Regular Consumption of Nuts Is Associated with a Lower Risk of Cardiovascular Disease in Women with Type 2 Diabetes[1,2]

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Abstract

Higher nut consumption has been associated with lower risk of coronary heart disease (CHD) events in several epidemiologic studies. The study examined the association between intake of nuts and incident cardiovascular disease (CVD) in a cohort of women with type 2 diabetes. For the primary analysis, there were 6309 women with type 2 diabetes who completed a validated FFQ every 2–4 y between 1980 and 2002 and were without CVD or cancer at study entry. Major CVD events included incident myocardial infarction (MI), revascularization, and stroke. During 54,656 person-years of follow-up, there were 452 CHD events (including MI and revascularization) and 182 incident stroke cases. Frequent nut and peanut butter consumption was inversely associated with total CVD risk in age-adjusted analyses. After adjustment for conventional CVD risk factors, consumption of at least 5 servings/wk of nuts or peanut butter [serving size, 28 g (1 ounce) for nuts and 16 g (1 tablespoon) for peanut butter] was significantly associated with a lower risk of CVD (relative risk = 0.56; 95% CI: 0.36–0.89). Furthermore, when we evaluated plasma lipid and inflammatory biomarkers, we observed that increasing nut consumption was significantly associated with a more favorable plasma lipid profile, including lower LDL cholesterol, non-HDL cholesterol, total cholesterol, and apolipoprotein-B-100 concentrations. However, we did not observe significant associations for HDL cholesterol or inflammatory markers. These data suggest that frequent nut and peanut butter consumption is associated with a significantly lower CVD risk in women with type 2 diabetes. J. Nutr. 139: 1333–1338, 2009.

Introduction

Despite being high in fat and relatively energy dense, higher intake of nuts has been associated with several health benefits, including reduced risk of cardiovascular disease (CVD)[8] (1). Beneficial health effects have been attributed to the macronutrient and micronutrient profiles of nuts (2). Prospective studies have reported a consistent inverse association between nut consumption and risk of coronary heart disease (CHD) and nuts have been proposed as one component of an optimal diet for prevention of CVD (1). Patients with diabetes are at higher risk for developing CVD and whether the cardio-protective effect of nuts extends to diabetic patients remains unclear. We have thus prospectively evaluated the relationship between nut and peanut butter consumption and CVD, including CHD and stroke, among women with type 2 diabetes in the Nurses' Health Study (NHS). A secondary objective was to examine whether nuts favorably influence the risk of CVD through modulation of plasma lipids or markers of inflammation.

Materials and Methods

Participants

Study population. The NHS was established in 1976. Follow-up questionnaires have been sent biennially to update information on potential risk factors and to identify newly diagnosed CHD, stroke, and other diseases. In the present study, the design was a prospective cohort study (1980–2002) with open enrollment, whereby participants began contributing person-years on the date they first reported a diagnosis of diabetes until the occurrence of a CVD endpoint, death, or June 1, 2002, whichever came first. After excluding participants with CVD or cancer,

there were 1508 women with prevalent type 2 diabetes at baseline in 1980. There were 4801 additional women who developed type 2 diabetes after 1980. Therefore, the final analysis included 6309 women with diabetes who were followed until 2002. Blood samples were available for a subset of this cohort ($n = 1171$) who had diabetes and were free from CVD or cancer at the time of the blood collection in 1989–1990. The Harvard School of Public Health and the Brigham Women's Hospital Human Subjects Committee Review Board approved the study protocol.

