaced milk with cola beverages in their diet for 10 days, Kristensen et al. (2005) concluded that replacement of cola for milk results in a low calcium intake, which may negatively affect bone health.

In summary, these reviews support that calcium and milk and milk products play an important role in bone mineral content in children. Results from adult trials are mixed.

### ***Milk and Milk Products and Cardiovascular Disease***

Recent studies report that intake of milk and milk products are protective against cardiovascular disease. The conclusion reached for this question is based on review of two systematic reviews/meta-analyses (Alvarez-Leon, 2006; Elwood, 2008) and one case-control study (Kontogianni, 2006).

Alvarez-Leon et al. (2006) systematically reviewed papers on the associations between consumption of dairy products and health outcomes, including CVD. The systematic review of these papers found an inverse association between the intake of dairy products and stroke.

Elwood et al. (2008) performed a systematic review and meta-analysis to investigate the literature on milk and dairy consumption and risk of vascular disease. The final review included 15 prospective studies on ischemic heart disease and stroke and 4 case-control studies on myocardial infarction. The data showed a reduction in risk associated with the highest level of milk consumption for myocardial infarction. There was also a reduction of about 10 to 15 percent in the incidence of ischemic heart disease and a 20 percent reduction in stroke events in the individuals who had reported drinking the most milk, relative to those drinking the least milk within each cohort. The authors concluded that the data provides support for the beneficial effects of milk and dairy consumption on risk for cardiovascular disease.

Finally, in a case-control study, Kontogianni et al. (2006) examined the association between dairy consumption and the prevalence of a first, non-fatal event of an acute coronary syndrome in Greek adults. They reported an inverse relationship between dairy product consumption and the odds of having acute coronary syndrome. An increase of one portion of a dairy product per week was associated with a 12 percent lower likelihood of having acute coronary syndrome.

### ***Milk and Milk Products and Type 2 Diabetes***

In a recent systematic review with meta-analysis (Elwood, 2008) of four prospective studies on diabetes, relative risk for T2D was estimated to be 10 percent lower in people who had a high milk intake relative to those with low consumption.

### ***Milk and Milk Products and Metabolic Syndrome***

Intake of milk and milk products is associated with reduced risk of metabolic syndrome and may even be protective in certain population groups. The conclusion reached for this question is

based on one systematic review with meta-analysis (Elwood, 2008), one prospective cohort study (Snijder, 2008), and three cross-sectional studies (Azadbakht, 2005; Beydoun, 2008; Ruidavets, 2007).

Elwood et al. (2008) performed a systematic review and meta-analysis and the data showed a reduction in risk associated with the highest level of milk consumption for metabolic syndrome (RR=0.74; 95% CI: 0.64, 0.84) compared to the risk in those with low consumption.

Snijder et al. (2008) conducted a prospective cohort study investigating the association between dairy consumption and changes in weight and metabolic disturbances. The authors concluded that dairy consumption was not associated with changes in metabolic variables in a Dutch elderly population. Three cross-sectional studies (Azadbakht, 2005; Beydoun, 2008; Ruidavets, 2007) looked at milk and milk product consumption and metabolic syndrome. Azadbakht et al. (2005) found an inverse relationship between dairy consumption and metabolic syndrome, and the French study by Ruidavets et al. (2007) determined that the intake of dairy products was associated with a lower probability of insulin resistance syndrome. No significant associations between whole milk (per 100 g), low-fat milk (per 100 g), or skim milk (per 100 g) and metabolic syndrome were observed in a study of NHANES 1999-2004 data (Beydoun, 2008).

### ***Milk and Milk Products and Blood Cholesterol***

Few studies have been conducted on the relationship between the intake of milk and milk products and blood cholesterol, although the high saturated fat content of milk fat would theoretically support a positive association with whole milk products. Three articles published since 2004 were reviewed on this topic: a randomized trial (Bowen, 2005), a prospective cohort study (Snijder, 2008) and a cross-sectional study (Houston, 2008).

In the dairy product feeding study (Bowen, 2005), intake of milk products was associated with reduced blood cholesterol, although this was associated with weight loss in the study. In a study of Dutch elderly (Snijder, 2008), baseline dairy consumption was not associated with changes in serum lipid levels over 6.4 years. A study of NHANES III data found that in women, more frequent cheese consumption was associated with higher HDL-cholesterol and lower LDL-cholesterol ( $p$  for trend  $< 0.05$ ), while in men, more frequent cheese consumption was associated with higher BMI, waist circumference, HDL-cholesterol, and LDL-cholesterol ( $p$  for trend  $< 0.05$ ). Thus, intake of milk and milk products in recent studies did not always show expected increases in total blood cholesterol, and may be linked to increased HDL-cholesterol.

### ***Milk and Milk Products and Blood Pressure***

Based on the current review of research of literature published since 2004, there is little evidence that supports an independent relationship between the intake of milk and milk products and blood pressure. This conclusion is based on one systematic review (Alvarez-Leon, 2006), one RCT (Bowen, 2005), six prospective cohort studies (Alonso, 2005; Engberink, 2009a; Engberink, 2009b; Snijder, 2008; Toledo, 2009; Wang, 2008a), and five cross-sectional studies (Azadbakht, 2005; Beydoun, 2008; Djousse, 2006; Houston, 2008; Ruidavets, 2006).

The systematic review by Alvarez-Leon et al. (2006) concluded that an inverse association exists between the intake of dairy products and hypertension. In the Bowen et al. (2005) RCT, the authors determined that weight loss following energy-restricted, high-protein diets is not affected by dietary calcium or protein source. Also, weight loss, not dietary calcium, was shown to improve blood pressure.

Results were reviewed from six prospective studies conducted in the Netherlands, Spain and the US. In the Women's Health Study (Wang, 2008a) decreased risk of hypertension was associated with low-fat dairy products, calcium and vitamin D. In the SUN cohort in Spain, Alonso et al. (2005) reported a 54 percent reduction in hypertension in participants with the highest consumption of low-fat dairy products compared to those with the lowest consumption, and they found no association between whole-fat dairy or total calcium intake and incident hypertension. Likewise, the Toledo et al. (2009) study in Spain found no significant relationship between high-fat dairy and blood pressure, but blood pressure was significantly lower among the highest consumers of low-fat dairy products.

In general, studies from the Netherlands did not show as strong a relationship between the intake of milk and milk products and blood pressure. Engberink et al. (2009a) followed more than 20,000 participants for 5 years in the Netherlands and concluded that dairy intake has little effect on population blood pressure. Snijder et al. (2008) concluded that dairy consumption was not associated with changes in metabolic variables in their study with a Dutch elderly population. Engberink et al. (2009b) followed older Dutch participants for 6 years, and they concluded that low-fat dairy may be related to hypertension prevention, but high-fat dairy and cheese did not show the same effect.

