Original article

Nut consumption is associated with lower incidence of type 2 diabetes: The Tehran Lipid and Glucose Study

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Abstract

Aim. – Nuts are rich in unsaturated fatty acids as well as other bioactive constituents. The present study investigated the association between nut consumption and the incidence of type 2 diabetes mellitus (T2DM) in a Middle Eastern population.

Methods. – The study was conducted within the framework of the Tehran Lipid and Glucose Study (TLGS), in which 1984 participants (920 men and 1064 women) free of DM, aged ≥ 20 years, were followed from phase III (2005–2008) to phase V (2011–2014). Dietary data were obtained from valid and reliable food-frequency questionnaires at baseline. Using multiple logistic regression, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, with adjustments for age, gender, BMI, serum cholesterol and triglycerides, smoking and energy intake.

Results. – Study participants' means $\pm$ SD of age and of BMI were 40.1 ± 13.1 years and 27.0 ± 4.8 kg/m^2, respectively. The median $\pm$ SE of their total daily consumption of nuts was 1.19 ± 0.11 servings. After 6.2 ± 0.7 years of follow-up, 150 cases of T2DM were confirmed. On comparing those who consumed ≥ 4 servings/week with those who consumed < 1 serving/week, the age-/energy-adjusted OR of incident T2DM for total nut consumption was 0.64 (95% CI: 0.36–1.12; *P* for trend = 0.03). In a fully adjusted model, nut consumption was associated with a lower risk of T2DM, and the ORs (95% CIs) of risk for those consuming 2–3.99 and ≥ 4 servings/week of nuts were 0.51 (0.26–0.97) and 0.47 (0.25–0.90), respectively, compared with those consuming < 1 serving/week (*P* < 0.001 for trend).

Conclusion. – Our findings suggest that consuming ≥ 4 servings/week of nuts reduced the risk of T2DM compared with < 1 serving/week.

1. Introduction

The latest incidence figures for type 2 diabetes mellitus (T2DM) in Iran are 9.36 in men and 10.1 in women [1]. Data from the Surveillance of Risk Factors of Non-communicable Diseases, documented from 2005 to 2011 in Iran, show a 35% increase in the prevalence of DM during this time period, and call for urgent action and implementation of preventative programmes [2]. Microvascular (retinopathy, neuropathy, nephropathy) and macrovascular (hypertension, hyperlipidaemia, coronary artery disease, cerebral vascular disease, ischaemic heart disease [IHD], stroke, peripheral vascular disease) complications are the main results of T2DM [3–6].

In general, an unhealthy lifestyle – with a combination of sedentarity and poor dietary habits, including high intakes of energy (calories), total and saturated fatty acids, red and processed meats as well as sugary foods, and a low consumption of fibre, fruit and vegetables – is one of the best-known modifiable risk factors of T2DM [1,3,4,6,7].

Given that nuts are low in carbohydrate, a number of previous studies have shown that eating nuts, either alone or with other foods, can modify insulin resistance and reduce levels of post-prandial glucose, thereby resulting in better glycaemic control

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[8,9]. However, the results of previous prospective studies on the association of nut consumption with DM risk have been inconclusive [10–12]. Two prospective studies, the Nurses' Health Study (NHS) [10] and Shanghai Women's Health Study [11], have both suggested that increasing the frequency of nut intake can contribute to a decrease in the risk of DM [10,11]; a report from the Physicians' Health Study [12], however, found no association between nut consumption and risk of DM. In addition, evidence from two recent reviews of nut consumption and risk of T2DM, hypertension and IHD documented different findings [13,14]. Afshin et al. [13] reported an inverse association between incidence of DM and nut consumption whereas, in the meta-analysis conducted by Guo et al. [14], it was shown that the consumption of > 2 servings/week of nuts had no effect on the risk of DM.

Given these conflicting results, the effect of eating nuts on the incidence of T2DM is still not clear. In addition, to our knowledge, there has been no prospective cohort study from the Middle East and North Africa (MENA) region on the association of nut consumption and risk of T2DM. This raises a concern as to whether the findings of previous studies can be generalized to populations living in these countries, as they have rather different social, economic and cultural backgrounds. Thus, to address this question, the present study aimed to investigate the association between nut consumption and the incidence of T2DM in a population-based study carried out in the MENA region.

