Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: a 1-y randomized controlled trial[1–3]

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ABSTRACT

Background: There remains no consensus about the optimal dietary composition for sustained weight loss.

Objective: The objective was to examine the effects of 2 dietary macronutrient patterns with different glycemic loads on adherence to a prescribed regimen of calorie restriction (CR), weight and fat loss, and related variables.

Design: A randomized controlled trial (RCT) of diets with a high glycemic load (HG) or a low glycemic load (LG) at 30% CR was conducted in 34 healthy overweight adults with a mean (±SD) age of 35 ± 6 y and body mass index (kg/m^2) of 27.6 ± 1.4. All food was provided for 6 mo in diets controlled for confounding variables, and subjects self-administered the plans for 6 additional months. Primary and secondary outcomes included energy intake measured by doubly labeled water, body weight and fatness, hunger, satiety, and resting metabolic rate.

Results: All groups consumed significantly less energy during CR than at baseline ($P < 0.01$), but changes in energy intake, body weight, body fat, and resting metabolic rate did not differ significantly between groups. Both groups ate more energy than provided (eg, 21% and 28% CR at 3 mo and 16% and 17% CR at 6 mo with HG and LG, respectively). Percentage weight change at 12 mo was −8.04 ± 4.1% in the HG group and −7.81 ± 5.0% in the LG group. There was no effect of dietary composition on changes in hunger, satiety, or satisfaction with the amount and type of provided food during CR.

Conclusions: These findings provide more detailed evidence to suggest that diets differing substantially in glycemic load induce comparable long-term weight loss. *Am J Clin Nutr* 2007;85: 1023–30.

KEY WORDS Glycemic load, caloric restriction, body weight, metabolism

INTRODUCTION

The prevalence of obesity and overweight continues to increase nationally and worldwide (1–3). Calorie restriction (CR) remains the cornerstone of most weight-management strategies, but there remains no consensus over the role of dietary macronutrient composition in optimizing long-term weight loss.

In part, the lack of consensus probably reflects the fact that most studies in this area have provided dietary advice, rather than food, with resulting uncertainty in the true extent of dietary change. For example, recent studies have examined whether low-carbohydrate or low-glycemic-load (GL) diets facilitate greater long-term weight loss than do conventional recommendations based on national dietary guidelines (4, 5); most (6–10), but not all (11), of the studies reported transiently greater weight loss at 6 mo in individuals consuming low-carbohydrate or low-GL diets that was attenuated in studies continuing to 12 mo (8, 10). However, unbiased assessments of adherence to the tested regimens were not performed, and there may have been differences between tested diets that influenced the results. It is recognized that dietary change in the absence of provided food is difficult because of formidable barriers, such as the need to alter central lifestyle factors such as established shopping and cooking habits and food preferences (12–16). For this reason, perhaps, subjects tend to inflate self-reports of the magnitude of dietary change (17). Moreover, in most of the reports of high- compared with low-carbohydrate regimens and weight loss, differential behavioral support was given to each treatment group because they were testing popular diet prescriptions rather than specifically different dietary compositions, which confounded the results (8, 11, 18). Thus, additional studies that use more detailed and consistent methods are needed to resolve the effects of different dietary patterns on long-term weight loss.

We describe here a detailed 1-y randomized controlled trial (RCT) designed to examine the effects of dietary patterns differing

