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Pecan-Enriched Diets Alter Cholesterol Profiles and Triglycerides in Adults at Risk for Cardiovascular Disease in a Randomized, Controlled Trial

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ABSTRACT

Background: Research indicates that tree nuts are cardioprotective, but studies on pecans are limited.

Objectives: We examined the impact of daily pecan consumption on blood lipids and glycemia in adults at-risk for cardiovascular disease (CVD).

Methods: This was a randomized, controlled trial where 56 adults (BMI ≥28 kg/m^2 or hypercholesterolemia) were randomly allocated into a control group (n = 18) or 1 of 2 pecan groups. The ADD group (n = 16) consumed pecans (68 g) as part of a free-living diet. The SUB group (n = 18) substituted the pecans (68 g) for isocaloric foods from their diet. At baseline and 8 wk, a high-fat meal was consumed with 4-h postprandial blood draws to determine changes in blood lipids and glycemia.

Results: There was a significant reduction from baseline to 8 wk in fasting total cholesterol (TC) (204 ± 8.76 to 195 ± 8.12; 205 ± 8.06 to 195 ± 6.94 mg/dL), LDL cholesterol (143 ± 8.09 to 129 ± 7.71; 144 ± 6.60 to 135 ± 6.16 mg/dL), triglycerides (TGs) (139 ± 12.1 to 125 ± 14.6; 133 ± 10.7 to 120 ± 10.3 mg/dL), TC/HDL cholesterol ratio (3.92 ± 0.206 to 3.58 ± 0.175; 4.08 ± 0.167 to 3.79 ± 0.151), non–HDL cholesterol (151 ± 8.24 to 140 ± 7.95; 155 ± 6.87 to 143 ± 6.00 mg/dL), and apolipoprotein B (99.1 ± 5.96 to 93.0 ± 5.35; 104 ± 3.43 to 97.1 ± 3.11 mg/dL) in the ADD and SUB groups, respectively ($P \leq 0.05$ for all), with no changes in control. There was a reduction in postprandial TGs ($P \leq 0.01$) in ADD, and a reduction in postprandial glucose ($P < 0.05$) in SUB.

Conclusions: Pecan consumption improves fasting and postprandial blood lipids in CVD at-risk adults. This trial was registered at clinicaltrials.gov as NCT04376632. *J Nutr* 2021;0:1–11.

Keywords: lipids, cardiovascular disease, tree nuts, low-density lipoprotein, glycemia

Introduction

Cardiovascular disease (CVD) is the leading cause of death for adults in the United States, with 1 in every 4 deaths attributed to CVD (1). Risk factors include increased adiposity, elevated blood pressure, smoking, insulin resistance, and dyslipidemia (2), which is characterized as elevated total cholesterol (TC), LDL cholesterol, triglycerides (TGs), or low concentrations of HDL cholesterol (3). Common interventions for mitigating dyslipidemia include modifying dietary intake and/or exercise patterns (4). One dietary strategy that has been shown to be effective for improving lipid metabolism (5, 6) and reducing CVD risk (7, 8) is to replace saturated fatty acid (SFA) and *trans*-fatty acids with MUFAs and PUFAs (9).

Tree nuts are rich sources of dietary MUFAs and PUFAs, as well as other vitamins, minerals, and phytonutrients (10), and have been shown to decrease blood lipids, lipid peroxidation, and overall CVD risk (11–16) while also improving lipid metabolism (17, 18). Although there is substantial health-related research available on tree nut consumption, most studies are on walnuts (13, 19), almonds (15, 20, 21), or pistachios (22–24). To date, only 4 studies have examined the impact of pecan consumption on chronic disease risk in adults (5, 25–27). Because pecans are a rich source of MUFAs, PUFAs, fiber, vitamin E, and polyphenols and are low in SFAs (28–30), it is plausible that pecan consumption could provide some cardioprotective effects, especially as it relates to lipid metabolism.

We have previously shown that acute pecan consumption suppresses postprandial TGs in healthy young men (5). Furthermore, 2 longer-term studies of 4–8 wk showed that dietary pecan supplementation results in decreased TC, LDL cholesterol, and fasting TGs in healthy adults (26, 27). However, a more recent study that investigated the impact of a smaller daily dose of pecans (~42.5 g/d) in a metabolically at-risk population (overweight with central adiposity) did not show

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reductions in blood lipids (25). It is unclear if the lack of change in blood lipids was due to the lower dose of pecans or the at-risk population. Finally, no study has investigated whether the method or instructions for nut incorporation into the diet affects blood lipid outcomes.

To address the discrepancies and questions listed above, the objective of this study was to examine the impact of daily pecan consumption (with and without dietary/isocaloric substitution instructions) for an 8-wk period on blood lipids (the primary outcomes) and markers of glycemia (secondary outcomes) in adults with hypercholesterolemia or at higher risk for CVD [BMI (in kg/m^2) ≥28]. We hypothesized that daily pecan consumption, regardless of the method of incorporation into the diet, would result in improvements in blood lipids and markers of glycemia and that the responses of the control group would be nonsignificant.

Methods

Study design

This study was a single-blind, randomized, parallel controlled trial involving an 8-wk intervention conducted at the University of Georgia. The single-blind categorization of this study is in reference to the participants' masking to the dietary substitution instructions that were provided to each pecan group. Participants were not blinded to whether they received a pecan intervention or were in the control group. Data collection occurred from August 2018 to December 2020, when the goal of 16 participants/group was obtained. The study protocol included a screening visit and 3 testing visits. Participants were randomly assigned (balanced blocks stratified by age, sex, and BMI) to 1 of 3 groups: a "no-nut" control or 1 of 2 pecan groups (ADD or SUB). Participants in ADD and SUB consumed 68 g of pecans/d for 8 wk; however, dietary instructions for the incorporation of pecans into the diet differed. For ADD, pecans were consumed as part of a free-living diet, whereas in SUB, participants received counseling at baseline on how to substitute pecans for isocaloric foods from their habitual diet. This study was approved by the Institutional Review Board from the University of Georgia for human participants, and informed written consent was obtained from each participant prior to testing.

Participants

Sixty-nine sedentary men and women between the ages of 30 and 75 y with high cholesterol or a BMI of ≥28 were assessed for eligibility. Inclusion based on "high cholesterol" concentrations was defined as either "borderline high/undesirable" in 2 blood lipid categories or "high" in TC or LDL cholesterol (**Supplemental Table 1**). To rule out individuals with familial hypercholesterolemia, participants with LDL cholesterol concentrations >95th percentile or HDL cholesterol concentrations <20th percentile were excluded. Other exclusion criteria included habitual nut consumption (56 g/wk); nut allergies; special diets (i.e., ketogenic diet, intermittent fasting); excessive alcohol use [42 g alcohol/d (men) or 28 g alcohol/d (women)]; tobacco or nicotine use; exercise >3 h/wk; weight loss or gain >5% of body weight in the past 3 mo; plans to begin a weight loss or exercise regimen; history of medical events or medication use affecting digestion, absorption, or metabolism; gastrointestinal surgery; and chronic or metabolic diseases. Individuals taking medications that could affect blood lipid or glycemic outcomes were also excluded. Finally, individuals with the following biomarkers were excluded: fasting glucose >126 mg/dL, fasting TG >350 mg/dL, and blood pressure >180/120 mmHg. Eligibility based on blood lipids and glucose was determined from fasting blood samples at the screening visit.

