Inclusion of walnut in the diets of adults at risk for type 2 diabetes and their dietary pattern changes: a randomized, controlled, cross-over trial

Valentine Yanchou Njike,1,2 Niloufarsadat Yarandi,2 Paul Petraro,2 Rocky G Ayettey,1,2 Judith A Treu,1,2 David L Katz1,2

ABSTRACT

Background: In our recently published study, including walnuts in the diets of adults with prediabetes led to overall improvement in diet quality. This report adds to those study findings by examining the food groups displaced during walnut inclusion in the diets of those adults with prediabetes.

Methods: Randomized, controlled, modified Latin square parallel design with 2 treatment arms. The 112 participants (31 men, 81 women) were randomly assigned to a diet with or without dietary counseling to regulate calorie intake in a 1:1 ratio. Within each treatment arm, participants were further randomized to 1 of 2 sequence permutations to receive a walnut-included diet with 56 g (366 kcal) of walnuts per day and a walnut-excluded diet. Participants in the calorie-regulated arm received advice from a diettian to preserve an isocaloric condition while including walnuts. We analyzed the 12 components of the 2010 Healthy Eating Index to examine dietary pattern changes of study participants.

Results: Seafood and plant protein foods intake significantly increased with walnut inclusion, compared with their exclusion (2.14±2.06 vs −0.49±2.33; p=0.003). The ingestion of healthful fatty acids also significantly increased with walnut inclusion, compared with their exclusion (1.43±5.53 vs −1.76±4.80; p=0.02). Dairy ingestion increased with walnut inclusion in the calorie-regulated phase, compared with walnut inclusion without calorie regulation (1.06±4.42 vs −2.15±3.64; p=0.02).

Conclusions: Our data suggest that walnut inclusion in the diets of adults at risk for diabetes led to an increase in intake of other healthful foods.

Trial registration number: NCT02330848.

Key messages

- The inclusion of walnuts in the diets of adults at risk for type 2 diabetes improved their overall diet quality.
- The inclusion of walnuts in the diets of adults at risk for type 2 diabetes facilitated the introduction of healthy food choices in their diets.
- The inclusion of walnuts in the diets of adults at risk for type 2 diabetes facilitated the replacement of unhealthy foods in their diets.

BACKGROUND

According to the WHO, the number of cases of adults with diabetes has quadrupled since 1980.1 This increase in the number of cases of diabetes could be attributed to changes in dietary patterns which include an increase in the consumption of obesigenic foods such as sugary foods and beverages.2 Currently, about 29.1 million Americans are known to have diabetes.3 An estimated 86 million Americans aged 20 and older have prediabetes.3 Among adults at risk of diabetes, 15–30% develop diabetes within 5 years.3

Potential complications of diabetes include heart attack, stroke, vision loss, kidney disease, nerve damage, and lower limb gangrene that could lead to amputation. The risk of death of individuals with diabetes is 50% more than that of those without diabetes. It is estimated that the total medical cost, work lost, and wages lost for individuals with diabetes is about $245 billion. The medical cost for individuals with diabetes is twice as high as that for those without diabetes.3

Although there is no known cure for diabetes, the progression from prediabetes to type 2 diabetes could be prevented.4–7 A study by Knowler et al4 demonstrated that modest lifestyle changes (ie, exercise and nutrition) led to a reduction of 5–7% of body weight and a 58% reduction in the risk of developing type 2 diabetes among individuals at high risk of diabetes. In addition, lifestyle interventions have been shown to be cost-effective for the primary prevention of type 2 diabetes.8 Foods that are low in fat and calories, and high in fiber, with a focus on fruit, vegetables and whole grains are typically recommended to prevent the
progression from prediabetes to diabetes. Improved diet quality has been associated with lower risk of type 2 diabetes. In our recently published study, the inclusion of walnuts in the diets of adults at risk for type 2 diabetes led to improvement in their overall diet quality. The foods displaced from the diets of these individuals with the inclusion of walnuts that led to the improvement in diet quality were unknown. We therefore examined the foods that were displaced with the inclusion of walnuts in the diets of these adults with prediabetes.

METHODS

Study population

One hundred and twelve adults at risk for type 2 diabetes (31 men, 81 women) were recruited from the Lower Naugatuck Valley of Connecticut through flyers and newspaper advertisements. Those responding to the advertisements (n=678) were prescreened using a semi-structured telephone interview. Details of the study methods, recruitment process, and participant flow have been previously published.

