Effect of Alternate-Day Fasting on Weight Loss, Weight Maintenance, and Cardioprotection Among Metabolically Healthy Obese Adults
A Randomized Clinical Trial

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IMPORTANCE Alternate-day fasting has become increasingly popular, yet, to date, no long-term randomized clinical trials have evaluated its efficacy.

OBJECTIVE To compare the effects of alternate-day fasting vs daily calorie restriction on weight loss, weight maintenance, and risk indicators for cardiovascular disease.

DESIGN, SETTING, AND PARTICIPANTS A single-center randomized clinical trial of obese adults (18 to 64 years of age; mean body mass index, 34) was conducted between October 1, 2011, and January 15, 2015, at an academic institution in Chicago, Illinois.

INTERVENTIONS Participants were randomized to 1 of 3 groups for 1 year: alternate-day fasting (25% of energy needs on fast days; 125% of energy needs on alternating “feast days”), calorie restriction (75% of energy needs every day), or a no-intervention control. The trial involved a 6-month weight-loss phase followed by a 6-month weight-maintenance phase.

MAIN OUTCOMES AND MEASURES The primary outcome was change in body weight. Secondary outcomes were adherence to the dietary intervention and risk indicators for cardiovascular disease.

RESULTS Among the 100 participants (86 women and 14 men; mean [SD] age, 44 [11] years), the dropout rate was highest in the alternate-day fasting group (13 of 34 [38%]), vs the daily calorie restriction group (10 of 35 [29%]) and control group (8 of 31 [26%]). Mean weight loss was similar for participants in the alternate-day fasting group and those in the daily calorie restriction group at month 6 (–6.8% [95% CI, –9.1% to –4.5%] vs –6.8% [95% CI, –9.1% to –4.6%]) and month 12 (–6.0% [95% CI, –8.5% to –3.6%] vs –5.3% [95% CI, –7.6% to –3.0%]) relative to those in the control group. Participants in the alternate-day fasting group ate more than prescribed on fast days, and less than prescribed on feast days, while those in the daily calorie restriction group generally met their prescribed energy goals. There were no significant differences between the intervention groups in blood pressure, heart rate, triglycerides, fasting glucose, fasting insulin, insulin resistance, C-reactive protein, or homocysteine concentrations at month 6 or 12. Mean high-density lipoprotein cholesterol levels at month 6 significantly increased among the participants in the alternate-day fasting group (6.2 mg/dL [95% CI, 0.1-12.4 mg/dL]), but not at month 12 (11.5 mg/dL [95% CI, 1.9-21.1 mg/dL]) compared with those in the daily calorie restriction group.

CONCLUSIONS AND RELEVANCE Alternate-day fasting did not produce superior adherence, weight loss, weight maintenance, or cardioprotection vs daily calorie restriction.

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The first-line therapy prescribed to obese patients for weight loss is daily calorie restriction. However, many patients find it difficult to adhere to a conventional weight-loss diet because food intake must be limited every day. As such, adherence to daily calorie restriction decreases after 1 month and continues to decline thereafter. In light of this limitation, another approach that requires individuals to restrict calories only every other day was developed. This strategy is called alternate-day fasting and involves a fast day where individuals consume 25% of their usual intake (approximately 500 kcal), alternated with a “feast day” where individuals are permitted to consume food ad libitum. Findings from short-term studies indicate that participants lose 3% to 7% of body weight after 2 to 3 months of alternate-day fasting and experience improvements in lipid profiles, blood pressure, and insulin sensitivity.

Alternate-day fasting regimens have increased in popularity during the past decade, and several best-selling diet books have promoted this approach. More than 1 million copies of these books have been sold in the United States and United Kingdom to date. Despite the growing popularity of alternate-day fasting, to our knowledge, no long-term randomized clinical trials have evaluated its efficacy or compared this regimen with a conventional weight-loss diet.

