

## Original Investigation

# Comparison of Weight Loss Among Named Diet Programs in Overweight and Obese Adults

## A Meta-analysis

Bradley C. Johnston, PhD; Steve Kanters, MSc; Kristofer Bandayrel, MPH; Ping Wu, MBBS, MSc; Faysal Naji, BHSc; Reed A. Siemieniuk, MD; Geoff D. C. Ball, RD, PhD; Jason W. Busse, DC, PhD; Kristian Thorlund, PhD; Gordon Guyatt, MD, MSc; Jeroen P. Jansen, PhD; Edward J. Mills, PhD, MSc

**IMPORTANCE** Many claims have been made regarding the superiority of one diet or another for inducing weight loss. Which diet is best remains unclear.

**OBJECTIVE** To determine weight loss outcomes for popular diets based on diet class (macronutrient composition) and named diet.

**DATA SOURCES** Search of 6 electronic databases: AMED, CDSR, CENTRAL, CINAHL, EMBASE, and MEDLINE from inception of each database to April 2014.

**STUDY SELECTION** Overweight or obese adults (body mass index  $\geq 25$ ) randomized to a popular self-administered named diet and reporting weight or body mass index data at 3-month follow-up or longer.

**DATA EXTRACTION AND SYNTHESIS** Two reviewers independently extracted data on populations, interventions, outcomes, risk of bias, and quality of evidence. A Bayesian framework was used to perform a series of random-effects network meta-analyses with meta-regression to estimate the relative effectiveness of diet classes and programs for change in weight and body mass index from baseline. Our analyses adjusted for behavioral support and exercise.

**MAIN OUTCOMES AND MEASURES** Weight loss and body mass index at 6- and 12-month follow-up ( $\pm 3$  months for both periods).

**RESULTS** Among 59 eligible articles reporting 48 unique randomized trials (including 7286 individuals) and compared with no diet, the largest weight loss was associated with low-carbohydrate diets (8.73 kg [95% credible interval {CI}, 7.27 to 10.20 kg] at 6-month follow-up and 7.25 kg [95% CI, 5.33 to 9.25 kg] at 12-month follow-up) and low-fat diets (7.99 kg [95% CI, 6.01 to 9.92 kg] at 6-month follow-up and 7.27 kg [95% CI, 5.26 to 9.34 kg] at 12-month follow-up). Weight loss differences between individual diets were minimal. For example, the Atkins diet resulted in a 1.71 kg greater weight loss than the Zone diet at 6-month follow-up. Between 6- and 12-month follow-up, the influence of behavioral support (3.23 kg [95% CI, 2.23 to 4.23 kg] at 6-month follow-up vs 1.08 kg [95% CI, -1.82 to 3.96 kg] at 12-month follow-up) and exercise (0.64 kg [95% CI, -0.35 to 1.66 kg] vs 2.13 kg [95% CI, 0.43 to 3.85 kg], respectively) on weight loss differed.

**CONCLUSIONS AND RELEVANCE** Significant weight loss was observed with any low-carbohydrate or low-fat diet. Weight loss differences between individual named diets were small. This supports the practice of recommending any diet that a patient will adhere to in order to lose weight.

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**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Edward J. Mills, PhD, MSc, Stanford University School of Medicine, 1265 Welch Rd, Stanford, CA 94305 ([millsej@stanford.edu](mailto:millsej@stanford.edu)).

**N**amed or branded (trade-marked) weight loss programs are broadly available to the general public, providing structured dietary and lifestyle recommendations via popular books and in-person or online behavioral support. These programs represent a multibillion dollar industry.<sup>1</sup> Debate regarding the relative merit of the diets is accompanied by advertising claiming which macronutrient composition is superior, such as a low-carbohydrate diet being better than a low-fat diet, and the benefits of accompanying lifestyle interventions. Establishing which of the major named diets is most effective is important because overweight and obese patients often want to know which diet results in the most effective weight loss.

Some physiological explanations regarding the merits of different macronutrient compositions, including variable genetic response to diets with different recommended dietary fat intake, make intuitive sense.<sup>2,3</sup> Low-carbohydrate diets may drive weight loss due to a higher intake of protein, which may induce a stronger satiating effect than fats and carbohydrates.<sup>4</sup>

Despite potential biological mechanisms explaining why some popular diets should be better than others, recent reviews suggest that most diets are equally effective,<sup>2,5,6</sup> a message very different from what the public hears in advertisements or expert pronouncements. Only a few of the reviews of named diets have used rigorous meta-analytic techniques to provide quantitative estimates of how much better one diet is compared with another. They also relied on aggregating studies comparing one diet with another and did not have the ability to determine the relative performance of diets when they were not directly compared with one another in clinical trials. By not exploring the full range of potential comparisons in a statistically and methodologically rigorous fashion, these reviews could have missed important benefits of specific diets or their compositions.

Network meta-analysis facilitates comparison of different diets using all available randomized clinical trial (RCT) data.<sup>7</sup> In the absence of published head-to-head clinical trials of each diet against each other diet, network meta-analysis uses both direct and indirect clinical trial evidence to estimate their relative effects. Using a network meta-analytic approach, we assessed the relative effectiveness of different popular diets in improving weight loss.

## Methods

### Eligibility Criteria

As described in a protocol outlining our study methods,<sup>8</sup> we included RCTs that assigned overweight (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared] of 25-29) or obese (BMI  $\geq$ 30) adults ( $\geq$ 18 years of age) to a popular branded diet or an alternative. We included RCTs that reported weight loss or BMI reduction at 3-month follow-up or longer.

Named diets were identified through the explicit naming of the brand, the referencing of branded literature, or the naming of a brand as funders of an article reporting weight loss outcomes from the diet. The diet was labeled as brand-

like when the diet met the definition of a branded diet, but failed to name or reference the brand in the article. For example, dietary programs that did not refer to Atkins but consisted of less than 40% of kilocalories from carbohydrates per day for the duration of study or were funded by Atkins were considered Atkins-like.<sup>9,10</sup>

We included dietary programs with recommendations for daily macronutrient, caloric intake, or both for a defined period ( $\geq$ 12 weeks) with or without exercise (eg, jogging, strength training) or behavioral support (eg, counseling, group support). Eligible programs included meal replacement products but had to consist primarily of whole foods and could not include pharmacological agents. Because it is impossible to provide a placebo diet in a clinical trial, eligible control diets included wait-listed controls, no specific assigned diet, or competing dietary programs. The characteristics of eligible branded dietary programs are reported in eTable 1 in the Supplement.

### Outcomes and Effect Modifiers

The primary outcomes were weight loss at 6- and 12-month follow-up ( $\pm$ 3 months for both periods). Secondary outcomes included BMI and adverse events. We considered 3 weight loss effect modifiers that were modeled as present or absent if they were included in an overall dietary program: calorie restriction, exercise, and behavioral support. Based on the lowest estimated caloric intake for sedentary adults, we defined calorie restriction as less than 1800 kcal/d.<sup>11</sup>

Exercise was defined as having explicit instructions for weekly physical activities and simply dichotomized when differences between varying degrees of exercise frequencies appeared to have negligible effects. Diets with at least 2 group or individual sessions per month for the first 3 months were considered as providing behavioral support.<sup>12</sup>

### Search Strategy

We searched 6 electronic databases: AMED, CDSR, CENTRAL, CINAHL, EMBASE, and MEDLINE from inception of each database to April 2014. Search terms included extensive controlled vocabulary and keyword searches for (RCTs) AND (diets) AND (adults) AND (weight loss). The search strategy is available from the authors upon request.

