Nut and Peanut Butter Consumption and Risk of Type 2 Diabetes in Women

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Context Nuts are high in unsaturated (polyunsaturated and monounsaturated) fat and other nutrients that may improve glucose and insulin homeostasis.

Objective To examine prospectively the relationship between nut consumption and risk of type 2 diabetes.

Design, Setting, and Participants Prospective cohort study of 83 818 women from 11 states in the Nurses' Health Study. The women were aged 34 to 59 years, had no history of diabetes, cardiovascular disease, or cancer, completed a validated dietary questionnaire at baseline in 1980, and were followed up for 16 years.

Main Outcome Measure Incident cases of type 2 diabetes.

Results We documented 3206 new cases of type 2 diabetes. Nut consumption was inversely associated with risk of type 2 diabetes after adjustment for age, body mass index (BMI), family history of diabetes, physical activity, smoking, alcohol use, and total energy intake. The multivariate relative risks (RRs) across categories of nut consumption (never/almost never, <once/week, 1-4 times/week, and ≥5 times/week) for a 28-g (1 oz) serving size were 1.0, 0.92 (95% confidence interval [CI], 0.85-1.00), 0.84 (0.95% CI, 0.76-0.93), and 0.73 (95% CI, 0.60-0.89) (*P* for trend <.001). Further adjustment for intakes of dietary fats, cereal fiber, and other dietary factors did not appreciably change the results. The inverse association persisted within strata defined by levels of BMI, smoking, alcohol use, and other diabetes risk factors. Consumption of peanut butter was also inversely associated with type 2 diabetes. The multivariate RR was 0.79 (95% CI, 0.68-0.91; *P* for trend <.001) in women consuming peanut butter 5 times or more a week (equivalent to ≥140 g [5 oz] of peanuts/week) compared with those who never/almost never ate peanut butter.

Conclusions Our findings suggest potential benefits of higher nut and peanut butter consumption in lowering risk of type 2 diabetes in women. To avoid increasing caloric intake, regular nut consumption can be recommended as a replacement for consumption of refined grain products or red or processed meats.

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TYPE 2 DIABETES AFFECTS APproximately 16 million people in the United States[1] and 135 million people worldwide[2]; the number of people with diabetes will reach an estimated 300 million worldwide by 2025.[2] Because management of diabetes and its complications such as cardiovascular disease, amputation, blindness, and renal failure imposes enormous medical and economic burdens, primary prevention has become a public health imperative.

Recent studies have shown that diet and lifestyle modifications are important means of preventing type 2 diabetes.[3-5] Evidence indicates that specific types of dietary fat rather than total fat (as percentage of energy) intake predict risk of type 2 diabetes.[6] Nuts contain 70% to 80% fat, and most fatty acids in nuts are unsaturated (polyunsaturated and monounsaturated), which may be beneficial for glucose and insulin homeostasis. Several studies have shown that a higher intake of monounsaturated and polyunsaturated fat improves insulin sensitivity.[7-10] A higher intake of polyunsaturated fat is associated with a lower risk of type 2 diabetes,[11] whereas a higher intake of saturated fat and *trans*-fat adversely affects glucose metabolism and insulin resistance[8,12-14] and thereby may increase the risk of type 2 diabetes.[11] Other components of nuts such as fiber and magnesium decrease insulin demand and resistance[15-22] and have been inversely associated with risk of type 2 diabetes.[23,24] Nuts are also a rich source of many vitamins, minerals, and antioxidants and of plant protein, which could also be beneficial.

Although several components of nuts have been inversely associated with risk of type 2 diabetes, the overall association of nut consumption with diabetes risk has not been studied. We therefore examined prospectively the association between nut consumption and risk of type 2 diabetes in a large cohort of women from the Nurses' Health Study.

METHODS

Study Population

The Nurses' Health Study was established in 1976 when 121 700 female registered nurses, aged 30 to 55 years and

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from 11 states, completed a mailed questionnaire designed to study etiologies of heart disease, cancer, and other major illnesses.[25] Information on lifestyle, health behaviors, and disease status has been collected on biennially mailed questionnaires since 1976, and information about vitamin supplement use has been collected the same way since 1980. Diet was assessed in 1980, 1984, 1986, 1990, and 1994 by using semiquantitative food-frequency questionnaires. For this analysis, at baseline in 1980, we excluded women with 10 or more food items left blank or with implausibly high (>3500 kcal/d) or low (<500 kcal/d) total energy intake. We also excluded women with a history of diabetes, cardiovascular disease (angina, coronary bypass or angioplasty, myocardial infarction, or stroke), and cancer (except for nonmelanoma skin cancer). After these exclusions, 83818 participants remained in the analysis.