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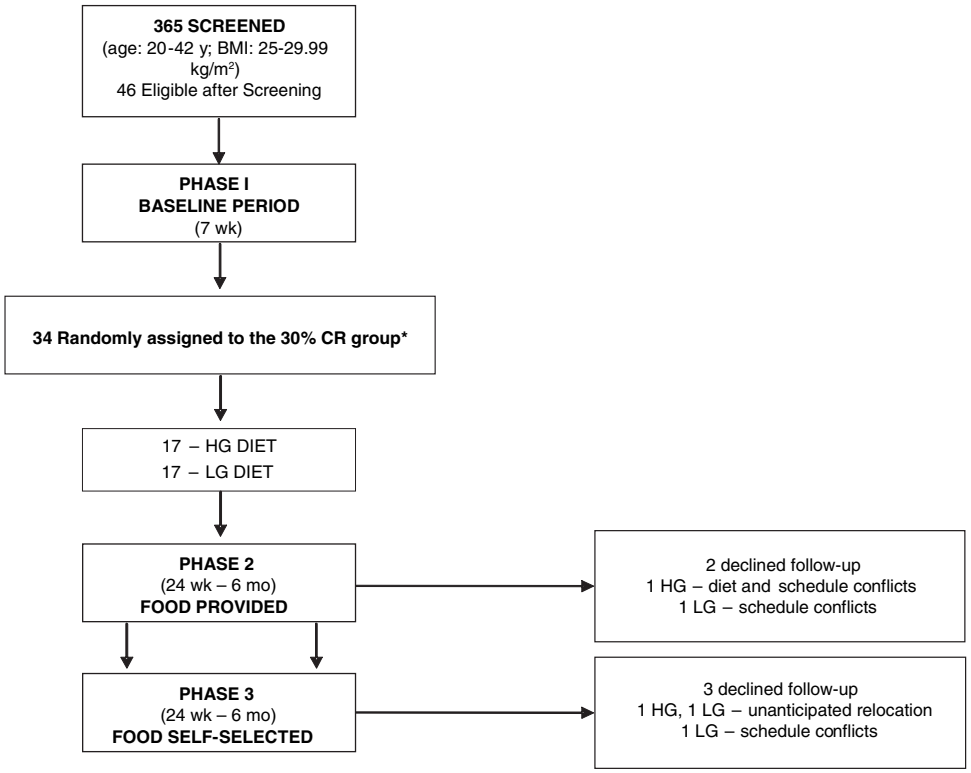

FIGURE 1. Flow of study participants from screening through study completion. The numbers shown in the figure are specific to the group that was prescribed a regimen of 30% calorie restriction (CR). *Twelve subjects were randomly assigned to a 10% CR control group (data not shown). HG, high glycemic load; LG, low glycemic load.

in glycemic load and fed at 30% CR on adherence to the regimens, weight and body fat losses, and underlying explanations for differential responses to the diets.

SUBJECTS AND METHODS

Study population

The subjects were 34 overweight [body mass index (in kg/m^2): 25–30] but otherwise healthy men and women aged 24–42 y who were recruited through a variety of local advertisements. Twelve additional subjects were recruited and randomly assigned to 2 different control groups for the purpose of gaining experience in retaining a control group but are not described here because the groups are very small ($n = 5$ in the HG group and $n = 4$ in the LG group at 12 mo). This study constitutes the first phase of the CALERIE (Comprehensive Assessment of the Long-term Effects of Restricting Intake of Energy) trial at Tufts University. CALERIE is a coordinated multicenter study of CR in human health and aging. During this first phase, independent studies were conducted at the different sites. Eligibility for the Tufts study was determined on the basis of a normal health-history questionnaire and a screening examination that included blood and urine tests, physical and psychological examinations, and assessment of anticipated lifestyle changes, such as pregnancy or moving out of the area. Additional exclusion criteria included high physical activity levels (ie, participation in sports or training for >12 h/wk), weight fluctuations (>6.8 kg in the past year), inability to complete an accurate 7-d dietary record (accuracy defined as 70–130% of estimated energy requirements), and any disease or medications that might influence the results obtained (including diabetes, cancer, coronary heart disease, endocrine disorders, psychiatric diagnosis, or eating disorder). The study was conducted at the Metabolic Research Unit of the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University with approval by the Institutional Review Board of Tufts–New England Medical Center Hospital. All subjects gave written informed consent before participating and were provided with a stipend. The study was independently monitored annually for overall compliance and data accuracy by an external clinical trial monitor from the Duke Clinical Research Institute, Durham, NC, and the safety and efficacy of the clinical trial were monitored by a Data Safety Monitoring Board.

Study protocol

As shown in **Figure 1**, this yearlong intervention study included a 7-wk baseline period (phase 1), during which time the subjects were requested to maintain a stable weight and continue eating their usual diet. Baseline weight-maintenance energy requirements [assumed to be equal to total energy expenditure (TEE), as measured by doubly labeled water (19)] and key outcome variables were assessed. Following phase 1, there was a 24-wk CR phase (phase 2: ≈6 mo) during which the subjects were randomly assigned to a diet with a low glycemic load (LG) or a high glycemic load (HG), and all food was provided at 70% of individual baseline weight-maintenance energy requirements. The last phase of the study consisted of a 24-wk CR phase (phase 3: ≈6 mo) during which the subjects were instructed to take overall responsibility for food preparation and to continue their phase 2 regimen. The subjects were expected to visit the research

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TABLE 1
Composition of the 2 diets[1]

