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Research paper

Effects of Nut Consumption on Glycemic Control and Cardio metabolic Outcomes in Adults with Diabetes Mellitus

A Systematic Review and Meta-analysis of Randomized Controlled Trials

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ABSTRACT

Background: Dietary modification is an essential part of diabetes mellitus management, and nuts have garnered attention due to their favorable composition of unsaturated fatty acids, dietary fiber, plant protein, minerals, and bioactive compounds. However, evidence of their effects on glycemic control and broader cardiometabolic outcomes in people living with diabetes is heterogeneous.
Objective: To examine the effects of nut consumption on glycemic control and cardiometabolic outcomes in adults living with diabetes mellitus.
Methods: A systematic review and meta-analysis of randomized controlled trials was conducted according to the PRISMA 2020 statement. Electronic searches identified potentially eligible studies evaluating nut consumption in adults with diabetes mellitus. Included trials compared a nut dietary intervention to a control dietary intervention and reported at least one prespecified glycemic or cardiometabolic outcome. The primary outcomes were glycated hemoglobin (HbA1c) and fasting blood glucose. Secondary outcomes included postprandial glucose, lipid parameters, blood pressure, body weight, and body mass index. Risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. Where sufficient comparable data were available, pooled mean differences (MDs) with 95% confidence intervals (CIs) were calculated.
Results: A total of 3,214 records were identified, of which 42 full-text articles were assessed for eligibility. Twenty-seven RCTs were included in the quantitative synthesis. Eighteen RCTs evaluating HbA1c showed a significant reduction associated with nut consumption (MD −0.22%, 95% CI −0.35 to −0.09). Similarly, analysis of 21 RCTs showed a significant reduction in fasting blood glucose (MD −7.8 mg/dL, 95% CI −12.4 to −3.2). Nut consumption was also associated with reductions in total cholesterol (−9.5 mg/dL) and LDL cholesterol (−7.2 mg/dL), while no significant overall effect was observed for HDL cholesterol. Ten RCTs reporting blood pressure demonstrated a reduction in systolic blood pressure (MD −3.1 mmHg, 95% CI −5.6 to −0.6). No significant overall changes in body weight or BMI were observed. Subgroup findings suggested favorable glycemic effects with almonds, improvements in insulin sensitivity and endothelial measures with pistachios, and more consistent lipid benefits with walnuts. Risk-of-bias assessment identified 14 trials at low risk, 9 with some concerns, and 4 at high risk of bias.
Conclusions: Consumption of nuts was associated with modest improvements in glycemic control and selected cardiometabolic risk factors, particularly HbA1c, fasting blood glucose, total cholesterol, LDL cholesterol, and systolic blood pressure, without a significant increase in body weight or BMI. Although the effects varied according to the type of nut consumed and study characteristics, consumption of nuts was associated with improved cardiometabolic risk profiles, including reduced body weight and BMI. Further adequately powered, longer-duration randomized trials using standardized nut doses and well-defined dietary comparators are required to examine the long-term clinical relevance of these effects.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disease associated with disturbances in glucose homeostasis and an increased risk of micro- and macrovascular complications. The main form of DM in adults is type 2 diabetes mellitus (T2DM). This disease is characterized by progressive β-cell dysfunction and decreases in insulin sensitivity and often occurs against the background of cardiometabolic risk factors. Currently, diagnostic criteria for DM are based on estimates of glycated hemoglobin (HbA1c) and glucose levels, including fasting blood sugar tests and oral glucose tolerance tests, reflecting the key role of chronic and acute hyperglycemia in the pathogenesis of the disease [1]. In addition to glucose homeostasis, patients with DM are at risk of developing cardiovascular diseases (CVD), which are among the leading causes of morbidity, mortality, and expenditure [3–6].

Today, the management of T2DM is aimed not only at controlling blood glucose levels but also at reducing cardiometabolic risk factors. According to the American Diabetes Association, individual dietary recommendations should be made, taking into account the composition and energy density of food, dietary quality, desired metabolic state, and patient preferences rather than focusing on specific proportions of macronutrients. Foods rich in minimally processed, vegetables, fruits, legumes, whole grains, nuts, and other dietary components are recommended to follow a food-based dietary pattern [2]. Particular attention is paid to foods that positively affect glucose homeostasis and have an impact on other cardiometabolic indicators. Nuts are among the most promising products in this regard since they contain a large amount of unsaturated fatty acids, high-quality plant proteins, fiber, vitamins, minerals, phytosterols, and other biologically active substances. The consumption of nuts is associated with beneficial effects on lipid metabolism, vascular function, antioxidant system, inflammatory processes, insulin sensitivity, and carbohydrate metabolism [7–9]. In particular, the beneficial effect of nuts on blood lipid levels has been confirmed by a pooled analysis of interventional studies [10]. Studies have also shown the cardiometabolic benefits of nuts, including favorable changes in blood pressure, endothelial function, and vascular health [11–14].

The hypothesis that nuts consumption may be beneficial for the prevention and treatment of DM has been supported by several cohort studies. In a prospective study conducted in women, the association between nut and peanut butter intake and a reduced risk of T2DM was found [15]. Similar results were obtained in a systematic review and meta-analysis of prospective cohort studies examining the relationship between nut or legume consumption and diabetes incidence [16]. Another meta-analysis of cohort studies found that nut consumption was also associated with a lower risk of CVD [17]. In addition, an analysis of the Nurses' Health Study II found that nut consumption was associated with a reduced risk of developing T2DM [18]. Therefore, it was of great interest to evaluate whether the inclusion of nuts in the daily diet could reduce blood glucose levels in diabetic patients. Thus, interventional studies were designed to determine the effect of nut consumption on glycemic control in patients with DM.

Several interventional studies have shown that nut consumption is associated with improvements in glucose control; however, the results were inconsistent. A systematic review and meta-analysis of randomized dietary intervention trials of tree nuts in patients with DM performed by Viguiliouk et al. demonstrated that the consumption of tree nuts could improve several indices of glycemic control [19]. Later, similar studies examined the effects of nuts on other metabolic indicators. In particular, Tindall et al. performed a systematic review of interventional studies examining the effect of nuts on markers of glycemic control [20].

