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# A randomized controlled-feeding trial based on the Dietary Guidelines for Americans on cardiometabolic health indexes

*Sridevi Krishnan,*[1,2] *Sean H Adams,*[3,4] *Lindsay H Allen,*[1,2] *Kevin D Laugero,*[1,2] *John W Newman,*[1,2] *Charles B Stephensen,*[1,2] *Dustin J Burnett,*[1,2] *Megan Witbracht,*[1,2] *Lucas C Welch,*[1,2] *Excel S Que,*[1] *and Nancy L Keim*[1,2]

[1]Western Human Nutrition Research Center, Agricultural Research Service, USDA, Davis, CA; [2]Department of Nutrition, University of California–Davis, Davis, CA; [3]Arkansas Children's Nutrition Center; and [4]Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR

## ABSTRACT

**Background:** The 2010 Dietary Guidelines for Americans (DGA) recommend nutrient needs be met by increasing fruit, vegetable, and whole-grain intake with the use of low-fat or fat-free dairy products and by reducing sodium, solid fats, and added sugars. However, the DGA, as a dietary pattern, have not been tested in an intervention trial.

**Objective:** The aim of this study was to evaluate the impact of a DGA-based diet compared with a representative typical American diet (TAD) on glucose homeostasis and fasting lipids in individuals at risk of cardiometabolic disease.

**Design:** A randomized, double-blind, controlled 8-wk intervention was conducted in overweight and obese women selected according to indexes of insulin resistance or dyslipidemia. Women were randomly assigned to the DGA or TAD group ($n$ = 28 DGA and 24 TAD). The TAD diet was based on average adult intake from the NHANES 2009–2010. The DGA and TAD diets had respective Healthy Eating Index scores of 98 and 62. All foods and beverages were provided during the intervention. Oral-glucose tolerance and fasting lipids were evaluated at 0, 2, and 8 wk of the intervention. Insulin resistance and sensitivity were estimated with the use of surrogates (e.g., homeostasis model assessment of insulin resistance).

**Results:** By design, volunteers maintained their weight during the intervention. Fasting insulin, glucose, triglycerides, oral-glucose tolerance, and indexes of insulin resistance were not affected by either of the diets. Systolic blood pressure decreased in the DGA group (∼−9 mm Hg; $P < 0.05$). Total and HDL cholesterol also decreased in both groups ($P < 0.05$). Exploratory analysis comparing volunteers entering the study with insulin resistance and dyslipidemia with those with only dyslipidemia did not show an effect of pre-existing conditions on glucose tolerance or fasting lipid outcomes.

**Conclusions:** The consumption of a DGA dietary pattern for 8 wk without weight loss reduced systolic blood pressure. There were no differences between the DGA and TAD diets in fasting insulin, glucose, indexes of insulin resistance, or fasting lipids. This trial was registered at www.clinicaltrials.gov as NCT02298725. *Am J Clin Nutr* 2018;108:266–278.

**Keywords:** insulin, glucose tolerance, blood lipids, metabolic syndrome, dietary pattern, Dietary Guidelines for Americans, DGA

## INTRODUCTION

The 2010 Dietary Guidelines for Americans (DGA) recommended a dietary pattern that meets nutrient needs while increasing intakes of fruit, vegetables, and whole grains with the use of lower-fat milk and dairy products and by reducing sodium, solid fats, and added sugars (1). The current 2015 DGA recommendations reaffirmed the general characteristics of the dietary pattern, adding only that seafood, legumes, and nuts are desirable protein sources (2). Dietary patterns, more than individual foods or nutrients, are associated with health benefits, due to the synergistic or additive influence of individual constituents (3). With the use of a data-driven approach, on the basis of epidemiologic studies, several dietary patterns have been described and associated with modifying the risk of chronic cardiovascular and metabolic disease (4). When normal-weight Chinese adults consuming a traditional dietary pattern were compared with those consuming a Western dietary pattern, the latter had a higher incidence of insulin resistance (5). Systematic reviews conducted during the past decade reported an inverse association between healthful dietary patterns and type 2 diabetes risk, but this relation disappeared when controlled for confounding variables (6), including BMI (7). Limitations of epidemiologic research, observational or prospective, should be considered in interpreting the relation between dietary patterns and health outcomes (8).

Few randomized controlled trials have evaluated food-based patterns. To our knowledge, no studies have tested food-based patterns without weight loss on outcomes related to the risk of type 2 diabetes or insulin resistance. The Prevención con Dieta Mediterránea (PREDIMED) trial, although not a strictly controlled feeding intervention, showed reduced fasting glucose, insulin, and HOMA-IR with 2 Mediterranean dietary patterns compared with a low-fat diet; body-weight changes were minimal (9). Apart from PREDIMED, there is little compelling

 

evidence that a dietary pattern intervention can attenuate the insulin-resistant state in the absence of weight loss (10). The Diabetes Prevention Program, one of the most effective, yet intensive lifestyle interventions tested in an at-risk population, improved insulin resistance in participants with type 2 diabetes, and concurrently reduced body weight (11). There are other controlled trials that manipulated the macronutrient composition of the diet and showed reductions in plasma glucose, glycated hemoglobin (HbA1c), HOMA-IR, and insulin secretion capacity in the absence of weight change (12–15), but these were not food pattern–based interventions.

With these studies in mind, there is clearly a knowledge gap in the scientific literature with respect to weight-independent cardiometabolic effects of high-quality, food-based diets, in particular the DGA. We hypothesized that the consumption of a diet patterned after the DGA compared with a typical American diet (TAD) would improve insulin sensitivity and blood lipids in a cohort of overweight and obese women at risk of metabolic disease. Our study was designed to keep each participant's body weight stable to eliminate a possible confounding effect of weight change. To test our hypothesis, we conducted a controlled intervention trial, providing 2 different dietary patterns, one based on the recommendations of the 2010 DGA and the other based on the average reported intake for women aged 20–65 y in the NHANES 2009–2010 to define TAD. To our knowledge, this is the first study that has provided all foods to meet DGA recommendations to test the effects of this dietary pattern on metabolic health.

## METHODS

### Study volunteers

Pre- and postmenopausal overweight to obese women who did not meet the minimal physical activity guidelines of 150 min/wk (16) and had ≥1 cardiometabolic risk factor were included in this trial. Inclusion criteria included age 20–65 y, BMI (kg/m$^2$) of 25–39.9, and resting blood pressure ≤140/90 mm Hg. Several indexes of glucose intolerance and insulin resistance were considered as inclusion criteria on the basis of American Diabetes Association guidelines. Participants qualified if they had ≥1 of the following: fasting glucose ≥100 and <126 mg/dL; oral-glucose-tolerance test (OGTT) 2-h glucose >140 and <199 mg/dL; Quantitative Insulin Sensitivity Check Index (QUICKI) score <0.315, homeostasis model assessment (HOMA) >3.67, or log HOMA >0.085; or HbA1c ≥5.7 and <6.5. The rationale for these cutoffs is detailed in Campbell et al. (17). As an alternative to qualifying on the basis of indexes of glucose intolerance alone, volunteers could also qualify on the basis of ATP III guidelines (Adult Treatment Panel) criteria (18): fasting triglyceride concentrations >150 mg/dL or HDL cholesterol <50 mg/dL. Participants were excluded on the basis of the following criteria: resting blood pressure >140/90 mm Hg, hemoglobin <11.5 g/dL, total cholesterol >300 mg/dL, LDL cholesterol >189 mg/dL, triglycerides >400 mg/dL, or clinically abnormal thyroid or liver function. Other exclusion criteria included the presence of any metabolic diseases, gastrointestinal disorders, cancer or other serious chronic disease; pregnancy or lactation; current use of tobacco; prescribed or over-the-counter weight-loss medications in the 6 mo before enrollment into the study; moderate or strenuous physical activity >30 min/d on ≥5 d/wk; weight change of >5% of body weight within 6 mo of entry into the study; "graveyard" work shifts or forced to stay awake all night; dietary restrictions that would interfere with consuming the intervention foods; or use of medications for elevated lipids or glucose.

