Nuts as a Replacement for Carbohydrates in the Diabetic Diet

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OBJECTIVE—Fat intake, especially monounsaturated fatty acid (MUFA), has been liberalized in diabetic diets to preserve HDL cholesterol and improve glycemic control, yet the exact sources have not been clearly defined. Therefore, we assessed the effect of mixed nut consumption as a source of vegetable fat on serum lipids and HbA_{1c} in type 2 diabetes.

RESEARCH DESIGN AND METHODS—A total of 117 type 2 diabetic subjects were randomized to one of three treatments for 3 months. Supplements were provided at 475 kcal per 2,000-kcal diet as mixed nuts (75 g/day), muffins, or half portions of both. The primary outcome was change in HbA_{1c}.

RESULTS—The relative increase in MUFAs was 8.7% energy on the full-nut dose compared with muffins. Using an intention-to-treat analysis ($n = 117$), full-nut dose (mean intake 73 g/day) reduced HbA_{1c} (−0.21% absolute HbA_{1c} units, 95% CI −0.30 to −0.11, $P < 0.001$) with no change after half-nut dose or muffin. Full-nut dose was significantly different from half-nut dose ($P = 0.004$) and muffin ($P = 0.001$), but no difference was seen between half-nut dose and muffins. LDL cholesterol also decreased significantly after full-nut dose compared with muffin. The LDL cholesterol reduction after half-nut dose was intermediate and not significantly different from the other treatments. Apolipoprotein (apo) B and the apoB:apoA1 ratio behaved similarly. Nut intake related negatively to changes in HbA_{1c} ($r = -0.20$, $P = 0.033$) and LDL cholesterol ($r = -0.24$, $P = 0.011$).

CONCLUSIONS—Two ounces of nuts daily as a replacement for carbohydrate foods improved both glycemic control and serum lipids in type 2 diabetes.

Replacement of carbohydrate by healthy fat, such as monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs), has been increasingly recognized as a possible therapeutic strategy in the treatment of diabetes (1) as concerns emerge over the impact of refined carbohydrate foods in increasing postprandial glycemia and reducing HDL cholesterol (1). At the same time, increased proportions of fat and protein in the diet, especially of plant origin (2,3), may confer metabolic benefits and reduce the risk of developing coronary heart disease (CHD) and diabetes. However, there is little guidance on the optimal foods with which to increase the fat and protein intakes, and fear persists that increasing the proportion of fat in the diet will increase body weight (1). Nevertheless, use of nuts to increase fat intake has not resulted in weight gain, and habitual nut consumption lowers LDL cholesterol (4). Furthermore, nut intake has been associated with reduced CHD risk, a major cause of death in diabetes (4–6). Despite these potential advantages of nuts, few studies have been undertaken in diabetes, and none have demonstrated advantages in glycemic control (7–10).

Therefore, we have carried out a study specifically to test the effect on glycemic control and serum lipids of substituting nuts as a source of fat and vegetable protein to replace carbohydrate foods (muffins) in the diets of patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

—Subjects were recruited by a newspaper advertisement and from previous studies. A total of 117 subjects were eligible and randomized (Supplementary Fig. 1). Recruitment took place from April 2007 to September 2008, with the last follow-up visit on 18 December 2008. Eligible participants were men or postmenopausal women with type 2 diabetes who were taking antidiabetic agents other than acarbose, with medications stable for the previous 3 months and who had HbA_{1c} values at screening between 6.5 and 8.0% (Table 1). No participants had clinically significant cardiovascular, renal, or liver disease (alanine aminotransferase more than three times the upper limit of normal) or a history of cancer. Subjects were accepted after surgery or myocardial infarction if they had an event-free 6-month period before the study. One subject had changed medications within 3 months before the start of the study. Nevertheless, all randomized subjects were retained for the intention-to-treat analyses.