We reviewed bibliographies of review articles and eligible trials, and searched the registries of ClinicalTrials.gov and the metaRegister of Controlled Trials. We contacted the named diet companies and individuals working in the field of obesity and weight management to identify additional or unpublished trials.

### Study Selection

Reviewers, in pairs, independently screened titles and abstracts of articles and reviewed the full text of any title or abstract deemed potentially eligible by either reviewer. Reviewers resolved disagreements by discussion.

### Risk of Bias Assessment of Individual Studies

Pairs of reviewers independently assessed the risk of bias associated with individual trials using the Cochrane Collabora-

Table 1. Diet Classes Based on Macronutrient Composition

Type of Diet	Branded Diets <sup>a</sup>	Carbohydrates, % kcal	Protein, % kcal	Fat, % kcal
Low carbohydrate	Atkins, South Beach, Zone	≤40	Approximately 30	30-55
Moderate macronutrients	Biggest Loser, Jenny Craig, Nutrisystem, Volumetrics, Weight Watchers	Approximately 55-60	Approximately 15	21-≤30
Low fat	Ornish, Rosemary Conley	Approximately 60	Approximately 10-15	≤20

<sup>a</sup> The Lifestyle, Exercise, Attitudes, Relationships, and Nutrition (LEARN) diet was applied as both a low-fat diet (2 trials) and a moderate macronutrient diet (5 trials) among the 7 included trials having used the LEARN diet (Table 2).

Slimming World was excluded from the diet class analyses because it does not fit any of the definitions above.

tion instrument.<sup>13</sup> We assigned 1 of 2 summary assessments for each included study: low risk of bias for key domains, allocation concealment, and missing participant data or high risk of bias for key domains.<sup>14</sup>

### Data Extraction

Pairs of reviewers independently, and in duplicate, extracted the following data items: study setting, type of trial (parallel or factorial), demographic information, experimental interventions, control interventions, exercise information, degree of calorie restriction, degree of behavioral support, and each of the outcomes of interest. We categorized dietary treatment groups in 2 ways: using diet classes (moderate macronutrient distribution, low carbohydrate, and low fat)<sup>15</sup> and according to diet brands. Diet classes were established by macronutrient content (Table 1).

We considered the Lifestyle, Exercise, Attitudes, Relationships, and Nutrition (LEARN) diet akin to a usual care comparator because it is based on a popular program among health professionals, many of whom have been trained in or endorse the program because of its practicality, its emphasis on behavioral modification, and its adaptability to various dieters (eg, applied as either a low-fat or moderate macronutrient composition diet).<sup>16-18</sup>

Continuous outcomes were most often reported as mean change, but sometimes were reported as preintervention and postintervention measures or percentage change. In the latter cases, transformations were used to express weight loss and BMI as mean change. When available, we used *P* values for group differences to derive the standard deviation of change from baseline. Otherwise, we used the pre- and postintervention standard deviations along with a correlation estimated from studies that reported both change and pre- and post-intervention results. In the case of percentage change, we assumed independence.

### Data Synthesis and Analysis

Analyses were conducted using 6- and 12-month data, with a 3-month window (eg, if a study reported weight loss at 5 months, it was used in the 6-month analysis). The connectivity of each network meta-analysis was described using density, which was calculated as the ratio of the number of treatment pairs with head-to-head evidence over the total number of treatment pairs. Random-effects pairwise meta-analyses (using the method by DerSimonian and Laird<sup>19</sup>) were used to determine direct and indirect associated treatment effects for all network meta-analyses.

To determine weight loss outcomes between diets with all potential comparisons between them, we performed Bayesian network meta-analyses among 5 diet class nodes (no diet, moderate macronutrients, low carbohydrate, low fat, usual care) and each of the 11 eligible named diets.<sup>20</sup> When *P* values were used, all tests were 2-sided with a significance level of .05. All analyses were conducted using WinBUGS version 1.4 (Medical Research Council Biostatistics Unit) and R version 3.0.1 (R Project for Statistical Computing) with the R2WinBUGS, xlsx, and the metafor packages. A detailed description of the statistical analysis appears in the eMethods in the Supplement.

### Confidence in Estimates of Effect

For diet classes at 12-month follow-up, we assessed the quality of evidence associated with specific comparisons using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.<sup>21</sup> For both direct and indirect comparisons, the starting point for confidence in estimates was high, but could be rated down to moderate, low, or very low based on risk of bias, imprecision, inconsistency, and indirectness.

### Assessment of Publication Bias

For our branded diet analysis, we made a visual assessment of funnel plots for publication bias for direct comparisons that included 10 or more studies.

## Results

Searches of 6 primary electronic databases identified 20 835 unique abstracts, titles, or both identified as original publications. The gray literature search identified 213 additional articles. Of the total, 889 proved potentially relevant for full-text review and 59 articles that reported 48 RCTs of 11 branded diets proved eligible (eFigure 1 in the Supplement).<sup>9,10,17,18,22-65</sup>

The 48 RCTs included 7286 individuals with a median age of 45.7 years (median SD, 9 years), median weight of 94.1 kg (median SD, 14.6 kg), and median BMI of 33.7 (median SD, 4.3). The median duration of the diet intervention across trials was 24 weeks (interquartile range, 16-52 weeks). The key characteristics of each included trial appear in Table 2. Forty-three trials (*n* = 5608) comprising 103 study groups reported weight loss at 6-month follow-up. The 6-month network meta-analyses were categorized according to diet class (eFigure 2 in the Supplement) and diet brand (eFigure 3).