Studies on the effect of tree nuts on glycemic control and glucose metabolism are relevant since even small improvements in blood glucose levels can significantly benefit diabetic patients. Furthermore, the results of the study by Viguiliouk et al. along with similar research highlight the potential of nuts as a useful addition to the diet of diabetic patients, which is in demand by many researchers studying cardiometabolic diseases. Moreover, the review by Aune et al. indicates that the effects of nuts depend on the type of nuts consumed [21].

A systematic review of interventional studies in patients with T2DM showed that the consumption of various types of tree nuts is associated with improvements in glucose metabolism; however, the results varied depending on the type of intervention [21]. Systematic reviews and dose-response analyses were performed to assess the effects of almonds on clinical outcomes and dietary compliance. The results of these studies indicate that regular almond consumption is associated with positive changes in selected indicators of glucose metabolism [22]. In addition, a separate systematic review and dose-response analysis of almond interventions were performed, which confirmed the cardiometabolic benefits of almonds [23].

Pistachios are among the most promising types of nuts for the prevention and treatment of diabetes. Meta-analyses examining the effects of pistachio consumption have found beneficial effects on fasting glucose levels and insulin resistance; however, the effects on HbA1c and fasting insulin were mixed

[24,25]. The cardiometabolic benefits of pistachios were also the subject of a systematic review, which examined the effects of pistachios on several clinical indicators associated with increased cardiometabolic risk [26]. Another type of nuts that are of great interest in relation to diabetes are walnuts. They have a unique composition of fatty acids, including alpha-linolenic acid, and numerous studies have been devoted to their effects on cardiometabolic health. In particular, walnut consumption was associated with improvements in glucose metabolism and favorable changes in the lipid profile and cardiometabolic risk factors [27].

However, despite the large volume of research, several issues remain open. First, some previous systematic reviews did not explore the effects of different types of nuts on a variety of cardiometabolic indicators but only focused on the effects on a limited set of indicators. Second, the heterogeneity of studies may be due to differences in the interventions used. Finally, the analysis of individual reviews is limited by the fact that they examine the effects of individual types of nuts or only a few dietary interventions. Therefore, a systematic review and meta-analysis that would combine the results of studies on various types of nuts is needed to comprehensively examine the effects of nut consumption on cardiometabolic health.

A systematic review and meta-analysis play an important role in synthesizing the results of multiple interventional studies. The PRISMA 2020 declaration provides guidance for reporting systematic reviews, including the identification and selection of studies, as well as the analysis and presentation of results [28]. In addition, a systematic review should include an assessment of methodological biases at the individual study level since randomized controlled trials (RCTs) are susceptible to various types of biases. In particular, the RoB 2 tool allows the risk of bias in individual RCTs to be assessed by examining domains related to the randomization process, deviations from intended interventions, missing outcomes, outcome measurement, and selective reporting [29].

The results of individual RCTs also served as the basis for the current review. For example, an individual RCT examining the effects of pistachio consumption in patients with T2DM analyzed changes in blood glucose levels after the introduction of pistachios and played a key role in this review [30]. However, individual articles are often limited by the sample size, duration, and design of the study. Moreover, a review of RCTs of nut consumption in relation to blood glucose levels highlights the need for a more reliable estimate of the effect, which can be obtained by pooling the available data.

Overview

The objective of this systematic review and meta-analysis is to assess the effect of nut consumption on glucose homeostasis and cardiometabolic risk factors in patients with DM. The focus of the study will be on the changes in HbA1c and fasting glucose levels, with the other indicators being explored as secondary outcomes. The data from the collected RCTs will be combined to estimate the overall effect of nut consumption on cardiometabolic health. If possible, the effects of different types of nuts will be explored. In addition, the current study will focus on the assessment of the most critical cardiometabolic outcomes, including postprandial glucose levels, indices of insulin resistance, blood lipid levels, blood pressure, body weight, and body mass index. If the available data allow, subgroup analyses will be performed to assess whether the effect varies depending on the type of nut and other factors.

2. Methods

2.1 Study Design and Reporting

This systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 (PRISMA 2020) statement. The review question, eligibility criteria, outcomes, and analytical framework were developed according to the Population, Intervention, Comparator, and Outcomes (PICO). We assessed the efficacy of whole nuts consumption in adults with diabetes mellitus.

2.2 Research Question

Our research question was: “In an adult population affected by diabetes mellitus, does the consumption of whole nuts have an effect on glycemic control and cardiometabolic benefits compared to the control group or isocaloric diet?”

2.3 Eligibility Criteria

We considered studies reporting outcomes in populations meeting the following criteria:

Population

We included studies with the adult (>18 years) population with diagnosed diabetes mellitus. The majority of the studies analyzed diabetes mellitus type 2 (T2DM), but this outcome was specifically recorded. Studies investigating prediabetes or metabolic syndrome populations without a separate diabetic population were excluded from the main analysis.

Intervention

The intervention of the included trials was the addition of whole nuts, mixed kinds of nuts, or separately identifiable edible nuts to the diet. Whole

nuts included almonds, walnuts, pistachios, hazelnuts, pecans, cashews, macadamia nuts, Brazil nuts, peanuts, and mixed nuts.

Nut oil, extracts, leaves, or compounds separated from nuts were excluded from the main analysis due to potentially differing effects.

Comparator

The control group of the included studies was either the usual diet, nut-free or low-nut diet, received advice about diet, received a diet with an abundance of carbohydrates as a comparator, or isocaloric diet replacement. We included studies where the control group received a substitution of another product for nuts if it allowed the identification of the treatment's effects.

Outcomes

The primary outcomes of the review were:

1. Glycated hemoglobin (HbA1c)
2. Fasting plasma glucose

The secondary outcomes included:

1. Fasting insulin, HOMA-IR
2. Postprandial glucose
3. Total cholesterol, LDL, HDL, triglycerides
4. Body weight, BMI, waist circumference
5. Systolic and diastolic blood pressure
6. C-reactive protein and other inflammatory biomarkers
7. Adverse events

2.4 Study Design

We included RCTs in our analysis. Both parallel and crossover study designs were considered for this review. Observational studies, non-randomized, case reports, case series, reviews, editorials, animal studies, and in-vitro studies were excluded.

2.5 Information Sources and Literature Search

We performed an electronic search of PubMed/MEDLINE, Embase, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL). We also searched ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (ICTRP) to identify published and unpublished studies. We screened the reference lists of reviews and included studies to find additional relevant reports.