	HG diet	LG diet
Carbohydrate (% of energy)	60	40[2]
Fat (% of energy)	20	30[2]
Protein (% of energy)	20	30[2]
Fiber (g/1000 kcal)	15.1 ± 0.8[3]	15.3 ± 0.6
Energy density (kcal/g)	1.0 ± 0.0	1.0 ± 0.0
Glycemic index	85.6 ± 2.8	52.4 ± 4.4[2]
Glycemic load (g/1000 kcal)	118.3 ± 4.1	45.4 ± 4.6[2]
Variety (food items[4]/d)	11	11
Appearance (100-mm VAS)[5]	55.0 ± 12.3	56.6 ± 12.1
Taste (100-mm VAS)[5]	64.5 ± 13.7	62.8 ± 11.8
Smell (100-mm VAS)[5]	61.5 ± 12.6	61.6 ± 9.3

[1] VAS, visual analogue scale (5-point anchors ranging from "not at all" to "extremely" at opposite ends).
[2] Significantly different from the HG diet, $P < 0.001$ (independent-sample t test).
[3] $\bar{x} \pm$ SD (all such values).
[4] Mixed dishes were considered as one food item.
[5] Paired-sample t tests were used for comparisons between groups because an independent group tested both diets before the study began; no significant differences were observed.

center weekly throughout the study for a variety of activities, including weekly behavioral support groups, individual meetings with the study dietitian, safety monitoring, and outcome testing.

Study diets

Two diets approximating the range of current dietary recommendations for healthful macronutrient ranges and containing the Dietary Reference Intakes (DRIs) of micronutrients and essential fatty acids (4) were developed for use in this study at 30% CR relative to baseline energy requirements. Diet compositions are summarized in **Table 1** for the HG and LG diets, and a list of actual foods that were provided for each type of diet is included in **Appendix A**. Both diets had consistent features designed to promote CR, including meeting DRIs for dietary fiber (4), limited inclusion of high-energy-density foods (20), limited liquid calories (21), and a relatively high variety of low-energy-density foods (eg, fruit and vegetables), and a relatively low variety of high-energy-dense foods (22). The diets differed in the ratio of macronutrients (HG: 60% carbohydrate, 20% fat, and 20% protein; LG: 40% carbohydrate, 30% fat, and 30% protein), and the carbohydrate sources in the LG diet had a lower glycemic index (GI) per published GIs of different carbohydrate sources (23). Because all 3 macronutrients varied between the diets, the study outcomes are most appropriately attributed to different dietary patterns. However, because the largest difference between the diets was in the GL, the diets are described as HG and LG diets. The daily glycemic load was calculated as [daily GI × (total available carbohydrate (g/d))/1000 kcal]. The amount of available carbohydrate for each food was calculated as total grams of carbohydrate – total dietary fiber. Please note that, although it was technically possible to change the GL of the diets by changing just the carbohydrate and fat contents (and leaving protein constant), it would have been hard to control other factors between the diets, including palatability and energy density. With the chosen approach, it was possible to match the diets for dietary variety and palatability [assessed by using a visual analogue scale (VAS) during a pilot test of the diets]. The subjects were also provided with a multivitamin supplement and 500 mg Ca/d to ensure that the DRIs of micronutrients were met.

All food was provided at the 30% reduced CR prescription to subjects during the first 6 mo of the CR intervention. The subjects were asked to consume only the provided food and were told that it was important to comply with the study but were also told that it was important to report both leftovers and any additional foods they consumed on data recording sheets that were provided for this purpose. After weeks 15–20 of the CR intervention, the subjects were allowed 1000 kcal/wk of discretionary foods not on the menu, and this amount was subtracted from the provided foods. The subjects were requested to bring back their leftover foods, which were weighed and the amounts recorded on the data recording sheets. The subjects were allowed to eat foods not included in the study diet on days such as Thanksgiving and Christmas (or other infrequent special occasions) and were given nonperishable foods and menu suggestions when traveling. Intakes were self-recorded during these times. The subjects or their designated representative came to the research center twice a week to pick up the meals.

During the second 6 mo of the study, the subjects were instructed to self-select and prepare their own food at home to maintain their randomization. To prepare for this phase, the subjects worked with the study dietitian to develop an individualized plan that included menus, recipes, portion sizes, and food lists that were consistent with their randomized diets, prescribed calorie levels, and food preferences. Food scales were provided to help with appropriate portioning, and the subjects participated in a preparatory grocery store tour and cooking class.