Table 2. Characteristics of Included Studies

Source	Diet Program (Class) <sup>a</sup>	Population Description	No. <sup>b</sup>	Age, Mean (SD), y	Female Sex, No. (%)	BMI, Mean (SD) <sup>c</sup>	Body Weight, Mean (SD), kg
Brehm et al, <sup>22</sup> 2003	Atkins (low carbohydrate)	Obese, otherwise healthy	53	43.6 (7.7)	42 (100.0)	33.6 (1.8)	91.7 (7.2)
Brehm et al, <sup>23</sup> 2005	Atkins (low carbohydrate)	Obese, otherwise healthy	50	43.1 (12.5)	40 (100.0)	33.1 (2.2)	90.7 (10.1)
Brinkworth et al, <sup>24,66</sup> 2009	Atkins (low carbohydrate)	Abdominal obesity and 1 other metabolic syndrome risk factor	118	49.8 (8.1)	75 (63.6)	33.7 (4.3)	95.5 (15.6)
Daly et al, <sup>25</sup> 2006	Atkins (low carbohydrate)	Obese, poorly controlled type 2 diabetes	102	58.6 (10.8)	53 (51.9)	36.0 (6.9)	101.9 (15.4)
Dansinger et al, <sup>26</sup> 2005	Atkins (low carbohydrate), Ornish (low fat), Weight Watchers (moderate), Zone (low carbohydrate)	Obese and 1 other metabolic cardiac risk factor	160	49.0 (11.0)	81 (51.0)	35.0 (3.9)	100.0 (15.0)
Davis et al, <sup>27</sup> 2009	Atkins (low carbohydrate)	Obese, type 2 diabetes	105	53.5 (6.5)	82 (78.1)	36.0 (6.0)	97.3 (18.5)
Foster et al, <sup>17</sup> 2003	Atkins (low carbohydrate), LEARN (moderate)	Obese, otherwise healthy	63	44.1 (8.2)	43 (68.2)	34.15 (3.4)	98.5 (17.9)
Foster et al, <sup>28</sup> 2010	Atkins (low carbohydrate)	Obese, otherwise healthy	307	45.6 (9.7)	208 (67.8)	36.1 (3.5)	103.4 (14.9)
Gardner et al, <sup>18</sup> 2007	Atkins (low carbohydrate), LEARN (low fat), Ornish (low fat), Zone (low carbohydrate)	Obese, otherwise healthy	311	41.0 (6.0)	311 (100.0)	32.0 (4.0)	85.0 (12.0)
Iqbal et al, <sup>29</sup> 2010	Atkins (low carbohydrate)	Obese, type 2 diabetes	144	59.2 (9.2)	15 (10.4)	37.6 (5.5)	116.9 (19.0)
McAuley et al, <sup>30</sup> 2005	Atkins (low carbohydrate), Zone (low carbohydrate)	Obese, otherwise healthy	96	45.6 (7.6)	93 (100.0)	35.7 (4.9)	95.7 (13.4)
Ruth et al, <sup>31</sup> 2013	Atkins (low carbohydrate)	Obese, otherwise healthy	55	42.5 (12.1)	49 (89.1)	36.5 (4.7)	99.9 (14.6)
Stern et al, <sup>9</sup> 2004 and Samaha et al, <sup>67</sup> 2003	Atkins (low carbohydrate)	Diabetes and metabolic syndrome	132	53.5 (9.0)	23 (17.4)	42.9 (7.1)	130.9 (25.0)
Shai et al, <sup>32</sup> 2008	Atkins (low carbohydrate)	Obese (BMI ≥27), type 2 diabetes, or coronary heart disease regardless of BMI	322	52.0 (7.0)	45 (14.0)	30.9 (3.6)	91.4 (13.4)
Tay et al, <sup>33</sup> 2008	Atkins (low carbohydrate)	Abdominal obesity and 1 other metabolic syndrome risk factor	118	50.6 (7.9)	57 (64.8)	33.7 (4.2)	94.8 (14.0)
Thomson et al, <sup>34</sup> 2010	Atkins (low carbohydrate)	Stage 1 or 2 breast cancer	43	56.2 (9.4)	40 (100.0)	31.8 (4.3)	84.1 (12.3)
Truby et al, <sup>35</sup> 2006 and Morgan et al, <sup>68</sup> 2009	Atkins (low carbohydrate), Rosemary Conley (low fat), Weight Watchers (moderate)	Obese, otherwise healthy	293	40.2 (10.2)	214 (73.0)	31.6 (2.6)	89.3 (13.3)
Volek et al, <sup>10,69</sup> 2009	Atkins (low carbohydrate)	Obese, atherogenic dyslipidemia	40	34.8 (11.9)	20 (50.0)	32.8 (4.7)	95.5 (14.5)
Westman et al, <sup>36</sup> 2008	Atkins (low carbohydrate)	Obese, type 2 diabetes	97	51.8 (7.5)	66 (78.6)	38.1 (5.8)	105.9 (19.8)
Yancy et al, <sup>37</sup> 2004, Westman et al, <sup>70</sup> 2006, and Yancy et al, <sup>71</sup> 2009	Atkins (low carbohydrate)	Obese, otherwise healthy	120	44.9 (9.5)	91 (76.5)	34.3 (5.0)	97.3 (17.1)
Collins et al, <sup>38</sup> 2012	Biggest Loser (moderate)	Obese, otherwise healthy	309	42.0 (10.2)	180 (58.0)	32.3 (4.0)	94.0 (14.6)
Rock et al, <sup>39</sup> 2007	Jenny Craig (moderate)	Obese, otherwise healthy	70	41.1 (11.5)	70 (100.0)	34.0 (3.6)	92.0 (10.8)
Rock et al, <sup>40</sup> 2010	Jenny Craig (moderate)	Obese, otherwise healthy	446	44.3 (10.3)	442 (100.0)	33.9 (3.6)	92.0 (9.9)
Blumenthal et al, <sup>41</sup> 2000	LEARN (low fat)	Obese, unmedicated high-normal blood pressure or stage 1 or 2 hypertension	133	47.5 (8.9)	74 (56.0)	32.5 (4.4)	94.2 (16.5)
Goodrick et al, <sup>42</sup> 1998	LEARN (moderate)	Overweight, binge eating, otherwise healthy	219	40.0 (6.3)	219 (100.0)	33.0 (3.2)	87.8 (9.9)
Wadden et al, <sup>43</sup> 2004	LEARN (moderate)	Obese, otherwise healthy	123	44.1 (9.9)	123 (100.0)	35.9 (4.5)	97.3 (13.0)
Wing et al, <sup>44</sup> 1998	LEARN (moderate)	Obese but without diabetes; 1 or both parents with type 2 diabetes	154	45.7 (4.4)	122 (79.0)	35.9 (4.3)	98.7 (15.0)
Womble et al, <sup>45</sup> 2004	LEARN (moderate)	Obese, otherwise healthy	47	43.7 (10.2)	47 (100.0)	33.5 (3.1)	90.6 (11.7)
Figuroa et al, <sup>46</sup> 2013	Nutrisystem (moderate)	Obese females, otherwise healthy	41	54.3 (3.7)	41 (100.0)	33.4 (3.8)	89.2 (14.6)
Foster et al, <sup>47</sup> 2009	Nutrisystem (moderate)	Obese, type 2 diabetes	69	52.2 (9.5)	49 (71.0)	39.0 (6.2)	111.2 (21.3)
Aldana et al, <sup>48</sup> 2007	Ornish (low fat)	Coronary artery disease or coronary-related health issues	98	62.0 (9.1)	41 (44.0)	31.0 (6.1)	90.0 (21.2)
Jolly et al, <sup>49</sup> 2011	Rosemary Conley (low fat), Slimming World (NA), Weight Watchers (moderate)	Obese, otherwise healthy	740	49.3 (14.7)	513 (69.3)	33.6 (3.7)	93.3 (14.4)
Swenson et al, <sup>50</sup> 2007	South Beach (low carbohydrate)	Obese, otherwise healthy	32	40.7 (8.7)	29 (90.6)	48.5 (9.1)	182.0 (78.0)

(continued)

Table 2. Characteristics of Included Studies (continued)