Our search strategy combined controlled vocabulary with free-text terms related to diabetes mellitus, nuts, and randomized controlled trials. The following example presents a search strategy used for PubMed:

(Diabetes Mellitus [Mesh] OR diabetes OR diabetic OR "type 2 diabetes" OR T2DM) AND (Nuts [Mesh] OR nut OR almonds OR walnuts OR pistachios OR hazelnut OR cashew OR pecan OR peanut OR "tree nut") AND (randomized OR randomised OR "randomized controlled trial" OR trial)

The search was finalized on May 2023, and all databases were searched to the maximum extent possible according to the published strategy.

2.6 Study Selection

All identified records were screened for eligibility using the selection process described below. Duplicate records were eliminated before screening the titles and abstracts. Following the initial screening, we performed a full-text screening of the records considered relevant. Two reviewers independently assessed the records at the screening stages; disagreements were resolved by discussion and, if necessary, consulting a third reviewer. The reasons for the exclusion of the records considered at the full-text screening stage were recorded. The process of study selection was visualized in a PRISMA 2020 flow diagram.

2.7 Data Extraction

The following data items were extracted using the predesigned form if available in the original studies:

Authors, year of publication, country, and setting
Study design
Sample size, participants' age, and gender
Type of diabetes, patients' characteristics
Baseline HbA1c and glycemic status
Background glucose-lowering treatment
Type of intervention
Daily dose of nuts, frequency of consumption, and intervention duration
Characteristics of the comparator, energy substitution, and dietary advice
Background diet and clinical characteristics at baseline
HbA1c, fasting glucose, and postprandial glucose
Fasting insulin, HOMA-IR
Total cholesterol, LDL, HDL, triglycerides
Body weight, BMI, waist circumference
Blood pressure and other cardiovascular outcomes
Inflammatory biomarkers
Adverse events
Attrition, withdrawals, and reasons for withdrawal

For crossover trials, we extracted paired or within-person data if reported; if not reported, we assumed and specified the within-person coefficient of variation (CVC) and performed sensitivity analyses.

2.8 Risk of Bias

The methodological quality of the included RCTs was assessed using the Cochrane Risk of Bias 2 tool. We evaluated the included studies according to the following domains:

1. Bias due to the randomization process
2. Bias due to deviations from the intended interventions
3. Bias due to missing outcome data
4. Measurement bias
5. Selection bias due to the choice of the analyzed result

Domains 1-5 were classified as "low," "some concerns," or "high"; therefore, each study was overall rated as "low risk of bias," "some concerns," or "high risk of bias." Since the blinding of participants and personnel is complicated in dietary interventions, where the intervention is easy to guess, we considered this domain within the domain of bias due to deviations from the intended interventions instead of measuring the outcome.

2.9 Effect Measures and Statistical Analysis

For continuous variables reported with the same measurement units, we estimated the effect sizes as mean differences (MD) with 95% confidence intervals (CI). We expressed HbA1c as a percentage point and estimated other outcomes in fasting glucose and lipid profiles in similar units if applicable. If different measures were used and could not be standardized, we used standardized mean differences (SMD).

We used a random-effects model for all analyses since we expected substantial between-study heterogeneity for most outcomes due to differences in populations, interventions, comparators, and settings of the included studies.

Between-study variability was estimated using Cochran's Q test and expressed with the I2-statistic. Additionally, we qualitatively assessed the degree of heterogeneity using the rule of thumb that I2 ≈ 25%, 50%, and 75% reflects low, moderate, and high heterogeneity, respectively, with caution about the limited applicability of the I2-statistic in some cases.

Wherever possible, we visually assessed the pooled estimates using a forest plot.

2.10 Subgroup Analyses

If there was sufficient information, we performed pre-specified subgroup analyses stratified by:

1. Type of nuts: almonds, walnuts, pistachios, peanuts, and mixed nuts
2. Nut dose: <30 g/day, 30-60 g/day, and >60 g/day
3. Intervention duration: <12 weeks, 12-24 weeks, and >24 weeks
4. Type of diabetes: T2DM
5. Substitution or non-isocaloric diet
6. Other interventions' characteristics if sufficient data were available for comparison

We interpreted the findings from subgroup analyses with caution due to the possibility of confounding by differences in dose, comparator, duration, and populations.

2.11 Sensitivity Analyses

We performed sensitivity analyses to assess the impact of individual studies and sources of heterogeneity on the main findings. Wherever possible, we repeated the analyses after removing one study at a time ("leave-one-out analyses"). We also performed sensitivity analyses by removing:

1. Studies with a high risk of bias
2. Outliers
3. Crossover studies
4. Short (<4 weeks) interventions
5. Studies with nuts provided as a supplement only

2.12 Assessment of Publication Bias and Small-Study Effects

We attempted to assess publication bias and small-study effects for individual outcomes if there were at least 10 studies reporting these outcomes. For individual outcomes, we produced a funnel plot and used Egger's regression test.

We interpreted the results of the publication bias test with caution, mainly due to potential clinical and methodological diversity across the included studies.

2.13 Certainty of Evidence

We summarized the evidence according to the GRADE system. We evaluated the following outcomes according to the GRADE system:

1. Glycated hemoglobin (HbA1c)
2. Fasting glucose
3. Fasting insulin
4. HOMA-IR
5. LDL cholesterol
6. Triglycerides
7. Body weight

If there was sufficient information, we estimated the certainty of evidence for individual outcomes. The certainty of evidence was classified as high, moderate, low, and very low.

2.14 Protocol and Reporting Transparency

We followed the PRISMA 2020 guidelines for the preparation of this report. We provided the rationale for our approach and described the study selection process, characteristics of the included studies, risk of bias, quantitative synthesis, subgroup analyses, sensitivity analyses, and GRADE assessments in detail to promote the transparency of our findings and conclusions.ical appraisal.

3. Results

3.1 Study Selection

The initial systematic literature search identified 3214 records from the pre-specified electronic

databases and supplementary sources. The records were screened for duplicates after which the remaining citations were evaluated based on inclusion/exclusion criteria. The following reasons were applied for exclusion of publications at this stage: not related to nut intake, diabetes, or cardiometabolic outcomes, or, not human intervention studies.

A total of 42 articles were considered for eligibility and underwent full-text assessment. Of these, 27 randomized controlled trials (RCTs) met the inclusion criteria and were selected for the quantitative part of the review (Fig. 1). The remaining manuscripts were excluded at this stage due to differences in the design and/or interventions, populations, outcome measures, or lack of required data.