TABLE 1 Nutrient breakdown for the high saturated fat meal challenge

Composition	SFA-rich meal
Percentage of total energy from	
Protein	5.0
Carbohydrate	25.0
Fat	69.5
Percentage of energy from fatty acids	
SFA	46.9
MUFA	15.7
PUFA	6.9

Protocol

Screening visit.

Individuals arrived at the laboratory following an 8- to 12-h overnight fast and 24 h without exercise or alcohol. A fasting blood draw for a lipid panel and glucose measurement was obtained, and anthropometrics and resting metabolic rate (RMR) were measured as previously described (31–33). Participants' RMR was multiplied by an average activity factor of 1.65 to estimate daily energy needs (34). Alcohol consumption habits were assessed by the Alcohol Use Disorders Identification Test (35). If individuals qualified for the study, participants were randomly allocated to 1 of 3 groups by a researcher who was not involved in data collection or analysis. An allocation ratio of 1:1:1, a permuted block design (balanced for age, sex, and BMI), and a random-number generator were used to randomly allocate participants.

Pre-diet intervention visit.

Participants completed a 2-d food diary containing 1 weekend day and 1 weekday (36) between the screening visit and the pre-diet intervention visit (V1). One of the food diaries took place the day before V1. In addition, the night before V1, participants consumed a lead-in dinner meal and snack (provided by research personnel) that contained 50% of total energy from carbohydrate, 15% of energy from protein, and 35% of energy from fat.

For V1, participants arrived following an 8- to 12-h overnight fast and 24 h without exercise or alcohol. Anthropometrics and RMR were measured. Baseline stress levels were obtained through the Perceived Stress Scale (PSS) (37), and physical activity was assessed by calculating total metabolic equivalent task (MET) min/wk with the International Physical Activity Questionnaire (IPAQ) (38).

Following the questionnaires, an intravenous (IV) catheter was inserted for the fasting blood draw, and the line was kept patent with saline. Participants then consumed an SFA-rich breakfast shake within 10 min. This high-fat meal provided 17% of total daily energy needs based on the RMR measurements from the screening visit and was made from an original milk chocolate ready-to-drink shake (Ensure; Abbott Nutrition, Abbott Laboratories), unsalted butter, red palm oil, coconut oil, soy lecithin granules, and powdered chocolate drink mix. The nutrient breakdown of this test meal is provided in **Table 1**. Then, 118 mL of water was used to rinse out the container and then ingested to ensure the entire liquid meal was consumed. A sensory questionnaire using a 9-point hedonic scale was administered after meal consumption to assess the sensory modalities (appearance, taste, texture, aroma, and overall acceptance) of the breakfast shake (39, 40). Following the SFA meal, blood draws occurred at 30, 60, 90, 120, 150, 180, 210, and

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Supplemental Tables 1–3 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.
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Abbreviations used: apoB, apolipoprotein B; CAD, coronary artery disease; CVD, cardiovascular disease; iAUC, incremental area under the curve; IPAQ, International Physical Activity Questionnaire; IV, intravenous; MET, metabolic equivalent task; NEFA, nonesterified fatty acid; PSS, Perceived Stress Scale; RMR, resting metabolic rate; TC, total cholesterol; TG, triglyceride; V1, pre-diet intervention visit; V2, mid-diet intervention visit; V3, post-diet intervention visit.

240 min, and 118 mL of water was provided once/h postprandially. After 4 h, the IV catheter was removed.

Eight-week dietary intervention.

The day after V1, all participants began the 8-wk intervention. Written diet instructions were provided to all participants. Participants in the control group were instructed to avoid all forms of nuts and to consume ≤64 g of nut butter/wk. Participants in ADD were provided with 68-g (~0.5-cup or 2.25-oz) portions of pecans to consume as part of their free-living diet with no additional diet instructions. Participants in SUB were instructed to substitute the 475 kcal provided by the 68 g of pecans for foods habitually consumed in their free-living diet (28). Trained research personnel guided the participants on how to make appropriate energy substitutions based on their previously completed food diaries. For example, if the participant habitually consumed snacks throughout the day, the research personnel highlighted the energy content of the snacks and asked the participant if it was feasible to replace the habitual snacks with the provided pecans. The guidance provided was individualized based on each participant's dietary intake. **Supplemental Table 2** shows the complete nutrition information for the 68-g portion of pecans. A 4-wk supply of pecans (in 68-g portions) was provided to participants in ADD and SUB at V1 and the mid-diet intervention visit (V2). Like the control group, the pecan groups were instructed to avoid all other nuts and limit nut butter to ≤64 g/wk (2 servings). In addition, they were instructed to eat pecans in their raw form (no roasting, cooking, or baking). Participants were permitted to add the pecans to other foods. Likewise, all participants were instructed to avoid consuming >42 g alcohol/d (men) or >28 g alcohol/d (women) and were asked not to make any other changes to their diet or activity levels. Participants were unaware of the diet instructions that were provided to other groups to prevent unintentional or intentional changes in behavior.

Weekly responsibilities.

Participants in ADD and SUB logged their intake of pecans on a daily nut compliance document, which was submitted to research staff weekly. Poor compliance was categorized as consumption of <75% of pecans throughout the 8-wk intervention. All participants completed a food diary once per week alternating between weekdays and weekend days. Daily nutrient intakes based on food diaries were assessed using the Food Processor SQL software (ESHA Research; version 10.12.0). The nutrients from the 2 baseline food diaries and then the food diaries from weeks 1–8 were averaged before analysis. The IPAQ was completed electronically during weeks 2 and 6.

Mid-diet intervention visit.

After 4 wk of the intervention, participants arrived at the laboratory following another 8- to 12-h overnight fast and 24 h without exercise or alcohol. The same dinner meal and snack that were consumed before V1 were consumed the night before V2. The same anthropometrics, PSS, IPAQ, and fasting blood draw from V1 were repeated exactly as stated above.

Post-diet intervention visit.

After 8 wk of the intervention, participants arrived for the post-diet intervention visit (V3) under the same previsit conditions as V1 and V2. Participants completed the same study procedures and measurements from V1, including anthropometrics questionnaires, and SFA meal.

Sample analysis

During all 3 testing visits, a portion of the fasting blood sample was drawn into a serum separator clot activator vacutainer and held at room temperature for 30 min before centrifugation for 15 min at 3000 × *g* at 4°C. The serum from the serum separator clot activator vacutainer was transferred into a transport tube and kept at 4°C until detailed blood lipid panel analyses were completed (Quest Diagnositics). This lipid panel was a primary outcome and included TC, TG, LDL cholesterol, HDL cholesterol, LDL particle number, LDL size, HDL size, total apolipoprotein B (apoB), and lipoprotein(a).

The rest of the fasting blood sample and all postprandial blood samples were drawn into an EDTA vacutainer, immediately placed on ice, and then centrifuged under the same conditions. The plasma was aliquoted and stored at −80°C until analysis. Sample analysis of primary outcomes included TGs and nonesterified fatty acids (NEFAs), whereas glucose and insulin were secondary outcomes. Fasting sample analysis of γ-tocopherol served as a marker of biological compliance (41). Plasma TGs and NEFAs were measured by enzyme-based calorimetric assays (Wako Chemicals USA). Plasma glucose and insulin were measured using a colorimetric glucose oxidase/peroxidase method (glucose oxidase: G2133, peroxidase: P8250; Sigma Aldrich) and radioimmunoassay (MilliporeSigma), respectively. Plasma γ-tocopherol was measured by HPLC (Eurofin Craft Technologies).