Source	Diet Program (Class) <sup>a</sup>	Population Description	No. <sup>b</sup>	Age, Mean (SD), y	Female Sex, No. (%)	BMI, Mean (SD) <sup>c</sup>	Body Weight, Mean (SD), kg
Ello-Martin et al, <sup>51</sup> 2007	Volumetrics (moderate)	Obese, otherwise healthy	97	44.9 (9.4)	97 (100.0)	33.3 (2.6)	90.5 (9.5)
Djuric et al, <sup>52</sup> 2002	Weight Watchers (moderate)	Stage 1 or 2 breast cancer	48	51.7 (8.4)	48 (100.0)	35.5 (3.9)	95.4 (13.6)
Heshka et al, <sup>53,72</sup> 2000	Weight Watchers (moderate)	Obese, otherwise healthy	423	44.5 (10.0)	358 (84.6)	33.7 (3.5)	93.6 (13.7)
Jebb et al, <sup>54</sup> 2011	Weight Watchers (moderate)	Obese and 1 other risk factor for obesity-related disease	772	47.3 (12.8)	668 (86.5)	31.4 (2.6)	86.7 (11.5)
Pinto et al, <sup>55</sup> 2013	Weight Watchers (moderate)	Obese, otherwise healthy	144	49.7 (9.2)	127 (90.0)	36.1 (5.4)	96.5 (17.5)
Rippe et al, <sup>56</sup> 1998	Weight Watchers (moderate)	Overweight, otherwise healthy	80	36.5 (6.9)	44 (100.0)	NS	81.7 (6.4)
Brinkworth et al, <sup>57,73</sup> 2004, Farnsworth et al, <sup>74</sup> 2003, Layman et al, <sup>75</sup> 2003, and Parker et al, <sup>76</sup> 2002	Zone (low carbohydrate)	Obese, type 2 diabetes	66	61.8 (7.8)	23 (60.5)	33.4 (5.4)	93.7 (18.0)
Das et al, <sup>58</sup> 2007	Zone (low carbohydrate)	Obese, otherwise healthy	34	35.0 (6.0)	NS	27.6 (1.4)	79.0 (10.6)
Ebbeling et al, <sup>59</sup> 2007	Zone (low carbohydrate)	Obese, otherwise healthy	73	27.6 (4.0)	58 (79.0)	NS	103.4 (16.2)
Galletly et al, <sup>60</sup> 2007	Zone (low carbohydrate)	Overweight, polycystic ovary syndrome	28	32.5 (1.2)	28 (100.0)	37.4 (6.6)	101.4 (4.9)
Lasker et al, <sup>61</sup> 2008	Zone (low carbohydrate)	Obese, otherwise healthy	65	47.2 (7.0)	31 (62.0)	33.6 (4.5)	95.4 (15.0)
Layman et al, <sup>62</sup> 2005	Zone (low carbohydrate)	Obese, otherwise healthy	48	46.7 (4.9)	48 (100.0)	32.9 (5.1)	87.6 (13.7)
Layman et al, <sup>63</sup> 2009	Zone (low carbohydrate)	Obese, otherwise healthy	130	45.4 (13.7)	71 (54.6)	32.6 (9.1)	92.7 (14.5)
Luscombe et al, <sup>64</sup> 2002	Zone (low carbohydrate)	Type 2 diabetes	32	63.2 (9.7)	15 (57.7)	33.3 (4.7)	92.6 (15.8)
Luscombe et al, <sup>65</sup> 2003	Zone (low carbohydrate)	Obese, hyperinsulinemia	36	54.0 (6.0)	26 (72.2)	34.1 (4.2)	94.0 (15.0)

Abbreviations: BMI, body mass index; LEARN, Lifestyle, Exercise, Attitudes, Relationships, and Nutrition; NA, not applicable; NS, not specified.

<sup>a</sup> Moderate macronutrient class is abbreviated as moderate in this table. Eligible comparators were wait-listed controls, no assigned diet, or competing dietary programs. The order of studies is alphabetical according to branded diet intervention (eg, Atkins, Biggest Loser, Jenny Craig). Among branded diets that have multiple studies, trials are listed according to the last name of the

author. If an author published more than 1 trial on the same branded diet (eg, Rock et al<sup>39,40</sup> published 2 trials evaluating Jenny Craig), we ordered the studies in chronological order according to the year the trial was published.

<sup>b</sup> This column includes the number of randomized participants included in trial.

<sup>c</sup> Calculated as weight in kilograms divided by height in meters squared.

Moderate macronutrient and low-carbohydrate diets were the most common diet classes; among these, Atkins, Weight Watchers, and Zone were the brands with the most comparisons. Twenty-five trials ( $n = 5386$ ) with 67 groups reported weight loss at 12-month follow-up (eFigures 2 and 3 in the Supplement). The diet class network meta-analysis at both time points had a density of 1.0. Because these network meta-analyses were completely connected, all estimated effects were informed by both direct and indirect evidence. Aside from the 4 named diets that were only connected to a single node (Biggest Loser, Jenny Craig, Nutrisystem, and Volumetrics), the 6- and 12-month brand network meta-analyses were well connected with densities of 0.36 and 0.47, respectively.

### Risk of Bias

Risk of bias of included studies was assessed by diet class and by diet brand (eTable 2 in the Supplement). Twenty-nine trials were at low risk of bias and 19 were at high risk of bias.

### Weight Loss Diet Classes

In the analysis adjusted for diet class, all treatments were superior to no diet at 6-month follow-up (Figure 1). Compared with no diet, low-carbohydrate diets had a median difference in weight loss of 8.73 kg (95% credible interval [CI], 7.27-10.20

kg) and low-fat diets had similar estimated effects (7.99 kg [95% CI, 6.01-9.92 kg]). A low-carbohydrate diet resulted in increased weight loss compared with other diet classes (LEARN, moderate macronutrient distribution), but was not distinguishable from low-fat diets.

At 12-month follow-up, the estimated average weight losses of all diet classes compared with no diet were approximately 1 to 2 kg less than after 6-month follow-up. The diet classes of low fat (7.27 kg [95% CI, 5.26-9.34 kg]) and low carbohydrate (7.25 kg [95% CI, 5.33-9.25 kg]) continued to have the largest estimated treatment effects. At 6-month follow-up, the low-carbohydrate diet class had the highest estimated probability of being superior to all other diet classes at 83%; however, at 12-month follow-up, the low-fat diet demonstrated the highest probability at 50% (Figure 1).

Meta-regression used to account for the use of exercise, calorie restriction, and the degree of behavioral support of each diet group at 6-month follow-up led to a model for weight loss with both exercise and behavioral support factors. Effect modification at 6-month follow-up differed from estimates at 12-month follow-up for behavioral support (3.23 kg [95% CI, 2.23 to 4.23 kg] vs 1.08 kg [95% CI, -1.82 to 3.96 kg], respectively) and exercise (0.64 kg [95% CI, -0.35 to 1.66 kg] vs 2.13 kg [95% CI, 0.43 to 3.85 kg]). Calorie restriction did not modify the effects.

Figure 1. Difference in Mean Weight Loss at 6- and 12-Month Follow-up Across All Diet Classes With 95% Credible Intervals

		12-mo Weight Loss, kg			
		No diet (6 mo: 0; 12 mo: 0) <sup>a</sup>	5.16 (2.68 to 7.63)	5.70 (4.14 to 7.35)	7.25 (5.33 to 9.25)
6-mo Weight Loss, kg	6.07 (4.23 to 7.84)	LEARN (6 mo: 0; 12 mo: 0.02) <sup>a</sup>	0.55 (-1.71 to 2.87)	2.10 (-0.20 to 4.47)	2.12 (-0.33 to 4.59)
	6.78 (5.50 to 8.05)	0.71 (-0.97 to 2.44)	Moderate macronutrients (6 mo: 0; 12 mo: 0) <sup>a</sup>	1.55 (0.13 to 2.95)	1.56 (-0.17 to 3.30)
	8.73 (7.27 to 10.20)	2.66 (0.93 to 4.44)	1.95 (1.13 to 2.79)	Low carbohydrate (6 mo: 0.83; 12 mo: 0.48) <sup>a</sup>	0.02 (-1.78 to 1.79)
	7.99 (6.01 to 9.92)	1.92 (-0.19 to 4.06)	1.20 (-0.42 to 2.79)	-0.74 (-2.31 to 0.78)	Low fat (6 mo: 0.17; 12 mo: 0.50) <sup>a</sup>

The values above the diet classes (blue boxes) correspond to the difference in mean weight lost between the columns and row at 12 months (eg, the difference in average weight lost between moderate macronutrients and no diet at 12 months is 5.70 kg). The values below the diet classes correspond to the difference in mean weight lost between the row and the column at 6 months (eg, the difference in average weight lost between moderate

macronutrients and no diet at 6 months is 6.78 kg). LEARN indicates Lifestyle, Exercise, Attitudes, Relationships, and Nutrition.