### Study approvals

The study is registered at clinicaltrials.gov (identifier: NCT02298725) and was approved by the University of California, Davis (UC Davis), Institutional Review Board. Several primary and secondary outcome measures were evaluated as part of this trial. In the present report, we focus on primary metabolic health outcomes, and our other outcomes are listed in the clinicaltrials.gov study page. Future articles will report on other outcomes that were evaluated, as data become available. Participants provided written informed consent to be screened and, if qualified, provided consent for participating in the intervention study. No adverse events or unintended harms were reported by study participants in this intervention trial.

### Study design and timeline

The study was conducted as a double-blinded, randomized, controlled-feeding clinical trial. The trial consisted of an orientation to study procedures, followed by a 1-wk baseline period during which participants continued to consume their usual diets, and all preintervention data were collected. The baseline period was followed by the 8-wk intervention (**Supplemental Table 1**). During the orientation, participants were introduced to study procedures and study requirements were reviewed. The baseline, preintervention period included activity monitoring, assessment of usual diet, energy requirement estimation, completion of an OGTT, and body-composition measurement. Once the intervention period started, the OGTT test protocol was repeated after 2 wk and again after 8 wk. Assignment to the dietary intervention was random.

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Supplemental Tables 1–11 and Supplemental Figures 1 and 2 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/ajcn/.

Present address for LCW: Department of Anatomy, CWRU SOM WG49, 10900 Euclid Ave., Cleveland, OH 44106–4930.

Present address for MW: Institute for Memory Impairments and Neurological Disorders, University of California, 1100 Gottschalk Medical Plaza, Irvine, CA 92697–4285.

Address correspondence to NLK (e-mail: nancy.keim@ars.usda.gov).

Abbreviations used: DASH, Dietary Approaches to Stop Hypertension; DGA, Dietary Guidelines for Americans; EER, estimated energy requirement; GIT, glucose intolerance/insulin resistance; HbA1c, glycated hemoglobin; HEI, Health Eating Index; HOMA, homeostasis model assessment; iAUC, incremental AUC; MET, metabolic task equivalent; OGTT, oral-glucose-tolerance test; PAEE, physical activity energy expenditure; QUICKI, Qualitative Insulin Sensitivity Check Index; REE, resting energy expenditure; TAD, typical American diet; UC Davis, University of California, Davis.

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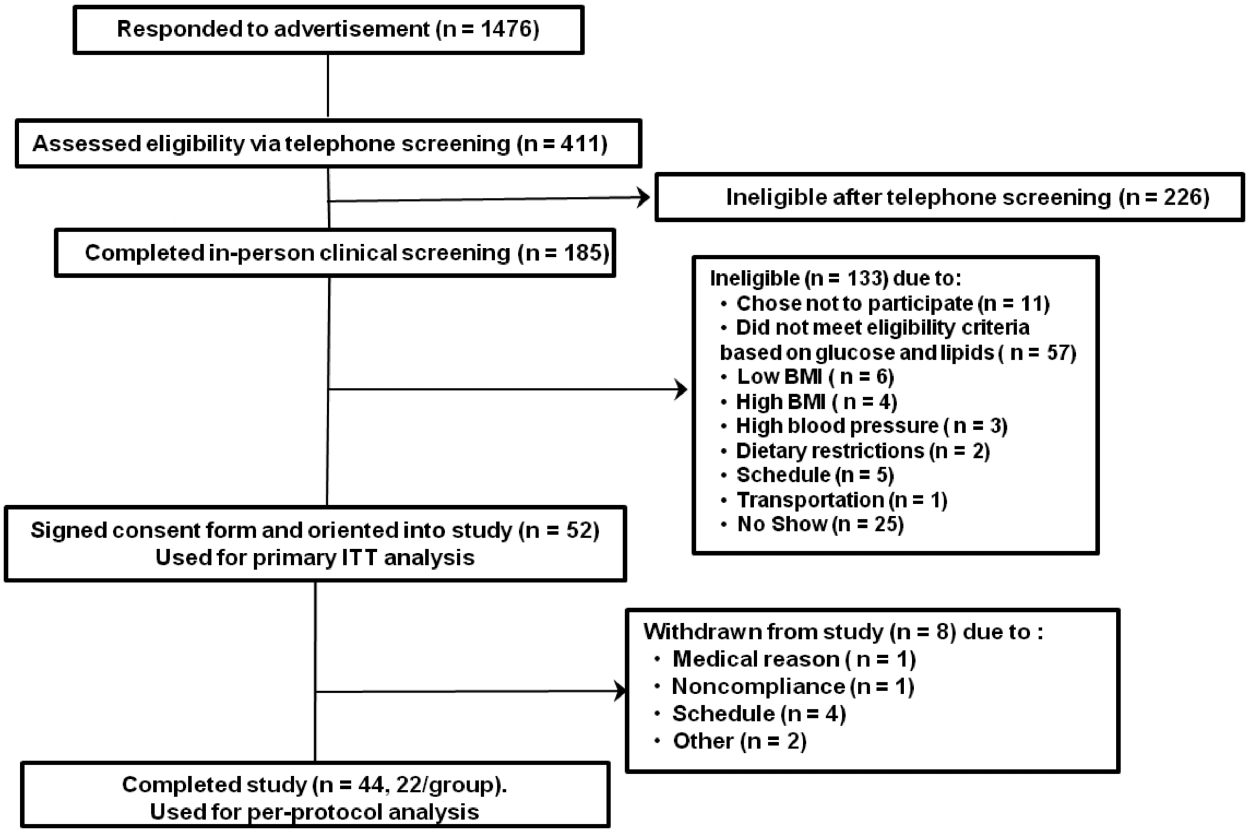


**FIGURE 1** CONSORT diagram representing the volunteers who were screened, consented, and completed the study. CONSORT, Consolidated Standards of Reporting Trials; ITT, intent-to-treat.

### Participant recruitment and screening for eligibility

Participants were recruited between January 2015 and February 2017 via posted flyers, Western Human Nutrition Research Center website posting, Craigslist advertising, newspaper and radio advertising, and referrals from UC Davis and the greater Sacramento area. A sample of women ($n = 52$), aged 20–65 y, were enrolled in the intervention trial after successfully completing the screening process. The first step of the screening process consisted of a telephone interview that assessed interest in the study, medical history, and reported height, weight, and age of the caller. For those women who met the general screening criteria for BMI, age, and reported absence of chronic disease, an in-person appointment was scheduled. At this appointment, height was measured to the nearest 0.1 cm with the use of a wall-mounted stadiometer (model S100; Ayrton Corporation) and weight was measured to the nearest 0.1 kg with the use of a calibrated electronic scale (Tanita BWB-627A Class III electronic scale; Toledo Scale). Volunteers then sat for a 3-min resting period before systolic and diastolic blood pressure measurements, pulse, and temperature were taken with the use of a noninvasive blood pressure monitor (GE DINAMAP vitals monitor; GE Healthcare). Waist and hip circumferences were measured in triplicate by using anthropometric tape. The waist measurement was taken at the minimum circumference between the iliac crest and the rib cage, whereas the hip measurement was taken at the maximum protuberance of the buttocks. An overnight-fasted blood sample was taken for a clinical chemistry panel, lipid panel, complete blood count, and glucose and insulin determinations. Finally, volunteers were given a 75-g oral-glucose-tolerance beverage (Limeondex, lemon-lime flavored; Fisherbrand), and a 2-h postbeverage blood sample was taken for glucose and insulin analysis. The screening clinical chemistry assays were performed by the UC Davis Medical Center clinical pathology laboratory.

The CONSORT (Consolidated Standards of Reporting Trials) diagram (**Figure 1**) shows the total number of people who responded to the advertisement, who were assessed for their eligibility via telephone screen, did not qualify after the telephone screen, moved forward with the in-person clinical screening appointment, did not qualify after the clinical screening, signed the intervention study consent form and were oriented to the study, withdrew from the study, and completed the study. Disqualifications after the in-person screen included loss of participant interest, not meeting laboratory inclusion criteria, BMI based on measured height and weight of $<25$ or $>39.9$, resting systolic and diastolic blood pressure $>140/90$ mm Hg, dietary restrictions, scheduling conflicts, transportation issues, or not showing up to the visit. After signing the consent form, a total of 8 participants withdrew for various reasons, which included unwillingness to comply with the diet, scheduling conflicts, or personal reasons related to family or medical concerns. Recruitment was closed upon enrollment of required volunteers based on our sample size calculation provided in the "Data analysis" section.

