

Priority Areas for Research on the Intake, Composition, and Health Effects of Tree Nuts and Peanuts^{1,2}

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Abstract

This article summarizes the main conclusions drawn from a conference on the health effects of nut consumption and identifies priority areas for future research. Individuals with higher intakes of nuts generally have higher intakes of many beneficial dietary constituents. More information is needed on nut composition, the bioavailability of nutrients, and other bioactive constituents. Better methods are needed to assess usual nut intake, including biomarkers, and the types, physical form, and amounts of nuts that are consumed. The feasibility of including nuts and seeds as a separate food group in the Dietary Guidelines should be tested, as should ways to increase nut intake. A moderate intake of nuts can be included in a weight loss regimen and further information is needed on whether nuts improve satiety as well as adherence to and efficacy of diets designed for weight reduction. There is substantial evidence that nut consumption reduces risk of cardiovascular disease. Future research should investigate their benefits for prevention of congestive heart failure, including clinical studies in patients with this condition, to evaluate the effects of nuts on markers of heart disease risk. Higher nut consumption is associated with lower risk of diabetes and associated cardiovascular disease. More remains to be learned about the effects of nuts on postprandial glycemic and insulin response, glycemic control, and improvement of disease risk factors in subjects with prediabetes and diabetes. Information is needed on nut-induced allergic reactions, including their prevalence and consequences, causes of sensitization, biomarkers of severe reactions, and cross-reactivity to different types of nuts. J. Nutr. 138: 1763S–1765S, 2008.

Nut composition, dietary quality, and nutrient intake

Based on studies of the diets of higher and lower consumers of nuts (defined here as tree nuts and/or ground nuts), those who consume higher amounts have been reported as consuming more PUFA and monounsaturated fatty acids, linoleic acid, folate, potassium, magnesium, copper, vitamins E and K, selenium, potassium, and fiber (1). Nuts are also a good source of many phytonutrients, including phytosterols, flavonoids, and proan-

thocyanidins, which may reduce the risk of cardiovascular disease, primarily via through their antioxidant properties but through other mechanisms, too. In epidemiological studies, subjects with the highest intakes consume ~30 g/d on average. Currently, the average serving of nuts in the United States averages only 3–7 g/d compared with the qualified health claim recommendation of 42 g/d, so it will be necessary to find new ways to increase nut consumption, especially in meals. An important question that needs further resolution is whether higher nut intake is generally a marker for a high quality diet, and how it affects the consumption of other foods (e.g. increasing intake when nuts are used as coatings or flavors, or replacing other foods in the diet). Higher consumers of nuts have been reported to consume less vitamin B-12, retinol, lycopene, and sodium. A potentially ideal scenario would be that when nuts are used as a snack, they replace high-energy, low-nutrient dense food items.

Nuts are now positioned with meat, poultry, fish, and eggs in the U.S. Food Guide Pyramid, but this is not consistent with the fact that most nuts (~60%) are consumed as snacks. The conference participants agreed that there should be a separate category for nuts and seeds in the guidelines. The recommendation should be to consume nuts with their skin, whenever possible, because of its high phytonutrient content.

Additional analyses are needed to obtain better information on the phytonutrient content of nuts, the bioavailability of both

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macro- and micronutrients, and the effects of variety, storage, and processing on nutrient content and bioavailability. Several studies provide evidence that not all the fat in nuts is absorbed, but little is known about the efficiency of absorption of other nutrients. In terms of both composition and health benefits, more remains to be learned about the value of specific types of nuts/peanuts, rather than viewing all nuts as having the same nutritional value.

Valid tools should be developed for assessing nut intake and thus for following trends in nut consumption over time. Experience in national surveys has shown that reporting consumption as a “handful” is not sufficiently accurate. There are no validated ways to estimate nut intake for use in either national surveys or individual diets. Dietary assessment tools should address how and when nuts are consumed and in what amounts in specific situations (e.g. as a meat replacement, source of fat and oil, ingredient, or a snack). There are no adequately validated biomarkers of nut consumption, although changes in serum tocopherol and magnesium concentrations have been used for this purpose. It may be useful to explore serum or erythrocyte membrane fatty acid composition for this purpose.