Inclusion criteria: Adults between 25 and 75 years of age; non-smokers; high risk for diabetes, defined as meeting at least one of the following criteria: (1) overweight with increased waist circumference; (2) prediabetes based on fasting blood glucose between 100 and 126 mg/dL or glycated hemoglobin 5.7–6.4%; or (3) metabolic syndrome.

Exclusion criteria: Allergy to walnuts or any other nuts; anticipated inability to complete the study protocol for any reason; current eating disorder; restricted diets by choice (ie, vegetarian, vegan); regular use of high doses of vitamin E (>400 IU/day) or vitamin C (>500 mg/day); use of fish oil, flaxseed oil, omega-3 fatty acid, and/or fiber supplements unless willing to discontinue supplementation for the study duration.

Study design

This was a randomized, controlled, modified Latin square parallel design study with two treatment arms to examine the effects of the inclusion of walnuts in the diets of adults at risk for type 2 diabetes on their dietary patterns over a 6-month period. After a 4-week run-in period of an ad libitum diet, participants were randomized to one of four possible sequence permutations, and then crossed over following inclusion of 56 g walnuts per day, or walnut exclusion, for 6 months in their diets in random sequence, with a 3-month washout between treatments.

Intervention

Walnut intake without caloric regulation: Participants were provided 392 g of walnuts (unshelled) per week (56 g or 2 oz/day) to include in their diets. Their calorie intake was not monitored or regulated, and thus allowed to float ad libitum.

Walnut intake with caloric regulation: The intervention group participants met with a registered dietitian and received instructions and recipes for inclusion of 392 g of walnuts per week (56 g or 2 oz/day) in their otherwise ad libitum meal plan. Participants received instruction to preserve an isocaloric condition after the addition of walnuts. The study dietitian customized dietary advice to make room calorically for walnuts in the diet, while accommodating the priorities of each study participant. The general approach emphasized a general reduction in portion sizes; participants also received advice, based on baseline dietary intake analysis, of food eliminations that they might want to consider. While the isocaloric condition was encouraged and monitored by the dietitian, participants were provided latitude in determining how to make room for the calories from the walnuts, to better approximate real-world conditions.

Control diet: During the control phase, participants also met with the dietitian and received instructions to follow their usual ad libitum diets, with the exception of avoiding intake of walnuts and specific walnut-containing products. Dietary monitoring and participant weighing was conducted to ensure that an isocaloric condition was maintained.

Outcome measure

To help the study team track any variation in dietary patterns over the course of the study, all participants were asked to provide information on the foods and beverages that they consumed by completing 24-hour recalls using a web-based Automated Self-Administered 24-Hour Recall (ASA24; available from the National Cancer Institute at http://riskfactor.cancer.gov/tools/instruments/asa24/), which guided them through the process of completing the recall data. Diet quality and the food groups were assessed using the Healthy Eating Index (HEI) 2010. The HEI measures the diet quality, independent of quantity, which is used to assess compliance with the US Dietary Guidelines for Americans and monitor changes in dietary patterns. The HEI is a scoring metric that is used to determine the quality of a given dietary pattern, set of foods, or menu. There are 12 components in the HEI-2010. All of the key Dietary Guidelines food choice recommendations that relate to diet quality are reflected in the HEI-2010’s 12 components. Nine of the components focus on adequacy (dietary components to increase) and three focus on moderation (dietary components to decrease). The performance of the HEI-2010 has been evaluated through an assessment of its content validity, construct validity, and reliability. We analyzed the 12 components of the HEI-2010 to assess the dietary pattern changes in the diets of our study participants.

Statistical analysis

Generalized linear models were used to analyze these data. Regression models were used to adjust for...
potential confounding factors (ie, age, gender, race, compliance, and treatment sequence). All analyses of end points were based on the intention-to-treat principle. Results are expressed as means±SD in text and tables except where otherwise stated. SAS software for Windows V.9.3 (SAS Institute, Cary, North Carolina, USA) was used to carry out all statistical analyses.