2. Materials and methods

2.1. Subjects

The present study was conducted within the framework of the Tehran Lipid and Glucose Study (TLGS), details of which have been reported previously [15]. The principal aim of the TLGS was to prevent non-communicable diseases (NCD) by designing and implementing programmes to promote healthy lifestyles and reduce NCD risk factors. In brief, this cohort study was first launched in 1999 and enrolled > 15,000 subjects with a minimum age of 3 years, selected using multistage random cluster sampling methods. All of the included subjects were residents under the coverage of three medical health centres in District no. 13 of Tehran, the capital city of Iran, and all were re-evaluated every 3 years. Phase I, which had a cross-sectional design, took place between 1999 and 2001, while phases II, III, IV and V were performed during 2002–2005, 2005–2008, 2008–2011 and 2011–2014, respectively, using a prospective cohort design.

Of the 12,523 subjects enrolled in phase III of the study, 3462 participants were randomly selected for information on their dietary intakes. For the present investigation, only participants who had complete dietary data, medical histories, laboratory and anthropometric measurements from phase III (2005–2008) were selected, and followed until phase V (2011–2014).

After exclusion of subjects who were aged < 20 years ($n = 199$), pregnant ($n = 19$), had a history of cancer, stroke or cardiovascular disease, or diabetes at baseline ($n = 176$), and over- and under-reporters ($n = 22$) during phase III, plus those who

were missing data for any of the covariates in phase V ($n = 70$), a total of 1984 subjects were finally eligible for inclusion.

The study protocol was approved by the institutional ethics committee of the Research Institute for Endocrine Sciences, affiliated with the Shahid Beheshti University of Medical Sciences in Tehran. All participants signed an informed written consent form to participate.

2.2. Dietary intakes

Each subject was interviewed by a trained nutritionist, who had at least 5 years of experience in the TLGS survey, to complete a valid and reliable 168-item semi-quantitative food-frequency questionnaire (FFQ) [16]. To evaluate the reproducibility of the FFQ, 132 subjects (61 men and 71 women), aged ≥ 20 years, completed this FFQ twice, with a 14-month interval between FFQ1 and FFQ2. Over a 1-year period, 12 dietary recalls (DRs) were collected (1 per month) to assess the validity of the FFQ. The age-/energy-adjusted and deattenuated Spearman correlation coefficients to assess validity of the FFQ for total food groups was 0.44 (nuts: 0.54) in men and 0.37 in women (nuts: 0.39). The median age-/energy-adjusted intraclass correlation coefficient, which reflects the reproducibility of food groups in the FFQ, was 0.51 in men (nuts: 0.34) and 0.59 in women (nuts: 0.52). During face-to face interviews, participants were asked to provide details about their usual consumption frequency of various food items (such as nuts, seeds, peanuts, almonds, pistachios and walnuts) during the previous year on a daily, weekly or monthly basis. To calculate the mean daily intake of each food item, the frequency of consumption was multiplied by the amount consumed according to the recorded portion sizes, which were reported in household measures and then converted to grammes (g) based on raw or cooked coefficients. Energy (calorie) and nutrient contents were calculated, using US Department of Agriculture (USDA) food composition tables (FCTs), with Iranian FCTs used for local food items not found in the USDA FCTs.

Nuts included all kinds of tree nuts and seeds, including peanuts, almonds, walnuts, pistachios, hazelnuts, sunflower seeds, watermelon seeds and pumpkin seeds, and the compounds derived from them. Total nut consumption was calculated by summation of the items listed.

2.3. Measurement of covariates

At the time of entry to the study, all subjects were interviewed by trained interviewers using pretested questionnaires, and asked to provide details of their demographic data (age and education level), medical history of diagnosed diseases (cancer, stroke, cardiovascular disease, DM) and use of medications as well as smoking habits. Weight was measured with subjects minimally clothed and without shoes, using seca 707 digital scales (seca GmbH & Co., Hamburg, Germany) with 100 g accuracy (range: 0.1–150 kg). Height was measured using a tape measure with 0.5 cm accuracy, with subjects in a standing position and no shoes, and shoulders in normal alignment. Waist circumference was recorded to the nearest 0.1 cm at the level of the umbilicus

over light clothing, using a non-stretchable measuring tape, with no pressure placed on the body surface. Body mass index (BMI) was calculated by dividing weight in kilogrammes by height in square metres (kg/m^2).