Nut consumption, satiety, and maintenance of body weight

Both epidemiological and clinical studies show that moderate consumption of nuts provides health benefits without threatening energy balance, and that nuts can be included in a weight loss regimen. Several mechanisms are implicated, including replacement of other food items by nuts due to their high satiety value, incomplete absorption of their fat content, and a slight increase in resting energy expenditure (2).

Future research in this area should be focused on how including nuts in weight reduction plans affects peoples’ dietary adherence and rate and maintenance of weight loss. A range of quantities of nuts should be tested to evaluate any dose-response effect of the amount consumed on appetite, energy intake, body composition, substrate oxidation, and substitution for other foods. It would be valuable to have more information on the health and dietary quality benefits of replacing specific snacks, especially those with high-carbohydrate content and low-nutrient density, with nuts. This information should be compared for both lean and obese individuals and obtained in a range of population groups. It is not known whether there are substantive differential effects depending on the form and flavor of nuts, which may affect oral processing and/or subsequent health outcomes. Another area of interest is the possible interactions between nut intake, the gut microflora, and the health effects of nuts.

Nut intake and risk of cardiovascular disease

There is substantial epidemiological evidence that nut intake is related to a reduced incidence of coronary heart disease (3). Higher consumption of nuts is also associated with lower mortality, and especially lower cardiovascular disease mortality, in both men and women. Such health benefits may be mediated by many factors in nuts, including their fatty acid composition, other macronutrients, and micronutrients, phytochemical, or other bioactive compounds, some of which have antiinflammatory properties. Such benefits would be expected to be greater where nuts and nut butters replace refined carbohydrates and saturated fats in the diet.

Specific evidence of reduction of risk factors for coronary disease has been obtained from a pooled analysis of studies that examined the effects of nuts on these factors. Across all studies,

diets higher in nuts lowered total cholesterol, LDL-cholesterol, the LDL:HDL ratio, and serum triglycerides for those with baseline concentrations > 1.7 mmol/L (> 150 mg/dL). There were no significant effects on serum HDL-cholesterol. These beneficial effects of nuts were greater in lean than in obese people, but individuals with higher LDL-cholesterol at baseline had greater absolute and proportional reductions in serum lipids. The effects were proportional to the amount of nuts consumed. In the Predimed study, compared with a low-fat diet, Mediterranean diets high in either nuts or olive oil had beneficial effects on blood pressure, insulin resistance, serum triglycerides, oxidized LDL, inflammation, and HDL-cholesterol without changing body weight. It is likely that the greater statistical power of the large sample size in this study resulted in more effects of nuts being detected. In limited, short-term feeding trials, nuts improved endothelial function (walnuts specifically), oxidative stress was improved or unchanged, but there was no evidence of an effect on inflammation (based on lack of change in serum C-reactive protein concentrations). Thus, nuts have beneficial effects on cardiovascular disease risk factors that go beyond their cholesterol-lowering effects.

Future epidemiologic analyses should assess whether nut and peanut consumption is associated with risk of congestive heart failure, the sequelae of disease in patients with congestive heart failure, and the risk of progression from diabetes to heart failure. It may be useful to obtain data on the association between nut consumption and cell membrane composition in relevant geographic regions and population groups to further the agenda of finding good biomarkers of usual nut consumption.

Clinical studies are needed in patients with heart failure to test the benefits (including prevention of recurrence) of treatment with diets rich in nuts/peanuts (as part of a diet rich in fruits, vegetables, and whole grains) on biomarkers for health and nutritional status. These would include antioxidant capacity, essential fatty acid and vitamin status, etc., as well as risk factors for cardiovascular disease. The effects of diets high in nuts and peanuts also should be studied to examine their effects on markers of subclinical atherosclerosis, such as intima media thickness, calcium deposition in coronary arteries, and vulnerable plaques.