### Randomization and blinding

Volunteers were stratified by menopausal status (pre- or post-) and glucose intolerance (normal compared with insulin resistant), and then randomly assigned within each stratum to the DGA or TAD diet (1:1 allocation ratio to each group) in blocks of 2 by using Microsoft Office Excel. The study statistician generated the randomization lists with the use of colors to indicate treatment (without knowledge of which would be which), and the principal dietitian assigned the colors to specific diets and implemented the randomization scheme. The randomization schedules were only communicated between the statistician and the dietitian; the dietitian's assistant, in addition to the former 2 individuals, was aware of and had access to the sequence. Nobody involved with data analysis had access to the assignment of the subjects. When the study coordinators sent out an e-mail announcing enrollment of a new subject, the dietitian added the subject to the next available slot per the stratification scheme. If the participant dropped out after commencing the diet, the space was not reused, and was marked with an "X" to signify that the participant dropped out. If the participant was enrolled but never started the diet, then the space was reused. If a participant enrolled and was randomly assigned but delayed commencement of the diet, then the space that was assigned was reserved for that subject until the date at which the participant commenced the diet. Once randomly assigned, the metabolic kitchen was given the participant ID, their kilocalorie prescription, and the color codes that identified the treatment. All of the recipes, foods, and documentation were coded only with these color codes according to which treatment the foods belonged. The use of "DGA" or "TAD" was never indicated on paperwork or through verbal exchange in the metabolic kitchen. Similarly, participants only saw diets referred to as the color diets. In addition, study coordinators and all staff interacting with the subjects knew only of treatments by colors, and not the true randomized diet group.

### Diet interventions and blinding during implementation

Two diets were designed, both with the goals of providing sufficient energy to maintain body weight and containing macronutrients falling within the acceptable range, as recommended by the Institute of Medicine (19). The primary objective of the menu design was to only include foods and beverages commonly available to consumers in grocery stores. The TAD was based on dietary intake reported by participants in the USDA's "What We Eat in America" survey, the dietary arm of NHANES, and the DGA diet was based on the food-group recommendations set forth by the 2010 DGAs (20). The food groups for the diets are listed in **Table 1**, which shows the primary differences between diets. The DGA diet contained more fruit and vegetables, whole grains, and dairy, whereas the TAD had more refined grains, solid fats, and added sugars. Each day's menu included 3 meals and snacks to meet the calculated caloric needs to maintain weight. Eight-day cyclic menus were designed for the 2 interventions. Sample menus and ingredients for the DGA and TAD are found in **Supplemental Tables 2** and **3**. Additional specific details of the menu and preparation are the subject of a follow-up article. All of the study foods were prepared by the Metabolic Kitchen and Human Feeding Laboratory at the USDA, Agricultural Research Service (Western Human Nutrition Research Center). Volunteers received study foods 2 times/wk.

**TABLE 1**
Servings of food groups in the DGA and TAD diets[1]

| Food group | TAD | DGA |
|---|---|---|
| Fruit (total), cups | 1.0 | 2.3 ⇧ |
| Whole fruit, cups | 0.4 | 1.6 ⇧ |
| Juice, cups | 0.6 | 0.7 ⇧ |
| Vegetables (total), cups | 1.5 | 3.4 ⇧ |
| Dark green, cups | 0.12 | 0.4 ⇧ |
| Red and orange, cups | 0.3 | 1.1 ⇧ |
| Beans and peas (legumes), cups | 0.1 | 0.3 ⇧ |
| Starchy vegetables, cups | 0.54 | 0.8 ⇧ |
| Other vegetables, cups | 0.5 | 0.9 ⇧ |
| Grains (total), ounces | 6.8 | 5.2 ⇩ |
| Whole grains, ounces | 1.1 | 2.8 ⇧ |
| Enriched refined grains, ounces | 5.7 | 2.4 ⇩ |
| Meat, fish, poultry, eggs, nuts and seeds (total), ounces | 6.5 | 5.2 ⇩ |
| Seafood, ounces | 0.6 | 1.1 ⇧ |
| Meat, poultry, eggs, ounces | 5.4 | 3.4 ⇩ |
| Nuts, seeds, soy products, ounces | 0.5 | 0.8 ⇧ |
| Dairy, cups | 1.5 | 3.3 ⇧ |
| Oils, g | 22.4 | 33.1 ⇧ |
| Solid fats and added sugars, kcal | 757 | 333 ⇩ |
| % of energy | 33 | 15 ⇩ |

[1]Food sources included a combination of fresh, frozen, canned, juiced, cured, manufactured, and dried. Most foods were conventional foods; some were organic. Examples of specific foods on the menu are provided in Supplemental Tables 1 and 2. Metric conversions: Ounces: 1 ounce = 28 g, 1 fluid ounce = 30 g, 1 cup = 237 mL/224 g. DGA, Dietary Guidelines for Americans; TAD, typical American diet; ⇧, more servings than TAD group; ⇩, fewer servings than TAD group.

Between the screening appointment and study week 0, three 24-h dietary recalls (unannounced) were completed on 2 weekdays and 1 weekend day with the use of the Automated Self-Administered 24-h dietary recall system (21) to obtain information about the usual dietary habits of each participant. Data from this were used to calculate Healthy Eating Index (HEI) scores, as well as prestudy nutrient intake summaries, which are presented in **Supplemental Table 4**. HEI scores were calculated according to guidelines set by the USDA (22) with the use of linear regression to estimate scores within the cutoffs that have been provided.

The target food patterns for both the TAD and DGA diets were adapted from data in Table 5-1 of the 2010 DGA policy document (1). The nutrient- and food group–controlled study menus were developed by a registered dietitian using the Nutrition Data System for Research 2014 (Nutrition Coordinating Center, University of Minnesota) and ProNutra3.5 (Viocare, Inc.) software programs.

The 8-d rotating-cycle menu was scaled to match each participant's estimated energy requirement (EER), as described below. The various food-group amounts were scaled proportionately from the 2200-kcal level in order to maintain equal distribution of foods in relation to body mass and EER. Each menu was scaled proportionately to create 3 core energy levels: 1700, 2200, and 2700 kcal. Unit foods were designed to further adjust kilocalories to match energy levels between the core menus; these foods were carefully calculated to match both the nutrient and food group pattern of the core kilocalorie levels in order to keep the overall dietary pattern proportionate.

The study diets used foods commonly available in the American retail market, as well as foods in a variety of forms: fresh, canned, frozen, juiced, cured, dried, and manufactured. Specific foods were selected because they were detailed in What We Eat in America's food categories (2001–2010) and the Food and Nutrient Database for Dietary Studies, they contained a specific nutritional profile that aided in the fine-tuning of the diet calculations, they assisted in improving palatability, or because they could remain acceptable to participants after portioning.

To design a double-blinded diet, menus were constructed primarily from a common core of selected foods so that the same general types of foods were used on both diets. During enrollment, the participants were never told about the DGA or TAD dietary patterns, only that we were evaluating 2 nutritionally adequate, weight-maintaining dietary patterns. Furthermore, the participants never interacted with each other while eating meals at the center so as to be able to compare diets. The same foods appeared in both of the diets (see Supplemental Table 2), but often the menu days did not overlap between volunteers at different stages (weeks) of the study. The energy density of the DGA diet (for all foods and caloric beverages, or just food or just caloric beverages) was lower (0.67, 0.75, or 0.43 kcal/g, respectively) than that of the TAD diet (0.86, 0.94, or 0.54 kcal/g, respectively) (see Supplemental Table 4). The major differences between the 2 diets were achieved by increasing or decreasing food groups and nutrients as detailed in the Key Recommendations of the 2010 DGA (1). Another difference between the TAD and DGA diets was the use of some healthier lines of manufactured foods containing fewer solid fats and added sugars, less sodium, more potassium, and more fruit and vegetables. Foods that are generally perceived as unhealthful (e.g., hot dogs) were puréed and stealthily incorporated into mixed dishes (e.g., chili). Furthermore, the assembly of food components was ordered in a way to disguise any perceived visual signs of healthfulness or unhealthfulness. Coffee, tea, and bottled water (still and sparkling) were provided by the metabolic kitchen to reduce variability in commonly consumed "free" beverages.