We conducted a 1-year, randomized clinical trial to compare the effects of alternate-day fasting vs daily calorie restriction on body weight and risk indicators for cardiovascular disease. We hypothesized that the participants in the alternate-day fasting group would be more adherent to their diet, achieve greater weight loss, and experience more pronounced improvements in risk indicators for cardiovascular disease during the 6-month weight-loss phase compared with those in the daily calorie restriction group. We also hypothesized that the alternate-day fasting group would better maintain their weight loss and sustain their improvements in risk indicators for cardiovascular disease during the 6-month weight-maintenance phase compared with the daily calorie restriction group.

Methods

Participants

We conducted the trial between October 1, 2011, and January 15, 2015, at the University of Illinois at Chicago. Participants were recruited from the Chicago area by means of flyers placed around the university and were screened via a questionnaire, an assessment of body mass index, and a pregnancy test. Individuals included were men and women between 18 and 65 years of age, with a body mass index between 25.0 and 39.9 (calculated as weight in kilograms divided by height in meters squared) who had previously been sedentary (<60 minutes per week of light activity for the 3 months prior to the study). Exclusion criteria were a history of cardiovascular disease or type 1 or 2 diabetes, use of medications that could affect study outcomes, unstable weight for 3 months prior to the beginning of the study (>4-kg weight loss or gain), perimenopause or otherwise irregular menstrual cycle, pregnancy, and current smoking. The protocol was approved by the Office for the Protection of Research Subjects at the University of Illinois at Chicago, and written informed consent was obtained from all participants. The full protocol is available in Supplement 1.

Randomization and Intervention Groups

Participants were randomized in a 1:1:1 ratio to an alternate-day fasting group, daily calorie restriction group, or no-intervention control group. Randomization was performed by a stratified random sampling procedure by sex, age (18-42 years and 43-65 years), and body mass index (25.0-32.5 and 32.6-39.9). Block size ranged from 1 to 11 participants. The active trial duration was 1 year and consisted of a baseline phase (1 month), a weight-loss phase (6 months), and a weight-maintenance phase (6 months) (eFigure 1 in Supplement 2). We chose this design because weight loss typically peaks at 6 months during a lifestyle intervention. During the baseline phase, all participants ate their usual diet and maintained a stable weight. Baseline total energy expenditure was measured using doubly labeled water. All participants were instructed not to change their physical activity habits throughout the trial (eg, not to join a gym) to avoid potential confounding.

Weight-Loss Phase

Participants in the alternate-day fasting group and those in the daily calorie restriction group were provided with all meals during the first 3 months of the trial and received dietary counseling thereafter (eFigure 1 in Supplement 2). During the 6-month weight-loss phase, the intervention groups were instructed to reduce their energy intake by a mean of 25% per day. To achieve this reduction, the alternate-day fasting group was instructed to consume 25% of baseline energy intake as a lunch (between 12 pm and 2 pm) on fast days and 125% of baseline energy intake split between 3 meals on alternating feast days. The daily calorie restriction group was instructed to consume 75% of baseline energy intake split between 3 meals every day. The provided meals were in accordance with the American Heart Association guidelines for macronutrient intake, with 30% of energy as fat, 55% as carbohydrate, and 15% as protein. From months 4 to 6, when food was no longer provided, intervention participants met individually with a dietitian or nutritionist weekly to learn how to continue with their diets on their own.
Weight-Maintenance Phase
At the beginning of the 6-month weight-maintenance phase, total daily energy expenditure was reassessed using doubly labeled water. Participants were instructed to maintain their body weight during this phase. Participants in the alternate-day fasting group were instructed to consume 50% of energy needs as a lunch on fast days and 150% of energy needs split between 3 meals on alternating feast days. Participants in the daily calorie restriction group were instructed to consume 100% of energy needs split between 3 meals every day. Intervention participants met with the dietician individually each month to learn cognitive behavioral strategies to prevent weight regain and received personalized energy targets for weight maintenance based on results from doubly labeled water.