Studies also should be designed to determine whether nuts and peanuts can prevent cardiovascular disease. For example, nut intake might act synergistically with physical activity to lower cardiovascular disease risk factors and nuts may lower lipoprotein particle size and specific apolipoproteins. In diets prescribed for obese and overweight patients with insulin resistance, it is important to learn whether the addition of nuts affects their cholesterol-lowering or insulin-resistance response.

Nut consumption to lower risk of diabetes

Higher nut consumption is associated with a reduced risk of diabetes and of the development of coronary heart disease in individuals with diabetes (4). Nuts have favorable effects on the postprandial response to consuming white bread in both those with normal blood glucose and those with type 2 diabetes, in a dose-related manner. A lower risk of gallstone disease, an indicator of the metabolic syndrome, is associated with higher nut consumption. Nuts modify postprandial oxidative stress and may alter serum adiponectin concentrations. Importantly, including nuts as a separate food group produces more favorable lipid profiles in patients undergoing diabetes nutrition therapy.

Future areas of research should include studies of the acute effects of nut consumption on postprandial serum glucose and

insulin responses, markers of oxidative stress, and inflammatory biomarkers. Clinical studies, of ~3-mo duration, should evaluate the effect of including nuts on glycemic control (e.g. hemoglobin A1c concentrations), risk factors for coronary heart disease, and flow-mediated dilation and intima media thickness in patients with type 2 diabetes. Longer-term interventions are needed to determine whether increasing usual nut intake will lower the risk of developing type 2 diabetes in high risk groups, such as those with impaired glucose tolerance. Cohort studies could assess the strength of the association and dose-response relationship between usual nut intake and diabetes incidence and complications. More information is needed on the extent to which dietary patterns that include nuts can lower the glycemic load and improve serum fatty acid profiles and cardiovascular disease risk factors in subjects with prediabetes and diabetes.

Emerging areas of research

An important emerging question is whether nut intake can lower the risk of cancer. The epidemiologic data, such as those obtained in the EPIC study, are weak in this regard because of limitations in dietary survey design that have prevented quantification of nut-specific effects. A potentially useful alternative approach is to focus on the common set of processes (central mechanisms) that underlie chronic diseases as a way of targeting investigations (e.g. nitrous oxide production and turnover, and inflammation) (5). An additional recommendation is to investigate responses in multiple pathways simultaneously, based on well-designed interventions aimed at testing specific *a priori* hypotheses.

Allergic reactions to nuts

There are new studies of the prevalence of allergic reactions to nuts and the associated rates of severity and fatality in Europe. It does appear to be a valid conclusion that the prevalence of allergy is increasing (5). One theory is that early oral exposure to nuts (in infancy) promotes tolerance, whereas a more hygienic home environment promotes sensitization, but this is still unproven. Improvements are needed in the detection and diagnosis of allergic reactions and in the labeling of food. Some progress is being made in reducing the allergenic property of peanuts. The intake threshold that increases risk of an allergic reaction is known for peanuts, but not for other nuts, and should be determined using modeling and meta-analyses of data from existing studies and clinical trials.

Additional data are needed on the prevalence and consequences of allergic reactions to nuts in regions of the world beyond Europe. These data should be collected along with information that can inform us about the reasons for the increasing prevalence of allergies in regions where this is occurring and to improve our knowledge of how the prevalence of allergy changes with age (specifically including nuts other than peanuts). More information is needed on the severity of allergic responses and what causes sensitization; a little exists for peanuts, but virtually nothing for other nuts or on cross-sensitization across different types. Better biomarkers of potential severe reactions would be useful. Improved methods are required for component-resolved diagnosis (i.e. to enable specification of the specific nuts to which an individual may be allergic) and detection. More information is needed on the strength of the correlation between oral challenge and *in vitro* IgE binding tests. More effort needs to be invested in improving labeling, and allergen control programs should be research driven and evaluated rigorously.

Although nuts clearly have many health benefits, this is a relatively new area of research. Consequently, more research needs to be conducted that includes *in vitro*, animal, and clinical studies to further our understanding of the health effects of nuts and the underlying mechanisms involved. Building this evidence base will provide important information for future dietary guidance about nuts.

Other articles in this supplement include reference (6).

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