Blood samples were collected from all study subjects at baseline and during follow-up between 0700 and 0900 h after 12–14 h of overnight fasting. All blood samples were analysed at the TLGS research laboratory on the day they were collected. Fasting plasma glucose (FPG) was measured by the enzymatic colorimetric method using glucose oxidase. An oral glucose tolerance test (OGTT) with 82.5 g of glucose monohydrate solution (equivalent to 75 g of anhydrous glucose; Cerestar, Barcelona, Spain) was performed, and a second blood sample obtained 2 h after glucose ingestion. Total cholesterol was measured using the enzymatic colorimetric method with cholesterol esterase and cholesterol oxidase. For triglyceride (TG) assays, the same method was used, but with glycerol phosphate oxidase.

All analyses were carried out using commercial kits (Pars Azmoon Inc., Tehran, Iran) and a Selectra 2 autoanalyzer (Vital Scientific, Spankeren, The Netherlands). Inter- and intra-assay coefficients of variation at baseline were both 2.2% for FPG, and 2% and 0.5% for total cholesterol, respectively, and 1.6% and 0.6% for TG, respectively.

After a 15-min resting period, blood pressure was measured twice, separated by at least 30 s, using a standard mercury sphygmomanometer; the mean of the two measurements was recorded as the patient's blood pressure [15].

2.4. Definitions

Over- or underreporting was defined as the reporting of energy intakes outside the range of ± 3 SD. Diagnosis of T2DM was ascertained if the subject had at least one of the following American Diabetes Association (ADA) criteria: FPG ≥ 126 mg/dL; 2-h plasma glucose (PG) ≥ 200 mg/dL during OGTT; and a history of diagnosed diabetes, or taking any diabetic medication or antihyperglycaemic treatment [17].

2.5. Statistical analysis

Nut consumption was reported in servings/week and categorized into four groups: < 1, 1–1.99, 2–3.99 and ≥ 4 servings/week.

Baseline characteristics were compared across categories of nuts, and presented as means ± standard deviations (SDs) and as proportions (n and %) for continuous and categorical variables, respectively. To test the trend of continuous variables across categories of nuts, linear regression models were used according to the median intake of nuts in each category. Multivariable logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association between nut consumption and incidence of T2DM. ORs were reported by comparing the risk of progression for subjects consuming 1–1.99, 2–3.99 and ≥ 4 servings/week of nuts compared with those consuming < 1 serving/week (reference group).

To test for linear trends across categories, the median value of each category of total nut consumption was used as a continuous variable. Initial regression models were only adjusted for age at recruitment (years; continuous variable) and total energy intake (kcal/day; continuous variable). A second set of multivariate models were additionally adjusted for gender (male or female), smoking status (ever-smoker, never-smoker), years of education (< 9 years, 9–12 years, academic degree), BMI (kg/m^2; continuous variable), waist circumference (cm; continuous variable), systolic blood pressure (SBP; mmHg; continuous variable), diastolic blood pressure (DBP; mmHg; continuous variable) and FPG (mg/dL; continuous variable), in addition to serum cholesterol and TG (mg/dL; continuous variables). In the final adjusted models, there was further adjustment for dietary intakes, including total fruit and vegetables (servings/day), red meat (servings/day), fish (servings/day), poultry (servings/day), total sugar (g/day), total fibre (g/1000 kcal), and total fats (% energy), carbohydrates (% energy) and proteins (% energy). All of these dietary items were considered continuous variables.

All P-values were two-sided, and statistical significance was set at P < 0.05. Analyses were performed using SPSS version 19 software (IBM SPSS Statistics, Armonk, NY, USA).

3. Results

Study participants' means ± SD of age and of BMI were 40.1 ± 13.1 years and 27.0 ± 4.8 kg/m^2, respectively, and the median ± SE (standard error) consumption of nuts in the study population was 1.19 ± 0.11 servings/week.

After 6.2 ± 0.7 years of follow-up, 150 incident cases of T2DM were confirmed. Table 1 presents the general characteristics and dietary intakes of the study participants according to categories of nut consumption. At baseline, with increasing nut intakes, the proportion of men and smoker participants also significantly increased (P < 0.01). In addition, those who consumed greater amounts of nuts had significantly higher intakes of energy, total fats (% energy), carbohydrates (% energy), fibre (g/1000 kcal), total sugar (g/day), fruit and vegetables (servings/day), and red meat, fish and poultry (servings/day) in comparison to those with lower intakes of nuts (P < 0.02). No statistically significant associations were observed for age, years of education, BMI, protein intakes (% energy), waist circumference, SBP, DBP, serum total cholesterol and TG across the different categories of nut consumption.