Statistical analyses

SAS version 9.2 statistical package (SAS Institute) was used for statistical analyses. All values were reported as mean ± SEM unless otherwise noted. Statistical significance was set at $P \leq 0.05$. A sample size of 48 (16/group) was estimated to detect a significant change in LDL cholesterol using G*power 3.19.7 assuming at least 80% power and an α of 0.05 based on the previous pecan study conducted by Morgan and Clayshulte (26). An unpaired *t* test was used to assess differences in nut compliance between the 2 pecan groups. For time course data, change from baseline was calculated (baseline value subtracted from each postprandial time point), and then a 3-factor (treatment, visit, time) repeated-measures ANOVA was used to test for within-group differences. In addition, the change in incremental area under the curve (iAUC) from pre- to post-intervention within each group was calculated for these outcomes for between-group comparisons. A 1-factor ANOVA was used to test for differences at baseline and across the intervention between groups, and a 2-factor repeated-measures ANOVA was used to test for differences within groups from pre- to post-intervention for anthropometrics, perceived stress, total MET minutes, dietary intake, and fasting biochemical outcomes. When significance was found, post hoc analyses were done using least squares means with no multiple testing adjustment. Continuous variables were examined for normality using the Shapiro–Wilk test, and an appropriate transformation was applied to nonnormal data before analysis.

Results

Participants

Fifty-six participants were randomly assigned to an intervention ($n = 20$ control, $n = 17$ ADD, and $n = 19$ SUB); however, 4 participants did not start or complete the intervention and were not included in final analyses (**Figure 1**). Therefore, 52 participants completed the intervention ($n = 12$ women and $n = 6$ men for control, $n = 11$ women and $n = 5$ men for ADD, and $n = 13$ women and $n = 5$ men for SUB) and were included in the per protocol analyses of primary and secondary outcomes. Five of those 52 participants did not complete the meal challenge, so only their fasting data were included (control = 2, ADD = 1, SUB = 2). Participant characteristics at baseline are presented in **Table 2**. There were no differences between groups at baseline for anthropometric or blood lipids. In addition, there were no differences between or within groups from pre- to post-intervention for body weight, BMI, waist circumference, hip circumference, systolic blood pressure, or diastolic blood pressure (**Supplemental Table 3**). Finally, the change in γ-tocopherol from baseline to 8 wk within ADD and SUB was significantly greater compared with control (0.41 ± 0.14 and 0.24 ± 0.08 compared with –0.06 ± 0.14 μg/mL, respectively; $P \leq 0.01$), indicating compliance in the 2 pecan groups.

On average, participants in ADD and SUB consumed 95 ± 1% and 94 ± 2% of pecans provided, respectively, and

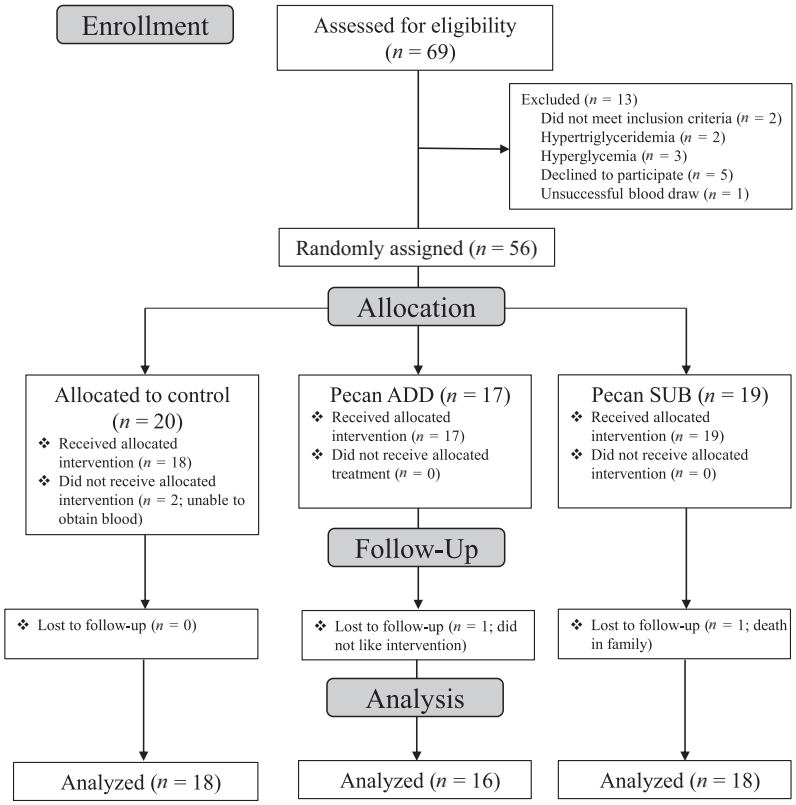

FIGURE 1 CONSORT flow diagram selection of participants. ADD, consumed pecans as part of a free-living diet; SUB, substituted pecans for isocaloric foods from their habitual diet.

compliance was not different between groups. No participant reported poor compliance, and there was no report of intake of nuts in the control group according to food diaries. Based on analysis of the weekly food diaries, as expected due to the daily pecan consumption, grams of total fat ($P < 0.0001$ and $P = 0.0003$), MUFA ($P < 0.0001$ for both), PUFA ($P < 0.0001$ and $P = 0.005$), and dietary fiber ($P < 0.0001$ and $P = 0.005$) increased significantly in ADD and SUB, respectively (Table 3). In addition, within ADD, there was an increase in protein intake ($P = 0.02$) and a trend for an increase in energy intake ($P = 0.07$). Regarding micronutrients, copper and magnesium increased significantly within ADD (0.38 ± 0.05 to

TABLE 2 Characteristics at baseline of adults at risk for cardiovascular disease in pecan or nut-free groups[1]

Characteristic	Control (n = 18)	ADD (n = 16)	SUB (n = 18)
Female, %	66	69	72
Age, y	50 ± 16	49 ± 11	46 ± 10
Height, cm	166.8 ± 11.7	167.6 ± 7.9	166.4 ± 10.1
Weight, kg	87.9 ± 28.5	84.9 ± 13.7	90.3 ± 20.6
BMI, kg/m^2	31.0 ± 7.1	30.2 ± 4.1	32.5 ± 6.9
Waist circumference, cm	112.6 ± 15.2	111.9 ± 9.1	115.0 ± 13.1
Hip circumference, cm	97.7 ± 18.0	96.4 ± 8.9	99.5 ± 15.9
Systolic blood pressure, mmHg	124 ± 14	128 ± 16	153 ± 17
Diastolic blood pressure, mmHg	81 ± 10	85 ± 15	83 ± 11
Body fat, %	32.1 ± 6.7	30.7 ± 6.6	33.1 ± 7.1
Total cholesterol, mg/dL	202 ± 44.6	204 ± 33.9	205 ± 33.2
LDL cholesterol, mg/dL	141 ± 43.5	143 ± 31.3	144 ± 27.2
HDL cholesterol, mg/dL	50.6 ± 15.6	52.9 ± 8.00	51.2 ± 11.0
Triglycerides, mg/dL	131 ± 39.1	139 ± 46.8	133 ± 44.0
Nonesterified fatty acids, mEq/L	0.458 ± 0.214	0.449 ± 0.182	0.436 ± 0.165
Glucose, mg/dL	101 ± 19.9	97.2 ± 12.3	95.4 ± 14.3
Insulin, μU/mL	16.1 ± 6.67	14.2 ± 7.39	20.1 ± 8.13
Total MET, min/wk	1,183 ± 257	1,312 ± 254	1,301 ± 408
Perceived Stress Scale	14 ± 1	13 ± 1	16 ± 1

[1]Values are mean ± SD unless otherwise indicated. There were no significant differences between groups at baseline for any outcome. All outcomes were measured in serum, except for nonesterified fatty acids, glucose, and insulin, which were measured in plasma. ADD, consumed pecans as part of a free-living diet; MET, metabolic equivalent task; SUB, substituted pecans for isocaloric foods from their habitual diet.