Protocol

The study was a 3-month randomized parallel study with two supplements and three treatments consisting of the following: a full portion of mixed nuts, a half portion of both nuts and muffins, or a full portion of muffins. After stratification by sex and HbA_{1c} (<7.1%), randomization was carried out using subject identification by a statistician who was geographically separate from the center

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Table 1—*Baseline characteristics of study participants*

	Number (%) of participants			
	Nuts	Half dose	Muffins	*P*
n	40	38	39	
Age (years)*	63 (9)	62 (8)	61 (10)	0.61†
Sex				
Male	26 (65)	26 (68)	26 (67)	0.97‡
Female	14 (35)	12 (32)	13 (33)	
Race/ethnicity				
European	23 (58)	25 (66)	18 (46)	0.83‡
Indian	10 (25)	8 (21)	13 (33)	
Far Eastern	4 (10)	3 (8)	3 (8)	
African	3 (8)	2 (5)	3 (8)	
Hispanic	0 (0)	0 (0)	1 (3)	
Native American	0 (0)	0 (0)	1 (3)	
Weight (kg)*	80 (15)	86 (16)	83 (15)	0.20†
BMI (kg/m^2)*	29 (5)	30 (5)	29 (4)	0.37†
Current smokers	2 (5)	4 (11)	3 (8)	0.57‡
HbA_{1c} (%)				
<7.0	20 (50)	20 (53)	22 (56)	0.84‡
≥7.0	20 (50)	18 (47)	17 (44)	
Duration of diabetes (years)*	7 (6)	8 (6)	8 (6)	0.57†
Medication use				
Hypoglycemic medications	40 (100)	38 (100)	39 (100)	1.00‡
Thiazolidinedione	12 (30)	11 (29)	11 (28)	1.00‡
Biguanide	35 (88)	36 (95)	35 (90)	0.62‡
Sulfonylurea	14 (35)	13 (34)	17 (44)	0.64‡
Meglitinides (nonsulfonylurea)	2 (5)	3 (8)	2 (5)	0.79‡
α-Glucosidase inhibitors	0 (0)	0 (0)	0 (0)	1.00
Dipeptidyl peptidase-4 inhibitor	0 (0)	0 (0)	1 (3)	0.66‡
Cholesterol-lowering medications	23 (58)[a]	31 (82)[b]	30 (77)[ab]	0.046‡
Blood pressure medications	23 (58)	29 (76)	28 (72)	0.12‡

Data are *n* (%) or *mean (SD). †*P* value is for overall *F* test for between-groups differences using the generalized linear model ANOVA. ‡*P* values for Fisher exact test where appropriate were calculated separately for distribution of each medication, since participants were from multiple nationalities or on multiple medications. A difference in superscript letters signifies a significant difference in percentage changes using the Q statistic.

at which subjects were seen. Neither the dietitians nor the participants could be blinded to the treatment allocation. However, equal emphasis was placed on the potential importance for health of both supplements. The analytical technicians were blinded to treatment, as was the statistician up to and during the preliminary assessment of the primary outcome of HbA_{1c}.

Participants were seen in the center for screening at week −1, baseline, and weeks 2, 4, 8, 10, and 12 of the study. At baseline and throughout the study, they received instructions on how to incorporate the supplement into their diets. At each center visit, participants were weighed in indoor clothing without shoes, and a fasting blood sample was taken. Only the baseline and week 12 body weight data were used in the final analysis. Also at each visit, blood pressure was measured seated on three occasions at 1-min intervals using an Omron (HEM 907 XL) automatic sphygmomanometer (Omron Healthcare, Burlington, Ontario, Canada), and the average of the three measurements was taken. In addition, participants brought with them their 7-day food record covering the week before the visit, and this record was discussed with the dietitian.

During the study, participants were asked to constantly maintain their oral antidiabetic medications and to have a form signed by their family physicians supporting their study involvement. If patients experienced symptoms of hypoglycemia with blood glucose levels <3.50 mmol/L (one patient on full-nut supplement) and provided that hypoglycemia was not explained by specific circumstances such as missed meals or increased physical activity, medications were reduced according to a predetermined protocol by the participants' physician. If HbA_{1c} rose to >8.5% on two successive occasions, participants were to be withdrawn from the study and referred back to their own physician. Only two subjects were withdrawn: one in the muffin group and the other on the half-nut dose. Both had recruitment HbA_{1c} levels of 8.0%, which rose above 8.5% on two successive occasions (Supplementary Fig. 1).

The study was approved by the research ethics board of St. Michael's Hospital and the University of Toronto, and written consent was obtained from all participants.