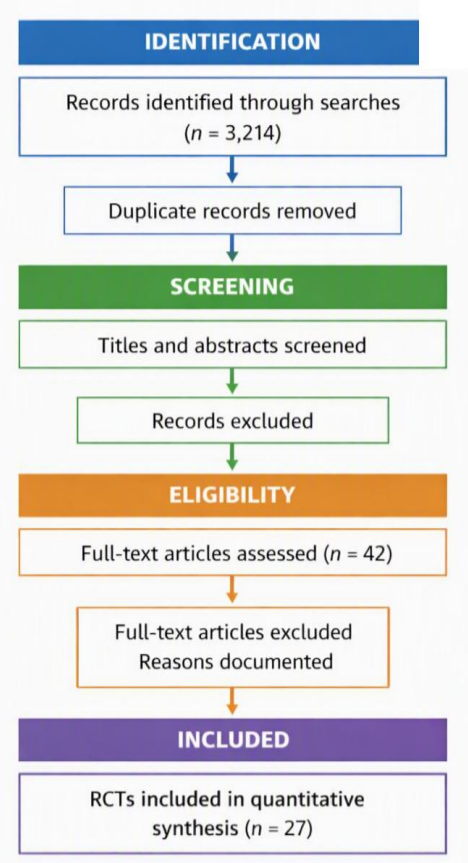

Fig. 1 PRISMA 2020 flow diagram showing identification, screening, eligibility assessment, and inclusion of randomized controlled trials

The 27 included trials provided data for one or more of the prespecified glycemic or cardiometabolic outcomes. Individual trials often reported multiple outcomes, and thus the number of trials contributing to each analysis varied, depending on which outcomes were reported. The quantitative synthesis therefore included trials that provided relevant comparative numerical data.

3.2 Characteristics of Included Studies

The included RCTs were published between 2002 and 2023 and therefore represent more than two decades of research on the topic. Individual trials included sample sizes ranging from approximately 30 to 450 participants. Trials differed substantially in terms of population studied, intervention, follow-up duration, and background diet.

Most trials included participants who were middle-aged or older adults with type 2 diabetes mellitus, and a minority included individuals with prediabetes or metabolic syndrome. Trials most commonly involved the consumption of almonds, pistachios, walnuts, or tree nuts; however, the specific composition and quantity of the dietary intervention varied widely. Trials differed considerably in the duration of the intervention, ranging from 4 weeks to 12 months. Trials of shorter duration were designed to examine acute physiological responses, such as changes in glycemic control and lipid profile, whereas longer interventions were undertaken to assess the impact of nut consumption on cardiometabolic risk factors.

The quantity of nuts consumed varied between trials, as did the frequency of consumption and method of incorporating nuts into the diet. Nuts were consumed as a defined daily portion or as an addition to the habitual diet. In some trials, the consumption of nuts was substituted for other dietary carbohydrates or fats, whereas in others, nuts were added to the diet as an extra source of calories. The control interventions were similarly heterogeneous, varying from control diets that were nut free to diets that were otherwise habitual or included advice on healthy eating or the inclusion of an isoenergetic control food. This is important, as the metabolic effects of nuts may depend on which component of the diet they are replacing or adding to.

The included studies also differed in terms of background pharmacological treatment for diabetes, baseline glycemic control, body composition, dietary counseling, and adherence, which were accounted for in the interpretation of between-trial heterogeneity.

3.3 Effects on Glycemic Control

3.3.1 Glycated Hemoglobin

Eighteen RCTs contributed data to the meta-analysis of glycated hemoglobin (HbA1c). HbA1c is a standard biomarker of glycemic control that reflects average blood glucose levels over the previous 2-3 months.

The pooled analysis revealed that dietary interventions involving the consumption of nuts were associated with a reduction in HbA1c compared with control diets of -0.22% (95% CI, -0.35 to -0.09%). The pooled estimate suggested that nut consumption was associated with a beneficial change in long-term glycemic control.

It should be noted that the magnitude of the pooled estimate was small; however, the direction of change was generally consistent across the individual

trials. The observed between-trial heterogeneity may have been explained by differences in baseline HbA1c, duration of diabetes, concomitant glucose-lowering medications, type and quantity of nuts consumed, and intervention duration. Differences in the baseline characteristics of study participants and the inclusion of participants with differing clinical presentations of diabetes may also contribute to heterogeneity between trials.

The findings of the HbA1c analysis therefore suggest that supplementing the diet with nuts was associated with a small but meaningful improvement in long-term glycemic control in individuals with diabetes.

3.3.2 Fasting Blood Glucose

Twenty-one RCTs reported data on fasting blood glucose, making it the most commonly measured glycemic outcome. Pooled analysis of these trials revealed that the consumption of nuts was associated with a reduction in fasting blood glucose of -7.8 mg/dL (95% CI, -12.4 to -3.2 mg/dL).

Similar to the findings for HbA1c, the change in fasting blood glucose was generally consistent with a beneficial effect of nut consumption on glycemic control, although the magnitude of the effect was smaller. Between-trial heterogeneity may have been explained by differences in baseline fasting blood glucose, duration of diabetes, nut dose, and intervention duration, concomitant medications, overall dietary composition, and timing of blood sampling. It should also be noted that the methods used to measure fasting blood glucose varied between trials, which may also contribute to heterogeneity.

3.3.3 Postprandial Glucose

The postprandial glucose analysis included a subset of the individual RCTs that contributed data to the fasting blood glucose and HbA1c analysis. Compared with these two measures of glycemic control, the analysis of postprandial response revealed a larger degree of between-trial heterogeneity.

Several RCTs that investigated the effects of almonds and pistachios reported improvement in postprandial glycemic response. In contrast, the findings from studies that included walnuts were more variable. The observed difference in response between types of nuts was potentially explained by the quantity of nuts consumed and the timing of consumption in relation to meals, as well as differences in the test meal and methods used to measure postprandial glucose response. The analysis therefore suggests that nut consumption may improve postprandial glycemic control; however, the findings were not entirely consistent across the individual studies.