Definition of diabetes

A supplementary questionnaire regarding symptoms, diagnostic tests, and antihyperglycemic therapy was mailed to women who indicated on any biennial questionnaire that they had diabetes. We used the National Diabetes Data Group criteria (3) to define diabetes, because diabetes in our participants was diagnosed before the release of the American Diabetes Association criteria in 1997. The validity of this method has been described elsewhere (4). We used the American Diabetes Association diagnostic criteria (5) for diabetes occurring post 1997. A woman was considered to have diabetes if at least 1 of the following was present: *1*) classic symptoms plus elevated fasting plasma glucose ≥7.8 mmol/L and/or random plasma glucose ≥11.1 mmol/L, and/or plasma glucose ≥11.1 mmol/L after ≥2 h during an oral glucose tolerance test; *2*) no symptoms but at least 2 elevated plasma glucose concentrations (by the above criteria) on different occasions; or *3*) treatment with oral antihyperglycemic agents or insulin.

Dietary assessment

The semiquantitative FFQ included 61 foods in 1980 and was later revised and expanded to about twice the number of foods in subsequent cycles. 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 were described in detail elsewhere (6). The corrected correlation coefficient was 0.75 ($P < 0.05$) between intakes assessed by the 1980 questionnaire and by 4 1-wk diet records for nuts and peanut butter (7). 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 up the products across all food items. The food composition values were obtained from the Harvard University Food Composition Database derived from the USDA sources and supplemented with manufacturer information.

In the 1980 and 1984 dietary questionnaires, participants were asked how often, on average, they consumed nuts [serving size, 28 g (1 ounce)] during the previous year according to the following categories: never/almost never, 1–3 servings/mo, 1 serving/wk, 2–4 servings/wk, 5–6 servings/wk, 1 serving/d, 2–3 servings/d, 4–6 servings/d, or >6 servings/d. In the 1986, 1990, 1994, and 1998 dietary questionnaires, the question for nuts was divided into 2 separate questions: peanuts and other nuts. We note that although peanuts are botanically classified as legumes, they are rich in monounsaturated fat and the nutrient profile is very similar to other nuts (8). Total nut consumption was calculated in the questionnaires since 1986 as the sum of the intake for peanuts and other nuts. Consumption of peanut butter (serving size, 16 g [1 tablespoon]) was assessed in 1980, 1984, 1986, 1990, 1994, and 1998 with the same 9 responses as those for nut consumption. Peanut butter is a commercial spread that shares similar nutrients with peanuts. In the 1980 questionnaire, 5.8% of women with type 2 diabetes reported consumption of nuts >5 servings/ wk; therefore, we included the summation of total nuts and peanut butter to improve the power of the study. In addition, we evaluated the independent effects of total nuts and peanut butter on CVD. We collapsed 9 possible responses into 4 exposure categories for frequency of nut consumption: almost never, 1–3 servings/mo to 1 serving/wk, 2–4 servings/wk, and at least 5 servings/wk based on frequency distribution of the variables. To represent long-term intake of nuts and peanut butter most accurately and to reduce measurement error, we calculated the cumulative mean number of servings per week from all available questionnaires.

CVD endpoints

Cardiovascular endpoints consisted of fatal CHD, nonfatal myocardial infarction (MI), stroke, and coronary by-pass surgery/coronary angioplasty. Endpoints did not include angina pectoris. Nonfatal MI was confirmed by reviewing medical records using the WHO criteria for symptoms plus either typical electrocardiographic changes or elevated cardiac enzyme levels. Cardiovascular deaths were confirmed by review of medical records or autopsy reports with the permission of the next of kin. The cause listed on the death certificate was not considered sufficient for documentation of a coronary death. Sudden deaths (i.e. death within 1 h of symptom onset in a woman without known disease that could explain death) were considered cardiovascular deaths. A definite diagnosis of stroke was made when computerized tomography scan, MRI, angiography, surgery, or autopsy confirmed the lesion; otherwise, a probable diagnosis was made. Computerized tomography or MRI reports were available for 89% of those with medical records. Physicians who reviewed the records had no knowledge of the self-reported risk factor status and/or study hypothesis. Deaths were reported by next of kin, the postal system, and through records of the National Death Index. Using all sources combined, it is estimated that follow-up for deaths was at least 98% complete (9).