Five cross-sectional studies (Azadbakht, 2005; Beydoun, 2008; Djousse, 2006; Houston, 2008; Ruidavets, 2006) conducted in Iran, France, and the US also were reviewed, and all showed some positive impact of milk and milk product consumption on blood pressure, although the results were not consistent for all population groups. Using data from NHANES 1999-2004, Beydoun et al. (2008) found that among all study participants, and among men in particular, fluid milk was inversely related to blood pressure (systolic and diastolic), and yogurt was associated with better systolic blood



pressure. In contrast, cheese was positively associated with systolic blood pressure. Using data on the intake of cheese from NHANES III, Houston et al. (2008) found that systolic blood pressure was not different across categories of cheese consumption, but diastolic blood pressure was higher among men in the highest category of cheese consumption compared to non-consumers. In a cross-sectional analysis of almost 5,000 participants from the National Heart, Lung, and Blood Institute Family Heart Study, there was an inverse association between dairy intake and the prevalence of hypertension that was independent of calcium intake and seen mainly among participants consuming less saturated fat. A cross-sectional analysis of 1,500 participants in Iran (Azadbakht, 2005) showed an inverse relationship between dairy consumption and hypertension. Finally, the French study by Ruidavets et al. (2006) concluded that the consumption of dairy products may be associated with reduced blood pressure.

Evaluating the research on this topic is complicated by the types of milk products consumed in the various studies, potential confounding with calcium intakes from other food sources, and the known relationship of blood pressure to weight loss.

### ***Milk and Milk Product Intake and Body Weight***

The Committee reviewed 18 studies conducted since 2004 that examined the link between the intake of milk and milk products and body weight and concluded that evidence supporting the hypothesis of a relationship between intake of milk and milk products and decreased body weight is not convincing. This conclusion is based on one systematic review (Lanou, 2008), one RCT (Bowen, 2005), four prospective cohort studies (Rajpathak, 2006; Rosell, 2006; Snijder, 2008; Vergnaud, 2008), and eight cross-sectional studies (Azadbakht, 2005; Beydoun, 2008; Brooks, 2006; Houston, 2008; Marques-Vidal, 2006; Mirmirin, 2005; Murakami, 2006; O'Neil 2009). The Committee also reviewed three studies that looked at energy intake as an outcome (Dove, 2009; Harper, 2007; Hollis, 2007), and one study (Olsen, 2007) that addressed pregnancy.

Lanou et al. (2008) reviewed the body of evidence on the effect of dairy product or calcium intake, with or without energy restriction, on body weight or adiposity. Of the 49 randomized clinical trials reviewed, 42 found no effect on weight of dairy or calcium consumption, and only 4 trials showed a potential effect of dairy products or calcium on weight loss. Of the 16 clinical trials, 15 showed no difference in body fat change between consumers of high and low levels of dairy or calcium. One study found greater fat loss among high-dairy consumers compared to low-dairy consumers. Overall, their review does not support a connection between dairy or calcium consumption and weight or fat loss.

In the Bowen et al. (2005) RCT, the effects on weight, body composition, metabolic parameters, and risk markers of two isocaloric, energy-restricted high-protein diets that differed in

dietary calcium and protein source on weight loss and body composition in healthy, overweight adults were compared. The authors concluded that weight loss following energy-restricted, high protein diets is not affected by dietary calcium or protein source.

The following four prospective cohort studies did not strongly support the hypothesis that increasing milk and milk products would result in a decrease in weight. Rajpathak et al. (2006) evaluated the association between calcium and dairy intakes and 12-year weight change among men in the US. Their results indicate that increasing calcium or dairy consumption is not associated with lower long-term weight gain in men. Rosell et al. (2006) examined the association between changes in dairy product consumption and self-reported weight change over 9 years among women. They concluded that the association between the intake of dairy products and weight gain differed according to the type of dairy product and the body weight status at baseline. Snijder et al. (2008) investigated the association between dairy consumption and 6.4-year changes in weight and metabolic disturbances in an elderly Dutch population. They concluded that higher dairy consumption does not protect against weight gain and the development of metabolic disturbances over time. Vergnaud et al. (2008) investigated the relationship between dairy consumption and calcium intake with 6-year changes in body weight and waist circumference in a French population. The authors concluded that sex, overweight status at baseline, and type of dairy product influences the associations between dairy product consumption and anthropometric changes. Eight cross-sectional studies (Azadbakht, 2005; Beydoun, 2008; Brooks, 2006; Houston, 2008; Marques-Vidal, 2006; Mirmirin, 2005; Murkami, 2006; O'Neil, 2009) were reviewed, and were more likely to support that calcium and/or dairy consumption was related to lower BMI.

Other studies included in the review measured whether consumption of milk or milk products was related to energy intake as an outcome. Dove et al. (2009) concluded that consumption of skim milk, in comparison with a fruit drink, leads to increased perceptions of satiety and to decreased energy intake at a subsequent meal. Harper et al. (2007) conducted a randomized cross-over design study to compare the effect on appetite and energy intake of consuming either a sugar-sweetened beverage (cola) or chocolate milk drink. The authors concluded that consuming chocolate milk increased subjective ratings of satiety and fullness compared with cola and decreased hunger and later consumption of food. However, this enhanced satiety did not translate into differences in ad libitum energy intake. Hollis and Mattes (2007) assessed the effect of daily intake of one or three portions of dairy foods on energy intake and appetite. The authors concluded that increasing dairy consumption from one to three portions each day led to increased energy intake. Thus, dairy foods may have some benefit for satiety when compared to fruit drinks, but increased consumption of any extra calories (versus substitution), including dairy products, will lead to increased energy intake.

Olsen et al. (2007) examined whether milk consumption during pregnancy is associated with greater infant size at birth in the Danish National Birth Cohort. Milk consumption was inversely

associated with the risk of small-for-gestational age birth and directly with both large-for-gestational age birth and mean birth weight.

## **Question 5: What is the Relationship between the Intake of Cooked Dry Beans and Peas and Selected Health Outcomes?**

### **Conclusion**

Limited evidence exists to establish a clear relationship between intake of cooked dry beans and peas and body weight. There is limited evidence that intake of cooked dry beans and peas lowers serum lipids. Limited evidence is available to determine a relationship between the intake of cooked dry beans and peas and type 2 diabetes.

### **Implications**

Legumes and soybeans, including dried beans and peas, are typically recommended foods because of their content of dietary fiber, protein, vitamins, and minerals (Mesina, 1999). Because soybeans are particularly high in isoflavones, a phytoestrogen, they have been more extensively studied than other legumes. Legumes are also promoted as a complementary protein source to grains since legumes are low in methionine and grains are low in lysine. Thus, legumes play an important role in vegan diets for enhancing protein quality. They may also provide a beneficial contribution to the general population in part to increase total vegetable consumption and dietary fiber intake.

### **Review of the Evidence**

#### ***Background***

Beans and peas are sources of protein, dietary fiber, minerals, and vitamins. As dietary fiber is linked to lower body weight, intake of beans and peas would be expected to also be linked to lower body weight. Consumption of dry beans, peas, and lentils is low in the US, with only 8 percent of adults consuming dry beans and peas on any one day (Mitchell, 2009), making it difficult to see relationships in existing cohorts. Dry beans and peas are concentrated sources of soluble dietary fiber, which is known to lower serum lipids. Vegetable protein from legumes has also been found to lower serum lipids, and the US has an existing health claim for the ability of soy protein to lower serum lipids. Most of the research in the lipid-lowering benefits of soy protein was done in hyperlipidemic individuals.

Unfortunately, few consumers include cooked dry beans and peas in their daily diet, and soy products are also not commonly consumed in the US. This makes it difficult to determine the protectiveness of intake of cooked dry beans and peas and soy when most prospective cohort studies include few participants who are consuming these products.