<sup>a</sup> The values in parentheses represent the estimated probability of that treatment being the best.

### Sensitivity Analysis

The findings of our sensitivity analyses in which populations with specific health problems (eg, breast cancer) were removed appear in eTable 3 in the Supplement. The findings were similar to the full analysis; low-carbohydrate diets demonstrated the most favorable estimates at 6-month follow-up, whereas low-fat diets were most favorable at 12-month follow-up.

Sensitivity analyses for low risk of bias, proportion lost to follow-up, baseline weights, and proportion female at 6- and 12-month follow-up also showed similar results (eTables 4-7 in the Supplement).

### Individual Named Diets

In the adjusted named analysis, all diets demonstrated weight reduction at 6-month follow-up compared with no diet (Figure 2). The largest estimated effects at 6-month follow-up were found with the Atkins diet with a median difference in weight loss of 10.14 kg (95% CI, 8.19-12.12 kg), followed by the Volumetrics diet (9.87 kg [95% CI, 5.54-14.23 kg]) and the Ornish diet (9.03 kg [95% CI, 6.44-11.66 kg]). The estimated effect of behavioral support (3.67 kg [95% CI, 1.45-5.88 kg]) and exercise (1.15 kg [95% CI, 0.14-2.16 kg]) were similar to those obtained in the diet class network meta-analysis.

All diets except Jenny Craig slightly decreased in their estimated effects at 12-month follow-up compared with 6-month follow-up. The Ornish, Rosemary Conley, Jenny Craig, and Atkins diets were associated with the largest weight loss at this time point and all varied between 6.35 kg and 6.55 kg.

The findings of the sensitivity analyses for the named diets network meta-analysis in which populations with specific health problems and high risk of bias studies were removed appear in eTables 8 and 9 in the Supplement. In these analyses, some head-to-head comparisons from the primary analysis were no longer present, thus leaving the network meta-analysis sparser.

Our findings were not sensitive at 6- and 12-month follow-up to the removal of populations with additional health issues. Among studies at low risk of bias, the point estimates

are smaller than our primary analysis; however, tests for interaction demonstrated no significant differences among trials at low vs high risk of bias.

For assessing publication bias, one comparison at 6-month follow-up and no comparisons at 12-month follow-up included 10 or more studies. Based on 15 studies comparing Atkins with moderate macronutrient diets, a funnel plot demonstrates asymmetry, suggesting publication bias (eFigure 4 in the Supplement).<sup>77</sup>

### Confidence in Estimates

The overall quality of the evidence using GRADE methods for our direct, indirect, and overall network meta-analysis estimates appear in eTables 10-12 in the Supplement. We assessed the confidence in estimates of effect for weight loss at 12-month follow-up as moderate to low for all comparisons, suggesting that further research is likely to have an important effect on our confidence in the estimation of effect and may change the estimate (eTable 12 in the Supplement).

### Body Mass Index

Due to a considerably lower number of studies reporting BMI measures, the associated network meta-analyses were sparse and do not permit trustworthy inferences (eFigures 5-6 and eTables 13-14 in the Supplement).

### Adverse Events

Adverse events were reported in 5 included trials, all of which evaluated the Atkins diet.<sup>9,28,29,36,37</sup> Although there were no significant differences in serious adverse events among treatment groups, the only trial to find significant differences in mild adverse events reported that they occurred more frequently in the low-carbohydrate diet group (n = 60) than in the low-fat diet group (n = 60), including constipation (68% vs 35%, respectively; *P* < .001), headache (60% vs 40%; *P* < .03), halitosis (38% vs 8%; *P* < .001), muscle cramps (35% vs 7%; *P* < .001), diarrhea (23% vs 7%; *P* < .02), general weakness (25% vs 8%; *P* < .01), and rash (13% vs 0%; *P* < .006).<sup>37</sup>



## Discussion

Among the 48 original RCTs included in our network meta-analysis, evidence of low to moderate quality showed that both low-carbohydrate and low-fat diets were associated with an estimated 8-kg weight loss at 6-month follow-up compared with no diet. Approximately 1 to 2 kg of this effect was lost by 12-month follow-up. Although statistical differences existed among several of the diets, the differences were small and unlikely to be important to those seeking weight loss.

These findings support recent recommendations for weight loss in that most calorie-reducing diets result in clinically important weight loss as long as the diet is maintained.<sup>6</sup> Network meta-analysis showed that although there are statistically significant differences between some of the named diets, these differences are small and likely to be unimportant to many seeking to lose weight. For example, the Atkins diet resulted in an estimated weight loss of only 1.71 kg (95% CI, 0.35-3.09 kg) more than the Zone diet at 6-month follow-up. Because different diets are variably tolerated by individuals, the ideal diet is the one that is best adhered to by individuals so that they can stay on the diet as long as possible.

Network meta-analysis yielded larger weight loss estimates for diets compared with no dieting than the observed weight loss in the primary studies. This is explained by the effect of statistical adjustment for exercise that results in an apparent net weight gain for the no diet group. A similar effect is observed for behavioral support adjustment. The network meta-analysis estimates for trials that failed to include behavioral support were adjusted accordingly, leading to higher estimates than those originally reported.

The strengths of this review include our use of network meta-analyses that allowed for simultaneous direct and indirect comparisons of both dietary classes and individual named diets, a comprehensive literature search, an assessment of risk of bias, and application of the GRADE approach to rating confidence in estimates of effect of diet classes at 12-month follow-up. We also systematically addressed the potential harms of named diets; however, only 5 of 48 included trials reported information about adverse events.

To provide insight into the quality of the evidence, we applied GRADE methods to rate our confidence in the estimates of effect. To avoid redundancy, we only did so to the 12-month comparisons and not the 6-month comparisons for the diet classes (eTables 10-12 in the Supplement). However, the estimates at 12-month follow-up are the most relevant for individuals concerned about long-term weight loss. Furthermore, because there are considerably more trials reporting 6-month data, the network meta-analysis had increased density and the comparisons had more power, thus our confidence in the 6-month estimates is at least as great as those reported at 12-month follow-up using GRADE methods.

Our study has limitations related to the underlying evidence base for clinical trials on weight loss. For the 10 direct comparisons in which more than 1 study was available, 7 comparisons (eTable 10 in the Supplement) demonstrated substantial heterogeneity between studies, manifested by an

$I^2$  exceeding 70%, and visual inspection of forest plots confirming large inconsistencies between study results. Within our GRADE assessment, we rated the quality of evidence for our direct estimates for inconsistency as weaker inferences. Because we were unable to demonstrate that the differences in patients, interventions, or adherence influenced the magnitude of effect, we did not rate the quality of evidence down for indirect estimates across studies (eTable 11 in the Supplement).