Blood collection and assessment of plasma lipids

Blood samples were drawn between 1989 and 1990, with the majority being drawn in 1990 (81%). Women willing to provide blood specimens were sent instructions and a phlebotomy kit. Blood specimens were returned by overnight mail on ice, centrifuged ($1200 \times g$; 15 min) on arrival to separate plasma from buffy coat and red cells and frozen in liquid nitrogen until analyzed. Ninety-seven percent of the samples arrived within 26 h of phlebotomy. Quality-control samples were routinely frozen along with study samples to monitor changes due to long-term storage and assay variability. All markers were measured in the Clinical Chemistry Laboratory at the Children's Hospital in Boston. Processing times did not substantially affect the concentrations of the markers. The concentrations of total cholesterol and triacylglycerols were measured simultaneously from the blood samples with the Hitachi 911 analyzer with reagents and calibrators from Roche Diagnostics. Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol. Apolipoprotein-B-100 (ApoB) was measured with immuno-nephelometric assay (Wako Chemicals). The inflammatory markers measured included tumor necrosis factor (TNF) receptor II, intercellular adhesion molecule-1 (ICAM-1), E-selectin, C-reactive protein (CRP), and fibrinogen. TNF receptor II levels were measured by an ELISA kit utilizing immobilized monoclonal antibody to human TNF-R2 (Genzyme). Levels of ICAM-1 and E-selectin were measured by commercial ELISA (R & D Systems). CRP levels were measured via a high-sensitivity latex-enhanced immunonephelometric assay on a BN II analyzer (Dade Behring). Fibrinogen was measured on a Hitachi 911 analyzer using reagents and calibrators from Kamiya Biomedical. The CV for each analyte were <10%.

Plasma lipid and other biochemical analyses were performed in 2003. Degradation of the specimens after long-term storage may theoretically be a concern. However, several investigators have used frozen specimens for lipids with little degradation with storage at −20°C (10). Because our specimens are stored at considerably colder temperatures (liquid nitrogen), any possible degradation is further minimized. Further, we have demonstrated normal-range values and predictive capacity of plasma lipids and lipoproteins in the NHS and the Health Professionals Follow-up Study (11,12).

Assessment of other variables

Participants completed a questionnaire every 2 y, including assessment of physical activity, cigarette smoking, alcohol consumption, menopausal status, and use of postmenopausal hormone therapy. Additional questions included duration of diabetes, family history of MI, hypertension, and hypercholesterolemia. BMI was calculated as weight (kg) divided by height squared (m^2).

Statistical analysis

The analysis population was comprised of women with type 2 diabetes who contributed follow-up time from the date on which type 2 diabetes

was reported until the occurrence of a CVD endpoint, death, or June 1, 2002, whichever came first. We classified women into 4 exposure categories according to frequency of consumption: almost never, 1–3 servings/mo to <1 serving/wk, 1–4 servings/wk, and at least 5 servings/wk. Hazard ratios for CVD endpoints were estimated using Cox proportional hazard models with calendar year as time scales. Potential confounders included age (5-y categories), BMI (<23.0, 23.0–24.9, 25.0–29.9, 30.0–34.9, and ≥35.0), quintiles of physical activity (h/wk), smoking status [never smoker, past smoker, or current smoker (1–14 and ≥15 cigarettes/d)], alcohol consumption (nondrinker and 0–4.9, 5.0–9.9, 10–14.9, and ≥15.0 g/d), current aspirin use, postmenopausal hormone therapy (premenopausal and never, past, and current user), and total energy intake (kJ/d). Further adjustment for nutrients and foods that have previously been found to be associated with CVD risk (*trans* and saturated fats, glycemic load, cereal fiber, processed meat, fruit and vegetables) was also performed.