Soluble fibers are thought to slow absorption of carbohydrates and lower the glycemic index of foods. In the original studies of glycemic index, intake of legumes was associated with the lowest glucose response. Independent of glycemic index and load, cooked dry beans and peas show promise for use in control of blood glucose for individuals with T2D.

We examined studies from January 2000 to present for this review. Overall, our review suggests that little evidence is available on the relationship between intake of cooked dry beans and peas and health outcomes.

### ***Cooked Dry Beans and Peas and Body Weight***

The few intervention studies on the relationship between intake of cooked dry beans and peas (not including soy) and body weight find mixed results. This conclusion is based on the review of one meta-analysis (Anderson and Major, 2002), one systematic review (Williams, 2008), four trials (Crujeiras, 2007; Pittaway, 2006; Pittaway, 2007; Pittaway, 2008), and one cross-sectional study (Papanikolaou, 2008) for beans and peas. Additionally, the Committee reviewed one systematic review (Cope, 2008) and one cohort study (Maskarinec, 2008) specifically pertaining to soy foods.

In a meta-analysis of 11 studies, Anderson and Major (2002) found that the intake of non-soy legumes was associated with decreased body weight. In a systematic review examining the role of whole grains and legumes in preventing and managing overweight and obesity, Williams et al. (2008) concluded that weight loss is achievable with energy-controlled diets high in legumes but felt there was insufficient evidence to draw conclusions about the protective effect of legumes on weight.

Results from feeding trials with beans and peas are mixed, but diet treatments with beans and peas are generally no more successful in weight loss than the control or comparison treatment. In two randomized crossover trials comparing chickpea- to wheat-supplemented diets, no significant differences between dietary interventions was observed (Pittaway, 2006; Pittaway, 2007). In a study that included chickpea-supplemented ad libitum, a non-significant decrease in body weight was observed during the chickpea phase compared to the control phase (Pittaway, 2008). In a RCT comparing hypocaloric diets high in non-soybean legumes to a diet without legumes, both groups lost weight with greater weight loss achieved by those consuming legumes. A comparison of bean eaters from NHANES 1999-2002 suggest that bean consumers had lower body weights, and waist circumferences in comparison to non-consumers (Papanikolaou, 2008).

In a systematic review of soy foods and weight loss, Cope et al. (2008) concluded that there was limited evidence to support the hypothesis that soy foods increase weight loss when fed at isocaloric levels or that soy foods affect caloric intake when included as part of a diet. In a cohort study, women consuming more soy during adulthood had a lower BMI, but the relation was primarily observed for Caucasian and postmenopausal participants (Maskarinec, 2008).

### ***Cooked Dry Beans and Peas and Cardiovascular Outcomes***

Limited evidence exists that dry beans and peas have unique abilities to lower serum lipids; most of the lipid lowering seen in studies is related to the soluble fiber content of these products. The conclusion reached for this question is based on the review of one meta-analysis (Anderson and Major, 2002), five trials (Crujeiras, 2007; Finley, 2007; Pittaway, 2006; Pittaway, 2007; Pittaway, 2008), two prospective cohort studies (Bazzano, 2001; Steffen, 2005), one case-control study (Kabagambe, 2005), and one cross-sectional study (Papanikolaou, 2008). The Committee also considered one randomized crossover trial (Welty, 2007), one prospective cohort study (Kokubo, 2007), and one longitudinal study (Nagata, 2000) regarding soy foods.

Anderson and Major (2002) quantitatively analyzed changes in serum lipoprotein levels resulting from intake of non-soya pulses. The authors concluded that regular consumption of pulses may have important protective effects on risk for CVD, including decreases in serum cholesterol, LDL-cholesterol, and triacylglycerols and increases in HDL-cholesterol.

In the intervention studies, dry beans and peas lowered serum lipids as expected based on soluble fiber content. In a series of studies including the daily consumption of more than 100 g of chickpeas per day for 5 to 12 weeks, Pittaway et al. (2006, 2007, 2008) observed improvements in serum total cholesterol and LDL-cholesterol compared to a control diet without legumes. Similar improvements in total cholesterol were observed following an 8-week weight loss intervention that included non-soybean legumes four days each week, and the decrease in total cholesterol was directly correlated with increased fiber intake (Crujeiras, 2007).

Bazzano et al. (2001) found a strong and independent inverse association between dietary intake of legumes and risk of CHD in the Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS), which is a prospective cohort study of the First National Health and Nutrition Examination Survey (NHANES I) from 1971 to 1975. Legume consumption four or more times per week compared with less than once a week was associated with a 22 percent lower risk of CHD and an 11 percent lower risk of CVD. In the Coronary Artery Risk Development in Young Adults (CARDIA) Study (Steffen, 2005), tertiles of legume intake were less than 0.1, 0.1 to 0.2, and more than 0.2 times per day, supporting extremely low usual intake of legumes. The authors noted that limited consumption of legumes and insufficient statistical power precluded definitive conclusions from being drawn about the relationship between intake of legumes and elevated blood pressure. However, it is unclear whether null findings were due to the lack of association or limited range in consumption. In a case-control study in Costa Rica, Kabagambe et al. (2005) observed an inverse association between myocardial infarction and the intake of one serving of beans per day (1/3 cup of cooked beans) in adjusted analyses. However, no additional benefit was observed with more than one serving per day.

In more than 12 years of follow-up of the Japan Public Health Center-Based Study Cohort I (Kokubo, 2007), investigators saw a decrease in the risk of myocardial infarction, cerebral infarction, and CVD mortality among women consuming soy at least five times per week compared to those consuming soy zero to two times per week. However, no associations were observed for men. In a longitudinal study in Japan, Nagata et al. (2000) also observed an inverse correlation between soy product intake and heart disease mortality in women, but not men.

In a randomized crossover trial in which hypertensive, prehypertensive, and normotensive postmenopausal women consumed the Therapeutic Lifestyle Changes (TLC) diet alone or with 1/2 cup unsalted soy nuts (25 g soy protein) replacing 25 g of non-soy protein, benefits to blood pressure and LDL-cholesterol were greater for the hypertensive women than the normotensive participants (Welty, 2007).

### ***Cooked Dry Beans And Peas And Type 2 Diabetes Mellitus***

Evidence is insufficient to determine a relationship between dry beans and peas and T2D. Only one study was found that measured the relationship between dry beans and peas and T2D. The association between the consumption of legume and soy foods and T2D was examined over an average follow-up of approximately 5 years in the Shanghai Women's Health Study (Villegas, 2005). Average daily intake of individual food items was combined for the following food groups: total legumes and three mutually exclusive groups [soybeans (dried and fresh), peanuts, and other legumes]. The median intake of total legumes was 30.5 g/d, for soybeans was 11.0 g/d, for peanuts was 0.7 g/d, and for other legumes was 15.5 g/d. Total legume consumption and consumption of soybeans and other legumes were each associated with a decrease in risk of T2D.

## **Chapter Summary**

Proteins are unique because they provide both essential amino acids to build body proteins and are a calorie source. Because the RDA of protein for any person is based on their ideal body weight (0.8 g protein/kg body weight/day for ages 19 and above), lower-calorie diets require higher percentage of protein intake. Protein quality varies greatly and is dependent on the amino acid composition of the protein and the digestibility. Animal sources of protein, including meat, fish, milk, and egg, are the highest quality proteins. Plant proteins can be combined to form more complete proteins if combinations of legumes and grains are consumed. As most Americans consume too many calories, the percentage of calories from protein may be higher – up to 35 percent of calories can come from protein on very low calorie diets. Higher-protein diets tend to

assist in initial weight loss, but long term studies of weight loss or maintenance of weight loss find no differences among diets lower or higher in protein.