Dietary interventions

Participants were counseled to substitute the supplement calories where possible for the carbohydrate foods in their original diets. General dietary advice conformed to the National Cholesterol Education Program Adult Treatment Panel III and the American Diabetes Association guidelines to reduce saturated fat and cholesterol intakes (Supplementary Table 1). Of the participants, 43% were obese (50/117, BMI >30 kg/m^2) and wished to lose weight. They were informed that this was not a weight-loss study but were given advice on portion size and fat intake to help them meet their weight-reduction objectives. Compliance was assessed from the mean of the five 7-day diet records per treatment (weeks 2, 4, 8, 10, and 12).

Supplements

The nuts supplied consisted of a mixture of unsalted and mostly raw almonds, pistachios, walnuts, pecans, hazelnuts, peanuts, cashews, and macadamias. The muffin was developed to be a healthy whole-wheat product, sweetened with apple concentrate, with no sugar added. The muffin had similar protein content to the nuts, by the inclusion of egg white and skim milk powder. The calories from MUFAs in the nuts were the same by design as the carbohydrate calories in the muffin (Supplementary Table 2).

Energy requirements

Energy requirements were calculated for each participant as referenced previously (3), using the Harris-Benedict equation, with allowance for physical activity. Those participants with energy requirements of

>2,400 calories received supplements of 630 kcal (100 g nuts [*n* = 0]; four muffins [*n* = 1]; or 50 g nuts and two muffins [*n* = 1]); individuals whose requirements were 1,600–2,400 kcal received supplements of 475 kcal (75 g nuts [*n* = 38]; 37.5 g nuts plus one and a half muffins [*n* = 36]; or three muffins [*n* = 36]); and individuals whose requirements were <1,600 kcal received supplements of 315 kcal (50 g nuts [*n* = 2]; 25 g nuts and one muffin [*n* = 1]; or two muffins [*n* = 2]) (Supplementary Table 2).

Biochemical analyses

HbA_{1c} was analyzed within 2 days of collection on whole blood collected in EDTA Vacutainer tubes and measured by a designated high-performance liquid chromatography (HPLC) method (Tosoh G7 Automated HPLC Analyzer; Tosoh Bioscience, Grove City, OH) (CV 1.7%). Blood glucose was measured in the hospital routine analytical laboratory by a glucose oxidase method. Serum samples stored at −70°C were analyzed for lipids, and apolipoproteins (apo) and oxidative products were analyzed at the end of the study. LDL cholesterol was calculated by the method of Friedwald et al. (3). C-reactive protein (CRP) was measured by end point nephelometry. Oxidized products were measured on participants who completed the study. Oxidized LDL was measured chemically as conjugated dienes and thiobarbituric acid–reactive substances in the LDL fraction (11,12), and oxidized serum proteins were measured as protein thiols (13).

Diets were analyzed in 115 participants with baseline data using a computer program based on the data from the U.S. Department of Agriculture (3) and international glycemic index tables (14), with additional measurements made on local foods.

Power calculations

The initial power calculation was based on an assumption of a 20% dropout and an effect size of 0.8% HbA_{1c} units with an SD of effect of 1.235% ($\alpha = 0.05$, $1\text{-}\beta = 0.8$), for which 30 subjects per group were required. This calculation was revised after publication of a low glycemic index trial. The effect size of the change in HbA_{1c} was adjusted to 0.45% HbA_{1c} units, similar to a modest effect of acarbose with an SD of effect of 0.60% HbA_{1c} units (15). These values were also in line with the HbA_{1c} data of the completer and intention-to-treat groups, respectively, from the recent low glycemic index study. For the comparison of nuts with muffins, 40 subjects would be required per group ($\alpha = 0.05$, $1\text{-}\beta = 0.8$). No prior adjustment was made for the multiple comparisons necessary for assessment of a dose response. To establish significance for the three comparisons using the Bonferroni correction, $P < 0.0175$ was required. The power was, therefore, designed to assess the primary outcome of the difference in change in HbA_{1c} between full-nut dose versus muffins.