There was a statistically significant decrease in T2DM risk in the third (2–4 servings/week) vs the lowest (< 1 serving/week) category of nut intake in the age-/energy-adjusted model (OR: 0.49, 95% CI: 0.27–0.90). However, these associations were slightly attenuated when comparing the highest category of nut intake (≥ 4 servings/week) with the lowest (OR: 0.64, 95% CI: 0.36–1.12). In the fully adjusted model, the ORs of incident DM were 0.50 (95% CI: 0.26–0.96; P < 0.001 for trend) and 0.53 (95% CI: 0.29–0.97; P < 0.001 for trend) for the third (2–3.99 servings/week) and fourth (≥ 4 servings/week) categories of nut consumption, respectively. Moreover, these associations did not change substantially in another model that was further adjusted for other dietary variables (OR: 0.51, 95% CI: 0.26–0.97 and

Table 1
Baseline characteristics and dietary intakes of study participants according to nut consumption: Tehran Lipid and Glucose Study.[a]

	Nut consumption (servings/week)				P for trend[b]
	<1 (n = 827)	1–1.99 (n = 504)	2–3.99 (n = 330)	≥ 4 (n = 323)	
Males (%)	44.0	44.0	49.1	53.3	0.01
Academic education (%)	26.8	27.5	26.7	23.8	0.12
Ever-smoker (%)	9.7	13.3	13.1	16.7	<0.001
Age (years)	41 ± 14	40 ± 13	39 ± 13	40 ± 12	0.16
Body mass index (kg/m^2)	27.1 ± 4.8	27.1 ± 4.9	26.7 ± 4.6	27.1 ± 4.8	0.75
Cholesterol (mg/dL)	184 ± 39	189 ± 38	186 ± 39	187 ± 38	0.47
Triglycerides (mg/dL)	138 ± 87	140 ± 71	132 ± 70	145 ± 87	0.34
Systolic blood pressure (mmHg)	112 ± 16	111 ± 17	110 ± 16	111 ± 15	0.75
Diastolic blood pressure (mmHg)	73 ± 10	74 ± 11	73 ± 11	74 ± 10	0.67
Waist circumference (cm)	90 ± 13	90 ± 12	89 ± 13	90 ± 13	0.49
Dietary intakes (per day)					
Energy (kcal)	2117 ± 787	2359 ± 801	2556 ± 928	2883 ± 1034	<0.001
Total vegetables and fruit (serving)	4.44 ± 2.74	5.43 ± 6.17	5.67 ± 2.92	6.82 ± 3.68	<0.001
Total sugar (g)	110.24 ± 57.74	127.65 ± 53.40	133.43 ± 56.23	157.39 ± 68.71	<0.001
Protein (% energy)	13.74 ± 2.58	13.56 ± 2.38	13.52 ± 2.42	13.77 ± 2.52	0.79
Carbohydrate (% energy)	57.89 ± 7.91	57.94 ± 6.96	56.53 ± 6.93	56.70 ± 7.00	<0.001
Total fat (% energy)	30.75 ± 7.77	31.10 ± 6.93	32.50 ± 6.84	32.67 ± 6.70	<0.001
Total fibre (g/1000 kcal)	17.20 ± 7.68	16.71 ± 6.49	16.06 ± 7.05	15.94 ± 6.08	<0.001
Red meat (serving)	0.64 ± 0.99	0.65 ± 0.71	0.68 ± 0.76	0.76 ± 0.88	0.02
Poultry (serving)	0.97 ± 1.14	1.03 ± 1.21	1.03 ± 1.28	1.22 ± 1.44	<0.001
Fish (serving)	0.34 ± 0.60	0.35 ± 0.40	0.42 ± 0.42	0.52 ± 0.57	<0.001

All data are presented as means ± SD unless otherwise stated.

[a] Phase III.

[b] By linear regression models across categories of nut consumption for continuous variables and chi-square tests for categorical variables; to test for linear trends for continuous variables across categories, the median value of each category of total nut consumption was used as a continuous variable.

Table 2
Odds ratios (95% CIs) for incidence of type 2 diabetes mellitus according to categories of nut consumption.

	Nut consumption (servings/week)				P for trend[c]
	<1 (n = 827)	1–1.99 (n = 504)	2–3.99 (n = 330)	≥ 4 (n = 323)	
Cases/non-cases	70/757	18/305	14/316	48/456	
Age-/energy-adjusted model	1.00	1.18 (0.79–1.76)	0.49 (0.27–0.90)	0.64 (0.63–1.12)	0.03
Multivariable adjusted model[a]	1.00	1.16 (0.76–1.77)	0.50 (0.26–0.96)	0.53 (0.29–0.97)	0.01
Multivariable adjusted model[b]	1.00	1.11 (0.72–1.71)	0.51 (0.26–0.97)	0.47 (0.25–0.90)	0.01

[a] Additionally adjusted for gender, years of education, smoking status, body mass index (kg/m^2), systolic and diastolic blood pressure (mmHg), cholesterol (mg/dL), triglycerides (mg/dL).