## Needs for Future Research

1. Develop standardized definitions for vegetable proteins and improve assessment methods for quantifying vegetable protein intake to help clarify outcomes in epidemiologic studies in this area.

**Rationale:** Assessing vegetarian eating patterns and their protein content is complex and current methodologies do not capture critical variations. Therefore, investigators' ability to quantify any possible association with health benefits is limited. Better standardized definitions and improved assessment methods will improve the ability to quantify health benefits associated with consumption of vegetable protein.

2. Develop better methods of conducting cohort studies of populations consuming plant-based diets compared to animal based diets, including defined classifications of vegetarian and "near vegetarian" eating patterns and more specific impacts of dried beans and peas on health.

**Rationale:** Large US cohorts do not include enough vegetarians and vegans to make comparisons on health outcomes including weight control and blood pressure. Widespread public interest and possible public health impacts of this dietary pattern raise the priority for this research.

3. Conduct studies of potential limitations of plant-based diet for key nutrients, including calcium, iron, vitamin B<sub>12</sub>, and protein quality, especially in children and the elderly.

**Rationale:** These data are needed to determine whether vegan children require dietary supplements to attain adequate nutrient status and growth.

4. Examine the role of dairy products in lipid profiles, especially through intervention trials in which all types of dairy products, both low and high fat, are fed. Bioactive components that alter serum lipid levels may be contained in milk fat.

**Rationale:** Consumption of milk products may not have predictable effect on serum lipids, weight control and metabolic syndrome. The ability of dairy consumption to increase HDL levels and their effect on weight gain or weight loss and metabolic syndrome is also of widespread public health interest and worthy of additional study.

5. Develop and investigate potential biomarkers for objective assessment of vegetable protein intake.

**Rationale:** Few measures of protein status exist in healthy individuals, so it is difficult to compare protein status of participants in cohort studies with diverse protein intakes.

6. Develop better assessment tools to classify vegetarian patterns in epidemiologic studies.

**Rationale:** No assessment methods are currently available to classify participants into the wide range of vegetarian eating patterns.

7. Conduct randomized controlled trials to answer the question whether intake of dairy products alters blood pressure.

**Rationale:** Results from prospective studies are inconsistent and suggest that many other variables that affect blood pressure, such as weight loss and other nutrients, will make associations difficult to determine.

8. Ensure that prospective cohort studies continue to track the association between intake of dairy products and metabolic syndrome.

**Rationale:** Evidence to date does not suggest that high fat dairy products are more likely than low fat dairy products to induce metabolic syndrome. Whether there are other protective compounds in milk products, such as calcium, protein, fatty acids, etc. that provide protection requires further research.



## References

- Alewaeters K, Clarys P, Hebbelinck M, Deriemacker P, Clarys JP. Cross-sectional analysis of BMI and some lifestyle variables in Flemish vegetarians compared with non-vegetarians. *Ergonomics*. 2005;48(11-14):1433-44.
- Alonso A, Beunza JJ, Bes-Rastrollo M, Pajares RM, Martínez-González MA. Vegetable protein and fiber from cereal are inversely associated with the risk of hypertension in a Spanish cohort. *Arch Med Res*. 2006;37(6):778-86.
- Alonso A, Beunza JJ, Delgado-Rodríguez M, Martínez JA, Martínez-González MA. Low-fat dairy consumption and reduced risk of hypertension: the Seguimiento Universidad de Navarra (SUN) cohort. *Am J Clin Nutr*. 2005;82(5):972-9.
- Alvarez-León EE, Román-Viñas B, Serra-Majem L. Dairy products and health: a review of the epidemiological evidence. *Br J Nutr*. 2006;96 Suppl 1:S94-9.
- Al-Zahrani MS. Increased intake of dairy products is related to lower periodontitis prevalence. *J Periodontol*. 2006;77(2):289-94.
- Anderson JW, Major AW. Pulses and lipaemia, short- and long-term effect: potential in the prevention of cardiovascular disease. *Br J Nutr*. 2002;88 Suppl 3:S263-71.
- Appleby P, Roddam A, Allen N, Key T. Comparative fracture risk in vegetarians and nonvegetarians in EPIC-Oxford. *Eur J Clin Nutr*. 2007;61(12):1400-6. Epub 2007 Feb 7.
- Appleby PN, Davey GK, Key TJ. Hypertension and blood pressure among meat eaters, fish eaters, vegetarians and vegans in EPIC-Oxford. *Public Health Nutr*. 2002;5(5):645-54.
- Azadbakht L, Mirmiran P, Esmailzadeh A, Azizi F. Dairy consumption is inversely associated with the prevalence of the metabolic syndrome in Tehranian adults. *Am J Clin Nutr*. 2005;82(3):523-30.
- Baines S, Powers J, Brown WJ. How does the health and well-being of young Australian vegetarian and semi-vegetarian women compare with non-vegetarians? *Public Health Nutr*. 2007;10(5):436-42.
- Bazzano LA, He J, Ogden LG, Loria C, Vupputuri S, Myers L, Whelton PK. Legume consumption and risk of coronary heart disease in US men and women: NHANES I Epidemiologic Follow-up Study. *Arch Intern Med*. 2001;161(21):2573-8.
- Beydoun MA, Gary TL, Caballero BH, Lawrence RS, Cheskin LJ, Wang Y. Ethnic differences in dairy and related nutrient consumption among US adults and their association with obesity, central obesity, and the metabolic syndrome. *Am J Clin Nutr*. 2008;87(6):1914-25.
- Bowen J, Noakes M, Clifton PM. Effect of calcium and dairy foods in high protein, energy-restricted diets on weight loss and metabolic parameters in overweight adults. *Int J Obes (Lond)*. 2005;29(8):957-65.

Brooks BM, Rajeshwari R, Nicklas TA, Yang SJ, Berenson GS. Association of calcium intake, dairy product consumption with overweight status in young adults (1995-1996): the Bogalusa Heart Study. *J Am Coll Nutr.* 2006;25(6):523-32.

Budek AZ, Hoppe C, Michaelsen KF, Mølgaard C. High intake of milk, but not meat, decreases bone turnover in prepubertal boys after 7 days. *Eur J Clin Nutr.* 2007;61(8):957-62. Epub 2007 Jan 17.

Chao A, Thun MJ, Connell CJ, McCullough ML, Jacobs EJ, Flanders WD, Rodriguez C, Sinha R, Calle EE. Meat consumption and risk of colorectal cancer. *JAMA.* 2005;293(2):172-82.

Chen CW, Lin YL, Lin TK, Lin CT, Chen BC, Lin CL. Total cardiovascular risk profile of Taiwanese vegetarians. *Eur J Clin Nutr.* 2008;62(1):138-44. Epub 2007 Mar 14.

Cho E, Chen WY, Hunter DJ, Stampfer MJ, Colditz GA, Hankinson SE, Willett WC. Red meat intake and risk of breast cancer among premenopausal women. *Arch Intern Med.* 2006;166(20):2253-9.

Cope MB, Erdman JW Jr, Allison DB. The potential role of soyfoods in weight and adiposity reduction: an evidence-based review. *Obes Rev.* 2008;9(3):219-35.