The sample size was estimated to provide ≥80% power to detect a minimal difference of 7.5 in HEI score between treatment groups, with maximum allowable type I error of 5% (adjusted for three pair-wise comparisons). An SD of 10 in HEI and an attrition rate of 25% were used to compute the sample size.

RESULTS

Study participants

A total of 112 adults at risk for type 2 diabetes enrolled in this study. Most of the participants were female (ie, 72.3%). The proportion of female participants randomized to the calorie-regulated group was comparable to those randomized to the no calorie-regulated group. At baseline, the consumption of vegetables; greens and beans; total fruits (ie, 100% fruit juice); whole fruits (ie, all forms except juice); whole grains; seafood and plant protein foods; fatty acids (ie, ratio of polyunsaturated and monounsaturated fatty acids to saturated fatty acids); sodium; refined grain and empty calories (ie, calories from solid fats, alcohol, and added sugars) was comparable in the participants randomized to the calorie-regulated group as compared with those randomized to the no calorie-regulated group. The consumption of dairy products (ie, milk products, such as fluid milk, yogurt, and cheese, and fortified soy beverages) was significantly higher in the calorie-regulated group as compared with the no calorie-regulated group (p=0.04). Baseline data of our study participants are presented in table 1.

Efficacy end point

Calorie-regulated arm: Participants’ consumption of seafood and plant protein foods significantly increased from baseline during the walnut phase, as compared with the control (2.14±2.06 vs −0.49±2.33; p=0.003). Their intake of sodium non-significantly decreased from baseline during the walnut-included phase, as compared with the walnut-excluded phase (−3.20±4.46 vs −0.52±5.03; p=0.07). Their intake of sodium, empty calories, and dairy products significantly decreased from baseline (ie, −3.20±4.46, p<0.01; −3.15±6.03, p<0.05; and −2.15±3.64, p<0.05, respectively) with the inclusion of walnuts in the diet. The consumption of refined grains significantly decreased from baseline during the control phase (−2.04±1.39; p<0.05). The consumption of fruits and proteins significantly increased from baseline during the walnut-excluded phase (ie, 1.52±2.26, p<0.05 and 0.90±2.07, p<0.05, respectively). The consumption of vegetables; greens and beans; whole fruit; whole grains; and fatty acids (ie, ratio of polyunsaturated and monounsaturated fatty acids to saturated fatty acids) did not change significantly (p>0.05) from baseline during the walnut-included phase, compared with the walnut-excluded phase.

No calorie-regulated arm: The consumption of seafood and plant protein foods and healthful fatty acids significantly increased from baseline during the walnut-included phase as compared with the walnut-excluded phase (1.67±2.32 vs −1.21±3.93; p=0.002 and 1.43±4.53 vs −1.76±4.80; p=0.02, respectively). The consumption of vegetables significantly decreased from baseline during the walnut-included phase compared with the walnut-excluded phase (−0.55±1.84 vs 0.80±2.21; p=0.04). Empty calorie consumption non-significantly decreased from baseline during the walnut-excluded phase as compared with the walnut-excluded phase (−3.03±8.24 vs 0.70±8.64; p=0.06). However, empty calorie consumption