Control Group Protocol
Participants in the control group were instructed to maintain their weight throughout the trial and not to change their eating or physical activity habits. Controls received no food or dietary counseling but visited the research center at the same frequency as the intervention participants (to provide outcome measurements). Controls who completed the 12-month trial received 3 months of free weight-loss counseling and a 12-month gym membership at the end of the study.

Outcome Measures
The primary outcome of the study was change in body weight, which was measured monthly via a digital scale while the participant was in a hospital gown. Fat mass and lean mass were measured every 6 months in the fasted state by dual-energy x-ray absorptiometry (QDR 4500W; Hologic). Visceral fat mass was measured every 6 months by magnetic resonance imaging performed with a 1.5-T magnet (Siemens Vision), and images were analyzed using validated software.

Mean percentage energy restriction during the weight-loss phase was retrospectively calculated by the intake balance method using doubly labeled water and changes in body composition. Physical activity was measured for 7 consecutive days every 6 months using an activity monitor (SenseWear Armband Mini; BodyMedia Inc.). Dietary intake and adherence to diets was assessed every 3 months with a 7-day food record and analyzed using Nutritionist Pro software (Axxya Systems LLC). Intervention participants were considered to be adherent when their actual energy intake, determined via food records, was within 200 kcal of their prescribed daily energy goal.

Blood samples were obtained following a 12-hour fast every 6 months (collected on the morning after a feast day for the alternate-day fasting group). Secondary outcomes included blood pressure, heart rate, and total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, fasting glucose, fasting insulin, C-reactive protein, and homocysteine concentrations (analytical methods are detailed in the full protocol in Supplement 1). The homeostasis model assessment of insulin resistance was calculated as insulin × glucose/405, where the unit of measure for insulin is in micro-international units per milliliter and the unit of measure for glucose is milligrams per deciliter.

Statistical Analysis
For the sample size calculation, we estimated that alternate-day fasting would reduce body weight by 15% by month 6 and that daily calorie restriction would reduce body weight by 10% by month 6. We calculated that 26 participants per group would provide 80% power to detect a significant difference of 5% in body weight between the alternate-day fasting group and the daily calorie restriction group at month 6, using a 2-tailed independent-samples t test with α = .05. We anticipated a dropout rate of 12%. Thus, we initially aimed to recruit 90 participants (30 per group), assuming that 78 participants (26 per group) would complete the trial. We later decided to recruit 100 participants to increase our statistical power because our dropout rate was higher than expected.

Data are shown as mean values (with 95% CIs) unless otherwise noted. A 2-tailed P < .05 was considered statistically significant. Tests for normality were included in the model, and all data were found to be normally distributed. We conducted an intention-to-treat analysis, which included data from all 100 participants who underwent randomization. Results are reported by intention-to-treat analysis unless indicated otherwise. A linear mixed model was used to assess time, diet, and time × diet effects for each outcome. This model provides unbiased estimates of time and treatment effects under a missing-at-random assumption. Time was not assumed to be linear in the model. This strategy allowed for estimation of time and diet effects (and their interaction) without imposing a linear time trend. The analyses were performed using SAS, version 9.4 (SAS Institute, Inc), and R software, version 3.2.2 (R Foundation for Statistical Computing).

Results
Participant Characteristics and Attrition
Of the 222 participants who were screened, 100 (45.0%) were randomly assigned to the diet or control groups, and 69 (69.0% of those assigned) completed the study (Figure 1). The dropout rate was highest in the alternate-day fasting group (13 of 34 [38%]), relative to the daily calorie restriction group (10 of 35 [29%]) and control group (8 of 31 [26%]). More participants in the alternate-day fasting group than in the daily calorie restriction group withdrew owing to difficulties adhering with the diet. All baseline characteristics had comparable distributions between the alternate-day fasting group, the daily calorie restriction group, and the control group (Table 1). The participants were primarily metabolically healthy obese women.