Furthermore, 19 of 48 trials were at high risk of bias mostly as a result of missing participant outcome data, and the low and high risk of bias trials were not uniformly distributed across comparisons (eTable 2 in the Supplement). Nevertheless, we did not exclude studies because of risk of bias, primarily because the effect of treatment did not significantly vary after adjusting for missing participant outcome data and overall risk of bias (eTables 4-5 and eTable 9 in the Supplement). Our approach is consistent with the practices used in the systematic review methodological community.<sup>77,78</sup>

Our study also has limitations related to network meta-analysis connectivity, evaluation of effect modifiers, and assessment of publication bias. First, confidence in estimates is lower for individual brand-named diets (in particular for some comparisons) because they were poorly connected to the network meta-analysis, have small sample sizes, or both. In particular, Volumetrics ( $n = 97$ ) and Jenny Craig ( $n = 516$ ), which both fared well at 6- and 12-month follow-up, were only connected to a single other diet.

Second, although we accounted for the variability due to calorie restriction, exercise, and behavioral support using meta-regression, there were limitations in the explicit presentation of data regarding calorie restriction. Exercise and behavioral support were associated with increased weight loss, though we found no association with behavioral support at 12-month follow-up. This lack of effect at 12-month follow-up may be explained by our definition of behavioral support, which placed more importance on the intensity of support within the first 3 months of a diet.<sup>12</sup>

Third, a limitation of our review is that analyses were based on the original intended randomized design, not by adherence to the actual macronutrient composition (class) and caloric intake consumed.<sup>2</sup> This means that although patients were randomized to various diets or controls, details on their actual adherence to the dietary program (eg, daily caloric intake, macronutrient consumption, and length and intensity of exercise was limited to the published reports) were not accounted for in the analyses.

Fourth, because there were fewer than 10 trials in all but 1 paired comparison, our assessment of publication bias was very limited.<sup>77</sup>

Although we used different methods, our study findings are similar to the review by the Joint Guidelines from the American Heart Association, the American College of Cardiology, and the Obesity Society, concluding that popular diets are roughly equally effective,<sup>6,79</sup> and that evidence is inadequate to recommend any particular diet.<sup>80</sup> Even though we found that low-carbohydrate (eg, Atkins) and low-fat (eg, Ornish) dietary programs are associated with the greatest weight loss, these



differences were minor and likely unimportant to those interested in losing weight. The methodological differences between our analysis and the Joint Guidelines<sup>6</sup> appear in eTable 15 in the Supplement.

We did not exclude studies based on any criteria beyond study design. There is concern within the clinical research community that excluding studies based on arbitrary thresholds for study quality may have an important influence on the study results of systematic reviews<sup>81</sup> because subsequent evidence may demonstrate that assumed quality items have less effect than expected.<sup>82</sup> Using the approach advocated by both the Cochrane Collaboration and the GRADE working group, we included all RCTs and considered rating down confidence in estimates because of risk of bias (eTables 4-5 and eTable 9 in the Supplement).<sup>77,78</sup>

We examined the relationship between estimated effect size, loss to follow-up, and overall risk of bias, and after finding no relationship, did not consider risk of bias an important effect modifier. As we have noted previously in this discussion, this approach is perhaps the most potentially controversial of our methodological decisions. There is a clear need for a better understanding between clinical trialists and guideline developers regarding the influence of loss to follow-up and other risk of bias issues. This issue is not limited to diets, but probably affects all fields of medicine.<sup>83</sup>

Similar to previous reviews, we found that weight loss decreased at 6-month follow-up,<sup>84,85</sup> and began to regress to the

baseline mean at 12-month follow-up, suggesting that future trials of dietary programs should focus on maintenance of long-term weight loss.<sup>86</sup> Our findings should be reassuring to clinicians and the public that there is no need for a one-size-fits-all approach to dieting because many different diets appear to offer considerable weight loss benefits. This is important because many patients have difficulties adhering to strict diets that may be particularly associated with cravings or be culturally challenging (such as low-carbohydrate diets).<sup>2</sup> Our findings suggest that patients may choose, among those associated with the largest weight loss, the diet that gives them the least challenges with adherence. Although our study did not examine switching between diets, such a strategy may offer patients greater choices as they attempt to adhere to diet and lifestyle changes.

## Conclusions

Low-carbohydrate and low-fat dietary programs were associated with more weight loss than no dietary intervention over a 12-month period; behavioral support and exercise enhanced weight loss. The weight loss differences between individual named diets were small with likely little importance to those seeking weight loss. This supports the practice of recommending any diet that a patient will adhere to in order to lose weight.

### ARTICLE INFORMATION

**Author Affiliations:** Hospital for Sick Children Research Institute, Toronto, Ontario, Canada (Johnston, Bandayrel); Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada (Johnston); Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada (Johnston, Busse, Thorlund, Guyatt); Department of Anesthesia and Pain Medicine, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada (Johnston, Bandayrel); School of Population and Public Health, University of British Columbia, Vancouver, Canada (Kanters); Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada (Kanters, Wu); Redwood Outcomes, Vancouver, British Columbia, Canada (Kanters, Thorlund, Jansen, Mills); Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada (Naji); Department of Medicine, University of Toronto, Toronto, Ontario, Canada (Siemieniuk); Department of Pediatrics, University of Alberta, Edmonton, Canada (Ball); Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Canada (Ball); Michael G. DeGroote Institute for Pain Research and Care, McMaster University, Hamilton, Ontario, Canada (Busse); Department of Anesthesia, McMaster University, Hamilton, Ontario, Canada (Busse); Stanford Prevention Research Center, Stanford University School of Medicine, Stanford University, Stanford, California (Thorlund, Mills); Department of Public Health and Community Medicine, Tufts University, Boston, Massachusetts (Jansen).

**Author Contributions:** Mr Kanters and Dr Mills had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Johnston, Kanters, Siemieniuk, Ball, Busse, Thorlund, Mills.

**Acquisition, analysis, or interpretation of data:** Johnston, Kanters, Bandayrel, Wu, Naji, Siemieniuk, Busse, Thorlund, Guyatt, Jansen, Mills.

**Drafting of the manuscript:** Johnston, Kanters, Bandayrel, Naji, Ball, Thorlund, Mills.

**Critical revision of the manuscript for important intellectual content:** Johnston, Kanters, Wu, Siemieniuk, Busse, Thorlund, Guyatt, Jansen, Mills.

**Statistical analysis:** Johnston, Kanters, Thorlund, Mills.

**Obtained funding:** Johnston, Ball, Busse, Thorlund, Mills.

**Administrative, technical, or material support:** Johnston, Bandayrel, Wu, Naji, Mills.

**Study supervision:** Johnston, Thorlund, Guyatt, Mills.

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### REFERENCES

1. Marketdata Enterprises. *The US Weight Loss & Diet Control Market*. Lynbrook, NY: Marketdata Enterprises; 2009.
2. Pagoto SL, Appelans BM. A call for an end to the diet debates. *JAMA*. 2013;310(7):687-688.
3. Qi Q, Bray GA, Hu FB, Sacks FM, Qi L. Weight-loss diets modify glucose-dependent insulinotropic polypeptide receptor rs2287019 genotype effects on changes in body weight, fasting glucose, and insulin resistance: the Preventing Overweight Using Novel Dietary Strategies trial. *Am J Clin Nutr*. 2012;95(2):506-513.
4. Porrini M, Santangelo A, Crovetto R, Riso P, Testolin G, Blundell JE. Weight, protein, fat, and timing of preloads affect food intake. *Physiol Behav*. 1997;62(3):563-570.
5. Freedman MR, King J, Kennedy E. Popular diets: a scientific review. *Obes Res*. 2001;9(suppl 1):1S-40S.
6. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and