Study foods were weighed to the nearest 0.1 g and produced in a multistep assembly system with embedded checks-and-balances to verify correct product and weight of each ingredient. When foods specific to one diet were received, they were coded upon delivery to reduce the risk of being used for the incorrect intervention diet. An inspection checkpoint was implemented at the final stage of assembly, where preprinted labels for all food items of each participant's meal were affixed to the meal after being verified. Furthermore, once meals were packed "to go," they were inspected by a study coordinator immediately before handing over to the participant.

Participants were provided a daily meal checklist (**Supplemental Figure 1**) that included each menu item with space for documenting the amount consumed; the time each item was consumed; a checkbox to confirm having only eaten study foods; a checkbox to confirm not taking any medications, supplements, or other remedies; space for documenting any adverse events related to eating the meals; and space for documenting any nonstudy foods, drinks, medications, supplements, or other remedies. They were also instructed to return all unwashed packaging; visual inspection was documented by the metabolic kitchen. In addition to the checklists and returned packaging, participants were educated on food safety as well as provided tips on managing challenging social situations while participating in a feeding study. Repeated reinforcement of the value of honesty over perfection was provided. Study coordinators reviewed the returned checklists with the participants to verify completeness.

### Estimating energy requirement to maintain body weight

The EER was based on preintervention measurements of resting energy expenditure (REE), physical activity energy expenditure (PAEE), and an adjustment for the thermic effect of food. Participant REE was measured by using an automated metabolic cart (TrueOne 2400; Parvo Medics) in the fasted state after quietly resting in a semireclined position for 20 min. Respiratory gas exchange was then measured for 20 min, with the goal of obtaining $\geq$10 min of "steady state" data (minute-by-minute CV $<$5% for volume of oxygen consumed and volume of carbondioxide produced). The Weir equation without urinary nitrogen correction was used to estimate REE (23). Average PAEE was measured over 7 consecutive days (kilocalories per day) with the use of an accelerometer (Actical; Respironics) beginning on the orientation day. Total energy expenditure was calculated by the addition of REE and PAEE and adjusting for the thermic effect of food, so that it represented 10% of REE. The Actical estimates different intensity physical activities on the basis of the metabolic equivalents (METs) using activity counts per unit time (using 60 epochs/count). Three to 6 METs are considered moderate-intensity physical activity, $<$1 counts as sedentary, 1–2.9 counts as light activity, 3–5.9 as moderate intensity, and vigorous as any activity $\geq$6 METs. The volunteers' age, height, weight, and sex were taken into account while setting up the Actical, which then estimates energy expenditure on the basis of these factors as well as the measured activity counts and their corresponding METs. Energy intake was prescribed for each participant on the basis of her specific estimate of total energy expenditure. Body-weight measurements during the study were used to ensure that the caloric prescription was appropriate to maintain weight. If the body-weight trajectory had a significant slope, increasing or decreasing at a rate yielding a change of $>$3% extrapolated over the first 2 study weeks, the caloric content of the diet was adjusted to offset the change in weight and then kept constant for the remainder of the study.

### Activity monitoring

In addition to measuring PAEE preintervention, activity was monitored during study weeks 4 and 7. The accelerometer was positioned atop the iliac crest of the left hip and secured with an elastic belt. During the monitoring weeks, participants wore the device for 7 consecutive days, removing it only for showering, bathing, or other activities in which the device might be submerged. Participants kept a daily log of waking and sleeping times, intervals when the device was removed, and intervals of activity patterns they considered out of the ordinary.

### Body-composition measurement

Once during baseline (week 0) and once during week 8, a whole-body scan was performed with the use of dual-energy X-ray absorptiometry (Hologic Discovery QDR Series 84994; Hologic, Inc.). This scan provided values for total lean mass,

total fat mass, estimates of gynoid and android fat distribution, and percentage body fat, bone density, bone mineral mass. All premenopausal women were given a commercial urine human chorionic gonadotropin immunoassay to confirm nonpregnant status before scanning.

### OGTT

At weeks 0, 2, and 8, a standard OGTT was administered to volunteers after a 12-h overnight fast. A registered nurse placed an indwelling catheter into the volunteer's antecubital vein and took a fasting blood sample. After this, the volunteer was given a 75-g glucose bolus to be consumed within 5 min. Four subsequent blood samples were taken at 30, 60, 90, and 120 min after drinking the glucose bolus. Antecubital vein blood was collected in Vacutainers (Becton Dickinson VACUTAINER Systems, Rutherford, New Jersey), with no additives for insulin determination or potassium oxalate/sodium fluoride for glucose determination. Once blood was obtained, the serum Vacutainers were kept at room temperature for 30 min, whereas the plasma Vacutainers were immediately chilled on ice. All of the Vacutainers were centrifuged in a refrigerated Centra CL3R (International Equipment Co.) for 10 min at 100 × *g* at 10°C, and serum and plasma aliquots were stored at –80°C for analysis. Plasma glucose was determined by using an enzyme-linked colorimetic assay on a Clinical Chemistry Analyzer (Cobas Integra 400+; Roche Diagnostics Corporation). Serum insulin concentrations were determined by using a competitive binding assay on an immunoanalyzer (Cobas E 411; Roche Diagnostics). Fasting values for glucose and insulin were used to calculate HOMA-IR (24), QUICKI (25) and McAuley (26) indexes. The Matsuda index was calculated by using fasting and OGTT values for glucose and insulin (27).

### Blood pressure and lipids

Systolic and diastolic blood pressures were measured at weeks 0, 2, and 8, as outlined previously. Similarly, fasting plasma samples were used to measure lipid panels (total, LDL, and HDL cholesterol) as well as triglycerides at the UC Davis Medical Center clinical pathology laboratory, as mentioned previously.

### Statistical analysis

*Power calculation*

The sample size for this study was based on a power calculation conducted with the use of a cohort of sedentary, obese, insulin-resistant women ($n = 21$), with repeated (twice) baseline fasting insulin concentrations, followed by 1 wk of a weight-maintenance DGA 2005–based diet intervention (17). Fasting insulin concentrations were measured again after the run-in diet phase. In order to account for the "regression to the mean effect" affecting the variation in these measures, a residual-corrected (the residual after the 2 baseline variances were accounted for) change in SD for insulin was calculated to be 7.11 mIU/mL. On the basis of this value, we calculated that 17 subjects/group would enable us to detect a difference of 5.32 mIU/mL between group means with 80% probability, assuming a 5% level of significance and a 2-tailed test. This translated to an effect size of 0.75. Adding in a 25% attrition rate to this number increased the sample size to 22/group, which was our final sample size.

*Data analysis*

Data from volunteers who started the full 8-wk intervention and testing were included (DGA = 28, TAD = 24; total: 52), in a primary intent-to-treat analysis. A secondary per-protocol analysis with only data from volunteers who completed the full 8-wk intervention was also performed ($n = 22$ each DGA and TAD; total: 44), followed by subgroup analyses. All of the analyses were performed in R single packages nlme and lsmeans (R statistical software) (28) and JMP Pro 13.1 (SAS Institute). The normality of data was checked by using the Shapiro-Wilk test, and nonnormal data were transformed to log or cube root for use in further analysis (transformed data were confirmed to be normal before using in parametric tests). Grubbs test was used to detect univariate outliers; transformed data used in parametric tests did not have any statistical outliers; van der Wearden's nonparametric tests were used to identify differences at baseline between volunteers randomly assigned to the DGA and TAD diet groups, as well as to compare adherence to diet between the groups. A linear mixed-effects model with subject as the random effect and group (DGA compared with TAD), week (0, 2, or 8), and blood collection minutes (0, 30, 50, 90, and 120) as fixed effects, and repeated measures with interactions (group × week × minutes) were tested for the outcome glucose and insulin after the OGTT. Some serum samples were hemolyzed (~3% of combined data for all weeks for both groups and at all time points), which is known to affect insulin analysis. In a sensitivity analyses, the hemolyzed sample insulin values were removed and imputed within each subject by using the multivariate imputation R package Amelia II (29). An ANOVA was conducted comparing the following 2 models: *1*) a linear mixed model using insulin values from hemolyzed and *2*) a similar model using imputed data. This was performed to evaluate differences between their fit and found not to be different ($P = 0.45$). Furthermore, an analysis comparing insulin outcomes (OGTT, fasting and postprandial) after removing the hemolyzed samples was also performed and showed no differences from the reported outcome in this study.