Prescribed vs Actual Energy Intake Determined via Food Records
On the fast day (Figure 2A), participants in the alternate-day fasting group exceeded their prescribed energy goal at months 3 and 6. On the fast day (Figure 2B), participants in the alternate-day fasting group ate less than their prescribed goal at months 3, 6, 9, and 12. Participants in the daily calorie restriction group (Figure 2C) met their prescribed energy goals at months 3, 6, and 12 but ate less than their prescribed goal at month 9. A higher proportion of participants in the daily calo-
rie restriction group were adherent to their energy goals at months 3, 6, 9, and 12 relative to those in the alternate-day fasting group.

**Percentage Energy Restriction Determined via Doubly Labeled Water**
From baseline to month 6, the alternate-day fasting group achieved a mean (SD) percentage energy restriction of 21% (16%), and the daily calorie restriction group achieved a mean (SD) percentage energy restriction of 24% (16%), with no significant difference between the intervention groups or compared with the control group (eFigure 2 in Supplement 2).

**Physical Activity and Dietary Intake**
Data on dietary intake are displayed in eTable 1 in Supplement 2. Percentage of energy intake from fat, carbohydrates, and protein did not differ significantly over time in any of the groups. Physical activity, measured as steps per day, did not change during the course of the trial in any group (eTable 2 in Supplement 2). This level of activity is approximately 1000 to 2000 steps per day higher than that of the average overweight or obese adult.25

**Weight Loss and Weight Maintenance**
Changes in body weight are displayed in Figure 3 and Table 2. Weight loss was not significantly different between the alternate-day fasting group and the daily calorie restriction group at month 6. At the end of the study, total weight loss was -6.0% (95% CI, -8.5% to -3.6%) for the alternate-day fasting group and -5.3% (95% CI, -7.6% to -3.0%) for the daily calorie restriction group, relative to controls, with no significant difference between the intervention groups. Weight regain from months 6 to 12 (-0.8%; 95% CI, -3.2% to 1.7%) was not significantly different between the alternate-day fasting group and the daily calorie restriction group. Moreover, weight regain from months 6 to 12 was not significantly different between the alternate-day fasting group and controls (0.8%; 95% CI, -1.8% to 3.3%), or the daily calorie restriction group and controls (1.5%; 95% CI, -0.8% to 3.9%). Changes in body composition are reported in Table 2. There were no statistically significant differences between the alternate-day fasting group and the daily calorie restriction group for fat mass, lean mass, or visceral fat mass at month 6 or month 12.

**Blood Pressure and Heart Rate**
Blood pressure was not significantly different between the intervention groups, or relative to controls, at month 6 or month 12 (Table 2). There were also no statistically significant differences in heart rate between the alternate-day fasting group and the daily calorie restriction group at month 6 or month 12 (Table 2).

**Plasma Lipids**
Changes in plasma lipids during the course of the trial are shown in Table 2. Total cholesterol levels were not significantly different between the intervention groups, or relative to controls, at month 6 or month 12. At month 6, high-density lipoprotein cholesterol levels were significantly elevated in the alternate-day fasting group by 6.2 mg/dL (95% CI, 0.1-12.4 mg/dL) (to convert to millimoles per liter, multiply by 0.0259) vs the daily calorie restriction group, but this effect was no longer observed by month 12. Low-density lipoprotein choles-
Table 1. Baseline Characteristics and Risk Factors of the Study Participants