TABLE 3 Daily nutrient intake of adults at risk for cardiovascular disease at baseline and throughout an 8-wk pecan or nut-free diet[1]

	Control		ADD		SUB	
Characteristic	Baseline	Intervention	Baseline	Intervention	Baseline	Intervention
Energy, kcal	1917 ± 156	1977 ± 174	1850 ± 136	2329 ± 170[2]	2066 ± 136	2201 ± 101
kcal from carbohydrate, %	48.3 ± 1.25	46.9 ± 1.45	47.6 ± 2.70	36.7 ± 1.46[3]	48.1 ± 1.74	40.5 ± 1.45[3]
kcal from protein, %	15.0 ± 0.66	15.6 ± 0.74	15.4 ± 0.65	13.8 ± 0.58[4]	14.4 ± 0.69	12.7 ± 0.35[4]
kcal from fat, %	35.9 ± 1.47	36.6 ± 1.02	36.3 ± 2.44	48.3 ± 0.96[3]	36.1 ± 1.44	45.5 ± 1.53[3]
kcal from alcohol, %	0.90 ± 0.52	0.87 ± 0.39	0.75 ± 0.42	1.11 ± 0.64	1.45 ± 0.79	1.33 ± 0.55
Carbohydrate, g	228 ± 16.6	236 ± 105	216 ± 18.4	214 ± 17.3	250 ± 20.7	226 ± 15.5
Fiber, g	16.5 ± 2.15	15.4 ± 1.21	12.4 ± 1.39	20.5 ± 1.52[3]	12.8 ± 2.30	18.1 ± 1.50[5]
Protein, g	69.4 ± 5.07	74.0 ± 4.69	70.2 ± 5.06	81.0 ± 7.40[4]	73.8 ± 6.50	69.8 ± 3.74
Fat, g	78.8 ± 8.53	80.3 ± 7.06	76.6 ± 8.45	126 ± 9.98[3]	83.3 ± 6.36	110 ± 4.84[3]
MUFA, g	27.8 ± 3.21	33.1 ± 3.04[2]	31.8 ± 3.66	63.2 ± 4.48[3]	34.1 ± 2.48	53.0 ± 2.12[3]
PUFA, g	19.6 ± 2.90	19.7 ± 2.64	16.8 ± 2.68	32.2 ± 2.20[3]	21.0 ± 2.86	29.3 ± 1.50[5]
SFA, g	30.7 ± 3.53	26.5 ± 2.25	27.3 ± 3.65	29.4 ± 3.75	27.4 ± 2.51	27.0 ± 1.89
Trans-FA, g	0.71 ± 0.19	0.92 ± 0.17	0.79 ± 0.16	0.83 ± 0.18	0.75 ± 0.19	0.70 ± 0.12
Cholesterol,mg	233 ± 34.8	253 ± 26.3	302 ± 53.7	307 ± 53.0	275 ± 33.3	206 ± 24.0

[1] All values are mean ± SEM ($N = 52$). ADD, consumed pecans as part of a free-living diet; FA, fatty acid; SUB, substituted pecans for isocaloric foods from their habitual diet.
[2] Indicates a trend for a change within a group ($P < 0.10$). There were no significant differences between groups at baseline.
[3] Indicates a significant difference from baseline within a group ($P \leq 0.001$).
[4] Indicates a significant difference from baseline within a group ($P \leq 0.05$)
[5] Indicates a significant difference from baseline within a group ($P \leq 0.01$).

1.30 ± 0.11 mg and 114 ± 11.3 to 205 ± 15.7 mg, respectively; $P < 0.0001$ for both) and SUB (0.54 ± 0.12 mg to 1.21 ± 0.07 and 117 ± 13.3 to 185 ± 13.2 mg, respectively; $P < 0.0001$ and 0.001), but there were no other changes for fat- or water-soluble vitamins or minerals. There was a trend for an increase in MUFA in control ($P = 0.07$), but no significant changes within this group. In addition, there were no changes in physical activity (total MET minutes) from baseline throughout the intervention in any of the 3 groups. There was also no change in sensory ratings from pre- to postintervention visits for the SFA shake within each group (overall acceptability: control: 6 ± 0 to 6 ± 0.0; ADD: 7 ± 0 to 6 ± 1; SUB: 6 ± 0 to 6 ± 0, respectively; $P = 0.23$). Finally, ratings of stress did not differ from pre- to postintervention within each group (control: 14 ± 1 to 14 ± 2; ADD: 13 ± 1 to 12 ± 1; SUB: 16 ± 1 to 14 ± 1, respectively; $P = 0.67$).

Change in fasting biochemical markers between groups

The change from pre- to postintervention for fasting TC, LDL cholesterol, HDL cholesterol, apoB, TG, NEFA, non–HDL cholesterol, and TC/HDL cholesterol ratio is displayed in **Figure 2**. From baseline to 8 wk, the decreases in TC ($P = 0.02$ for both), LDL cholesterol ($P = 0.0004$ and $P = 0.004$), apoB ($P = 0.003$ and $P = 0.001$), TG ($P = 0.02$ and $P = 0.01$), non–HDL cholesterol ($P = 0.003$ for both), and TC/HDL cholesterol ratio ($P < 0.001$ for both) were greater in ADD and SUB compared with control, respectively. There were no differences between pecan groups. Furthermore, the reduction in fasting NEFA from pre- to post-intervention was greater in ADD compared with control ($P = 0.01$), whereas SUB was not different from either group.

Many of the aforementioned differences between groups across the 8 wk were already different at the midway point of the intervention. Specifically, from baseline to 4 wk, the decreases in LDL cholesterol ($P = 0.004$ and 0.05) and TC/HDL cholesterol ratio ($P = 0.003$ and 0.01) were greater in ADD and SUB compared with control, respectively. Furthermore, the change in HDL cholesterol was higher in SUB compared with control ($P = 0.01$), and there was a trend in ADD compared with control ($P = 0.09$). Similarly, the change in TG was lower in ADD compared with control ($P = 0.007$), and there was a trend for a greater decrease in SUB compared with control ($P = 0.09$). There were no differences between any group for the change in LDL particle number, LDL size, LDL medium, HDL large, LDL peak size, lipoprotein(a), glucose, and insulin from baseline to 4 or 8 wk.

Fasting biochemical markers

Fasting blood lipids at baseline, 4 wk, and 8 wk are displayed in **Table 4**. For TC, there was a reduction from baseline to 4 and 8 wk for ADD ($P = 0.05$ and $P = 0.03$, respectively) and a reduction at 8 wk for SUB ($P = 0.02$). Similarly, there was a reduction in LDL cholesterol from baseline to 4 and 8 wk within ADD ($P = 0.0002$ and $P = 0.002$, respectively) and a reduction at 8 wk within SUB ($P = 0.02$). There were no differences in TC or LDL cholesterol within control.