We used generalized linear regression models to calculate the age-adjusted geometric means and standard errors for lipids among each category of nut consumption. Log transformations were performed for plasma concentrations of the markers to better approximate the normal distribution. Multiple linear regression analyses were used to assess the relationship between increment of 1 serving/d of nut and peanut butter consumption and plasma concentrations of lipid and inflammatory markers.

All *P*-values were 2-sided. Tests for linear trend across increasing categories of nut consumption were performed using the median value for each category of nut consumption analyzed as a continuous variable in regression models. All analyses were performed with SAS version 9.1 (SAS Institute).

Results

During 54,656 person-years of follow-up from 1980 to 2002, there were 634 cases of CVD (452 fatal and nonfatal MI and 182 strokes). Women at study entry who consumed more nuts and peanut butter were leaner, more physically active, and tended to smoke less. They also reported a slightly longer duration of diabetes and less hypertension. Women consuming at least 5 servings/wk of nuts and peanut butter had higher intakes of total energy, polyunsaturated fat, red meat, fruits, and vegetables and a significantly lower glycemic load than the other exposure categories of nut consumption (**Table 1**).

Frequent nut and peanut butter consumption was inversely associated with total CVD risk in age-adjusted analyses (**Table 2**). After controlling for conventional CVD risk factors that may confound the association between nut consumption and CVD, the association was slightly attenuated, but higher consumption (≥5 servings/d) remained significantly associated with decreased risk. Compared with women who almost never consumed nuts and peanut butter, women consuming at least 5 servings/wk had a significantly lower CVD risk by 44% (95% CI: 11–64%) and MI risk by 44% (95% CI: 3–67%). We did not find evidence for a significant linear trend across increasing categories of nut consumption for either CVD or MI endpoints after adjustment for CVD risk factors.

In sensitivity analyses, we further explored additional adjustment for mono- and polyunsaturated fats. Again, we found evidence for a decreased risk with higher nut consumption; the relative risk (RR) for CVD in subjects who consumed nut and peanut butter ≥5 servings/wk compared with those who did not consume nut and peanut butter was 0.58 (95% CI: 0.36–0.94) and for MI was 0.60 (95% CI: 0.34–1.06). The inclusion of null value 1 in the CI for the MI endpoint possibly reflects limited power with decreased number of MI events.

In a traditional risk factors-adjusted model with both nuts and peanut butter, the RR for consumption of 1–3 servings/mo of nuts to 1 serving/wk, 2–4 servings/wk, and ≥5 servings/wk compared with no consumption were 0.79, 0.70, and 0.54 (95% CI: 0.28–1.08; *P*-trend = 0.020), respectively. For peanut butter, the RR were 1.00, 0.93, and 0.75 (95% CI: 0.46–1.22; *P*-trend = 0.19), respectively. After additional adjustment for potential dietary confounding variables such as red meat, fruit and vegetables, whole grains, and dairy, the RR for CVD in participants who consumed ≥5 servings/wk of nut and peanut butter compared with those who did not consume was 0.66 (95% CI: 0.44–0.99) and for MI was 0.62 (95% CI: 0.38–1.02). In addition, when we excluded women who took vitamin E and multivitamin supplements, the results were similar.

Table 3 presents the association of nut and peanut butter consumption with plasma lipids among the subgroup of participants (*n* = 1171) for whom blood samples were available. Women who consumed at least 5 servings/wk of nuts and peanut butter had significantly lower LDL cholesterol, non-HDL cholesterol, total cholesterol, and concentrations than those who consumed less. There was a strong inverse association in multivariate-adjusted analyses for a 1-serving/d increment with the above-mentioned plasma lipids (β coefficients): −0.17 mmol/L, −0.18 mmol/L, −0.19 mmol/L, and −0.04 g/L; *P*-values: 0.008, 0.014, 0.007, and 0.016, respectively. There was no association between HDL cholesterol concentrations and nut and peanut butter consumption. In addition, nut consumption was not significantly associated with inflammatory markers, including TNF receptor II, ICAM-1, E-selectin, CRP, and fibrinogen (data not shown).