<table>
<thead>
<tr>
<th>Characteristic or Risk Factor</th>
<th>Alternate-Day Fasting Group (n = 34)</th>
<th>Daily Calorie Restriction Group (n = 35)</th>
<th>Control Group (n = 31)</th>
<th>All Participants (N = 100)</th>
<th>Participants Who Completed the Study (n = 69)</th>
<th>Participants Who Did Not Complete the Study (n = 31)</th>
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<td>1.69 (0.11)</td>
<td>1.64 (0.08)</td>
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<td>1.66 (0.09)</td>
<td>1.68 (0.09)</td>
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<td>Weight, mean (SD), kg</td>
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<td>101 (16)</td>
<td>92 (16)</td>
<td>96 (15)</td>
<td>95 (16)</td>
<td>99 (13)</td>
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<tr>
<td>Fat mass</td>
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<td>40 (7)</td>
<td>36 (10)</td>
<td>38 (8)</td>
<td>37 (8)</td>
<td>41 (8)</td>
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<td>Lean mass</td>
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<td>53 (10)</td>
<td>56 (11)</td>
<td>55 (11)</td>
<td>57 (9)</td>
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<td>Visceral fat mass</td>
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<td>2.4 (1.2)</td>
<td>1.9 (1.2)</td>
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<td>2.1 (1.1)</td>
<td>1.9 (1.2)</td>
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<td>35 (4)</td>
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<td>10 (10)</td>
<td>10 (15)</td>
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<td>30.0-40.0</td>
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<td>27 (87)</td>
<td>90 (90)</td>
<td>59 (85)</td>
<td>31 (100)</td>
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<td>Waist circumference, mean (SD), cm</td>
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<td>108 (11)</td>
<td>104 (12)</td>
<td>105 (11)</td>
<td>105 (12)</td>
<td>104 (10)</td>
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<td>Blood pressure, mean (SD), mm Hg</td>
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<td>Systolic</td>
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<td>122 (17)</td>
<td>121 (16)</td>
<td>123 (15)</td>
<td>124 (16)</td>
<td>120 (11)</td>
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<td>Diastolic</td>
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<td>80 (11)</td>
<td>81 (11)</td>
<td>81 (10)</td>
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<td>80 (9)</td>
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<tr>
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<td>75 (9)</td>
<td>75 (10)</td>
<td>74 (10)</td>
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<td>74 (9)</td>
<td>75 (11)</td>
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<td>Glucose, mean (SD), mg/dL</td>
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<td>92 (18)</td>
<td>87 (8)</td>
<td>90 (14)</td>
<td>92 (10)</td>
<td>86 (20)</td>
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<td>Insulin, mean (SD), μIU/mL</td>
<td>16 (14)</td>
<td>20 (18)</td>
<td>16 (9)</td>
<td>18 (14)</td>
<td>18 (14)</td>
<td>17 (15)</td>
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<tr>
<td>HOMA-IR, mean (SD)</td>
<td>3.7 (3.6)</td>
<td>5.1 (5.9)</td>
<td>3.5 (2.1)</td>
<td>4.1 (4.3)</td>
<td>4.1 (3.5)</td>
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<td>Cholesterol, mean (SD), mg/dL</td>
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<td></td>
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<tr>
<td>Total</td>
<td>188 (35)</td>
<td>184 (35)</td>
<td>190 (30)</td>
<td>187 (33)</td>
<td>188 (36)</td>
<td>185 (27)</td>
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<tr>
<td>HDL</td>
<td>57 (14)</td>
<td>53 (11)</td>
<td>59 (13)</td>
<td>56 (13)</td>
<td>56 (13)</td>
<td>58 (13)</td>
</tr>
<tr>
<td>LDL</td>
<td>111 (30)</td>
<td>112 (31)</td>
<td>112 (31)</td>
<td>111 (30)</td>
<td>113 (33)</td>
<td>108 (24)</td>
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<td>Triglycerides, mean (SD), mg/dL</td>
<td>101 (59)</td>
<td>97 (27)</td>
<td>98 (43)</td>
<td>98 (44)</td>
<td>99 (46)</td>
<td>92 (40)</td>
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<tr>
<td>HS CRP, mean (SD), mg/dL</td>
<td>0.32 (0.23)</td>
<td>0.58 (0.52)</td>
<td>0.53 (0.53)</td>
<td>0.48 (0.46)</td>
<td>0.47 (0.43)</td>
<td>0.50 (0.53)</td>
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<td>Homocysteine, mean (SD), mg/L</td>
<td>1.31 (0.37)</td>
<td>1.31 (0.39)</td>
<td>1.32 (0.28)</td>
<td>1.31 (0.35)</td>
<td>1.31 (0.32)</td>
<td>1.31 (0.41)</td>
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</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance (calculated as insulin × glucose/405, where the unit of measure for insulin is in micro-international units per milliliter and the unit of measure for glucose is milligrams per deciliter); HS CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; to convert insulin to picomoles per liter, multiply by 6.945; to convert total, HDL, and LDL cholesterol to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0113; and to convert homocysteine to micromoles per liter, multiply by 7.397.