Recruitment and randomization

A total of 365 eligible subjects were screened for this study over a 1-y period from October 2002 to December 2003, and 34 subjects were enrolled to the 30% CR groups (Figure 1). A block randomization stratified on body mass index, sex, and diet group was used. All outcome-assessment staff were blinded to participant randomization, and the subjects were not informed of their randomization until month 3 of CR.

Body weight, height, and composition

Height was measured at the research center, once at the beginning of the study, with a wall-mounted stadiometer to ±0.1 cm, and weight was measured at weekly intervals to ±50 g with a calibrated scale (model CN-20; DETECTO-Cardinal Scale Manufacturing Co, Webb City, MO). All subjects were provided with a home weight scale (model HS301 TANITA body weight scale; Tanita Corporation of America Inc, Arlington Heights, IL), and a daily home weight measure was obtained. Air-displacement plethysmography (BOD POD; Life Measurement Inc, Concord, CA) was used to measure body density in duplicate at baseline and at 3, 6, and 12 mo. The principles of this accurate density-based method and its validation and practical use are described elsewhere (24–26). The test-retest CV for percentage body fat measured by BOD POD in human adults is 1.7% ± 1.1% (24).

Resting metabolic rate

Resting metabolic rate (RMR) was measured on 2 mornings at baseline and at 6 mo and 12 mo of CR, after the subjects slept

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overnight in the research center and fasted for 12 h according to our usual procedures (27). Measurements were obtained while the subjects were resting supine in comfortable thermoneutral conditions by indirect calorimetry (Deltatrac portable metabolic cart; Sensor Medics Corp, Yorba Linda, CA), and subjects were instructed to relax and avoid hyperventilation, fidgeting, or sleeping during the measurements. Measurements of oxygen consumption and carbon dioxide production were obtained for 40 min, and the last 30 min of the data were used to calculate RMR with the use of de Weir's equation (28). The calorimeter was assessed periodically with an alcohol burn test to ensure that the accuracy of the measurements was within ±1%.

Calculated energy intake and dietary adherence to CR

The TEE of the subjects was measured in duplicate over successive 14-d periods at baseline, and additional 14-d measurements were made at 3, 6, and 12 mo of CR. This standard, nonradioactive isotopic method has been extensively validated and is described elsewhere (29, 30). Briefly, at the start of each TEE measurement, the subjects fasted overnight and were given an oral dose of doubly labeled water ($^2H_2{}^{18}O$) containing 0.22 g $H_2{}^{18}O$/kg estimated total body water and 0.115 g ^2H_2O/kg total body water after collection of 2 independent baseline urine specimens. The subjects were then required to remain fairly sedentary and not to consume any food or water while urine samples were collected from complete voids made at 3, 4.5, and 6 h after dose administration. After completion of urine collections, the subjects were discharged from the unit and carried out their usual daily activities for 14 d, with supervised urine specimen collection on days 7 and 14. All samples were portioned in duplicates into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, Newton, NC) immediately after collection and stored at −20 °C.

Abundances of $H_2{}^{18}O$ and ^2H_2O in dilutions of the isotope doses and in urine specimens were measured in duplicate by using isotope ratio mass spectrometry (31), and deuterium was prepared for analysis by using an automated chromium reduction system (32). The urine samples were analyzed at the Pennington Biomedical Research Center (Baton Rouge, LA). Isotope elimination rates (k_h and k_o) were calculated by using linear regression of logged values, and carbon dioxide production was calculated by using the equations of Schoeller (19), as modified by Racette et al (33). TEE was then calculated on the basis of an assumed respiratory quotient of 0.86. Please note that large errors in respiratory quotient have a small effect on the error of calculations of TEE (34).

Measurements of TEE obtained at 3, 6, and 12 mo during the CR intervention were used to calculate the actual energy intake of the subjects at these time periods. Because energy intake is equal to TEE plus the change in energy balance (when a subject is not in neutral energy balance), TEE data can be used to calculate a value for energy intake unbiased by subject reporting, by correcting for the estimated change in body energy stores during the same period based on weight change (35). Individual values for weight change during the doubly labeled water period were calculated from the regression of daily measurements of body weight made for up to 7 d before and 7 d after the period of TEE measurements (for a maximum of 28 d). The energy content of weight change was calculated assuming an energy content of weight loss of 7.4 kcal/g (36).