Table 1 | Baseline characteristics of study participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Calorie regulated/ walnuts (N=53)</th>
<th>No calorie regulated/ walnuts (N=49)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>69.6%</td>
<td>75.0%</td>
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<tr>
<td>Age (years)</td>
<td>56.5±11.7</td>
<td>53.3±11.1</td>
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<tr>
<td>2010 Healthy Eating Index score</td>
<td>57.1±17.4</td>
<td>54.0±15.7</td>
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</tr>
<tr>
<td>Total vegetables*</td>
<td>3.7±1.5</td>
<td>3.4±1.6</td>
<td>0.23</td>
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<tr>
<td>Greens and beans*</td>
<td>2.3±2.4</td>
<td>2.0±2.3</td>
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</tr>
<tr>
<td>Total fruit†</td>
<td>2.7±2.0</td>
<td>2.7±2.0</td>
<td>0.92</td>
</tr>
<tr>
<td>Whole fruit‡</td>
<td>3.0±2.2</td>
<td>3.0±2.3</td>
<td>0.99</td>
</tr>
<tr>
<td>Whole grains</td>
<td>4.1±3.9</td>
<td>3.0±3.6</td>
<td>0.17</td>
</tr>
<tr>
<td>Dairy§</td>
<td>6.4±3.1</td>
<td>5.1±3.7</td>
<td>0.04</td>
</tr>
<tr>
<td>Total protein foods¶</td>
<td>3.8±1.6</td>
<td>4.3±1.3</td>
<td>0.10</td>
</tr>
<tr>
<td>Seafood and plant protein foods¶**</td>
<td>2.5±2.2</td>
<td>2.4±2.4</td>
<td>0.91</td>
</tr>
<tr>
<td>Fatty acids††</td>
<td>4.2±3.8</td>
<td>4.6±3.8</td>
<td>0.60</td>
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<tr>
<td>Sodium</td>
<td>4.4±3.6</td>
<td>4.0±3.9</td>
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<tr>
<td>Refined grains</td>
<td>6.8±3.4</td>
<td>7.3±3.3</td>
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<tr>
<td>Empty calories†‡</td>
<td>13.9±5.5</td>
<td>13.8±6.1</td>
<td>0.95</td>
</tr>
<tr>
<td>Total calories</td>
<td>2054.7±788.6</td>
<td>1892.8±867.5</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*includes any beans and peas not counted as total protein foods. †includes 100% fruit juice. ‡includes all forms except juice. §includes all milk products, such as fluid milk, yogurt, and cheese, and fortified soy beverages. ¶includes seafood, nuts, seeds, soy products (other than beverages) as well as beans and peas counted as total protein foods. ††Ratio of polyunsaturated and monounsaturated fatty acids to saturated fatty acids. **Includes seafood, nuts, seeds, soy products (other than beverages) as well as beans and peas counted as total protein foods.


decreased significantly from baseline in the walnut-included phase (−3.03±8.24; p<0.05). The consumption of greens and beans; fruit; whole fruit; whole grains; dairy products; protein foods; sodium; and refined grains from baseline during the walnut-included phase was comparable to that found during the walnut-excluded phase (p>0.05).

Calorie-regulated arm versus no calorie-regulated arm: The decrease in the consumption of dairy products from baseline observed in participants in the calorie-regulated arm during the walnut-included phase was significant as compared with those in the no calorie-regulated arm (−2.15±3.64 vs 1.06±4.42; p=0.02). No differential treatment effects were observed (p>0.05) in the consumption of vegetables; greens and beans; fruit; whole fruit; whole grains; protein foods; sodium; refined grains; or empty calories from baseline with the inclusion of walnuts in the diets of these adults at risk for type 2 diabetes. The consumption of greens and beans, whole fruit, and whole grains did not change significantly with the inclusion of walnuts in the diet.

Our efficacy data are reported in table 2.

**DISCUSSION**

Our data suggest that the consumption of seafood and plant protein foods and healthful fatty acids significantly increased, while the consumption of sodium, empty calories, vegetables, and dairy foods significantly decreased, with the inclusion of walnuts in the diets of these adults at risk for type 2 diabetes. The consumption of greens and beans, whole fruit, and whole grains did not change significantly with the inclusion of walnuts in the diet.

There was a significant reduction in dairy product consumption in the participants randomized in the calorie-regulated arm as compared with those in the no calorie-regulated arm. All of these dietary changes observed during the walnut-included phase led to an overall significant improvement in diet quality among this group of adults at risk for type 2 diabetes.

Studies have shown that improved diet quality is associated with lower risk for type 2 diabetes. Further, in a study by Dominguez et al,14 dietary-based diabetes risk score, which integrates optimal food patterns, with the risk of developing type 2 diabetes was inversely associated with the development of type 2 diabetes. The American Diabetes Association (ADA) recommends intake of plant-based protein sources, for example, beans, nuts, seeds, or tofu; fish and seafood; chicken and other poultry; eggs; and low-fat dairy products. The ADA also recommends intake of natural sources of vegetable fats, such as nuts, seeds, or avocados; foods that provide omega-3 fatty acids, such as salmon, tuna, mackerel, or walnuts; and plant-based oils, such as canola, grapeseed, or olive oils as the healthful choices for blood glucose control in diabetes and prediabetes.