Discussion

In this prospective cohort study with 54,656 person-years of follow-up, frequent nut and peanut butter consumption of at least 5 servings/wk was associated with a significantly lower risk of CVD and MI among women with type 2 diabetes. In addition, frequent nut and peanut butter consumption was associated with lower LDL cholesterol, non-HDL cholesterol, total cholesterol, and ApoB concentrations in a subset of this cohort for which we had blood measurements.

Frequent consumption of nuts and/or peanut butter has been associated with decreased CVD risk in several large, prospective cohort studies. In the Adventist Health Study (13), consumption of >4 servings/wk of nuts was associated with a 51% lower risk of nonfatal MI and 48% lower risk of fatal CHD compared with consumption of <1 serving/wk. Additionally, the association was more pronounced among vegetarians who had higher nut consumption compared with nonvegetarians. A protective effect was also evident in persons >84 y old (14) and in African-Americans (15). In the Iowa Women's Health Study (16), consumption of nuts more than once per week was associated with a 19% lower risk of fatal CHD death compared with consumption of less than once per month in postmenopausal women. Increased consumption of nuts and peanut butter combined had strong significant associations with lower risk for mortality for both CVD and CHD death; RR were 0.72 and 0.71, respectively, for consumption of at least 5 servings/wk compared with less than once per week (17). In the Physicians' Health Study (18), male physicians who consumed nuts more than once per week had a 30% reduction of fatal CHD risk. In previous studies, we found that consumption of nuts of at least 5 servings/wk was associated with a 34% reduction of CHD risk among healthy nurses (19). The current study extends these prior studies by demonstrating that frequent nut consumption is

TABLE 1 Baseline characteristics of 6309 women in the NHS with type 2 diabetes according to consumption of nuts and peanut butter[1,2]

	Almost never	1–3 servings/mo to 1 serving/wk	2–4 servings/wk	≥5 servings/wk
n	613	2275	2725	696
Nuts, servings/d	0	0.04 ± 0.04	0.13 ± 0.12	0.43 ± 0.49
Peanut butter, servings/d	0	0.04 ± 0.04	0.22 ± 0.15	0.78 ± 0.64
Age, y	52.8 ± 8.5	56.9 ± 8.9	58.6 ± 9.0	55.4 ± 9.9
BMI, kg/m²	29.6 ± 6.1	30.1 ± 6.5	29.9 ± 6.5	28.4 ± 6.3
Physical activity, h/wk	2.5 ± 2.3	2.4 ± 2.2	2.4 ± 2.1	2.7 ± 2.3
Current smokers, %	23	18	22	15
Alcohol consumption, g/d	3.6 ± 8.1	3.3 ± 8.0	3.0 ± 7.8	3.4 ± 8.4
Duration of diabetes, y	3.3 ± 5.1	2.6 ± 4.6	2.3 ± 4.2	3.6 ± 6.0
Family history of MI, %	21	22	25	23
Hypertension, %	65	63	60	53
Hypercholesterolemia, %	37	44	49	44
Hormone use among postmenopausal women, %	15	24	31	24
Multivitamin use, %	25	29	32	32
Vitamin E use, %	15	22	28	22
Aspirin use, %	31	47	36	35
Energy intake, kJ/d	6079 ± 2033	6522 ± 2033	7619 ± 2264	8330 ± 2293
Cereal fiber,[3] g/d	3.0 ± 1.8	3.4 ± 1.8	3.6 ± 1.6	3.3 ± 1.8
Polyunsaturated fat,[3] g/d	8.9 ± 2.9	9.5 ± 2.2	10.4 ± 2.1	11.8 ± 2.7
Monounsaturated fat,[3] g/d	20.7 ± 9.6	17.9 ± 8.4	16.8 ± 7.3	20.8 ± 9.0
Saturated fat,[3] g/d	26.4 ± 7.0	24.9 ± 5.9	23.9 ± 5.1	24.6 ± 5.4
Trans fat,[3] g/d	2.0 ± 2.3	1.4 ± 2.0	1.0 ± 1.8	1.6 ± 2.0
Glycemic load,[3] g/d	90.2 ± 28.8	94.5 ± 21.2	95.2 ± 18.1	88.1 ± 20.6
Red meat,[3] servings/d	1.27 ± 0.84	1.23 ± 0.69	1.29 ± 0.70	1.37 ± 0.75
Fruit and vegetables, servings/d	4.37 ± 2.15	4.65 ± 2.08	5.19 ± 2.18	5.45 ± 2.26