* Data are presented as number (percentage) of patients unless otherwise indicated.

terol concentrations did not differ significantly between the intervention groups at month 6. At month 12, low-density lipoprotein cholesterol levels significantly increased in the alternate-day fasting group (11.5 mg/dL [95% CI, 1.9-21.1 mg/dL]) (to convert to millimoles per liter, multiply by 0.0259) relative to the daily calorie restriction group. Triglyceride levels did not differ significantly between the intervention groups at month 6 or month 12.

Glucoregulatory and Inflammatory Factors
Changes in glucoregulatory and inflammatory factors are displayed in Table 2. Fasting plasma glucose did not differ
significantly between the intervention groups, or relative to controls, at month 6 or month 12. There were also no significant differences in fasting insulin or the homeostasis model assessment of insulin resistance between the intervention groups at month 6 or month 12. High-sensitivity C-reactive protein and homocysteine levels did not differ significantly between the intervention groups, or relative to controls, at month 6 or month 12. We also performed a sensitivity analysis, in which sex and race/ethnicity were included as adjustment covariates in the intention-to-treat mixed model. The inclusion of sex and race/ethnicity did not affect any of the estimated treatment effects reported in Table 2.

Discussion

The results of this randomized clinical trial demonstrated that alternate-day fasting did not produce superior adherence, weight loss, weight maintenance, or improvement in risk indicators for cardiovascular disease compared with daily calorie restriction.

Alternate-day fasting has been promoted as a potentially superior alternative to daily calorie restriction under the assumption that it is easier to restrict calories every other day. However, our data from food records, doubly labeled water, and regular weigh-ins indicate that this assumption is not the
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Original Investigation Research