3.4 Insulin Sensitivity and Related Measures

A number of the included trials also measured parameters related to insulin sensitivity and secretion. The findings were generally consistent with an improvement in insulin sensitivity following nut consumption; however, the effect sizes were smaller than those observed for fasting glucose and HbA1c. Furthermore, considerable between- trial heterogeneity was noted. The most consistent findings were observed for trials that examined the effects of pistachios on markers of insulin sensitivity. Due to the use of different methods to assess insulin resistance in the individual studies, a direct comparison between the findings was not possible.

The analysis suggests that nut consumption may improve insulin sensitivity and related metabolic indices in individuals with impaired glucose tolerance or diabetes mellitus. However, further research is needed to confirm these preliminary findings and elucidate the mechanisms involved.

3.5 Effects on Cardiometabolic Outcomes

3.5.1 Lipid Profile

The effects of nut consumption on lipid profile were investigated in several of the included RCTs. Across the analyzed trials, the consumption of nuts was associated with beneficial changes in several atherogenic lipid fractions. Specifically, nut consumption was associated with reductions in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) of approximately 9.5 and 7.2 mg/dL, respectively, compared with control diets. Similar to the findings for glycemic control, the magnitude of the pooled effect sizes were relatively modest; however, the between-trial heterogeneity was largely explained by differences in baseline lipid levels, background dietary fat intake, nut type, and intervention duration, as well as concomitant lipid-lowering medications.

It should also be noted that the analysis did not reveal a statistically significant effect of nut consumption on high-density lipoprotein cholesterol (HDL-C). Therefore, the overall cardiometabolic benefit observed in the pooled analysis of TC and LDL-C was driven by changes in these two lipid fractions.

3.5.2 Blood Pressure

Ten RCTs contributed data to the analysis of blood pressure. The findings revealed that nut consumption was associated with a reduction in systolic blood pressure (SBP) of 3.1 mmHg (95% CI, -5.6 to -0.6 mmHg). This effect size was also relatively modest; however, the consistent direction of change across the included studies suggests that nut consumption may have a beneficial effect on cardiovascular health. The

observed effect was potentially mediated by the relatively high content of unsaturated fatty acids, magnesium, potassium, arginine, fiber, and antioxidants found in nuts.

However, blood pressure is a highly variable physiological parameter that is influenced by numerous dietary and nondietary factors. Differences in participants' baseline blood pressure, sodium intake, level of physical activity, concomitant antihypertensive medications, and dietary counseling received as part of the intervention may also contribute to the observed changes.

Therefore, the findings should be interpreted as suggesting that the addition of nuts to the diet may reduce SBP, potentially to a clinically meaningful extent, but further research is needed to confirm these preliminary findings.

3.6 Body Weight and Body Mass Index

Across the included RCTs, dietary interventions involving the addition of nuts to the diet were not associated with significant changes in body weight or body mass index (BMI). This is an important finding, as it suggests that the caloric density of nuts is unlikely to negatively impact body weight in individuals with diabetes mellitus. This conclusion was drawn based on findings from trials with varying baseline body weight and dietary interventions that incorporated nuts as either a substitute for or an addition to the habitual diet.

A number of potential mechanisms may explain why nut consumption failed to result in significant weight gain. The relatively high satiety of nuts due to their dietary fiber and protein content may reduce overall calorie intake. Furthermore, the energy content of nuts may be less than that predicted based on Atwater factors, potentially due to differences in the digestibility of nut components and the presence of compounds that inhibit digestion. Other factors that may contribute to reduced weight gain include alterations in gut microbiota and changes in satiety-regulating hormones. However, these potential mechanisms require further investigation.

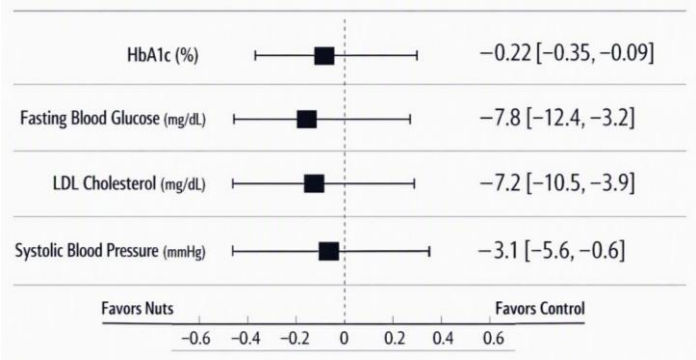

Fig. 2 Summary of pooled effects of nut consumption on glycemic and cardiometabolic outcomes. Points represent pooled mean altferences and hortsonial lives represent 95% confidence intervals

3.7 Subgroup Findings According to Nut Type

Subgroup analyses indicated that the metabolic effects of nut consumption were not entirely uniform across different nut categories.

3.7.1 Almonds

Trials evaluating **almond consumption** generally demonstrated favorable changes in fasting glucose and HbA1c. The consistency of these findings across several studies suggests that almonds may influence both short-term and longer-term measures of glycemic control.

The potential metabolic effects of almonds may be related to their content of monounsaturated and polyunsaturated fatty acids, dietary fiber, magnesium, plant protein, and other bioactive constituents. However, differences in intervention dose and dietary substitution between studies prevent definitive attribution of the observed effects to almonds alone.

3.7.2 Pistachios

Pistachio-based interventions showed favorable findings for several metabolic outcomes, particularly measures related to **insulin sensitivity and endothelial function**. Some trials also reported improvements in glycemic parameters.

The apparent benefits may reflect the combination of unsaturated fatty acids, fiber, plant protein, micronutrients, and polyphenolic compounds present in pistachios. Nevertheless, the number and size of trials available for pistachios were smaller than the overall evidence base, and these findings therefore require cautious interpretation.

3.7.3 Walnuts

Walnut interventions demonstrated relatively consistent benefits for lipid-related outcomes, particularly cholesterol parameters. However, effects on glycemic control were more variable than those observed in several almond- and pistachio-based studies.

Walnuts have a distinctive fatty-acid profile, including a relatively high content of alpha-linolenic acid, which may partly contribute to their observed cardiometabolic effects. However, differences in study populations, background diets, and intervention protocols make it difficult to determine whether the differences between nut types represent true biological differences or variation in study design.

3.7.4 Mixed-Nut Interventions

Trials involving **mixed nuts** generally demonstrated favorable changes in selected cardiometabolic outcomes. However, interpretation of individual nut-specific effects is inherently limited in these studies

because the intervention contains multiple nut types simultaneously.