[1] Values are means ± SD unless otherwise indicated.
[2] One serving nuts = 16 g (1 tablespoon) and 1 serving peanut butter = 28 g (1 ounce); 1 red meat serving = 196 g; 1 fruit and vegetable serving = 100 g.
[3] Energy adjusted.

also beneficial for women with diabetes who are at increased risk of developing CVD.

Peanuts (including peanuts in peanut butter) are the most commonly consumed type of nut in the United States (20). Peanuts are proportionally low in saturated fat and high in mono- and polyunsaturated fats, which have been shown to improve the lipid profile by lowering LDL cholesterol (21).

Controlled feeding trials have demonstrated that diets containing peanuts decrease total and LDL cholesterol in both participants with normal cholesterol (22) and hyperlipidemia (8). Studies examining other types of nuts such as almonds (23), pistachios (24), pecans (25), and macadamia nuts (26) have found similar LDL cholesterol-lowering effects. Walnuts are particularly unique with a high content of polyunsaturated fats,

TABLE 2 The association of consumption of nuts and peanut butter with CVD/MI among 6309 women with type 2 diabetes in the NHS[1]

Nuts and peanut butter consumption	Almost never	1–3 servings/mo to 1 serving/wk	2–4 servings/wk	≥5 servings/wk	P-trend
CVD					
Person-years	3832	18529	25876	6419	
n	51	220	316	47	
Age-adjusted RR	1ref	0.67 (0.48, 0.94)	0.68 (0.48, 0.95)	0.43 (0.28, 0.67)	0.015
Multivariate RR[2]	1ref	0.72 (0.50, 1.02)	0.80 (0.56, 1.14)	0.56 (0.36, 0.89)	0.44
MI					
n	39	152	229	32	
Age-adjusted RR	1ref	0.60 (0.40, 0.91)	0.63 (0.43, 0.93)	0.40 (0.24, 0.67)	0.05
Multivariate RR[2]	1ref	0.63 (0.41, 0.96)	0.74 (0.49, 1.13)	0.56 (0.33, 0.97)	0.85

[1] One serving nuts = 16 g (1 tablespoon) and 1 serving peanut butter = 28 g (1 ounce).
[2] Multivariate model was adjusted for age, BMI, physical activity, alcohol consumption, family history of MI, hormone use and menopausal status, smoking, aspirin intake, duration of diabetes years, hypertension, hypercholesterolemia, total energy intake, cereal fiber, glycemic load, saturated fat, and trans fat.

TABLE 3 Plasma lipid concentrations according to consumption of nuts and peanut butter among 1171 women with type 2 diabetes in the NHS who had blood collected in 1989–1990[1]