For HDL cholesterol, there was an increase from baseline to 4 wk for ADD ($P = 0.03$) and SUB ($P = 0.001$) but not at 8 wk. Furthermore, the TC/HDL cholesterol ratio was reduced at 4 and 8 wk in ADD ($P = 0.001$ and $P = 0.008$, respectively) and SUB ($P = 0.02$ for both), and there was a trend for an increase in TC/HDL cholesterol ratio at 8 wk in control ($P = 0.08$). There was also a reduction at 4 and 8 wk for non–HDL cholesterol in ADD ($P = 0.01$ for both) and at 8 wk in SUB ($P = 0.009$). There were no differences in non–HDL cholesterol within control. Finally, for total apoB, there was a reduction at 8 wk in ADD ($P = 0.04$) and SUB ($P = 0.02$) and an increase at 8 wk in control ($P = 0.05$). LDL particle number, LDL small, LDL medium, LDL peak size, and lipoprotein(a) did not change within any treatment group across the intervention.

For TG, there was a reduction from baseline to 8 wk in ADD ($P = 0.009$) and SUB ($P = 0.05$) and an increase in control ($P = 0.04$). In addition, there was a decrease in fasting NEFA in ADD from baseline to 8 wk ($P = 0.003$) and a decrease in SUB at 4 wk ($P = 0.01$) but not at 8 wk. Finally, analysis of glycemic measures revealed no change within any group across the intervention for insulin or glucose (Table 4).

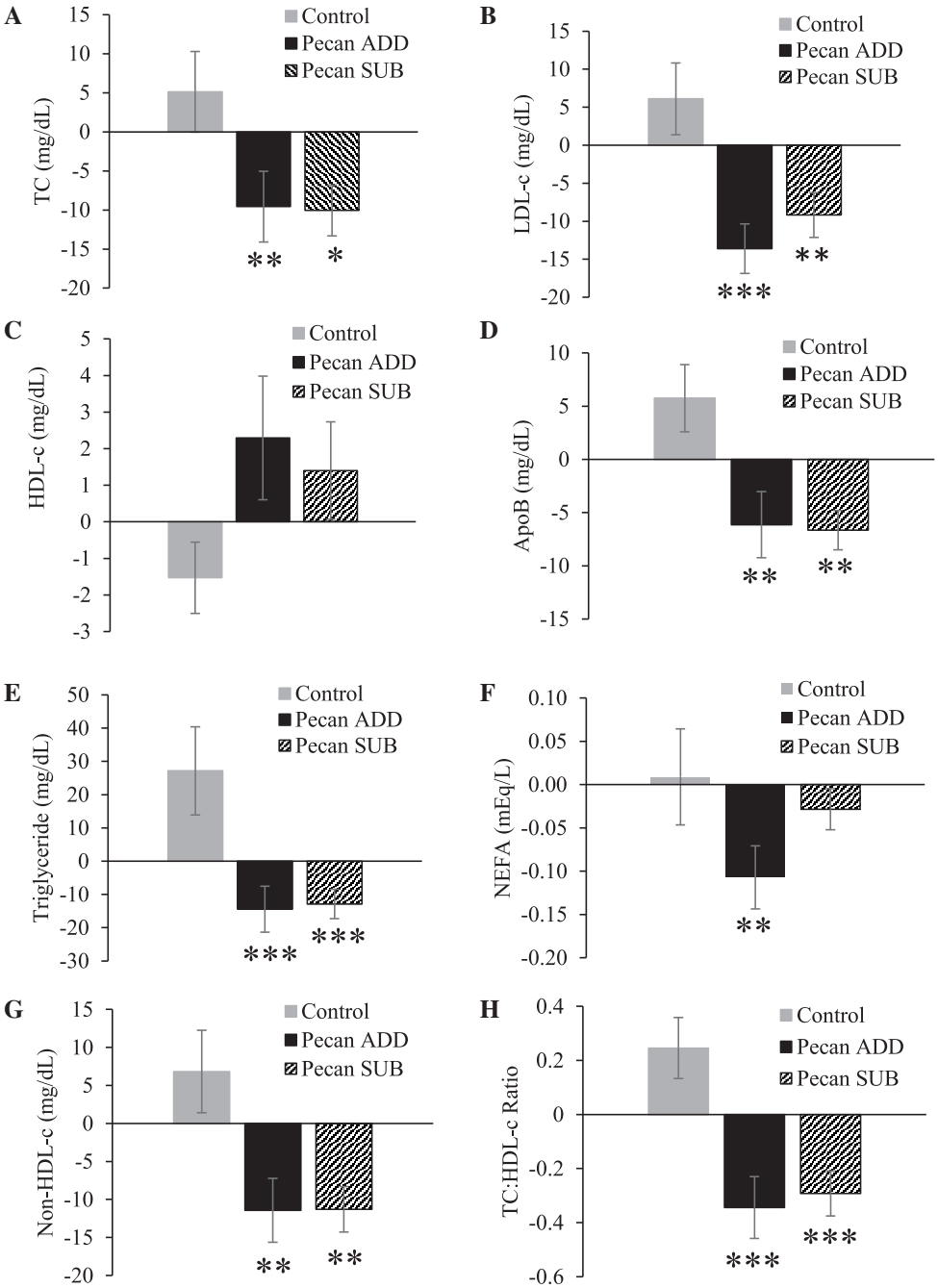

FIGURE 2 Change in serum fasting (A) total cholesterol (TC), (B) LDL cholesterol, (C) HDL cholesterol, (D) apolipoprotein B (apoB), (E) triglycerides (TGs), (F) nonesterified fatty acids (NEFAs), (G) non–HDL cholesterol, and (H) TC/HDL cholesterol ratio from pre to post pecan-enriched diets or nut-free diets in adults at risk for cardiovascular disease (control: $n = 18$; ADD: $n = 16$; SUB: $n = 18$). Asterisks denote level of statistically significant difference compared with the control group ($^{*}P \leq 0.05$, $^{**}P \leq 0.01$, and $^{***}P \leq 0.001$). All values are presented as mean ± SEM. ADD, consumed pecans as part of a free-living diet; SUB, substituted pecans for isocaloric foods from their habitual diet.

Postprandial biochemical markers

The meal responses for TG, NEFA, insulin, and glucose are presented in **Figure 3**. Postprandial TGs were suppressed at postintervention compared with baseline in ADD ($P \leq 0.05$) (Figure 3B) but not in SUB or control. Furthermore, postprandial glucose was suppressed at postintervention compared with baseline in SUB ($P \leq 0.01$) (**Figure 4F**) but not in ADD or control. In addition, the meal response for NEFA (Figure 3D–F) and insulin (Figure 4A–C) did not differ from pre- to postintervention for any of the 3 groups (Figure 3B–D). Finally, the change in meal response from V1 to V3 was not significantly different between groups for TG (change in iAUC: control: –13.0 ± 44.2; ADD: –36.8 ± 29.5; SUB: 1.18 ± 28.9 mg/dL; $P = 0.77$), NEFA (control: –0.05 ± 0.22; ADD: 0.27 ± 0.14; SUB: 0.15 ± 0.11 mEq/L; $P = 0.36$), insulin (control: 0.10 ± 6.89; ADD: 5.77 ± 5.99; SUB: 1.53 ± 3.32 mg/dL; $P = 0.75$), or glucose (control: –7.96 ± 24.4; ADD: 10.9 ± 8.70; SUB: –36.7 ± 22.0 mg/dL; $P = 0.125$).