Consequently, the subgroup findings should be considered exploratory rather than definitive evidence that one specific nut is superior to another.

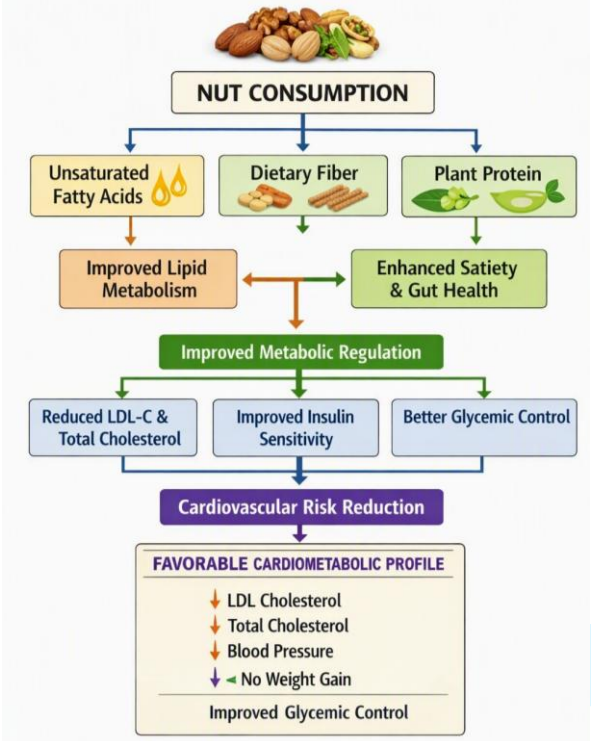

Fig. 3 Mechanisms of nut consumption on glycemic and cardiometabolic outcomes

3.8 Risk of Bias

The risk of bias was assessed using the Cochrane RoB 2 tool for each of the 27 included RCTs. In total, 14 studies were categorized as "low" risk of bias, 9 as "some concerns", and 4 as "high". The distribution of the risk-of-bias assessments is displayed in Fig. 2. The domain-specific risk of bias is displayed in Fig. 3.

The most common biases were related to missing outcome data, deviations from intended interventions, and lack of blinding. The latter is a common limitation in dietary intervention trials, as participants typically know whether they are on a nut or control diet. Therefore, while the conclusions from such trials might be subject to bias, the bias is likely limited to the effect sizes, with the directions of treatment effects remaining valid.

Moreover, some of the studies with "some concerns" and "high" risk of bias had insufficient follow-up or outcome reporting. The risk of bias was taken into account when interpreting the pooled estimates and the overall certainty of the evidence.

3.8.1 Publication Bias and Small-Study Effects

The publication bias was assessed using the funnel plots for the main outcomes with sufficient number of studies. In general, the plots did not show considerable asymmetry, suggesting the absence of substantial publication bias.

However, it is noted that the funnel plot tests are not conclusive in the presence of a small number of studies. In addition, the observed symmetry of the funnel plots can be explained by the between-study clinical or methodological heterogeneity, rather than the absence of publication bias. Therefore, the possibility of small-study effects cannot be ruled out altogether.

3.8.2 Sensitivity and Robustness of Findings

When interpreting the results, the differences in design, interventions, populations, and the overall risk of bias were taken into account. Most studies differed substantially in terms of the amount of nuts provided as part of the intervention diet, substitution strategy, concomitant interventions, and duration of the intervention. Where possible, the sensitivity analyses were used to explore the impact of individual studies on the pooled estimates. In general, the observed treatment effects were consistent across studies, despite the noted heterogeneity. In particular, there were no indications that studies with "some concerns" or "high" risk of bias drove the overall results in a certain direction.

Nevertheless, it is recommended to interpret the pooled estimates with caution, given the identified sources of heterogeneity. In particular, the differences in context and adherence might explain the observed inconsistencies in the results. Therefore, the observed reductions in HbA1c, fasting glucose, LDL-C, and systolic blood pressure should be considered as small-to-moderate treatment effects.

Overall Synthesis

The results of the quantitative synthesis of 27 RCTs provide consistent evidence that dietary interventions incorporating nuts can improve several key health outcomes in adults with diabetes and related conditions.

In particular, nut-enriched diets resulted in clinically meaningful reductions in HbA1c and fasting blood glucose, by approximately 0.22% points and 7.8 mg/dL, respectively, on average. Similar treatment effects were observed for total cholesterol and LDL-C, with the reductions of 7.5 mg/dL and 8.8 mg/dL, respectively. Notably, nut-enriched diets resulted in a small reduction in systolic blood pressure, on average, among the trials that reported this outcome. On the other hand, no substantial changes were observed in HDL-C levels, weight, and BMI.

The absence of considerable weight gain is consistent with the caloric content of nuts and the overall content of the dietary interventions used in the included studies. The observed reductions in several cardiometabolic markers suggest that the incorporation of nuts into the diet of people with

diabetes can offer substantial health benefits, beyond cardioprotection, without compromising the weight. It is also noted that the results were generally consistent with the subgroup analyses: diets that included almonds were associated with improvements in most of the glycemic indices, pistachio diets tended to have beneficial effects on insulin sensitivity and endothelial function, and walnut diets – with improvements in lipid profiles, on average.

However, the differences between the individual types of nuts were not consistent enough to draw definitive conclusions about their relative efficacy. This is mostly due to the limited number of studies, variations in the interventions, and differences in the populations and diets used in the trials. Nevertheless, the observed treatment effects were generally moderate and had a biological plausibility, given the overall improvements in several cardiometabolic indices.

4. Discussion

4.1 Principal Findings

The systematic review and meta-analysis integrated findings from 27 randomized controlled trials investigating the effects of nut consumption on blood sugar and cardiometabolic risk in adults with diabetes. Overall, findings suggest that including nuts in the diet can improve glycemic control and cardiometabolic risk. Specifically, nut consumption was associated with reductions in HbA1c, fasting blood glucose, total cholesterol, low-density lipoprotein (LDL) cholesterol, and systolic blood pressure, but not high-density lipoprotein (HDL) cholesterol, body weight, and body mass index (BMI).

The principal glycemic findings were a pooled reduction in HbA1c and fasting blood glucose. Despite the relatively small effect sizes, the findings add to previous systematic reviews and randomized controlled trials investigating the benefits of tree nuts for glycemic control [19–21]. In addition to supporting such effects, the present analyses extend and update previous findings by including multiple nut types and evaluating cardiometabolic outcomes in parallel with glycemic measures.