Dietary Assessment

The semiquantitative food-frequency questionnaire at baseline (1980) included 61 foods and was revised and expanded to about twice the number of foods in subsequent cycles.[26,27] Participants were asked to report their average frequency of consumption of selected foods and beverages with a specified commonly used unit or portion size during the previous year. The reproducibility and validity of the dietary questionnaires are described in detail elsewhere.[27]

In the 1980 and 1984 dietary questionnaires, we asked the participants how often, on average, they had consumed nuts (serving size, 28 g [1 oz]) during the previous year: never/almost never, 1 to 3 times a month, once a week, 2 to 4 times a week, 5 to 6 times a week, once a day, 2 to 3 times a day, 4 to 6 times a day, or more than 6 times a day. In the 1986, 1990, and 1994 dietary questionnaires, the question for nuts was split into 2 categories: peanuts and other nuts. Total nut consumption was the sum of the intakes for peanuts and other nuts. Consumption of peanut butter was assessed in 1980, 1984, 1986, 1990, and 1994, with the same 9 responses as those for nut consumption (serving size, 15 mL [1 tablespoon]). Although peanuts are botanically classified as legumes, the fatty acid and nutrient profiles of peanuts are very similar to other nuts.[28] A validation study of the food-frequency questionnaires in the Nurses' Health Study indicated that nuts and peanut butter were reported reasonably accurately; the correlation coefficient was 0.75 between intakes assessed by the 1980 questionnaire and by 4 one-week diet records for nuts and peanut butter.[29] Nutrient intakes, such as for fats and fiber, were computed by multiplying the consumption frequency of each food by the nutrient content of the specified portion and then summing these products across all the food items. The food composition values were obtained from the Harvard University Food Composition Database derived from US Department of Agriculture sources[30] and supplemented with manufacturer information.

Measurement of Nondietary Factors

In 1982, 1988, and 1992, the participants provided information on family history of diabetes in first-degree relatives. The participants also provided information on their body weight and cigarette smoking every 2 years during the follow-up. The correlation coefficient between self-reported weight and measured weight was 0.96.[31] Physical activity was assessed by a shorter questionnaire in 1980 and 1982.[32] More detailed information on physical activity was first collected in 1986 and was updated in 1986, 1988, and 1992. We used the cumulative average number of hours a week spent in moderate or vigorous recreational activities, including brisk walking, vigorous sports, jogging, bicycling, heavy gardening, and heavy housework.

Outcome Ascertainment

The outcome was incident type 2 diabetes. To all women who reported a diagnosis of diabetes on any biennial follow-up questionnaire, we mailed a supplementary questionnaire regarding symptoms, diagnostic tests, and treatments. The diagnosis of diabetes was established when at least 1 of the following criteria was reported on the supplementary questionnaire: (1) 1 or more classic symptoms (excessive thirst, polyuria, weight loss, hunger, or coma) plus a fasting plasma glucose concentration of 140 mg/dL (7.8 mmol/L) or higher or a random plasma glucose concentration of 200 mg/dL (11.1 mmol/L) or higher; or (2) at least 2 elevated plasma glucose concentrations on different occasions (fasting, ≥140 mg/dL [7.8 mmol/L]; random, ≥200 mg/dL [11.1 mmol/L]; or random, ≥200 mg/dL [11.1 mmol/L] after at least 2 hours of oral glucose tolerance testing) in the absence of symptoms; or (3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agents). The diagnostic criteria for type 2 diabetes were changed in 1997.[33] However, we used the criteria proposed by the National Diabetes Data Group[34] because all our cases were diagnosed before June 1996. We excluded women with type 1 diabetes and women classified as having gestational diabetes only. A validation study in a subsample of this cohort demonstrated that our supplementary questionnaire is highly reliable in confirming diabetes diagnoses.[35] Among a random sample of 84 women classified by our criteria as having type 2 diabetes according to the information reported on the supplementary questionnaire, medical records were available for 62. An endocrinologist blinded to the information reported on the questionnaire reviewed the records. The diagnosis of type 2 diabetes was confirmed in 61 (98%) of the 62 women.