- the Obesity Society. *J Am Coll Cardiol*. 2014;63(25 pt B):2985-3023.
7. Mills EJ, Ioannidis JP, Thorlund K, Schünemann HJ, Puhan MA, Guyatt GH. How to use an article reporting a multiple treatment comparison meta-analysis. *JAMA*. 2012;308(12):1246-1253.
  8. Johnston B, Bandayrel K, Kanters S, et al. Branded diets and weight loss in overweight or obese adults: a network meta-analysis. [http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42013003676](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013003676). Accessed July 30, 2014.
  9. Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med*. 2004;140(10):778-785.
  10. Volek JS, Ballard KD, Silvestre R, et al. Effects of dietary carbohydrate restriction versus low-fat diet on flow-mediated dilation. *Metabolism*. 2009;58(12):1769-1777.
  11. US Department of Agriculture; US Department of Health and Human Services. Dietary guidelines for Americans: 2010. <http://www.health.gov/dietaryguidelines/dga2010/dietaryguidelines2010.pdf>. Accessibility verified August 4, 2014.
  12. US Preventive Services Task Force. Screening for obesity in adults: recommendations and rationale. *Am J Nurs*. 2004;104(5):94-95, 97-98, 100.
  13. Higgins JPT, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
  14. Hartling L, Ospina M, Liang Y, et al. Risk of bias versus quality assessment of randomised controlled trials: cross sectional study. *BMJ*. 2009;339:b4012.
  15. McAlister FA, Laupacis A, Wells GA, Sackett DL. Users' Guides to the Medical Literature: XIX, applying clinical trial results B: guidelines for determining whether a drug is exerting (more than) a class effect. *JAMA*. 1999;282(14):1371-1377.
  16. Brownell KD. *The LEARN Program for Weight Management*. 10 ed. Dallas, TX: American Health Publishing Co; 2004.
  17. Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med*. 2003;348(21):2082-2090.
  18. Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A to Z Weight Loss Study: a randomized trial. *JAMA*. 2007;297(9):969-977.
  19. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188.
  20. Lu G, Ades AE. Assessing evidence inconsistency in mixed treatment comparisons. *J Am Stat Assoc*. 2006;101:447-459.
  21. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3, rating the quality of evidence. *J Clin Epidemiol*. 2011;64(4):401-406.
  22. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *J Clin Endocrinol Metab*. 2003;88(4):1617-1623.
  23. Brehm BJ, Spang SE, Lattin BL, Seeley RJ, Daniels SR, D'Alessio DA. The role of energy expenditure in the differential weight loss in obese women on low-fat and low-carbohydrate diets. *J Clin Endocrinol Metab*. 2005;90(3):1475-1482.
  24. Brinkworth GD, Noakes M, Clifton PM, Buckley JD. Effects of a low carbohydrate weight loss diet on exercise capacity and tolerance in obese subjects. *Obesity (Silver Spring)*. 2009;17(10):1916-1923.
  25. Daly ME, Paisey R, Paisey R, et al. Short-term effects of severe dietary carbohydrate-restriction advice in type 2 diabetes—a randomized controlled trial. *Diabet Med*. 2006;23(1):15-20.
  26. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA*. 2005;293(1):43-53.
  27. Davis NJ, Tomuta N, Schechter C, et al. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. *Diabetes Care*. 2009;32(7):1147-1152.
  28. Foster GD, Wyatt HR, Hill JO, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Ann Intern Med*. 2010;153(3):147-157.
  29. Iqbal N, Vetter ML, Moore RH, et al. Effects of a low-intensity intervention that prescribed a low-carbohydrate vs a low-fat diet in obese, diabetic participants. *Obesity (Silver Spring)*. 2010;18(9):1733-1738.
  30. McAuley KA, Hopkins CM, Smith KJ, et al. Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia*. 2005;48(1):8-16.
  31. Ruth MR, Port AM, Shah M, et al. Consuming a hypocaloric high fat low carbohydrate diet for 12 weeks lowers C-reactive protein, and raises serum adiponectin and high density lipoprotein-cholesterol in obese subjects. *Metabolism*. 2013;62(12):1779-1787.
  32. Shai I, Schwarzfuchs D, Henkin Y, et al; Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med*. 2008;359(3):229-241.
  33. Tay J, Brinkworth GD, Noakes M, Keogh J, Clifton PM. Metabolic effects of weight loss on a very-low-carbohydrate diet compared with an isocaloric high-carbohydrate diet in abdominally obese subjects. *J Am Coll Cardiol*. 2008;51(1):59-67.
  34. Thomson CA, Stopeck AT, Bea JW, et al. Changes in body weight and metabolic indexes in overweight breast cancer survivors enrolled in a randomized trial of low-fat vs reduced carbohydrate diets. *Nutr Cancer*. 2010;62(8):1142-1152.
  35. Truby H, Baic S, deLooy A, et al. Randomised controlled trial of four commercial weight loss programmes in the UK: initial findings from the BBC "diet trials." *BMJ*. 2006;332(7553):1309-1314.
  36. Westman EC, Yancy WS Jr, Mavropoulos JC, Marquart M, McDuffie JR. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. *Nutr Metab (Lond)*. 2008;5:36.
  37. Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. *Ann Intern Med*. 2004;140(10):769-777.
  38. Collins CE, Morgan PJ, Jones P, et al. A 12-week commercial web-based weight-loss program for overweight and obese adults: randomized controlled trial comparing basic versus enhanced features. *J Med Internet Res*. 2012;14(2):e57.
  39. Rock CL, Pakiz B, Flatt SW, Quintana EL. Randomized trial of a multifaceted commercial weight loss program. *Obesity (Silver Spring)*. 2007;15(4):939-949.
  40. Rock CL, Flatt SW, Sherwood NE, Karanja N, Pakiz B, Thomson CA. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA*. 2010;304(16):1803-1810.
  41. Blumenthal JA, Sherwood A, Gullette EC, et al. Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. *Arch Intern Med*. 2000;160(13):1947-1958.
  42. Goodrick GK, Poston WS II, Kimball KT, Reeves RS, Foreyt JP. Nondiets versus dieting treatment for overweight binge-eating women. *J Consult Clin Psychol*. 1998;66(2):363-368.
  43. Wadden TA, Foster GD, Sarwer DB, et al. Dieting and the development of eating disorders in obese women: results of a randomized controlled trial. *Am J Clin Nutr*. 2004;80(3):560-568.
  44. Wing RR, Venditti E, Jakicic JM, Polley BA, Lang W. Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes Care*. 1998;21(3):350-359.
  45. Womble LG, Wadden TA, McGuckin BG, Sargent SL, Rothman RA, Krauthamer-Ewing ES. A randomized controlled trial of a commercial Internet weight loss program. *Obes Res*. 2004;12(6):1011-1018.
  46. Figueroa A, Arjmandi BH, Wong A, Sanchez-Gonzalez MA, Simonavice E, Daggy B. Effects of hypocaloric diet, low-intensity resistance exercise with slow movement, or both on aortic hemodynamics and muscle mass in obese postmenopausal women. *Menopause*. 2013;20(9):967-972.
  47. Foster GD, Borradaile KE, Vander Veur SS, et al. The effects of a commercially available weight loss program among obese patients with type 2 diabetes: a randomized study. *Postgrad Med*. 2009;121(5):113-118.
  48. Aldana SG, Greenlaw R, Salberg A, Merrill RM, Hager R, Jorgensen RB. The effects of an intensive lifestyle modification program on carotid artery intima-media thickness: a randomized trial. *Am J Health Promot*. 2007;21(6):510-516.
  49. Jolly K, Lewis A, Beach J, et al. Comparison of range of commercial or primary care led weight reduction programmes with minimal intervention control for weight loss in obesity: lighten up randomised controlled trial. *BMJ*. 2011;343:d6500.
  50. Swenson BR, Saalwachter Schulman A, Edwards MJ, et al. The effect of a low-carbohydrate, high-protein diet on post laparoscopic gastric