The incremental AUCs (iAUCs) for glucose and insulin were calculated by using the trapezoidal rule, while correcting for the fasting value (30). Linear mixed-effects modeling was also used to compare fasting values for glucose, insulin, HbA1c, HOMA, QUICKI, the Matsuda index, the Disposition index, the McAuley index, triglycerides, and LDL, HDL, total cholesterol at weeks 0, 2, and 8, with their week 0 value as a covariate to adjust for baseline differences between the groups. This was followed by pairwise least-square means tests with Tukey's method, where appropriate. $P < 0.05$ was considered significant for all tests.

### Subgroup analyses

Exploratory analyses were performed using linear mixed-effects modeling to determine if certain participant phenotypes affected study outcomes related to glucose tolerance: fasting and postprandial glucose, insulin, HOMA-IR, QUICKI, HbA1c, Matsuda index, or iAUC glucose and insulin. The phenotype subgroup comparisons were as follows: *1*) premenopausal compared with postmenopausal participants, *2*) participants

**TABLE 2**
Characteristics of study volunteers measured at screening, by diet group[1]

| Variables | TAD ($n = 24$) Mean ± SD | TAD ($n = 24$) Range (minimum–maximum) | DGA ($n = 28$) Mean ± SD | DGA ($n = 28$) Range (minimum–maximum) |
|---|---|---|---|---|
| Anthropometric | | | | |
| Age, y | 47.1 ± 9.5 | 26–64 | 46.8 ± 14.9 | 21–63 |
| Height, cm | 164.7 ± 7.9 | 152.1–179.6 | 166.0 ± 7.4 | 147.1–179.0 |
| Weight, kg | 88.8 ± 14.2 | 65.2–119.7 | 89.4 ± 15.0 | 59.9–115.5 |
| BMI, kg/m$^2$ | 32.4 ± 3.9 | 26.0–39.8 | 31.9 ± 3.9 | 25.2–38.3 |
| Waist-to-hip ratio | 0.81 ± 0.08 | 0.6–0.9 | 0.80 ± 0.09 | 0.7–0.9 |
| Waist circumference, cm | 96.9 ± 14.2 | 81.3–149.5 | 95.0 ± 8.9 | 78.7–111.0 |
| Systolic blood pressure, mm Hg | 119.7 ± 12.1 | 94–141.5 | 125.1 ± 13.5 | 99–142.0 |
| Diastolic blood pressure, mm Hg | 71.0 ± 8.9 | 60–89.5 | 71.5 ± 8.9 | 56.0–87.0 |
| Clinical | | | | |
| Fasting glucose, mg/dL | 89.6 ± 6.8 | 77–102 | 93.9 ± 10.8 | 78–115 |
| 2-h Glucose, mg/dL | 126.0 ± 33.7 | 78–188 | 126.8 ± 33.5 | 63–199 |
| Fasting insulin, mIU/mL | 11.5 ± 7.4 | 4.2–33.3 | 13.7 ± 8.3 | 4.7–35.9 |
| 2-h Insulin, mIU/mL | 93.0 ± 82.4 | 15.2–366.4 | 97.9 ± 71.4 | 18.7–320.4 |
| HOMA-IR | 3.7 ± 2.3 | 0.6–10.8 | 4.2 ± 3.2 | 0.5–14.2 |
| QUICKI | 0.33 ± 0.04 | 0.28–0.42 | 0.33 ± 0.04 | 0.27–0.44 |
| Matsuda index | 3.1 ± 2.0 | 0.9–11.3 | 2.9 ± 2.5 | 0.7–11.9 |
| McAuley index | 10.2 ± 1.1 | 8.2–12.7 | 9.9 ± 1.2 | 7.4–12.8 |
| HbA1c, % | 5.6 ± 0.3 | 5.0–6.2 | 5.6 ± 0.3 | 5.0–6.1 |
| Total cholesterol, mg/dL | 206.3 ± 30.6 | 127–285 | 209.6 ± 36.6 | 147–299 |
| LDL cholesterol, mg/dL | 130.3 ± 28.5 | 78–212 | 129.0 ± 27.8 | 69–206 |
| HDL cholesterol, mg/dL | 48.8 ± 11.4 | 27–77 | 50.1 ± 10.4 | 33–75 |
| Triglycerides, mg/dL | 136.3 ± 71.4 | 50–282 | 146.5 ± 94.8 | 57–354 |

[1]DGA, Dietary Guidelines for Americans; HbA1c, glycated hemoglobin; QUICKI, Qualitative Insulin Sensitivity Check Index; TAD, typical American diet.

entering the study with criteria related to insulin resistance and dyslipidemia compared with those with dyslipidemia only, *3*) comparison of participants assigned to the DGA intervention who had improvement in their usual diet quality with participants assigned to the TAD intervention who had no change or a decrease in their diet quality. The difference between HEI total score for the participant's usual diet and intervention diet was calculated as intervention − usual diet, and used to categorize volunteers into groups on the basis of whether their score increased (by ≥5 units), decreased (by ≥5 units), or had no change (within ±5 units).

## RESULTS

### Primary intent-to-treat approach

Study participants were between 21 and 64 y of age, with BMIs ranging from 25.2 to 39.8. Physical and clinical characteristics measured at screening were not different between the groups (**Table 2**). Across the intervention, fasting glucose, insulin, lipids, systolic and diastolic blood pressure, and indexes related to glucose homeostasis and insulin resistance/sensitivity are presented in **Table 3**.

Systolic blood pressure showed a significant group ($P = 0.044$) and week ($P = 0.017$) effect, and a trend for interaction ($P = 0.090$). Tukey's adjusted multiple-comparison tests showed a significant reduction at week 8 compared with week 0 in the DGA ($P = 0.006$) but not in the TAD group ($P = 0.919$). Total fasting cholesterol had a significant group × week interaction ($P = 0.050$); however, multiple-comparison tests identified only a trend for lowered values at week 8 in the DGA compared with week 0 ($P = 0.090$), but not in the TAD group. HDL cholesterol had a week and a group main effect ($P = 0.001$), with no interaction effect. Weeks 0, 2, and 8 were different in both TAD and DGA groups based on multiple-comparison tests (week 0 compared with week 2: $P = 0.004$; week 0 compared with week 8: $P < 0.001$; week 2 compared with week 8: $P = 0.053$).

Results from the OGTTs at weeks 0, 2, and 8 for DGA and TAD groups are presented in **Figure 2**. No significant differences between the diet groups were identified when analyzed as repeated measures (glucose: diet effect $P$ value = 0.405, insulin: diet effect $P$ value = 0.534) and as a summary measure using the iAUC (iAUC glucose diet effect $P$ value = 0.505; iAUC insulin diet effect $P$ value = 0.864). There was no effect of week and no interaction of diet × week on iAUC insulin or glucose.

Anthropometric and physical activity data are presented in **Supplemental Table 5**. Body weight and body fat percentage were maintained during the study in both groups. No participants experienced >5% weight loss, and $n = 14$ (DGA = 7, TAD = 7) experienced weight loss of ~3%. Lean mass also showed a significant main effect of week ($P = 0.043$), with Tukey's pairwise test confirming the difference between weeks 0 and 8 ($P = 0.051$). There was a main effect of week ($P = 0.015$) and group ($P = 0.031$) on android fat mass, with no significant interaction effects ($P = 0.206$). Pairwise Tukey's adjusted $P$ values indicated significantly different android fat mass at week 8 compared with week 1 ($P = 0.009$), but no group differences. No significant differences by group or week were identified in BMI, percentage body fat, hip circumference, or gynoid fat mass. Moderate-intensity physical activity minutes were not different [DGA:

**TABLE 3**
Primary metabolic outcome variables by diet group and study week[1]

| | TAD ($n = 24$) | | | DGA ($n = 28$) | | |
|---|---|---|---|---|---|---|
| | Week 0 | Week 2 | Week 8 | Week 0 | Week 2 | Week 8 |
| Fasting glucose, mg/dL | 99.7 ± 6.8 | 99.1 ± 9.1 | 95.2 ± 7.2 | 98.5 ± 10.9 | 99.7 ± 11.8 | 99.7 ± 10.6 |
| HbA1c, % | 5.5 ± 0.3 | 5.5 ± 0.4 | 5.4 ± 0.3 | 5.4 ± 0.3 | 5.4 ± 0.3 | 5.5 ± 0.3 |
| Fasting insulin, mIU/mL | 14.7 ± 9.5 | 15.0 ± 9.2 | 14.8 ± 10.0 | 17.1 ± 12.1 | 18.3 ± 13.6 | 15.2 ± 11.2 |
| Matsuda index | 3.1 ± 1.9 | 2.8 ± 1.6 | 3.8 ± 4.5 | 2.9 ± 2.4 | 2.6 ± 1.7 | 3.2 ± 1.9 |
| HOMA-IR | 3.7 ± 2.3 | 3.7 ± 2.1 | 3.5 ± 2.2 | 4.2 ± 3.2 | 4.5 ± 3.6 | 3.9 ± 3.1 |
| QUICKI | 0.33 ± 0.04 | 0.32 ± 0.03 | 0.33 ± 0.04 | 0.33 ± 0.04 | 0.32 ± 0.03 | 0.33 ± 0.03 |
| McAuley index | 10.2 ± 1.1 | 9.9 ± 0.9 | 10.0 ± 1.2 | 9.9 ± 1.2 | 9.8 ± 1.6 | 9.9 ± 1.2 |
| Fasting total cholesterol,[2] mg/dL | 195.8 ± 26.1 | 203.7 ± 23.7 | 197.6 ± 24.9 | 200.8 ± 37.5$^{a}$ | 193.1 ± 37.1$^{a,b}$ | 190.7 ± 34.4$^{b}$ |
| Fasting LDL cholesterol, mg/dL | 127.2 ± 22.4 | 133.7 ± 22.9 | 130.2 ± 22.3 | 123.3 ± 28.1 | 122.0 ± 28.3 | 117.4 ± 21.2 |
| Fasting HDL cholesterol,[3] mg/dL | 45.6 ± 9.4$^{x}$ | 44.1 ± 10.3$^{y}$ | 41.5 ± 10.3$^{z}$ | 50.4 ± 11.1$^{a}$ | 48.0 ± 8.0$^{b}$ | 47.0 ± 9.5$^{c}$ |
| Fasting triglycerides, mg/dL | 112.5 ± 58.7 | 129.4 ± 66.7 | 130.4 ± 77.8 | 141.1 ± 101.3 | 130.0 ± 78.8 | 142.6 ± 93.1 |
| Systolic blood pressure,[4] mm Hg | 119.7 ± 10.2 | 119.7 ± 8.4 | 117.3 ± 8.3 | 125.1 ± 14.9$^{a}$ | 121.5 ± 9.8$^{a,b}$ | 118.8 ± 9.1$^{b}$ |
| Diastolic blood pressure, mm Hg | 72.8 ± 6.9 | 70.9 ± 4.4 | 70.3 ± 6.3 | 72.0 ± 8.5 | 71.7 ± 7.4 | 71.0 ± 7.4 |

[1] Values are means ± SDs. Linear mixed-model analyses with week as a repeated effect and volunteer as a random effect were performed. DGA, Dietary Guidelines for Americans; HbA1c, glycated hemoglobin; QUICKI, Qualitative Insulin Sensitivity Check Index; TAD, typical American diet.

[2] Significant interaction effect of group × week ($P = 0.05$); no main group or week effect. Tukey's pairwise tests identified trends for differences between weeks 0 and 8 ($P = 0.09$), indicated by different superscript letters.

[3] Main effect of group and week ($P < 0.05$), and no interaction effect. Differences are indicated by different superscript letters within groups.

[4] Main effect of group and week ($P < 0.05$) and a trend for interaction ($P = 0.09$). Differences are indicated by different superscript letters.

12.9 ± 14.1 compared with TAD: 20.8 ± 21.4 min/d; $p = 0.120$ (group); 0.215 (week) and 0.311 (group × time interaction)], and neither were low [$P = 0.309$ (group), 0.984 (week), and 0.991 (group × week)] or vigorous-intensity [$P = 0.310$ (group), 0.485 (week), and 0.338 (group × week)] physical activity minutes.

### Per-protocol approach

With the use of the per-protocol approach ($n = 22$ each, TAD and DGA), our study volunteers' anthropometric and clinical characteristics were not different at baseline, with the exception of systolic blood pressure, which was higher in the DGA group than in the TAD group ($P = 0.051$) (**Supplemental Table 6**). The study volunteers (96% of the cohort) were considered at risk on the basis of a combination of fasting glucose, insulin, and triglycerides (**Supplemental Figure 2**). The reported usual food intake in these volunteers yielded HEI scores between 65 and 69 (**Supplemental Table 7**), which are very similar to the intervention TAD diet (score: 62), but considerably lower than the intervention DGA diet (score: 98) (Supplemental Table 4).

Fasting glucose, insulin, lipids, systolic and diastolic blood pressure, and indexes related to glucose control and insulin resistance/sensitivity are presented in **Supplemental Table 8.** In total cholesterol, significant week ($P = 0.020$) and group ($P = 0.020$) effects were identified with no interaction effects, and pairwise tests indicated a significant difference between weeks 2 and 8 ($P = 0.020$) and a group difference as well ($P = 0.050$). HDL cholesterol showed significant main week ($P < 0.001$) and group ($P < 0.001$) effects, with Tukey's adjusted pairwise comparisons indicating a week 0 compared with week 8 difference ($P < 0.001$), but no group effect. In a pairwise test, there was a trend for a difference in LDL cholesterol between DGA and TAD groups ($P = 0.090$), but this was not significant. In systolic blood pressure, there was a significant week effect ($P = 0.002$) and a significant group × week interaction ($P = 0.04$). Multiple-comparison tests (adjusted by Tukey's) showed significantly lower systolic blood pressure at weeks 2 and 8 compared with week 0 in the DGA group ($P = 0.050$ and $P = 0.001$, respectively) but no change in the TAD group. Furthermore, although 16 women in the DGA group had reduced systolic blood pressure by ≥ 2 mm Hg, only 9 women in the TAD group had a reduction of ≥2 mm Hg. No significant main (week or group) or interaction effects were identified in fasting and 2-h glucose and insulin, HOMA-IR, QUICKI, or the McAuley, Disposition, or Matsuda indexes. The OGTT time-course data showed no significant effects for glucose or insulin (data not shown; similar to intent-to-treat data).

Dietary adherence in completers ($n = 22$ each, DGA and TAD) was measured by using diet logs that were scored in combination with weight maintenance and surveillance of returned packaging. Taking both groups together, the study volunteers logged an average of 34 ± 33 deviances from eating 100% of prescribed foods, and 5 ± 8 deviances in eating nonstudy foods; this represents adhering an average of ~88% and ~95%, respectively. Both the DGA and TAD diets had equivalent overall adherence scores, with 30 ± 35 (10.4% ± 0.1% deviation) instances of reported deviance from full dietary compliance in the DGA group and 39 ± 31 (13.9% ± 0.1%) instances of reported deviance in the TAD group. Similarly, there were 3.5 ± 4.3 (1.2% ± 0.1%) reported instances of eating nonstudy foods in the DGA group and 5.7 ± 10.6 (2.0% ± 0.1%) instances in the TAD group. No significant differences were identified between the groups in any of the nonadherence categories.