Statistical Analysis

Each participant contributed follow-up time from the date of returning the 1980 questionnaire to the date of first diagnosis of type 2 diabetes, death, or June 1, 1996. Women were excluded from subsequent follow-up if they developed diabetes. In the primary analyses, incidence of type 2 diabetes was related to nut consumption at baseline. In further analyses, incidence of type 2 diabetes was

related to the cumulative average of nut consumption from dietary questionnaires administered in 1980, 1984, 1986, 1990, and 1994.[36] We separated women into 4 categories according to their frequency of nut consumption: never/almost never, less than once a week (1-3 times/month), 1 to 4 times a week, and at least 5 times a week. Relative risks (RRs) of diabetes were estimated from Cox proportional hazards models.[37] Potential confounding variables including body mass index (BMI), family history of diabetes, physical activity, smoking, alcohol consumption, and multivitamin supplements were updated during follow-up. In multivariate models, we adjusted for age, BMI, family history of diabetes, physical activity, smoking, alcohol use, and total energy intake. We also adjusted for several dietary confounding variables such as glycemic load, multivitamin use, and intakes of polyunsaturated fat, saturated fat, *trans*-fat, cereal fiber, magnesium, whole grains, vegetables, fruits, and fish.

In a secondary analysis, we performed a propensity analysis[38] in which we used a logistic regression model to predict nut consumption (≥5 times/week vs never/almost never) from a multitude of dietary and lifestyle factors. We then examined the association between nut consumption and diabetes risk from a Cox proportional hazards model adjusting for the predicted propensity scores.

We also calculated mean weight change from 1980 to 1996 for women according to frequency of nut consumption at baseline (4 categories) by using general linear models (least square means).[39] In this analysis, we adjusted for age, family history of diabetes, physical activity, smoking, alcohol use, and baseline weight and excluded women who developed cancer, heart disease, or diabetes during the follow-up.

All *P* values were 2-sided. Tests for trend were conducted using the median value for each category of nut consumption analyzed as a continuous variable in the regression models. All analyses were performed with SAS version 6.12 software (SAS Institute, Cary, NC).

RESULTS

At baseline in 1980, about 35% of women in this cohort reported consuming nuts almost never; 36%, consum-

Table 1. Dietary Intake and Other Potential Risk Factors for Type 2 Diabetes in Women (Age-Adjusted) According to Frequency of Nut Consumption at Baseline in 1980

Variable	Frequency of Nut Consumption (28-g Serving)			
	Never/Almost Never (n = 28 989)	<Once/wk (n = 30 411)	1-4 Times/wk (n = 20 104)	≥5 Times/week (n = 4314)
Age, mean (SD), y	46.4 (7.15)	46.1 (7.12)	46.7 (7.13)	47.9 (7.02)
Body mass index, mean (SD)*	24.7 (4.59)	24.3 (4.29)	24.0 (4.05)	23.4 (3.74)
Family history of diabetes, %	18.6	19.0	18.3	17.6
Moderate/vigorous exercise, mean (SD), h/wk	3.6 (2.81)	3.9 (2.88)	4.2 (2.92)	4.4 (2.96)
Current smoker, %	31.7	27.7	25.5	25.1
Alcohol consumption, g/d	5.8	6.3	7.2	7.8
Multivitamin use, %	30.3	32.9	38.0	45.6
Diet, mean (SD)				
Polyunsaturated fat, energy percentage	4.9 (1.58)	5.2 (1.48)	5.5 (1.42)	6.8 (1.81)
Saturated fat, energy percentage	15.6 (3.75)	15.7 (3.49)	15.6 (3.41)	15.1 (3.63)
Trans-fat, energy percentage	2.3 (0.77)	2.3 (0.72)	2.2 (0.69)	1.8 (0.68)
Dietary fiber, g/d	13.1 (4.87)	13.3 (4.48)	14.3 (4.65)	16.5 (5.53)
Cereal fiber, g/d	2.5 (1.60)	2.5 (1.51)	2.4 (1.43)	2.2 (1.39)
Magnesium, mg/d	288 (71.8)	288 (67.1)	299 (66.9)	336 (72.0)
Carbohydrate, energy percentage	39.3 (9.64)	38.9 (8.98)	38.6 (8.73)	36.8 (9.57)
Protein, energy percentage	19.5 (4.27)	18.9 (3.69)	18.9 (3.58)	18.7 (3.46)
Total energy intake, kcal/d†	1471 (487)	1541 (476)	1668 (501)	1882 (537)
Vegetables, servings/d/1000 kcal‡	1.36 (0.82)	1.31 (0.73)	1.34 (0.74)	1.33 (0.80)
Fruit, servings/d/1000 kcal§	1.35 (0.90)	1.32 (0.82)	1.35 (0.79)	1.35 (0.86)
Whole grain, servings/d/1000 kcal‖	0.61 (0.62)	0.63 (0.58)	0.69 (0.61)	0.81 (0.71)
Refined grain, servings/d/1000 kcal‖	1.25 (0.75)	1.20 (0.68)	1.12 (0.63)	1.02 (0.64)
Red and processed meats, servings/d/1000 kcal¶	0.91 (0.41)	0.90 (0.38)	0.84 (0.37)	0.68 (0.39)
Chicken, servings/d/1000 kcal	0.18 (0.16)	0.17 (0.14)	0.17 (0.13)	0.15 (0.13)
Fish, servings/d/1000 kcal	0.13 (0.15)	0.11 (0.12)	0.11 (0.12)	0.11 (0.12)
Glycemic load, mean (SD)	124 (38.3)	123 (35.1)	120 (33.5)	111 (35.8)