Self-reported hunger, desire to eat, and dietary satisfaction

The subjects were asked to record the level of hunger, desire to eat nonstudy foods, and satisfaction with the amount of food using a 100-mm VAS completed at the end of each study day (37, 38). Daily values were averaged for analyses of different study periods; on average, 50% of the daily records were completed for the analyses presented here.

Biochemical measures

Biochemical measures were determined in 12-h fasting blood samples collected at baseline and at 6 and 12 mo. Plasma total cholesterol, triacylglycerol, HDL, and LDL were measured on a Hitachi 911 automated analyzer (Roche Diagnostics, Indianapolis, IN) with the use of enzymatic reagents. Blood glucose was measured with a coupled enzyme kinetic method on a Cobas Mira Analyzer (Roche Diagnostics). Insulin was measured with a competitive binding radioimmunoassay with a commercial human insulin specific kit (Linco Research Inc, St Charles, MO) and a Packard Cobra II gamma counter. All assays had a CV of 2.7–6%.

Statistics

Statistical analyses were performed by using SAS for WINDOWS (version 8.2; SAS Institute, Cary, NC). Values are expressed as means ± SDs unless otherwise specified. Analyses were performed by using all available data from randomly assigned subjects and by restricting attention to subjects with complete data (n = 15 for HG and n = 14 for LG). Diet characteristics were compared by using t tests for independent samples for all variables except for the palatability variables, for which paired-samples t tests were used because an independent group of subjects tasted both diets for the VAS ratings before the start of the study. Baseline characteristics of the subjects were compared by using independent-sample t tests. Changes in hunger, satiety, and dietary satisfaction between baseline and 12 wk of CR were compared by using analysis of variance. Percentage weight change over time was examined by using a linear model with diet group and time as independent variables. For all other outcome variables, a mixed-model analysis with repeated measures was performed to determine the effects of diet (HG and LG) and the change over time. All P values were 2-sided, and a P value ≤0.05 was considered to indicate statistical significance.

RESULTS

Of the 34 subjects randomly assigned to 30% CR, 85% (n = 29) completed the 1-y study and subjects who dropped out mostly did so because of scheduling conflicts and unplanned life changes (Figure 1). Baseline characteristics for the subjects are shown in **Table 2**. There were no statistically significant differences between the groups for any of the baseline variables.

Baseline TEE (equivalent to energy requirements in the weight-maintenance state) and energy intake calculated from TEE at intervals during the intervention (expressed as a percentage of baseline TEE, ie, %CR) are provided in **Table 3**. There was no statistically significant difference in baseline TEE between the diet groups. Both groups had significant %CR from

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TABLE 2
Characteristics of the subjects in the 2 diet groups at baseline[1]

	HG diet (n = 4 M, 13 F)	LG diet (n = 4 M, 13 F)
Age (y)	34 ± 5	35 ± 6
BMI (kg/m^2)	27.5 ± 1.6	27.6 ± 1.2
Height (cm)	169.1 ± 10.7	169.0 ± 10.2
Weight (kg)	79.0 ± 12.1	79.1 ± 9.2
Body fat (%)	34.8 ± 7.1	34.9 ± 8.2

[1] All values are $\bar{x}$ ± SD. HG, high glycemic load; LG, low glycemic load. There were no statistically significant differences between the diet groups (independent-sample t tests).

baseline ($P < 0.01$). However, %CR was not statistically significantly different between the groups at 3, 6, or 12 mo of the intervention. On average, the subjects ate somewhat more food than prescribed at all time points. Consistent with the actual measured %CR values, percentage weight loss was significant over time in both groups ($P < 0.0001$) but was not significantly different between the groups ($P = 0.59$) (**Figure 2**). In other words, there was no difference in percentage weight loss between individuals randomly assigned to different diets, and mean values at 12 mo were not statistically significantly different (**Table 4**).

Baseline body weight, percentage body fat, and RMR, and percent change from baseline at 6 and 12 mo of CR, respectively, are also shown in Table 4. There was a statistically significant decrease in mean percentage fat over time ($P < 0.0001$) consistent with body weight change; however, the difference between diet groups was not statistically significant over time. RMR also decreased significantly from baseline to 6 and 12 mo ($P < 0.01$), but changes in RMR over time were not statistically significant between diet groups. There was no diet-by-time interaction for both the measured and percentage change data. It should be noted that there were also no group differences in changes in fat-free mass and fat mass with CR, and the change in RMR adjusted for the change in fat-free mass was also not significant (data not shown). Results for weight, fat loss, and change in RMR when all participants were included were not statistically different from the results obtained when noncompleters were.