TABLE 4 Fasting biochemical markers of adults at risk for cardiovascular disease at baseline and throughout an 8-wk pecan-enriched or nut-free diet[1]

	Control			ADD			SUB		
Characteristic	Week 0	Week 4	Week 8	Week 0	Week 4	Week 8	Week 0	Week 4	Week 8
TC, mg/dL	202 ± 43.6	209 ± 44.7	208 ± 47.8	204 ± 33.9	196 ± 35.2[2]	195 ± 31.4[2,3]	205 ± 33.2	206 ± 33.4	195 ± 28.6[2,3]
LDL cholesterol, mg/dL	141 ± 43.5	146 ± 45.0	148 ± 39.3	143 ± 31.3	127 ± 30.6[3,4]	129 ± 29.9[3,5]	144 ± 27.2	139 ± 25.9[3]	135 ± 25.4[2,3]
HDL cholesterol, mg/dL	50.6 ± 11.5	50.8 ± 12.8	49.1 ± 12.3	52.9 ± 8.00	56.5 ± 7.85[2]	55.2 ± 6.88	51.2 ± 11.0	56.5 ± 14.9[3,4]	52.6 ± 9.70
TG, mg/dL	131 ± 39.1	163 ± 75.0	158 ± 83.9[2]	139 ± 46.8	128 ± 60.4[3]	125 ± 56.5[3,5]	133 ± 44.0	138 ± 65.3	138 ± 65.3[2,3]
NEFA, mEq/L	0.46 ± 0.21	0.41 ± 0.19	0.47 ± 0.19	0.45 ± 0.18	0.40 ± 0.17	0.34 ± 0.14[3,5]	0.44 ± 0.17	0.35 ± 0.19[2]	0.40 ± 0.19
TC/HDL cholesterol ratio	4.14 ± 1.25	4.38 ± 1.50	4.41 ± 1.23	3.92 ± 0.80	3.53 ± 0.68[3,5]	3.58 ± 0.68[3,5]	4.08 ± 0.69	3.79 ± 0.67[2,3]	3.79 ± 0.622[2,3]
Non–HDL cholesterol, mg/dL	150 ± 43.1	156 ± 46.3	157 ± 45.5	151 ± 31.9	141 ± 34.8[5]	140 ± 30.8[3,5]	155 ± 27.5	152 ± 23.1	143 ± 24.0[3,5]
LDL-P, nmol/L	1303 ± 391	1314 ± 366	1356 ± 326	1332 ± 294	1249 ± 305	1311 ± 371	1310 ± 248	1313 ± 183	1269 ± 273
LDL small, nmol/L	253 ± 125	255 ± 117	266 ± 107	221 ± 74.5	210 ± 89.4	236 ± 123	199 ± 59.9	180 ± 47.8	183 ± 64.0
LDL medium, nmol/L	295 ± 117	288 ± 122	300 ± 99.3	314 ± 98.6	289 ± 107	312 ± 123	298 ± 70.6	274 ± 68.3	263 ± 51.3
HDL large, nmol/L	4580 ± 787	4890 ± 839	5090 ± 1220	5170 ± 900	5810 ± 1380	5610 ± 911	5210 ± 880	5660 ± 1630	5030 ± 1070
LDL peak size, nm	21.7 ± 0.54	21.7 ± 0.68	21.5 ± 0.48	21.9 ± 0.43	22.0 ± 0.48	21.9 ± 0.44	21.9 ± 0.51	22.0 ± 0.62	22.0 ± 0.55
ApoB, mg/dL	96.9 ± 25.4	98.5 ± 28.5	103 ± 23.2[2]	99.1 ± 22.3	96.1 ± 24.0	93.0 ± 20.0[2,3]	104 ± 13.7	100 ± 11.0	97.1 ± 12.4[2,3]
Lp(a), nmol/L	31.9 ± 27.1	34.3 ± 30.4	31.1 ± 29.2	79.3 ± 82.6	78.8 ± 76.7	80.5 ± 74.8	73.1 ± 103	69.1 ± 106	71.2 ± 108
Insulin, μU/mL	16.1 ± 6.67	17.3 ± 7.86	19.3 ± 12.4	14.2 ± 7.39	14.7 ± 8.18	15.2 ± 7.58	20.1 ± 8.13	23.4 ± 10.5	21.4 ± 9.93
Glucose, mg/dL	101 ± 19.9	101 ± 17.7	100 ± 20.2	97.2 ± 12.3	94.4 ± 7.43	94.8 ± 10.3	95.4 ± 14.3	97.1 ± 14.0	101 ± 16.0

[1] All values are mean ± SD (control: $n = 18$; ADD: $n = 16$; SUB: $n = 18$). ADD, consumed pecans as part of a free-living diet; ApoB, apolipoprotein B; LDL-P, LDL particle number; Lp(a), lipoprotein(a); NEFA, nonesterified free fatty acid; SUB, substituted pecans for isocaloric foods from their habitual diet; TC, total cholesterol; TG, triglyceride.
[2] Indicates a significant difference from baseline within a group ($P \leq 0.05$).
[3] Indicates that the change from baseline to 4 or 8 wk was significantly different from that of the control group ($P \leq 0.05$). All outcomes were measured in serum, except for nonesterified fatty acids, insulin, and glucose, which were measured in plasma.
[4] Indicates a significant difference from baseline within a group ($P \leq 0.001$).
[5] Indicates a significant difference from baseline within a group ($P \leq 0.01$).

Discussion

To our knowledge, for the first time in a population at risk for CVD, we have shown that daily pecan consumption (68 g) for 8 wk, with or without dietary isocaloric substitution instructions, resulted in significant improvements in fasting TC, LDL cholesterol, TGs, HDL cholesterol, TC/HDL cholesterol ratio, non–HDL cholesterol, and apoB. In addition, there were improvements in fasting NEFA and postprandial glucose or TGs in at least 1 of the 2 pecan groups. Based on the energy intake data, the dietary substitution instructions were effective because there no change in energy intake within SUB, whereas there was a trend for an increase in ADD. Contrary, to our hypothesis, there were no changes in fasting LDL particle number, LDL particle size, lipoprotein(a), or fasting or postprandial insulin or glucose. There were no changes in body weight, physical activity, or stress between or within groups, and the changes in self-reported food intake were as expected in the pecan groups. Moreover, the increase in γ-tocopherol was significantly greater in both pecan groups compared with control, confirming compliance with the pecan interventions, and thus the improvements in blood lipids are likely attributable to the daily consumption of pecans.

It is of equal importance to study physiologic/clinical significance along with statistical significance. One way to do this is by examining the magnitude of change due to an intervention. We found that pecan consumption lowered TC by 4.7% and 4.9% and LDL cholesterol by 9.5% and 6.4% in ADD and SUB, respectively. These findings are clinically meaningful because a 1.0% reduction in LDL cholesterol is associated with a 1.2–2.0% reduction in the risk of coronary artery disease (CAD) (42, 43). The similar reduction of blood lipids in ADD and SUB is also a novel finding and indicates that dietary substitution instructions are not required when recommending daily pecan consumption for patients with dyslipidemia. In addition, compared with other types of interventions, our results show a larger degree of success. A meta-analysis of 51 exercise interventions reported that, on average, the reduction in TC and LDL cholesterol was 1.0% and 5.0%, respectively (44), whereas another meta-analysis reported no benefit of weight loss exercise interventions focusing on weight loss on blood lipids (45). It has also been shown that exercise and weight loss are often time-consuming and difficult to adhere to long term (46, 47). Therefore, the addition of pecans to the diet, or substituting foods in the typical diet with pecans, not only produced a greater and more consistent reduction in TC and LDL cholesterol compared with exercise and weight loss interventions (44–47) but may also be a more sustainable approach for long-term health.