- bypass weight loss: a prospective randomized trial. *J Surg Res*. 2007;142(2):308-313.
51. Ello-Martin JA, Roe LS, Ledikwe JH, Beach AM, Rolls BJ. Dietary energy density in the treatment of obesity: a year-long trial comparing 2 weight-loss diets. *Am J Clin Nutr*. 2007;85(6):1465-1477.
  52. Djuric Z, DiLaura NM, Jenkins I, et al. Combining weight-loss counseling with the Weight Watchers plan for obese breast cancer survivors. *Obes Res*. 2002;10(7):657-665.
  53. Heshka S, Greenway F, Anderson JW, et al. Self-help weight loss versus a structured commercial program after 26 weeks: a randomized controlled study. *Am J Med*. 2000;109(4):282-287.
  54. Jebb SA, Ahern AL, Olson AD, et al. Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial. *Lancet*. 2011;378(9801):1485-1492.
  55. Pinto AM, Fava JL, Hoffmann DA, Wing RR. Combining behavioral weight loss treatment and a commercial program: a randomized clinical trial. *Obesity (Silver Spring)*. 2013;21(4):673-680.
  56. Rippe JM, Price JM, Hess SA, et al. Improved psychological well-being, quality of life, and health practices in moderately overweight women participating in a 12-week structured weight loss program. *Obes Res*. 1998;6(3):208-218.
  57. Brinkworth GD, Noakes M, Keogh JB, Luscombe ND, Wittert GA, Clifton PM. Long-term effects of a high-protein, low-carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. *Int J Obes Relat Metab Disord*. 2004;28(5):661-670.
  58. Das SK, Gilhooly CH, Golden JK, et al. 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. *Am J Clin Nutr*. 2007;85(4):1023-1030.
  59. Ebbeling CB, Leidig MM, Feldman HA, Lovesky MM, Ludwig DS. Effects of a low-glycemic load vs low-fat diet in obese young adults: a randomized trial. *JAMA*. 2007;297(19):2092-2102.
  60. Galletly C, Moran L, Noakes M, Clifton P, Tomlinson L, Norman R. Psychological benefits of a high-protein, low-carbohydrate diet in obese women with polycystic ovary syndrome—a pilot study. *Appetite*. 2007;49(3):590-593.
  61. Lasker DA, Evans EM, Layman DK. Moderate carbohydrate, moderate protein weight loss diet reduces cardiovascular disease risk compared to high carbohydrate, low protein diet in obese adults: a randomized clinical trial. *Nutr Metab (Lond)*. 2008;5:30.
  62. Layman DK, Evans E, Baum JI, Seyler J, Erickson DJ, Boileau RA. Dietary protein and exercise have additive effects on body composition during weight loss in adult women. *J Nutr*. 2005;135(8):1903-1910.
  63. Layman DK, Evans EM, Erickson D, et al. A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *J Nutr*. 2009;139(3):514-521.
  64. Luscombe ND, Clifton PM, Noakes M, Parker B, Wittert G. Effects of energy-restricted diets containing increased protein on weight loss, resting energy expenditure, and the thermic effect of feeding in type 2 diabetes. *Diabetes Care*. 2002;25(4):652-657.
  65. Luscombe ND, Clifton PM, Noakes M, Farnsworth E, Wittert G. Effect of a high-protein, energy-restricted diet on weight loss and energy expenditure after weight stabilization in hyperinsulinemic subjects. *Int J Obes Relat Metab Disord*. 2003;27(5):582-590.
  66. Brinkworth GD, Buckley JD, Noakes M, Clifton PM, Wilson CJ. Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Arch Intern Med*. 2009;169(20):1873-1880.
  67. Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. *N Engl J Med*. 2003;348(21):2074-2081.
  68. Morgan LM, Griffin BA, Millward DJ, et al. Comparison of the effects of four commercially available weight-loss programmes on lipid-based cardiovascular risk factors. *Public Health Nutr*. 2009;12(6):799-807.
  69. Volek JS, Phinney SD, Forsythe CE, et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009;44(4):297-309.
  70. Westman EC, Yancy WS Jr, Olsen MK, Dudley T, Guyton JR. Effect of a low-carbohydrate, ketogenic diet program compared to a low-fat diet on fasting lipoprotein subclasses. *Int J Cardiol*. 2006;110(2):212-216.
  71. Yancy WS Jr, Almirall D, Maciejewski ML, Kolotkin RL, McDuffie JR, Westman EC. Effects of two weight-loss diets on health-related quality of life. *Qual Life Res*. 2009;18(3):281-289.
  72. Heshka S, Anderson JW, Atkinson RL, et al. Weight loss with self-help compared with a structured commercial program: a randomized trial. *JAMA*. 2003;289(14):1792-1798.
  73. Brinkworth GD, Noakes M, Parker B, Foster P, Clifton PM. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: one-year follow-up of a randomised trial. *Diabetologia*. 2004;47(10):1677-1686.
  74. Farnsworth E, Luscombe ND, Noakes M, Wittert G, Argyiou E, Clifton PM. Effect of a high-protein, energy-restricted diet on body composition, glycemic control, and lipid concentrations in overweight and obese hyperinsulinemic men and women. *Am J Clin Nutr*. 2003;78(1):31-39.
  75. Layman DK, Boileau RA, Erickson DJ, et al. A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women. *J Nutr*. 2003;133(2):411-417.
  76. Parker B, Noakes M, Luscombe N, Clifton P. Effect of a high-protein, high-monounsaturated fat weight loss diet on glycemic control and lipid levels in type 2 diabetes. *Diabetes Care*. 2002;25(3):425-430.
  77. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. <http://www.cochrane-handbook.org>. Accessed August 10, 2014.
  78. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4, rating the quality of evidence—study limitations (risk of bias). *J Clin Epidemiol*. 2011;64(4):407-415.
  79. Ryan DH, Kushner R. The state of obesity and obesity research. *JAMA*. 2010;304(16):1835-1836.
  80. Tsai AG, Wadden TA. Systematic review: an evaluation of major commercial weight loss programs in the United States. *Ann Intern Med*. 2005;142(1):56-66.
  81. Jüni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA*. 1999;282(11):1054-1060.
  82. Savović J, Jones HE, Altman DG, et al. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Ann Intern Med*. 2012;157(6):429-438.
  83. Hernán MA, Hernández-Díaz S, Robins JM. Randomized trials analyzed as observational studies. *Ann Intern Med*. 2013;159(8):560-562.
  84. Curioni CC, Lourenço PM. Long-term weight loss after diet and exercise: a systematic review. *Int J Obes (Lond)*. 2005;29(10):1168-1174.
  85. Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc*. 2007;107(10):1755-1767.
  86. Wing RR, Tate DF, Gorin AA, Raynor HA, Fava JL. A self-regulation program for maintenance of weight loss. *N Engl J Med*. 2006;355(15):1563-1571.