Statistical analyses

Results are expressed as means ± SD or 95% CIs. The significance of treatment differences was assessed by the CONTRAST statement in SAS version 9.2 (16), which allows comparisons of repeated measures over time based on a *t* test statistic with equal weighting for each value. In this study, the three values for the last month (end of weeks 8, 10, and 12) were expressed individually as changes from the mean baseline (mean of weeks −1 and 0). The model also used baseline as a covariate. The primary analysis was an intention-to-treat analysis, including all randomized subjects (*n* = 117) with the baseline observation carried forward for subjects who did not have at least one value in the last month (i.e., end of weeks 8, 10, and 12) (*n* = 14). Subjects who were randomized but did not start (*n* = 1) had their screening value used as baseline, and this value was carried forward (Supplementary Fig. 1). Unadjusted significance levels are given in the text, tables, and figures. Using the Bonferroni correction, for three-way comparisons, these differences were significant when the *P* value was <0.0175. Where only start and end values were available (diet, markers of oxidative stress, and body weight), significance was assessed by the least square means procedure in SAS with a Tukey adjustment for multiplicity of comparisons. Pearson correlations were used to examine the relation of nut intake to changes in HbA_{1c}, lipids, and apolipoproteins. Nut consumption was defined as the difference in total tree nut, peanut, and nut butter intake in grams per day between the pretreatment and end of treatment week assessed from the 7-day diet records. The dose-response analyses on nut and MUFA intakes (% energy) and change in study outcomes were performed by regression analyses pooling the responses across the three treatment groups.

RESULTS—Of the participants, 39 of 40 (97.5%) completed the full-nut dose (i.e., provided a blood sample in the final month), compared with 32 of 38 (84%) of those taking the half-nut dose and 32 of 39 (82%) on muffins. In the half-nut dose group, one subject dropped out after randomization but was unaware of his treatment allocation, and one participant was withdrawn because of two consecutive HbA_{1c} levels >8.5%. In the muffin group, one participant developed allergic symptoms. In the full-nut dose group, one participant developed a nut allergy. These subjects' data were retained for the intention-to-treat analyses.

No treatment differences were seen at baseline in diet, blood pressure, or anthropometric measurements (Tables 1 and 2 and Supplementary Table 1). During the study, MUFA intake, expressed as percent of total energy, increased significantly after full-nut dose consumption (Supplementary Tables 1 and 2) compared with muffins (8.7%, 95% CI 7.1–10.4, $P < 0.001$). There was good compliance with all treatments (90.6–97.3).

Glycemic control and body weight

In the intention-to-treat analysis, oral hypoglycemic medication dosages increased in one participant in the half-nut dose group, with reductions for two participants. Three participants (one in each group) had their Avandia switched to Actos after media alerts.

The mean HbA_{1c} fell −0.21% absolute HbA_{1c} units (95% CI −0.30 to −0.11, $P < 0.001$) on the full-nut supplement; −0.07% absolute HbA_{1c} units (−0.19 to 0.05, $P = 0.270$) on the half-nut dose supplement; and −0.05% absolute HbA_{1c} units (−0.16 to 0.06, $P = 0.355$) on the muffin supplement (Fig. 1). The reduction in HbA_{1c} on full-nut dose was significantly different from the half-nut dose ($P = 0.004$) and muffins dose ($P = 0.001$) (Fig. 1). The significance of the difference between full-nut dose and muffins in HbA_{1c} remained after adjustment for duration of diabetes or body weight using an ANCOVA model ($P = 0.023$ and $P = 0.004$, respectively). No significant changes from baseline were seen in blood glucose or body weight, and there were no significant differences in responses between treatments (Table 2 and Supplementary Tables 1 and 3). Nut intake related negatively to change in HbA_{1c} ($r = -0.20$, $n = 115$, $P = 0.033$). Through regression analysis, the full-dose (of 100 g/day) nut intake corresponded

Table 2—*Mean study measurements and significance of treatment differences in the intention-to-treat analysis*