Because there are so few previous studies on daily pecan consumption, there are limited data to compare our results to (25, 27, 48). Previously, beneficial results from daily pecan consumption were only observed in healthy populations following 4–8 wk of daily pecan consumption (27, 48). McKay et al. (25) found no change in TC or LDL cholesterol following 4 wk of pecan consumption (~42.5 g/d) in overweight or obese adults. Because our study was also in an overweight and obese population, it is possible that the smaller dosage of pecans in McKay et al. (25) was not enough to elicit improvements in blood lipids. A previous meta-analysis concluded that tree nut doses of ≥60 g/d are necessary to observe a reduction in LDL cholesterol (49). Therefore, cardioprotective dietary recommendations should include pecans in doses of at least 68 g/d.

Although this study was not designed to be mechanistic, previous work and knowledge, as well as the analysis of the food diaries, suggest 2 nutrients in the pecans may elicit the observed reduction in TC and LDL cholesterol following pecan consumption. The first is the fatty acid composition of the

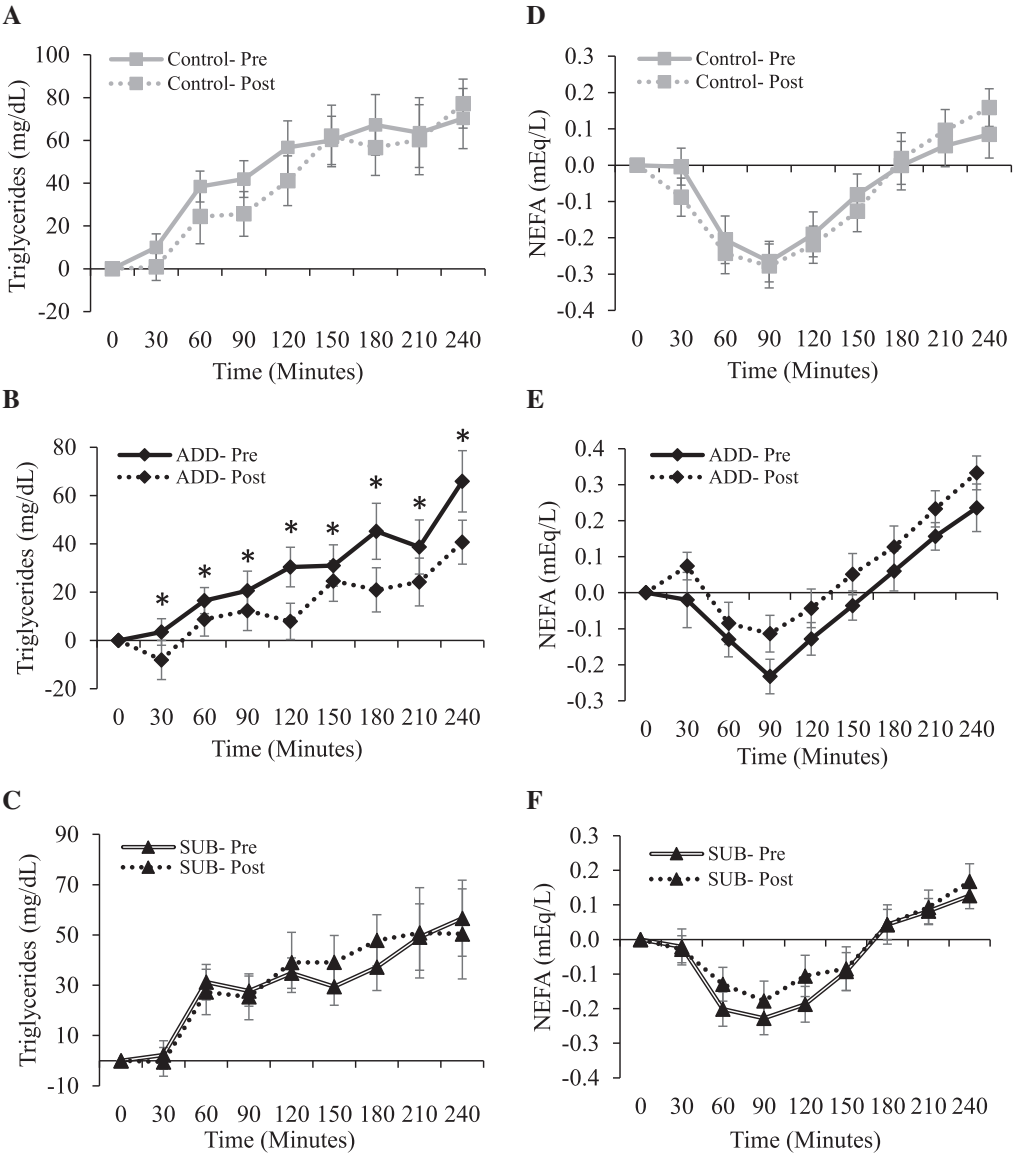

FIGURE 3 Time course for change in plasma triglycerides (TGs) (A–C) and nonesterified fatty acids (NEFAs) (D–F) for each group before and after pecan-enriched diets or nut-free diets in adults at risk for cardiovascular disease (control: $n = 16$; ADD: $n = 15$; SUB: $n = 16$). Participants consumed a high-fat breakfast meal immediately after time 0. *Indicates a significant difference between the pre- and postintervention meal responses within a group ($P \leq 0.05$). All values are presented as mean ± SEM. ADD, consumed pecans as part of a free-living diet; SUB, substituted pecans for isocaloric foods from their habitual diet.

pecans. The dose of pecans in this study contained 24.9 g MUFA and 13.6 g PUFA (28, 50), and this fatty acid profile was reflected in the nutrient analysis from the food diaries in which significant increases in MUFA and PUFA were observed in both nut groups. Previous research has shown that diets rich in unsaturated fats produce favorable effects on cholesterol (7, 51, 52). Those clinical trials are supported by mechanistic research, which indicates that SFAs increase LDL cholesterol by downregulating LDL receptors and increasing LDL formation, whereas unsaturated fatty acids have the opposite effect (7, 53, 54). The second is the high fiber content of pecans because moderate and high fiber intake is associated with decreased CVD risk due to the reduction of LDL cholesterol (55, 56). The dose of pecans provided 6.5 g/d of dietary fiber, which corresponded to significant increases of 8.1 g and 5.3 g/d of fiber in the ADD and SUB groups' overall diet during the intervention, respectively. Although the details of this complex mechanism still need to be elucidated, one can conclude that the higher daily fiber intakes, along with the favorable fatty acid profile, from the pecans likely contributed to the observed LDL cholesterol reduction in the present study.