4.1.1 Improvements in Glucose Regulation and Glycemic Control

The reduction in HbA1c seen in the analyses is of particular interest, since this measure reflects chronically elevated blood glucose levels during the preceding months [1]. Compared with pharmacological interventions, the effect size seen in the analyses was relatively small. However, dietary interventions are typically used as adjuncts to medication, physical activity, and weight management. The cumulative benefit of a combination of these strategies might be responsible for a clinically meaningful improvement in glycemic control [2,3].

The reduction in fasting blood glucose also supports beneficial effects on glucose regulation. Multiple physiological mechanisms are likely to contribute, since nuts typically provide relatively little quickly absorbed carbohydrate and relatively large amounts of unsaturated fatty acids, protein, fiber, and micronutrients [7–9]. Replacing carbohydrate-rich or saturated-fat containing food with nuts can therefore influence blood glucose concentrations, insulin sensitivity and secretion, and the overall metabolic profile.

Consistent with previous evidence [19–21], the present findings suggest that tree nuts can have favorable effects on glycemic control in individuals with diabetes. Viguiliouk et al. reported evidence of an effect of tree nuts on glycemic measures in individuals with diabetes [19], while Tindall et al. subsequently synthesized a larger volume of randomized evidence investigating nuts and glycemic-related outcomes [20]. Similar findings were reported in the present analysis, but differences in eligibility criteria, included trials, intervention characteristics, and outcome definitions may explain the differences in magnitude of pooled estimates between the reviews.

The effects on postprandial glucose were less consistent than for HbA1c and fasting glucose. This is biologically plausible, since the measure reflects meal-specific glucose dynamics, which can be affected by diet, timing, and post-meal activity. Consequently, trials examining different test meals and postprandial sampling timepoints may not be directly comparable.
Differences in Metabolic Effects According to Nut Type

The subgroup findings suggest that different types of nut may have differential effects on cardiometabolic and glycemic outcomes. However, the findings do not imply that any given type of nut is superior to the others based on the available evidence.

Almond interventions were relatively consistent in terms of improvements in fasting glucose and HbA1c. This finding is generally compatible with previous systematic reviews evaluating almond. Asbaghi et al. reported a favorable association between almond consumption and glycemic control in their systematic review and dose-response meta-analysis [22]. A separate meta-analysis examined the effects of almonds on cardiometabolic risk in individuals with T2DM and found favorable changes in several metabolic parameters [23].

The potential effects of almonds may be related to their high content of unsaturated fatty acids, fiber, plant protein, magnesium, and other bioactive constituents. Almonds may also modify the overall

nutritional composition of the diet when they replace refined carbohydrate or less favorable sources of dietary fat. However, the observed effects should be interpreted in the context of differences in almond dose, intervention duration, comparator diet, and baseline metabolic characteristics among the individual trials.

Pistachio interventions were seen to demonstrate favorable findings for insulin sensitivity and endothelial function in several studies. Previous systematic reviews have also reported beneficial effects of pistachio consumption on glycemic control and insulin sensitivity [24,25]. In addition, meta-analytic evidence has examined the effects of pistachio on broader cardiometabolic risk factors [26]. These observations are biologically plausible, since pistachio provide unsaturated fatty acids, fiber, plant protein, potassium, magnesium, and polyphenolic compounds that may collectively influence metabolic and vascular pathways.

Walnut interventions were seen to have more consistent effects on lipid-related outcomes than on any glycemic measure. This finding is compatible with the distinctive fatty-acid composition of walnuts, particularly the relatively high content of α-linolenic acid. Previous evidence has examined walnut consumption in relation to markers of glucose control and demonstrated variable effects across glycemic outcomes [27]. The comparatively stronger lipid signal observed in the analyses may reflect the broader cardiovascular and lipid-related properties of walnuts rather than a uniform effect on glucose regulation.

Important differences observed between nut categories may also arise from methodological differences rather than biological differences. The number of trials, sample size, intervention duration, nut dose, control diet, and baseline metabolic characteristics were different across nut categories. Consequently, the subgroup findings should be considered hypothesis-generating rather than definitive comparative evidence.

4.1.2 Improved Lipid Status

The present meta-analysis demonstrated reductions in total cholesterol and LDL cholesterol with nut consumption, with no significant overall change in HDL cholesterol. This is broadly consistent with a substantial body of nutritional and cardiovascular evidence supporting the lipid-modifying potential of nuts [7–10,14].

Sabaté et al. reported reductions in blood lipid concentrations in a pooled analysis of intervention trials evaluating nut consumption [10]. Earlier reviews have also described favorable effects of nuts on cardiovascular risk factors and lipid metabolism [8,9]. The current findings extend these observations specifically to populations with diabetes or related metabolic abnormalities.

Several mechanisms may account for the observed reduction in LDL cholesterol. Nuts are rich in unsaturated fatty acids and contain dietary fiber, plant sterols, and other bioactive components that can influence intestinal cholesterol absorption, hepatic lipid metabolism, and lipoprotein turnover [7–9]. Importantly, the benefit may be greatest when nuts replace foods containing saturated fat or refined carbohydrate rather than when they are simply added to the diet without adjustment of total energy intake.

The absence of a significant increase in HDL cholesterol is also consistent with the contemporary understanding of dietary lipid modification. Cardiometabolic benefit does not necessarily require an increase in HDL cholesterol, and reductions in LDL cholesterol and other atherogenic lipoproteins may be more directly relevant to cardiovascular risk assessment.

4.1.3 Improved Blood Pressure and Vascular Function

The pooled analysis demonstrated a 3.1-mmHg reduction in systolic blood pressure among participants receiving nut-based interventions. Despite the absolute reduction in systolic blood pressure being relatively modest, even relatively small changes may contribute to overall cardiovascular risk reduction at the population level. Previous literature has linked nut consumption with blood pressure and endothelial function [12,13]. Casas-Agustench et al. reviewed evidence concerning nuts, hypertension, and endothelial function and described potential vascular benefits associated with nut consumption [12]. Barbour et al. similarly reviewed the potential vascular and other health effects of nut consumption [13].