We observed a significant increase in the consumption of seafood and plant protein foods with the inclusion of walnuts in the diets of adults at risk for diabetes. In a study by Patel et al,15 consumption of lean fish, total fish and shellfish was not associated with the risk of type 2 diabetes. However, fatty fish consumption was inversely associated with the risk of type 2 diabetes. Wu et al36 also demonstrated no association between the consumption of fish/seafood and the risk of type 2 diabetes, and

<table>
<thead>
<tr>
<th>Variable</th>
<th>CRW</th>
<th>Calorie regulated/walnut excluded</th>
<th>p Value</th>
<th>NCRW</th>
<th>No calorie regulated/walnut excluded</th>
<th>p Value</th>
<th>CRW vs NCRW p Value</th>
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<tbody>
<tr>
<td>Healthy Eating Index score</td>
<td>9.14±17.71**</td>
<td>0.40±15.13</td>
<td>0.02</td>
<td>7.02±15.89¥</td>
<td>−5.92±21.84¥</td>
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<tr>
<td>Total vegetables</td>
<td>−0.35±1.93</td>
<td>−0.30±1.8</td>
<td>0.93</td>
<td>−0.55±1.84</td>
<td>0.80±2.21</td>
<td>0.04</td>
<td>0.76</td>
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<tr>
<td>Greens and beans</td>
<td>−0.60±2.83</td>
<td>−0.31±2.74</td>
<td>0.76</td>
<td>−0.69±2.71</td>
<td>−0.14±3.72</td>
<td>0.59</td>
<td>0.93</td>
</tr>
<tr>
<td>Total protein foods</td>
<td>−0.11±2.39</td>
<td>1.52±2.26¥</td>
<td>0.06</td>
<td>−0.55±2.91</td>
<td>−0.13±3.30</td>
<td>0.64</td>
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<td>Whole fruit</td>
<td>−0.36±2.52</td>
<td>1.23±2.40</td>
<td>0.10</td>
<td>−0.51±3.40</td>
<td>−0.34±3.85</td>
<td>0.87</td>
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<td>Whole grains</td>
<td>−1.01±4.64</td>
<td>−0.11±4.95</td>
<td>0.55</td>
<td>0.82±4.87</td>
<td>−0.35±4.56</td>
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<tr>
<td>Dairy</td>
<td>−2.15±3.64¥</td>
<td>−0.51±4.39</td>
<td>0.20</td>
<td>1.06±4.42</td>
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<tr>
<td>Seafood and plant protein foods</td>
<td>0.72±1.46</td>
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<td>0.04</td>
<td>0.40±1.00</td>
<td>0.14±2.04</td>
<td>0.64</td>
<td>0.57</td>
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<tr>
<td>Fatty acids</td>
<td>2.14±2.06**</td>
<td>−0.49±2.33</td>
<td>0.003</td>
<td>1.67±2.32</td>
<td>−1.21±3.93*</td>
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<tr>
<td>Sodium</td>
<td>0.93±6.51</td>
<td>0.02±4.26</td>
<td>0.51</td>
<td>1.43±4.53</td>
<td>−1.76±4.80</td>
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<td>0.72</td>
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<tr>
<td>Refined grains</td>
<td>−3.20±4.46¥</td>
<td>−0.52±5.03</td>
<td>0.07</td>
<td>−1.77±6.27</td>
<td>−1.79±5.71</td>
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<tr>
<td>Empty calories</td>
<td>−1.13±3.18</td>
<td>−2.04±4.39¥</td>
<td>0.42</td>
<td>−0.98±3.88</td>
<td>−0.47±5.02</td>
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<td>0.90</td>
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<tr>
<td>Total calories</td>
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<td>0.63</td>
<td>−3.03±8.24¥</td>
<td>0.70±8.64</td>
<td>0.06</td>
<td>0.95</td>
</tr>
</tbody>
</table>

¥<0.05, ¥<0.01, **<0.001 indicates significant changes from baseline.

CRW, calorie regulated/walnut included; NCRW, no calorie regulated/walnut included.
observed an inverse relationship between the consumption of α-linolenic acid and the risk of diabetes. However, epidemiological studies have shown an association between the consumption of animal proteins and the increased risk of type 2 diabetes.\textsuperscript{17-19} In a meta-analysis by Viguiliouk \textit{et al.}\textsuperscript{20} replacing animal protein sources with plant protein food sources improved glycemic control in individual with diabetes. Seafood and plant-based proteins have a relatively low glycemic index. Foods with a low glycemic index are typically recommended for patients with or at risk for diabetes. Increased consumption of seafood and plant protein foods in the diets of patients at risk for diabetes or diabetes could help in blood glucose control. On the other hand, animal proteins, particularly red meats, are rich in saturated fatty acids that could adversely affect blood glucose levels.