Cross AJ, Leitzmann MF, Gail MH, Hollenbeck AR, Schatzkin A, Sinha R. A prospective study of red and processed meat intake in relation to cancer risk. *PLoS Med.* 2007;4(12):e325.

Cross AJ, Peters U, Kirsh VA, Andriole GL, Reding D, Hayes RB, Sinha R. A prospective study of meat and meat mutagens and prostate cancer risk. *Cancer Res.* 2005;65(24):11779-84.

Crujeiras AB, Parra D, Abete I, Martínez JA. A hypocaloric diet enriched in legumes specifically mitigates lipid peroxidation in obese subjects. *Free Radic Res.* 2007;41(4):498-506.

Djoussé L, Gaziano JM, Buring JE, Lee IM. Egg consumption and risk of type 2 diabetes in men and women. *Diabetes Care.* 2009;32(2):295-300. Epub 2008 Nov 18.

Djoussé L, Gaziano JM. Egg consumption in relation to cardiovascular disease and mortality: the Physicians' Health Study. *Am J Clin Nutr.* 2008;87(4):964-9.

Djoussé L, Pankow JS, Hunt SC, Heiss G, Province MA, Kabagambe EK, Ellison RC. Influence of saturated fat and linolenic acid on the association between intake of dairy products and blood pressure. *Hypertension.* 2006;48(2):335-41.

Dos Santos Silva I, Mangtani P, McCormack V, Bhakta D, Sevak L, McMichael AJ. Lifelong vegetarianism and risk of breast cancer: a population-based case-control study among South Asian migrant women living in England. *Int J Cancer.* 2002;99(2):238-44.

Dove ER, Hodgson JM, Puddey IB, Beilin LJ, Lee YP, Mori TA. Skim milk compared with a fruit drink acutely reduces appetite and energy intake in overweight men and women. *Am J Clin Nutr.* 2009;90(1):70-5. Epub 2009 May 27.

- Elliott P, Stamler J, Dyer AR, Appel L, Dennis B, Kesteloot H, Ueshima H, Okayama A, Chan Q, Garside DB, Zhou B. Association between protein intake and blood pressure: the INTERMAP Study. *Arch Intern Med.* 2006;166(1):79-87.
- Elwood PC, Givens DI, Beswick AD, Fehily AM, Pickering JE, Gallacher J. The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer. *J Am Coll Nutr.* 2008;27(6):723S-34S.
- Engberink MF, Geleijnse JM, de Jong N, Smit HA, Kok FJ, Verschuren WM. Dairy intake, blood pressure, and incident hypertension in a general Dutch population. *J Nutr.* 2009a;139(3):582-7. Epub 2009 Jan 21.
- Engberink MF, Hendriksen MA, Schouten EG, van Rooij FJ, Hofman A, Witteman JC, Geleijnse JM. Inverse association between dairy intake and hypertension: the Rotterdam Study. *Am J Clin Nutr.* 2009b;89(6):1877-83. Epub 2009 Apr 15.
- English DR, MacInnis RJ, Hodge AM, Hopper JL, Haydon AM, Giles GG. Red meat, chicken, and fish consumption and risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev.* 2004;13(9):1509-14.
- Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride.* Washington, DC: National Academy Press, 1997.
- Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids.* Washington, DC: The National Academies Press; 2005.
- Ferrucci LM, Cross AJ, Graubard BI, Brinton LA, McCarty CA, Ziegler RG, Ma X, Mayne ST, Sinha R. Intake of meat, meat mutagens, and iron and the risk of breast cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Br J Cancer.* 2009;101(1):178-84. Epub 2009 Jun 9.
- Finley JW, Burrell JB, Reeves PG. Pinto bean consumption changes SCFA profiles in fecal fermentations, bacterial populations of the lower bowel, and lipid profiles in blood of humans. *J Nutr.* 2007;137(11):2391-8.
- Flood A, Velie EM, Sinha R, Chatterjee N, Lacey JV Jr, Schairer C, Schatzkin A. Meat, fat, and their subtypes as risk factors for colorectal cancer in a prospective cohort of women. *Am J Epidemiol.* 2003;158(1):59-68.
- Fung TT, Hu FB, Holmes MD, Rosner BA, Hunter DJ, Colditz GA, Willett WC. Dietary patterns and the risk of postmenopausal breast cancer. *Int J Cancer.* 2005;116(1):116-21.
- Fung TT, Schulze M, Manson JE, Willett WC, Hu FB. Dietary patterns, meat intake, and the risk of type 2 diabetes in women. *Arch Intern Med.* 2004;164(20):2235-40.
- Grant R, Bilgin A, Zeuschner C, Guy T, Pearce R, Hokin B, Ashton J. The relative impact of a vegetable-rich diet on key markers of health in a cohort of Australian adolescents. *Asia Pac J Clin Nutr.* 2008;17(1):107-15.

- Halton TL, Liu S, Manson JE, Hu FB. Low-carbohydrate-diet score and risk of type 2 diabetes in women. *Am J Clin Nutr*. 2008;87(2):339-46.
- Halton TL, Willett WC, Liu S, Manson JE, Albert CM, Rexrode K, Hu FB. Low-carbohydrate-diet score and the risk of coronary heart disease in women. *N Engl J Med*. 2006;355(19):1991-2002.
- Harland JI, Haffner TA. Systematic review, meta-analysis and regression of randomised controlled trials reporting an association between an intake of circa 25 g soya protein per day and blood cholesterol. *Atherosclerosis*. 2008;200(1):13-27. Epub 2008 Apr 15.
- Harper A, James A, Flint A, Astrup A. Increased satiety after intake of a chocolate milk drink compared with a carbonated beverage, but no difference in subsequent ad libitum lunch intake. *Br J Nutr*. 2007;97(3):579-83.
- He J, Gu D, Wu X, Chen J, Duan X, Chen J, Whelton PK. Effect of soybean protein on blood pressure: a randomized, controlled trial. *Ann Intern Med*. 2005;143(1):1-9.
- Hollis JH, Mattes RD. Effect of increased dairy consumption on appetitive ratings and food intake. *Obesity* (Silver Spring). 2007;15(6):1520-6. Erratum in: *Obesity* (Silver Spring). 2007;15(10):2520.
- Houston DK, Driver KE, Bush AJ, Kritchevsky SB. The association between cheese consumption and cardiovascular risk factors among adults. *J Hum Nutr Diet*. 2008;21(2):129-40.
- Huncharek M, Muscat J, Kupelnick B. Impact of dairy products and dietary calcium on bone-mineral content in children: results of a meta-analysis. *Bone*. 2008;43(2):312-21. Epub 2008 Mar 15.
- Hung CJ, Huang PC, Li YH, Lu SC, Ho LT, Chou HF. Taiwanese vegetarians have higher insulin sensitivity than omnivores. *Br J Nutr*. 2006;95(1):129-35.
- Järvinen R, Knekt P, Hakulinen T, Rissanen H, Heliövaara M. Dietary fat, cholesterol and colorectal cancer in a prospective study. *Br J Cancer*. 2001;85(3):357-61.
- Kabagambe EK, Baylin A, Ruiz-Narvarez E, Siles X, Campos H. Decreased consumption of dried mature beans is positively associated with urbanization and nonfatal acute myocardial infarction. *J Nutr*. 2005;135(7):1770-5.
- Kabat GC, Cross AJ, Park Y, Schatzkin A, Hollenbeck AR, Rohan TE, Sinha R. Meat intake and meat preparation in relation to risk of postmenopausal breast cancer in the NIH-AARP diet and health study. *Int J Cancer*. 2009;124(10):2430-5.
- Kanis JA, Johansson H, Oden A, De Laet C, Johnell O, Eisman JA, Mc Closkey E, Mellstrom D, Pols H, Reeve J, Silman A, Tenenhouse A. A meta-analysis of milk intake and fracture risk: low utility for case finding. *Osteoporos Int*. 2005;16(7):799-804. Epub 2004 Oct 21.
- Kelemen LE, Kushi LH, Jacobs DR Jr, Cerhan JR. Associations of dietary protein with disease and mortality in a prospective study of postmenopausal women. *Am J Epidemiol*. 2005;161(3):239-49.

Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Cancer incidence in vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009a;89(5):1620S-1626S. Epub 2009 Mar 11.

Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Mortality in British vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009b;89(5):1613S-1619S. Epub 2009 Mar 18.

Kojima M, Wakai K, Tamakoshi K, Tokudome S, Toyoshima H, Watanabe Y, Hayakawa N, Suzuki K, Hashimoto S, Ito Y, Tamakoshi A; Japan Collaborative Cohort Study Group. Diet and colorectal cancer mortality: results from the Japan Collaborative Cohort Study. *Nutr Cancer*. 2004;50(1):23-32.

Kokubo Y, Iso H, Ishihara J, Okada K, Inoue M, Tsugane S; JPHC Study Group. Association of dietary intake of soy, beans, and isoflavones with risk of cerebral and myocardial infarctions in Japanese populations: the Japan Public Health Center-based (JPHC) study cohort I. *Circulation*. 2007;116(22):2553-62. Epub 2007 Nov 19.

Konstantynowicz J, Nguyen TV, Kaczmarek M, Jamiolkowski J, Piotrowska-Jastrzebska J, Seeman E. Fractures during growth: potential role of a milk-free diet. *Osteoporos Int*. 2007;18(12):1601-7. Epub 2007 May 22.

Kontogianni MD, Panagiotakos DB, Chrysohoou C, Pitsavos C, Stefanadis C. Modelling dairy intake on the development of acute coronary syndromes: the CARDIO2000 study. *Eur J Cardiovasc Prev Rehabil*. 2006;13(5):791-7.

Koutros S, Cross AJ, Sandler DP, Hoppin JA, Ma X, Zheng T, Alavanja MC, Sinha R. Meat and meat mutagens and risk of prostate cancer in the Agricultural Health Study. *Cancer Epidemiol Biomarkers Prev*. 2008;17(1):80-7.

Kristensen M, Jensen M, Kudsk J, Henriksen M, Mølgaard C. Short-term effects on bone turnover of replacing milk with cola beverages: a 10-day interventional study in young men. *Osteoporos Int*. 2005;16(12):1803-8. Epub 2005 May 11.

Lanou AJ, Barnard ND. Dairy and weight loss hypothesis: an evaluation of the clinical trials. *Nutr Rev*. 2008;66(5):272-9.

Larsson SC, Rafter J, Holmberg L, Bergkvist L, Wolk A. Red meat consumption and risk of cancers of the proximal colon, distal colon and rectum: the Swedish Mammography Cohort. *Int J Cancer*. 2005;113(5):829-34.

Lee SA, Shu XO, Li H, Yang G, Cai H, Wen W, Ji BT, Gao J, Gao YT, Zheng W. Adolescent and adult soy food intake and breast cancer risk: results from the Shanghai Women's Health Study. *Am J Clin Nutr*. 2009a;89(6):1920-6. Epub 2009 Apr 29.

Lee SA, Shu XO, Yang G, Li H, Gao YT, Zheng W. Animal origin foods and colorectal cancer risk: a report from the Shanghai Women's Health Study. *Nutr Cancer*. 2009b;61(2):194-205.

- Liao FH, Shieh MJ, Yang SC, Lin SH, Chien YW. Effectiveness of a soy-based compared with a traditional low-calorie diet on weight loss and lipid levels in overweight adults. *Nutrition*. 2007;23(7-8):551-6. Epub 2007 Jun 15.
- Linos E, Willett WC, Cho E, Colditz G, Frazier LA. Red meat consumption during adolescence among premenopausal women and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev*. 2008;17(8):2146-51. Epub 2008 Jul 31.
- Mahon AK, Flynn MG, Stewart LK, McFarlin BK, Iglay HB, Mattes RD, Lyle RM, Considine RV, Campbell WW. Protein intake during energy restriction: effects on body composition and markers of metabolic and cardiovascular health in postmenopausal women. *J Am Coll Nutr*. 2007;26(2):182-9.
- Marques-Vidal P, Gonçalves A, Dias CM. Milk intake is inversely related to obesity in men and in young women: data from the Portuguese Health Interview Survey 1998-1999. *Int J Obes (Lond)*. 2006;30(1):88-93.
- Maskarinec G, Aylward AG, Erber E, Takata Y, Kolonel LN. Soy intake is related to a lower body mass index in adult women. *Eur J Nutr*. 2008;47(3):138-44. Epub 2008 Apr 22.
- McCabe LD, Martin BR, McCabe GP, Johnston CC, Weaver CM, Peacock M. Dairy intakes affect bone density in the elderly. *Am J Clin Nutr*. 2004;80(4):1066-74.
- McVeigh BL, Dillingham BL, Lampe JW, Duncan AM. Effect of soy protein varying in isoflavone content on serum lipids in healthy young men. *Am J Clin Nutr*. 2006;83(2):244-51.
- Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: A systematic review and meta-analysis. *Circulation*. 2010;121:2271-83.
- Michaud DS, Augustsson K, Rimm EB, Stampfer MJ, Willett WC, Giovannucci E. A prospective study on intake of animal products and risk of prostate cancer. *Cancer Causes Control*. 2001;12(6):557-67.
- Mirmiran P, Esmailzadeh A, Azizi F. Dairy consumption and body mass index: an inverse relationship. *Int J Obes (Lond)*. 2005;29(1):115-21.
- Mitchell DC, Lawrence FR, Hartman TJ, Curran JM. Consumption of dry beans, peas, and lentils could improve diet quality in the US population. *J Am Diet Assoc*. 2009;109(5):909-13.
- Miura K, Greenland P, Stamler J, Liu K, Davi GL, Nakagawa H. Relation of vegetable, fruit, and meat intake to 7-year blood pressure change in middle-aged men: the Chicago Western Electric Study. *Am J Epidemiol*. 2004;159(6):572-80.
- Murakami K, Okubo H, Sasaki S. No relation between intakes of calcium and dairy products and body mass index in Japanese women aged 18 to 20 y. *Nutrition*. 2006;22(5):490-5. Epub 2006 Feb 24.

Nagata C. Ecological study of the association between soy product intake and mortality from cancer and heart disease in Japan. *Int J Epidemiol.* 2000;29(5):832-6.

Nakamoto K, Watanabe S, Kudo H, Tanaka A. Nutritional characteristics of middle-aged Japanese vegetarians. *J Atheroscler Thromb.* 2008;15(3):122-9.

Nakamura Y, Iso H, Kita Y, Ueshima H, Okada K, Konishi M, Inoue M, Tsugane S. Egg consumption, serum total cholesterol concentrations and coronary heart disease incidence: Japan Public Health Center-based prospective study. *Br J Nutr.* 2006;96(5):921-8.