### Exploratory subgroup analyses

The distribution of postmenopausal (DGA: $n = 13$; TAD: $n = 8$) and premenopausal (DGA: $n = 9$; TAD: $n = 14$) women in this study was not different between the diet groups (chi-square

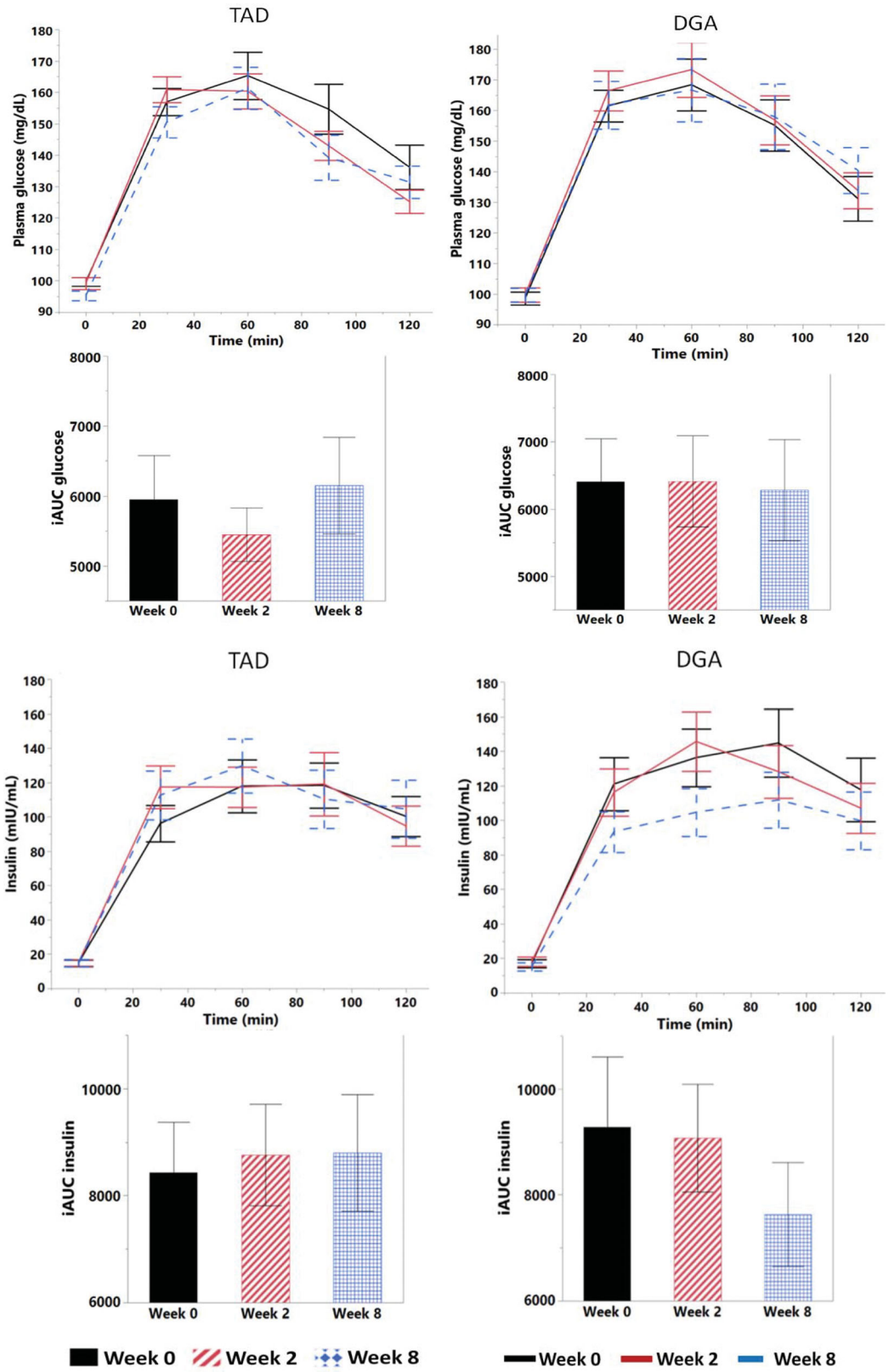


**FIGURE 2** Glucose and insulin responses to OGTT, depicted by group, week, and time in minutes (top) and as the iAUC (bottom), in women before (week 0), during, and after 8-wk dietary patterns consistent with a TAD or the DGA. Linear mixed-model analyses with time (for time course) or week (for iAUC) as repeated effects and volunteer as a random effect were performed. No significant effects for diet group, week, or interaction of diet group × week were found in OGTT responses. Values are means ± SDs, $n = 24$ in the TAD group and $n = 28$ in the DGA group. DGA, Dietary Guidelines for Americans; iAUC, incremental AUC; OGTT, oral-glucose-tolerance test; TAD, typical American diet.

test, $P = 0.13$). No interactions between diet group, week, and menopausal status were found for fasting glucose, insulin, and OGTT variables (**Supplemental Table 9**).

Of the 44 women who completed this study, 18 were dyslipidemic ($n = 9$ each in the TAD and DGA groups); the remaining 26 presented evidence of dyslipidemia and glucose intolerance/insulin resistance (GIT) ($n = 13$ each in the TAD and DGA groups). The distribution of dyslipidemia compared with dyslipidemia+GIT was not different between DGA and TAD (chi-square test, $P = 1.00$). No differences were identified in fasting or postprandial glucose and insulin, or any of the insulin resistance measures by group, week, or dyslipidemia compared with dyslipidemia+GIT interaction (**Supplemental Table 10**).

All 22 women in the DGA group improved their diet quality on the basis of a change in HEI score, whereas 2 of the 22 women in the TAD group increased their diet quality on the basis of HEI score (**Supplemental Table 11**). The total HEI score, on average, relative to the intervention diet increased by 32.7 points in the DGA group and decreased by 6.5 points in the TAD group. No interactions between HEI category and week and group were identified.

Participants who had >3% weight loss did not have significantly different diet group responses in fasting or 2-h OGTT insulin (diet group effects: $P = 0.560$ and $P = 0.760$, respectively) or fasting or 2-h glucose (diet group effects: $P = 0.850$ and $P = 0.830$, respectively), week, or diet × week interaction compared with the group that experienced <3% bodyweight change.

## DISCUSSION

To our knowledge, this is the first controlled-feeding trial to test the effect of a food-based dietary pattern following recommendations of the DGA. We measured cardiometabolic disease risk factors in an at-risk female cohort, while maintaining body weight, with the use of foods that are accessible and acceptable to the consumer. The higher quality of the DGA diet relative to the TAD was confirmed by HEI scores of 98 and 62, respectively. We found that, in the absence of weight loss, consuming a diet based on recommendations of the DGA did not change glucose homeostasis or fasting lipids in our cohort. The 2015 DGA Advisory Committee report concluded that there was moderate evidence for reduction in type 2 diabetes risk associated with nutrient-dense diets (2); however, the results from our short-term intervention trial did not align with this evidence. By design, the intervention did not lead to significant weight loss, and because changes in body weight and body fat can play a role in the pathogenesis of type 2 diabetes (31), this may also explain why improvements in blood sugar control were not observed despite the improvement in diet quality.

### Evidence based on whole diets

Epidemiologic evidence suggests that dietary patterns are associated with the risk of developing type 2 diabetes (i.e., a plant-based dietary pattern reduces risk, whereas an animal-based dietary pattern increases risk) (32). A recent meta-analysis of epidemiologic evidence supports the notion that dietary patterns that score high in diet quality using Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and the Alternate HEI techniques have strong potential for preventing type 2 diabetes (33). A recent population-based prospective cohort study identified that following the 2015 Dutch Dietary Guidelines was associated with reduced mortality due to some (stroke, colorectal cancer) but not all (coronary heart disease, type 2 diabetes, breast cancer) chronic diseases (34). Interventions aimed at reducing type 2 diabetes risk (31, 35) or managing glycemia in patients with type 2 diabetes (36) have typically involved increasing physical activity, reducing body weight, or both. To our knowledge, no data exist to determine if the consumption of a DGA-based diet while maintaining excess body weight can reduce type 2 diabetes risk. The Diabetes Prevention Program was an effective intervention found to be superior to metformin in reducing type 2 diabetes risk (37). This intensive intervention included both diet and exercise guidelines and achieved and maintained a 7% weight loss as part of the program. Similarly, the DGA recommend that adults should engage in moderately intense physical activity for ≥150 min/wk to achieve health benefits (2), higher than the average activity of the women in our trial. The results herein suggest that a DGA dietary pattern alone is not sufficient to elicit significant improvements, at least over a short period of time, in clinical cardiometabolic risk factors in women. Furthermore, a recent report that compiled data from 3 large studies [diet, obesity and genes dietary study (DiOGenes), dietary intervention with shop model (SHOPUS), and nutrient-gene interactions in human obesity (NUGENOB)] identified that high fasting glucose was associated with weight gain, or lack of weight maintenance, while following a diet that was low in whole grains and dietary fiber and had a high glycemic load (38). This indicates an association between fasting glucose and body weight, as well as the role of dietary pattern in regulating their association. Hence, intervention trials aimed at improving cardiometabolic health may require both increased physical activity, weight loss, or both in tandem with high-quality dietary patterns to be clinically meaningful.