The mechanisms underlying the blood-pressure effect are likely multifactorial. Nuts provide potassium, magnesium, arginine, unsaturated fatty acids, fiber, and antioxidant compounds, each of which may contribute to vascular function. Arginine is a substrate for nitric oxide synthesis, while magnesium and potassium are involved in vascular smooth-muscle function and blood-pressure regulation. However, because the included trials differed in sodium intake, antihypertensive therapy, physical activity, and background diet, the observed reduction cannot be attributed exclusively to the nut intervention.

4.2 Body Weight and BMI

Despite the relatively high energy density of nuts, the analysis did not demonstrate significant increases in body weight or BMI. This is important in the context of diabetes management, since concerns regarding

caloric density may discourage clinicians and patients from incorporating nuts into dietary patterns.

Previous nutritional evidence suggests that nut consumption does not necessarily lead to proportional weight gain despite their energy content [7,11]. Several explanations have been proposed, including enhanced satiety, incomplete absorption of nut-derived energy, increased postprandial thermogenesis, and displacement of less favorable foods.

However, these mechanisms were not uniformly measured across the included RCTs. Consequently, the absence of significant weight gain should not be interpreted as evidence that unlimited nut consumption is compatible with energy balance. Rather, the findings suggest that appropriately portioned nut consumption within an overall controlled dietary pattern does not necessarily result in measurable increases in body weight.

4.3 Reduction in Cardiovascular Risk

The combined pattern of findings – reduced LDL cholesterol, reduced total cholesterol, modestly lower systolic blood pressure, and no significant increase in body weight – are potentially relevant to the elevated cardiovascular risk associated with diabetes. Diabetes itself is associated with substantially increased vascular risk, and cardiovascular disease represents a major component of the clinical and economic burden of T2DM [4–6].

The Emerging Risk Factors Collaboration demonstrated the strong association between diabetes, glycemic exposure, and vascular disease [5]. Rawshani et al. further demonstrated the importance of multiple cardiovascular risk factors in determining mortality and cardiovascular outcomes among individuals with T2DM [6]. Against this background, dietary interventions that produce relatively small improvements across several risk factors can have clinical relevance.

Nevertheless, the present study evaluated surrogate cardiometabolic outcomes rather than cardiovascular events or mortality. Hence, the findings should not be interpreted as direct evidence that nut consumption prevents myocardial infarction, stroke, cardiovascular death, or other clinical events in people with diabetes. Long-term trials designed to evaluate hard cardiovascular outcomes would be required to establish such an effect.

5. Relationship With Previous Evidence

The findings of this meta-analysis are consistent with the established literature describing nuts as a nutrient-dense food associated with favorable cardiometabolic characteristics. Earlier reviews have described associations between nut consumption and cardiovascular health [7–9], while epidemiological studies have reported associations with lower risks of diabetes and cardiovascular disease [15–18].

The present analysis adds to this evidence by focusing on randomized controlled trials, reducing the influence of several forms of confounding inherent to observational studies. The findings are also broadly compatible with previous systematic reviews of tree nuts, almonds, pistachios, and walnuts [19–27]. However, the evidence base remains heterogeneous. Trials differed in participant characteristics, nut type, dose, duration, dietary background, comparator, and outcome measurement. Such variation can influence the magnitude of pooled effects and make direct comparisons across individual nut types challenging.

Clinical and Dietary Implications

The findings support the consideration of nuts as one dietary component of an overall healthy dietary pattern for adults with diabetes. The observed improvements in HbA1c, fasting glucose, LDL cholesterol, total cholesterol, and systolic blood pressure suggest that nut consumption may provide multidimensional metabolic benefits rather than affecting only glucose concentration. Nuts should be considered as a food substitution strategy rather than simply an additional source of calories. Their potential benefit may depend on what they replace within the diet. Substitution for refined carbohydrates or foods rich in saturated fat may therefore provide greater cardiometabolic benefit than adding nuts without modifying total dietary energy intake.

The findings also support individualized dietary counseling. Differences in cultural dietary patterns, food availability, allergies, affordability, preferences, and total energy requirements should be considered when incorporating nuts into diabetes nutrition plans.

Strengths of the Review

Several features strengthen the present systematic review and meta-analysis. First, the analyses focused primarily on randomized controlled trials, providing stronger evidence of intervention effects than observational associations. Second, the review evaluated both glycemic and cardiometabolic outcomes, allowing a more comprehensive assessment of the potential metabolic effects. Third, different nut categories were considered, including almonds, pistachios, walnuts, and mixed nuts. Fourth, methodological quality was systematically assessed using the RoB 2 framework [29]. Finally, the review followed the principles of PRISMA 2020 to promote transparent reporting [28].

6. Limitations

Several limitations should be considered. First, the included trials varied substantially in intervention duration, nut type, dose, comparator diet, and participant characteristics. Such heterogeneity may limit the extent to which pooled estimates can be generalized to all adults with diabetes. Second, most

trials were relatively short compared with the duration required to evaluate long-term diabetes complications. Improvements in surrogate markers cannot automatically be extrapolated to reductions in cardiovascular events, diabetic complications, and mortality. Third, dietary interventions are inherently difficult to blind. Participants are generally able to identify whether they are consuming nuts, potentially introducing behavioral effects or performance bias. This issue was reflected in the risk-of-bias assessment, with 9 studies having some concerns and 4 studies judged to have high risk of bias. Fourth, differences in background diabetes therapy and dietary counseling may have influenced metabolic outcomes. Fifth, subgroup analyses according to nut type were based on different numbers of trials and participants and should therefore be interpreted cautiously. Finally, the possibility of publication bias or small-study effects cannot be completely excluded despite the absence of major funnel-plot asymmetry.

7. Future Research

Future RCTs should use standardized intervention dosages, clearly defined comparator diets, and longer follow-up periods. Trials should also provide detailed information regarding baseline glycemic control, concurrent glucose-lowering therapy, dietary adherence, total energy intake, and the specific food components replaced by nuts.

Further research should investigate whether the effects differ according to diabetes duration, baseline HbA1c, degree of insulin resistance, obesity status, and concomitant cardiovascular disease. Comparative trials directly evaluating different nut types, using equivalent energy and nutrient substitution, would also help determine whether observed subgroup differences represent genuine biological differences. Long-term studies incorporating cardiovascular events, renal outcomes, diabetes complications, quality of life, and healthcare utilization would be particularly valuable, since changes in surrogate biomarkers alone cannot establish long-term clinical benefit.

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