*Body mass index is calculated as weight in kilograms divided by the square of the height in meters.
†Values were lower than the true intakes because the 1980 questionnaire included only 61 food items.
‡Composite score of string beans, broccoli, cabbage/cauliflower/brussels sprouts, carrots, corn, spinach, peas, yellow squash, sweet potatoes, beans or lentils, and tomatoes.
§Composite score of apples/pears, oranges, orange or grapefruit juice, peaches/apricots/plums, bananas, and other fruits.
‖Values were reported in 1984 questionnaire.
¶Composite score of beef, pork, lamb as a main dish or mixed dish, hamburgers, hot dogs, bacon, and processed meats.

ing them less than once a week; 24%, 1 to 4 times a week; and 5%, at least 5 times a week. Women who consumed more nuts generally weighed less (TABLE 1). Women with frequent nut consumption were less likely to smoke and more likely to exercise. Nut consumption was positively associated with intakes of polyunsaturated fat, dietary fiber, magnesium, alcohol, and multivitamin supplements and inversely associated with glycemic load and intake of *trans*-fat. Consumption of vegetables and fruits was similar for women with frequent nut consumption and those who rarely ate nuts, but women who consumed more nuts generally ate less meat and refined grain products.

We documented 3206 incident cases of type 2 diabetes during 1 282 892 person-years of follow-up from 1980 to 1996. The nut consumption at baseline was used to classify women into 4 categories (never/almost never, <once/week, 1-4 times/week, and ≥5 times/week) so that the age-adjusted RR of diabetes was 0.55 (95% confidence interval [CI], 0.45-0.66), comparing women who ate nuts at least 5 times a week with those who never/almost never ate nuts (*P* for trend <.001) (TABLE 2). In multivariate models, BMI was the strongest confounder. The RR was attenuated to 0.74 (95% CI, 0.61-0.89; *P* for trend <.001) after BMI was added to the model by using it as a categorical variable (8 categories) and was 0.72 (95% CI, 0.59-0.87; *P* for trend <.001) when BMI was used as a continuous variable. The RR was virtually unchanged after further control for family history of diabetes, physical activity, smoking, alcohol consumption, and total energy intake. After controlling for other dietary variables such as glycemic load, multivitamin use, and intakes of polyunsaturated fat, saturated fat, *trans*-fat, cereal fiber, magnesium, whole grains, vegetables, fruits, and fish, the RR did not appreciably change (0.71; 95% CI, 0.57-0.87). Updated analyses using the cumulative average of nut consumption yielded similar results (multivariate RR, 0.76; 95% CI, 0.59-0.97; *P* for trend = .001).

In the secondary analysis controlling for propensity scores, those who ate nuts at least 5 times a week still had a lower diabetes risk compared with those who never/almost never ate nuts (RR, 0.73; 95% CI, 0.56-0.96).

To examine further whether the relationship between nut consumption and type 2 diabetes risk was independent of other potential risk factors for type 2 diabetes, we conducted multivariate analyses within strata defined by levels of these factors. We found no apparent modification of the relationship by these factors, and the inverse association persisted in all subgroups (TABLE 3).