	Baseline*			End point*			Treatment difference†		
	Full-nut dose	Half-nut dose	Muffins	Full-nut dose	Half-nut dose	Muffins	Full-nut dose vs. muffins (*P*)	Full- vs. half-nut dose (*P*)	Half-nut dose vs. muffins (*P*)
n	40	38	39	40	38	39			
Glucose (mmol/L)	7.3 (6.9–7.7)	7.4 (6.9–7.8)	7.1 (6.7–7.5)	7.2 (6.7–7.6)	7.4 (6.7–8.1)	7.2 (6.7–7.7)	0.079	0.304	0.681
HbA_{1c} (%)	7.1 (6.9–7.3)	7.1 (6.9–7.3)	7.1 (7.0–7.3)	6.9 (6.7–7.1)	7.0 (6.8–7.3)	7.1 (6.9–7.2)	0.001	0.004	0.863
Lipids (mmol/L)									
Total cholesterol	4.4 (4.1–4.8)	4.0 (3.8–4.2)	4.2 (3.9–4.5)	4.2 (3.9–4.6)	4.0 (3.8–4.3)	4.3 (3.9–4.6)	<0.001	0.042	0.203
LDL cholesterol	2.5 (2.1–2.8)	2.2 (2.0–2.4)	2.3 (2.0–2.5)	2.3 (1.9–2.6)	2.1 (1.9–2.4)	2.3 (2.1–2.6)	<0.001	0.123	0.048
HDL cholesterol	1.2 (1.1–1.2)	1.1 (1.0–1.2)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	0.405	0.364	0.995
Triglycerides	1.8 (1.5–2.0)	1.6 (1.3–1.8)	1.6 (1.4–1.9)	1.7 (1.3–2.0)	1.6 (1.3–1.9)	1.6 (1.4–1.8)	0.158	0.064	0.970
Total cholesterol:HDL cholesterol ratio	3.9 (3.6–4.3)	3.8 (3.3–4.2)	3.8 (3.4–4.2)	3.6 (3.3–3.9)	3.7 (3.2–4.1)	3.7 (3.3–4.1)	0.006	0.163	0.047
LDL cholesterol:HDL cholesterol ratio	2.2 (1.9–2.5)	2.1 (1.8–2.4)	2.1 (1.8–2.4)	1.9 (1.7–2.2)	1.9 (1.7–2.2)	2.0 (1.7–2.3)	0.002	0.163	0.013
ApoA1	1.5 (1.4–1.5)	1.5 (1.4–1.5)	1.5 (1.4–1.5)	1.5 (1.4–1.5)	1.5 (1.4–1.6)	1.5 (1.4–1.6)	0.26	0.249	0.976
ApoB	0.85 (0.76–0.93)	0.76 (0.70–0.82)	0.79 (0.72–0.85)	0.80 (0.72–0.88)	0.75 (0.69–0.81)	0.80 (0.73–0.87)	<0.001	0.147	0.012
ApoB:apoA1	0.58 (0.52–0.63)	0.54 (0.48–0.60)	0.55 (0.49–0.62)	0.54 (0.49–0.59)	0.52 (0.46–0.58)	0.55 (0.49–0.61)	0.004	0.537	0.001
Serum CRP (nmol/L)	1.6 (1.1–2.1)	1.8 (0.9–2.7)	1.9 (1.1–2.6)	2.2 (1.2–3.2)	1.5 (1.1–2.0)	2.0 (1.2–2.8)	0.682	0.186	0.042
Blood pressure (mmHg)									
Systolic	121 (118–125)	123 (119–128)	125 (121–129)	119 (116–123)	124 (120–128)	124 (120–128)	0.084	0.005	0.274
Diastolic	70 (67–73)	71 (69–74)	71 (68–75)	69 (66–72)	72 (70–74)	72 (68–75)	0.024	0.021	0.888

Data are means (95% CI). $n = 117$. *Baseline is an average of weeks −1 and 0 and end point is an average of weeks 8, 10, and 12, except for body weight (week 0). †Mean treatment differences (95% CI) were determined and *P* values were estimated by CONTRAST using average baseline and the difference from week 8, 10, and 12. Significance by Bonferroni, $P < 0.0175$.

to a −0.26% (95% CI −0.41 to −0.11) reduction in absolute HbA_{1c} units.