[b] Further adjusted for dietary intakes of total vegetables and fruit (servings/day), red meat (servings/day), fish (servings/day), poultry (servings/day), total sugar (g/day), total fibre (g/1000 kcal), total fats (% energy), carbohydrates (% energy), proteins (% energy).

[c] To test for linear trends across categories, the median value of each category of total nut consumption was used as a continuous variable.

OR: 0.47, 95% CI: 0.25–0.90, respectively; *P* < 0.001 for trend; Table 2 and Fig. 1).

Fig. 2 is a scatterplot of nut consumption (servings/week) at baseline in relation to FPG levels during follow-up. Nearly all of the DM patients (FPG levels ≥ 126 mg/dL) and subjects with FPG levels ≥ 110 but < 126 mg/dL consumed fewer than 2–3 servings/week of nuts. In addition, the frequency of subjects who consumed fewer than 5–6 servings/week of nuts had FPG levels < 110 mg/dL, which was higher than in those having > 6 servings/week, whose FPG levels were normal.

4. Discussion

To the best of our knowledge, this was the first study to investigate the effects of nut consumption on DM in a Middle Eastern (MENA) population. In this population-based cohort study with > 6 years of follow-up, the level of nut consumption was inversely associated with the risk of T2DM, independently of other known risk factors. Compared with those consuming < 1 serving/week of nuts, those who consumed ≥ 4 servings/week had a 53% lower T2DM risk, findings that are in line with the results of previous prospective cohort studies of the relationship between nut intake and risk of T2DM [10,11,18,19]. An analysis by Jiang et al. [10] of women in the NHS indicated that more frequent intakes of nuts and peanut butter decreased the risk of T2DM incidence by 29%; this inverse relationship was also confirmed by findings in the Shanghai Women's Health Study [11]. In addition, the "second-generation" of this large prospective cohort study (NHS II) showed that an increased frequency of walnut intake, but not total nut consumption, lowered the risk of DM independently of BMI and other potential confounders [20]. Similarly, the findings of the Physicians' Health Study I failed to
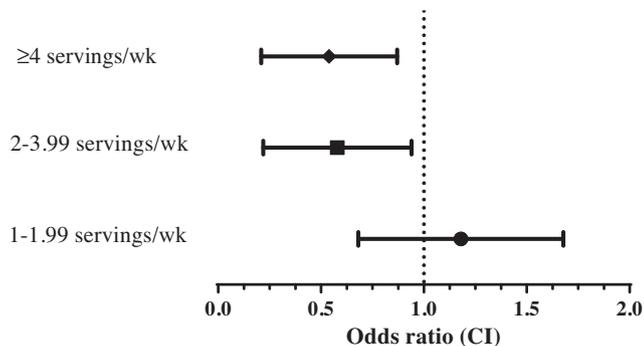
Fig. 1. Multivariable adjusted odds ratios and 95% confidence intervals for incidence of type 2 diabetes by categories of nut consumption. Adjusted for age, energy intake, gender, years of education, smoking status, BMI, SBP, DBP, fasting plasma glucose (FPG), cholesterol, triacylglycerol (TG), and dietary intakes of total vegetables and fruits, red meat, fish, and poultry, fibre, sugar, fat, carbohydrate, and protein.
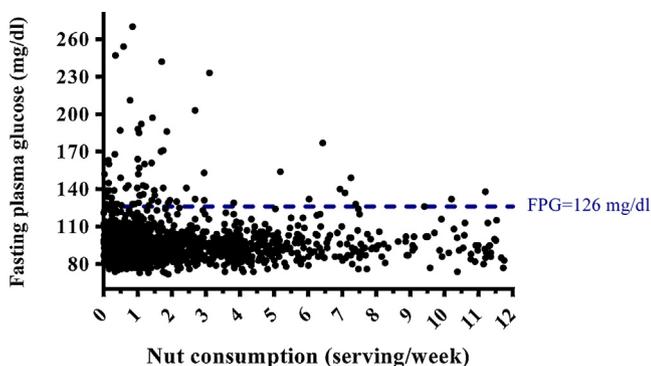

Fig. 2. Scatter plot of nut consumption in servings per week at baseline against fasting plasma glucose level after 6.17 ± 0.74 years of follow-up.

show any significant inverse relationship between intake of nuts and risk of DM after adjusting for BMI and other confounders, whereas an inverse association was shown in the age-adjusted model [12]. Furthermore, based on the results of two prospective studies examining the long-term outcomes of DM, a higher consumption of nuts was found to be associated with a lower risk of mortality among DM patients and a lower CVD risk among DM women [18,19].