We observed a decrease in the consumption of dairy products with the inclusion of walnuts in the diet. Chen \textit{et al.}\textsuperscript{21} demonstrated that increased yogurt consumption was associated with low risk of type 2 diabetes, while the consumption of other dairy foods or total dairy products was not associated with the incidence of type 2 diabetes. Malik \textit{et al.}\textsuperscript{22} demonstrated that high dairy product consumption during adolescence was associated with lower risk of type 2 diabetes. Meta-analyses\textsuperscript{23, 24} have shown that modest increases in consumption of dairy products such as low fat dairy, cheese and yogurt have been associated with reduced incidence of type 2 diabetes. On the contrary, in a large prospective study by Slujs \textit{et al.}\textsuperscript{25} total dairy product consumption was not associated with the risk of type 2 diabetes. However, an inverse relationship was observed between cheese intake and combined fermented dairy product consumption and the risk of type 2 diabetes.

We observed a non-significant decrease in empty calorie consumption from baseline during the walnut-included phase as compared with the walnut-excluded phase. However, the consumption of empty calories decreased significantly from baseline in the walnut-included phase. Pan \textit{et al.}\textsuperscript{26} demonstrated that substitution of plain water consumption for sugar sweetened beverages or fruit juice was associated with a lower risk for type 2 diabetes. Fagherazzi \textit{et al.}\textsuperscript{27} demonstrated that the consumption of sugar sweetened and artificially sweetened beverages was associated with increased incidence of type 2 diabetes. These empty calorie foods typically have a relatively high glycemic index. Foods with a high glycemic index are typically not recommended in diabetes and prediabetes due to the risk of adversely affecting blood glucose levels.

In our study, the consumption of whole grains did not differ significantly during the walnut-included phase as compared with the walnut-excluded phase. However, the consumption of refined grains decreased from baseline during the walnut-excluded phase. O’Neill \textit{et al.}\textsuperscript{28} demonstrated that tree nut consumption was associated with improved diet quality and improved nutrient intake. A meta-analysis by Blanco Mejia \textit{et al.}\textsuperscript{29} demonstrated that tree nuts improved triglycerides and blood glucose levels in individuals with metabolic syndrome. Another meta-analysis by Ye \textit{et al.}\textsuperscript{30} also demonstrated that whole grain consumption was associated with vascular disease prevention. In another study by Sahyoun \textit{et al.}\textsuperscript{31} high whole grain consumption was inversely associated with metabolic syndrome and cardiovascular mortality. Aune \textit{et al.}\textsuperscript{32} also showed that high whole grain consumption was associated with reduced risk of type 2 diabetes. Sun \textit{et al.}\textsuperscript{33} demonstrated that substituting brown rice for white rice reduced the risk for type 2 diabetes. Whole grains, as compared with refined grains, have a low glycemic index. The decrease in the consumption of refined grains in the walnut-excluded phase in our study may be due to the Hawthorn effect.

Our study showed a significant increase in the consumption of fatty acids with the inclusion of walnuts in the diet, as compared with their exclusion, among participants who did not receive counseling to regulate caloric intake. In a study by Guasch-Ferré \textit{et al.}\textsuperscript{34} higher olive oil consumption was associated with a lower risk of type 2 diabetes. Increased animal fat consumption has been associated with an increased risk of type 2 diabetes.\textsuperscript{35} Diets rich in monounsaturated fatty acids have been shown to decrease fasting insulin and improve the homeostasis model assessment of insulin resistance and the low-density lipoprotein to high-density lipoprotein ratio.\textsuperscript{36} Salmerón \textit{et al.}\textsuperscript{37} demonstrated that intakes of total fats and saturated and monounsaturated fatty acids are not associated with risk of type 2 diabetes in women, but that trans fatty acids increase the risk, while polyunsaturated fatty acids reduce the risk. Fatty acids affect glucose metabolism by modifying cell membrane function, enzyme activity, insulin signaling, and gene expression.\textsuperscript{38}