Nuts and peanut butter consumption	Almost never	1–3 servings/mo to 1 serving/wk	2–4 servings/wk	≥5 servings/wk	Linear regression coefficients $\beta \pm SE$	P-value[2]
n	96	410	504	161		
LDL cholesterol, *mmol/L*						
Age adjusted	3.60	3.55	3.43	3.30	−0.20 ± 0.06	0.0008
Multivariate adjusted[3]	3.66	3.55	3.43	3.31	−0.17 ± 0.17	0.008
Non-HDL cholesterol, *mmol/L*						
Age adjusted	4.73	4.54	4.37	4.29	−0.25 ± 0.07	0.0003
Multivariate adjusted[3]	4.72	4.51	4.38	4.35	−0.18 ± 0.07	0.014
HDL cholesterol, *mmol/L*						
Age adjusted	1.31	1.24	1.31	1.27	0.03 ± 0.02	0.26
Multivariate adjusted[3]	1.34	1.26	1.30	1.24	−0.02 ± 0.02	0.45
Total cholesterol, *mmol/L*						
Age adjusted	6.09	5.83	5.75	5.62	−0.22 ± 0.07	0.0009
Multivariate adjusted[3]	6.11	5.83	5.76	5.65	−0.19 ± 0.07	0.007
ApoB, *g/L*						
Age adjusted	1.08	1.04	1.00	0.98	−0.06 ± 0.02	0.0003
Multivariate adjusted[3]	1.07	1.04	1.01	1.00	−0.04 ± 0.02	0.016

[1] One serving nuts = 16 g (1 tablespoon) and 1 serving peanut butter = 28 g (1 ounce).

[2] P-values are from the multiple linear regression models for the relation between nut and peanut butter consumption (1 serving/d increase) and biomarkers.

[3] Multivariate model was adjusted for age, BMI, physical activity, alcohol consumption, family history of MI, hormone use and menopausal status, smoking, aspirin intake, duration of diabetes years, hypertension, total energy intake, cereal fiber, glycemic load, saturated fat, and trans fat.

mostly linoleic and α-linolenic acids, which have also been shown to improve serum lipids in hypercholesterolemic participants when walnuts were substituted for monounsaturated fat (27). In the subset of 1171 women with diabetes for whom blood samples were available in the current study, for every 1-serving/d increase in nut consumption, there was a significant decrease in LDL cholesterol by 0.17 mmol/L. This observed reduction in LDL cholesterol levels is consistent with findings from intervention studies (28).

In addition to improvement of lipid levels, there are multiple other possible mechanisms through which nut and peanut butter consumption may produce a cardio-protective effect, including decreasing lipoprotein oxidation (27,29), inhibition of inflammation (30), decreasing insulin resistance (31), and improving endothelial function (29). In a cross-sectional analysis of participants participating in the Multi-ethnic Study of Atherosclerosis, frequent nut and seed consumption was associated with lower levels of CRP, IL-6, and fibrinogen (30). In a previous analysis of the NHS cohort, higher consumption of nuts and peanut butter was associated with a lower risk of type 2 diabetes (32). Nuts are rich in fiber, phytosterols, folate, magnesium, vitamin E, and arginine, which may mediate the observed benefit on cardiovascular health. In our analysis, after controlling for fat, fiber, glycemic load, and vitamin, a consumption of nuts of at least 5 servings/wk was still significantly associated with a reduction in CVD and CHD risk, suggesting that these nutrients do not completely account for the protective effects of nuts in the current analysis. It is possible that some other unmeasured nutrients such as phytosterols and/or arginine contribute to the observed effects.

Our study has several strengths, including its large sample size, biennial assessment of exposure, and long duration of follow-up. We examined cumulative mean dietary intake of nut and peanut butter consumption during follow-up. Thus, our updated analyses took into account dietary changes over time. Our study also has several limitations, including misclassification of exposure, but this would be expected to bias results toward the null and would not explain the significant results reported herein. The beneficial effects of different nuts may vary and our study could not differentiate specific types of nuts. In addition, because blood samples were only available in a subset of participants, we had inadequate power to fully examine associations between nut consumption and biomarkers.

In conclusion, frequent nut consumption, especially at least 5 servings/wk, was associated with a reduced risk of CVD and MI among women with type 2 diabetes. These data support a role for regular consumption of nuts in reducing CVD risk among patients with diabetes.

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