Changes in self-reported hunger and satisfaction with the amount and type of provided food and the desire to eat nonstudy foods between baseline and 3 mo of CR were examined by using daily VAS. The first 3 mo of CR were chosen for this analysis because this is the period when adherence to the prescribed CR was at its highest; therefore, eating-behavior variables could be compared between groups to indicate true composition effects. The results from this analysis showed that there was a significant increase from baseline in the desire to eat nonstudy foods ($P < 0.01$) and a significant decrease in the satisfaction with the type of provided food ($P < 0.05$) within the HG group but not within the LG group. However, there was no statistically significant difference between the diet groups for change in these variables over time (data not shown).

Fasting values for triacylglycerols, insulin, glucose, and total, HDL, and LDL cholesterol at baseline and the percent change in these variables at 6 and 12 mo of CR are shown in **Table 5**. The decreases over time in percentage change from baseline were statistically significant for triacylglycerol ($P < 0.001$), insulin ($P < 0.0001$), and total ($P < 0.001$), HDL ($P < 0.0001$), and LDL ($P < 0.05$) cholesterol, but not for glucose. There were no statistically significant diet-by-group interactions over time for any of the variables. Insulin and glucose data for the 30% CR group with the 2 diets are reported in more detail elsewhere (39), but are summarized here for completeness.

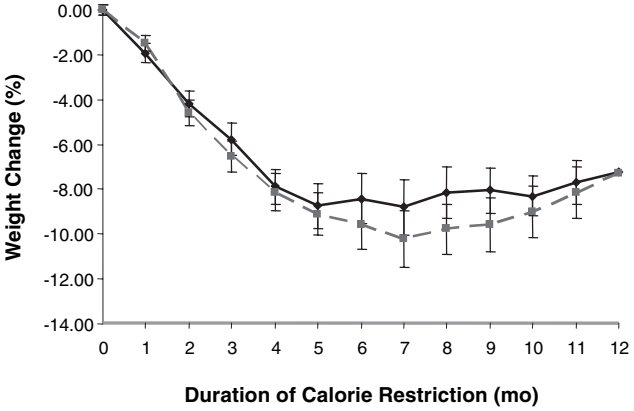

FIGURE 2. Mean (±SD) percentage weight change during 12 mo of calorie restriction in the groups randomly assigned to consume a diet with either a high glycemic load (n = 15; ●) or a low glycemic load (n = 14; ■). Percentage weight change over time was analyzed with the use of a linear model with diet group and time as independent variables.

TABLE 3
Prescribed energy intake during calorie restriction (CR) and energy intake expressed as a percentage of baseline total energy expenditure (TEE) at 3, 6, and 12 mo of CR[1]

	HG diet (n = 15)	LG diet (n = 14)
Baseline TEE (kcal/d)	2825 ± 499	2708 ± 373
Prescribed energy intake (kcal/d)	1960 ± 364	1900 ± 251
Measured CR at 3 mo (%)[2]	21.1 ± 10.3	27.5 ± 13.0
Measured CR at 6 mo (%)[2]	15.7 ± 12.7	17.5 ± 15.3
Measured CR at 12 mo (%)[2]	17.1 ± 13.0	9.5 ± 14.2

[1] All values are $\bar{x}$ ± SD. HG, high glycemic load; LG, low glycemic load.

[2] There was a statistically significant difference over time ($P < 0.01$) but not between groups ($P = 0.922$) (mixed-model analysis of repeated measures). There was no significant diet-by-time interaction ($P = 0.125$).

DISCUSSION

This detailed RCT in healthy overweight women and men is the first to examine the effects of HG compared with LG diets on weight loss in a long-term protocol not confounded by group differences in other factors that strongly influence energy intake, including type of behavioral support, diet palatability, and dietary variety of the regimens. Under the conditions of this study, which tested diets that differed in all 3 macronutrients but mostly in glycemic load (40% carbohydrate from low-GI sources compared with 60% of energy intake from high-GI sources), we found no significant difference between the groups in mean energy intake, weight loss, and body fat loss throughout the 12 mo study. These findings provide more rigorous support than available previously for the view that wide variability in the balance of different dietary macronutrients has little effect on mean long-term weight loss during CR (40).