In line with the present and previous cohort studies, the positive effects of nut consumption on T2DM and its complications were also confirmed in previous clinical trials. According to the results of a recent randomised trial of non-DM participants in the Prevencion con Dieta Mediterranea (PREDIMED) study, the risk of DM was reduced by 52% by a Mediterranean diet supplemented with 30 g/day of nuts compared with a low-fat control diet [21]. In addition, some clinical trials have shown that intakes of different kinds of nuts can attenuate DM markers and its related complications, and also have beneficial effects on obesity, weight control, glycaemic control, HbA$_{1c}$, adiposity, lipid profiles and inflammatory markers [22–27].

Moreover, the beneficial effects of nuts in terms of modulating inflammation, insulin resistance, serum lipids and glycaemic control were confirmed by three recent systematic reviews and meta-analyses [28–30]. Considering that persistent

hyperglycaemia and insulin resistance, as well as inflammation and oxidative stress, play critical roles in the development of DM and its complications, any agents that can ameliorate these adverse conditions can also reduce the risk of DM [31–33].

According to the ADA, glycaemic control has a crucial role in preventing and managing DM [34]. The results of previous studies suggest that, because of the low carbohydrate content of nuts, they may be beneficial in glycaemic control by modulating insulin responses and lowering postprandial glucose when consumed either alone or with meals [8,9]; the beneficial health effects of nuts may also be related to their special fatty acid contents, including high levels of mono- and polyunsaturated fatty acids (MUFAs and PUFAs, respectively), and especially omega-3 fatty acids, as well as their exceptional nutrient profiles, including high levels of antioxidant vitamins, minerals and phytochemicals (for example, folate, niacin, vitamins E and B6, potassium, phosphorus, calcium, copper, zinc, selenium, magnesium, arginine, carotenoids, polyphenols and phytosterols) [27,35–37]. The high MUFA and PUFA contents of nuts can reduce fat accumulation in the human body by boosting oxidation, and increasing thermogenesis as well as resting energy expenditure. Furthermore, nuts are good sources of plant-based protein and dietary fibre, which can delay gastric-emptying and, consequently, reduce gastrointestinal transit time and absorption, thereby eventually leading to increased satiety [27,35–39].

Thus, our present results suggest that an increased consumption of nuts in a healthy population can potentially reduce the risk of incident DM through various mechanisms, including attenuating inflammation, lowering lipids, and antioxidative and antihyperglycaemic effects, as well as increasing satiety, improving weight control, modifying insulin resistance and modulating glycaemic control [27–30,35–37].

Our study has a few limitations. Although the statistical models for potential risk factors of DM and other confounders were carefully controlled, it was not possible to substantially rule out the effect of unknown factors and residual confounders. On the other hand, our study has several strengths, such as a prospective design with 6 years of follow-up. In addition, as biochemical markers of T2DM were available for all participants, the T2DM diagnosis was based on ADA criteria and not on self-reporting. Furthermore, information on a variety of covariates was available for analyses. As this was the first investigation to look for any association between nut intake and incidence of T2DM within the framework of a population-based study in a developing country with people who have different lifestyles and socioeconomic statuses compared with those in the developed Western countries, those differences may help to establish the independence of any putative associations. Also, the use of a valid and reliable FFQ, which was carefully completed by a trained nutritionist, reduced any possible measurement error in the assessment of dietary intakes.

5. Conclusion

Our findings suggest that the consumption of ≥ 4 servings/week of nuts reduced the risk of T2DM compared with consuming <1 serving/week. Indeed, this study extends our

currently available knowledge by demonstrating that increased nut consumption is associated with a reduced risk of T2DM incidence independent of potential confounders. Future clinical trials should examine the effects of consuming various amounts of different kinds of nuts on attenuating both the symptoms and complications of T2DM.

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Contribution statement

GA and ZG contributed to the data analysis, interpretation of data and drafting the manuscript. PM and FA contributed to the design, and revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript for publication.

Disclosure of interest

The authors declare that they have no competing interest.

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