Furthermore, by design, the study aimed to maintain body weight, which may be a primary reason we did not observe the positive impact that the DGA pattern may impart. However, the use of change in body weight, android fat mass, or waist circumference in the current study did not have a significant effect on primary outcome variables—glucose, insulin, and lipids (data not shown). Hence, the 3% weight loss seen in 50% of our volunteers, and the significant android fat mass and waist circumference change in both groups, did not affect our outcomes or groups differently.

### Dietary fiber (whole grains, fruit, and vegetables)

One of the major differences between the 2 intervention diets was the greater amount of fiber provided in the DGA diet. Whole-grain intake and type 2 diabetes risk factors have been inversely associated in epidemiologic studies (39). Whole-grain foods can reduce insulin resistance and postprandial insulin and glucose response in hyperinsulinemic adults (40), but this effect is not apparent in healthy normal-weight (41) or overweight (42) individuals. Juntunen et al. (43) theorized that the effect of whole grain on blood sugar and insulin is not due to the fiber content but to the form and structure of the fiber, with rye showing stronger effects than wheat, for example. A current meta-analysis reported a plateauing effect of whole-grain intake, especially on type 2

diabetes risk (39), with high intakes not having a strong risk-lowering association. These studies suggest that specific whole-grain types in a high-quality diet may be important to elicit robust effects on blood sugar control and insulin sensitivity. Our diet plans did not include rye, barley, or oats, and wheat and rice were the major sources of whole grain in the DGA diet. Therefore, this difference in grain products may have contributed to the lack of improvement in fasting insulin, glucose, or insulin resistance surrogates.

Plant-based dietary patterns with an emphasis on fruit and vegetables are associated with a reduced risk of type 2 diabetes (32). In the current study, the usual (preintervention) total vegetable intake (reported to be 1.2 cups/d for both diet groups; data not shown) increased to 3.4 cups in the DGA group. However, the true benefits from the antioxidants, carotenoids, and other phenolics would have to be evaluated by measuring appropriate markers in blood or other tissues before and after the intervention, and linking these to specific changes in outcomes.

### Dietary added sugars

The DGA diet provided fewer calories as added sugar than did the TAD diet. Epidemiologic studies have reported a link between high added-sugar consumption, primarily in the form of sugar-sweetened beverages, with increased type 2 diabetes risk (44), likely through weight gain with very high intakes of added sugar (45). A recent meta-analysis and systematic review, however, reported no association between total sugar consumption and type 2 diabetes risk (46), while also suggesting that current evidence is limited, both in the number of studies as well as heterogeneity of study types, to draw sound conclusions. Intervention studies conducted in adolescents and young adults, aimed at reducing type 2 diabetes risk factors by reducing sugar intake (to $<$10% of total energy intake), do show significant improvements in glucose and insulin iAUC, insulin secretion, and body fat (47). Our current study did not identify a significant impact of the overall change in dietary pattern and reduced intake of added sugar on risk factors for type 2 diabetes. Our participants reported (albeit via self-reports) low added-sugar intake before the intervention, averaging 15 g/d or ~3% of total energy intake (see Supplemental Table 5). Even with the difference in added sugars between the DGA (7.6% of energy) and TAD (14.2% of energy) groups, we did not see any effects of the added-sugar contents of the intervention diets on the outcome measures.

### Dietary total and saturated fats

Studies conducted almost 3 decades ago implicated dietary saturated fat in the pathogenesis of type 2 diabetes (48). Replacing saturated with mono- or polyunsaturated fats can improve insulin sensitivity in healthy people (49). In the current study, we reduced the saturated fat intake by 40–50% compared with reported usual intake, whereas MUFA and PUFA intake remained relatively similar to habitual reported intake. This resulted in an increase in the polyunsaturated-to-saturated ratio. Higher polyunsaturated-to-saturated ratios are associated with a reduced risk of type 2 diabetes (50). Despite these dietary fat changes, there was no impact on type 2 diabetes risk factors or triglyceridemia with the DGA diet, suggesting that the classification of saturated fat, MUFAs, or PUFAs may be too general and other considerations, such as the fat matrix or individual fatty acids, need to be considered.

### Dietary sodium and potassium

Reducing dietary sodium intake has been associated with reduced systolic blood pressure in both individuals with and without hypertension (51, 52). In the current study, we found that the DGA diet resulted in an improvement in systolic blood pressure, but no change in diastolic blood pressure. There was also no effect of the TAD diet on blood pressure measures. The decrease in systolic blood pressure could have been due to reduced sodium, as well as the increased potassium in the DGA diet (53). However, the study design did not allow for an evaluation of the salt-specific effects on blood pressure and other variables. Following the DASH diet recommendations, our study supports the idea that reducing sodium intake and increasing potassium intake reduces systolic blood pressure, despite the lower quantity of potassium than is recommended in both DGA and DASH studies (only matching the sodium-to-potassium ratio with the DASH study) (54).

### Diet habits and study outcomes

In an exploratory analysis, we examined whether the usual diet consumed by each participant before entering the study might have influenced the study outcomes. On the basis of self-reported diet intake data, the mean preintervention HEI score of the participants of the DGA group was 69, ~30 points lower than the DGA intervention diet score of 98. On the other hand, the mean preintervention HEI score of the TAD group, 65, was very similar to the HEI score of the TAD intervention, which was 62. The average HEI score for adults (aged 18–64 y, which is the age range in the current study) is 58.3 (55), which is lower than that observed in our volunteers' habitual intake, and significantly lower than that of the DGA diet in the current study. However, this score from NHANES is a combination for both men and women, and may likely be different if it is observed just in women. The DGA intervention vastly improved the quality of diet for women assigned to this group as assessed by the HEI scores. In a subset analysis, we compared women in the DGA group who improved their HEI score with women in the TAD group whose pretrial diet HEI was similar or even higher than the TAD HEI score. This subject stratification did not alter the overall findings—namely, no diet group differences in the risk factors for type 2 diabetes were detected as a result of the interventions or as a function of study week.

We monitored adherence to the intervention diets with the use of a combination of techniques: an adherence scoring tool (56) based on daily food logs (Supplemental Figure 1), weight maintenance, meeting the volunteers 2 times/wk to troubleshoot and reinforce honesty over perfection, ensuring that volunteers ate 2 meals during the week at the research center, and continually surveilling and documenting returned foods and packaging. Our volunteers reported strong adherence to the study foods and low inclusion of nonstudy foods.

### Strengths and limitations

Strengths of the study include the selection of "at risk" volunteers, albeit using diverse endpoints, and the fact that the

study, although relatively small in terms of sample size, was adequately powered to test our hypotheses. To our knowledge, this is the first controlled-feeding trial testing the efficacy of a diet following the food group and nutrient recommendations of the DGA compared with a more representative American diet. We did not observe improvements in our primary outcome variables as a result of consuming the DGA diet pattern, possibly due to the short, 8-wk duration of the intervention or the heterogeneity of inclusion criteria. It is also possible that adherence to the weight-maintenance requirement of the study in both diet groups had benefit, which could mask between-group differences. However, because systolic blood pressure improved in just the DGA group we think that this change can be attributed to the DGA. Furthermore, volunteers in the TAD group reported more moderate physical activity than the DGA group, albeit not significantly different, which could have affected our results. Our sample size was appropriate for the population of women we targeted and recruited. However, the diversity in the "at risk" definition (to include insulin resistance, glucose intolerance, and dyslipidemia) we used to include women may have affected our results (see Supplemental Figure 2), and a refinement in metabolic syndrome characteristics to only focus on one outcome may have yielded different results. Finally, because this was a controlled-feeding trial, ad libitum intake on such a pattern and how it affects appetite regulation was not within the scope of our investigation. Furthermore, self-report and visual inspection of returned food and packaging are imperfect tools for measuring adherence. Further investigation with the use of more-objective measurements of adherence is needed.

The DGA include other recommendations that were not built into the design of this study, specifically that achieving and maintaining a healthy body weight is important and that moderate-to-vigorous physical activity should be included in one's daily routine on most, if not all, days of the week. Sustaining a practice of consuming a high-quality diet may provide important benefits, but these other guidelines may be critical to induce clinically meaningful improvements in cardiometabolic health.

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