Another meaningful finding from this study was the significant reduction in apoB within each pecan group. Although never previously reported with pecan consumption alone, the reduction in apoB observed in this study is consistent with previous findings in other tree nuts (49). ApoB is a large protein found on atherogenic lipoproteins such as chylomicron remnants, LDL cholesterol, VLDL, intermediate-density lipoprotein, and lipoprotein(a) (57). One might be surprised that the reduction in apoB was not accompanied by a reduction in LDL particle number. However, because apoB is found on numerous lipoproteins, it is possible that the reduction in apoB occurred due to the reduction of another lipoprotein. Emerging research indicates that apoB is

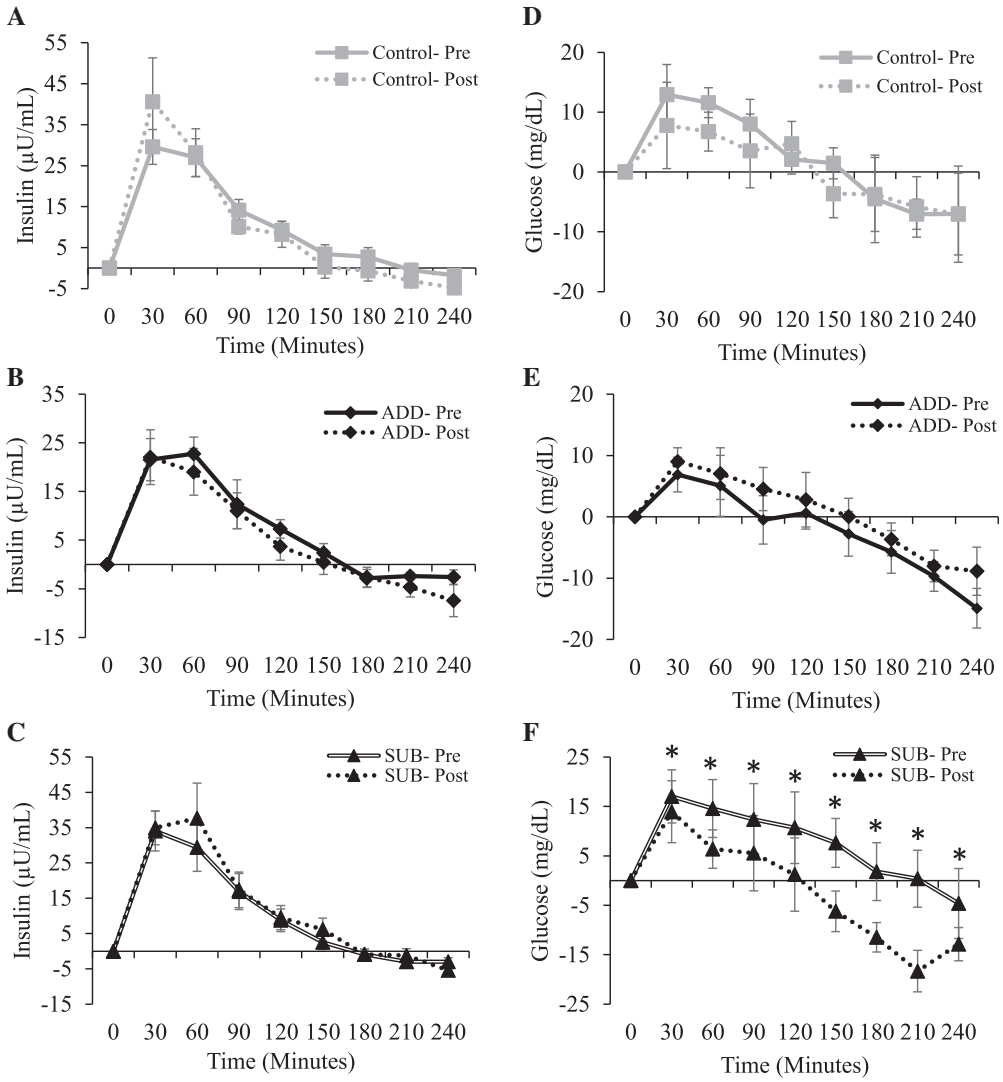

FIGURE 4 Time course for change in plasma insulin (A–C) and glucose (D–F) for each group before and after pecan-enriched diets or nut-free diets in adults at risk for cardiovascular disease (control: $n = 16$; ADD: $n = 15$; SUB: $n = 16$). Participants consumed a high-fat breakfast meal immediately after time 0. *Indicates a significant difference between the pre- and postintervention meal responses within a group ($P \leq 0.01$). All values are presented as mean ± SEM. ADD, consumed pecans as part of a free-living diet; SUB, substituted pecans for isocaloric foods from their habitual diet.

more useful in predicting atherosclerotic CVD risk than LDL cholesterol (58, 59). A meta-analysis concluded that a 10-mg/dL decrease in apoB reduces the risk of coronary heart disease and overall CVD risk by 9% and 6%, respectively (60). The magnitude of reduction in apoB that occurred in the pecan groups corresponds to a 5–6% reduced risk of CHD and 3–4% reduced risk of CVD, further illustrating the cardioprotective benefits of pecan consumption.

We previously reported that acute consumption of a muffin containing pecans resulted in lower postprandial TG responses in males compared with a muffin made with butter (5). However, no study had ever investigated the postprandial TG and glucose responses to a high-fat meal following a long-term tree nut intervention. To our knowledge, for the first time, we showed a reduction in postprandial TG and glucose responses following a high-SFA meal in at least one of the pecan groups. Importantly, this effect occurred with a test meal that was absent of pecans. This outcome is clinically meaningful because elevated postprandial TGs and glucose are an independent risk factor for CVD (61–63). Because Americans consume more SFAs on the weekend compared with weekdays (64), habitual pecan consumption may provide a cardioprotective benefit when the occasional high-SFA meal is consumed. It is unclear why this effect was observed in only 1 pecan group for each outcome (TGs for ADD and glucose for SUB), especially because there were no significant differences in the self-reported intake of any nutrient between the 2 pecan groups.

This study was not without limitations. As previously mentioned, measurements of dietary intake, physical activity, and stress were all self-reported, which may contain some degree of under- or overreporting. In addition, significant increases in TGs and apoB were observed within the control group. Although the change within the control group was unexpected, it is also not uncommon, as evidenced by significant increases in TC within the control group of a previous pecan trial by Morgan and Clayshulte (26). We can only speculate why this effect was observed. The self-reported dietary intake data do not provide a logical answer because no changes in nutrient intake, such as carbohydrate content, occurred during the intervention; however, we know that "no-treatment" control groups are

at risk of expectation bias, in which the expectation of no benefit from the study leads to a less favorable outcome (65). Furthermore, we only controlled the dinner meal the evening before each testing visit rather than including a multiday lead-in diet. This design was intentional to isolate the effects of adding pecans to one's habitual diet. Another limitation is the generalizability of results because we used a relatively high dose of pecans and a shorter duration. We can only speculate on the effectiveness of a smaller dose over a longer duration, but it is helpful to consider that 42.5 g (1.5 oz) within a low saturated fat diet is recommended by the FDA as a qualified health claim (66). Finally, this study was not powered or designed to detect differences between sexes or races.

In conclusion, daily pecan (68 g) consumption reduced fasting blood lipids, including TC, LDL cholesterol, apoB, postprandial TGs, and postprandial glucose in adults with high cholesterol or those at a greater risk for CVD (BMI ≥28). The results of this study are clinically meaningful because the magnitude of reduction in LDL cholesterol in the pecan groups (6.4–9.5%) could correspond to a 6.5–11.4% reduction in the risk for CAD. Furthermore, the reduction in postprandial TGs and glucose provides additional protection in the fed state. This study shows that a simple and cost-effective method to reduce risk factors of CVD in susceptible populations is achievable. Future studies should investigate the impact of pecan consumption for a longer duration at a lower dose in a variety of populations.

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