Serum lipids and apolipoproteins

Two participants in the full-nut dose group increased and one participant on the half-nut dose decreased lipid medications during the study. There were no changes in lipid medications in the muffin group. Significant between-treatment differences were seen with greater cholesterol reductions for the full-nut dose compared with muffins for total cholesterol (−0.24 mmol/L, 95% CI −0.44 to −0.04, $P < 0.001$); LDL cholesterol (−0.22 mmol/L, −0.41 to −0.03, $P < 0.001$) (Supplementary Fig. 2); and total cholesterol:HDL cholesterol (−0.23, −0.47 to 0.02, $P = 0.006$) (Table 2 and Supplementary Table 3). All three diets significantly raised the HDL cholesterol (full-nut dose: 0.04 mmol/L, 0.01–0.08, $P = 0.017$; half-nut dose: 0.03 mmol/L, 0.00–0.06, $P = 0.025$; and muffins: 0.03 mmol/L, 0.01–0.05, $P = 0.012$). Nut intake related negatively to total cholesterol ($r = -0.19$, $n = 115$, $P = 0.039$) and LDL cholesterol ($r = -0.24$, $n = 115$, $P = 0.011$). Through a regression analysis, the full-dose nut intake would be predicted to lower LDL cholesterol by −0.26 mmol/L (−0.42 to −0.10). Adjustment for lipid medications still resulted in a significant LDL cholesterol difference between full-nut dose and muffins ($P = 0.007$).

The changes in lipids were reflected in the corresponding changes in apolipoproteins. ApoB showed a greater reduction on full-nut dose versus muffins ($P < 0.001$) and half-nut dose versus muffins ($P = 0.012$) as did the apoB:apoA1 ratio (full-nut dose versus muffins, $P = 0.004$, and half-nut dose versus muffins, $P = 0.001$) (Table 2). Nut intake related to a reduction in apoB ($r = -0.26$, $n = 115$, $P = 0.006$).

Oxidized LDL cholesterol and plasma proteins, CRP, and blood pressure

No significant differences were seen between treatments for CRP (Table 2 and Supplementary Table 3) or measures of oxidative damage (data not shown). Blood pressure difference was not significant with or without adjustment for blood pressure medication use.

CONCLUSIONS—Increased mixed nut consumption as a source of unsaturated (monounsaturated and polyunsaturated) fat intake to replace dietary starch favorably affected both HbA_{1c} and serum

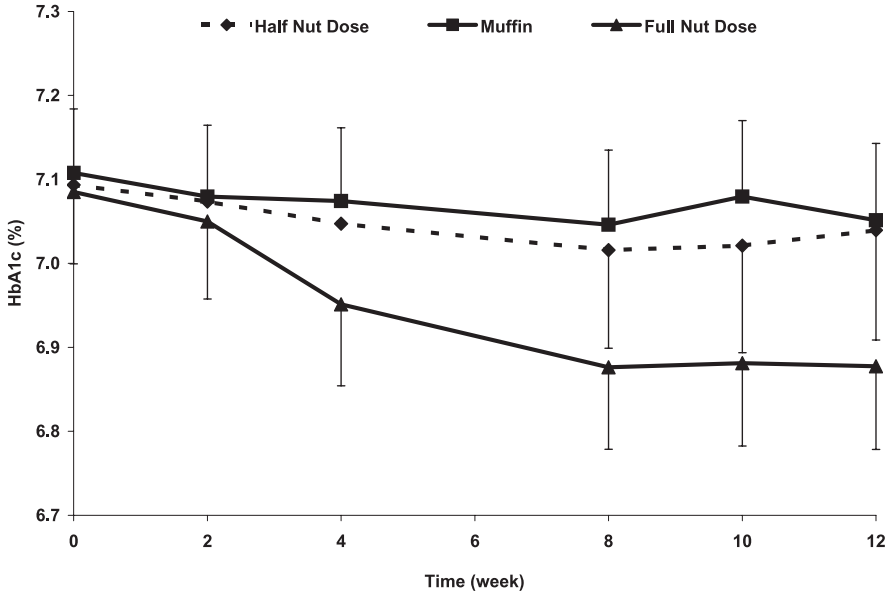

Figure 1—*Mean HbA_{1c} measurements in participants with type 2 diabetes consuming full-nut dose, half-nut dose, or muffins.*

lipids. These data provide a specific food option for individuals wishing to lower the carbohydrate content of the diet in type 2 diabetes.

Recently, there has been renewed interest in reducing carbohydrate content in the diet of diabetic patients. In 1994, on the basis of emerging evidence (17), the American Diabetes Association first suggested the possibility of exchanging dietary carbohydrate for MUFA in dietary recommendations for type 2 diabetes (18). Although not all studies have shown beneficial effects of MUFAs in diabetes (19), general interest has persisted, especially in the context of the Mediterranean diet. However, low carbohydrate intakes have also been achieved on the Atkins diet by increasing animal fats and proteins. This influential dietary pattern is reflected in the relatively lower prestudy carbohydrate intakes of ~45% in the current study rather than the 50–60% once recommended (20,21).