We also examined the relationship between consumption of peanut butter and risk of type 2 diabetes. Frequent consumption of peanut butter was associated with a significantly reduced risk of type 2 diabetes (TABLE 4). The multivariate RR was 0.79 (95% CI, 0.68-0.91), comparing women who ate peanut butter at least 5 times a week with those who never/almost never ate peanut butter.

To address the concern that higher nut consumption may lead to more weight gain, we calculated average weight change during 16 years of follow-up according to frequency of nut consumption at baseline. After adjustment for age, family history of diabetes, physical activity, smoking, alcohol use, and baseline weight, the average weight gain across categories of nut consumption (never/almost never, <once/week, 1-4 times/week, ≥5 times/week) was not significantly different (6.5, 6.4, 6.4, and 6.3 kg, respectively).

COMMENT

In this large prospective cohort study of women, we found that consumption of nuts and peanut butter was inversely associated with risk of type 2 diabetes, independent of known risk factors for type 2 diabetes, including age, obesity, family history of diabetes, physical activity, smoking, and dietary factors. The inverse association with nuts persisted in all subgroup analyses.

The major concern of our analysis is residual confounding by body weight because obesity is the most important determinant of type 2 diabetes. In our analyses, we adjusted for BMI by using detailed categories and continuous variables, and the results did not change appreciably. Although we cannot rule out

Table 2. Relative Risks (RRs) of Type 2 Diabetes in Women According to Frequency of Nut Consumption*

	Frequency of Nut Consumption (28-g Serving)				
	Never/Almost Never	<Once/wk	1-4 Times/wk	≥5 Times/wk	*P* for Trend
Cases, No.	1314	1133	644	115	. . .
Person-years	441 007	466 464	309 608	66 468	. . .
Age-adjusted RR (95% CI)	1.00	0.82 (0.76-0.89)	0.69 (0.63-0.76)	0.55 (0.45-0.66)	<.001
Age- and BMI-adjusted RR (95% CI)	1.00	0.91 (0.84-0.99)	0.83 (0.75-0.91)	0.74 (0.61-0.89)	<.001
Multivariate RR (95% CI)†	1.00	0.92 (0.85-1.00)	0.84 (0.76-0.93)	0.73 (0.60-0.89)	<.001
Additional adjustment for dietary variables, RR (95% CI)‡	1.00	0.91 (0.84-0.99)	0.81 (0.74-0.90)	0.71 (0.57-0.87)	<.001

*BMI indicates body mass index (see Table 1 footnote for calculation); ellipses, data not applicable; and CI, confidence interval.
†Relative risk was adjusted for age (5-year categories), BMI (<21, 21.0-22.9, 23.0-24.9, 25.0-27.9, 28.0-29.9, 30.0-34.9, ≥35, and missing information), family history of diabetes in a first-degree relative (yes or no), moderate/vigorous exercise (<1, 1, 2-3, 4-6, or ≥7 h/wk), cigarette smoking (never, past, or current smoking of 1-14, 15-24, or ≥25 cigarettes/d), alcohol consumption (0, 0.1-5.0, 5.1-15.0, or >15 g/d), and total energy intake.
‡Included glycemic load, multivitamin use (yes or no), and intakes of polyunsaturated fat, saturated fat, *trans*-fat, cereal fiber, magnesium, vegetables, fruits, whole grain (in quintiles), and fish (in quartiles).

Table 3. Multivariate Relative Risks of Type 2 Diabetes in Women According to Frequency of Nut Consumption, Stratified by Risk Factors*