Nakamura Y, Okamura T, Tamaki S, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H; NIPPON DATA80 Research Group. Egg consumption, serum cholesterol, and cause-specific and all-cause mortality: the National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged, 1980 (NIPPON DATA80). *Am J Clin Nutr.* 2004;80(1):58-63.

National Cancer Institute. Risk Factor Monitoring and Methods Branch. Applied Research Program. Usual Energy Intake from Protein. <http://riskfactor.cancer.gov/diet/usualintakes/energy/t1.html>. Updated April 13, 2010. Accessed April 19, 2010.

Newby PK, Tucker KL, Wolk A. Risk of overweight and obesity among semivegetarian, lactovegetarian, and vegan women. *Am J Clin Nutr.* 2005;81(6):1267-74.

Norat T, Bingham S, Ferrari P, Slimani N, Jenab M, Mazuir M, Overvad K, Olsen A, Tjønneland A, Clavel F, Boutron-Ruault MC, Kesse E, Boeing H, Bergmann MM, Nieters A, Linseisen J, Trichopoulou A, Trichopoulos D, Tountas Y, Berrino F, Palli D, Panico S, Tumino R, Vineis P, Bueno-de-Mesquita HB, Peeters PH, Engeset D, Lund E, Skeie G, Ardanaz E, González C, Navarro C, Quirós JR, Sanchez MJ, Berglund G, Mattisson I, Hallmans G, Palmqvist R, Day NE, Khaw KT, Key TJ, San Joaquin M, Hémon B, Saracci R, Kaaks R, Riboli E. Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. *J Natl Cancer Inst.* 2005;97(12):906-16.

Oba S, Shimizu N, Nagata C, Shimizu H, Kametani M, Takeyama N, Ohnuma T, Matsushita S. The relationship between the consumption of meat, fat, and coffee and the risk of colon cancer: a prospective study in Japan. *Cancer Lett.* 2006;244(2):260-7. Epub 2006 Mar 6.

Olsen SF, Halldorsson TI, Willett WC, Knudsen VK, Gillman MW, Mikkelsen TB, Olsen J; NUTRIX Consortium. Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study. *Am J Clin Nutr.* 2007;86(4):1104-10.

O'Neil CE, Nicklas TA, Liu Y, Franklin FA. Impact of dairy and sweetened beverage consumption on diet and weight of a multiethnic population of Head Start mothers. *J Am Diet Assoc.* 2009;109(5):874-82.

Pan A, Franco OH, Ye J, Demark-Wahnefried W, Ye X, Yu Z, Li H, Lin X. Soy protein intake has sex-specific effects on the risk of metabolic syndrome in middle-aged and elderly Chinese. *J Nutr.* 2008;138(12):2413-21.

- Papanikolaou Y, Fulgoni VL 3rd. Bean consumption is associated with greater nutrient intake, reduced systolic blood pressure, lower body weight, and a smaller waist circumference in adults: results from the National Health and Nutrition Examination Survey 1999-2002. *J Am Coll Nutr.* 2008;27(5):569-76.
- Park SY, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN. Fat and meat intake and prostate cancer risk: the multiethnic cohort study. *Int J Cancer.* 2007;121(6):1339-45.
- Pittaway JK, Ahuja KD, Cehun M, Chronopoulos A, Robertson IK, Nestel PJ, Ball MJ. Dietary supplementation with chickpeas for at least 5 weeks results in small but significant reductions in serum total and low-density lipoprotein cholesterol in adult women and men. *Ann Nutr Metab.* 2006;50(6):512-8. Epub 2006 Dec 21.
- Pittaway JK, Ahuja KD, Robertson IK, Ball MJ. Effects of a controlled diet supplemented with chickpeas on serum lipids, glucose tolerance, satiety and bowel function. *J Am Coll Nutr.* 2007;26(4):334-40.
- Pittaway JK, Robertson IK, Ball MJ. Chickpeas may influence fatty acid and fiber intake in an ad libitum diet, leading to small improvements in serum lipid profile and glycemic control. *J Am Diet Assoc.* 2008;108(6):1009-13.
- Qureshi AI, Suri FK, Ahmed S, Nasar A, Divani AA, Kirmani JF. Regular egg consumption does not increase the risk of stroke and cardiovascular diseases. *Med Sci Monit.* 2007;13(1):CR1-8. Epub 2006 Dec 18.
- Rajpathak SN, Rimm EB, Rosner B, Willett WC, Hu FB. Calcium and dairy intakes in relation to long-term weight gain in US men. *Am J Clin Nutr.* 2006;83(3):559-66.
- Reynolds K, Chin A, Lees KA, Nguyen A, Bujnowski D, He J. A meta-analysis of the effect of soy protein supplementation on serum lipids. *Am J Cardiol.* 2006;98(5):633-40. Epub 2006 Jul 12.
- Rockell JE, Williams SM, Taylor RW, Grant AM, Jones IE, Goulding A. Two-year changes in bone and body composition in young children with a history of prolonged milk avoidance. *Osteoporos Int.* 2005;16(9):1016-23. Epub 2004 Nov 23.
- Rodriguez C, McCullough ML, Mondul AM, Jacobs EJ, Chao A, Patel AV, Thun MJ, Calle EE. Meat consumption among Black and White men and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev.* 2006;15(2):211-6.
- Rohrmann S, Platz EA, Kavanaugh CJ, Thuita L, Hoffman SC, Helzlsouer KJ. Meat and dairy consumption and subsequent risk of prostate cancer in a US cohort study. *Cancer Causes Control.* 2007;18(1):41-50.
- Rosell M, Appleby P, Spencer E, Key T. Weight gain over 5 years in 21,966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-Oxford. *Int J Obes (Lond).* 2006;30(9):1389-96. Epub 2006 Mar 14.
- Rosell M, Håkansson NN, Wolk A. Association between dairy food consumption and weight change over 9 y in 19,352 perimenopausal women. *Am J Clin Nutr.* 2006;84(6):1481-8.