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TABLE 4
Resting metabolic rate (RMR) and body composition in the 2 diet groups[1]

	Baseline[2]	Change from baseline 6 mo	Change from baseline 12 mo
		%	
Body weight (kg)[3]			
HG diet (n = 15)	78.5 ± 12.3	−9.1 ± 4.2	−8.0 ± 4.1
LG diet (n = 14)	78.0 ± 9.3	−10.4 ± 4.1	−7.8 ± 5.0
Body fat (%)[3]			
HG diet	35.0 ± 7.1	−17.1 ± 11.6	−14.8 ± 8.8
LG diet	35.2 ± 8.7	−23.3 ± 16.6	−17.9 ± 12.5
RMR (kcal/d)[4]			
HG diet	1582 ± 255	−5.9 ± 5.7	−3.3 ± 7.1
LG diet	1605 ± 182	−6.6 ± 5.6	−2.2 ± 7.8

[1] All values are $\bar{x}$ ± SD. CR, calorie restriction; HG, high glycemic load; LG, low glycemic load.
[2] There were no statistically significant differences between the groups (independent-sample t tests).
[3,4] There was a statistically significant change over time: [3]$P < 0.001$, [4]$P < 0.01$. There were no statistically significant differences between the diet groups over time (mixed-model analysis of repeated measures). There was no significant diet-by-time interaction.

Several recent long-term studies have examined the effects of diet composition on weight loss and reported greater weight loss with LG diets than with HG diets at 6 mo, but no difference in mean weight loss at 12 mo (8, 10, 41). Perhaps the most important difference between those studies and the one described here is that those studies recommended dietary compositions to the subjects, whereas we provided subjects with a complete set of meals and snacks every day for 6 mo in menus controlled for other factors that have well-established influences on energy intake (42, 43). The compositions recommended in those studies were also more extreme (eg, less carbohydrate in the LG groups), but self-reported intakes indicated similar actual compositions to those used in this study. The greater initial weight loss seen in the LG groups in the previous studies may therefore have been due to inadvertent dietary changes that the subjects made to accommodate protocol requirements, for example, in dietary variety, palatability, and fiber (which are known to have independent effects on energy intake) rather than in macronutrients and glycemic load. By 12 mo, both the previous studies and our new investigation found no difference in weight loss between the HG and LG regimens and a tendency for weight and body fat regain in the LG groups. Taken together, these findings suggest that reduced energy intake may be somewhat harder to sustain with LG regimens in the long term. This could be true for a number of

TABLE 5
Clinical indicators in the 2 diet groups[1]

	Baseline[2]	Change from baseline 6 mo	Change from baseline 12 mo
		%	
Triacylglycerol (mg/dL)[3]			
HG diet (n = 15)	90.6 ± 47.2	−14.3 ± 21.9	−16.5 ± 29.9
LG diet (n = 14)	98.6 ± 33.1	−24.7 ± 27.7	−15.2 ± 24.8
Total cholesterol (mg/dL)[4]			
HG diet	168.4 ± 25.3	−11.1 ± 8.3	−4.2 ± 9.3
LG diet	176.7 ± 26.7	−13.4 ± 12.1	−5.3 ± 10.5
HDL cholesterol (mg/dL)[5]			
HG diet	55.4 ± 8.5	−2.8 ± 10.6	13.3 ± 16.2
LG diet	51.0 ± 11.5	−3.1 ± 19.1	11.9 ± 10.2
LDL cholesterol (mg/dL)[6]			
HG diet	96.9 ± 21.5	−13.2 ± 11.0	−7.1 ± 11.3
LG diet	107.6 ± 24.2	−13.4 ± 18.2	−7.0 ± 17.5
Glucose (mg/dL)			
HG diet	83.5 ± 6.1	−2.5 ± 6.1	−2.3 ± 6.2
LG diet	84.4 ± 5.8	−1.8 ± 7.8	5.0 ± 9.9
Insulin (μIU/mL)[4]			
HG diet	10.5 ± 3.6	−14.9 ± 20.0	−18.0 ± 15.0
LG diet	12.1 ± 4.3	−25.4 ± 24.2	−21.2 ± 16.7

[1] All values are $\bar{x}$ ± SD. HG, high glycemic load; LG, low glycemic load. There were no statistically significant differences between diet groups over time.
[2] There were no statistically significant differences at baseline between the groups (independent-sample t tests).
[3,4,6] There was a statistically significant change over time (mixed-model analysis of repeated measures): [3]$P < 0.001$, [4]$P < 0.0001$, [6]$P < 0.05$.
[5] There was a statistically significant change over time at the 12-mo time point only, $P < 0.0001$ (mixed-model analysis of repeated measures).