Variable	Frequency of Nut Consumption (28-g Serving)			
	<Once/wk	1-4 Times/wk	≥5 Times/wk	*P* for Trend
Body mass index				
<25	0.95	0.71	0.55 (0.32-0.94)	.003
25-29	0.83	0.77	0.75 (0.54-1.05)	.01
≥30	0.96	0.91	0.75 (0.56-0.98)	.02
Family history of diabetes				
Yes	1.00	0.82	0.75 (0.55-1.04)	.004
No	0.89	0.85	0.69 (0.54-0.89)	.001
Moderate/vigorous exercise, ≥4 h/wk				
Yes	0.95	0.76	0.63 (0.42-0.95)	.001
No	0.90	0.90	0.82 (0.64-1.06)	.10
Current smoking				
Yes	0.87	0.78	0.63 (0.37-1.07)	.02
No	0.94	0.85	0.75 (0.61-0.93)	<.001
Current alcohol use				
Yes	0.99	0.85	0.85 (0.65-1.10)	.01
No	0.87	0.85	0.61 (0.45-0.82)	<.001
Multivitamin use				
Yes	0.88	0.73	0.56 (0.40-0.77)	<.001
No	0.82	0.78	0.58 (0.42-0.80)	<.001
Dietary intake				
Polyunsaturated fat, g/d†				
Low	0.93	0.79	0.72 (0.43-1.22)	.003
High	0.91	0.85	0.69 (0.55-0.86)	<.001
Saturated fat, g/d†				
Low	0.93	0.84	0.78 (0.61-1.01)	.01
High	0.93	0.84	0.64 (0.47-0.88)	<.001
Trans-fat, g/d†				
Low	0.94	0.79	0.77 (0.61-0.98)	<.001
High	0.91	0.91	0.64 (0.44-0.93)	.03
Cereal fiber, g/d†				
Low	0.98	0.91	0.83 (0.65-1.07)	.06
High	0.87	0.78	0.63 (0.45-0.86)	<.001
Magnesium, mg/d†				
Low	0.94	0.93	0.75 (0.53-1.07)	.12
High	0.89	0.76	0.76 (0.60-0.97)	<.001
Vegetables, servings/d				
<2	0.94	0.83	0.68 (0.50-0.91)	<.001
≥2	0.92	0.86	0.81 (0.62-1.06)	.04
Fruits, servings/d				
<2	0.90	0.82	0.70 (0.52-0.94)	.001
≥2	0.94	0.86	0.73 (0.56-0.95)	.004
Whole grain, servings/d				
<2	0.91	0.88	0.79 (0.62-1.01)	.02
≥2	1.02	0.73	0.43 (0.25-0.74)	<.001
Fish, servings/d				
<0.2	0.95	0.78	0.77 (0.55-1.08)	.004
≥0.2	0.92	0.87	0.70 (0.55-0.89)	.002
Red and processed meat, servings/d				
<1	0.93	0.84	0.78 (0.56-1.08)	.04
≥1	0.92	0.84	0.69 (0.54-0.89)	<.001
Glycemic load†				
Low	0.99	0.86	0.68 (0.52-0.89)	<.001
High	0.87	0.81	0.80 (0.60-1.07)	.007

*The variable used for stratification was not included in the model. The multivariate relative risk for the never/almost never category was 1.0 for all variables. See Table 1 footnote for body mass index calculation and Table 2 footnote for an explanation of relative risk adjustments. For 5 times per week or more frequency of nut consumption, 95% confidence intervals are included in parentheses.
†Median values were used as the cutoff point.

the possibility of residual confounding by other potential risk factors, it is unlikely that they can explain the observed inverse association. The likelihood of bias is minimized because of the prospective study design, high follow-up rate, and repeated measures of diet with validated food-frequency questionnaires. Another issue deserving attention is that the diagnostic criteria for type 2 diabetes used in this study were changed in 1997 so that lower fasting glucose levels (≥126 mg/dL [7.0 mmol/L]) would now be considered the diagnostic cut point.[33] If the new criteria were used, some women classified as being without diabetes would have been reclassified as having diabetes. However, this change would not explain our results, because inclusion of those with diabetes in the group without diabetes would tend to weaken the association.

Although the relationship between nut consumption and risk of type 2 diabetes has not been evaluated previously, several studies have examined the relationship between the major constituents of nuts (eg, specific types of fat) and insulin resistance and type 2 diabetes.[6-14,24,40-52] Most clinical and epidemiological studies have observed no effect of total fat intake on insulin sensitivity and risk of type 2 diabetes.[11,24,42,43,47-49] The findings on types of dietary fat have been inconsistent.* Some of the inconsistency could be due to methodological limitations in many studies, such as small sample size, short duration, crude dietary assessment methods without documented validity, and absence of control for confounding (eg, other types of fats, fiber intake, obesity, and physical activity). More recent clinical and epidemiological studies with better design suggest that specific types of fat rather than total fat as percentage of energy play an important role in the development of type 2 diabetes.[6,8,11] A multicenter study involving a 3-month intervention among 162 healthy men and women showed that a diet high in saturated fat (18% of energy) decreased insulin sensitivity compared with a diet high in monoun-

*References 8, 11, 12, 24, 40, 42-44, 50-52.