Cohort studies have provided additional support showing that higher vegetable fat and protein intakes are associated with a reduced risk of developing diabetes and CHD (2). The macronutrient profile of nuts fits well with low-carbohydrate, high–vegetable fat, and high-protein diets. Furthermore, neither in the current study nor in previous reports has nut consumption been associated with weight gain (22). If anything, nuts appear to be well suited as part of weight-reducing diets.

The reduction in HbA_{1c} was achieved despite baseline HbA_{1c} concentrations, which on entry were close to the target of <7.0% in participants who were already treated with one or more (average 1.5) antihyperglycemic medications. Furthermore, a reduction in LDL cholesterol was achieved even though the majority of subjects (84/117, or 72%) were already taking statins and had low mean baseline LDL cholesterol concentrations of 2.03 mmol/L (95% CI 1.90–2.16).

The full-nut dose reduced HbA_{1c} by two-thirds of the reduction recognized as clinically meaningful by the U.S. Food and Drug Administration (>0.3% absolute HbA_{1c} units) in the development of antihyperglycemic drugs (23). In addition, the number of participants who achieved an HbA_{1c} concentration of >7% (19 prestudy participants, down to 13 poststudy participants) was significantly greater on the nut treatment than on the muffin treatment (20 prestudy participants, remaining at 20 poststudy participants, Mantel-Haenszel test, $P = 0.040$). Based on data from the UK Prospective Diabetes Study and the ADVANCE study (24), the HbA_{1c} reduction for the full-nut dose would translate into a predicted 7–8% reduction in microvascular complications.

Methodological weaknesses included use of a 7-day diet history with the errors and inaccurateness associated with self-reported data, lack of blinding for participants and dietitians, and the attempt to demonstrate a dose response to nuts when the primary objective of establishing whether nuts improved glycemic control had not first been demonstrated. In addition, in the current study, nut consumption was substantial (37.5 g for the half-nut dose and 75 g/2,000 kcal) for the full-nut dose. However, the baseline nut intake was 12 g/day, and the compliance levels were high (i.e., 95.7 and 97.3% for the full-nut and half-nut groups, respectively). Therefore, we believe that, with the appropriate advice, nut intake at these levels can be achieved and maintained. Furthermore, the resulting relative increase in MUFA intake was modest at 8.7% of total calories for the full-nut dose.

The strengths of the study include its novelty as one of the first studies to assess nuts in type 2 diabetes coupled with measurement of HbA_{1c} and blood lipids at three time points in the last month to increase the validity of the assessment of blood lipids and glycemic control. The study length was adequate to see an HbA_{1c} effect. There was good compliance with the supplement and a dropout rate of 12%, which was lower than that seen in many other longer-term diet trials (25). Finally, there is a requirement for pharmacological interventions aimed at improving glycemic control to demonstrate that they have no negative impact on CHD (23). In this respect, nut consumption not only improved glycemic control but also lipid risk factors for CHD.

We have no explanation for the lack of antioxidant effects of nuts seen with previous studies but may relate to antioxidants in wheat bran and apple concentrate used in the muffins.

We conclude that mixed, unsalted, raw, or dry-roasted nuts have benefits for both blood glucose control and blood lipids and may be used to increase vegetable oil and protein intake in the diets of type 2 diabetic patients as part of a strategy to improve diabetes control without weight gain.

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C.W.C.K. and D.J.A.J. are responsible for the study concept and design and for acquiring funding. D.J.A.J., C.W.C.K., and E.V. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. D.J.A.J. researched data, wrote the manuscript, reviewed and edited the manuscript, and contributed to the discussion. C.W.C.K. reviewed and edited the manuscript and contributed to the discussion. M.S.B. researched data. K.S. wrote the manuscript, reviewed and edited the manuscript, and contributed to the discussion. E.V. and S.M. researched data. T.P., S.N., B.B., R.d.S., and C.I. researched data and contributed to the discussion. R.G.J. reviewed and edited the manuscript and contributed to the discussion.

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