Blood pressure, mm Hg

Systolic

Diastolic

Heart rate, beats/min

Cholesterol, mg/dL

Total

HDL

LDL

Triglycerides, mg/dL

Glucose, mg/dL

Insulin, μU/mL

Homocysteine, μg/L

Effect of Alternate-Day Fasting Among Metabolically Healthy Obese Adults

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Change in ADF − Change in DCR (95% CI) At 6 mo</th>
<th>Change in ADF − Change in Control (95% CI) At 6 mo</th>
<th>Change in DCR − Change in Control (95% CI) At 6 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, % change</td>
<td>0.0 (−2.2 to 2.2)</td>
<td>−0.7 (−3.1 to 1.6)</td>
<td>−6.8 (−9.1 to −4.5)</td>
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<tr>
<td>Fat mass, kg</td>
<td>0.9 (−1.3 to 3.1)</td>
<td>0.0 (−2.4 to 2.4)</td>
<td>−4.2 (−6.6 to −1.8)</td>
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<td>Lean mass, kg</td>
<td>0.6 (−1.0 to 2.2)</td>
<td>0.5 (−1.2 to 2.2)</td>
<td>−1.5 (−3.2 to 0.2)</td>
</tr>
<tr>
<td>Visceral fat mass, kg</td>
<td>0.2 (−0.1 to 0.5)</td>
<td>0.1 (−0.2 to 0.5)</td>
<td>−0.4 (−0.7 to −0.1)</td>
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<tr>
<td>Blood pressure, mm Hg</td>
<td>0.8 (−7.1 to 8.7)</td>
<td>−1.1 (−9.5 to 7.4)</td>
<td>−3.1 (−11.3 to 5.2)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>6.2 (0.1 to 12.4)</td>
<td>1.0 (−5.9 to 7.8)</td>
<td>8.4 (1.9 to 14.7)</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>2.5 (−6.0 to 10.9)</td>
<td>11.5 (19.1 to 21.1)</td>
<td>2.6 (−11.5 to 6.4)</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>−10.5 (−26.7 to 5.8)</td>
<td>−9.9 (−28.3 to 8.6)</td>
<td>−19.1 (−36.3 to −1.8)</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>−1.4 (−8.5 to 5.2)</td>
<td>5.7 (−16.3 to 1.0)</td>
<td>−6.7 (−13.3 to 0.7)</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>0.3 (−0.1 to 0.7)</td>
<td>0.03 (−0.12 to 0.18)</td>
<td>0.10 (−0.04 to 0.24)</td>
</tr>
<tr>
<td>Insulin, μU/mL</td>
<td>−0.4 (−5.5 to 4.7)</td>
<td>−1.3 (−6.9 to 4.3)</td>
<td>−7.5 (−12.9 to −2.0)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.07 (−1.56 to 1.70)</td>
<td>0.02 (−1.78 to 1.81)</td>
<td>−2.49 (−4.22 to −0.76)</td>
</tr>
<tr>
<td>HS CRP, mg/dL</td>
<td>−0.04 (−0.19 to 0.11)</td>
<td>0.00 (−0.16 to 0.17)</td>
<td>−0.07 (−0.23 to −0.08)</td>
</tr>
<tr>
<td>Homocysteine, μg/L</td>
<td>0.03 (−0.10 to 0.17)</td>
<td>0.03 (−0.12 to 0.18)</td>
<td>0.10 (−0.04 to 0.24)</td>
</tr>
</tbody>
</table>

Abbreviations: ADF, alternate-day fasting; DCR, daily calorie restriction; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance (calculated as insulin × glucose/405, where the unit of measure for insulin is micro-international units per milliliter and the unit of measure for glucose is milligrams per deciliter); HS CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

SI conversion factors: To convert total, HDL, and LDL cholesterol to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0555; to convert insulin to picomoles per liter, multiply by 6.945; and to convert glucose to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0555; to convert insulin to picomoles per liter, multiply by 6.945; and to convert glucose to millimoles per liter, multiply by 0.0259.

SI conversion factors: To convert homocysteine to micromoles per liter, multiply by 7.397.

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conjunction with modulations in appetite hormones (ghrelin, peptide YY, and glucagon-like peptide-1) could offer some insight into why daily calorie restriction may allow for easier adherence compared with alternate-day fasting.

Contrary to our original hypotheses, the participants in the alternate-day fasting group did not experience more pronounced improvements in risk indicators for cardiovascular disease compared with the participants in the daily calorie restriction group. However, the trial included primarily metabolically healthy obese adults. Since many of the participants had normal cholesterol levels and normal blood pressure at baseline, it is not surprising that most risk indicators for cardiovascular disease did not change in response to diet.

Limitations
Our study has several limitations. First, the duration of the maintenance phase was short (6 months). Second, the control group was imperfect, in that they received no food, no counseling, and less attention from study personnel, relative to the intervention groups, which may have confounded our findings. We also failed to include the control group in our initial power calculation. Third, since the dropout rate was higher than anticipated, our power to detect the hypothesized difference of 5% weight loss between the intervention groups at month 6 decreased from 80% to 60%. The higher dropout rate in the alternate-day fasting group may have also introduced a possible selection bias between groups. Finally, we enrolled predominantly metabolically healthy obese individuals, which may have hindered the abilities of the interventions to produce greater improvements in our measured cardiovascular disease risk indicators.24,25

The generalizability of our findings is also limited by the enrollment.

Conclusions
The alternate-day fasting diet was not superior to the daily calorie restriction diet with regard to adherence, weight loss, weight maintenance, or improvement in risk indicators for cardiovascular disease.

REFERENCES