We did not observe any difference between the inclusion versus the exclusion of walnuts in the consumption of greens and beans; fruit; and whole fruit. In a study by Cooper \textit{et al.}\textsuperscript{39} consumption of fruit or vegetables was not associated with the risk of diabetes, while the consumption of green leafy vegetables was inversely associated with the risk of diabetes. Bazzano \textit{et al.}\textsuperscript{40} also demonstrated that the consumption of green leafy vegetables and fruit was associated with a lower risk of diabetes, whereas consumption of fruit juices may be associated with an increased risk among women. In a meta-analysis by Carter \textit{et al.}\textsuperscript{41} increased daily intake of green leafy vegetables was associated with a significantly reduced risk of type 2 diabetes. In another meta-analysis by Li \textit{et al.}\textsuperscript{42} the consumption of fruit or green leafy vegetables was associated with a reduced risk of type 2 diabetes. A study by Wu \textit{et al.}\textsuperscript{43} showed that 2–3 servings per day of vegetables and 2 servings per day of fruits reduced the risk of type 2 diabetes when compared with other levels of vegetable and fruit consumption, respectively. Green leafy vegetables are relatively low in saturated and trans fatty acids, and have a low glycemic index.
Cardiovascular and metabolic risk

In our study, while the consumption of sodium decreased non-significantly from baseline in the walnut-included phase compared with the walnut-excluded phase, we observed a significant decrease in the consumption of sodium from baseline with the inclusion of walnuts in the calorie-regulated arm. In a study by Horikawa et al., high sodium consumption was associated with increased risk of cardiovascular disease (CVD) in individual with type 2 diabetes. A synergistic effect of the risk of CVD was also identified when high sodium consumption was coupled with poor glucose control. A review by Poggio et al. also concluded that high sodium consumption was associated with higher CVD mortality. However, other studies have shown no association between sodium consumption and CVD. High sodium consumption affects the cardiovascular system by adversely affecting blood pressure. The reduction of consumption of sodium with the inclusion of walnuts could therefore reduce our participants risk for CVD.

Limitations
This study had several limitations. First, the participants were predominantly Caucasians and female, which limit us in extrapolating our findings to the general population. Second, the study had a small sample size. This limitation was overcome to some extent by crossing over the participants to the two different treatment assignments, thereby improving the power of the study. Third, the study relied on self-report by the participants for their dietary records, which can introduce measurement and recall biases. Fourth, the participants were not monitored on a daily basis and were not administered a supervised diet. However, this can also be viewed as a strength of the study because it provides a more realistic scenario and potentially increases external validity. In addition, the variation of the dietary patterns among participants may make it difficult to interpret the findings. Fifth, the advice given by the dietitian to the calorie-regulated group may explain some of the dietary changes observed. However, generally similar dietary changes were observed among those who did not receive advice to regulate their calorie intake. Sixth, another limitation is that intake of dairy products was significantly higher in the calorie-regulated arm as compared with the group not receiving guidance for total calorie, vegetables, and dairy foods decreased significantly with the inclusion of walnuts in the diets of these adults. The inclusion of walnuts in the diets of adults with prediabetes facilitated the introduction of healthful foods in their diets that are suitable for blood glucose control. Our study suggests that adding walnuts produces changes in intake of other foods. Future studies should routinely examine the impact of single food interventions on overall dietary patterns, since the addition of any given food almost invariably means changes in the intake of others.

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REFERENCES

CONCLUSIONS
The inclusion of walnuts in the diets in these adults at risk for type 2 diabetes led to the inclusion in their diets of healthful foods typically recommended for blood glucose control. We observed a significant increase in intake of seafood and plant-based proteins and healthful fatty acids, while the consumption of sodium, empty calorie, vegetables, and dairy foods decreased significantly with the inclusion of walnuts in the diets of these adults. The inclusion of walnuts in the diets of adults with prediabetes facilitated the introduction of healthful foods in their diets that are suitable for blood glucose control. Our study suggests that adding walnuts produces changes in intake of other foods. Future studies should routinely examine the impact of single food interventions on overall dietary patterns, since the addition of any given food almost invariably means changes in the intake of others.
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Valentine Yanchou Njike, Niloufarsadat Yarandi, Paul Petraro, Rockiy G Ayettey, Judith A Treu and David L Katz

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