- Ruidavets JB, Bongard V, Dallongeville J, Arveiler D, Ducimetière P, Perret B, Simon C, Amouyel P, Ferrières J. High consumptions of grain, fish, dairy products and combinations of these are associated with a low prevalence of metabolic syndrome. *J Epidemiol Community Health*. 2007;61(9):810-7.
- Ruidavets JB, Bongard V, Simon C, Dallongeville J, Ducimetière P, Arveiler D, Amouyel P, Bingham A, Ferrières J. Independent contribution of dairy products and calcium intake to blood pressure variations at a population level. *J Hypertens*. 2006;24(4):671-81.
- Sato Y, Nakaya N, Kuriyama S, Nishino Y, Tsubono Y, Tsuji I. Meat consumption and risk of colorectal cancer in Japan: the Miyagi Cohort Study. *Eur J Cancer Prev*. 2006;15(3):211-8.
- Schulze MB, Manson JE, Willett WC, Hu FB. Processed meat intake and incidence of Type 2 diabetes in younger and middle-aged women. *Diabetologia*. 2003;46(11):1465-73. Epub 2003 Oct 24.
- Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. *Arch Intern Med*. 2009;169(6):562-71.
- Sluijs I, Beulens JW, van der A DL, Spijkerman AM, Grobbee DE, van der Schouw YT. Dietary intake of total, animal, and vegetable protein and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)-NL study. *Diabetes Care*. 2010;33(1):43-8. Epub 2009 Oct 13.
- Snijder MB, van Dam RM, Stehouwer CD, Hiddink GJ, Heine RJ, Dekker JM. A prospective study of dairy consumption in relation to changes in metabolic risk factors: the Hoorn Study. *Obesity (Silver Spring)*. 2008;16(3):706-9. Epub 2008 Jan 17.
- Song Y, Manson JE, Buring JE, Liu S. A prospective study of red meat consumption and type 2 diabetes in middle-aged and elderly women: the women's health study. *Diabetes Care*. 2004;27(9):2108-15.
- Spencer EA, Appleby PN, Davey GK, Key TJ. Diet and body mass index in 38000 EPIC-Oxford meat-eaters, fish-eaters, vegetarians and vegans. *Int J Obes Relat Metab Disord*. 2003;27(6):728-34.
- Stamler J, Liu K, Ruth KJ, Pryer J, Greenland P. Eight-year blood pressure change in middle-aged men: relationship to multiple nutrients. *Hypertension*. 2002;39(5):1000-6.
- Steffen LM, Kroenke CH, Yu X, Pereira MA, Slattery ML, Van Horn L, Gross MD, Jacobs DR Jr. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr*. 2005;82(6):1169-77.
- Taylor EF, Burley VJ, Greenwood DC, Cade JE. Meat consumption and risk of breast cancer in the UK Women's Cohort Study. *Br J Cancer*. 2007;96(7):1139-46. Erratum in: *Br J Cancer*. 2007;96(11):1780.
- Teede HJ, Dalais FS, Kotsopoulos D, Liang YL, Davis S, McGrath BP. Dietary soy has both beneficial and potentially adverse cardiovascular effects: a placebo-controlled study in men and postmenopausal women. *J Clin Endocrinol Metab*. 2001;86(7):3053-60.

Teixeira Rde C, Molina Mdel C, Zandonade E, Mill JG. Cardiovascular risk in vegetarians and omnivores: a comparative study. *Arq Bras Cardiol.* 2007;89(4):237-44.

Thorpe DL, Knutsen SF, Beeson WL, Rajaram S, Fraser GE. Effects of meat consumption and vegetarian diet on risk of wrist fracture over 25 years in a cohort of peri- and postmenopausal women. *Public Health Nutr.* 2008;11(6):564-72. Epub 2007 Aug 9.

Toledo E, Delgado-Rodríguez M, Estruch R, Salas-Salvadó J, Corella D, Gomez-Gracia E, Fiol M, Lamuela-Raventós RM, Schröder H, Arós F, Ros E, Ruíz-Gutiérrez V, Lapetra J, Conde-Herrera M, Sáez G, Vinyoles E, Martínez-González MA. Low-fat dairy products and blood pressure: follow-up of 2290 older persons at high cardiovascular risk participating in the PREDIMED study. *Br J Nutr.* 2009;101(1):59-67.

Umesawa M, Sato S, Imano H, Kitamura A, Shimamoto T, Yamagishi K, Tanigawa T, Iso H. Relations between protein intake and blood pressure in Japanese men and women: the Circulatory Risk in Communities Study (CIRCS). *Am J Clin Nutr.* 2009;90(2):377-84. Epub 2009 Jun 10.

van Dam RM, Willett WC, Rimm EB, Stampfer MJ, Hu FB. Dietary fat and meat intake in relation to risk of type 2 diabetes in men. *Diabetes Care.* 2002;25(3):417-24.

Vang A, Singh PN, Lee JW, Haddad EH, Brinegar CH. Meats, processed meats, obesity, weight gain and occurrence of diabetes among adults: findings from Adventist Health Studies. *Ann Nutr Metab.* 2008;52(2):96-104. Epub 2008 Mar 18.

Vergnaud AC, Péneau S, Chat-Yung S, Kesse E, Czernichow S, Galan P, Hercberg S, Bertrais S. Dairy consumption and 6-y changes in body weight and waist circumference in middle-aged French adults. *Am J Clin Nutr.* 2008;88(5):1248-55.

Villegas R, Gao YT, Yang G, Li HL, Elasy TA, Zheng W, Shu XO. Legume and soy food intake and the incidence of type 2 diabetes in the Shanghai Women's Health Study. *Am J Clin Nutr.* 2008;87(1):162-7.

Wagemakers JJ, Prynne CJ, Stephen AM, Wadsworth ME. Consumption of red or processed meat does not predict risk factors for coronary heart disease; results from a cohort of British adults in 1989 and 1999. *Eur J Clin Nutr.* 2009;63(3):303-11.

Wang L, Manson JE, Buring JE, Lee IM, Sesso HD. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged and older women. *Hypertension.* 2008a;51(4):1073-9. Epub 2008 Feb 7.

Wang YF, Yancy WS Jr, Yu D, Champagne C, Appel LJ, Lin PH. The relationship between dietary protein intake and blood pressure: results from the PREMIER study. *J Hum Hypertens.* 2008b;22(11):745-54. Epub 2008 Jun 26.

Wang L, Manson JE, Buring JE, Sesso HD. Meat intake and the risk of hypertension in middle-aged and older women. *J Hypertens.* 2008c;26(2):215-22.

Wang YF, Chiu JS, Chuang MH, Chiu JE, Lin CL. Bone mineral density of vegetarian and non-vegetarian adults in Taiwan. *Asia Pac J Clin Nutr.* 2008d;17(1):101-6.

- Weggemans RM, Trautwein EA. Relation between soy-associated isoflavones and LDL and HDL cholesterol concentrations in humans: a meta-analysis. *Eur J Clin Nutr.* 2003;57(8):940-6.
- Wei EK, Giovannucci E, Wu K, Rosner B, Fuchs CS, Willett WC, Colditz GA. Comparison of risk factors for colon and rectal cancer. *Int J Cancer.* 2004;108(3):433-42.
- Welty FK, Lee KS, Lew NS, Zhou JR. Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women. *Arch Intern Med.* 2007;167(10):1060-7.
- Williams PG, Grafenauer SJ, O'Shea JE. Cereal grains, legumes, and weight management: a comprehensive review of the scientific evidence. *Nutr Rev.* 2008;66(4):171-82.
- 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.
- Wu K, Giovannucci E, Byrne C, Platz EA, Fuchs C, Willett WC, Sinha R. Meat mutagens and risk of distal colon adenoma in a cohort of US men. *Cancer Epidemiol Biomarkers Prev.* 2006;15(6):1120-5.
- Xu F, Yin XM, Tong SL. Association between excess bodyweight and intake of red meat and vegetables among urban and rural adult Chinese in Nanjing, China. *Asia Pac J Public Health.* 2007;19(3):3-9.
- Yang G, Shu XO, Jin F, Zhang X, Li HL, Li Q, Gao YT, Zheng W. Longitudinal study of soy food intake and blood pressure among middle-aged and elderly Chinese women. *Am J Clin Nutr.* 2005;81(5):1012-7.
- Yen CE, Yen CH, Huang MC, Cheng CH, Huang YC. Dietary intake and nutritional status of vegetarian and omnivorous preschool children and their parents in Taiwan. *Nutr Res.* 2008;28(7):430-6.
- Zhan S, Ho SC. Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. *Am J Clin Nutr.* 2005;81(2):397-408.