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reasons, including the difficulty in sustaining a self-selected LG diet because of the challenges in maintaining acceptable variety and palatability or, perhaps, to the difficulties associated with the significant lifestyle changes required to shop and cook for an unfamiliar LG regimen.

Some short-term studies have also examined the effects of HG compared with LG diets on weight and body composition (44–46). However, those studies did not control the diets for other factors, such as dietary variety (42), palatability (42), and fiber (43), which are known to have substantial independent effects on energy intake, and typically had other differences between diet groups, such as different methods for self-reporting relevant variables, such as energy intake. In the present study, energy intake was measured by using the objective doubly labeled water method by calculating energy intake from TEE (19) and the change in energy balance during the measurement period based on body weight change as outlined previously (35). This was an important element of the protocol because underreporting of dietary intake by the subjects in self-reports is essentially a universal phenomenon, with the extent of underreporting varying between 5% and 50%, depending on the population (35, 47–49). Using the doubly labeled water method, we found that, although both groups of 30% CR subjects consumed some nonstudy food, there was no significant difference in the degree of nonadherence between the dietary groups.

It should also be noted that there were no differences in self assessments of changes in hunger over time by subjects in the HG and LG groups during the first 12 wk of the protocol, when adherence was generally highest. This finding of no difference in hunger between the HG and LG diet groups might have been due to a lack of power in this relatively small study, especially because the desire to eat nonstudy foods increased in the HG group but not in the LG group. It is also possible, however, that the suggested greater satiation from high-protein meals and low-GI meals than from low-protein and high-GI meals in previous studies (50, 51) was not seen here because of the common features anticipated to minimize hunger in both the diets, including very high amounts dietary fiber (43), low energy density (20), and low amounts of liquid energy sources (21). We speculate that these common satiety-inducing features may have overridden any possible additional satiety effects of the higher-protein content and lower GI of the LG diet.

This long-term and detailed RCT, which provided diets extensively matched for confounding variables, found no evidence of any differential effect of dietary GL on group mean values for energy intake, hunger, satiety, metabolic rate, and weight and body fat loss up to 12 mo. Although the results obtained cannot be attributed to any one macronutrient, because we aimed to create different macronutrient patterns that mimicked common patterns of consumption, the present results suggest that a broad range of healthy diets can successfully promote weight loss.

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The authors' responsibilities were as follows—SKD: study design, clinical trial coordination and outcome assessment, intervention management, data management and analysis, and manuscript preparation; CHG: clinical trial intervention implementation, data management, and manuscript review; JKG, AGP, and PJF: clinical trial outcome assessment and manuscript review; RAC: clinical trial intervention implementation and manuscript review; ST: clinical trial outcome assessment; MT: clinical trial outcome assessment and data management; MAM and AHL: clinical trial outcome assessment and manuscript review; GED: statistical expertise and manuscript review; CD: study design and manuscript review; MVB: data analysis and manuscript review; JPD: doubly labeled water assessment, data analysis, and manuscript review; ES: assessment of adverse events, medical monitoring, and manuscript review; SBR (principal investigator): study design, clinical trial intervention implementation management, and manuscript preparation. None of the authors had a conflict of interest.

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APPENDIX A

Sample of foods provided in the diets with a high glycemic load (HG) or low glycemic load (LG)

HG diet
Candied sweet potatoes
Carrots
Chicken and pea casserole
Chef salad
Chicken and rice
Couscous
English muffins and bagels
Jelly
Jasmine rice
Lactose-free skim milk[1]
Oatmeal
Pizza
Sugar cookies and graham crackers
Shepherd's pie with mashed potatoes
Sweet and sour chicken
Turkey with cranberry sauce
Tuna sandwich
Waffles
Yogurt with added fruit—canned pears, peaches, figs, pineapple, oranges, and bananas
LG diet
Baked chicken
Bean and barley stew
Bulgur and beans
Broccoli and beans
Cottage cheese, low-fat
Curried lentils
Fish
Fruit: oranges, grapefruit, plums, pears, apples, and berries
Flaxseed cookies
Green salad
Kashi[2] and Muesli[3] cereal
Lentils with tomato sauce
Nuts
Pumpernickel bread
Salisbury steak
Skim milk
Tomato cucumber bean salad
Wheat berry salad
Yogurt

[1] Lactaid; McNeil Nutritionals, LLC, Fort Washington, PA.
[2] Kashi, La Jolla, CA.
[3] Kellogg's Co, Battle Creek, MI.

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