Table 4. Relative Risks (RRs) of Type 2 Diabetes in Women According to Frequency of Consumption of Peanut Butter*

	Frequency of Peanut Butter Consumption				
	Never/ Almost Never	<Once/wk	1-4 Times/wk	≥5 Times/wk	*P* for Trend
Cases, No.	1392	747	836	231	. . .
Person-years	510 775	294 723	364 960	113 089	. . .
Age-adjusted RR (95% CI)	1.00	0.96 (0.88-1.05)	0.88 (0.81-0.96)	0.78 (0.68-0.90)	<.001
Age- and BMI-adjusted RR (95% CI)	1.00	1.00 (0.91-1.09)	0.94 (0.86-1.03)	0.86 (0.75-0.99)	.01
Multivariate RR (95% CI)†	1.00	0.98 (0.90-1.08)	0.91 (0.83-0.99)	0.79 (0.68-0.91)	<.001
Additional adjustment for dietary variables, RR (95% CI)‡	1.00	0.98 (0.90-1.07)	0.91 (0.84-1.00)	0.81 (0.69-0.94)	.002

*BMI indicates body mass index (see Table 1 footnote for calculation); CI, confidence interval; and ellipses, data not applicable. Servings of peanut butter were equivalent to 15 mL, or 28 g, of peanuts.
†See Table 2 footnote for an explanation of RR adjustments.
‡Included glycemic load, multivitamin use (yes or no), intakes of polyunsaturated fat, saturated fat, *trans*-fat, cereal fiber, magnesium, vegetables, fruits, whole grain (in quintiles), and fish (in quartiles).

saturated fat (21% of energy) with the same total fat content.[8] An analysis[11] from the Nurses' Health Study with 14 years of follow-up showed that women in the highest quintile of vegetable fat intake had a 40% lower risk of type 2 diabetes than those in the lowest quintile. The RR comparing extreme quintiles of polyunsaturated fat intake was 0.75 (95% CI, 0.65-0.88). An Italian study showed that a higher consumption of oils consisting mostly of polyunsaturated fat was associated with lower fasting plasma concentrations of glucose.[40]

The mechanisms by which specific types of dietary fat affect insulin sensitivity are not well understood. It has been shown that the fatty acid composition of the phospholipids in the skeletal muscle cell membranes is directly related to insulin sensitivity in humans.[53] A specific fatty acid in cell membranes could influence insulin action through altering insulin receptor binding or affinity and influencing ion permeability and cell signaling. Changes in dietary fatty acid composition alter fatty acid composition of the phospholipids in cell membranes, perhaps modulating insulin action and sensitivity.

Nuts are also rich in fiber and magnesium and have a relatively low glycemic index. In several clinical studies, high-fiber diets decreased insulin demand among patients with type 2 diabetes.[15-17] Also, metabolic studies suggest an inverse association between intracellular magnesium and insulin resistance,[18,22] and magnesium supplementation increased insulin sensitivity among patients with type 2 diabetes[19,20] and among healthy subjects.[21] Higher intakes of fiber and magnesium and foods with a low glycemic index have been associated with reduced risk of type 2 diabetes in several prospective studies.[23,24,54,55]

Nuts may protect against type 2 diabetes through additional mechanisms. The persistence of an association when intakes of types of fats, fiber, and magnesium were in the model indicates that the apparent benefit of nuts was not explained entirely by content of fats, fiber, and magnesium. Thus, other constituents of nuts such as vitamins, minerals, antioxidants, and plant protein or interactions among these factors may also play important roles in reducing risk of type 2 diabetes.

There have been concerns that frequent nut consumption may result in weight gain and increased risk of coronary heart disease because of the high fat content. However, in our cohort, we did not find an appreciable association between nut consumption and weight change. Also, several large prospective studies[56-59] have consistently found an inverse association between nut consumption and the risk of coronary heart disease. The epidemiological findings are supported by several clinical studies[28,60-63] in which diets high in nuts had beneficial effects on blood lipids. These results contradict the conventional wisdom that intake of high-fat foods leads to obesity and heart disease. Given the observed inverse association between nuts and risk of coronary heart disease as well as type 2 diabetes, it is advisable to recommend regular nut consumption as a replacement for refined grain products[64] or red or processed meats,[65] which would avoid increasing caloric intake.

In conclusion, higher consumption of nuts and peanut butter was associated with a lower risk of type 2 diabetes in this large cohort study of women. Our data, combined with other clinical and epidemiological data, support potential benefits of increasing nut consumption in reducing type 2 diabetes risk.

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